ECRO XXXII ANNUAL MEETING – ABSTRACT BOOKLET

Wed, 31 Aug 2022

17:45 - 18:00

Welcome

Goethe Hall

18:00 - 19:00

Christophe Laudamiel: FROM SCIENCE TO FUN - a scent tour of the past three years

Goethe Hall

Thu, 1 Sep 2022

08:30 - 09:30

Keynote Lecture: Greg Jefferis: Smell, Love and Memory

Goethe Hall

Chair/s: Silke Sachse

Thu-L2-001

Smell, love and memory

Gregory Jefferis

Division of Neurobiology, MRC Laboratory of Molecular Biology and Department of Zoology, University of Cambridge, UK

At this meeting, we can all agree that the chemical senses are endlessly fascinating in their own right. However, they also provide a powerful entry point for a range of strategies to study the neural circuit basis of behaviour. Two examples of this are the close association between olfaction and memory in many species and the processing of pheromones to control sexually dimorphic behaviour. Another theme of growing importance in neuroscience is the use of synaptic resolution brain wiring diagrams (connectomes) in order to reveal circuit logic. I will discuss examples from our own work in Drosophila that apply experimental and connectomics approaches to olfaction to reveal general principles of sensory processing and behaviour.

10:00 - 12:00

Symposium 1: Piriform cortex: From synapses to behaviour

Goethe Hall

Chair/s: Friedrich Johenning

The primary olfactory (piriform) cortex receives direct input from the olfactory bulb and is a central hub for processing olfactory information. Recent evidence has suggested a role for piriform cortex in representing behaviorally relevant variables beyond odor identity. This symposium brings together researchers focused on understanding synaptic plasticity, population dynamics, and computations in piriform cortex necessary for odor-guided behaviors. The aim is to further our understanding of the functional role of the piriform cortex in complex behaviors.

Thu-S1-001

Dendritic mechanisms of odor representation and plasticity in piriform cortex pyramidal neurons

Jackie Schiller, Amit Kumar
Technion Medical School

The piriform cortex (PCx) receives direct input from the olfactory bulb (OB) and is the brain's main station for odor recognition and memory. The transformation of the odor code from OB to PCx is profound: mitral and tufted cells in olfactory glomeruli respond to individual odorant molecules, whereas pyramidal neurons (PNs) in the PCx responds to multiple, apparently random combinations of activated glomeruli. How these “discontinuous” receptive fields are formed from OB inputs remains unknown. To study these questions, we used brain slices of PCx combined with electrophysiology, calcium imaging, optogenetics, uncaging and modeling. We found that counter to the prevailing view that olfactory PNs sum their inputs passively, NMDA spikes within individual dendrites can both amplify OB inputs and impose combination selectivity upon them, while their ability to compartmentalize voltage signals allows different dendrites to represent different odorant combinations. Moreover, we find that these NMDA spikes can serve as a strong and robust postsynaptic signal for long term potentiation of LOT inputs into distal apical dendrites of PCx PNs. We conclude that dendrites of PCx PNs provide the nonlinear integrative and plasticity mechanisms necessary for odor learning and representation.

Thu-S1-002

Ascribing function to principal neuron cell types in mouse piriform cortex.

Kevin Franks
Duke University, Durham, United States

The piriform cortex contains two main classes of principal neurons: semilunar cells (SLs) and pyramidal cells (PYRs). Both SLs and PYRs receive direct olfactory bulb input. However, while SLs only receive excitatory inputs from the olfactory bulb, PYRs also receive excitatory synaptic inputs from SLs and other PYRs, forming an extensive, long-range recurrent network within the piriform cortex. SLs only receive excitatory inputs from the olfactory bulb. By contrast, PYRs receive direct olfactory bulb input and excitatory synaptic inputs from SLs and other PYRs, forming an extensive, long-range recurrent network within the piriform cortex. What specific roles do SLs and PYRs play in odor processing and guiding odor-driven behaviors? Based on observations in brain slices, cortical odor processing has been proposed to occur in two sequential stages in which SLs first receive and integrate olfactory bulb input. PYRs then receive, transform, and transmit SL input. Is odor information sequentially processed in vivo? We have developed a mouse line that expresses Cre recombinase selectively in SLs in the piriform cortex, providing a genetic handle to identify and control the activity of SLs in vivo. We found that cortical odor processing in vivo occurs primarily through parallel channels of SLs and PYRs, with PYRs exhibiting little dependence on SL input. In preliminary investigations, we found that SLs decorrelate similar inputs while PYRs generalize according to the dominant odor component in mice performing an odor discrimination task. Moreover, SLs are required to form, but not to retrieve, learned odor associations. Together, these observations support a model in which SLs and PYRs may function analogously to the dentate gyrus and CA3 regions in the hippocampus.

Thu-S1-003

Differential encoding of odor and place in the mouse olfactory and lateral entorhinal cortex

Wilson Mena [1], Keeley Baker [2], Shaun Kohli [2], Yun Yoo [2], Shahab Razaei Mazinani [3], Alexander Fleischmann [2]
[1] Department of Neuroscience, Institut Pasteur, Paris, France, [2] Department of Neuroscience and Carney Institute for Brain Science, Brown University, Providence, USA, [3] Departement BEL, Centre CMP, Ecole des Mines de Saint-Étienne, Gardanne, France

Associating odor cues with spatial information in the environment is critical for animal behavior. The lateral entorhinal cortex (LEC) is reciprocally interconnected with the olfactory (piriform, PCx) cortex and the hippocampus and thus ideally positioned to play key roles in encoding odor-place associations. Here, we used mini-endoscopes to record neural activity in the LEC and PCx of head-fixed and freely moving mice. We show that odor identity is encoded in LEC ensembles, but less accurately than in PCx. Interestingly, odor-encoding ensembles in head-fixed mice are substantially reorganized in freely moving mice sampling odor cues at ports on a linear track. Compared to PCx, LEC ensembles carry

more accurate information about the location of the odor ports and the position of the mouse along the track. Finally, we found that overlap between neural ensembles activated by odors and spatial position is more pronounced in LEC than in PCx. Together, our data suggest robust context-dependent modulation of cortical odor representations and a gradient of odor and place information coding along the PCx-LEC axis.

Thu-S1-004

State prediction in primary olfactory cortex

Hanne Stensola [1, 2], Tor Stensola [1, 2], Megha Patwa [2], Eric DeWitt [2], Zach Mainen [2]
[1] University of Agder, [2] Champalimaud Centre for the Unknown

While primary sensory areas are robustly activated by sensory input signals, both theory and experiment suggest that the same cortices are modulated by internally generated activity. Predictive coding theories propose that sensory cortical responses incorporate comparisons between incoming sensory signals and expectations generated by internal models of the sensory scene. Yet several aspects of how sensory expectation is expressed in sensory circuits remain unclear. A fundamental question is whether distinct prediction effects accompany functional and anatomical differences between sensory modalities. The primary olfactory cortex (OC) receives unpatterned sensory inputs via the main olfactory bulb, and OC responses to odors reflect local associative dynamics more so than input activity. How sensory predictions are implemented in this system is not well understood. To address this, we chronically recorded neural populations in the mouse OC during presentation of odor pairs without reinforcement. 12 odors were systematically paired to establish stimulus-specific sensory predictions. In a subset of trials, the second odor was either presented alone (unpredicted) or omitted. After odor pairing, we observed changes to odor responses in both single cells and on the population level. Prediction-matched responses were bidirectionally modulated across the neural population, and became decodable from neural activity prior to odor onset. Surprisingly, after just one session, we observed reinstatement of the predicted odor representation instead of a mismatch response in trials where the predicted odor was omitted. These data indicate that prediction generates activity in the primary olfactory cortex that differs from what has been observed in other sensory modalities. This work was funded by an ERC advanced grant and an FCT SR&TD grant.

Thu-S1-005

Binge eating suppresses flavor representations in the mouse olfactory cortex

Hung Lo [1, 2], Anke Schoenherr [1], Malinda L. S. Tantirigama [3, 5], Matthew E. Larkum [3], Benjamin Judkewitz [1, 2, 5], Katharina Stumpenhorst [4], Marion Rivalan [5], York Winter [4], Dietmar Schmitz [1, 2, 5, 6], Friedrich Johenning [1, 2]
[1] Charité – Universitätsmedizin Berlin, Neuroscience Research Center, Berlin, Germany, [2] Einstein Center for Neurosciences Berlin, Berlin, Germany, [3] Institut für Biologie, Humboldt Universität zu Berlin, Berlin, Germany, [4] Cognitive Neurobiology, Humboldt Universität zu Berlin, Berlin, Germany, [5] NeuroCure Cluster of Excellence, Berlin, Germany, [6] Center for Neurodegenerative Diseases (DZNE), Berlin, Germany

Appropriate feeding behavior is the foundation of maintaining homeostasis. Elevated feeding rate (binge eating) is a common trait of eating disorders, and it is associated with obesity. It is also known that flavor perception has an active role in regulating feeding. However, the effects of feeding rate on flavor sensory feedback remain unknown. We developed a liquid food delivery system that mice can consume flavored milk with different feeding rates, e.g., slow eating mode (4-second interval) and binge eating mode (0.4-second interval). Using miniscope in mice, we showed that binge eating suppresses neuronal activity in the anterior olfactory (piriform) cortex (aPC), while slow eating does not. The strength of binge-induced suppression in the aPC predicts animals' consumption and duration of feeding. This suppression is unlikely due to the activation of local GABAergic interneurons (PV^+ & SOM^+) in the aPC. Odor inputs from olfactory bulb mitral cells remain stable upon binge eating, suggesting the suppression is not due to degraded odor inputs. We further excluded the inhibitory effect from serotonergic modulation in the aPC by using in vivo serotonin imaging. Taken together, our results provide clear circuit mechanisms of binge-induced flavor modulation, which may contribute to binge-induced overeating due to reduced sensory feedback of food items.
This project is funded by DFG 458236353.

10:00 - 12:00

Symposium 2: The chemosensory roles of cilia: Integral roles beyond odor detection

Hahn Lecture Hall

Chair/s: Nathalie Jurisch-Yaksi, Jeremy McIntyre

In the olfactory system, the cilia that extend from olfactory sensory neurons (OSNs) are well known for their role in detecting chemical stimuli. In addition to OSNs, cilia project from nearly all cell types and contribute in various ways to the detection of chemical cues. This symposium will address the numerous roles cilia play in chemosensory systems. Talks will focus on the development of olfactory cilia, bitter and sweet receptor function in motile cilia, as well as the roles of primary cilia in neuronal migration and in modulating olfactory signaling in the brain.

Thu-S2-001

The peculiar cilia of olfactory sensory neurons

Nathalie Jurisch-Yaksi

Department of Clinical and Molecular Medicine, Norwegian University of Science and technology, Trondheim, Norway

Cilia are hair-like structures enriched in receptors and signaling molecules, which play key roles in signal transduction. Notably, olfactory sensory neurons (OSN) cilia harbor all the machinery necessary for odor detection, and thus are indispensable for olfaction. To date, the regulatory pathways involved in controlling cilia formation in OSN remain elusive. Particularly, OSN cilia have properties of motile cilia, akin to those on respiratory and ependymal cells, yet in most vertebrates, OSN cilia lack motility. In our study, we reveal that mammalian and zebrafish OSN express the master regulator of motile ciliogenesis, foxj1. Interestingly, the expression of foxj1 target genes involved in cilia motility are actively repressed in OSN as compared to motile ciliated respiratory cells, explaining their immotility. Next, we investigated the function of foxj1 in cilia formation in zebrafish OSNs. We observed that OSN cilia are lacking in foxj1 mutants. In line with ciliogenesis defects, we identified that foxj1 mutant display aberrant responses to olfactory cues. Altogether, we identified a novel and critical role of foxj1 in OSN cilia formation but not motility. We argue that understanding the regulatory pathways underlying diversity in cilia formation and function is necessary to better understand sensory deficits in patients with ciliary disorders.

Thu-S2-002

Ciliary MCHR1 signaling in the olfactory bulb

Jeremy McIntyre

Department of Neuroscience University of Florida, Center for Smell and Taste

In the brain, a subset of neuromodulatory GPCRs localize to the primary cilia of neurons, altough their function remains unclear. To investigate a role for primary cilia in modulating neuronal function in the olfactory bulb (OB) we characterized the expression and localization of several known ciliary GPCRs. Using in situ hybridization and immunofluorescence labelling we analyzed the expression of SSTR3, MCHR1, DRD1, DRD2, HTR6, CHRM2, CHRM3, CHRM5, and GPR161. Of these, DRD1, HTR6, SSTR3, and MCHR1 localized to cilia of neurons in the OB. MCHR1, the only melanin-concentrating hormone (MCH) receptor in the mouse genome, localized to inhibitory granule cells and glomerular interneurons, but not excitatory mitral and tufted cells. The localization of MCHR1 suggests a mechanism by which interneurons can be modulated by the hypothalamic neuropeptide MCH. To further support this connection, we labelled hypothalamic MCH neurons using cre-dependent AAVs expressing fluorescent reporters. Fibers from MCH neurons were detected in both the glomerular and granule cell layers of the OB, and could be seen in close proximity to cilia. To determine if MCHR1 signaling influences odor coding we perfromed calcium imaging of the OB. Using anesthetized Thy1-GCaMP6 mice we find that application of MCH to the OB reduces glomerular responses to odors ($t(99) = 10.98$, $p < 0.0001$). Conversely, application of the MCHR1 antagonist SNAP-94847 increases responses ($t(157) = 5.425$, $p < 0.0001$). To test specificity, we crossed Thy1-GCaMP6 mice with a novel MCHR1 knockout model we created. In contrast to wildtype littermates, MCHR1 knockout mice do no show increased glomerular responses when the MCHR1 antagonist is applied. Combined these data higlight both a role for ciliary signaling in the modulation of neuronal activity, and identify a specific hypothalamic peptide capable of modulating odor responses in the OB.

This project is supported by NIH NIDCD R01DC019379

Thu-S2-003

APEX-based proximity labeling for time-resolved, quantitative cilia proteomics reveals proteome dynamics during active signaling

Elena May [1], Marian Kalocsay [2], David Mick [1, 3]

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The primary cilium is a central signaling hub and provides a special environment that concentrates signaling proteins to generate adequate responses to external stimuli. Effective signaling of vertebrate primary cilia depends on the dynamic transport of central signaling components such as receptors and effectors into and out of primary cilia. Yet, apart from select factors, the extent of the proteomic remodeling of primary cilia during active signaling remains largely unknown. We employ proximity labeling methods using cilia-localized ascorbate peroxidase (cilia-APEX) in combination with tandem-mass-tag-based quantitative mass spectrometry approaches to reveal the comprehensive proteomic alteration of primary cilia in response to signal in cells. By profiling the cilia proteome in a time-resolved manner after inducing the hallmark primary cilium signaling pathway by Sonic Hedgehog stimulation, we could reconcile previously described changes in the localization of known Hedgehog signaling components, including low abundant membrane receptors, such as GPCRs. Importantly, we revealed a rapid removal of the cAMP-dependent protein kinase (PKA) holoenzyme, including the orphan GPCR GPR161, which functions as the A-kinase anchoring protein (AKAP) in primary cilia. Hierarchical clustering identified the putative phosphatase PALD1 that accumulates in primary cilia in response to active Hedgehog signaling to dampen signaling in a cell type-specific manner. Surprisingly, we find PALD1 enriched in primary cilia also in response to other stimuli, suggesting a more general function in ciliary signal transduction.
Our unbiased analyses demonstrate that proximity labeling in combination with quantitative proteomics allows time-resolved proteomics of primary cilia and provide novel insights into how primary cilia orchestrate signaling processes.
Funding: Our research is funded by the German Research Foundation (DFG).

Thu-S2-004

Long-range migration of centrioles to the apical surface of the olfactory epithelium

Jennifer Wang [1], Kaitlin Ching [2], Tim Stearns [3]

[1] Department of Biology, Washington University in St. Louis, [2] Department of Molecular, Cell, and Developmental Biology, University of California Los Angeles, [3] Department of Biology, Stanford University, Department of Genetics, Stanford University School of Medicine

The multiple sensory cilia that protrude from olfactory sensory neuron dendrites each require a unique structure, known as a centriole, for their formation. Cells control centriole formation and maturation to ensure that the requisite number of centrioles and cilia are created. We have previously shown that in the mouse olfactory epithelium, centrioles are amplified in progenitor cells located near the basal lamina, often 50–100 µm from the apical surface. Objective: Here, we define how OSN centrioles traverse this distance from the basal lamina to the apical surface, and how they mature to allow for cilia formation.
Methods: High-resolution expansion microscopy, live imaging, explant culture system.
Results: During dendrite outgrowth, centrioles migrate together, with multiple centrioles per group and multiple groups per OSN. Centrioles migrate slowly, with a maximum rate of 0.18 µm/minute. Centriole migration can be perturbed ex vivo by stabilizing microtubules. Migrating centriole groups are associated with microtubule nucleation factors. In mature OSNs, centrioles also matured, as marked by the acquisition of rootletin and centriolar appendages. One cilium, that nucleated by the parental centriole, has a unique appendage structure and forms a single cilium before other centrioles.
Conclusions: Our results support a model in which the microtubule cytoskeleton is critical for slow centriole migration, perhaps through centrosome-directed microtubule nucleation. Our results also indicate that centriole maturation is spatiotemporally regulated to only occur in mature OSNs, after centrioles arrive in the forming dendritic knob. Finally, our discovery that a single cilium formed before all others and bears unique structural properties suggests that this

cilium may be involved in unique signaling important for OSN differentiation.
Funding: National Institutes of Health and the National Science Foundation.

13:30 - 15:30

Symposium 3: Chemosensory perception of social signals in the context of human interaction

Goethe Hall

Chair/s: Ilona Croy

Human interaction is controlled by how we perceive each other. Smells play a subtle but significant role in this because they provide the background against which we interpret other sensory stimuli. In this symposium, we will clarify the social aspects of chemosensory perception: How are body odors perceived? How do body odors transport familiarity and closeness? And how are body odors in various states emitted? The aim of the symposium is thus to trace the sender-receiver chemosensory interaction.

Thu-S3-001

Future trends in human chemosignalling research

Monique A.M. Smeets

Faculty of Social & Behavioral Sciences, Utrecht University, Utrecht, The Netherlands, Unilever R&D, Beauty & Wellbeing and Personal Care Science & Technology, Consumer Science, Rotterdam, the Netherlands

Human chemosignalling science has progressed from chemosignalling being regarded as a dodgy phenomenon to a recognized mode of social communication. While it has been shown that individuals can transmit information about their trait and state via body odour there are still gaps in our scientific understanding of how chemosignalling “works” and what it can afford.

A future research roadmap should address outstanding questions around Need, Mechanism, and Application. Need relates to the “So what?” question of why we need this research? Mechanism refers to unravelling the “chemical codes”, olfactory receptors implicated and brain processing to produce successful sender-receiver communication. Application deals with how to exploit our understanding of relevance and impact (Need), and mode of action (Mechanism) for societal benefits.

In an increasingly digital society, social online interactions are limited to audio-visual input with chemosensory input being mostly absent. But has the field provided sufficient evidence to support the additional impact of chemosignalling over other sensory channels to convince stakeholders of its benefits? Are these signals private? We need a narrative about benefits as well as risks to society from utilizing scientific insights about chemosignalling to address these concerns.

Mechanism and Application go hand in hand, in that understanding how chemosensory signals differ will enable technical solutions to detect or produce these distinctive signals as well as personal care product applications that can mask or boost them as desired. Based on the above, future research should prioritize 1) an unequivocal demonstration of impact from chemosignalling research, 2) creating a narrative addressing both benefits and risks to society, 3) a research focus on signal identification, both theory and data-driven, and 4) the pursuit of technical and personal care applications closely collaborating with technical start-ups and personal care industry.

Thu-S3-002

Sensory-analytical characterization of body odor samples of different age groups

Diana Owsienko [1], Katharina Hierl [2], Laura Schäfer [2], Ilona Croy [3], Helene M. Loos [1, 4]

[1] Chair of Aroma and Smell Research, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), 91054 Erlangen, Germany, [2] Department of Psychotherapy and Psychosomatics, Technical University of Dresden, 01062 Dresden, Germany, [3]Department of Clinical Psychology, Friedrich-Schiller-University of Jena, 07743 Jena, Germany, [4] Fraunhofer Institute for Process Engineering and Packaging IVV, 85354 Freising, Germany

During infancy, childhood and adolescence, cues towards the respective developmental status are conveyed by human body odorants and volatiles and serve as a basis for chemical communication in social interactions, e.g. between parents and their child. To find out more about the underlying molecular principles, the aim of this work was to characterize the body odor profiles of different age groups and further investigate the age-related changes in the composition of body odor samples. For this purpose, axillary samples of two age groups, namely from infants and toddlers (age range: 0-3 years) and teenagers (age range: 14-18 years), were collected using cotton pads that were worn over night. Per age group, six participants were recruited. Solvent extraction followed by solvent assisted flavor evaporation (SAFE) was applied to isolate volatiles from the samples, whereby samples obtained from all six participants of an age group were pooled. The distillates were measured by gas chromatography-mass spectrometry/olfactometry to identify volatile and odor-active compounds. Further, target compounds were determined and quantified. The qualitative composition of odor-active compounds in samples obtained from both age groups was dominated by aldehydes and acids. The compounds 5α-androst-16-en-3-one and 5α-androst-16-en-3α-ol were only detected in the samples of adolescents. Further, quantitative differences were observed for squalene and its degradation products 6-methyl-5-hepten-2-one and geranyl acetone. In conclusion, developmental changes induce a change in body odor. Such alteration becomes evident in the qualitative as well as quantitative composition of body odor samples which may explain differences in olfactory perception.

This research was funded by the German Research Foundation, grant number BU 1351/24-1 and CR 479/11-1.

Thu-S3-003

Parental perception of olfactory kin recognition

Laura Schäfer [1], Ilona Croy [1, 2]

[1] Department of Psychosomatics, TU Dresden, [2] Institute of Psychology, Friedrich-Schiller-Universität Jena

Children´s body odours are effective chemosignals in the parent-child relationship. Mothers are able to identify their children by smell and prefer this smell over that of unfamiliar children. This is mediated by genetic similarity and developmental stage - presumably to promote parental care at pre-pubertal stage, while facilitating incest avoidance at (post)pubertal stage. The here presented study tested whether similar mechanisms apply to fathers. Therefore n = 56 fathers evaluated body odour samples of their own and of unfamiliar children in varying genetic and developmental stages from birth to adolescence. Genetic status was mapped via human leucocyte antigen (HLA-) profiling, developmental status by standardized assessment of pubertal status and steroid hormone concentration (estradiol, testosterone). Fathers recognized their own child´s body odour above chance and preferred that odour over unfamiliar odours. The paternal preference did not relate to HLA similarity but decreased with increasing age of the child. The decline was linked to higher pubertal stages in daughters only, which supports the hypothesis of odour-mediated incest prevention in opposite-sex parent-child dyads.

Funding: This research was funded by the German Research Foundation, grant number CR 479/4-1.

Thu-S3-004

Association between self-reported and third-party rated attractiveness in body odour

Lucie Kuncová [1], Zuzana Štěrbová [1, 2], Jitka Třebická Fialová [1], Dagmar Schwambergová [1], Vít Třebický [1, 3], Žaneta Pátková [1], Vladimír Kunc [4], Jan Havlíček [1]

[1] Faculty of Science, Charles University, Prague, Czech Republic, [2] Faculty of Arts, Charles University, Prague, Czech Republic, [3] Faculty of Physical Education and Sports, Charles University, Prague, Czech Republic, [4] Faculty of Electrical Engineering, Czech Technical University in Prague, Prague, Czech Republic

Human mate choice is driven by various characteristics including body odour attractiveness. The estimation of own attractiveness modulates one's self-perceived mate value and consequently mate choice. Previous studies tested self-assessment of various characteristics such as facial attractiveness, but similar data on body odour attractiveness is missing.

We focused on the association between self-reported and third-party rated body odour attractiveness (BOA) in women and men. We included data from nine different studies. In total, the body odour samples were provided by 277 men and 249 women. Participants also reported the estimation of their BOA, body hair density and perspiration intensity on a 7-point Likert scale. Each sample was evaluated at least by 14 raters (105 men and 965 women in total) for attractiveness. The results showed a significant correlation between self-reported and third-party rated BOA in women ($r = 0.22$), but not in men ($r = 0.09$). Interestingly, self-reported BOA was negatively modulated by the self-reported perspiration intensity, but it did not influence the third-party ratings of BOA. Both men and women tended to overestimate their BOA.

Our results are in line with previous studies in other modalities which reported correlation between the self and third-party rated attractiveness around $r = 0.2$. However, we found a significant association only in women. This could be due to the better olfactory abilities in women or higher social pressure on women's physical attractiveness. Further, we found a tendency for overestimation of self-reported BOA both in men and women. The overestimation could serve as a self-protective mechanism for one's well-being.

LK is supported by the START grant (no. START/SOC/064, MŠMT).

Thu-S3-005

Exploring the links between body odour exposure, disgust sensitivity, relationship commitment and attachment style.

Mem Mahmut

Food, Flavour and Fragrance Lab, Macquarie University, Australia

This talk presents the findings of a series of studies exploring the links between olfactory ability, experiences of partner body odours and attachment styles in romantic relationships. Specifically, we explored whether attachment style predicts experiences of a partner's body odour and sexual disgust sensitivity and whether olfactory ability and experiences of partner body odours were related to attachment style and relationship intimacy and commitment. The broad findings across these studies indicated that poorer olfactory ability was associated with attachment insecurity, avoidant attachment styles were associated with higher disgust towards partner body odours and higher sexual disgust, and that exposure to partner body odours may be associated with stronger relationship commitment.

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13:30 - 15:30

Symposium 4: Higher order processing of chemosensory cues in the fly brain

Hahn Lecture Hall

Chair/s: Sophie Caron, Marcus Carl Stensmyr

Our symposium will highlight recent advances in our understanding of how chemosensory information is decoded and processed by higher brain centers in the fly. The invited speakers will cover taste, olfaction, as well as thermosensation, and how these sensory inputs are integrated in the fly brain to yield appropriate behavioral responses. All invited speakers are leaders in their respective fields, and each have their own approach to tackle the central question of how sensory input is translated to behavioral output.

Thu-S4-001

Adaptive traits in the drosophila mushroom body

Sophie J. C. Caron [1], Kaitlyn E. Ellis [1], Hayley Smihula [1], Ishani Ganguli [2], Ashok Litwin- Kumar [2], Thomas Auer [3], Richard Benton [3]

[1] School of Biological Sciences, University of Utah, Salt Lake City, United States, [2] Center for Theoretical Neuroscience, Columbia University, New York, United States, [3] Center for Integrative Genomics, University of Lausanne, Lausanne, Switzerland

How the brain adapts in response to changes in the environment remains largely unknown. Thus far, adaptive traits have been primarily identified in sensory systems, suggesting that sensory neurons might be more malleable to evolutionary pressures than neurons embedded in higher brain centers. In Drosophila, comparative studies of closely related species that live in drastically different chemosensory ecology revealed that olfactory sensory neurons can rapidly evolve new detection capabilities. For instance, the obligate noni specialist Drosophila sechellia, a close relative of the generalists Drosophila melanogaster and Drosophila simulans, is equipped with olfactory sensory neurons finely tuned to noni volatiles. In this presentation, I will summarize our recent findings showing that adaptive traits can be found downstream of the olfactory sensory neurons. We used a neuronal tracing technique to determine how the projection neurons of the olfactory system connect to the Kenyon cell of the mushroom body. We mapped over 2000 projection neuron—Kenyon cell connections in Drosophila melanogaster, Drosophila sechellia and Drosophila simulans. Statistical analyses of these connections revealed global architectural features that are species-specific. Specifically, we found that the projection neurons activated by noni volatiles connect more frequently to Kenyon cells in Drosophila sechellia than they do in the generalist species. We also found that this increased connectivity results from a larger number of projection neurons as well as a larger number of pre-synaptic sites. Finally, we have evidence suggesting that increased connectivity in the mushroom body leads to differences in learning abilities. Altogether, this study shows that higher brain centers are just as malleable to evolutionary pressures as sensory systems, suggesting that the brain might adapt to novel sensory environments through cellular changes distributed along neuronal circuits.

Thu-S4-002

Gut-brain axis controls food ingestion in Drosophila

Xinyue Cui, Matthew R. Meiselman, Haein Kim, Nilay Yapici

Cornell University, Ithaca, NY 14850, USA

In many animals, food intake is strictly regulated by sensory, homeostatic, and hedonic neural circuits that balance energy intake with energy expenditure. Although neural circuits that regulate food intake have been extensively investigated in rodent models, the entire sensory-motor neural circuits that generate food perception and accordingly regulate food ingestion have not been fully understood in any model organism. We use the fly (Drosophila melanogaster) to understand the fundamental principles of how the brain integrates the sensory percept of food with the sensation of hunger and satiety to regulate food intake on the level of circuits. Previously, we identified a novel group of interneurons, IN1 neurons, as a regulator of food ingestion in flies. Here, we used optogenetics and two-photon calcium imaging to investigate the neural circuitry of IN1 neurons. We found that IN1 neurons receive specific excitatory input from sugar-sensing chemosensory neurons and mechanosensitive neurons that respond to food texture. Using, intersectional genetics, we investigated which sugar-sensing neurons activate IN1 neurons. Our detailed analysis showed that taste neurons expressing Gr43a generated a strong and sustained calcium response in IN1

neurons. We further investigated which Gr43a neurons produce this excitatory effect and found that IN1 neurons receive specific excitatory input from interoceptive Gr43a neurons that innervate the fly digestive system. Finally, we developed a new imaging preparation to capture the activity of gut neurons in vivo in behaving flies. Using this imaging prep, we showed that Gr43a gut neurons indeed respond to sugar ingestion. Our research revealed that the gut-brain axis might regulate food ingestion in flies in a similar way to in rodents and humans.

Thu-S4-003

Convergence of olfactory and thermosensory stimuli in the Drosophila brain

Genevieve Jouandet, Michael Alpert, Miguel Simoes, Alessia Para, Marco Gallio
Department of Neurobiology, Northwestern University, 60208, Evanston, IL, USA

The avoidance of unfavorable temperature is a fundamental behavior in the repertoire of all motile animals, from flatworms to whale sharks. Because temperature preference is both innate and species-specific, it is an ideal system to study how behavior emerges from the activity of the brain and how it evolves under selective pressure, allowing animals to colonize new environments. The primary focus of the Gallio Lab is the study of the molecular and circuit mechanisms underlying temperature sensing and preference in the fruit fly Drosophila. Our efforts have been directed towards following the full transformation of temperature stimuli: from detection at the periphery, to representation and processing in the brain, to the appearance of directed behavioral responses. Yet even when avoiding unfavorable temperature, flies are constantly exposed to additional sensory cues. If these stimuli also happen to be aversive, they may ultimately produce stronger responses (avoid/walk away). If they are attractive, a sensory conflict may emerge. One of our current objectives is to identify the brain circuits that process stimulus valence (attractive/aversive) across modalities. We are using olfaction and thermosensation to understand how stimuli of different nature but similar valence (unfavorable temperature and aversive odors) may be processed together to produce coherent responses, and -conversely- to understand how flies may be able to suppress innate avoidance of unfavorable temperatures when confronted with the possibility of a reward (attractive odors).

Thu-S4-004

Dissecting olfactory processing and plasticity in the fly brain

Florencia Campetella [1], Benjamin Fabian [1], Bill Hansson [2], Silke Sachse [1]
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Most animals rely on their olfactory system to accomplish behavioral tasks that guarantee their survival and reproduction. Since the odor space consists of an enormous, nearly infinite number of possible stimuli, olfactory systems require special strategies to perceive, identify and evaluate the highly diverse odor information from the environment. The vinegar fly Drosophila melanogaster represents a premier model system for studying olfactory processing mechanisms 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, molecular and behavioral methods, my group is dissecting the neural circuits that are involved in coding, processing and perception of odors. We identified and dissected the neuronal correlates to specific behavioral outputs resulting from the perception of odor mixtures, we demonstrated that the neural composition of every olfactory glomerulus is unique and correlated to its functional relevance, and we were able to show that higher brain centers decode the behavioral value of an odor. We are currently examining whether the olfactory circuitry is hardwired or can be modulated by previous experience. The talk will summarize our recent insights into coding strategies and plastic components of the olfactory circuitry of Drosophila.

Thu-S4-005

Hungry glia cells modulate odor foraging and feeding

Ilona C. Grunwald Kadow, Jean-Francois De Backer
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The main goal of my research is to understand how chemosensory information is translated into a state- and context-dependent percept of the environment guiding decisions and behavior. To this end, we combine novel methodology

such as in vivo fast lightfield wholebrain calcium imaging of neurons and glia cells with (opto)genetic manipulations and behavioral analysis. We employ methods for large scale analysis of imaging and behavioral data with computational modelling and anatomy to unravel how neural circuits across the brain encode what the animal experiences and direct its next action. Most recently, we became interested in how cellular metabolism and energy state of neurons and glia cells relate to feeding and foraging behavior. In the meeting, I would like to discuss unpublished data suggesting that metabolic sensing of different types of glia cells shape foraging and feeding behavior. We hypothesize that similar basic metabolic pathways guide foraging behavior both in single cell organisms as well as in animals with highly complex brains.

15:30 - 17:00

Poster Session (No. 1-59)

Planck Lobby & Meitner Hall

Thu-P1-001

Microfluidic BRET assays of GPCRs with a smartphone

Margriet Roelse [1], Jasper Snoep [2], Maurice Henquet [1], Aria Samimi [2], Maarten Jongsma [1]

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In our lab we have previously established a reverse-transfected cell array technology in a microfluidic system to screen GPCR libraries against sequentially injected samples. Activated receptors induce a transient calcium increase that is visualized by a fluorescence-based ratiometric FRET calcium sensor using a fluorescence microscope. However, such specialized read-out equipment is costly and not easily miniaturized for use as a screening tool outside a biological lab. Furthermore, complex samples like coffee and milk are problematic to measure due to sample fluorescence and light reflection. To avoid the need for a fluorescence-excitation light source we switched to a luciferase-based calcium reporter system. Bioluminescent calcium sensors are available as ratiometric BRET-sensors like CalfluxVTN and intensity-based split luciferase sensors like GeNL Ca^{2+}. The aim of this study was to evaluate these sensors for GPCRs activation in the context of a smartphone-based recording system.

Luciferase enzymes yield a constant glow of light at a stable concentration of substrate, but typically these substrates may be rapidly oxidized when mixed prior with different samples. To prevent oxidation we developed a substrate mixing setup where the substrate stock solution is merged immediately prior to entering the receptomics flowcell. We found that an iPhone12ProMax colour camera operated by a low light imaging app, mounted with a macro-lens and placed upon a light-tight box containing a microfluidic flowcell attached to a pump was all we needed to perform a BRET-analysis using the separate RGB signals of the colour camera. One to two second exposures resulted in high quality calcium signals from 300 receptor spots on a 1 square cm array. This demonstrated the potential of the development of robust BRET assays in small instruments outside the lab.

This work was supported by NWO project TO2 Luminose, a joint project between BU Bioscience and Insectsense BV.

Thu-P1-002

Laser-induced oxidized metal oxide semiconductor gas sensor arrays with high compositional tunability for artificial olfaction

Hyeokjin Kwon, Hyuk-Jun Kwon

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The electronic nose (e-nose), one of the electronic sensor systems, is an analysis system composed of arrays of chemical sensors to mimic the mammalian olfactory system that recognizes different odors. The e-nose analyzed many odor components quickly, analyzing individual odor components and simultaneously detecting patterns of overall odor components. Metal oxide semiconductors (MOS), a chemo-resistive material that changes its electrical resistance in response to changes in the nearby atmosphere, are a great candidate for the building block of the e-nose system due to their high sensitivity, low cost, and simplicity. Also, the low selectivity issue of MOS can be supplemented with the

assembly of sensors to be a cross-reactive sensor array.
Herein, we suggested the metal oxide array with high compositional tunability by laser-induced oxidation. When the laser beam irradiates the metallic film, oxidation occurs depending on the amount of light due to the interaction between oxygen and materials. As a result, various metal oxide layers with the controlled composition of oxygen are fabricated and operated differently because of their oxygen nonstoichiometry. To verify the laser-induced oxidation, we analyze the composition of metal oxide films by Raman spectroscopy and X-ray Photoelectron Spectroscopy (XPS). Also, we measured the sensing behaviors of the laser-oxidized MOS sensor array during the exposure of 8 different odor molecules (Heptanol, 2-ethylfenchol, D-limonene, Octanal, Decanal, Cis-3-hexenol, 2,3,5-trimethylpyrazine, and Geraniol) by bubbler system. And then, we classified 8 different recognized patterns by extracting the characteristics of gas sensors.
Acknowledgment: This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education(2020R1A6A1A03040516). Also, this work was supported by the NRF grants (2019M3C1B8090840) funded by the Ministry of Science and ICT (MSIT).

Thu-P1-003

Detecting malodours using odorant binding proteins from hermetia illucens

Marisa Nardiello [1, 2], Carmen Scieuzo [2, 3], Rosanna Salvia [2, 3], Donatella Farina [2, 3], Jonathan Cammack [4], Jeffrey Tomberlin [4], Patrizia Falabella [2, 3], Krishna Persaud [1]
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Hermetia illucens (Diptera: Stratiomyidae) is a voracious scavenger insect with great capacity for bioconversion of organic waste. It can recognize and discriminate a wide range of chemical compounds that influence the choice of substrates for oviposition. Adult gravid females are attracted by VOCs from decomposing organic substrates and some species of bacteria present on decaying matter. The larval and adult transcriptome indicates an arsenal of odorant binding proteins (OBPs), that may facilitate the colonization of disparate environments with characteristic smells of decomposition. There is interest in development of sensing systems for malodours as often these indicate the presence of harmful components and can cause negative health and environmental effects. We report the expression, characterisation and performance of immobilised H. illucens OBPs (HillOBPs) on quartz crystal microbalance (QCM) transducers. The heterologous expression of recombinant HillOBPs was carried out with specific plasmids transformed in Escherichia coli BL21 (DE3) pLys and inoculated in 1 L of LB medium and four OBPs were expressed – HillOBP_C57, HillOBP_C11107, HillOBP_21691, HillOBP_C1173. Once delipidated and concentrated, HillOBPs were immobilized and used as biorecognition elements in quartz crystal microbalances (QCMs), to test the ability to detect volatile organic compounds (VOCs) of interest associated with organic decomposition. The resonant frequency changes of the QCMs were measured on exposure to various odorants. It was found that the HillOBPs-based biosensor array has a strong affinity for Isobutyraldehyde, Isovaleraldehyde, 2-Methylbutyraldehyde and Butyric acid at high and low concentrations in vapour phase. The performance of this HillOBP-based biosensor (high sensitivity, low limit of detection and good reversibility) may be of interest for the creation of fast, inexpensive and reliable malodour sensors for applications in environmental and agri-food monitoring.

Thu-P1-004

IL-6 release by a human gingival fibroblast cell line correlates with the bitter taste threshold of the stimulant

Johanna Tiroch [1, 2], Andreas Dunkel [3], Sonja Sterneder [1, 2, 3], Sofie Zehentner [1, 2], Maik Behrens [3], Antonella Di Pizio [3], Jakob Ley [4], Barbara Lieder [1], Veronika Somoza [1, 3, 5]

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Fibroblasts are the predominant cell type in gingival connective tissues and play an essential role during acute inflammation, releasing cytokines that recruit immune cells to counter environmental stimuli. Activation of bitter sensing chemoreceptors (TAS2Rs) has been demonstrated to repress the release of lipopolysaccharide (LPS)-induced pro-inflammatory cytokines by the human gingival fibroblast cell line HGF-1. Since these results indicate that TAS2Rs activation in HGF-1 cells mediates the release of pro-inflammatory cytokines, we hypothesized that the release of the pro-inflammatory interleukin 6 (IL-6) by HGF-1 cells is correlated with sensory bitter taste thresholds.

In previous work, we showed that trans-resveratrol repressed the LPS-induced IL-6 release in HGF-1 cells via TAS2R50 involvement. We, therefore, performed molecular docking on TAS2R50 and functional cell-based experiments using a number of TAS2R agonists selected from the chemical bitter space in combination with TAS2R antagonists to demonstrate that this cellular response to taste-relevant concentrations is not TAS2R50 specific. In a next set of experiments, the number of test compounds selected from the chemical bitter space was expanded to cover the structural diversity of bitter compounds with reported psychophysical threshold. Functional experiments revealed a correlation between the reported bitter taste threshold of tastants and their modulating effect on the LPS-induced IL-6 release by HGF-1 cells. These results were validated against our previously established parietal cell assay using the HGT-1 cell line, and found to have an improved correlation with bitter taste thresholds (HGF-1: R^2=0.60, $p<0.01$ vs. HGT-1: R^2=0.15, p=0.26).

In conclusion, the HGF-1 cell assay presents a suitable model for the identification of bitter compounds and modulators. In addition, our results strongly support the anti-inflammatory potential of bitter compounds which has to be substantiated by clinical studies.

Thu-P1-005

Machine learning-enabled biomimetic electronic olfaction using graphene single-channel sensors

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Background: Olfaction is an evolutionary old sensory system, which provides sophisticated access to information about our surroundings. [1] Inspired by the biological example, electronic noses (e-noses) in combination with efficient machine learning techniques aim to achieve similar performance and thus to digitize the sense of smell. [2, 3] Objectives: In this work, the discriminative recognition of odors using graphene single-channel nanosensor-based electronic olfaction in conjunction with machine learning were investigated at room temperature. Experimental methods: Functionalized graphene-based single-channel nanosensor were prepared and sensing signal was acquired towards exposure to various odors. The fingerprint information of odors was then represented by feature vector extracted from sensing signal and applied to discriminate as well as identify odors by machine learning. Results: The developed prototype exhibits excellent odor discrimination (83.3%) and identification performance (97.5%) at room temperature, maximizing the obtained results from a single nanosensor. Upon exposure to binary odor mixture, the response features behave similarly to one of the existing individual odor component, mimicking the overshadowing effect in human olfactory perception. Conclusions: We present the excellent performance of graphene single-channel nanosensor based electronic olfaction in conjunction with machine learning. The developed platform may facilitate miniaturization of e-noses, digitization of odors, and distinction of volatile organic compounds (VOCs) in various emerging applications.

Sources of funding: We appreciate the funding support from Volkswagen Stiftung (grant no. 9B396).
References:
1. Sarafoleanu, C.et.al. J Med Life 2009, 2 (2), 196-8.
2. Gardner, J. W.et.al. Sensors and Actuators B: Chemical 1994, 18 (1-3), 210-211.
3. Covington, J. A.et.al. IEEE Sensors Journal 2021, 1-1.

Thu-P1-006

Does the farming environment impact the vomeronasal organ condition?

Violaine Mechin, Patrick Pageat, Marion Boutry, Eva Teruel, Florian Frandjian, Celine Portalier, Laura Bouyer, Pietro Asproni

IRSEA - Research Institute in Semiochemistry and Applied Ethology, Quartier Salignan, Apt, Fance

Chemical communication is used by mammals to maintain the social harmony in groups through the exchange of pheromones. The reception of these molecules is mainly insured by the vomeronasal organ (VNO). When altered, this organ cannot properly detect cues strongly impacting the animal life.

Intensive farming exposes animals to dangerous substances such as ammonia, a gas produced during litter degradation and responsible of the respiratory tract damages. Due to the anatomical proximity to these structures, the aim of this study was to investigate if an environment rich in ammonia can induce VNO conditions.

We characterized ammonia exposure effects on murine VNOs using histology. Animals were split in 3 groups of 10 mice: G1 = mice in normal laboratory environment; G2 = mice in the cage with an increase of the natural ammonia concentration; G3 = mice in the cage with a litter changed every 5 days to limit the ammonia concentration at 0 ppm. After 21 days, VNO were histologically analyzed and a qualitative score (0 = healthy, 1 = weak, and 2 = strong) was used to evaluate the condition of non-sensorial (NSE) and sensorial (VNSE) epithelium and VNO soft tissue. In normal housing, mice VNO were significantly less impacted than mice in the cage, concerning the NSE inflammation ($p=0.0016$), the VNSE degeneration ($p=0.0023$), and the alteration of the VNO soft tissue ($p<0.0001$) (Fisher's exact test). Even if no significant differences were observed, mice exposed to natural ammonia presented stronger signs of VNO alteration than non-exposed ones.

In conclusion, mice housed in a closed environment presented more VNO alterations than those in a normal housing, as probable consequence of dust and gas accumulation. Furthermore, natural ammonia seems to increase the onset of these lesions. These preliminary results on a murine model suggest that the housing environment can strongly impact VNO conditions, opening interesting perspectives for farm animals.

Thu-P1-007

Influence of stress chemosignals on empathy and emotion recognition in depressed individuals and healthy controls

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Human body odors contain various chemosignals that play an important role in our non-verbal communication regarding health status, genetic identity, immune system, fitness and emotional state. Studies on human chemosignalling in individuals with psychiatric diseases are scarce, but it has been indicated that patients with depression show alterations regarding smell perception and emotion recognition. In the current project, we investigated emotional stress behavior and the influence of chemosignals in axillary sweat on other individuals. For this

purpose, chemosensory cues from Trier Social Stress Test (TSST) and a friendly version of TSST were obtained in 39 healthy participants. Those chemosignals and an odor-free blank sample (cotton pad) were used to stimulate another group of healthy participants (n = 40) and patients with depression (n = 37). The various stimuli were examined regarding their influence on subjective feelings of stress and empathic reactions. We were able to show that depressed individuals improve their ability to assess grief emotions when in contact with stress chemosignals. These influences on emotion processing were observed particularly for male stress sweat donors or a high donor stress level. The results implicate, that stress chemosignals subconsciously sharpen the senses of patients with depression, leading to a better emotion assessment and therefore an improved ability to empathize especially for emotions heightened by this psychiatric disease. Healthy individuals remained unaffected in their recognition of grief. Knowledge of the influence of human chemosignals on processing emotional cues could be crucial for a better understanding of the psychopathology behind depression and help develop new treatment options.

Thu-P1-008

Emotional body odors enhance the effects of mindfulness treatment in individuals with social anxiety: a pilot study

Cinzia Cecchetto [1], Claudio Gentili [1, 2], Elisa Dal Bò [1, 2]

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Previous studies have shown that individuals exposed to emotional body odors report a partial reproduction of the affective state of the sender. The present study aimed to investigate if emotional body odors can increase the benefits of a mindfulness-based intervention in individuals with social anxiety symptoms (SAD), a mental disorder characterized by intense fear and avoidance of social situations. Thirty women (mean age: 22.2) with SAD were recruited and divided into one of three odor conditions (happiness or fear body odors or clear air). The study was conducted over two consecutive days. Each day, participants performed the mindfulness intervention while being exposed to one of the three odor conditions. At the beginning of day 2, participants were subjected to a social stress induction. Heart rate variability (HRV) was measure during the intervention. At the beginning and at the end of each day, anxiety was measured with the STAI scale. Results on anxiety level showed a significant interaction of odor and time both for day 1 [$F(2,27) = 3.59$, $p = .041$] and day 2 [$F(2,25) = 6.04$, $p = .007$]. On day 1, participants doing the intervention in the happiness condition reported a reduction of anxiety (happiness: $p = .003$, fear: $p = .08$, clean air: $p = .99$), whereas on day 2 both participants in the happiness and fear conditions reported a reduction of anxiety (happiness: $p = .002$, fear: $p = .002$, clean air: $p = 1.00$). Moreover, HRV analysis revealed a main effect of odor [$F(2,25) = 3.9$, $p = .033$]: HRV was higher during the intervention with happiness compared to fear odor ($p = .026$) indicating overall increasing well-being. The results give potential insight of how body odors may be utilized to support positive outcomes of psychological therapy.

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Thu-P1-009

Do emotional body odors modulate the processing of neutral faces in individuals with social anxiety and depressive symptoms?

Elisa Dal Bò [1, 2], Alejandro Luis Callara [3], Claudio Gentili [1, 2], Francesca Mura [1, 2], Nicola Vanello [3], Ludovica Natali [2], Enzo Pasquale Scilingo [3], Alberto Greco [3], Cinzia Cecchetto [2]

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Human body odors are an effective modality of social communication. Individuals exposed to emotional body odors report a partial reproduction of the affective state of the sender. The present study aimed to explore how body odors collected in happiness and fearful conditions modulate the subjective ratings, the psychophysiological response and the neural processing of neutral faces in individuals with depressive symptoms, with social anxiety symptoms, and healthy controls (N = 22 for each group). To this aim, electrocardiogram (ECG) and EEG (using a 256-channel system) were recorded continuously. As for subjective ratings, we found a significant group main effect of the arousal ratings: individuals with depressive and social anxiety symptoms rated the neutral faces as more arousing than control

individuals. Moreover, we found that individuals with depressive symptoms, compared to social anxiety and healthy individuals, rated the neutral faces as more arousing when they were presented in concomitant with the fear odor ($p = 0.002$), but not with happiness or clean air. This result was replicated when continuous measure of depressive symptoms was analysed in respect of odor condition, confirming that individuals with depressive symptoms seem to be especially sensitive to fear body odor as contextual information. From the ECG we extracted the heart rate variability (HRV). Results showed a main effect of odor: HRV increased during the fear and happiness body odors compared to clean air, suggesting that at peripheral level the two emotional body odors seem to show similar affective reactions. Finally, regarding EEG data, analyses are ongoing. Results of both ERPs and time-frequency analyses will be presented. These preliminary results confirm the role of body odors in modulating both the subjective and physiological responses.
FUNDING: European Commission Horizon 2020 research and innovation program [grant numbers 824153] to the POTION project

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Thu-P1-010

Feedback regulation of dopamine signalling tunes reward intensities

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Regulation of reward signals in the brain is crucial for appropriate evaluation of values and behavioral adaptation. In the fruit fly Drosophila melanogaster, a group of dopaminergic neurons (DANs) in the protocerebral anterior medial (PAM) cluster mediates the reinforcing property of the sugar reward. Recent studies suggest that localized regulation at the presynaptic site of DANs is critical for determining reward in olfactory memory. Cell-type specific visualization of the two dopamine receptors, DopR1 and D2R, also known as Dop2R, revealed their protein localization in presynaptic terminals of the PAM neurons. Based on the sequence similarity, DopR1 and D2R are classified as the fly orthologs to vertebrate D1 and D2 receptors, respectively. Here, we show that DopR1 and D2R in the DAN terminals fine-tune reward signaling for appetitive olfactory memory. In vivo calcium recording of the PAM neurons revealed that the sugar response at the PAM terminals was locally inhibited by D2R, indicating the function as an autoreceptor. Silencing DopR1 and D2R respectively altered appetitive memories in different ranges of sugar concentrations. Interestingly, we found that selective regulation of the PAM neurons by DopR1 and D2R applied to alcohol preference. This dose-dependent tuning by the opposing dopamine autoreceptors may thus represent a general mechanism for defining the dynamic range of reward.

Thu-P1-011

Neural circuits for wind guided olfactory navigation in Drosophila

Katherine Nagel, Andrew Matheson, Aaron Lanz, Tim Currier, Nick Kathman
NYU School of Medicine

Many animals navigate towards odor sources by combining olfactory cues with flow cues that indicate the source direction. We have identified neural circuits in Drosophila that encode and integrate these two cues to promote navigation towards an odor source. We first show that two distinct pathways from the periphery to the fan-shaped body, a part of the insect navigation center, encode wind and odor cues respectively. Wind pathway neurons encode wind direction independent of odor, while odor pathway neurons encode odor independent of wind direction. Moreover, optogenetic activation of odor pathway neurons promotes upwind navigation. Within the fan-shaped body, we identify hΔC local neurons that receive input from both wind and odor pathways and encode an odor-gated wind direction signal. We show that hΔC activity is required for persistent upwind navigation, while sparse activation of hΔC neurons promotes navigation in a reproducible direction. A computational model based on connectivity motifs within the fan-shaped body can reproduce both of these phenotypes, and illustrates how hΔC activity can specify a goal direction for navigation. Ongoing work imaging from behaving flies aims to understand how hΔC activity evolves during navigation in complex odor environments.

Thu-P1-012

Processing of sweet, astringent and pungent oral stimuli in the human brain.

Yunmeng Zhu [1], Divesh Thaploo [1], Pengfei Han [2], Thomas Hummel [1]

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Abstract: Taste and oral somatosensation are intimately related to each other from peripheral receptors to the central nervous system. Oral astringent sensation is thought to contain both gustatory and oral somatosensory components. In the present study, using functional magnetic resonance imaging (fMRI) we compared the cerebral response to astringent stimuli (tannin), with the response to one typical taste stimulus (sweet - sucrose) and one typical somatosensory stimulus (pungent - capsaicin). We observed three distributed brain sub-regions respectively located in Lobule IX of cerebellar hemisphere, right side of dorsolateral superior frontal gyrus and left side of middle temporal gyrus, which responded significantly different to the three types of oral stimulations, suggesting that these regions play a role in the discrimination of sucrose, tannin and capsaicin solutions. In addition, we observed overlapping activations in sub-region of the insula co-activated by three types of stimulations, suggesting the convergence of gustatory and oral somatosensory inputs in the insula. This study was supported by in-house funds from the department of Otorhinolaryngology of the TU Dresden.

Thu-P1-013

Characterization of the volatile fraction of Zebra Finch preen oil & feathers

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The olfactory sense was long-time underestimated in avian intra- and interspecific communication. First studies demonstrating that birds use their olfactory sense in communication processes were published in the sixties by Bang and colleagues (Bang 1965, Bang and Cobb 1968). Now, it is known that birds use olfaction in different social- and non-social contexts, amongst others in navigation and orientation, predator avoidance, foraging, reproduction and kin recognition. In Zebra Finches, it has recently been shown that the begging behavior of hatchlings lasts longer when their parents' scent is provided compared to the scent of unfamiliar adults (Caspers et al. 2017). To unravel the molecular principles of such chemical communication processes in birds, a characterization of the entirety of substances in avian odor sources is essential. In our current work, we established methods for the analysis of the volatile fraction of preen oil and feathers of Zebra Finches. Solvent extraction, solvent-assisted flavor evaporation, as well as gas chromatography-mass-spectrometry and one- and two-dimensional gas chromatography-olfactometry/mass spectrometry were applied. Using this methodology enabled us to identify so far 59 volatile compounds, with some of them not having been identified in avian samples before. We want to encourage further researchers to apply these and complementary methods on other bird species or even other animals to gain knowledge about the role of the volatilome in communication processes.

Funding: DFG (LO 2545/5-1 and CA 889/9-1)

Thu-P1-014

Ultrasonic vocalization and social behaviors in anophthalmic mice

Nouhaila Bouguiyoud [1, 2], Elena Morales-Grahl [4], Gilles Bronchti [1], Florence Roullet [3], Johannes Frasnelli [1, 2], Syrina Al Aïn [1, 2]

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Ultrasonic vocalizations (USVs) are calls produced by mice in multiple social contexts, including mother-pup separation, social play in juveniles, social interactions, and mating in adults. Whereas sensory deprivation may alter USV emission

and some social behaviors in deaf and anosmic rodents, little is known about the effects of visual deprivation in rodents. The aim of this longitudinal study was to assess acoustic communication and social behaviors in a congenitally blind mouse model, the ZRDBA strain. This strain generates litters comprising half the pups born blind (absence of eyes and optic nerves), and the other half born sighted. Anophthalmic and sighted mice were assayed to a series of behavioral tests at three different ages. Our findings showed that (1) at Post-Natal Day (PND) 7, USVs' total number between both groups was similar, all mice vocalized less during the second maternal isolation period than the first period, and both phenotypes showed similar discrimination and preference, favoring exploration of the home bedding odor; (2) at PND 30–35, anophthalmic mice engaged less in social behaviors in the juvenile play test than sighted ones, but the number of total USVs produced is not affected; and (3) at adulthood, when exposed to a female urine spot, anophthalmic male mice displayed faster responses in terms of USVs' emission and sniffing behavior, associated with a longer time spent exploring the female urinary odor. Interestingly, anxiety levels assessed in adult mice were significantly lower in anophthalmic mice compared with sighted mice. Together, our study reveals that congenital visual deprivation had no effect on the number of USVs emitted in the pups and juveniles, but affected the USVs' emission in the adult male and impacted the social behavior in juvenile and adult mice.

Thu-P1-015

Geosmin strongly modulates the honey bee defence behaviour and elicits unusual neuronal response patterns.

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Geosmin is an odorant produced by bacteria e.g. in moist soil. It has been found to be of extraordinary relevance to some insects, although for different reasons. Here we report the first tests on the effect of geosmin on honey bees. Behavioural experiments have shown that in bees exposed to the alarm pheromone component isoamyl acetate (IAA), geosmin strongly suppresses the defence behaviour, although, surprisingly, only at very low concentrations of geosmin. Electroantennography and antennal lobe (AL) calcium imaging provided insights into the underlying mechanisms. At the level of the olfactory receptor neurons, responses to mixtures of geosmin and IAA were lower than to pure IAA, suggesting an interaction of both compounds at the receptor level. In the AL, geosmin elicited a broad activity pattern but with decreasing amplitudes as concentration increases, which again correlates with the observed behaviour. Computational modelling of odour transduction and coding in the AL suggests that a broader activation of olfactory receptor types by geosmin in combination with lateral inhibition could lead to the observed non-monotonic increasing-decreasing responses to geosmin and thus underlie the specificity of the behavioural response to low geosmin concentrations. Finally, we speculate on a potential ecological relevance.

Thu-P1-016

Input-output transformation of odour representation in the mouse olfactory bulb via inhibitory network activity

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Convergence of olfactory sensory neurons (OSNs) onto discrete glomeruli generates a topographic map of olfactory receptor identity in the olfactory bulb (OB). Sensory input activates stereotypical glomerular patterns determined by the molecular receptive range of individual glomeruli. The combinatorial code of activated glomeruli holds information about the identity of an odour stimulus, before being processed by central circuits. Within a glomerulus information gets transferred to OB output neurons (mitral and tufted cells (MTCs)) which in turn form synaptic connections with inhibitory granule cells (GCs) via their lateral dendrites.

Here we monitored glomerular input and output signals in mice in response to a panel of 48 odours that cover a wide range of chemical space using in vivo 2-photon Ca^{2+} imaging. We employed triple-transgenic mouse lines that either

express GCaMP6f under the OMP-promoter (input) or the Tbet-promoter (output), alongside a fluorescently tagged M72 or O174 glomerulus. The resulting response profiles revealed higher and more structured correlations of activity patterns for the input (n = 148 glomeruli, 5 mice) compared to the output (n = 185 glomeruli, 13 mice). A similar decorrelation, or whitening, of odour representations from input to output has previously been observed in the zebrafish OB (Friedrich and Laurent, 2001) and has been attested to be mediated by inhibitory interneurons (Wanner and Friedrich, 2020).
To investigate potential mechanisms underlying the whitening that we observed, we created an artificial neural network (ANN) that models the contribution of GCs to the output signal. Our results show that implementing the modelled inhibitory GC-MTC connection faithfully recapitulates the physiological responses observed in vivo both in terms of level and pattern of decorrelation.

Thu-P1-017

Automated tracing of regenerating olfactory neurons in organotypic cultures

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Olfactory sensory neurons (OSN) regenerate from progenitors residing within the olfactory epithelium (OE). The OE pseudostratified architecture as well as soluble factors from the environment provide important cues for progenitors to differentiate into mature OSN. In case of severe injury with loss of cell-to-cell contact, regeneration is no longer possible: the OE is irreversibly replaced by respiratory, non-sensory epithelium. The molecular mechanisms triggering regeneration vs replacement of OSN are not fully understood. To address this, we developed a 2-D organotypic model which preserved the OE pseudostratified architecture. We investigated the influence of the coating (laminin, fibronectin, or collagen IV). Survival and growth of OSN were further assessed comparatively in response to different growth factor treatments (BDNF, GDNF, NT3, retinoic acid, FGF, and combinations of those). To quantify axonal growth, an automated quantification tool was developed . Axonal growth was significantly increased in Fibronectin and Collagen IV conditions compared to Laminin and Control (p= 0.001). Furthermore, combinations of growth factors simultaneously inducing proliferation and differentiation were significantly more efficient compared to growth factors inducing only differentiation. In conclusion, the organotypic OE culture allows for efficient qualitative and quantitative assessment of OSN outgrowth in response to different coatings and growth factor treatments. The developed quantification tool was helpful to assess OSN outgrowth in an objective, accurate (ICC between automated and manual tracing: 0.96) and repeated manner, saving 87% of examination time. This model combined with the automated tracing tool provides a more representative and time-saving method to characterize OSN regeneration. It may facilitate high-throughput screens of regenerative compounds and transcription factors in the future. Funded by: Foundation Louis-Jeantet, Auris, and Sir Jules Thorn.

Thu-P1-018

Intracranial recordings from the human olfactory cortex in response to pleasant and unpleasant odors

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The cerebral olfactory processing involves the limbic system at very first steps. Little is known about local field potentials elicited by odors in humans, especially the way the limbic system processes odor pleasantness. Here, we describe the single case of a patient (man, 39 years old) with pharmaco-resistant epilepsy monitored via stereotactically implanted depth electrodes (stereoelectroencephalography, SEEG) while passively receiving odors with different hedonic valences (peach or fish). SEEG was recorded from 96 contacts in the right hemisphere, located amongst others close to the piriform cortex, in the amygdala, hippocampus, and parahippocampal gyrus. Odors were

delivered 20 times and for 3s each using a computer-controlled olfactometer in precise timing and constant airflow. Respiration was monitored to align the stimulus onset on the following inspiration. Using time-frequency analysis, oscillations of different frequency bands were described. From the closest contact to the piriform cortex in the amygdala, a specific olfactory pattern was observed for peach in the form of early theta/beta oscillations linked to the inspiration phase, followed by beta and gamma oscillations, as described in the literature. Only in the amygdala, and not in other brain areas, a similar pattern was observed. The fish odor induced the same activation pattern with, however, a delayed peak of activity. Unlike the pleasant peach odor, the unpleasant fish odor produced an early and sustained reinforcement of the delta band. For both odors, contrary to active sniff-induced olfactory processing seen in the literature, the gamma oscillations seemed to last less for passive smelling, with periodic repetition of the olfactory pattern. The parahippocampal gyrus showed differential oscillations between fish and peach. Taken together, these results provide first insights into differential oscillations patterns in the human primary olfactory cortex for pleasant and unpleasant odors.

Thu-P1-019

Predicting the combinatorial code for any odorant molecule: a graph neural networks approach

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Our sense of smell relies on the use of approximatively 400 genes expressing functional odorant receptors (ORs), endowing us with the power to discriminate a vast number of chemical stimuli. ORs can accept several different classes of molecules – ligands, and one molecule can activate different ORs, leading to a complex combinatorial code of olfaction. Cracking this code is a long-standing challenge and its first step relies on the identification of OR-ligand pairs. To date, common procedure for OR's ligand identification has been based on in vitro search with rather low success rates of ~2%. Moreover, the data linking a molecule to a set of ORs are scarce and only 131 human ORs have an identified ligand. Thus, building a machine learning protocol linking molecules with ORs' sequence remains challenging. To tackle this issue, we leverage recent advances in representation learning and combine them with graph neural networks (GNN) to build a receptor-ligand prediction model. To our knowledge, this is the first model for ORs' ligand prediction that takes an entire protein sequence into account.
Several methods inspired by success of representation learning in the natural language processing (NLP) have been proposed to represent protein sequences. Here we use BERT which was previously trained on more than 200M protein sequences. We treat molecules as graphs and process ORs and molecules simultaneously using GNN.
Multiple experimental assays have been done to identify new ORs' ligands, yet curated dataset of OR-molecule pairs is still missing. Therefore, to train and evaluate our model, we gathered a new dataset of more than 46 000 OR-molecule pairs putting together results from 31 publications. Using this data, we evaluated our model on a test set comprising more than 1500 high-accuracy tertiary screening data (EC_{50}). Our receptor-ligand model correctly identifies 70% of ligands with 69% precision and achieves Matthew's correlation coefficient (MCC) of 0.60.

Thu-P1-020

Brief sensory deprivation triggers synaptic plasticity in the glomerular layer of the murine olfactory bulb

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The ability of neural circuits to adapt to changing stimuli is critical for learning, memory, and adaptation. In sensory systems, homeostatic forms of neuronal plasticity can be triggered by sensory deprivation. In the olfactory bulb, it has recently been demonstrated that while excitatory neurons remain unchanged, only a subtype of interneurons, axon-bearing dopaminergic (DA) neurons, decrease their intrinsic excitability in response to 24h of deprivation—a functional change complemented at the structural level with shortening of the axon initial segment.
However, whether this experience-dependent alteration is mirrored at the synapses remains unclear. Using whole-cell patch-clamp in brain slices of P20-40 mice who underwent 24h naris occlusion, this project investigated the synaptic changes in spontaneous excitatory and inhibitory events occurring in glomerular layer neurons, external tufted cells (ETCs) and the DA neurons of both subtypes (i.e.axon-bearing and anaxonic).

After 24h occlusion, anaxonic DA neurons–which have been previously shown resistant to change their intrinsic firing–display synaptic plasticity through receiving excitatory currents of reduced amplitude (EPSC,control:-26.91pA±2.247pA,occluded: -18.86pA±1.14pA, p<.05). This change was not found in their axon-bearing DA counterparts. Moreover, ETCs, excitatory interneurons also previously found to show no change intrinsically after 24h deprivation, received larger inhibitory currents (IPSC:control:377.9fC±77.51fC,occluded:614.2fC±60.42fC,p<.01). Taken together with the role of these cells, these results suggest a network mediated up-regulation of activity after deprivation. Moreover, this provides support to the notion that the circuit is able to flexibly recruit different types of plasticity at different cell types depending on the demand it faces.
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Thu-P1-021

Heterogeneity of bulbar dopaminergic cells

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Dopaminergic (DA) neurons in the murine olfactory bulb (OB) control the gain of the first olfactory synapse. They are known for adult neurogenesis, but recent work found that a subset of them cannot regenerate. These, unlike the anaxonic DA cells born throughout life, have an axon. Further differences in soma size, dendritic branching, excitability, odour tuning and plasticity suggest different roles in the OB.
Their connectivity is still unknown, so we began studying this using rabies tracing. By timing the floxed starter virus injection in a DAT-Cre mouse – embryo lateral ventricles, or adult rostral migratory stream – and waiting respectively 6 or 2 months before delivering rabies to the OB, we attempted to differentially trace the two subtypes. To validate, we checked DA identity of starter cells (cells infected by starter and rabies virus) by staining for tyrosine hydroxylase and used soma area as a proxy for subtype classification (axon-bearing cells >=100µm^2).
Embryonic-injected brains (n=6) showed a mixed traced population of axon-bearing and anaxonic DA cells. Although there was a soma size difference between embryonic- and adult-injected brains (means 69.7µm^2 and 48.5µm^2 respectively, p=0.0002), this was due to high variability in embryonic-injected brains (range 8 - 198µm^2, SD = 33.19) rather than consistently larger cell sizes. This indicated that anaxonic cells born in the embryo had survived the six-month window between starter and rabies injection, contrasting previous findings of their short lifespan.
If a mixed population has been traced, the pre-synaptic partners will nonetheless enlighten general DA connectivity in the OB which is thus far undefined. This could guide future physiological approaches to connectivity in the future, in which subtypes can be more clearly defined.
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Thu-P1-022

Robotic validation of stereo-olfaction for navigating turbulent plumes

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Turbulent odour plumes are challenging to track since there is usually no smooth gradient leading to the source. Instead, it was thought that insects used odour encounters and wind direction as main clues for foraging or locating mates. Recently, it was described that fruit flies can also use "stereo"-information inferred from temporal correlations between their two antennas [1].
Here we validate this strategy using robotic experiments in a turbulent environment.
We had previously constructed a stereo artificial nose based on metal-oxide sensors [2] which could resolve the onset of odorants with sub-second accuracy, inferring odour direction from temporal correlations similar to fruit flies.
We equipped a wheeled robot with a pair of sensors and placed it in a room with a fan and an intermittent odour

source. Sensor output spikes fed into a Time Difference Encoder (TDE) [3], a neural model encoding the time difference between two events into the number of spikes contained in an output burst.
A neural network comprising onset filters, TDEs and cross inhibition was able to perform lateralization of the gas source. A reactive navigation algorithm directed the robot towards the side of first detection and finally to the source, supporting the concept of stereo olfaction for plume navigation.
Further work could evaluate, e.g., the optimal sensor separation distance and use wind direction as an additional clue. Using stereo olfaction to bias a random walk could allow the robot to start outside the odour plume.
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References
[1] Kadakia et al. (2021) https://doi.org/10.1101/2021.09.29.462473
[2] Drix & Schmuker (2021) https://doi.org/10.1021/acssensors.0c02006
[3] Gutierrez-Galan et al. (2021) https://doi.org/10.1109/TNNLS.2021.3108047

Thu-P1-023

Diabetes-induced modulation of electrical activity of olfactory receptor neurons in an odorant receptor-dependent manner

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Olfactory receptor neurons (ORNs) express a single olfactory receptor (OR) to recognize odorants. Once an odorant ligand is bound to the OR, odorant-evoked neural activity is generated to drive olfactory perception. Each OR characterizes a different pattern of spontaneous ORN activity in the absence of odorant stimulation and both basal and odorant-induced activities play important roles in ORN maturation and odor perception.
Diabetes disturbs glucose metabolism and a changed metabolic status can alter odor perception. Insulin is involved in neural survival as a neural growth factor and may modulate ORN activity. However it remains unclear how diabetes, in particular type 1, changes the neural activity and the odor response properties of ORNs. We examined the effects of hypoinsulinemia on the odorant response properties and ORN activity using a drug-induced type 1 diabetic mouse model that lacks insulin. We used the suction pipette technique to examine activity of ORNs expressing specific ORs, using mouse lines that express GFP in ORNs that express the mOR-EG- or I7-OR. 3 months of diabetes did not induce any significant structural changes of the olfactory epithelium. But in diabetic mice I7-expressing ORNs showed a significant reduction of basal activity when compared to control mice, but those expressing the mOR-EG OR, which already have a low basal activity, did not. In the ligand-evoked responses, the maximal current responses of ORNs expressing mOR-EG- or I7 OR were not significantly different between control and diabetic mice. But the responses of I7 ORNs in diabetic mice decayed much more rapidly, while those of mOR-EG ORNs did not. Similarly, the odorant response recorded by electroolfactogram decayed more rapidly without significant reduction of the maximal response in diabetic mice. These results suggest that type 1 diabetes can alter odorant perception beginning in the periphery and that changes in the ORN activity are OR-dependent.

Thu-P1-024

Representational drift in a neural network model of the piriform cortex

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Recent experimental findings suggest that the stimuli representation in the piriform cortex may drift over weeks in animals. Nevertheless, the exact mechanism underlying this phenomenon is still not fully understood. In this work, we use theoretical and computational analyses to study this phenomenon in a simple two-layer network model of the olfactory system. The network receives inputs form the olfactory receptors and yields an output mimicking olfactory percepts. The representation in the expansive hidden layer is expected to model odor representation in the piriform

cortex. We show that the stochasticity during learning, arising merely from the experienced stimuli, could lead to a diffusion of neural network parameters, even when the training is complete. As a result, the similarity between the representations of the same odorant decays exponentially over time, as observed in the experiments. We also show that the representation of a stimulus which is presented more often than others drifts at a slower rate, similarly to the experimental observations. We further explore mechanisms underlying the stimulus-dependent drift in the model and relate them to the experimental findings.

Thu-P1-025

Decoding odour source location in realistic plumes from spatiotemporal concentration dynamics

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In natural environments, odours are dispersed through turbulent processes. The resulting spatiotemporal concentration fluctuations provide odour localisation cues [1]. But plume dynamics also differ according to their proximity to the ground, as illustrated by recent recordings of odour plumes released in free-stream (mid-air) and near-bed (ground-based) configurations in a wind tunnel [2]. We applied bout analysis to these plume recordings, a bio-inspired, event-based approach to process sensory information. A bout is defined as an event of rising gas concentration. Bout counts were previously shown to predict odour source proximity in a concentration invariant manner [1]. We found marked differences in the distribution of bout features for free-stream and near-bed release configurations. Bout counts decreased more rapidly in free-stream downwind from the source. Bout amplitudes decreased over distance for both plumes, with greater amplitudes and variation in the near-bed condition. Bout durations were, on average, greater in the free-stream than near-bed, but unaffected by source distance. For both configurations, the length and variance of inter-bout intervals (IBIs) increased downwind, with the free-stream showing a greater increase with distance. Crosswind from the plume midline counts decreased for both conditions, but variance increased, and bout durations were longer and sparser with longer IBIs. Our results indicate that temporal features of odour concentration not only encode source proximity but also the release configuration close to the ground or in mid-air. Further research should explore the utility of these cues in practical navigation settings.

References

[1] Schmuker et al. (2016) Sens Act B Chem, https://doi.org/10.1016/j.snb.2016.05.098

[2] Connor et al. (2018) Exp Fluids, https://doi.org/10.1007/s00348-018-2591-3

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Thu-P1-026

The effect of situational anxiety on olfactory perception using event-related potentials: preliminary results.

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Study Objectives:

Anxiety can influence cognitive or sensory tasks. However, few studies have examined the influence of situational anxiety on olfaction, and none have used olfactory event-related potentials to measure olfactory functioning. It has been proposed that the olfactory component P3, a latent component reflecting conscious perception, may be an indicator of emotional engagement following olfactory stimulation. This research attempts to elucidate whether there is an association between situational anxiety and the amplitude and latency of the P3 olfactory component.

Experimental Methods:

In this study, 14 healthy participants aged 18 to 35 years old, completed a validated questionnaire to measure situational anxiety (STAI) and their brain activity was recorded during 40 olfactory stimulations of rose delivered by a Burghart OL023 olfactometer (used to control airflow, humidity and temperature). The latency and amplitude of the P3

were measured for each participant. Correlations were then made between latencies and amplitudes and situational anxiety scores.
Preliminary Results:
Our preliminary results, on our sample of 14 participants (6 males) with a mean age of 25 years (SD=3), show a negative correlational trend between P3 amplitudes in Fz and situational anxiety scores (r_s = -0.417, p = 0.14), and a positive correlational trend between P3 latencies in Cz and situational anxiety scores (r_s = -0.463, p = 0.10). With the final sample (including 45 participants), we should reach the power necessary to exhibit a significant relation (0.05).
Conclusion:
This study is important because it provides insight into the association between anxiety and olfaction. Specifically, it suggests that situational anxiety may be an important factor to consider in olfactory evaluation, as the shape of latent components, such as the P3, may be affected in their latencies and amplitudes.

Thu-P1-027

Pheromone-induced odour learning and outstanding detection abilities in the newborn rabbit

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Perception of the wide, complex and changing odour environment requires that the olfactory system engages processing mechanisms ensuring efficient detection and discrimination of stimuli ending in specific motor actions and in adaptation. In newborn rabbits detecting and responding to the mammary pheromone (MP) emitted by the mother is crucial for survival, since the MP is a strong releaser of typical head-searching/oral grasping behaviour allowing to locate and orally grasp the maternal nipples during the daily nursing. Strikingly, the MP also functions as a natural reinforcer, i.e. as an unconditioned stimulus able to promote appetitive conditioning to a new odorant (CS) in a single and very brief (5 min) association. We have already shown that such MP-induced odour learning, which involves peripheral plasticity (induction) and cerebral plasticity, results in an increase in detection threshold of the CS. These results were obtained when the CS was used at a single concentration (10-5 g/ml). Here, we investigated whether and how the use of a CS (ethyl isobutyrate) at different concentrations (from 10-5 to 10-23 g/ml) during pairing with the MP, influences post-conditioning detection threshold of the CS. The results highlight that the lower the CS concentration, the lower the detection threshold. However, below a certain concentration level, the response range no longer includes the highest CS concentrations but shifts and focuses around the conditioning concentration. These results are original both because they pinpoint 1) detection capability of a learned odorant at exceptionally low concentrations, and 2) that for low concentrations, the perceived quality of the CS is altered. The study provides a novel insight into olfactory perceptual sensitivity in neonates, as well as evidence of discontinuity in perceived odorant quality at very low intensity.
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Thu-P1-028

Olfactory fat perception in meats: how volatile odor composition influence olfactory discrimination of fat content in beef and pork

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Previous studies indicate that fat can be perceived by humans through olfaction, but whether such ability is still valid in meat matrix and what volatiles facilitates fat odor still remain unclear. The aims of this study were (a) to investigate olfactory fat discrimination of meat and (b) to reveal the relationship between volatile composition and olfactory discrimination ability of meat differing in fat content. Olfactory triangle tests and ranking tests were performed (n=43 participants in duplicate) to determine odor discrimination between samples (raw and grilled meat differing in three fat levels) and ranking capability based on perceived fat content. HS-SPME-GC-MS analysis was performed to profile the volatile odor composition of the headspace of all meats. PLSR and PLS-DA were performed among sensory and chemical data to explore the relationship between fat odor perception and volatile compounds. The results showed

that most beef and pork meats differing in fat content can be discriminated through olfaction. Only raw beef with the lowest fat content, and grilled beef and pork with the highest fat content were correctly ranked for their fat content based on smell, suggesting that odor differences between meat samples were not always perceived as differences in fat content. The result of volatile compound composition profiling revealed octane, 2-octene, and acetic acid were related to odor discriminability between grilled beef samples. We conclude that differences in fat content in beef and pork can be distinguished through olfaction, but such odor differences are not always perceived as differences in fat content. Different volatile compositions contribute to olfactory discrimination of meat differing in fat content.
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Thu-P1-029

Differentiation of food liking and wanting using olfactory and visual cues

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Hedonic stimulus properties significantly influence food reward processing. The underlying mechanisms remain poorly understood, warranting precise delineation of the contributing processes. This is complicated by the fact that consummatory and anticipatory perceptual reward properties of food stimuli (pleasant and appetizing) are correlated in real world settings, processed in parallel, and across several sensory modalities. In this study, we test whether consummatory and anticipatory hedonic processing of visual and olfactory stimuli can be separated by comparing food stimuli (pleasant, appetizing), to non-food (pleasant, unappetizing), and disgusting (unpleasant, unappetizing) stimuli. In two separate experiments, participants rated content-matched sets of 28 odors (N=37) and 50 pictures (N=42) for consummatory reward properties and appetitive food reward value. Our results indicate that participants differentiate clearly between the anticipatory appetitive value and the consummatory reward value for both odors and pictures ($p<.001$). Hedonic properties were higher for visual than olfactory stimuli in the food category, but lower in the non-food category ($p=.004$), suggesting a higher risk for odor misidentification compared to pictures. The same is true for the consummatory part of the disgusting category ($p=.013$), indicating a need for stimulus matching in multisensory batteries. Our data demonstrate reliable separation of consummatory and anticipatory evaluation by category for both the olfactory and visual domain. Stimulus sets that vary these factors independently may provide novel insight into food reward processing, such as their integration with gastrointestinal feedback and their independent roles underlying disturbed processing of food reward in individuals with eating disorders.
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Thu-P1-030

Distraction effects on chemosensory perception in lean and obese volunteers

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Within this project, we explored the neurocognitive mechanism of distracted eating. Olfactory and gustatory performance under different levels of distraction was systematically compared between lean and overweight participants. Odors and tastes were delivered using constant-flow olfactometry and a modular pump gustometer. An ecologically valid paradigm, a Tetris game utilizing two difficulty levels (low vs. high) was used as distraction task. We observed that overweight participants rated intensity of taste and flavor stimuli as significantly diminished compared to lean participants within the high distraction condition. Thus, we assume changes on behavioral level induced by distraction are orchestrated by neural alternations that might be a unique biological marker of obesity. Noteworthy, the hedonic properties of gustatory stimuli were also significantly influenced by distraction. Both lean and

obese participants perceived the stimuli as significantly less pleasant within high-distraction compared to low-distraction condition.
Moreover, lean participants also perceived pleasantness of different food-associated odors as significantly decreased within the condition of high compared to low distraction. Contrary to our assumptions, the intensity perception of olfactory stimuli was not affected by distraction.
Within our sample, the overweight participants perceived intensity of olfactory and gustatory stimuli as significantly higher in comparison to the lean participants. This supports the assumption that overweight participants have higher sensitivity towards food-related chemosensory stimuli.
In conclusion, our findings suggest that the neurocognitive mechanism of distracted eating is different in effect and structure between the lean and obese populations and distracted eating is a contributing factor to obesity.

Thu-P1-031

ChemOddity : machine learning to predict odorant detection threshold

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Electronic noses mimic the sense of smell using a combination of molecular sensors. These sensors have selective affinities for compounds. In order to approximate the human sense of smell, the affinity of these sensors must be close to the detection threshold of the molecules. However, only a subset of the detection threshold is available in the scientific literature.
Here, we propose a machine learning model that aims to determine the odour detection threshold (ODT) for any molecules. A database of more than 3500 compounds has been gathered to train and evaluate a predictive model. We assessed several combinations of models' architecture (Random Forest, k-Nearest Neighbors, Support Vector Machine, Graph Neural Network, Ensemble models) and molecular descriptors (3D molecular descriptors, fingerprints, molecular graphs). We selected the Ensemble regressor, after optimizing parameters for each combination, whose performances are RMSE= 1.14, MAE=0.8 log (ODT) and an R^2 of 0.61. Our model predicts detection limits ranging from parts-per-million concentration (ppm) to parts-per-trillion (ppt). This allows us to custom design a series of chemicals to calibrate the e-nose according to specific needs. The predictive model and the entirety of the data will be available.

Thu-P1-032

How cross-modal touch-smell congruence can impact emotional responses to cosmetic product?

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The phenomenon of cross-modal association between sensory modalities can influence the perception of our environment. In cosmetic, smell and touch are intuitively the two most important senses involved in product perception and cross-modal associations between these two modalities have been explored. Thanks to our study, we have demonstrated that specific texture-fragrance associations lead to more or less congruent cross-modal pairing product. We want now to explore whether these different products can produce different emotional responses. We created combinations with 6 fragrances (floral, fruity, citrus, green, spicy and oriental) and 4 textures (cream, gel, oil and balm) to form so-called congruent or incongruent paring. While self-report is an easy and rapid measure of emotions, we also measured psychophysiological reactions as they can provide implicit or more objective responses of participants' emotional experience. We try to answer the following question: How physiological and behavioral measurements allow us to get emotional information about cross-modal odor and texture perception? To do so, we recorded verbal responses; heart rate (HR), breathing rate (BR), skin conductance (SC) and facial expressions (FACS) of 29 participants during the evaluation of cosmetic fragrance-texture combinations at the laboratory. Our preliminary results have shown that smell-touch cross-modal interactions remain complex and that the relevance of psychophysiological parameters is dependent on the texture/fragrance pairing. Experimental evaluation at the laboratory can be far from the reality of cosmetic use and may bias verbal and/or behavioral responses. Thus, extend more ecologicaly the study with home product use phase and establishing the relationship between verbal and psychophysiological responses can be useful to better understand emotional user.

Thu-P1-033

Decoding the bimodal perception of odor mixtures.

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Previous studies of this group examined the masking effect of eucalyptol when in a mixture with ammonia both on a behavioral, physiological and neural network level. We were able to find that eucalyptol can mask the olfactory, but not the trigeminal sensation of ammonia. Furthermore, behavioral data showed that only half the participants perceived the odor mixture as pleasant, which is a precondition for malodor coverage. The other half perceived the odor mixture as unpleasant, which was also apparent on a neuronal level, where these participants showed activation in the anterior insula and SII, indicating an attentional shift towards the unpleasant ammonia odor. While examining the signal intensity in other brain regions involved in odor processing, namely piriform cortex, anterior midcingulate gyrus, inferior frontal gyrus and anterior insula, we found both an expected peak at approximately 8 sec after stimulus presentation as well as an unexpected second peak at around 26 sec after stimulus presentation. Our ongoing analysis of this phenomenon concentrates on multiple aspects: First, we suspect a correlation with respiratory data, therefore we are currently using multiple regression approaches to examine the effect of respiration on the neurological correlates. Second, a delayed trigeminal sensation could be the reason. It is possible that the task to rate the pleasantness of the stimulus causes this delayed response, potentially by triggering an unconscious deep inhalation and therefore a repeated perception of the stimulus. Third, we aim to apply multi-voxel pattern analysis with which activation patterns can be used to better differentiate the initial stimulus. These analyses will be accompanied by a behavioral study examining the effect of the pleasantness rating and a deeper inhalation on odor intensity perception. We will here discuss several options for the explanation of the delayed neural network response to olfactory-trigeminal stimulation.

Thu-P1-034

Effects of smell training on short-term olfactory memory in children – preliminary results

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The olfactory system is highly plastic and susceptible to training. Systematic exposure to odors has been reported to increase olfactory receptor expression levels in rodents, as well as enhance behavioral response to odors, alter brain structure and neural processing of odors in humans. Due to an interplay between olfaction and cognitive functions several studies verified if olfactory training (OT) effects may reach beyond olfaction. However, most of the available data has been collected from adult and elderly populations. Here we present preliminary results of a study aiming to verify if OT in early-school children (n=29, aged 7-9 years, 14 females) would increase their short-term olfactory memory. Participants in the OT group received sets of four odors (rose, lemon, eucalyptol, cloves) and were asked to smell them twice a day for twelve consecutive weeks. Control group performed the same training procedure with odorless training sets. To measure short-term olfactory memory we prepared a game called “Smellory”. The came consists of a set of six pairs of odors, all stored in brown glass jars in odorant-soaked cotton balls. Participants’ task was to select two jars from the set, compare their content and decide if the odors are matching. The task has been repeated until all six pairs have been found. Two equivalent sets were performed and distributed randomly before and after OT to rule out a possible learning effect. Our analyses revealed that the number of trials needed to complete the task was lower after OT (M=23.82±4.55) as compared with the baseline score (M=26.73±2.25). Contrary, in the control group the number of tries required to finish the task increased between baseline (M=24.22±1.76) and post-intervention measurement (M=30.06±3.56). These results suggest that systematic exposure to odors may enhance higher olfactory functions like olfactory memory.

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Thu-P1-035

Olfactory training enhances emotion recognition in primary-school children – preliminary results

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Olfaction is associated with emotional functioning. Decreased olfactory performance has been found in patients who suffer from emotional disorders such as depression and conversely, people with anosmia more often report depressive symptoms. Most of the evidence linking olfaction and emotional functioning comes from the adult population, whereas it appears extremely interesting, whether enhanced olfactory performance may relate to the improvement of emotional processing in young children who rapidly develop emotional skills. This poster presents the results of a preliminary study on the effects of olfactory training on emotion recognition in healthy children. A total of 70 children participated in our study, of whom 45 performed a 12-week olfactory training twice a day using Sniffin Sticks with four scents: lemon, rose, eucalyptus, and clove. The children in the control group (n = 25) performed the same training regimen but used odorless Sniffin Sticks. Emotion recognition was assessed using Emotion Matching Test (EMT). After excluding participants who did not complete at least 50% of the training and those with hyposmia, the groups included in the analyses consisted of 33 children (66% girls; M_{age} = 7.30 ± 0.51 years) in the experimental group and 24 children (49% girls; M_{age} = 7.96 ± 0.75 years) in the control group. We analyzed whether olfactory training improved emotion recognition in children using a general linear model. We found that emotion recognition improved in the experimental group but not in the control group. These results suggest regular olfactory training can be used as a safe, accessible, and inexpensive method of enhancing emotional processing in primary-school children. This work was supported by National Science Centre in Poland (#2020/37/B/HS6/00288 awarded to AO).

Thu-P1-036

Adaptive plasticity in specialists and generalists

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Rise in global temperature and gaseous pollutants disturb the ecological interactions and the insect biodiversity. A recent study from our lab showed that levels of ozone found in rural areas disrupt the innate attraction of the tobacco hawkmoth Manduca sexta to the odour of one of its preferred flowers (Cook et al. 2020). However, this study showed that moths are able to learn ozone-altered floral odours through reward learning. Therefore, we speculate that insects such as Drosophilids might also possess similar ability in coping with modified odours through anthropogenic pollutants. We therefore investigate the effect of ozonated odours on the behaviour of “generalists” (Drosophilids that live in a wide ecological niche) and “specialists” (Drosophilids that live in a particular place). We hypothesize that “generalists” could adapt better than “specialists” in an increasingly polluted atmosphere. For instance, D.sechellia, a specialist Drosophilid, has adapted peripheral receptors and neural circuits in the brain allowing the insect to feed on noni fruit which other drosophilids strongly repel. These specialized changes which are beneficial to thrive in a specific niche might be the cause for specialists like D.sechellia to be less adaptive to increasing levels of pollutants in the environment. The objective of the project is to study the adaptations and plasticity of various drosophilids in response to pollutants. Through behavioral experiments, we found that D.melanogaster flies upon ozonation exhibit a decreased response to attractive odours and an increased aversion to aversive odors. Further functional imaging and electrophysiological experiments will reveal the neuronal mechanism behind the observed modified odour perception in ozonated flies at a functional and behavioral level. Furthermore, we aim to analyze the learning abilities of the different drosphilids to adapt to modified food odors.

Thu-P1-037

Analysis of fMRI data related to olfactory stimulation

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Functional MRI (fMRI) is frequently used for measurement of neural activity of living human brain. Block design experiment in fMRI is basic and frequently used. In this design, some stimulation or psychological task is presented to participants (stim condition) and no stimulation is presented (rest condition) are repeated. In analyzing, we shall make assumptions that blood flow will increase in stim condition and turn to normal state in rest condition in some brain areas related to this stimulation or task. On the other hand, numerous studies related to neural activities related to olfactory function on human have reported, and neural anatomical areas related to olfactory function were sometimes not consistent among studies. We, therefore, hypothesized that the cause of this variation may be due to the different temporal patterns of blood flow of brain activity among olfactory-related neural regions.

We performed simple block design experiment with presentation of olfactory stimulation. A pair of twenty seconds stim condition and same duration rest one was repeated thirty times, using 3T MRI scanner. Time of repetition was 2 seconds. In analysis, we put several conditions (hemodynamics models), about duration or slices of activation and latency from stimulus onsets, and shall present results.

Thu-P1-038

Context-dependent prioritization of odor representations by top-down inputs

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Specific combinations of volatile chemicals are detected by the nose and are interpreted by the brain as signatures for the presence of relevant objects. In natural environments, chemicals from many objects mix in the air prior to reaching the nose, making the task of identifying the underlying objects much more difficult. In such rich environments, mechanisms of attention are used by sensory systems to prioritize perception of specific objects over others. These mechanisms are believed to rely on feedback connectivity from central to peripheral sensory brain regions. Such feedback connectivity is abundant in the olfactory system, but how it serves to prioritize odors is currently unknown. We built a biologically-realistic model of the olfactory bulb and piriform cortex to study the mechanisms of odor-specific attention. The model captures key properties of feedforward and feedback circuitry and takes into account the nonlinear interactions between odorants at the olfactory epithelium. A contextual input that defines the target odor is fed into piriform cortex. This input modifies basal activity within piriform cortex. Via feedback piriform modifies olfactory bulb dynamics. We modelled naturalistic mixtures to test the effectiveness of different mappings of feedback connectivity and show that a mapping in which cortical neurons avoid innervating glomeruli they receive inputs from, but otherwise project randomly to the olfactory bulb, is efficient in prioritizing the target odor. Moreover, we demonstrate that the modified input impacts each neuron in olfactory cortex almost insignificantly, while the ensemble representation of a prioritized odor increased dramatically. Our model explains the relationship between feedback projections and attention, provides predictions for feedback connectivity, and demonstrates the unique contribution of collective dynamics for supporting behavioral functions.

Thu-P1-039

Lateral axo-axonal neuromodulation is required for stimulus-specific aversive olfactory conditioning in Drosophila

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Stimulus-specific associative learning, which is essential for animals' survival, is aided by temporal correlation between sensory and reinforcing signals and accurate neuronal sensory representations. However, reinforcing signals alone

could induce neuromodulation without coincident sensory-evoked neuronal activity, thereby generating unspecific associations. Here, we use two-photon in vivo functional imaging, along with pharmacological and optogenetics manipulations, and behavior experiments to report a crucial neuromodulatory mechanism that prevents unspecific association by counteracting the signals evoked by sensory and reinforcing cues. In Drosophila, olfactory signals are sparsely represented by cholinergic Kenyon cells (KCs), which receive dopaminergic reinforcing input. We find that KCs have numerous axo-axonic connections, mediated by the muscarinic type-B receptor (mAChR-B), which suppress both odor-evoked calcium responses and dopamine-evoked cAMP signals in neighboring KCs. Strikingly, mAChR-B knockdown impairs olfactory learning by inducing undesired changes to the valence of an odor that was not associated with reinforcer. Thus, this local neuromodulation acts in concert with sparse sensory representations and global dopaminergic modulation to achieve effective and accurate memory formation.

Thu-P1-040

Transient inhibition of olfactory output shortly after birth leads to limbic dysfunction and cognitive impairment in pre-juvenile mice

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Objectives: Cognitive processing requires directed interactions between several brain areas of the limbic system, such as hippocampus (HP) and lateral entorhinal cortex (LEC). They are modulated by multiple sensory systems. During development, the olfactory system might have a particular impact on these areas in mice that at birth are blind, deaf, do not whisker and have poor motor abilities. We previously showed that neonatal olfactory activation boosts the oscillatory entrainment of LEC via mono-and polysynaptic projections from in the olfactory bulb (OB). However, the long-lasting impact of olfactory inputs on the limbic function and cognitive abilities of later life is fully unknown.
Methods: We chemogenetically decreased the synaptic outputs of mitral/tufted cells (M/TCs), the main projecting neurons in the OB, during postnatal days 8-10 and monitored the long-lasting consequences on the downstream areas LEC and HP, and on cognitive performance.
Results: In vivo extracellular recordings revealed that after the transient decrease of the olfactory output, the oscillatory activities of downstream areas were diminished along development, in line with the long-lasting decrease in the dendritic complexity of HP-projecting pyramidal neurons in LEC. Correspondingly, pre-juvenile mice experiencing the early life manipulation had declined performance in cognitive tasks.
Conclusions: These results indicate that the early olfactory processing before eye-opening might be critical for the functional development of cognitive abilities.

Thu-P1-041

Synaptic properties support a high-level role for the nucleus of the lateral olfactory tract in odor processing.

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Odor information is processed by several olfactory cortical regions, all receiving direct input from the olfactory bulb. While much attention has been focused on some of these, others remain largely unexplored. The nucleus of the lateral olfactory tract (nLot) is one such brain region that has been very little studied and the function it serves in olfactory processing is unknown. It is located at the rostral end of the lateral olfactory tract, medially to piriform cortex, and has a 3 layered organization. The nLot contains about 5000 pyramidal neurons in the mouse and anatomical studies show that it is interconnected with several olfactory brain regions. The physiological properties of nLot neurons and its synaptic organization are currently completely unknown and revealing them may shed light on potential functions it serves.
We analyzed the biophysical properties of nLot pyramidal neurons, and the properties of various synaptic inputs onto them. We show that nLot neurons are bursters and that this burstiness stems from voltage activated calcium channels that are activated below the threshold for somatic action potentials. Olfactory bulb inputs make synaptic connections with distal dendrites of layer 2 nLot neurons and these manifest at the soma as very small EPSCs that do not reach

threshold for action potential generation. Occasionally, activation of the mitral and tufted cell axons elicited dendritic regenerative responses that were able to evoke somatic action potentials. Associative inputs into nLot terminate within layer 2 and their activation evokes much larger EPSCs that can reach threshold without requiring dendritic spikes. The increased responsivity to associative inputs compared to olfactory bulb inputs, indicates that the nLot is a high-level node in the olfactory circuit.

Thu-P1-042

Prediction error coding underlying adaptive olfactory behavior in Drosophila melanogaster.

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Insects are ideally suited for studying fundamental mechanisms of nervous system function. Here, we propose a basic circuit mechanism in the insect mushroom body (MB) that establishes prediction error coding through the integration of present and expected reinforcement. It employs a circuit motif with feed-forward and plastic converging connections from the Kenyon cell (KC) population to a MB output neuron (MBON) and feedback from the MBON to a dopaminergic neuron (DAN) via an inhibitory interneuron. This motif has been described in the connectome of adult [1] and larval [2]fruit fly.

In a systems level model approach to sensory-motor transformation we integrate olfactory processing in the antennal lobe, sparse stimulus representation in the KC population, prediction error coding in the KC-MBON-DAN motif, presynaptic plasticity in the KC-MBON synapse and postsynaptic homeostasis in the MBON. This model accounts for the experimentally observed features of acquisition and extinction of associative memories during appetitive and aversive learning in dependence on the magnitudes of odor and reinforcer as well as on the relative timing between sensory and reinforcing stimuli. To allow for the comparison of our simulation results with behavioral data we model learning induced plasticity over the full time course of behavioral experiments, both in the adult [3] and larva (unpublished). In the larva we entail a detailed locomotory model [4] allowing us to simulate artificial agents in virtual experiments.

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[1] Eichler et al. (2017) Nature, doi.org/10.1038/nature23455

[2] Eschbach et al. (2020) Nat Neurosci, doi.org/10.1038/s41593-020-0607-9

[3] Springer M, Nawrot MP (2021) eNeuro 8(3), doi.org/10.1523/ENEURO.0549-20.2021

[4] Sakagiannis P, Jürgensen AM, Nawrot MP (2021) bioRxiv, doi.org/10.1101/2021.07.07.451470

Thu-P1-043

Modulation of innate behaviour by learning.

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Drosophila has been used as model organisms to understand the neural basis of sensory behaviour, both innate and learned behaviour. Learning can modulate innate behaviours of animals ensuring flexible and appropriate behavioural responses to changing environmental . We are using larval chemotaxis to understand how innate behaviour is modified by learning and memory.

It has been proposed that a group of neurons in the Drosophila larvae integrates stimuli from innate and learning/memory circuits associated with olfaction. Previous studies have shown the role of group of neurons called Odd neurons in larval innate chemotaxis behaviour. They are situated downstream of the fly olfactory learning and memory centre, the Mushroom Body (MB), and the projection neurons (PNs), which respond directly to odour and as such represent innate sensory input. In this study, we have identified using Trans-Tango method that the Odd neurons receive inputs from the MB neurons depicting their role in learning and memory. We have also identified a role of the Odd neurons in larval odour associated appetitive learning behaviour. Inactivation of Odd neurons inhibit learning and memory in larvae. Temporal inactivation experiments suggests that Odd neurons are required during memory retrieval

and not in memory formation suggesting that Odd neurons could integrate olfactory memory with innate olfactory input. We are now investigating how the Odd neurons process both innate and learned stimuli for appropriate behavioural output.
This work would help in understanding the neural mechanisms by which learning and memory modulate different aspects of behaviour.

Thu-P1-044

Rapid odor processing by layer 2 subcircuits in lateral entorhinal cortex

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Olfactory information is encoded in lateral entorhinal cortex (LEC) by two classes of layer 2 (L2) principal neurons: fan and pyramidal cells. However, the functional properties of L2 cells and how they contribute to odor coding are unclear. Here, we show in awake mice that L2 cells respond to odors early during single sniffs and that LEC is essential for rapid discrimination of both odor identity and intensity. Population analyses of L2 ensembles reveals that rate coding distinguishes odor identity, but firing rates are only weakly concentration-dependent and changes in spike timing can represent odor intensity. L2 principal cells differ in afferent olfactory input and connectivity with inhibitory circuits and the relative timing of pyramidal and fan cell spikes provides a temporal code for odor intensity. Downstream, intensity is encoded purely by spike timing in hippocampal CA1. Together, these results reveal the unique processing of odor information by LEC subcircuits and highlight the importance of temporal coding in higher olfactory areas.

Thu-P1-045

Strikingly different neurotransmitter release strategies amongst interneuron subtypes of the olfactory bulb

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Neurons establish morphological polarity by specifying two different compartments: the axon and the somatodendritic domain. This polarity is also functional, because in most neurons dendrites receive the majority of inputs while axons generate output signals via neurotransmitter release. However, many exceptions to this dogma occur in the olfactory bulb (OB), where most GABAergic interneurons are anaxonic and can only release neurotransmitters from their dendrites. OB glutamatergic cells, however, have classic morphological polarity but release neurotransmitters from both axonal and somatodendritic domains. Dendritic release is, therefore, a common feature of OB neurons.
A subset of GABAergic interneurons in the OB also release dopamine. These dopaminergic (DA) cells comprise two groups – axonic and anaxonic – depending on the presence or absence of an axon. Here, we provide structural and functional evidence showing that, unlike their anaxonic counterparts, axon-bearing DA neurons rarely if ever release GABA from their dendrites. We injected a Cre-dependent AAV in embryonic VGAT-Cre mice to obtain sparse cell morphology (GFP) plus structural evidence for putative neurotransmitter release sites (synaptophysin-mRuby), finding dendritic mRuby puncta almost exclusively in anaxonic cells. We then obtained electrophysiological recordings in acute slices from DAT-tdT mice, using an auto-evoked inhibition (AEI) protocol to detect dendritic GABA release. All anaxonic neurons displayed an AEI response, while almost all axonic DA cells did not. Our results suggest that axon-bearing DA neurons are the only OB cell type to not effect dendritic neurotransmitter release, placing a key spatial constraint on their ability to shape olfactory sensory processing.

Thu-P1-046

Generation and characterization of N-GFP-Orco Drosophila melanogaster fly line

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Insects perceive countless odors with the help of odorant receptors (ORs) expressed by olfactory sensory neurons (OSNs) located in antenna and maxillary palps. OR complexes are composed of odor specific proteins OrX and olfactory co-receptor proteins Orco, both with extracellular C-terminus and intracellular N-terminus. In this study, we generated a genetically modified Drosophila melanogaster fly line that expresses green fluorescent protein (GFP) at the Orco N-terminus (UAS-N-GFP-ORCO) in Orco null mutant background (Orco1) using GAL4-UAS system. We first obtained four phenotypes for which we performed cryosectioning and immunolabeling in the antenna. In preliminary observations, we see that these fly lines have differences in OR expression patterns. Therefore we investigate the differences in fluorescence intensities from stomata and outer dendrites from the antennal cross sections. We also tested the olfactory capability of these flies using single sensillum recording (SSR). We could show that olfaction was not impaired by GFP insertion. As Orco guides OR trafficking to the OSN dendrites, we check whether insertion of GFP at the Orco N-terminus affects the trafficking. Further we want to use this transgenic fly line to resolve the structure of OR complexes using Cryo electron microscopy (cryo-EM).

Thu-P1-047

Transcriptional adaptation of olfactory sensory neurons to GPCR identity and activity

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In mammals, chemoperception relies on a diverse set of neuronal sensors able to detect chemicals present in the environment, and to adapt to various levels of stimulation. The contribution of endogenous and external factors to these neuronal identities remains to be determined. Taking advantage of the parallel coding lines present in the olfactory system and the improved sequencing techniques currently available, we explored the potential variations of neuronal identities before and after olfactory experience. We found that at rest, the transcriptomic profiles of mouse olfactory sensory neuron populations are already divergent, specific to the olfactory receptor they express, and are associated with the sequence of these latter. These divergent profiles further evolve in response to the environment, as odorant exposure leads to reprogramming via the modulation of transcription. These findings highlight a broad range of sensory neuron identities that are present at rest and that adapt to the experience of the individual, thus adding to the complexity and flexibility of sensory coding.

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Thu-P1-048

Norepinephrine enhances spiking discharge in vomeronasal sensory neurons through voltage-gated sodium channels modulation

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Norepinephrine (NE) is the neurotransmitter of the sympathetic branch of the autonomous nervous system in charge of fight and flight responses at physiological and behavioral level. NE-receptors are expressed in different organs of the body including many brain regions and peripheral nervous system. Olfactory sensory neurons (OSNs) express NE-receptors, and NE application to OSNs modulates action potential firing. Vomeronasal organ (VNO) makes part of the mouse accessory olfactory system and its main function is to detect pheromones and regulate social behaviors of the animal. While the effect of NE on the OSN has been studied, the effect of NE on the accessory olfactory systems remains unknow. Here we investigated whether NE directly affects the electrical properties of mouse vomeronasal sensory neurons (VSN) from acute slices, using the patch clamp technique in whole cell mode. We found that in VSNs ($n = 10$; $*p < 0.05$, t-test), NE (50 µM) application increases spiking frequency in response to current injection steps. To

explain this effect on VNO neurons, one the candidates is the AP machinery, that's because the experiments were performed in absence of transduction cascade activation, underlying an independent mechanism, which is downstream of it. To test the current involved in the AP, were used voltage clamp recording, the first candidate is the voltage-activated sodium channels, we isolate sodium current using an internal solution contained 140 mM CsCl a typical impermeable cation by voltage-activated potassium channels and the application in the extracellular bath of 100 µM of CdCl2 to block calcium conductance, we found that NE modulates voltage-activated sodium channel activation in VSNs shifting the activation curve to negative potentials (8.65 mV ± 2.3 mV ,n=6-9 ,**p<0.01).

Thu-P1-049

Electro-olfactogram analysis of odor responses from wild-type and knock-out mice for TMEM16B

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The sense of smell in animals can strongly influence feeding and social behaviors. In order to accomplish these tasks, all the events starting from the detection of odorants by olfactory sensory neurons (OSNs) in the olfactory epithelium (OE) must be properly tuned in terms of amplitude and kinetics. After the odorant binding to its receptor, a series of events leads to the activation of adenylyl cyclase III that produces cAMP that in turn opens the cyclic nucleotide-gated channels causing a first depolarizing current mediated by Na^+ and Ca^{2+} entry. In addition, the increase of the intracellular Ca^{2+} concentration activates the TMEM16B channel providing a further amplification of the odorant response. Since its relatively recent characterization in the OE, the contribution of TMEM16B to the amplitude and kinetics of the odor transduction process is still puzzling. We investigated the role of TMEM16B in odorant-induced responses using electro-olfactograms, that record the summated generator potential of the OSN population. Surprisingly, we found that the odorant responses were bigger in Tmem16b knock-out (KO) than in wild-type (WT) mice. In addition, the lack of TMEM16B altered the kinetics of the response that had a faster rising phase and shorter recovery time in the KO. To investigate response adaptation we used a double pulse protocol with different inter-pulse intervals and found that the recovery from adaptation at high odorant concentration was faster in KO than in WT mice. In another adaptation paradigm we applied an odorant conditioning stimulation followed by test pulses with different odorant concentrations. We found that the amplitude of the responses to the test stimulations was significantly smaller in WT whereas no significant difference was found in KO mice showing that TMEM16B plays an important role in the molecular mechanisms that mediate OSNs adaptation.

This work was funded by the Italian Ministry of Education, University and Research.

Thu-P1-050

Aquaporin-4 water channel as a new modulator of neuronal activity in the olfactory system

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Aquaporin-4 (AQP4) is a water-selective transport protein expressed in glial cells throughout the nervous system. The protein is the main water channel in the neuropil, and it has different isoforms that play several physiological roles ranging from astrocyte volume regulation to neuronal activity modulation. AQP4 isoforms are expressed in the supporting cells of the olfactory epithelium (OE) and astrocytes of the olfactory bulb (OB). Interestingly, a mouse lacking all APQ4 isoforms has been shown to have olfactory deficits. Hence, we wondered whether we could dissect the physiological role of two AQP4 isoforms, namely AQP4M23 and AQP4ex, in the olfactory system. We performed electro-olfactogram recordings founding that odorant responses are reduced in mice lacking the isoforms AQP4ex or AQP4M23 compared to wild type, indicating that they are involved in odorant detection. Both isoforms are also expressed in the OB. By analyzing the expression of the immediate early gene c-Fos, we evaluated the neuronal activity in the glomerular layer in response to a novel environmental odorant stimulus such as amyl acetate and compared it with a neutral, odorless stimulus. We found a decrease in the number of c-Fos positive cells in AQP4M23-KO compared to wild type only after the exposure to the neutral stimulus, suggesting that the astrocytic expression of AQP4M23

contributes to setting the basal levels of neuronal activation in the glomerular layer.
Altogether, these results establish that AQP4 isoforms have a critical role in odorant-evoked responses acting via a glial-like cell type: the supporting cells of the OE. Moreover, AQP4M23 could be involved in modulating neuronal activity in the OB, providing a foundation for future work investigating the precise physiological function of the water channel in the olfactory system.

Thu-P1-051

Computational prediction of the odorant receptor OR5K1 binding site structure and its interactions with pyrazine-based agonists

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The odorant receptor OR5K1 was recently and comprehensively characterized in terms of cognate agonists.[1] Despite the recent advancements in structural biology, no experimental structures of human odorant receptors are available. We computationally investigated the binding modes of OR5K1 ligands into the orthosteric binding site using structural information both from AI-driven modeling, as recently released in the AlphaFold Protein Structure Database, and from template-based modeling. Our work provides a comparison of different computational techniques for modeling odorant receptors and a model refinement protocol that succeeded to rationalize the different activity values of known OR5K1 agonists.[2] Moreover, by integrating modeling analyses with functional and mutagenesis experiments, we could characterize the binding site for alkylpyrazines in OR5K1, and identify residues that are necessary for receptor activation.

(1) Marcinek et al. An evolutionary conserved olfactory receptor for foodborne and semiochemical alkylpyrazines. FASEB J 2021, 35 (6), e21638.
(2) Nicoli et al. Modeling the Orthosteric Binding Site of the G Protein-Coupled Odorant Receptor OR5K1. bioRxiv 2022.06.01.494157; doi: 10.1101/2022.06.01.494157

Thu-P1-052

Dissecting odor mixture interactions in the fly brain

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In the natural environment, odors are often blends of many compounds at different concentrations. A question arises then, how does the olfactory system encode different mixtures of odors? The vinegar fly represents hereby a premier model system to study olfactory processing and mixture coding since the olfactory circuitry exhibits a stereotyped architecture which is similar to its mammalian counterpart, but which is less complex and highly tractable as well as susceptible to genetic manipulations. In a previous paper, we demonstrated that mixtures of odors having opposing hedonic valances valences (at certain ratios) are encoded and processed by a mixture-specific activation of projection neurons, the output neurons of the fly antennal lobe (Mohamed et al., 2019). This mixture code is maintained through lateral inhibition in an anisotropic manner initiated between glomeruli encoding opposing odor valences. We found that the activity of patchy and sparse local interneurons mediate this specific form of mixture inhibition. The goal of this project is to study the calcium dynamics of these patchy local interneurons in response to diverse odor mixtures, at the level of their pre- and post-synaptic activitiessites. We will investigate both the population dynamics, as well as activities at the single neuron level using two-photon functional imaging of the fly antennal lobe using SPARC.
This work is supported by the DFG as a part of SPP 2205: Evolutionary Optimisation of Neuronal Processing project

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Thu-P1-053

The order code in the olfactory bulb: can odorants be represented by the temporal order of glomerular activation?

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The representation of odor identity (ID) in the responses of olfactory neurons is not fully understood. Here, we test the hypothesis that odor ID is carried by the temporal order of activation of olfactory receptor (ORs) types. The order of OR activation is approximately preserved for different concentrations suggesting that it can carry information about the concentration-invariant odor ID. To test this hypothesis, we obtained glomerular calcium responses from the dorsal surface of the olfactory bulb to a large array of odorants, including mixtures, in multiple animals. Using this data, we computed the temporal order of glomerular activations. We proposed a neuronal distance metric in the odorant space based on rank correlation (Kendall-tau). We also measured perceptual distances in mice for the same set of odorants. We made the following observations. We find that the order-based odorant ID representations are similar across different concentrations of the same odorant. Odor IDs can be embedded into a low dimensional space (D~6). These embeddings can be accurately aligned between different animals. The representations of mixtures satisfy triangle inequality suggesting that the Kendall-tau based distances define a metric space. Using Canonical Correlation Analysis (CCA), we observed a strong correlation between the space on neural responses and the perceptual spaces of low dimension. Finally, we developed a method of embedding individual ORs into the odor space using the order-based measures. We showed that the glomeruli close to each other in the functional space can be found at similar locations in different animals, suggesting that they receive inputs from the same ORs. Overall, we developed and validated the metric for odorant representations based on the temporal sequence of OR activations. This metric yields robust representations of odor identity which generalize well across stimulus conditions and individual animals.

Thu-P1-054

Anatomical analysis of main and accessory olfactory bulb principal neuron projections

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The rodent olfactory system comprises at least two complementary central pathways: the main and the accessory olfactory pathway. Chemosensory signals that are detected by nasal olfactory sensory neurons are projected to the main olfactory bulb. However, many semiochemicals and other social chemosignals are detected by vomeronasal sensory neurons and relayed to the accessory olfactory bulb. As principal projection neurons, both main and accessory olfactory bulb mitral cells integrate chemosensory input and forward this information to distinct downstream target regions. Despite separate anatomical investigations of the main or accessory olfactory circuitry, parallel comparative analysis of individual projection paths using modern tracing techniques and largely intact brain samples is lacking. Here, we implemented state-of-the-art viral tracing and confocal imaging to allow for the detailed anatomical depiction of both main and accessory olfactory bulb mitral / tufted cell projections. Cre-dependent expression of adeno-associated viral genomes enabled optical tracing in transgenic mice that selectively express Cre recombinase in olfactory bulb projection neurons under the t-box protein 21 (tbx21) promoter. Three-dimensional reconstruction of olfactory bulb principal neuron projections is achieved by utilizing whole-brain slice preparations and cleared tissue samples. Altogether, this study provides detailed anatomical insight into unique and common target areas along each olfactory pathway, thus, laying a solid foundation for future investigations into parallel olfactory information processing by the main and accessory olfactory systems.

Thu-P1-055

Influence of fermented food consumption on taste and oral microbiota of rats

Maria Ibarlucea-jerez [1, 2], Magali Monnoye [3], M.C Canivenc-Lavier [1], Eric Beuvier [4], Philippe Gérard [3], Hélène Licandro [2], Eric Neyraud [1]

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Oral microbiota varies throughout the individual's life. These changes are due to several factors (environmental, physiological, lifestyle...) that shape its diversity and composition. However, little is known about the physiological impact of this persistence. Taste perception is one of the possible targeted functions. Indeed, our team has recently established relationships between oral microbiota and taste sensitivity in humans. The objective of this work was to see if fermented food bacteria were able to persist in the oral cavity and consequently influence the oral microbiota and the taste by using a rodent experimental design: two groups of rats (n=27/group) were fed for 3 weeks with experimental cheeses containing live or dead bacteria. Rat saliva was collected weekly for bacterial composition analysis (qPCR and 16S rRNA sequencing). Taste sensitivity was evaluated using the 2 bottles test method with 4 decreasing sucrose concentrations. First results, we found that 1/3 of the rats who consumed cheese with alive bacteria have these bacteria transiently in their oral cavity. However, their sucrose taste sensitivity was not significantly affected by comparing with rats without cheese bacteria persistence. This work shows that fermented food can modulate temporarily the composition of rat oral microbiota without leading to changes in the sucrose perception. However, this work needs to be reinforced by performing a longer exposure and by investigating the sensitivity to other tastes.

Thu-P1-056

Is taste linked to oral microbiota?

Hélène Licandro [1], Caroline Truntzer [2, 3], Sébastien Fromentin [4], Nicolas Pons [4], Christophe Martin [5, 6], Hervé M Blottière [4], Eric Neyraud [5]

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Taste perception varies strongly between individuals but the factors at the origin of this variability are not fully understood. For example, different events occurring at the vicinity of the taste receptors on the tongue can modulate taste perception. Our group has recently suggested that the microbiota at the surface of the tongue could be involved by controlling the taste compounds concentration in the lingual film (the biological material covering the tongue).
The aim of this work is to evaluate the contribution of the oral microbiota to taste.
To do this, taste sensitivity (5 basic tastes) was determined in 100 healthy adult subjects and the microbiota of their lingual film and saliva was characterized using quantitative metagenomics.
A total of 666 bacterial species have been identified and the large majority of the species are shared between saliva and lingual film (571) but the number of non-shared species is higher in saliva. The relationship between the bacterial profiles and taste sensitivity depends on the medium considered (saliva vs lingual film) and of the taste nature.
This work opens new perspectives on the implication of the oral microbiota on physiological functions occurring in the oral cavity.
Funding: This work was supported by grants from the French "Investissements d'Avenir" program, project ISITE-BFC (contract ANR-15-IDEX-0003) TOM and the French Institut Carnot Qualiment (project MORGoM).

Thu-P1-057

Anxiety reduces sweet and sour, awareness of anxiety enhances bitter

Naoya Zushi [1, 2], Monica Perusquia-Hernandez [3, 4], Saho Ayabe-Kanamura [5]

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Previous studies reported our perceived taste may be altered by our affective states. The aim of this study was to examine the effects of affective states introspection on taste perception. Eighty-three healthy Japanese participated in this study. All participants watched two types of 15-minute videos that evoked relaxation and anxiety. After watching each video, half of the participants were manipulated to introspect on their affective states by answering an anxiety questionnaire after viewing each video. The other half of the participants were asked to answer a personality test and introspect their personality traits. After completing each questionnaire, participants rated the intensity of sweetness, saltiness, sourness, bitterness, and liking of the taste stimulus by using Visual Analog Scale. Considering the possibility of different perceptual changes depending on the type of taste stimulus, half of the participants in each introspection group rated unsweetened coffee and the other half rated sweetened coffee as a taste stimulus. Analysis was conducted by a generalized linear mixed model with affect (relaxed/anxiety), target of introspection (affective state/personality trait), taste stimulus (unsweetened/sweetened) as fixed effects, and participant and taste stimuli as random effects. The results showed that anxiety significantly enhanced bitterness only in the group that introspected their own anxiety. In addition, we found that anxiety significantly suppressed sweetness and sourness, regardless of the presence or absence of affective states introspection. These results indicate that there are two types of effects of anxiety on taste perception, depending on the taste quality. One type of taste quality changes in perceived intensity with or without introspection, and the other type changes only with introspection. The effect of the affective state on the perception of taste quality may depend on the biological significance of the change in it.

Thu-P1-058

Prior exposure amplifies effects of hunger on subjective food value across the congruency spectrum.

Putu Agus Khorisantono, Janina Seubert

Department of Clinical Neuroscience, Division of Psychology, Karolinska Institutet

Flavour is a multisensory experience where increasing concordance between its components. For example, approximating a combination of fruity odour and a sweet taste, enhances the reported pleasantness of the percept. How these multisensory effects interact with the impact of metabolic states on reported pleasantness remains unknown, as both generalised alliesthesia and sensory-specific satiety act on the perceived pleasantness of food items. The goal of our study was to determine whether metabolic and sensory-specific effects differentially affect pleasantness ratings for multisensory flavour stimuli across the spectrum of sensory concordance. Participants completed two experimental sessions where they rated the pleasantness and object-likeness of beverages composed of taste and odor components varying in sensory concordance. Prior to each session, subjects fasted for 6 hours. In the hungry condition, they then directly performed the task, whereas in the sated condition they first consumed a meal of either chicken noodle soup or lemon meringue pie. Initial linear mixed-effect modelling showed an effect of sensory concordance on pleasantness ($\beta = 0.133$, $p < .0001$) but neither hunger state nor the taste of the food item eaten were reliable predictors of pleasantness. Post-hoc exploratory analyses showed that model fit was significantly improved by accounting for exposure effects imposed by the session order ($\beta = -0.127$, $p = .037$), which interacted with hunger state, ($\beta = 0.097$, $p = .0046$). Sensory-specific effects remained a poor predictor of pleasantness. Taken together, our results indicate an additive effect of alliesthesia and multisensory concordance on perceived pleasantness. Alliesthesia effects, however, are subject to interaction effects with prior exposure, where pleasantness enhancement through hunger is stronger after prior exposure under sated conditions.

Thu-P1-059

Consumption of a sugar-sweetened soft drink in combination with a Western-type diet alters taste markers independent of body weight development

Barbara Lieder [1], Jozef Čonka [2], Agnes Reiner [1], Victoria Zabel [1], Dominik Ameur [3], Mark Somoza [3,4], Katarína Šebeková [2], Peter Celec [2], Veronika Somoza [1,4]

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Taste dysfunction has been reported for obese individuals in mice and men, but more recent studies indicated that certain dietary stimuli also lead to taste deficits in mice without the onset of obesity. Here we investigated whether the long-term intake of a typical caffeinated sugar-sweetened soft drink (SSB) alters markers for taste function when applied in combination with a standard chow (STD) or a Western-type Diet (WD).

Adult male CD1 mice had ad libitum access to tap water or SSB in combination with either STD (n=10-12) or a WD (commercial cheeseburgers, n=7-8) for 24 weeks. Energy intake from fluid and food was monitored three times a week. Body weight and composition, waist circumference, glucose and lipid profile, and blood pressure were analyzed at the end of the intervention. The number and size of the fungiform papillae for calculation of the chemosensory surface at the tip of each tongue was examined after staining of the tongue with brilliant blue and mRNA levels of genes associated with the different cell types of taste buds and taste receptors were analyzed in the circumvallate papillae (CV) using a cDNA microarray and qPCR.

Although the overall energy intake was higher in the WD groups, there was no difference in body weight and composition, in the blood lipids, and markers for glucose intolerance between the SSB and water groups at the end of the experiment. The total chemosensory surface from the fungiform papillae was reduced after SSB compared to water intake in the WD group by 36 ± 19 % ($p<0.05$). Transcriptome analysis of the CV revealed an upregulation of marker genes for basal taste bud cells, of GLUT-1, and several bitter taste receptors targeted by caffeine and in the SSB group fed a WD.

In conclusion, the study supports an interplay of sugar, high-nutrient diets, and chemosensory function on a molecular level independent of body weight development in mice, which could influence food selection.

17:00 - 18:00

Keynote Lecture: Masha Niv: Bitter and sweet molecules and receptors: insights from integrating modeling and experiment

Goethe Hall

Chair/s: Michael Schmuker

Thu-L3-001

Bitter and sweet molecules and receptors: integrating modeling and experiment

Masha Niv

The Robert H Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Israel

Ligands of taste GPCRs are numerous, chemically diverse and often have multiple biotargets. Extraoral expression of taste receptors suggests that yet unknown, endogenous ligands and modulators may be essential for their physiological roles. We integrate machine learning and modeling with experimental testing to obtain a deeper understanding of the bitter and sweet chemical space and its biological implications.

I will present the BitterMatch approach that matches molecules to bitter taste receptors, predictions for large chemical datasets, and future extensions of the algorithm. I will next introduce an iterative data-driven approach that lead us towards discovery of several T2R14 antagonists, and propose receptor features involved in agonists and antagonists recognition.

While bitter taste recognition is achieved by multiple T2R subtypes, typically via their orthosteric binding sites, the

versatility of T1R2/T1R3 heterodimeric sweet taste receptor is facilitated by multiple binding sites. I will present our recent findings on T1R2 and T1R3 roles in recognition of sweet molecules, including deuterated water.
Finally, I will highlight the advantages of integrating experimental data and computational tools, and the opportunities provided by zooming on the “chemical” in “chemoreception research”.

Fri, 2 Sep 2022

08:30 - 09:30

Keynote Lecture: Yoshihiro Yoshihara: Olfactory receptors, circuits and behaviors in zebrafish

Goethe Hall
Chair/s: Ivan Manzini

Fri-L4-001

Olfactory receptors, circuits and behaviors in zebrafish

Yoshihiro Yoshihara
RIKEN Center for Brain Science, Saitama, Japan

Many olfactory cues pervade the aquatic environment of fish and induce various behaviors important for their survival and species preservation, such as searching foods, escaping from danger, and finding potential mates. Zebrafish has become one of the most useful model organisms in neurobiology. In addition to its general advantageous properties (external fertilization, rapid development, transparency of embryos, etc.), zebrafish is amenable to various genetic engineering technologies such as transgenesis, mutagenesis, gene knockdown/knockout, and transposon-mediated gene transfer. Our transgenic approach unraveled two segregated neural pathways originating from ciliated and microvillous sensory neurons in the olfactory epithelium to distinct regions of the olfactory bulb. Furthermore, the two basic principles, one neuron - one receptor rule and axon convergence to target glomeruli, are essentially preserved also in zebrafish, rendering this organism a suitable model vertebrate for the olfactory research. In this lecture, I will summarize advances in our knowledge on the functional architecture of the olfactory neural circuits in zebrafish, which mediate specific odor-induced behaviors. In particular, I will focus on molecular genetic dissection of the neural elements involved in the attraction to food odors, the aversion from alarm pheromone, and the social response to sex pheromones.

10:00 - 12:00

Symposium 5: Waves and wafts: oscillations in central olfactory processing

Goethe Hall
Chair/s: Veronica Egger, Diego Restrepo
The sense of smell has the complicated task of processing qualitatively multidimensional sensory input conveyed by turbulent odor plumes and paced by the respiratory rhythm. In addition, signal processing of olfactory input takes place under drastically different contextual circumstances. Our symposium will bring together an exciting set of speakers using a variety of experimental approaches that will discuss how olfactory system oscillations are generated, how they entrain activity in non-olfactory brain regions, how distance and direction of an odor source is encoded, and how oscillations contribute to multidimensional circuit processing and integrate with contextual circuit modulation.

Fri-S5-001

Intrinsic bulbar theta oscillations: a precise clockwork that synchronizes spontaneous mitral cell activity even in the absence of respiration.

Veronica Egger [1], Luna Jammal Salameh [1], Mathias Dutschmann [2]

[1] Regensburg University, [2] Florey Institute, Melbourne, Australia

Both spontaneous and odor-evoked network activity in rodent olfactory bulbs (OB) are patterned by respiration, resulting in oscillations within the θ regime. Previously, we observed θ rhythms in local field potential recordings (LFP) in semi-intact nose-brain preparations (NBP) of rats that were uncoupled from respiration (Perez et al. 2015). Thus, we hypothesized that the respiratory θ rhythm taps into an intrinsic θ resonance of the bulbar network.

Here we investigate the properties of these intrinsic θ rhythms via LFP recordings at the mitral cell layer within NBPs. Oscillations occurred within a range of 2.5 – 4 Hz and frequently displayed harmonics. All the respective spectral peaks were highly stable with regard to power and frequency and surprisingly narrow, with a bandwidth below 0.01 Hz. θ frequency and power did not change across a set of different recording locations, suggesting that the oscillation is a global feature of the OB network. θ oscillations disappeared upon degradation of the overall network activity, proving their neuronal origin.

The substantial spontaneous spiking activity recorded at the mitral cell layer was found to be correlated with the ongoing θ rhythm, replicating previous in vivo observations, also with regard to the preferred phase of spiking. Possible mechanisms for intrinsic θ generation might involve globally synchronized bursting of external tufted cells in the glomerular layer. These bursts are known to rely on low-voltage Ca^{2+} channel activation. Local injections of the Na^{+} channel blocker lidocaine reduced mitral cell spiking and local network activity but did not interfere with θ. In contrast, global perfusion with the Ca^{2+} channel blocker $NiCl_2$ resulted in decreasing θ power - but also reduced mitral cell spiking. These findings are coherent with an essential role for external tufted cells in intrinsic θ and a concomitant modulation of mitral cell activity, which itself does not contribute to intrinsic θ generation.

Fri-S5-002

Nasal breathing entrains brain activity and modulates behavior in mice

Minghong Ma

Department of Neuroscience, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

The mammalian olfactory system transmits respiration-entrained signals to widespread brain regions including the medial prefrontal cortex (mPFC), which critically regulates numerous cognitive functions. Breathing is dynamically modulated by metabolic needs, orofacial movements, and emotional states. It remains unclear how nasal breathing impacts the mPFC activity across behaviors and the underlying neural pathway(s). I will update our recent progress on this topic by discussing two ongoing projects in my lab. First, we recorded nasal breathing in mice via a pressure sensor across a broad spectrum of spontaneous, attractive odor-, stress-, and fear-induced behaviors, and extract respiratory features using BreathMetrics. Using K-means clustering, we grouped 11 well-defined behavioral states into four clusters with distinct key features. We then implemented the K nearest neighbor classifier and found that breathing patterns could predict these behaviors with an accuracy of 70%. These findings highlight the tight relationship between breathing and behavior. Second, several neural pathways can potentially transmit respiration-related signals, and we studied the potential contribution of the anterior olfactory nucleus/tenia tecta (AON/TT) – mPFC pathway. Using the CRISPR-cas9 gene-editing technique, we generated a new mouse line which allows genetic access to the AON/TT neurons. We characterized the synaptic properties of the AON/TT – mPFC pathway and monitored the neural activity of this pathway across different behaviors. Currently we are testing the effects of chemogenetic inactivation of the AON/TT - mPFC pathway on several behaviors. Our study may have important implications on how respiration-related olfactory inputs contribute to higher cognitive functions by influencing the mPFC activity.

Fri-S5-003

Bilateral sensory signals for odor source localization in freely-moving mice

Kevin Bolding [1], Jiayue Tai [2], Daniel Leman [3], Ian Davison [4]

[1] Monell Chemical Senses Center, [2] Tufts University, Department of Biology, [3] Brandeis University, Department of Biology, [4]Boston University, Department of Biology

During sensory-guided navigation, animals refine their ongoing movement through a series of dynamic, iterative sensory-motor algorithms. In natural contexts, odors signal the location of resources and hazards, offering an ethologically relevant window on motivated sensory search. While odor responses has been studied intensively in head-fixed animals, little is known about the dynamic sensory signals that guide freely moving animals during active sampling of their environment or the sensory-motor strategies available to the animal at each stage of their search. Animals may navigate using comparison of signals across successive 'sniff' samples, using instantaneous 'stereo' comparison across hemispheres, or employ both under different conditions. To overcome the challenges of measuring bilateral odor responses in unrestrained animals, we developed new miniaturized microscopy tools for large-scale visualization of neural activity, and used them to image both hemispheres of the main olfactory bulb in mice exploring odor sources in an open arena. Sensory-evoked activity was detectable in discrete bursts occurring in a restricted area of ~10 cm surrounding the odor source. Increasing proximity to the source activated additional glomeruli, revealing that spatial information is encoded by progressive recruitment of receptors of varying affinity.

A subset of glomeruli exhibited a directional bias in activity for stimuli near the corresponding naris. Homologous pairs of glomeruli in either hemisphere were identified by their correlated signals in bilateral imaging. Subtracting left and right signals produced strongly biased directional tuning and predicted turning in a motivated foraging task. These data suggest that animals may employ multiple strategies to localize odor sources during free exploration, initially comparing the degree of glomerular recruitment across time during early approach phases, and ultimately reading out a bilateral direction code at close proximity.

Fri-S5-004

Upstream Gamma-Synchronization Enhances Odor Processing in the Downstream Neurons

Tal Dalal, Rafi Haddad

The Gonda Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, 5290002, Israel

Gamma-oscillatory activity is ubiquitous across brain areas. Numerous studies and theoretical models have suggested that γ-synchrony is likely to enhance the transmission of sensory information in the brain. However, direct causal evidence is still lacking. Here we tested this hypothesis in the mouse olfactory system, where local GABAergic granule cells (GC) in the olfactory bulb shape mitral/tufted cell (MTC) excitatory output from the olfactory bulb. By optogenetically modulating GC activity, we successfully dissociated MTC γ-synchronization from MTC firing rates. Recording of odor responses in downstream piriform cortex neurons showed that increasing MTC γ-synchronization enhanced cortical neuron odor-evoked firing rates, reduced their response variability, and improved their odor ensemble representation. These gains occurred despite a reduction in MTC firing rates. Furthermore, reducing MTC γ-synchronization without changing the MTC firing rates, by suppressing GC activity, degraded piriform cortex odor-evoked responses. These findings provide causal evidence that increased γ-synchronization enhances the transmission of sensory information between two brain regions.

Fri-S5-005

Olfactory learning elicits changes in oscillations and dimensionality in neural activity in hippocampal CA1

Diego Restrepo [1, 3], Daniel Ramirez-Gordillo [1], Andrew Parra [1], Fabio M. Simoes de Souza [1, 2], Ming Ma [1], Jose Riguero [1], Emily Gibson [3, 4]

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The hippocampus is classically associated with learning and memory, spatial navigation and sequence storage, but there is evidence for a role of CA1 neurons in olfactory associative learning. To explore encoding of olfactory identity

by CA1 neurons, we performed tetrode recording of local field potential and 2-photon imaging in dorsal CA1 of mice exposed to odorants in passive and active tasks. A pseudorandom odorant sequence was presented to head-fixed mice without water reward in the passive task, while in the active task the head-fixed mouse performed go/no-go associative learning where they obtained a water reward when they licked on a spout in the presence of the rewarded odorant.
We found that as the animal learns to discriminate odorants in the go-no go task, the coupling of high frequency neural oscillations to the phase of theta oscillations (theta-referenced phase-amplitude coupling or tPAC) in dorsal CA1 changes in a manner that results in divergence between rewarded and unrewarded odorant-elicited changes in the theta-phase referenced power (tPRP) for beta and gamma oscillations. Furthermore, the changes in tPAC resulted in a marked increase in the accuracy for decoding contextual odorant identity from tPRP when the animal became proficient. Additionally, the identity of the odorants could be decoded from calcium responses in the active task. For the passive task only a small subset of the neurons contributed to successful decoding of the odorant and odorant prediction fluctuated between trials. In contrast, for the active task in the proficient animal a large fraction of neurons contributed to decoding and odorant prediction defaulted to the unrewarded odorant in between trials. Our findings are significant because they show that ensembles of neurons in dorsal CA1 represent stimuli in strikingly different manners under different behavioral conditions.
Funded by NIH DC000566, NSF BIO-1926676 and U01NS099577.

10:00 - 12:00

Symposium 6: Young Investigators (selected from abstracts)

Hahn Lecture Hall
Chair/s: Jessica Freiherr, Silke Sachse

Fri-S6-001

Regulation of CXCL12 availability in the olfactory stem cell niche

André Dietz [1,2], Katja Senf [1,2], Julia Karius [1], Eva M. Neuhaus [1]
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The olfactory epithelium (OE) is not solely exposed to odorants, but also to cell damaging substances and pathogens in the inhaled air and therefore it has to undergo lifelong renewal. Ongoing neurogenesis was shown to be dependent on the chemokine receptor CXCR4, expressed by the globose basal cells and neuronal progenitor cells (Senf et al. 2021). By using immunofluorescent staining, we demonstrate here that tight regulation of the CXCR4-ligand CXCL12 by horizontal basal cells and sustentacular cells is crucial to maintain homeostasis of tissue regeneration. Horizontal basal cells accumulate CXCL12 at the cell surface due to heparan sulfate expression and stimulate the CXCR4-expressing cells within the OE. Using a knock-out mouse model lacking the heparan sulfate degrading enzyme alpha-L-Iduronidase, we show that over accumulation of CXCL12 led to increased activation and thereby downregulation of CXCR4. Additionally, CXCL12 abundance was regulated by sustentacular cells due to the expression of CXCL12 by themselves and by expressing the scavenging receptor atypical chemokine receptor 3 (ACKR3). Absence of functional ACKR3 in sustentacular cells using different knock-out mouse models increased CXCR4 activation and promoted intracellular localization of CXCR4 close to the Golgi-apparatus. The intracellular localization of CXCR4 led to an increase in differentiation into mature neurons, also reflected by effects on distribution and morphology of the Golgi-apparatus and redistribution of the neuronal signaling proteins GAP43 and MARCKS. Conversely, we show that knocking-out CXCL12 expression in sustentacular cells reversed the effect of intracellular clustering of CXCR4 and led to decreased neuronal differentiation. Together, our data reveal a critical role of the extracellular CXCL12 availability for intracellular localization of CXCR4, and its importance for proliferation and differentiation of neuronal stem cells in the OE. The study was supported by the DFG.

Fri-S6-002

Predicting intensity interactions in odor mixtures.

Robert Pellegrino [1], Matthew Andres [1], Vijay Singh [2], Josh Nsubuga [1], Joel Mainland [1, 3]
[1] *Monell Chemical Senses Center, Philadelphia, Pennsylvania,* [2] *Department of Physics, NC A&T State University, Greensboro, North Carolina,* [3] *Department of Neuroscience, University of Pennsylvania, Philadelphia, PA 19104, USA*

Most odors encountered in daily life are complex mixtures where molecules interact to overshadow, suppress, inhibit and synergize with each other. Multiple models exist to predict the odor intensity of a mixture from the intensity of its components; however, these interaction models have not been compared systematically and are not based on biophysical interactions. In this study, 15 panelists rated the intensity of binary and complex mixtures where each component was presented at varying concentrations. Both additive and strongest-component model consistently overestimated mixture intensity, as most mixtures were less intense than the strongest component. An accurate intensity of the mixture was predicted when incorporating more information on the intensity of the components along their respective concentration-intensity function. These interactions suggest that most previous models, which only predict mixture intensity using the intensity of the components, would be improved by adding information about each components' concentration-intensity function.

Fri-S6-003

Tas2R expression and function in the murine tracheal epithelium

Alexander Perniss, Silke Wiegand, Tamara Papadakis, Uwe Pfeil, Wolfgang Kummer
Institute for anatomy and cell biology, Justus Liebig University Giessen

Objectives: As shown by single cell sequencing and corresponding reporter mice various Tas2R are expressed by murine tracheal brush cells. Activation of tracheal brush cells by specific pathogen-associated formyl peptides results in an acetylcholine (ACh) dependent increase in mucociliary clearance (MC). In this study, we asked if Tas2R expression within the trachea is restricted to brush cells and if stimulation of Tas2R also leads to a release of ACh by brush cells and thereby alters MC.
Methods: Expression of all known murine Tas2R in the whole trachea and mechanically abraded tracheal epithelium was analyzed by RT-PCR (n = 3-6 each). As a readout for MC particle transport speed (PTS) was measured in response to 11 different Tas2R agonists in WT (C57BL/6J) and brush cell-deficient mice (Pou2f3$^{-/-}$).
Results: Messenger-RNA-transcripts for 34 of 35 murine Tas2R were present in samples of whole tracheas of WT mice. In contrast to that, mRNA for only 18 of 35 Ta2R was detected in abraded tracheal epithelium of WT mice. Three Tas2R-agonists (cycloheximide (100 µM), allylisothiocyanate (300 µM) and 3-oxo-C12-HSL (100 µM)) increased PTS independent of brush cells by 12%, 54% and 24%, respectively, since the effect persisted in Pou2f3$^{-/-}$-mice.
Conclusions: RT-PCR experiments suggest an alternative source of Tas2R expression in the trachea besides brush cells. Tested Tas2R agonists increased PTS independent of brush cells, pointing towards a brush cell-independent expression of Tas2R or to Tas2-independent actions on MC of these agonists.

Fri-S6-004

The search for olfactory receptors tuned to pheromones in the honey bee

Benjamin Andreu [1], Nicolas Montagné [2], Thomas Chertemps [2], Emmanuelle Jacquin-Joly [3], Julie Carcaud [1], Jean-Christophe Sandoz [1]
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Being social insects, honeybees use pheromones to ensure intraspecific communication allowing colony cohesion in a wide range of contexts: queen retinue, brood care, foraging, colony defense, swarming, etc. Honeybees constitute an interesting model to study the neurobiological basis of pheromonal processing, as the anatomy of the honey bee brain has been well characterized. Despite increasing knowledge already acquired on olfactory processing in this species, the nature of pheromonal coding is still poorly understood. Knowledge from other insects suggest that pheromones would be detected and processed by highly-specific and isolated subsystems ("labeled lines") while general odorants would be encoded in a combinatorial fashion ("across-fiber pattern"). But, with a such a plethora of different pheromonal

compounds, more than most insects, can the bee brain really harbor as many labeled lines? Or did this social insect evolve a more cost-effective strategy using combinatorial coding of pheromone information? To answer these questions, we study the responses of individual olfactory receptors and attempt to determine their ligands (receptor deorphanization). To this aim, we use heterologous expression in the “empty neuron system” of Drosophila, coupled to transcuticular calcium imaging. We will present here the work that lead to the identification of ligands for a first olfactory receptor in our panel. Once the ligands of each receptor are identified, we will study their neural representations in the honey bee brain using in vivo calcium imaging, aiming to produce a complete picture of the circuits involved in pheromone processing in this social insect.

Fri-S6-005

OWSum – Algorithmic odor prediction and insight into structure-odor-relationships

Doris Schicker [1, 2], Satnam Singh [1], Jessica Freiherr [1, 2], Andreas Grasskamp [1]

[1] Sensory Analytics and Technologies, Fraunhofer Institute for Process Engineering and Packaging IVV, Giggenhauser Straße 35, 85354 Freising, Germany, [2] Department of Psychiatry and Psychotherapy, Friedrich-Alexander-Universität Erlangen-Nürnberg, Schloßplatz 4, 91054 Erlangen, Germany

We derived and implemented the linear classification algorithm Olfactory Weighted Sum (OWSum) to predict molecules’ odors. The presented approach relies solely on structural patterns of the molecules as features for algorithmic treatment. In addition to the prediction of molecular odor, OWSum provides insights into properties of the dataset and allows to understand how algorithmic classifications are reached. OWSum achieves an accuracy of 90.5% on our database consisting of molecules belonging to six different odor classes. Using OWSum, we can quantitatively assign structural patterns to odors and identify the most important ones, giving chemists an intuitive understanding of underlying interactions. To deal with ambiguities of the natural language used to describe odor, we introduce a descriptor overlap as a metric for the quantification of semantic overlap between descriptors. This allows for grouping of descriptors and derivation of higher-level descriptors.

Fri-S6-006

Body odor disgust sensitivity is positively related to concern about COVID-19 pandemics

Marta Zakrzewska [1], Sandra Challma [1], Marco Tulio Liuzza [2], Teodor Jernsäther-Ohlsson [1], Torun Lindholm [1], Jonas Olofsson [1]

[1] Department of Psychology, Stockholm University, Sweden, [2] Department of Surgical and Medical Sciences, "Magna Graecia" University of Catanzaro, Italy

The SARS-CoV-2 virus and the resulting COVID-19 pandemic has drastically changed the way we interact with each other. In a time of this salient pathogen threat, individual differences in how we avoid contagion become more visible. Research on disease avoidance behaviors showed that they are related to several individual characteristics, one of them being disgust sensitivity. Interestingly, disgust sensitivity to body odors in particular (body odor disgust sensitivity, BODS) has recently been studied in more detail and seems to be important for avoidance behaviors. This is understandable as olfaction helps in recognizing and evading the (often invisible) threat of disease. In this project, we used online surveys to investigated the relationship between BODS and disease avoidance during salient pathogen threat (COVID-19 pandemics). We collected data in three waves between April 2020 and June 2022, in various locations around the world. Wave 1 (N = 2068) was done in Italy and Sweden; wave 2 (N = 4595) in Canada, Chile, Hong Kong, Kenya, Nigeria, Mexico, New Zealand and the United Kingdom (UK); wave 3 (N = 2893) in Australia, Colombia, India, Italy, Nigeria, Sweden and UK. Participant completed the BODS questionnaire and answered questions about attitudes towards and concern about behaviors related to COVID-19 (e.g., wearing masks, avoiding contact with strangers etc.). We used Bayesian parameter estimation and model comparison to study the relationship between BODS and attitudes towards COVID-19. In all three datasets, participants who reported greater body odor disgust sensitivity were also more concerned about COVID-19 pandemics. Our findings support the idea that body odor disgust is relevant to disease avoidance by showing that it is related to attitudes about disease spread limiting behaviors during a salient pathogen threat situation. These studies were funded by the Swedish Research Council.

13:30 - 15:30

Symposium 7: Making (chemo)sense of evolution - taste across animal phyla

Goethe Hall

Chair/s: Thomas O. Auer

In this symposium we will cover taste research in bird, cephalopod, fish and fly species drawing a broad picture of taste receptor and circuit evolution across animal phyla. We will highlight the strength of a comparative framework to extract general principles of chemosensory circuit function based on novel genomic, transcriptomic and physiological methods in classical model and non-model species in aquatic and non-aquatic environments.

Fri-S7-001

Molecular and cellular basis of octopus touch-taste

Lena van Giesen

Norwegian University of Science and Technology (NTNU), Trondheim, Norway

The ability to detect and process salient sensory information from diverse environments is crucial to an organism's survival. Animals exhibit a broad variety of cellular and molecular adaptations that enable them to detect, filter and process relevant chemical information from their specific ecological niche. While molecular, cellular and behavioral aspects of chemosensation have been studied in detail in a variety of terrestrial animals, these aspects are less well studied in aquatic context, where chemosensation is subjected to different physiochemical constraints.
I recently described the molecular basis of the "taste by touch" sense in octopus that guides complex and autonomous arm behaviors, including the characterization of a cephalopod specific family of chemotactile receptors (CRs). CRs are co-expressed in diverse patterns and form heteromeric ion channel complexes to specify signal detection and transduction. Thus, CRs offer a uniquely-suited protein family to understand how single protein complexes facilitate the detection and filtering of cellular signals to elicit sophisticated behaviors. Furthermore, we can transfer knowledge from this system to sensory systems of other marine invertebrates and study how chemosensory systems evolved to suit an animal's particular environmental niche.

Fri-S7-002

Evolution of gene expression in the taste tissues of ecologically diverse Drosophila species

Roman Arguello [1, 2], Gwénaëlle Bontonou [1, 2], Bastien Saint Leandre [1, 2], Tane Kafle [1, 2], Tess Baticle [1], Afrah Hassan [1], Justine Pascual [3], Enrico Bertolini [3], Juan Sanchez-Alcañiz [4], Thomas Auer [3]

[1] University of Lausanne Department of Ecology and Evolution, [2] Swiss Institute of Bioinformatics, [3] University of Lausanne Center for Integrative Genomics, [4] Instituto de Neurociencias UMH-CSIC

Insect taste organs display incredible morphological and functional diversity between species, as well as having variable sex-specific functions within species. In light of these differences, we have been addressing open questions about the evolution of gene expression in taste tissues. Our focus has been on closely-related species where insights into the early stages of sensory diversification can still be detected. We have generated transcriptomes for four sensory tissues (proboscis + maxillary palp, forelegs, ovipositor, and larval head) for males and females of six ecologically diverse Drosophila species. Species comparisons revealed pervasive gene expression changes associated with both morphological and chemosensory functions. In proboscis for instance, ~ 27% of 1:1 orthologs have changed in expression at least once over the past 15 million years. When examining expression breadth according to gene ages, we found that young genes and highly duplicated gene families were disproportionately tissue specific, suggesting a role in taste organ specialization. Given the roles that these organs play in sex-specific behavior, we examined the patterns of sex-biased gene expression. Patterns of sex-biased expression vary remarkably among taste tissues and do not reflect the phylogenetic relationship of the species. To relate these tissue-level expression changes to evolutionary modifications at the level of cell populations, we are generating cross-species single cell atlases. Analyses of these data are revealing species-specific elevated gene expression associated to the expansion of single neuron populations as well as surprising cell-specificity of sex-biased genes. Together, our work demonstrates the power of combining cross-species bulk RNA-sequencing with matched single cell RNA transcriptome data for understanding the origins of chemosensory diversification.

Fri-S7-003

Molecular evolution of taste in jawed fish and an unexpected link to olfaction

Sigrun I Korsching, Kanika Sharma, Günes Birdal
Institute of Genetics, MNF, University at Cologne, Germany

Evolution and cognate ligands of mammalian taste receptors - T1Rs and T2Rs – have been studied in some detail, whereas comparatively little is known about their counterparts in earlier-diverging vertebrates. Here we report phylogenetic studies to evaluate the evolutionary dynamics of these families in fish. Both families are absent in lamprey, but T1Rs can already be found in cartilaginous fish. In bony fish a clear distinction between ray-finned and lobefinned fish is seen for the evolution of T2Rs. In ray-finned fish four ancestral T2R genes exhibit little evolutionary dynamics, with few exceptions such as the Mexican cavefish that shows a moderate degree of gene duplications in one of the four ancestral genes1. In contrast, a lobe-finned fish, coelacanth, exhibits a very large T2R gene repertoire equaling that of amphibians and clearly surpassing mammalian T2R repertoires2. Remarkably, the ligand profile of the most basal coelacanth receptor, T2R01, is identical to that of its ortholog in zebrafish3, consistent with functional conservation over 400 million years of separate evolution.

In mammals taste is an intraoral sense which mainly serves to evaluate the nutritious content and potential toxicity of food taken in. In teleosts taste buds can also be found on the body surface such as head skin and lips, consistent with a possible additional function of taste as a distant sense similar to olfaction. Here we show that the nostrils of zebrafish possess a high density of T1R and T2R-expressing cells surpassing that of the oral cavity and of head skin by far. Thus, the incoming stream of odors first is sampled by sentinel taste cells on the nostrils, before it reaches the olfactory epithelium, opening up the possibility of cross-talk between these two sensory modalities.

1 Shiriagin and Korsching, Chem Senses 44, 23–32 (2019).
2 Syed and Korsching, BMC Genomics 15, 650 (2014).
3 Behrens et al., Genome Biology and Evolution 13, evaa264 (2021).

Fri-S7-004

A novel mechanism underlying selective loss of sugar-sensing in wrynecks

Julia F. Cramer [1], Eliot T. Miller [2], Meng-Ching Ko [1], Qiaoyi Liang [1], Glenn Cockburn [1], Tomoya Nakagita [3, 4], Massimiliano Cardinale [5], Leonida Fusani [6, 7], Yasuka Toda [3], Maude W. Baldwin [1]
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Changes in sensory receptors can shift how organisms perceive the world, directly affecting their interaction with the environment. Although receptor sensitivities can be highly contingent on changes occurring early in a lineage's evolutionary history, subsequent shifts in a species' behavior and ecology may exert selective pressure to modify and even reverse sensory receptor capabilities. The extent to which sensory reversion occurs, as well as the mechanisms underlying such shifts are not well understood. In our study, we use functional cell assays for receptor profiling as well as behavioral preference tests and uncover both an early gain as well as an unexpected mechanism for a surprising subsequent loss of sugar sensing in woodpeckers and wrynecks, members of the widespread and primarily insectivorous Picidae family of landbirds. Our analyses show that, similar to hummingbirds and songbirds, the ancestors of woodpeckers repurposed their T1R1-T1R3 savory (umami) receptor to detect sugars. Unexpectedly, while woodpeckers seem to have broadly retained this ability, wrynecks (an enigmatic ant-eating group sister to all other woodpeckers) selectively lost sugar sensing through a novel mechanism involving a single amino acid change in the T1R3 transmembrane domain. The identification of this molecular microswitch responsible for a sensory shift in taste receptors uncovers the molecular basis of a sensory reversion in vertebrates and offers novel insights into structure-function relationships during sensory receptor evolution.

Fri-S7-005

The progresion of change in neuronal activity that underlie the formation and consolidation of a gustatory associative memory

Neta Dagan [1], Anan Moran [1, 2]

[1] Department of Neurobiology, School of Neurobiology, Biochemistry & Biophysics The George S. Wise Faculty of Life Science Tel Aviv University Israel, [2] Sagol School of Neuroscience Tel-Aviv University Israel

Memory formation is not an instantaneous event, but rather a dynamic process that progressively evolves. Notable phases of memory formation include the early acquisition in which the memory is still labile, and the consolidation phase wherein the memory stabilizes. In conditioned taste aversion (CTA) learning, for instance, two such phases were identified in the gustatory cortex (GC) during the formation of a taste-malaise memory: an early acquisition phase (2-3 hours following training), followed by a consolidation phase 3 hours later. While these memory phases were characterized by their underlying molecular underpinnings, their associated progression in neuronal activity, neuronal network connectivity, and neuronal coding of taste identity, palatability, and novelty is still largely unknown. To study these unknowns we record continuously from the GC of rats while they undergo CTA. We found that the progression of activity changes depends on the neuronal organizational level: whereas the population response changed continuously, the known quickening of the ensemble-state dynamics associated with the faster rejection of harmful foods appeared only after consolidation. These results suggest a role of the consolidation phase in network optimization. In a new set of experiments we aim to characterize the network-level connectivity map and the cell-specific coding changes that underlie the progression of the CTA memory. To that end we implant Neuropixels probes in the GC and neighboring brain regions, and record the activity of hundreds of neurons simultaneously before, during, and after CTA. Using generalized linear modeling techniques over the pairwise neuronal cross-correlation we set to characterize the connectivity map between the recorded neurons. Creating this map during different time points following CTA will allow us to portray the fine network functional connectivity changes that underlie early acquisition and late consolidation phases.

13:30 - 15:30

Symposium 8: Sex-steroid hormones in olfaction

Hahn Lecture Hall

Chair/s: Tatjana Abaffy

Symposium theme revolves around the circulation derived sex-steroid hormones and also locally synthetized neurosteroids and their effects on the olfactory system. The idea is to present the current knowledge around the effects of these steroids on the olfactory system development, odor perception, pheromonal responses and social behavior.

Fri-S8-001

Estrogens regulate early embryonic development of the olfactory sensory system via estrogen-responsive glia

Aya Takesono [1], Paula Schirrmacher [1, 2], Aaron Scott [1, 3], Jon Green [1], Okhyun Lee [1], Matthew Winter [1], Tetsuhiro Kudoh [1], Charles Tyler [1]

[1] Biosciences, College of Life and Environmental Sciences, University of Exeter, Exeter, Devon, EX4 4QD, United Kingdom, [2]Department of Biological and Marine Sciences, Faculty of Science and Engineering, University of Hull, Hull, HU6 7RX, United Kingdom, [3] School of Physiology, Pharmacology & Neuroscience, University of Bristol, Bristol, BS8 1TD, United Kingdom

Estrogen is well-known to regulate development of sexual dimorphisms of the brain, however its role in the brain during early embryonic development prior to sex-differentiation is unclear.

Using estrogen biosensor zebrafish models, we demonstrate that estrogen activity in the embryonic brain occurs specifically in a type of glia located within the OB, which we name estrogen-responsive olfactory bulb/EROB cells. In response to estrogen, EROB cells overlay the outermost layer of the OB and interact tightly with olfactory sensory

neurons at the olfactory glomeruli. Pharmacologically Inhibiting estrogen activity by an estrogen receptor antagonist, ICI182,780 (ICI), and/or EROB cell ablation impede olfactory glomerular development, including topological organisation of olfactory glomeruli and inhibitory synaptogenesis in the OB. Furthermore, activation of estrogen signalling inhibits both intrinsic and olfaction-dependent neuronal activity in the OB, whereas ICI or EROB cell ablation results in the opposite effect on neuronal excitability. Altering the estrogen signalling disrupts olfaction-mediated behaviour in later larval stage. We propose that estrogen acts on glia to regulate development of functional OB circuits, thereby modulating the local excitability in the OB and olfaction-mediated behaviour. Our data also suggest a possibility that the estrogen/EROB cascade may be an important site of action for environmental estrogens causative of neurodevelopmental impairments in animals and humans.

Fri-S8-002

Integrative circuits for social behavior in the medial amygdala

Joseph Bergan

University of Massachusetts at Amherst

Social behaviors are essential for survival and social circuits must rapidly integrate, process, and communicate with brain-wide behavior networks. The medial amygdala is an important center for social integration that both processes social input and generates behavioral outputs. Aromatase-expressing neurons in the medial amygdala drive behavioral responses including aggression and social recognition. We recently identified the brain regions that provide synaptic input to aromatase-expressing neurons in the medial amygdala using rabies tracing and light sheet microscopy. These results confirm the central role of the medial amygdala in sex-specific social behavior and also highlight an unexpected level of integration of multiple sensory and homeostatic factors which may serve to modulate social behaviors. Broad integration is also clear in the moment-to-moment activity of aromatase neurons during social interactions. By understanding the detailed circuitry and physiology, as well sex differences and similarities in these properties, we are starting to understand medial amygdala-dependent social behaviors such as affiliation, parenting, social memory, predator avoidance, and aggression at a mechanistic level.

Fri-S8-003

Brain-derived estradiol and odor hedonics

Natalie Johnson [1], Katherine Wright [1], Anamaria Cotelo [1], Minghong Ma [2], Daniel Wesson [1]

[1] Dept of Pharmacology & Therapeutics, Center for Smell & Taste, University of Florida, [2] Dept of Neuroscience, University of Pennsylvania

The brain's tubular striatum (TuS, also known as the olfactory tubercle) receives both monosynaptic input from the olfactory bulb and midbrain dopaminergic input, which uniquely positions it to influence odor-guided motivated behaviors and odor hedonics. Furthermore, the TuS has abundant expression of aromatase, allowing for local, de novo synthesis of 17β-estradiol (E2). Given local E2's ability to rapidly influence neural activity and the established role of the TuS in odor valence, we reasoned that E2 in the TuS may influence attraction to odors. Using plethysmography, we examined odor-evoked high-frequency sniffing as a measure of odor attraction. Bilateral infusion of the aromatase inhibitor letrozole into the TuS of gonadectomized female adult mice induced a resistance to habituation over successive trials in their investigatory sniffing for female mouse urinary odor. Therefore, E2 in the TuS impacts attraction to ethologically relevant odors. We next sought to determine the role of TuS dopamine (DA) in odor-guided behaviors. Using in vivo fiber photometry and the DA sensor GRABDA, we observed a relationship between high frequency sniff bouts and DA release in the TuS. Since the TuS is largely comprised of neurons that express either DA 1 (D1) or DA 2 (D2) receptors, we then bilaterally infused either a D1 or D2 receptor antagonist, SCH23390 or raclopride, respectively, into the TuS of gonadally-intact mice. We found that inhibition of both D1 and D2 receptors reduced bouts of exploratory sniffing. Furthermore, inhibition of D2 receptors reduced investigatory sniffing to innately attractive odors. These data suggest that DA's actions in the TuS also impact behavior toward attractive odors. Because E2 can affect brain DA, including enhancement of DAergic transmission, ongoing work aims to explore the combined role of E2 and DA in odor-guided behaviors.

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Fri-S8-004

Trpm4 and hormone regulation in the vomeronasal organ

Frank Zufall

Center for Integrative Physiology and Molecular Medicine (CIPMM), Saarland University, Homburg, Germany

This lecture will summarize our studies identifying the transient receptor potential (TRP) channel TRPM4, a Ca^{2+}-activated Na^{+}-permeable ion channel, as a second TRP channel present in mouse vomeronsasal sensory neurons (VSNs), in addition to the diacylglycerol-sensitive and Ca^{2+} permeable TRPC2 channel. Three major results emerge from this work. First, unlike TRPC2, TRPM4 is not detectable in the microvilli of VSNs, suggesting that TRPM4 does not mediate primary chemoelectrical transduction in VSNs but rather would be ideal for a downstream, modulatory function in these neurons. Second, TRPM4 is expressed in a sex-specific manner in VSNs, in contrast to TRPC2. In the VNO of female mice, the expression of TRPM4 is synchronized to the female reproductive cycle and is upregulated specifically during proestrus and estrus, at a time when female mice are about to ovulate and become sexually active and receptive. Third, this cyclic regulation is governed by ovarian sex hormones because ovariectomy (OVX) results in permanent downregulation of TRPM4 expression, an effect that can be restored by systemic treatment of OVX mice with 17ß-estradiol but not with progesterone. On the basis of these results and other evidence, we propose that TRPM4 could be part of a novel hormone signaling cascade in the VNO, possibly required for modulating experience-dependent social behaviors through vomeronasal signaling. Our ongoing experiments are testing this central hypothesis. TRPM4 activation by hormonal signaling offers an attractive neural mechanism by which female mice could regulate the relative strength of sensory signals in their VSNs, depending on hormonal state.

Supported by Deutsche Forschungsgemeinschaft grant SFB-Transregio 152.

15:30 - 17:00

Poster Session (No. 60-123)

Planck Lobby & Meitner Hall

Fri-P2-060

Sampling, identification and sensory evaluation of odors of a newborn baby's head as a putative communication tool with grownups.

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For baby odor analyses, noninvasive, stress-free sample collection is important. Using a simple method, we succeeded in obtaining fresh odors from the head of fve newborn babies. These odors were chemically analyzed by two-dimensional gas chromatography coupled with mass spectrometry (GC×GC-MS), and compared with each other or with the odor of amniotic fuid from the baby’s mother. We identifed 31 chemical components of the volatile odors from neonate heads and 21 from amniotic fuid. Although 15 of these components were common to both sources, there was an apparent diference in the GC×GC patterns between the head and amniotic fuid odors, so the neonate head odor might be individually distinct immediately after birth. Therefore, we made artifcial mixtures of the major odor components of the neonate head and maternal amniotic fuid, and used psychological tests to examine whether or not these odors could be distinguished from each other. Our data show that the artifcial odor of a neonate head could be distinguished from that of amniotic fuid, and that the odors of artifcial head odor mixtures could be correctly discriminated for neonates within an hour after birth and at 2 or 3 days of age.

Fri-P2-061

Objective and subjective perception of different chemosensory stimuli by healthy subjects

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Human chemosignals originating from axillary sweat are becoming increasingly attractive in neuroscience research. In this study, we were particularly interested in the subjective and objective perception of chemosignals sampled during a TSST and a friendly version of the TSST concerning the time and the body region of sampling. Participants were asked to rate intensity, pleasantness, dominance, arousal, masculinity/femininity, and sexual attractiveness of the samples using visual analog scales. We did not determine significant differences between the two stress conditions (TSST/friendly TSST) but demonstrated significant differences in the perception of stress sweat concerning sampling time. Samples donated during the stress test were rated as more unpleasant, less sexually attractive, and more male-related than samples donated before and after the stress test. Regarding the body region, neck samples were evaluated as more pleasant, sexually attractive, and feminine-related, while armpit samples were rated as more intense, arousing, and dominant.

During objective assessment by a trained panel, the samples were characterized as sweaty-mouldy, sulphury and grapefruit-like. Additionally, sweat samples from the armpit collected during the stress test were evaluated as most arousing and dominant.

With this research, we were not only able to characterize stress sweat with attributes in a descriptive manner but did also prove that sampling during the stress test shows the most potent behavioral response. Finally, we here show differences in perception of stress sweat from different body regions, which can be important for subsequent attractiveness-specific chemosignal studies.

Fri-P2-062

AI-guided reverse chemical ecology applied to pest control

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Reverse chemical ecology is an innovative chemical ecology approach that consists in targeting olfactory receptors to accelerate the identification of new semiochemicals active on the behavior of crop pest insects. We recently demonstrated that machine learning approaches guided the discovery of novel natural ligands for the noctuid moth Spodoptera littoralis Olfactory Receptors 24 and 25 (SlitOR24 and SlitOR25). However, the applicability domain of the models limits the chemical space to explore to molecules similar to the training set. To overcome this limitation, a structure-based virtual screening (SBVS) protocol was optimized as follows. First, we collected experimental data of two recent studies and set up a database of 184 odorants for SlitOR24 and SlitOR25. Then the structure of the receptors has been obtained with Alphafold. The ligand binding site has been deduced from the experimental structure of the insect olfactory receptor MhOR5 (from Machilis hrabei) in complex with eugenol. Docking simulations have been performed using Vina and optimized by testing various parameters and rescoring functions. The performance of the SBVS (AUC ~0.75 for both receptors) seems sufficient to expand the chemical space of potentially active odorants.

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References: [1] G. Caballero-Vidal et al. Cell. Mol. Life Sci., 2021, 78, 6593-6603. [2] G. Caballero-Vidal et al. Sci. Rep, 2020, 1655.

Fri-P2-063

Enhanced neural processing of chemosensory happiness

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Previous research has shown enhanced neural processing of chemosensory anxiety, stress, and aggression signals. The current study is the first that examines event-related potentials (ERPs) in response to chemosensory happiness signals. Axillary sweat was collected via cotton pads from 25 women while they were waiting for the arrival of loved ones (friends or lovers) from whom they had been separated for a while (happiness condition), and during light ergometer training with adjusted heart rate (sport control condition). These donor women reported being happier during the happiness condition compared to the sport control condition ($p < .001$). Sweat samples per condition and additionally sweatless cotton were pooled, and presented to 26 men and 27 women (0.5 s, ISI: 18.5-22.5 s) via a constant-flow olfactometer (100 ml/s). EEG was recorded (61 electrodes), and the N1, P2, and P3 components of the chemosensory ERP were detected at fronto-central (Fz), centro-central (Cz), and parieto-central (Pz) electrode positions. The N1-P2 and N1-P3 interpeak amplitudes in response to happiness related sweat in reference to cotton (happiness – cotton) and sport control sweat in reference to cotton (sport – cotton) were analyzed. N1-P3 interpeak amplitudes were larger in response to chemosensory happiness compared to emotionally neutral information (sport control sweat, $p = .033$, $\eta_p^2 = 0.086$) across men and women. Happiness and sport sweat did not differ in intensity ($p = .171$) or pleasantness ($p = .535$).

The enlarged N1-P3 amplitudes in response to chemosensory happiness indicate evaluative importance of positive affect for men and women. These results suggest that happiness related sweat contains important social information sufficient to release an enhanced ERP response. Chemosensory transmission of positive affect seems to function as successful as the transmission of negative affect.

Fri-P2-064

The role of the main and accessory olfactory system in the "ram effect": an immunohistochemical study

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The ram effect is a well-known phenomenon in sheep, whereby the introduction of a sexually active ram in a group of anoestrous ewes induces luteinizing hormone (LH) secretion and ovulation. Previous studies verified the implication of the chemical communication in this phenomenon, also describing the role of the ram anteorbital gland secretion in this effect induction. However, the olfactory pathways involved in the treatment of these cues haven't been fully investigated. This study aimed to use the anti-c-Fos immunohistochemistry (IHC) to evaluate if the main and accessory olfactory bulb (MOB and AOB) are differentially activated by the anteorbital gland secretion of subjects having a different sexual status. Sixteen anoestrous ewes were divided into 4 groups to test the anteorbital gland secretions from entire rams, neutered males, and females. The fourth was the control group. After 20 minutes of inhalation, ewes were humanely euthanized and the brains submitted to IHC. The number of c-Fos+ neurons was counted in 1 mm2 in the MOB and AOB of each ewe, and the Kruskal-Wallis one-way ANOVA and the Wilcoxon two-sample test were used. The MOB was activated without statistical difference by the neutered and entire male secretion (170±4 vs 201±23 cells/1mm2, $p>0.05$). Male secretions activated the MOB more than females (140±5, $p<0.05$). The AOB was significantly more activated by the entire ram secretion (113±5, $p>0.05$) than other treatments, which showed a statistical difference in this order: neutered (89±2), females (58±2) and control group (15±2). Our data suggest that the MOB

recognizes male secretion without distinguishing between entire and neutered males. This distinction is then done by the AOB. In conclusion, the main olfactory system seems necessary to identify the presence of a male, probably inducing sheep vomeronasal organ opening, entire male pheromones detection and AOB activation, triggering then the brain circuit leading to LH peaks and ovulation.

Fri-P2-065

Aroma and taste effects of ethanol on components of whisky flavour

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The spirit industry has in recent years begun producing no and low alcohol spirit-like products and there is a demand for innovation within this category. To create a no or low alcohol whisky-like product we must first understand how the flavour and aroma of whisky congeners are perceptually different in variable alcohol strengths and our best tool for this is sensory analysis. The whisky industry typically dilutes samples to 20% abv and generally assesses by nosing as indicative of the flavour effects of whisky. There is little published work on the flavour effects of dilution or the variation between what can be perceived by nosing and tasting whiskies.

This study assessed aroma and taste effects of individual compounds, identified as major flavour-active constituents of whisky, in variable water/ethanol solutions. Descriptive analysis was performed by an expert panel of whisky tasters. Early results have shown that there are clear differences in flavour and aroma of the compounds that is variable and affected by ethanol percentage. There is some indication that there is an effect due to chemical groupings, related to compound stability.

Whisky is a complex medium that contains a plethora of flavour contributing compounds that can be introduced in the various stages of spirit production from grain selection to maturation. The ethanol/ water matrix which forms the base of all alcoholic products has complex interactions between water and ethanol molecules forming an incomplete mixture. Ethanol and water also have reactive relationships with many of the compounds that may be present in whisky. These compounds differ in solubility and hydrophobicity and their influence on the flavour active mechanisms of whisky compounds in the ethanol/water medium has been little understood until this current study. Work is ongoing and expected completion is July 2022.

Fri-P2-066

Multisensory olfactory training: a new treatment for post-covid-19 olfactory loss

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According to the quantitative studies, 45-60% of people suffer from olactory loss after being diagnosed with COVID-19. Olfactory training is the most effective methods used for the treatment of olfactory loss following viral infection of the upper respiratory tract. It consists of sniffing odors twice a day for 12 weeks.

Our aim is to improve the current olfactory training protocol. We hypothesize that providing odors in a multi-sensory context enhances the effects of olfactory training thus leading to more successful recovery in patients.

We recruited 45 patients (33 women, 12 men, aged Mean = 42.8) with olfactory dysfunction following COVID-19. We tested 36 patients (26 women, 10 men, aged Mean = 42.5) in follow-up. Participants were divided into two groups, namely (I) an olfactory training group and (II) multi-sensory training. Whereas group I (n=20) followed a classical olfactory training paradigm with odors of strawberry, lemon, coffee, cheese; we prepared equivalent multi-sensory stimuli for group II (n=16). We dissolved the odorants in the water, together with a corresponding gustatory stimulus (strawberry-sugar, lemon-citric acid, coffee-sucrose octaacetate, cheese-salt). Group II put a droplet of the solution on their tongue, while looking at a cardboard on which we color printed an image of the stimulus.

We evaluated olfactory function before and after the training with UPSIT, the Questionnaire of Olfactory Dysfunction (QOD) and rating scales in the 36 participants who completed the protocol. For all variables, both interventions revealed a significant effect of training, but we did not observe any significant difference between groups.

In conclusion, both the classical olfactory training and the novel multi-sensory training protocol showed significant effects on subjective and objctive olfactory function in olfactory dysfunction following COVID-19. However, multi-sensory training does not seem to provide any advantage over the classical approach.

Fri-P2-067

Bimodal sensory processing and learning in Drosophila melanogaster.

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Insects utilize a myriad of sensory signals to navigate natural environments. They show remarkable abilities to learn these cues and form memories associated with them. This learned information is essential to make crucial decisions at a later point in time. Conventional conditioning experiments have been used in the past to observe associative learning abilities of vinegar flies (Drosophila melanogaster) using individual sensory modalities. In our work, we established a T-maze choice assay that combines the presentation of both visual and olfactory stimuli in an aversive conditioning paradigm to study the effect of bimodal integration on learning performance. We show that the presence of an additional modality during training aids in better learning of visual and olfactory stimuli and in the retention of these memories. The results from these behavioural experiments provide evidence for the presence of neuronal substrates that can integrate sensory information and use that to form associations. Further physiological investigation in the higher brain regions such as the mushroom bodies and the lateral horn can reveal the identities of these neurons that are involved in multimodal information processing. This project is funded by the Deutscher Akademischer Austauschdienst (DAAD) and the Max Planck Gesellschaft (MPG).

Fri-P2-068

Gustatory modulation of olfactory preference in Drosophila larvae

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Integrating information from several sensory cues to make optimal foraging decisions is crucial for all animals. Previously we found that Drosophila larvae switch their odor response from aversion to attraction when food-deprived. We now investigate how the larval behavior towards an aversive olfactory cue is modified by pre-exposure to different food components, such as carbohydrates and proteins. In addition, we also analyze how food deprivation and food component exposure affect locomotion behavior in Drosophila larvae. We find that only exposure to nutritious, protein-rich, food is sufficient to retain a fed olfactory response, however, it is not sufficient to display fed locomotion behavior. Thus, olfactory responses and locomotion behavior are regulated independently during food deprivation.

Fri-P2-069

Association between natural images and natural odors

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Naturalness is more than a marketing trend. Neuroscientific studies brought evidence of distinct cognitive and cerebral processing of naturally occurring objects vs. human-made objects. However, these studies have focused on the visual modality and little knowledge is available concerning olfaction. If smells do not seem less capable of evoking nature, we wonder whether naturalness would share the same meaning between the visual and olfactory domains. Images have been considered natural when representing natural objects. Thus, one assumption that may be made is that, as for images, the naturalness of a smell would rely on what that smell evokes (i.e. a naturally occurring or a human made entity).

Following this hypothesis, we set up an Implicit Association Task testing for association between odors and images representing natural or human-made objects. In this task, 34 French participants were asked to categorize as fast as possible images and smells into one of four categories: fruit or candy for smells, mountains or building for images. It was expected that participants would be faster in congruent condition, i.e. when associated concepts (e.g. natural

smells and natural images) shared the same respond key, compared to incongruent condition, i.e. when dissociated concepts (e.g. natural smells and artificial images) shared the same respond key. We ran a linear mixed model with reaction time (RT) as dependent variable, participants and stimuli as random factors, and conditions (congruent vs. incongruent), modality (images vs. odors) and their interaction as fixed effects. Results showed a significant effect of conditions, RT being lower in congruent condition, and of modality, RT being lower for images. These results suggest that smells and images are associated based on the naturalness of the object they represent.
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Fri-P2-070

Modulation of the peripheral olfactory response by trigeminal agonists

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The olfactory epithelium (OE) contains both olfactory sensory neurons (OSNs) and trigeminal fibers, one detecting odorants and the other irritants. However, it is unclear if these two chemosensory systems interact. In trigeminal primary cell cultures, we characterized the calcium responses of trigeminal neurons to odorants with different trigeminal potencies. Using electro-olfactograms (EOGs), we then characterized responses to the same odorants in wild-type (WT) and knockout (KO) mice, which lack the chemosensory trigeminal receptors TRPA1 and TRPV1. The TRPA1 agonists, allyl- isothiocyanate (AITC) and cinnamaldehyde (CNA), showed reduced EOG responses in KO compared to WT mice. No significant differences were observed in response to the odorants pentyl acetate (PA), β-phenyl ethyl alcohol (PEA), both with low trigeminal potency, and the TRPM8 agonist, menthol. Furthermore, brief activations of peptidergic trigeminal fibers by strong trigeminal agonists (AITC and CO 2) induced a progressive decrease of OSN responses to a pure olfactory stimulus (PEA). Such modulation is lacking in KO mice and also in the WT when stimulating trigeminal fibers with menthol. Interestingly, when stimulated with CNA or PA, moderate TRPA1 agonists, PEA responses in WT were increased compared to the KO.
We conclude that irritants can modulate EOG responses. We determined that the trigeminal and olfactory systems interact in the OE, with the trigeminal system potentially having a bimodal modulation on olfactory responses. Strong trigeminal irritants cause a reduction of the odor response, while moderate trigeminal agonists might induce an enhancement. The relatively slow (minutes) temporal dynamics of the trigeminal modulation of olfactory responses, and the lack of any modulation by agonists of non- peptidergic fibers (menthol), suggest a mechanism of olfactory modulation mediated by TRPA1/V1 positive trigeminal peptidergic fibers.

Fri-P2-071

Analysis of adult neurogenesis in the mouse vomeronasal organ

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Throughout the lifetime of a rodent, sensory neurons in the vomeronasal organ (VNO) are continuously replaced by adult neurogenesis. However, the precise physiological processes that characterize adult neurogenesis in the VNO remain unclear. Here, we will begin to describe characteristics of neurogenesis in the vomeronasal sensory epithelium. We aim to label newly generated vomeronasal sensory neurons (VSNs) using a novel genetic approach: upon tamoxifen injection, neuronal stem cells in Id2CreER^{T2} :: Rosa26R-tdTomato mice express tdTomato upon coincident Id2 promoter activity. Descendants of these stem cells are thus labelled by red fluorescence. Using the Id2 stem cell marker as a VSN lineage tracer, we describe (i) the proportion of new-born neurons within the VSN population. Furthermore, we identify (ii) the epithelial position and morphology of individual new-born neurons and characterize their age-dependent migration patterns within the sensory epithelium. Finally, by analysing marker protein co-staining of tdTomato-positive cells, we assess the differentiation and maturation state of new-born neurons after 1, 3, 7, 14, 21, and 57 days post injection.

Fri-P2-072

Odor direction sensing with stereo antennae improves simulated odor source localization in realistic turbulent plumes

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A recent study suggested that Drosophila exploit lagged temporal correlation in odor signals between their antennae for navigation [1], similar to the Reichardt-Detector-model measuring optical flow in the fly's eye [2]. Here we ask how well this "odor-flow" navigation strategy works in realistic plumes.

Turbulent plumes were recorded in a wind tunnel using Planar Laser-Induced Fluorescence [3]. Recordings cover near-bed (NB) and mid-air ("free-stream", FS) gas release configurations, since plumes exhibit different behaviors depending on odor release and sensing height.

We simulated Drosophila-inspired virtual agents performing source localisation in these plume recordings. The agents turned and moved depending on the odor signal they received in each timestep. Direction-sensing (DS+) agents turned towards the odor when odor-flow (lagged correlation between antennae) was above a threshold. Otherwise, they followed the DS- strategy: turn and move in upwind direction when odor concentration is above a threshold; or pursue a random walk below threshold.

DS+ agents reached the source in 77% of the trials in NB plumes, and 45% in FS conditions, while DS- achieved 74% success rate in NB and 30% in FS conditions, after optimization of all parameters for each combination.

Our results suggest that odor-flow detection via stereo antennae could be most beneficial in NB conditions, consistent with walking flies, and to a lesser amount in FS conditions. We plan to validate these strategies using robotic agents, with a view toward improving real-world odor source navigation.

References

[1] Kadakia et al. (2021) biorxiv https://doi.org/10.1101/2021.09.29.462473

[2] Haag et al. (2004) PNAS https://doi.org/10.1073/pnas.0407368101

[3] Connor et al. (2018) Exp Fluids https://doi.org/10.1007/s00348-018-2591-3

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Fri-P2-073

Angular Gyrus takes part in the processing of odors associated to well-being- a finding from 2 consecutive neuroimaging studies

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Objective- A lot is known about the effect of odors on mood, cognition and behavior. We investigated the central nervous processing of odors with and without an association to well-being (WB) in two consecutive studies.

Methods-The experiment included 2 parts: pre-testing and fMRI scans. During pre-testing subjects rated intensity, valence and WB association for 14 (study 1) and 8 (study2) different odors. Pre-testing resulted in selection of two odors as WB associated and two odors without WB association or neutral odors. These odors were further delivered to the subjects that underwent fMRI scanning.

Results-In study 1, WB associated odors when compared to neutral odors showed increased and only activation in the right angular gyrus whereas in study 2 along with left angular gyrus, other olfactory and emotional processing areas such as anterior cingulate cortex, inferior and superior frontal parts along with left posterior orbitofrontal cortex were activated. In both the studies subjects filled up WB questionnaires, scores of which were controlled during analysis.

Conclusion-The consistent involvement of the angular gyrus in wellbeing related odor processing in these two independent studies suggests that angular gyrus may have a key role when attention shifts towards the presented stimuli with high reference to emotions, value and meaning.

Fri-P2-074

Validation of novel odor delivery presentation for human olfactory testing

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Careful control of perceptual stimuli is essential for collecting robust psychophysical data. In static olfactometry, odors are commonly diluted in an odorless solvent and presented to panelists in a rigid container. In this delivery method, the amount of odor is typically quantified as a liquid dilution rather than the concentration in vapor phase. While the number of molecules present in the vapor phase at steady state follows Raoult's law for ideal solutions or Henry's law for ideal dilute solutions it is not uncommon to observe deviations from these laws (Haring, 1974). In addition, sniffing from a rigid container draws in room air along with the stimulus, thereby diluting the stimulus. To address these issues, we developed a static odor delivery system that uses gas-sampling bags. To validate this method, 15 trained panelists rated the perceived intensity of seven concentrations of two odors (benzaldehyde and 2-heptanone) on a generalized Labeled Magnitude Scale for both gas-sampling bags and glass jars. Panelists more consistently reported the intensity of the gas-sampling bags ($r = 0.88$) than the glass jars ($r = 0.81$, $p < 0.005$). In addition, the maximum reported intensity of a fitted concentration-intensity curve was higher for gas-sampling bags than for jars ($p < 0.001$) - and odors had different max intensities in bags ($p < 0.001$), but not jars ($p = 0.93$). Gas-sampling bags are a valuable tool for olfactory psychophysics, eliminating the need for liquid solvents and the confound of dilution from room air.

Fri-P2-075

Delivering olfactory stimuli based on odor categories for multimedia contents as a feasible method

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Although we have five senses to perceive numerous stimuli, multimedia has mainly focused on visual and auditory senses. As one of the attempts to extend senses used in multimedia, olfactory stimuli have been used in multimedia content to enhance the sense of multimedia's reality. Matching odors with objects in scenes is mainly conducted when selecting odors for multimedia. However, it is impractical to select and offer all odors matched with all objects in scenes to viewers. As an alternative, offering an odor in a category was suggested to represent odors belonging to the category. Indeed, matching odors based on these categories has been used in the multimedia and film industries. However, it is still unclear whether viewers' responses to videos with multiple odors (e.g., rose, lavender, lily) from a category (e.g., flower) can be comparable. Therefore, we studied whether odors belonging to the same categories could be similar by monitoring congruency and five frequency bands (delta, theta, alpha, beta, and gamma) of the EEG data in videos. We conducted questionnaires and EEG experiments to validate the effects of odors belonging to similar categories. Our result showed that odors in similar odor categories had higher congruency to videos than those in the different odor categories. Our EEG data mainly clustered delta and theta bands when odors were offered in similar categories in both videos. Primarily, the theta band was related to neural signals of odors during olfactory processing. However, alpha, beta, and gamma bands were not clustered depending on the categories despite being related to human emotional responses. Our studies showed the possibility that choosing the odors based on odor categories in multimedia can be partially feasible.

Fri-P2-076

Electrophysiological and morphological characterization of periglomerular cells in the mouse accessory olfactory bulb

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The mouse accessory olfactory system plays a key role in detecting chemosignals during social interactions between conspecifics. Sensory information is detected by the system's peripheral structure, the vomeronasal organ, and information is sent via the vomeronasal nerve to the accessory olfactory bulb (AOB). At this first central stage of information processing, AOB mitral cells (AMCs) receive excitatory synaptic input from vomeronasal sensory neurons via multiple glomeruli. Local interneurons surrounding glomeruli are collectively identified as periglomerular cells (PGCs). The physiological function(s) of this AOB neuron population remains elusive. Furthermore, it is unknown whether PGCs form a homo- or heterogeneous neural population. Here, we detail the biophysical properties of PGCs by performing whole-cell patch-clamp recordings from visually identified PGCs in acute slices of the mouse AOB. In addition, after labeling PGCs with biocytin via diffusion loading or single-cell electroporation, post-hoc morphological analysis allows correlation of structural and functional characteristics. Cell-type specific features are determined by analyzing passive and active membrane properties. Voltage-dependent currents, including potassium, sodium and calcium currents, display distinct activation and inactivation properties. With fast action potential kinetics, PGCs discharge at relatively high frequencies. Our results reveal both the biophysical properties and morphological features of an elusive AOB neuron population and, thus, provide first insight into physiological PGC characteristics.

Fri-P2-077

The primacy model and the structure of olfactory space

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Understanding sensory processing relies on establishing a consistent relationship between the stimulus space, its neural representation, and perceptual quality. In olfaction, the difficulty in establishing these links lies partly in the complexity of the underlying odor input space and perceptual responses. Based on the recently proposed primacy code for concentration invariant odor identity representation and a few assumptions, we have developed a theoretical framework for mapping the odor input space to the response properties of olfactory receptors. We analyze a geometrical structure containing odor representations in a multidimensional space of receptor affinities and describe its low dimensional implementation, the primacy hull. We propose the implications of the primacy hull for the structure of feedforward connectivity in early olfactory networks. We test the predictions of our theory by comparing the existing receptor-ligand affinity and connectivity data obtained in the fruit fly olfactory system.

Fri-P2-078

Neuronal organization of the olfactory bulb in adult zebrafish

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Transformations of sensory input by the olfactory bulb (OB) are considered fundamental for downstream processing and memory. To understand the composition and wiring of the OB >400 neurons were reconstructed at ultra-structural resolution in an automatic segmentation of a SBEM volume (~18% of adult zebrafish OB volume).

Using multiple classification approaches we identified 10 distinct morphological classes of interneurons (INs) and three subclasses of mitral cells (MCs), the major type of projection neuron (PNs). The reconstruction of hundreds of PNs within the same brain allowed me to determine ruffed cells (RCs) to be an integral part of a zebrafish glomerulus and uncover anatomical evidence implicative of a paracrine interaction between MCs and RCs. Further, this investigation revealed that the majority of IN classes contradict the Law of Dynamic Polarization, i.e., axonless IN classes making reciprocal, dendro-dendritic synapses clearly dominate in zebrafish OB. In addition, I found the large and widespread

anatomy of deep layer INs in agreement with a widely distributed interaction with MCs as it has been proposed for mammals.
A qualitative assessment of synaptic and non-synaptic physical interactions between INs and PNs revealed differences between superficial and deep layer IN classes. Reciprocal dendro-dendritic synapses were frequent and interactions suggestive of paracrine transmission were observed between specific neuron types. Furthermore, we discovered a striking preference in individual IN classes for specific interactions with one of the two mayor PN types.

Fri-P2-079

Patients with Parkinson's disease share a unique olfactory perceptual fingerprint

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Although the olfactory decline in Parkinson's disease (PD) precedes the motor symptoms by several years or decades, it has yet to provide for a specific early biomarker in PD. Typical olfactory tests probe olfactory performance, in tasks such as detection, discrimination, and identification. Because of the myriad possible causes for the decline in olfactory performance, such performance-based tests lack specificity. An alternative to performance-based tests is the olfactory perceptual fingerprint (OPF). OPFs characterize how the world smells to an individual. OPFs are related to genetic makeup (Secundo et al., 2015), and provide specificity where performance-based tests do not (Weiss et al., 2020). To test the hypothesis that PD is associated with a specific typical OPF, we tested 10 PD patients (9M, mean age = 66.3 ± 7.4 years, disease duration = 9.3 ± 7.9 years, MDS-UPDRS total score = 57.9 ± 21.6) and 10 healthy controls (9M, mean age = 64.9 ± 5.4 years) using 10 odors and 11 descriptors. We found that OPFs were similar within the two groups but significantly different between them. In other words, healthy participants had higher descriptor correlations with other healthy participants, rather than with the PD group (paired t-test, t(8)=-3.05, P=.01), and PD participants had higher descriptor correlations with other PD participants, rather than with the healthy group (paired t-test, t(8)=-2.46, P=.03). Moreover, we could use OPFs alone to classify PD (unsupervised k-means clustering, 90% specificity, 70% sensitivity). These pilot data raise the possibility of a specific olfactory biomarker in PD.

References:

Secundo L, Snitz K, Weissler K, et al. (2015). Individual olfactory perception reveals meaningful nonolfactory genetic information. PNAS. 112:8750-5.
Weiss T, Soroka T, Gorodisky L, et al. (2020). Human Olfaction without Apparent Olfactory Bulbs. Neuron. 105:35-45.e5.

Fri-P2-080

Patients with persistent or transient Covid19-related olfactory deficits show a different gene expression pattern in the olfactory mucosa

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Objective: COVID-19 (C19) is caused by SARS-CoV-2, a Beta-Coronavirus eliciting a variety of symptoms, which may involve the chemical senses. It may replicate in the olfactory epithelium, triggering olfactory dysfunction and possibly anosmia. Olfactory symptoms may last for weeks or months, thus pertaining to the Long Covid-19 disease. In order to unravel the determinants of olfactory symptom persistence, we examined olfactory mucosa from patients with different symptoms.
Methods: We enrolled twenty-one patients (Comitato Etico Sperimentazione Clinica prot. N. 056881) after their recovery from infection, and assigned them to one of the following groups: C19 with persistent olfactory symptoms, C19 with transient olfactory symptoms, C19 without olfactory symptoms and controls (never had C19). Cells from the olfactory mucosa were harvested and their transcriptome analyzed. Olfactory performance was assessed with Sniffin' Sticks.

Results: The expression profile of miRNA appeared significantly altered after C19 infection, despite no relationship with olfactory symptoms was found. However, RNA-seq showed gene expression levels is altered for a long time after infection. Patients with persistent anosmia have altered levels of expression of genes involved in the neutrophil-mediated immune response and zinc homeostasis.
Conclusions: We suggest that miRNA are not directly involved in the appearance of C19-related olfactory disturbances, while the pattern of gene expression allows to segregate the four clinical groups and may suggest involvement of some pathways in olfactory symptoms persistence.
Funding: CARIPARO NEUROCOVID 2020 to AC, GO, AA, CP, CM.

Fri-P2-081

Molecular odor characteristics and their influence on perception in healthy individuals and subjects with olfactory dysfunction.

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The way odors are perceived by humans is determined by their chemical structure. The association of physico-chemical properties of the stimulus with the corresponding perception is so far incompletely understood and known only for some specific functional groups. Furthermore, the role of olfactory disorders on the perception of odorous substances with different chemical structures has rarely been studied before. With this study, we investigate the way in which subjective measures of human odor perception are related to the chemical properties of odor molecules and to what extent the perceptual impression differs between healthy participants and patients with olfactory disorders.
For this purpose, we examine a sample of 240 healthy volunteers and 120 patients with reduced olfactory performance (hyposmia and anosmia). From all healthy participants and patients, sociodemographic and questionnaire data on personality, mental health and odor significance are collected in an online survey conducted at the participants' homes. In a subsequent examination session, ten chemically different odors are first freely described and then evaluated according to various predetermined descriptors using visual analogue scales or dichotomous questions. Each participant completes a Sniffin' Sticks test for objective assessment of their olfactory function.
We present the olfactory perception of pleasantness and intensity for the first 30 healthy subjects and the first 30 patients. We focus on a comparison between and within healthy participants and participants with hyposmia or anosmia. The relationship to the chemical structure as well as inter-individual differences in the perception of the odors are considered. Qualitative descriptors are analyzed in an exploratory fashion.

Fri-P2-082

Chemosensory functions in patients with inflammatory bowel disease and their association with clinical disease activity

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Purpose: Decreased olfactory and gustatory functions are present in various systemic autoimmune diseases. However, little is known about the chemosensory functions of patients with inflammatory bowel disease (IBD). The present study aimed to investigate olfactory and gustatory functions in patients with IBD and their correlation with clinical disease activity.
Methods: 103 patients with IBD were included (52 men, 51 women, mean age 40.3 ± 1.2 years) in the present study. Chemosensory measurements consisted of olfactory testing using the "Sniffin' Sticks" test battery and gustatory testing using "taste sprays". The clinical disease activity of patients was graded as remission, mild, and moderate-severe. In addition, inflammatory markers (blood leucocyte count, fecal calprotectin, and C-reactive protein) were recorded.

Results: 70% of IBD patients were normosmic, 30% were hyposmic, and none of them was functionally anosmic; 6% of the patients showed signs of hypogeusia. Patients with moderate-severe IBD reached a higher olfactory threshold score compared with patients with remission (p=0.011) and mild IBD (p<0.001). The BMI of IBD patients was inversely correlated with their olfactory threshold (r=-0.25, p=0.010). Olfactory and gustatory function in IBD patients did not correlate with duration of disease, blood leucocyte count, CRP level, or fecal calprotectin level. However, patients' olfactory function significantly increased after 4 months of TNF-α inhibitor treatment (p=0.038).
Conclusions: IBD patients are more likely to present with hyposmia. Olfactory thresholds were mainly affected. They were significantly associated with clinical disease activity and BMI. As shown in a subgroup, treatment with TNF-α inhibitors appeared to improve olfactory function.
Keywords: Olfactory and gustatory function; smell disorder; taste disorder; inflammatory bowel disease; autoimmune diseases
Funding: intramural funding

Fri-P2-083

Functional connectivity patterns in patients with parosmia

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Introduction:
Imagine smelling a pleasant odor like peach as completely disgusting and unpleasant, as faeces. Very less is known about this condition called "parosmia" which has a direct impact on diet, mental health and quality of life. Among other suggestions, aberrant recovery of olfactory sensory neurons has been suggested as possible explanation for this phenomenon. We aim to study parosmia associated with anosmia and hyposmia using functional imaging and try to explain this shift from pleasant to unpleasant.
Methods:
In total, 152 functional anosmic and hyposmic patients (with and without parosmia) underwent resting state functional magnetic resonance imaging (rs-fMRI) using a 3T scanner (Siemens, Germany). Patients were asked to fixate on a cross during the entire duration of scanning. In total 240 volumes were acquired with a TR = 2060ms. We also acquired a high resolution T1 structural image. Currently, we analysed 6 parosmic patients with functional anosmia (47 ± 13 years, 3 women) and 9 parosmic patients with hyposmia (44 ± 20 years, 6 women) using functional connectivity based on the following seeds: bilateral piriform cortex and bilateral orbitofrontal cortex. Seed based functional connectivity tells which other brain area have similar activity patterns as the seed. All analysis was carried out using FSLv6.0.2 and results are reported at p<0.05 and cluster size>3.1.
Results:
The left piriform cortex was functionally connected with bilateral insula in the group with functional anosmia while the left orbitofrontal cortex was more connected with right dorsal anterior cingulate cortex. In the hyposmic group the left piriform cortex was functionally connected with the bilateral putamen while the left orbitofrontal cortex was more connected with the left prefrontal cortex and left angular gyrus.
Conclusions: Patients with parosmia seem to exhibit different patterns of connectivity in relation o the degree of olfactory loss.
No funding was available.

Fri-P2-084

Validation of SCENTinel in a large COVID-19 testing sample

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SCENTinel, a rapid multifunction smell test, is a candidate tool to enable population surveillance of smell disorders. To examine its potential, we carried out a cross-sectional investigation on a sample seeking outpatient SARS-CoV-2 testing

at Northwestern Medicine sites throughout the COVID-19 pandemic from April 2021. Up to April 2022, individuals conducted 2,413 SCENTinel tests, of which 1,557 (64%) were examined after participants were matched to medical record data containing contemporaneous SARS-CoV-2(PCR) findings. Data collection is still ongoing. These preliminary analyses include data from 1,557 SCENTinel tests (64%, initial N = 2,413) matched with medical record data containing SARS-CoV-2(PCR) results concurrent to SCENTinel completion. This preliminary sample includes 62%F, 76% white, age: 49±16 years old; 4-5% tested positive for SARS-CoV-2 infection (ndelta=50; ndelta+omicron=74). The SCENTinel components (odor detection, intensity, and identification) had moderate-to-high correlations (r=0.35-0.84, average to Cronbach's alpha of 0.44) with the total SCENTinel score. Self-reported smell loss was only related to SCENTinel's odor intensity (r=-0.11). The SCENTinel-overall score was marginally related to SARS-CoV-2+ in the delta group (r=-0.09), with major influence by SCENTinel's odor intensity (r=-0.27), whose mean scores were significantly lower (Cohen's d=-0.76). Both self-reported smell loss and SCENTinel-overall were uniquely predictive of SARS-CoV-2delta+, according to regression analysis. SCENTinel-overall was highly specific (89%) and predictive of SARS-CoV-2delta+, even controlling for self-reported smell loss. The low sensitivity of SCENTinel (28%) could reflect asymptomatic infection.

Fri-P2-085

Is there a common structure to the molecules which trigger parosmia, across a broad range of foods?

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A number of molecules have been identified recently as triggering the perception of disgust when those with parosmia are exposed to coffee (a common trigger). Many of these trigger molecules are highly potent aroma compounds which are formed via the Maillard reaction during thermal processing and have similar structural motifs, often based on sulfur or nitrogen heterocycles.

In an effort to determine whether these molecules, or their structural motifs, are conserved in other trigger foods, we broaden the scope for identification of potential triggers by looking at other foods which are thermally processed (meat, cocoa, toast), those with different volatile profiles (onions and garlic), those that are not traditionally heated (strawberries, bananas, lemons, cucumbers, cola drinks) and toothpaste which is one of the major triggers.

For this study we used GC-Olfactometry – an instrumental method which separates the volatile components in the headspace of any food and allows the participants to smell and assess the molecules one by one as they elute from the end of the GC-column. The participants are asked to describe each aroma, rate its intensity and indicate whether it contributes to the sense of disgust which they perceive when exposed to these trigger foods. GC-mass spectrometry was carried out on the same samples to identify the trigger molecules. The foods were each assed by 3-6 parosmic participants.

For thermally processed foods, we find that the trigger molecules are often the same as those found in coffee, and their common source is the Maillard reaction. For onion and garlic, although the molecules are different, the thiol/sulfide/disulfide motif is present in most of the trigger molecules. For fruits and vegetables, some new trigger molecules were identified.

The implications for our understanding of the underlying mechanism of parosmia will be discussed.

Fri-P2-086

Association between olfactory mental imagery and smell abilities in individuals affected by COVID-19

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Research on the ability to form olfactory images has received little attention as compared to other sensory domains. Olfactory mental imagery is represented along a continuum with experts (e.g., perfumers) and anosmic individuals presenting the strongest and weakest ability, respectively. The Vividness of Olfactory Imagery Questionnaire (VOIQ) is the most used tool to assess olfactory imagery ability. Following the idea that individuals with smell loss, a frequent and often long-term symptom associated with COVID-19, exhibit reduced olfactory imagery, we aimed to quantify and compare the olfactory imagery ability of individuals affected by COVID-19 (COVID+, n=98) and without COVID-19

(COVID-, n=66). Participants completed the VOIQ online where they had to mentally evoke four different situations of everyday life and think of four different odors in each one. They rated the vividness of the imagined odors on a 5-point scale; lower scores indicate higher olfactory imagery ability. Participants also completed the Smell-&-Taste-Check by the Global Consortium for Chemosensory Research, which included self-reports on smell, taste and chemesthetic abilities and direct intensity ratings of household items. The COVID+ group showed reduced olfactory imagery ability ($p=0.034$) as compared to the COVID- group, as well as reduced smell ability ($p<0.001$) and experienced intensity of odor items ($p=0.012$). As expected, VOIQ scores were negatively correlated with smell ability ($r=-0.42$, $p<0.001$) and experienced intensity ratings ($r=-0.39$, $p<0.001$). Conversely, smell ability and experienced intensity correlated positively ($r=0.62$, $p<0.001$); all associations were stronger in the COVID+ group. Our results suggest that olfactory mental imagery, as assessed via the VOIQ, could be an economic and fast means to screen for smell ability in individuals with acquired olfactory dysfunction due to COVID-19.
This work was funded by the University of Trento.

Fri-P2-087

Development of a chemical-perceptual space of olfaction

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As a chemical sense, the molecular structure of an odor determines whether and how it is perceived by humans. However, a clear stimulus-percept mapping as in other sensory systems is yet unknown and studies with large psychophysical datasets remain scarce. The aim of this study is to investigate the ways in which measures of human odor perception are related to the chemical properties of odor molecules and the extent to which personality traits and experience with odors influence them.
To achieve these goals, a sample of 1200 healthy young participants receive a set of ten out of 74 monomolecular odors, which differ in their position in a physicochemical space of odors. The odors are first freely described and then rated according to perceptual dimensions such as pleasantness, intensity, and familiarity. In order to account for interinvididual differences, participants fill in questionnaires about their personality, odor significance and socio-demographic background.
We will present results from the first 500 study participants and focus on relations to chemical structure as well as interinvididual differences in perception.

Fri-P2-088

A semantic analysis of parosmia identifying underlying semantic factors and determining parosmia severity on the basis of natural language data

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Parosmia is an olfactory disorder that involves distortions of specific odors (e.g., experiencing the smell of freshly brewed coffee as rotten fruit). Parosmia for some odors may co-occur with anosmia for other odors. Little is known about which odors are most frequently parosmia triggers, and tools for determining parosmia severity are lacking.
We present a new approach to understand and diagnose parosmia that is based on semantic properties of words associated with specific odors. Using a new data-driven method based on natural language data (Hörberg et al. 2020; Hörberg et al. under review), we identified 38 source-based olfactory descriptors (e.g., garlic) that are evenly dispersed across a large olfactory-semantic space. Parosmia patients (n = 48) classified these 38 descriptors in terms of whether their corresponding odors were perceptually distorted (i.e., parosmic), or whether they were completely odorless (i.e., anosmic). We then investigated whether these parosmic and anosmic classifications are related to lexical-semantic properties of the original words. We found parosmic experiences to most commonly be reported for words denoting unpleasant odors of inedibles that are highly associated to olfaction (e.g., excrement). Anosmic experiences, on the

other hand, were most frequently reported for words that describe highly specific odor experiences of edibles but that are less strongly associated to olfaction (e.g., pistachio) in comparison to other descriptors (e.g., perfume).
Based on PCA modeling of our data, we finally derived the Parosmia Severity Index-a measure of the severity of parosmia that can be determined solely on the word classification task. We found this index to be predictive of olfactory sensitivity, self-reported olfactory impairment, and depression. Our work provides a novel approach for investigating parosmia and a novel tool for establishing parosmia severity that does not require perceptual screening with odors.

Fri-P2-089

Self-assessment of olfactory function using the "Sniffin' Sticks"

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A large portion of the general population shows olfactory dysfunction. Hence, it is important to find the best treatment for every patient, starting with a precise and reliable assessment of the disorder. Despite of this, in a clinical context, often there is no place in daily routine for time-consuming procedures. This study aimed to examine if the assessment of olfactory function using the "Sniffin' Sticks" is suitable for self-assessment by the patients. "Sniffin' Sticks" (based on marker-like odor-dispensers) comprise odor threshold, discrimination and identification (TDI) testing designed for execution by medical staff. For this study a TDI set was split into two parts, each containing a modified version of the original set. In the first part medical staff administered the pens, whereas in the second part participants applied the test themselves. The sessions were repeated to assess test-retest reliability; 84 healthy subjects and 37 patients with olfactory dysfunction completed both sessions. Sniffin' Sticks self-assessment was efficient in distinguishing between self-reported healthy subjects and patients with olfactory dysfunction ($p's<0.01$). The overall self-administered Sniffin' Sticks test exhibited excellent test-retest reliability (ICC=0.90, $p<0.01$) and strong correlation with the assisted assessment ($r=0.80$ to 0.83, $p's<0.05$). The "Sniffin' Sticks" test battery is suitable for self-assessment rendering olfactory testing more cost effective and thus more appealing to its broad application in larger segments of patients.
Key words: Self-assessment, Self-test, Sniffin' Sticks, Olfactory dysfunction, Test-retest reliability
There is no funding for the current study.

Fri-P2-090

Retronasal olfaction is relatively less affected in older individuals with subjectively normal olfactory function

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Background: Orthonasal and retronasal olfaction are intimately connected. Still, they exhibit differences. The present study aimed to compare orthonasal and retronasal olfaction at both suprathreshold and threshold levels in a healthy population considering age.
Material and methods: A total of 171 participants with subjective normal olfactory function were divided into 2 groups (Young = 98 participants, mean age = 25.8 ± 5.3 vs. Old = 73 participants, mean age = 68.3 ± 10.6) according to their age. Groups were compared in terms of orthonasal odor threshold and identification (Sniffin' sticks test), retronasal odor threshold (Odor delivery container) and identification (Taste powder).
Results: Both orthonasal and retronasal olfaction decreased with age, while retronasal odor identification tended to decline to a lesser degree than orthonasal olfaction. In addition, retronasal odor identification ability of those unaware of their olfactory loss (hyposmia and anosmia) was less affected than their orthonasal olfaction. Age correlated negatively with orthonasal and retronasal olfaction. Orthonasal and retronasal olfaction related to each other.
Conclusion: In older individuals retronasal odor identification appears to be less affected than orthonasal odor identification. This may be partly due to differential changes at the level of the olfactory mucosa. The maintained retronasal olfactory function probably helps to maintain the pleasures of eating, contributing to the unawareness of the gradual age-related olfactory loss.
Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Fri-P2-091

Recognizing emotions triggered by fragrances using virtual reality and physiological measurement.

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Introduction: The analysis of human physiological responses to stimuli is a topic of interest to both academic and industrial researchers. Emotion identification remains a challenge due to: i) the difficulty of labeling an odor-induced emotion, ii) the lack of a reference database that can be used to associate physiological data with the emotional label. We developed a new methodology based on the combination of a self-report survey and physiological analysis. The identification of an emotion is determined by a comparison of olfactory and visual responses, the latter being previously associated with an emotion. Our protocol paves the way for accurate labeling of odor-induced emotions.
Method: 30 participants without smell disorder (mean age 37.6 +/- 10.4, 26 females) were recruited. They were stimulated by 22 selected raw materials, 31 fragrances and 20 virtual reality movies. Physiological data such as heart rate, skin conductance, and respiratory volume were collected from the participants. Participants were also asked to rate the valence, arousal, intensity, and naturalness of each stimulation. K-means clustering analysis was performed with the olfactory and visual stimuli. Stimuli were clustered using k-means analysis.
Results: 13 relevant groups of responses were obtained. The intra-class variation is about 1.90 and the inter-class variation is about 6.43. Videos with the same emotional label were associated in the k-means clustering. Each cluster is defined by at least one emotional term. Olfactory stimulations are classified in those groups.
Discussion: The results show that the response patterns following an olfactory stimulation are comparable to those obtained during virtual reality stimulation. We were also able to highlight the importance of the subjective perception of the stimulation on the responses and finally on the triggered emotion.
Conclusion: This methodology involving virtual reality allows to easily create databases of emotional references.

Fri-P2-092

Environmental signal interactions impact the food choice behaviour in mice

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The ability to search for food and to acquire environmental knowledge is vital for animal survival. Most of this knowledge comes from olfactory sensing via multiple olfactory systems. For example, a mouse that has eaten a novel source of food is able to socially transfer its expertise to littermates, a behaviour known as “Social Transmission of Food Preference” (STFP). This behaviour implies the activation of the neurons of the Main Olfactory Epithelium (MOE). On the other hand, the essential environmental detection of predator scents to avoid predation in the wild takes place via the activation of the Grueneberg Ganglion (GG) neurons.
We demonstrated thanks to immunostainings that the MOE and the GG neuronal projections into the olfactory bulb (OB) interact via periglomerular cells suggesting a potential signalling collaboration. To assess this notion, we investigated the STFP under different environmental conditions in vivo in mice. We showed that the STFP process is impacted by the presence of danger cues increasing the acquisition of food preference and highlighting the interaction between the GG and the MOE signals. Interestingly, in the process of these STFP experiments, we identified a subpopulation of mice unable to perform STFP correctly and to acquire a food preference. They displayed an increased number of oral-nasal investigations, which moreover lasted a significantly longer time. In the light of these results, we decided to assess the phosphoserine 6 expression in the MOE of these mice with immunostainings and western blots. Interestingly, we observed that they showed an alteration of MOE neuronal activation. We are further investigating these mice at the odorant detection level with calcium imaging experiments and at the signal integration level looking at OB glomeruli activation. Our findings might lead to the identification of a new gene or of a gene population playing a role in odorant detection and thus in the food decision-making.

Fri-P2-093

Odor threshold differs for some but not all odorants between older and younger adults

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Objectives of the study: Olfactory function deteriorates with age, and definitive mechanisms by which this decline occurs are likely multifactorial. The present study, conducted on a large cohort of healthy participants, aimed to investigate whether olfactory thresholds would differ for variable odors with different physico-chemical (e.g., heavy vs light weight molecules) and perceptual characteristics. Experimental methods used: In 81 participants (51% ≥ 50 years old), we assessed odor threshold in two sessions. Essential results: Linear Mixed Model analyses revealed that odor thresholds in younger and older adults changed with different odor conditions, presumably due to the common exposition to some of the odors, their trigeminality, and lipophilicity. This effect was observed for piperine, eucalyptol, 2-nonanone, gamma-valerolactone and pinene alpha, but not for the other 15 odorants studied. Furthermore, suprathreshold perception, i.e., intensity and, to some extent, irritation, contributed independently to sensorial odor detection, the later ones particularly in older adults. We also found that the molecular weight of the odorants did not add to their detection by, respectively, younger and older adults. Conclusions: To conclude, the present findings are in line with previous studies showing that the age-related change of chemosensory abilities is a multifaceted phenomenon, which does not affect all odorants. Identification of sources of funding: none.

Fri-P2-094

Why do we like so much the smell of roses: relationship between odorant compounds and perception

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Rose is one of the most widely cultivated ornamental plants in the world. In particular, its fragrance is known to be very pleasant and attractive to humans. Here, we aimed to understand if particular volatile odorant compounds (VOCs) play a role in such pleasantness or if it is due to the mixture of several compounds. To this end, 20 participants smelled 10 freshly picked modern roses. The perceptual and conscious characteristics associated to the roses were measured through quantitative ratings (on pleasantness, attractiveness, intensity, familiarity, "fruity", "lemony", "floral" and "rosy" quality), as well as analysis of motor behavior (speed and distance of approach/withdrawal, duration of sniffing and number of samplings, all reflecting inconscient motivation to approach the odor source). Using perceptual rating, we first revealed that the 10 roses present different levels of pleasantness, wanting, familiarity, intensity, floral and roses perception.

VOCs emitted by the different roses were then captured by headspace and analyzed by gas chromatography coupled with mass spectrometry. Principal Component Analysis and correlation analysis were used to reveal relationships between biochemical, perceptual and behavioral spaces. First results show that there is a positive correlation between the quantity of some VOCs and several perceptual and behavioral parameters, providing new information about the complex relationship between chemical composition and perception of roses in humans. This work was funded by Pack Ambition Recherche from the AURA Region and supported by CNRS, INSERM and University Jean Monnet of Saint-Etienne.

Fri-P2-095

Episodic memory evoked by odors, musical excerpts and faces: modality-specific effect of wanting, but modality-unspecific effect of pleasantness.

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The aim of this study was to unravel the effects of emotion and sensory modality of the memory cues, as well as their potential interaction, on episodic memory retrieval. Using a non-immersive virtual reality device presenting a three-room house, participants freely and incidentally explored three unique rich episodes over three consecutive days. Episodes were constructed around the three dimensions characterizing episodic memory: What (odor, music, face), Where (the rooms: bedroom, living room, office), and in Which context (the periods of the day: daytime, nighttime or twilight). During retrieval, on the fourth day, participants were told to recognize the encoded odors, music and faces among distractors and to select both the room and the period in which they have encountered the stimulus at encoding. Participants then rated each cue in terms of pleasantness, emotional intensity and motivation (i.e., to be perceived again). Results demonstrated that episodic memory retrieval was influenced by both the sensory modality and the emotion of the memory cues, the two dimensions interacting with each other. In a modality-unspecific manner, recognition and episodic memory were improved for the most pleasant and unpleasant cues. Moreover, odors were shown to be the most powerful memory cues. EM scores were higher when odors were rated as being more motivational. Musical excerpts specifically led to high levels of recognition memory, which was favored by the emotion (emotional intensity, motivation) of the cues, but no episodic retrieval. Faces evoked the retrieval of the period of the day only, and it was not influenced by emotional evaluations of the cues. These findings highlight the power of odors to evoke complex associative memories, such as episodic memory, probably via its links with motivational processes. This work was supported by the Lyon Neuroscience Research Center, and Lucile Rey was funded by the Roudnitska Foundation.

Fri-P2-096

OR7C1: a new mediator of melanogenesis

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ChemCom s.a.

Olfactory receptors (ORs) belong to the family of G-protein-coupled receptors and are expressed in olfactory neurons where they play a critical role in the recognition of thousands of odorants by the olfactory sensory system. Many ORs are also ectopically expressed in non-sensory tissues where they mediate a variety of cellular functions. Here, we expressed different OR7C1 variants in HEK293-RTP1/RTP2 cells and identified 44 agonists of this receptor using a luciferase reporter gene assay. In addition, we detected the expression of this OR at the transcriptional level (RNAseq and RT-PCR) in primary cultures of human epidermal melanocytes from different ethnical origins. Interestingly, a 4 days stimulation of these cells with OR7C1 activators led to an accumulation of eumelanin both intracellularly and in the culture medium, without any effect on cell viability (MTS). We further demonstrated that melanogenesis can be stimulated dose-dependently in human skin explants from different donors using OR7C1 agonists AmberKetal® and Ambermax®, while leaving skin explants viability or melanocyte proliferation unaffected. Finally, immunostaining of tyrosinase, a key player of melanin synthesis, revealed a significant 16% increase of this enzyme expression in skin explants after treatment. Altogether, our findings demonstrate that OR7C1 is expressed in human melanocytes and its activation by agonists identified in house can modulate melanogenesis, probably by increasing the tyrosinase expression. Both in-vitro and ex-vivo increases of melanin production are in the range of those elicited by UVB or by a benchmark product used in the same time interval. Clinical studies aiming to evaluate the potential of OR7C1 agonist as UV-free tanning agents on healthy volunteers are currently ongoing. This work is the subject of the patent application WO2021260168.

Fri-P2-097

Study of feline olfactory receptors using a computational reverse chemical ecology approach

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Semiochemicals can induce physiological and behavioural responses using chemical communication in mammals. These molecules can be detected by the olfactory receptor (OR) in the main olfactory epithelium (MOE) and trigger signals to the olfactory bulb and to the brain regions. Several computational studies have been reported about the structural modelling of mouse and human ORs and the receptor deorphanization from the ligands. However, the experimental structures of ORs are unavailable. Therefore, in silico studies are necessary to build the OR models. In this study, we aimed to deorphanize ORs of cats using semiochemicals and related odorants. We used a computational "reverse chemical ecology strategy" on cat ORs to analyze the conservation, phylogeny, and topology and to build models to identify their ligands. We have selected 54 deorphanized human ORs and found the feline orthologs using 10 human ORs which are known to bind at least 5 semiochemicals and odorants. The present results showed that cat ORs sequences share an average of 80% to 90% identity with other mammals. Phylogenetic studies showed the evolution between cat ORs and other mammalian orthologs of the 10 selected ORs. Further, the cat ORs were screened based on the 7-transmembrane (TM) OUT topology analysis. Then, the 6 selected OR sequences were modelled using multi-template modeling and 3 of them (OR1A1, OR2W1, OR52D1) were validated by dynamics simulations with a lipid membrane (DPPC). The virtual screening and docking study showed that the cat ORs depicted potential interactions with the ligands of the human ORs and the ligands of IRSEA patents CAP, FFP, and FIS. The androstadienone, linoleic acid, and oleic acid were evaluated as best-fit ligands by the binding-free energy, H-bonds, and 2D residual interactions. The results revealed that the best-fit ligands would be suitable for deorphanizing the receptor models, which will improve the understanding of chemical communication in cats.

Fri-P2-098

Olfactory habituation to food and non-food odours during fasted and fed states

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Olfactory habituation is a reduced behavioural response to repetitive odour stimulation which can be modulated by both bottom-up and top-down processes. Edibility is a top-down feature that can affect olfactory perception, but whether and how it can modulate olfactory habituation remains unclear. Further, food stimuli attract attention due to their intrinsic salience, which might slow down habituation. Here, we investigated whether olfactory habituation shows a different trend to food or non-food odours. Fifty participants were tested under fasted and fed states in separated sessions. In each session, participants were exposed to the same food and non-food odour in blocks of 20 trials. They rated the perceived odour intensity and pleasantness after each trial. Linear mixed-effects models showed that, regardless of the participants' hunger state, the perceived odour intensity decreased over time only for non-food odours ($p=0.007$). Conversely, the odour pleasantness decreased more significantly across trials for food (vs. non-food) odours ($p<0.001$). Our results showed that odour edibility modulates olfactory habituation, supporting the olfactory specific satiety theory, which describes a decrease in the pleasantness of an odour of food repeatedly smelled, without changes in the perceived intensity. However, the influence of other bottom-up features (e.g., trigeminality) cannot be ruled out. To minimize such influences, we are conducting an experiment in which participants complete the same habituation paradigm while being presented with a perceptually malleable odour in terms of edibility. The perceived odour edibility of vanilla odour is induced following a conditioning protocol and participants are assigned to one of two groups (edible vs. non-edible). We hypothesize a habituation trend in the edible (vs. non-edible) group like the one obtained in the above research for food (vs. non-food) odours, respectively.

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Fri-P2-099

Visualization of the secondary olfactory pathway in transgenic NBT-Katushka γ-cry Venus Xenopus laevis

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In the African clawed frog Xenopus laevis, class II β-tubulin (tubb2b) is expressed exclusively in neurons, and its promoter is used in different transgenic frog lines. In the frog line NBT-Katushka γ-cry Venus, tubb2b drives the expression of the red fluorescent protein Katushka. In this study, we used tubb2b-dependent fluorescence to visualize the olfactory system from the olfactory epithelium (OE) to the olfactory cortex (OC) and to label olfactory projection neurons (PNs) in the olfactory bulb (OB). We performed immunohistochemical stainings of the whole OE and OB as well as coronal brain sections of premetamorphic NBT-Katushka γ-cry Venus Xenopus laevis. We further injected and electroporated groups and single PNs in whole-mount preparations of the OB with various fluorescent dyes. We found that tubb2b was not active in all neurons of the olfactory system and the forebrain. In the OE, we detected tubb2b-positive cell bodies of olfactory receptor neurons and associated axons in the olfactory nerve. Axon terminals in the OB also show tubb2b-dependent fluorescence. In the OB mitral cell layer, we found tubb2b-positive cells separated into a lateral and medial group. Individual cells of both groups are morphologically similar, but differ in their axonal projection pattern to the OC. We found that axons of medial and lateral PNs divide into two olfactory tracts targeting the subpallium and the ventral pallium. Together, we found that transgenic frog lines, which use the promotor tubb2b, are a great tool to visualize main components of the olfactory system and the forebrain, but notably expression is not panneuronal. Moreover, we found that the secondary olfactory pathway of lateral and medial PNs is segregated into two independent streams that target different areas of the forebrain. Overall, this study builds the foundation for further analysis of odor-processing in larval Xenopus.

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Fri-P2-100

Temporal activity characterization of vomeronasal versus main olfactory system neurons, in behaving mice during associative learning

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The vomeronasal system (VNS) is a chemosensory system which is present in most vertebrates and is devoted to processing cues from other organisms. One of the distinctions of this system from the main olfactory system (MOS) concerns stimulus dynamics. Unlike MOS responses which are coupled to breathing and can follow a sub-second temporal scale, responses in the VNS are dictated by a relatively sluggish uptake by the vomeronasal organ (VNO) and develop over seconds. We have recently shown that in contrast to the main olfactory bulb (MOB), output neurons of the accessory olfactory bulb (AOB), do not support decoding at fine temporal scales (Yoles-Frenkel et al. 2018). However, it was not tested whether fine temporal structure can nevertheless be read by downstream processing stages of the VNS. Here, we exploited the ability of the VNS to form stimulus response associations (Marom et al. 2019), and used optogenetic stimulation in a GO-NOGO paradigm in mice. The optogenetic approach was used as it is challenging to activate one of the two systems without activating the other with natural stimuli. Our approach allowed us to selectively activate projection neurons from either the MOB or the AOB, and compare the ability of behaving, head fixed mice to discriminate various temporal patterns. I will present our latest results regarding the comparison of the two systems' abilities to discriminate between different stimulus durations and patterns of activation. I will also present our findings concerning the comparison of the MOS and the VNS sensitivity to timing relative to the breathing phase, where we tested the ability of mice to discriminate between stimulation patterns presented at the different phases of the ongoing breathing cycle.

Fri-P2-101

The development of a “fear-vitro” system allows the investigation of chemical danger signalling

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Mice are able to sense volatile cues that warn them from danger. This detection is mostly taking place in the Grueneberg ganglion (GG) olfactory subsystem. GG neurons can detect alarm pheromones released by stressed conspecifics to signal danger as well as kairomones involuntarily released in predator biological secretions allowing an interspecies danger communication. The precise signalling pathways occurring in GG neurons are still unclear. We thus focused on the investigation of the different cascade elements in a new in vitro model. We first incorporated the three bitter taste receptors (TAS2Rs) present in GG neurons in a heterologous system using HEK 293 cells and we demonstrated that we could mimic neuronal responses after stimulation with biological secretions from predators. We identified by calcium imaging experiments that the biological secretions from the skunk (Mephitis mephitis) are a potent source of kairomones. Indeed they can activate these TAS2R-expressing cells as well as GG neurons and induce fear-related behaviours in mice. We can thus correlate the fear signalling observed in vivo to ex vivo (GG tissue slices) and to in vitro experiments. We investigated further the other cascade elements such as the cyclic nucleotide-gated channel type A3 (CNGA3), essential for the entry of Ca^{2+}, which induces the depolarization of the membrane after the detection of alerting molecules. The use of pharmacological inhibitors such as L-Cis diltiazem allowed to verify its implication ex vivo. We then additionally transfected CNGA3 in our TAS2Rs in vitro model. We could demonstrate its membrane expression by immunocytochemistry and verify its functionality pharmacologically by calcium imaging using 8 Br-cGMP and a series of inhibitors. We thus managed to “upgrade” our in vitromodel as with TAS2Rs and CNGA3 co-expression we observed a synergistic effect after stimulation by predator danger cues. This “fear-vitro” model can now be used to identify new alerting cues.

Fri-P2-102

The role of purinergic signaling in neuronal stem cell activation and differentiation in the olfactory epithelium of larval Xenopus laevis

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The mechanisms underlying neurogenesis and regeneration after injury are still poorly understood. The olfactory epithelium is a site of continuous cell turnover. Olfactory receptor neurons and non-neuronal supporting cells are constantly replenished from a pool of neural stem cells, known as basal cells. Among others, purinergic signalling pathways have been identified to mediate epithelial damage and initiate regenerative processes. Here, we study the olfactory epithelium of larval Xenopus laevis to specify the purinergic receptors involved and how they link to intraepithelial signalling pathways. Using immunohistochemistry and in situ hybridization, we found that the majority of supporting cells and a subpopulation of basal cells express $P2Y_2$ receptor subtypes. This finding supports that basal cells express additional P2Y receptor subtypes, which remain to be identified. These results also support a differential expression of purinergic receptors based on basal cell type or physiological state. Additionally, we first established a reliable method for cultivating primary cells from Xenopus, which allows us to utilize different molecular and functional approaches. We investigated the response characteristics of these receptors upon application of nucleotides via functional calcium imaging in primary epithelial cell cultures and whole mounts of the olfactory epithelium. ATP was confirmed as a potent activator. Thus, ATP release within the olfactory epithelium is potentially an important part of intraepithelial signalling. The source of extracellular ATP in the olfactory epithelium is still unclear and we are currently searching for possible pathways of nucleotide release.

Fri-P2-103

Heterogeneity of principal neurons in murine olfactory bulb

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The olfactory bulb is an ideal model system to investigate sensory processing given its location, well defined circuitry, and established behavioral paradigms. Despite these advantages, our definition of its projection neurons haven't changed since being first defined in the late 1800s: laminarly arranged mitral cells and diffusely spread tufted cells. In lieu of further classification, few studies discriminate between the two and even fewer pay heed to heterogeneity within cell types. Instead many studies choose to collapse them into a single class: mitral/tufted.

Recent work has illustrated that these neurons encode complementary olfactory information that is reflected in their physiology & morphology, hinting that they may be more distinct than originally described. Using whole-cell patch clamp electrophysiology in acute slices from mice, this project aims to find a simple way to classify projection neurons based on their intrinsic properties.

Immunohistochemistry & DIC microscopy demonstrated that projection neurons in the mitral cell layer are diverse in their soma size; a k-means analysis returned a diameter based classifier that aligns with literature. In our physiological data this classifier divides the cells into putative mitral(pMC) and putative tufted cells(pTC). Preliminary results show that the two populations are distinct in key parameters like action potential threshold (pMC(n=24) 2.8±0.34 pA/pF; pTC(n=12) 5.5±0.98 pA/pF; unpaired t-test p=0.0025) and relative afterhyperpolarization (pMC(n=20) 17.6±0.94 pA; pTC(n=9) 12.6±1.1 pA; unpaired t-test p=0.007) and homogenous in others. These results offer further proof of mitral and tufted heterogeneity and implies that they may be classified and independently evaluated in routine patch-clamp experiments.

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Fri-P2-104

Trace amine associated receptors (TAARs) response to amines are largely affected by sequence variants.

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Volatile amines are recognized by a family of chemosensory receptors: the Trace Amine Associated Receptors (TAARs). Compared to regular olfactory receptors, TAARs are few (6 receptors expressed in the olfactory epithelium) and highly conserved. Thus, polymorphisms in this family can drastically alter our perception of amine compounds.

A joint approach of numerical simulations and in vitro experiments has revealed the activation mechanisms of hTAAR5. hTAAR5-S95P is a polymorphism found at high frequency in Nordic countries. People with this mutation have their perception of trimethylamine affected, making them less able to perceive the rotten fish smell caused by this molecule. Our 3D model captures both the inability of hTAAR5-S95P to be activated by trimethylamine (TMA) in vitro, and the activation of the receptor by different agonists. Long-scale molecular dynamics simulations of the system bound to ligands with different efficacies are performed and recover that the receptor is activated only when stimulated by agonists, capturing the features of a prototypical active state of GPCR. 2 specific features of the TAAR family were studied.

Fri-P2-105

Deciphering the ligand binding properties of the mouse odorant-binding protein OBP5 from Mus musculus

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Odorant-binding proteins (OBPs) are abundant soluble proteins secreted in the nasal mucus of a variety of species which are believed to be involved in the transport of odorants towards olfactory receptors. In this study, we report the functional characterization of mouse OBP5 (mOBP5). mOBP5 was recombinantly expressed as a hexahistidine-tagged protein in bacteria and purified by metal affinity. Oligomeric state and secondary structure composition of mOBP5 was investigated using gel filtration and circular dichroism spectroscopy. Fluorescent experiments revealed that mOBP5 interacts with the fluorescent probe N-phenyl naphthylamine (NPN) with a micromolar affinity. Competitive binding experiments with 40 odorants indicated that mOBP5 binds a restricted number of odorants with a good affinity. Isothermal titration calorimetry (ITC) confirmed that mOBP5 binds these compounds with association constants in the micromolar range. Finally, protein homology modelling and molecular docking analysis revealed the amino acid residues of mOBP5 guiding its binding properties.

Fri-P2-106

Phospholipase C and G proteins are involved in pheromone transduction of the hawkmoth Manduca sexta

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Insect odor transduction employs different mechanisms. In the fruitfly olfactory receptor (OR) olfactory coreceptor (Orco) tetramers underly both, an insensitive ionotropic and a sensitive metabotropic odor transduction pathway coupling to adenylyl cyclase. In hawkmoths Manduca sexta patch clamp recordings of primary cell cultures of antennal olfactory receptor neurons (ORNs) revealed that the first pheromone-dependent current to be elicited was a transient Ca2+ current that resembled IP3 -dependent Ca2+ currents, but not OR-Orco-based non-specific cation currents. Thus, we hypothesized that highly sensitive pheromone transduction in the hawkmoth employs G-protein-dependent activation of phospholipase Cβ. Furthermore, ELISAs measured diurnal oscillations of octopamine-dependent cAMP- and IP3 levels in hawkmoth antennae. Thus, here, in tip recordings of antennal pheromone-sensitive trichoid sensilla in vivo, we tested, whether pharmacological interference with antagonist of phospholipase C (U73122) and of various G proteins interferes with sensitive hawkmoth pheromone transduction. We found that U73122 reduced sensitivity and kinetics of pheromone transduction daytime-dependently. Infusion of Pasteurella multocida toxin that was described to cause declines of cAMP and increases of IP3 levels had variable, not significant effects. However, pertussis toxin that decreases IP3 and increased cAMP levels, and cholera toxin activating Gαs both decreased kinetics and sensitivity of pheromone responses at the end of the hawkmoth´s activity phase. We conclude that hawkmoth pheromone transduction involves G-protein-dependent activation of a phospholipase Cβ. Pheromone transduction cascades vary daytime-dependently, since a circadian clock in ORNs makes different cyclic nucleotide and Ca2+-dependent ion channels available for signal transduction during the sleep-wake cycle of the hawkmoth. [Supported by DFG grants STE531/20-1,2 to MS and GRK2749/1]

Fri-P2-107

Sensory alliesthesia in the following study, characteristics of individual sensory function

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Alliesthesia describes the phenomenon that for the same stimulus, the cued sensory pleasure can be modified according to the internal state. Food sensory alliesthesia (SA) is thus expressed as a difference between pleasures cued by the same food from hunger to satiety states, an experience observed in daily life. Since sensory cued pleasure was intimately linked to food intake, the aim here is to explore what role may be played by the SA in food intake.
In a 5-day experimental protocol, 20 men (20-35 y.o.) were recruited. Olfactory/visual alliesthesia to food stimuli was measured for 14 consecutive meals (4 breakfast, 5 lunches, and 5 dinners). Each alliesthesia measurement consisted of

olfactory and visual tests, 15 min before and 20 min after a meal. The olfactory test consisted of 4 olfactory stimuli representing sweet and salty foods for breakfast, or 10 stimuli representing different food types (sweet vs. salty; starter/main course/dessert) for lunch/dinner. Olfactory stimuli were presented in a bottle labeled with a 3-digital letter code. Visual stimuli were corresponding images of olfactory stimuli, presented on screen in front of the subjects. For each stimulus, participants rated sensory pleasure, wanting to eat, familiarity, and disgust using a line scale displayed on the screen. Our results show that participants had relatively stable alliesthesia from meal to meal during their 5-day stay. Moreover, independent of the level of hunger or satiety, the amplitude of alliesthesia is rather a characteristic of an individual's sensory function. The results of this first study on consecutive measures of SA suggested that, unlike the previous view that the SA may be involved in instantaneous food intake control, the SA in this following study manifests rather as an individual's sensory response profile, which might determine a habitual food intake pattern characterizing an individual food intake behavior.
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Fri-P2-108

Development of Saccharomyces cerivisiae as a platform for high-throughput insect olfactory receptor deorphanization

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Insects are essential to biodiversity and represent key elements of our food supply chains as pollination strongly contributes to global food production. On the flipside, insects are causing devastating swarms and pests affecting agricultural crop yields. Monitoring, understanding, and control of insect behavior is of burning importance for securing prosperous ecosystems and the development of control agents for sustainable pest management and food supply of a growing human population. Seven-transmembrane (7TM) receptors used to detect, communicate and execute timely behavior in diverse environments, as well as in relation to changing endogenous chemical cues are key to insect behavior. A better understanding of 7TM receptors' connections to insect behavior will improve our ability to model and arm insects with improved abilities to help tackle environmental concerns. Deorphanization of insect 7TM receptors using existing platforms (Drosophila “empty neuron”, frog oocyte, and HEK cells) is relatively low throughput. We are working toward developing a novel platform for insect 7TM receptor deorphanization based on the well-characterized and genetically tractable yeast Saccharomyces cerevisiae. In this study, we construct and characterize several calcium reporters in S. cerevisiae for reporting on the functionality of insect olfactory receptors (ORs), which are ligand-gated ion channels. We then expressed insect OR receptor co-receptors (ORCos) and several well-characterized olfactory receptors (ORs) and compare their functionality to that previously reported using more traditional characterization platforms. We also investigate the use of water/oil/water double emulsions for the maintenance of volatile odors during analysis.

Fri-P2-109

Understanding allosteric binding sites as ligand mediated gates in olfactory receptors

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G protein-coupled receptors (GPCRs) constitute a central component of cellular signal transduction processes, and are the major pharmaceutical target for a host of human diseases and disorders. However, the underlying molecular mechanisms by which endogenous ligands access the active site are still unclear. We have recently shown for an olfactory receptor, TAAR13c the presence of a second binding site in a vestibule on the external surface, which blocks the passage of the ligand towards the inner binding site. Hence, such ligand-gating mechanism might constitute a regulatory mechanism to determine ligand sensitivity for an entire class of olfactory receptors. Elimination of the external binding site generated supersensitive receptors suggesting this site to act as a gate. We also observed such a gating for another member of taar gene family, Taar13d and for zebrafish serotonergic receptor 5-HTR4 which is the ancestral gene from which the taar gene family originated. Hence, the proposed gating mechanism for olfactory

receptors surprisingly exhibits pronounced similarity to processes described for access of binding site for some neurotransmitter receptors.

Fri-P2-110

Extensive co-expression of tuning receptors across the olfactory system of Aedes aegypti

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Mosquitoes use their keen sense of smell to identify key resources in the environment. This sense relies on olfactory receptors expressed in hundreds of sensory neurons scattered across the antennae and maxillary palps. Until recently, it was assumed that individual sensory neurons express just one tuning receptor—as is the rule in both vinegar flies (Drosophila) and mice. However, a decade of bulk RNA sequencing shows that there are many more receptors present in adult mosquito olfactory organs than can be accounted for by this one neuron–one receptor rule. To reconcile these observations, we have generated the genetic tools necessary to sort and sequence the transcriptomes of tens of thousands of single neurons from Aedes aegypti antennae. We recover nearly all ~60 types of olfactory sensory neuron and characterize the precise patterns of receptor expression/co-expression therein. Our results have important implications for odor coding and olfactory system evolution in this important disease vector mosquito.

Fri-P2-111

The sensation of nasal obstruction in chronic rhinosinusitis: Involvement of the intranasal trigeminal system

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In chronic rhinosinusitis (CRS), nasal obstruction can be explained by structural deformities, polyps, or edematous nasal mucosa. In some cases, no major deformity or inflammation is present to explain the sensation of nasal obstruction of these patients. Here, nasal obstruction may result from an alteration of the afferent neural pathways of the trigeminal system responsible for airflow perception. The aim of this study is to assess the involvement of the intranasal trigeminal system in reduced nasal patency in CRS.

Methods: We carried out a prospective case-control study of 15 patients with CRS, 18 patients with a deviated nasal septum (DNS) and 16 healthy controls. We used Peak Nasal Inspiratory Flow (PNIF) and Visual Analog Scale (VAS) to assess objective and subjective nasal patency respectively. We further examined sensitivity of the intranasal trigeminal system using the Trigeminal Lateralization Task (TLT) with eucalyptol and cinnamaldehyde. Finally, we measured expression of trigeminal receptors TRPM8, TRPA1 and TRPV1 in mucosal biopsies taken intraoperatively from CRS patients and DNS patients by quantitative real-time PCR.

Results: CRS patients had significantly lower objective ($p=0.046$) and subjective ($p<0.001$) nasal patency than controls. DNS patients scored significantly lower than controls for subjective nasal patency ($p<0.001$). Regarding the trigeminal sensitivity, CRS patients scored significantly lower than DNS ($p=0.047$) and controls ($p=0.005$) with eucalyptol, while no difference was observed for cinnamaldehyde. We did not observe a group difference in the expression of TRPM8, TRPA1 and TRPV1.

Conclusion: The present data suggests that reported nasal obstruction in CRS patients may be linked to a combination of deficient perception of nasal airflow by the trigeminal system and a mechanical obstruction not visible by nasal endoscopy. The association with trigeminal receptors remains to be elucidated.

Funding: Fonds de recherche du Québec – Santé

Fri-P2-112

Cysteinyl leukotrienes and acetylcholine are biliary tuft cell cotransmitters

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Background & Aims: The gall bladder stores bile between meals and empties into the duodenum upon demand, thereby being exposed to the intestinal microbiome. This raises the need for antimicrobial factors, among them mucins produced by gall bladder epithelial cells. The role of the much less frequent biliary tuft cells in this scenario is still unknown.

Methods: Gall bladder contraction and mucin granule exocytosis were measured by force recording and electron microscopy, respectively, in wildtype and genetically modified mice. Stimuli were blue light in an appropriate optogenetic model, expressing channelrhodopsin-2 selectively in tuft cells, and short chain fatty acids. Acetylcholine, prostanoids and cysteinyl leukotrienes were directly assayed in supernatants of stimulated, explanted gall bladders. Reporter mice, in situ-hybridization and immunolabeling localized mediator synthesizing enzymes and receptors.

Results: Selective optogenetic stimulation of gall bladder tuft cells revealed corelease of acetylcholine and cysteinyl leukotrienes. Acetylcholine triggers exocytosis of mucin granules from cholangiocytes through the muscarinic receptor M3, and cysteinyl leukotrienes cause bladder contraction through the receptor CysLTR1. We identify propionate, a major metabolite of intestinal bacteria, as a naturally occurring stimulus activating tuft cells via the short chain free fatty acid receptor 2 and downstream signalling involving the cation channel TRPM5.

Conclusions: Our results establish gall bladder tuft cells as sensors of a microbial product, initiating two independent innate defence mechanisms through cotransmission. Acetylcholine, best characterized as a neurotransmitter, serves here as a paracrine factor triggering epithelial defence, and cysteinyl leukotrienes, known from immune effector cells, target the muscular component, emptying and closing the bladder.

Fri-P2-113

Mucin MUC1: a key protein in oral physiology and the molecular mechanisms of sensory perception of astringency.

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Astringency is a sensation of dryness, roughening, and puckering, occurring during the consumption of tannin-rich foods. Recently, we came up with a new hypothesis on the molecular origin of astringency. It relies on the role of the transmembrane mucin MUC1, which may act as a sensor of the surface of the oral mucosa. MUC1 also participates to the formation of the mucosal pellicle (MP), a thin layer of salivary proteins that lubricates the surface of the oral cells. To check this new theory, we have developed an innovating in vitro model of oral mucosa based on the TR146 oral epithelial cell line. We have stably transfected this cell line with various isoforms of MUC1, which differ by the length of the variable number of tandem repeat modules and the SEA module, which includes a cleavage site leading to the formation of two subunits. The characterization of the cellular models was made upon 3 criteria: the level of MUC1 expression, its addressing to the plasma membrane, and its capacity to anchor salivary proteins, in particular MUC5B.

Then, we studied the impact of MUC1 and its structure on the physico-chemical properties of the MP, using atomic force microscopy coupled with scanning microwave microscopy. It provides information on the surface topography, but also on the impedance, conductance, and dielectric properties at the cells' surface and more deeply in the intracellular compartment. Initial results indicate differences in the structure of the MP and in the local conductance, due to the increase in the dielectric properties, depending on MUC1 isoforms. Moreover, the addition of tannins changed the surface topography by inducing the formation of aggregates, in which the forces of interactions increase significantly. This study demonstrates the impact of MUC1 on the physico-chemical properties of the oral mucosa, impacting probably its interactions with food compounds and in particular with flavor compounds.

Fri-P2-114

Activation of the TRPV1 channel via [6]-gingerol facilitates cellular immune responses in primary human neutrophils

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Clarifying the function of sensory active transient receptor potential (TRP) channels in non-sensory tissue is of growing interest, especially with regard to food ingredients in nutritionally relevant concentrations. The TRPV1 channel may probably be, by far, the most intensively investigated member of the TRP superfamily. However, its function in non-neuronal cell types like blood leukocytes is still under extensive investigation. Neutrophils are the most abundant leukocytes in human blood, accounting for 60-70% of all circulating white blood cells. They are the first immune cells which are recruited to the sites of infection. Besides direct defense mechanisms like ROS production, neutrophils contribute to subsequent immune responses via the release of various cytokines and chemokines.

The study hypothesized the TRPV1 agonist [6]-gingerol to facilitate cellular immune responses of primary human neutrophils, after treatment with 50 nM, a concentration that can be reached in the circulation after habitual dietary intake. RNA expression analyses revealed a high abundancy of TRP channel expression in the types of primary leukocyte investigated, namely neutrophils, monocytes, NK-cells, T-cells, and B-cells. Incubation of neutrophils with 50 nM of the known TRPV1 ligand [6]-gingerol led to an increased surface expression of CD11b, CD66b, and the fMLF receptor FPR1. Upon subsequent stimulation with fMLF, the neutrophils displayed an about 30% ($p<0.05$) increase in CXCL8 secretion as well as in ROS production. Pharmacological inhibition of TRPV1 by trans-tert-butylcyclohexanol abolished the [6]-gingerol induced effects.

In conclusion, the TRPV1 channel is functionally expressed in human neutrophils. Activation of the channel with [6]-gingerol as a food-derived ligand in nutritionally relevant concentrations leads to an enhanced responsiveness of the cells towards activating stimuli, thereby facilitating a canonical cellular immune response of human neutrophils.

Fri-P2-115

Olfactory and vomeronasal epithelia in a transgenic BACHD rat model of Huntington´s disease

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Background. For neurodegenerative diseases such as Huntington's disease (HD), early diagnosis is essential to treat patients and delay symptoms. Impaired olfaction, as observed as an early symptom in Parkinson´s disease, may also constitute a key symptom in HD. However, there are few reports on olfactory deficits in HD. Therefore, we aimed to investigate in a transgenic rat model of HD 1) if there is a general olfactory impairment, and 2) if there exist disease-

specific dynamics of olfactory dysfunction when vomeronasal (VNE) and main olfactory epithelium (MOE) are compared. Methods. We used male rats of the transgenic line 22 (TG22) of the bacterial artificial chromosome Huntington disease model (BACHD), aged 3 days or 6 months. Cell proliferation, apoptosis and macrophage activity were examined by immunohistochemistry in VNE and MOE. Results. No differences were observed in cellular parameters in the VNE between the groups. However, the MOE of the 6-month-old HD animals showed a significantly increased number of mature olfactory receptor neurons. Other cellular parameters were not affected. Conclusion. The results obtained in TG22 line suggest a relative stability of the VNE, whereas the MOE seems at least temporarily affected.

Fri-P2-116

Differences in taste perception in hyposmic patients compared to healthy controls

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Introduction: Olfactory deficits inhibit flavor perception and influences food intake. The aim of the study was to evaluate the role of hyposmia on the taste perception in patients compared to healthy controls.
Materials and Methods: One hundred forty-eight subjects were enrolled, 57(35 women and 22 men) were hyposmic patients (mean age±SD, 35.7 ± 14.1) and 91 (62 women and 29 men) were healthy controls (mean age±SD, 31.4 ± 13.6). Among hyposmic subjects, 23 (40%) showed a post-acute Coronavirus (COVID-19) Syndrome. Olfactory function was assessed with the Sniffin' Sticks Extended Test which evaluated odor Threshold (OT), Discrimination (OD), Identification (OI) and their sum Threshold-Discrimination-Identification (TDI) scores. Whereas gustatory function was evaluated using the Taste strips test with four concentrations for each modality: sweet, bitter, sour, and salty.
Results: Hyposmic patients showed a significant decrease in the perception of salty, sweet, sour and in the total taste perception compared to controls, while no significant differences for bitter perception were found. Moreover, significant correlations were observed between TDI score versus salty ($r=0.285$, $p<0.01$), sweet ($r=0.243$, $p<0.01$), and sour perception ($r=0.321$, $p<0.01$). In order to confirm these correlations multivariate linear regression analyses were performed using TDI score as a dependent variable. Significant associations emerged between TDI score versus salty ($p<0.01$) and sour perception ($p<0.01$). This model explained 19% of variance ($R^2 = 0.188$) for the salty and taste perception. In hyposmic subjects with a post-acute Coronavirus (COVID-19) Syndrome a significant decrease only in bitter perception ($p<0.05$) was observed.
Conclusions: Patients with hyposmia reported alterations of salty and sour taste preference. In particular, patients reported lower perception of salty and sour compared to controls as consequence of the damage of flavor perception.

Fri-P2-117

Impact of sucrose and non-caloric sweeteners on the intestinal barrier function: a comparison of Caco-2 monoculture and Caco-2/HT29-MTX coculture model

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Activation of TAS1R3 in undifferentiated Caco-2 cells by aspartame and sucralose has been associated with increased intestinal permeability. However, the impact of a chronic treatment of Caco-2 cells during differentiation to an enterocyte-like phenotype with physiological relevant concentrations of sweeteners in comparison to sugar is not known yet. Here, we investigated the long-term effects of sucrose and the selected non-caloric sweeteners Rebaudioside M, Sucralose, and NHDC on the intestinal barrier function using Caco-2 cells and a coculture of Caco-2 and mucus producing HT29-MTX-E12 cells, which more closely resembles the physiological conditions. The transepithelial electrical resistance and the permeability of the fluorescent dye Lucifer Yellow (LY) as markers for the barrier function were measured after treatment with the test compounds in two concentrations (equisweet to 5% sucrose and equimolar 0.1 mM) on day 7, 14, and 21 of cultivation. Effects of the treatments on selected tight-junction proteins were determined with qRT-PCR and immunostaining.
Treatment with 150 mM sucrose led to an increase in the permeability of LY compared to the control in both cell models, the highest increase was on day 7 in the monoculture (176 ± 34 %). An osmotic effect of sucrose was excluded,

as well as an effect of the sweetness and the sweet taste receptor TAS1R3 by using the TAS1R3 inhibitor lactisole. However, treatment with 150 mM sucrose led to a decrease of CLDN2 and an increase in gene expression of TJP1, CLDN1, OCLN, and F11R, which may argue for a counter-regulatory effect. Overall, the coculture showed a higher resistance to osmotic stress and treatment with the test compounds than the monoculture.
In conclusion, treatment with sucrose showed a dose- and time-dependent effect on intestinal permeability independent of TAS1R3 and osmotic pressure, with potential protective effect of the mucus layer.

Fri-P2-118

Pt-based chemotherapeutic drugs induce bitterness responses in HGT-1 cells via regulation of bitter taste receptors

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Taste dysfunctions like bitter phantogeusia belong to the most prevalent chemotherapy-related side effects and impair the food intake and the nutritional status as well as the overall quality of life of patients. In order to enable the development of effective treatment strategies, the aim of this study was to elucidate the cellular and molecular mechanisms that are involved in the development of bitter phantogeusia during platinum (Pt)-based chemotherapy. For this purpose, we used human gastric tumour cells (HGT-1), functioning as a cellular model system (i) to identify bitter and bitter modulating compounds and (ii) to identify the involvement of bitter taste receptors (TAS2Rs). Our in vitro results demonstrate that cisplatin and carboplatin increased the bitterness response by HGT-1 cells, with cisplatin showing a stronger effect. Homoeriodictyol (HED), a bitter masking compound targeting various TAS2Rs, counteracted the cellular bitterness response caused by 50 µM cisplatin by -75 % ± 15 %, whereas the effect of 200 µM carboplatin was reduced by -76 % ± 11 %. Gene expression analysis revealed that expression levels of various TAS2Rs were altered due to Pt-based treatment. Finally, a functional role of the TAS2R5 in the HGT-1 bitterness response induced by the Pt-based drugs was verified by a siRNA knockdown approach. Along with data from cellular uptake studies carried out by means of ICP-MS, these results strongly support our hypothesis that Pt-based chemotherapeutics administered i.v. contribute to bitter phantogeusia experienced by cancer patients. Whether the administration of HED to cancer patients could help to reduce bitter phantogeusia and improve side effects like loss of appetite and body weight, has to be elucidated in a clinical study.

Funding: This research was funded by the Vienna Science and Technology Fund, grant number LS18-059.

Fri-P2-119

An unexpected link between taste and olfaction: taste bud sentinels on the passageway for olfactory signals

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Olfaction and taste are specialized chemical senses in arthropods and vertebrates. In terrestrial species, taste is considered a proximal sense whereas olfaction is considered distal. However, in some fish species, taste buds are also present on the outer body surface. This points to the possibility that in aquatic species taste also has a function in sensing the outer chemical environment. Zebrafish possess 4 T1Rs and 7 T2Rs, which makes a comprehensive analysis of their expression possible. Here we show that there is a taste organ-like high density of T1Rs and T2Rs on the nostrils of zebrafish, Danio rerio. In situ hybridization (TSA) was performed on coronal sections of adult zebrafish head to label all T1R- and T2R-expressing taste cells using complete mixes of individually validated RNA probes. The density of T1R- and T2R-expressing taste cells were measured on the nostrils, lower lip, oral cavity, and top head skin surfaces. Data was analysed using two-tailed unpaired Student's t-test. The results show the highest density of T1R-expressing taste cells in the nostrils, in stark contrast to the very low density observed in head skin, with intermediate density found in

the oral cavity. T2Rs show overall lower densities in all four organs, but with similar ratios between organs. These results suggest that the nostrils of zebrafish should be considered as a novel taste organ and point to a possible link between the detection and processing of gustatory and olfactory signals. This study was funded by DFG within the PhD Program "Research Training Group – Neural Circuit Analysis (RTG-NCA), GRK 1960".

Fri-P2-120

The sensitivity of dogs (Canis familiaris) to the bitter tasting deterrent denatonium benzoate

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Denatonium benzoate (DB) is an extremely bitter tasting chemical to humans and is used as a deterrent in various products where ingestion is unwanted, including antifreeze, laundry detergent, and treatments to discourage nail biting. In the case of antifreeze, some formulations contain ethelyne glycol, which is toxic not only to humans but also to dogs, cats and other mammals. DB serves as a deterrent for all vulnerable species, but published data on its efficacy in dogs and cats is not available. In this study we assessed the sensitivity of dogs to DB in vivo and then investigated the responses of dog bitter receptors (Tas2r) to DB in vitro. We found that in a two-bottle choice test 10 miniature schnauzer dogs on average did not reject a solution of 10µM (4.47ppm) DB ($p = 0.883$) but a larger sample (31 miniature schnauzers, 26 Labrador retrievers, 19 cocker spaniels) on average did reject 100µM (44.66ppm) ($p < 0.001$), although this was not true for every dog on every exposure. Accordingly, dog Tas2rs were less sensitive to DB than their human orthologues, with dTas2r4 being the only sensitive receptor (EC_{50} = 3.78mM). In humans TAS2R47 Is the most sensitive receptor for DB, followed by TAS2R10. Dogs lack a functional orthologue for TAS2R47 but do have one for TAS2R10. However, we found that dTas2r10 was completely insensitive to DB. By generating and testing a series of dog/human chimeric Tas2r10 receptors we identified that this difference was related, at least partly, to differences in the second extracellular loop (ECL2) region. We hope these data will help to inform the debate on the use, inclusion rate, and selection of bitter deterrents when considering dogs and also stimulate further research on the efficacy of bitter taste deterrents in other vulnerable species.

Fri-P2-121

Chemoreceptors TAS1R3 and GRM2 heterodimerize in human blood leukocytes

Lena Ball, Julia Bauer, Dietmar Krautwurst

Leibniz Institute for Food Systems Biology at the Technical University of Munich

The expression of canonical chemosensory receptors, such as the sweet taste receptor (TAS1R2/TAS1R3), has been demonstrated in a variety of extra-oral cells and tissues. Gene expression studies have revealed transcripts of all three TAS1R subunits, and all 25 bitter taste receptor (TAS2R) genes, as well as of some of the eight human metabotropic glutamate receptors (GRMs), in different types of immune cells, where they are involved, for example, in the chemotaxis of human neutrophils and the protection of T-cells from activation-induced cell death. TAS1Rs and GRMs both belong to the class C GPCRs whose characteristic structures are the large extracellular N-terminal and cysteine-rich domains. These distinctive components enable the assembly into constitutive dimeric complexes to accomplish their diverse functions.

Here we show that GRM2 and TAS1R3 co-localize and heterodimerize in human blood leukocytes, by means of immunocytochemistry and co-IP/Western analysis. We validated a heterodimerization of recombinant GRM2/TAS1R3 in heterologous test cells by means of BRET, and a gain-of-function luminescence assay with physiological concentrations of monosodium glutamate.

Our results demonstrate a heterodimerization across different families of class C GPCRs in leukocytes, suggesting previously unnoticed, new cellular function-tailored chemoreceptor combinations, enabling our immune system to cope with a vast variety of stimuli.

Fri-P2-122

Expression of ENaC regulators in δ-ENaC positive cultured adult human fungiform (HBO) taste cells

Vijay Lyall [1], Sunila Mahavadi [2], Shobha Mummalaneni [1], Mehmet Hakan Ozdener [3]

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In addition to α, β, and γ subunits of ENaC, human salt-sensing taste receptor cells (TRCs) also express the δ-subunit. We used human fungiform taste papillae (HBO) cell culture model along with molecular and imaging techniques to investigate if the expression and function of ENaC δ-subunit in human salt-sensing TRCs is also modulated by the ENaC regulatory hormones and intracellular signaling effectors known to modulate salt responses in rodent TRCs. Our results show that: (i) ENaC subunits are expressed in a subset of type II human taste cells; (ii) TRPV1, ACE2, MASR1, AT1R, GPER1, and CALHM1/3 are expressed in human taste cells; (iii) TRPV1 co-localizes in human taste cells that express the ENaC δ-subunit; (iv) Modulating TRPV1 activity by high salt and capsaicin altered ENaC mRNA expression; (v) Some of the ENaC regulators are most likely present in a complex, and that changes in the expression of one or more regulators can alter the expression of other effectors; We hypothesize that changes in ACE2 expression in human fungiform taste cells can alter the balance between the two major RAAS pathways, ACE1/Ang II/AT1R and ACE2/Ang-(1-7)/MASR, leading to changes in ENaC expression and responses to NaCl. Supported by VCU CCTR and VETAR grants to VL and an independent VETAR grant to SM.

Fri-P2-123

Functional conservation of bitter taste receptors

Silvia Schaefer, Florian Ziegler, Maik Behrens

Leibniz-Insitute for Food Systems Biology at the Technical University of Munich

The human bitter taste receptors (TAS2R) are rather well characterised by extensive screenings, resulting in the deorphanisation of 21 of the 25 TAS2Rs. The receptive ranges of receptors of other species, however, initially remained quite unexplored. After realising the importance of comparisons between receptor characteristics of different species in order to fully understand e.g. human TAS2R evolution and function, bitter taste receptor repertoires of other vertebrates were examined. The comprehensive analysis of mouse bitter taste receptors revealed that functional conservation, even among one-to-one orthologues of human and mouse, was rarely seen.

On the contrary, recent research indicated that agonist profiles among related receptors of different species may be more conserved than previously thought. Overlapping agonist profiles were found among distantly related bird species as well as among even more distantly related bony fish species. To see how widespread functional conservation of bitter taste receptors in different species is, we investigated whether the perception of evolutionary stable and hence "old" agonists such as metal salts, that activate the human TAS2R7, is also conserved across species. Thus, we performed functional calcium mobilization assays in transiently transfected HEK293T cells to identify conservation. In doing so, we were able to identify metal ions, especially Mg^{2+}, as additional conserved agonists in one-to-one orthologues of the human TAS2R7 of distant relatives of Boreoeutheria, namely desmodus rotundus, cavia porcellus and felis catus.

In conclusion, we can assume that conservation of bitter taste responses between species occurs more often than primarily thought and, in spite of the evolutionary distant relationship of the four investigated species, the conservation of metal ion response of TAS2R7 over millions of years indicates an important physiological function in mammals.

17:00 - 19:00

Symposium 9: Olfactory plasticity in a clinical context

Goethe Hall

Chair/s: Thomas Hummel

The sense of smell is plastic. This plasticity is based on the regenerative capacity of the olfactory mucosa. The regeneration is the basis for recovery after olfactory loss which is especially significant since the SARS-CoV-2 pandemic. In COVID19 the virus attacks the olfactory mucosa and olfactory receptor neurons are destroyed during the process of the disease. During recovery, ORNs are regrown from the globose basal cells. In addition to these changes at a peripheral level, the volume of the olfactory bulb also changes in relation to olfactory function. The same has been shown for the primary and secondary olfactory cortex where also changes in functional responsiveness have been observed. It appears that the effectiveness of "olfactory training" is based on these effects.
Aim of the symposium is to highlight these plastic changes at several levels. To this end a group of excellent researchers will present work that touches upon several aspects of plasticity in the chemical senses. In terms of career levels the group is mixed, with a PhD student, four relatively young colleagues in their early career, and one established senior colleagues.
Because of the high significance of this topic in terms of recovery from COVID-19 associated olfactory loss we believe that it is highly attractive to ECRO participants!

Fri-S9-001

Regeneration of the olfactory mucosa

Bradley Goldstein

Department of Head and Neck Surgery and Communication Sciences, Department of Neurobiology, Duke University School of Medicine, Durham, NC, USA

Olfaction can be impaired due to damage caused by trauma, infection, inflammation or aging. Damage can occur anywhere along the pathway from the peripheral olfactory epithelium in the nose to the cortex. The olfactory system exhibits a degree of plasticity that underlies an ability to recover function following certain types of injury. Nonetheless, lasting anosmia or hyposmia remain challenging clinical problems. At the periphery, recovery involves the generation of new olfactory neurons and related cell populations from tissue-resident stem cells. Functional recovery necessarily involves an ability to incorporate newly generated cells into the sensory system. Objectives: here, we consider mechanisms involved in damage and repair in the periphery, the olfactory epithelium in the nose. Methods: rodent models have long been used to experimentally injure the olfactory epithelium, including chemical injuries (including Triton X-100, zinc sulfate, methyl bromide, methimazole), surgical injury (olfactory bulb ablation, Cranial Nerve 1 section, blunt head trauma), genetic or pharmacogenetic alterations (gene deletion, conditional gene knockout, conditional toxin expression), or viral infection (for instance, influenza or coronavirus models). Results/conclusions: we review here details emerging from animal studies, identifying the horizontal basal cell as a reserve population, and globose basal cells as a heterogenous pool of active progenitors, harboring functional plasticity. Details regarding the functional potential and molecular mechanisms regulating basal cells are considered. Recent efforts to define patterns of olfactory epithelial damage in humans are also considered, including the potential roles of immune cells. Finally, we review potential therapeutic strategies emerging from these studies.
Funding: NIH/NIDCD

Fri-S9-002

Changes in stem cell proliferation and receptor expression profile in response to odor exposure

Vittoria Avaro [1], Thomas Hummel [2], Federico Calegari [1]

[1] Centre for Regenerative Therapies Dresden (CRTD), TU Dresden, Fetscherstrasse 105, 01307 Dresden, Germany, [2] Smell & Taste Clinic, Department of Otorhinolaryngology, TU Dresden, Fetscherstrasse 74, 01307 Dresden, Germany

Olfaction underlies our ability to detect chemicals in the environment. Often underappreciated, olfactory dysfunctions affect one out of twenty individuals and aging and infections are the leading causes for these changes. Olfactory Training, consisting of repeated short-term exposures to specific sets of odorants, is one of the few established

treatments effective in rescuing olfactory dysfunctions. Effective in only 50% of patients, biological mechanisms behind it are still unknown, limiting the identification of novel and more efficient treatments. Olfactory Epithelium, part of the peripheral nervous system, is the area with the highest regenerative potential in our nervous system and the only adult neurogenic niche confirmed to exist in both, rodents and humans. scRNA-Seq was recently employed, in both species, to characterize the Neural Stem Cells in the OE, identifying the molecular signatures of quiescent and active NSCs which in turn give rise to olfactory sensory neurons, maintaining the homeostasis of the tissue. Using in combination molecular, cellular, and functional approaches, my project aims to unravel a possible link between olfactory training and adult neurogenesis in the OE. Here, I reproduced human OT in wild type adult mice to address its effect on NSCs behaviour. Ongoing analysis suggest that OT was sufficient to induce NSCs to exit their quiescent state in mice. Upon training, increases were observed also in the number of proliferating neural progenitors, confirming the neurogenic nature of the effect and suggesting a connection between neurogenesis and olfactory functions. To further confirm our hypothesis, our plan now is to dig into the transcriptional landscape of patients' cells, addressing if and to which extent the same mechanisms apply in humans. In the future, our study may provide new insight and a better understanding of the basic biology of olfactory functions towards new strategies to treat related dysfunctions.

Fri-S9-003

Central-nervous changes during olfactory recovery in Covid-19?

Sanne Boesveldt, Birgit van Dijk, Paul Smeets, Elbrich Postma

Sensory science and Eating behavior group, division of Human Nutrition and Health, Wageningen University, The Netherlands

Smell loss is one of the most frequent symptoms -and predictor- of Covid-19, can be long-lasting and have devastating impact on eating behavior and daily life. In particular, patients often report that after a period of smell loss (anosmia), they develop a distorted sense of smell (parosmia). Yet the course and frequency of this conversion is unknown, as is its pathophysiology. Neuroimaging, as (f)MRI, could help us understand the possible pathways of olfactory disorders in Covid-19 patients. E.g. it has been shown that the olfactory bulb is compromised in patients with persistent Covid-19 olfactory dysfunction. We here set out to investigate the (structural and functional) neurophysiological correlates of anosmia and parosmia in Covid-19, and assess potential recovery over a 6 month period. The study is ongoing and preliminary data will be presented at the meeting.

Fri-S9-004

Compensation of sensory loss and effects of olfactory training on chemosensory and cognitive function

Anna Oleszkiewicz

Smell and Taste Clinic, TU Dresden, Institute of Psychology, University of Wroclaw

Constant alterations of the olfactory system as a result of interaction with the chemosensory environment are a matter of interdisciplinary interest. Studies have shown that exposure to odors leads to changes at both peripheral and central levels of the olfactory system, and this may result from both bottom-up and top-down processes. It seems reasonable to expect that the olfactory system would adapt to sensory loss and compensate for the lack of visual or auditory input. Yet, results in this regard are contradictory, reporting either enhanced olfactory performance in blindness or no significant difference between people with blindness and their respective control groups. Inspired by this discrepancy, we have conducted a series of studies comparing people with blindness and people with deafness, with their respective control groups (sighted or blind, respectively). This work led us to the general conclusion of no major advantage of people with blindness over sighted people in the behavioural response to odours, but we did observe decreased chemosensory performance in people with deafness.

Plasticity of the olfactory system has also been used in the rehabilitation of people with olfactory loss (anosmia). Olfactory training (OT) is a systematic exposure to a defined set of odorants – e.g., lemon, rose, cloves, and eucalyptus, twice a day over the period of at least 12 weeks. OT has been found to effectively rehabilitate the sense of smell, particularly in patients who lost their sense of smell due to a viral infection. Given the proximity of the brain structures responsible for olfactory processing and the limbic system, we hypothesized that OT may be beneficial for cognitive and emotional processing. Presented evidence suggests that the effects of OT may extend beyond olfactory performance and provide support in cognitive aging and emotional development.

Fri-S9-005

Supersmellers! What are they? How could we become one?

Katherine L. Whitcroft

NHS – Pinderfields Hospital South Yorkshire, Centre for Olfactory Research Applications, Institute of Philosophy, School of Advanced Study, London, UCL Ear Institute, London, Smell and Taste Lab, TU Dresden

During this talk I will first address the concept of the 'supersmeller' – what exactly defines hyperosmia and what are the controversies surrounding its nature? I will cover the psychophysical and neuroimaging characteristics of this cohort, highlighting differences compared with normosmics and those with olfactory dysfunction. I will also briefly cover the small amount of animal research on this topic. I will then address how one might achieve the purported 'supersmeller' status – both in terms of practical, evidenced steps that a person or patient can take, and in terms of the underlying mechanism behind such steps

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Fri-S9-006

Exploitation of brain plasticity using olfactory implants and transplants

Susanne Menzel, Thomas Hummel

Smell & Taste Clinic, Department of Otorhinolaryngology, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany.

The prevalence of low olfactory function is approximately 20%, with around 5% having anosmia. Existing therapies and outcomes are limited. More recent approaches may offer new options such as electrical stimulation at different levels of the olfactory system that could lead to an olfactory implant, or transplantation of cells from the olfactory mucosa. These approaches exploit the neuronal plasticity which plays a central role for the olfactory system. In addition, the therapeutic effect of "olfactory training" (OT: repeated and regular exposure to odors for weeks/months) is based on this plasticity. It has been shown that OT is associated with an improvement of olfactory function, an increase of the volume of olfactory bulb and also the cortical thickness of different brain structures like frontal gyrus and entorhinal cortex. In summary, plasticity of the olfactory system is of high significance to a range of new and emerging treatments of olfactory dysfunction.

17:00 - 19:00

Symposium 10: New developments in vomeronasal system research - from sensory organ to central processing

Hahn Lecture Hall

Chair/s: Yoram Ben-Shaul, Marc Spehr

The symposium presents new research developments related to the mouse vomeronasal system. The talks will describe new developments related to the entire VNS pathway, from sensory neurons and sensory organ, via the accessory olfactory bulb, all the way to the amygdala and the hypothalamus.

Fri-S10-001

Following and changing the developmental trajectories of the vomeronasal sensory neurons.

Paolo Forni

Department of Biological Sciences,University at Albany., The RNA Institute,University at Albany. Albany,NY,USA

The vomeronasal organ (VNO) of rodents contains Gαi2+ and Gαo+vomeronasal sensory neurons (VSNs) as the two major neuronal types. Gαo-expressing VSNs localize to the basal portion of the vomeronasal epithelium (basal VSNs), while Gαi2-expressing VSNs localize to the apical territories (apical VSNs). Basal and apical VSNs are continuously formed starting from a common pool of Achaete Scute-like-1 (Ascl-1)-positive neural progenitor cells. However, how the apical or basal cell fate of the VSNs is established has not been fully addressed thus far. By combining single-cell sequencing and mouse genetics we discovered that active Notch signaling plays a pivotal in triggering the Gαo/basal differentiation program. Conversely, Notch signaling loss-of-function prevents the formation of Gαo/basal VSNs. In this presentation, I will illustrate the basic mechanisms controlling the differentiation dichotomy of the vomeronasal

sensory neurons. Moreover, I will share some of our new findings about the molecular mechanisms controlling the maturation of the VSNs after the differentiation dichotomy is established.
This research is supported by the National Institute of Deafness and Other Communication Disorders of the National Institutes of Health under the Award R01-DC017149.

Fri-S10-002

Investigation of Ca^{2+}-activated currents in mouse vomeronasal sensory neurons

Victoria K. Switacz, Rudolf Degen, Marc Spehr
Department of Chemosensation, Institute for Biology II, RWTH Aachen University, Germany

The accessory olfactory system of mice regulates inter-and intraspecific communication and triggers a multitude of essential behaviors. A variety of semiochemicals serve as social cues and are detected by vomeronasal sensory neurons (VSNs) in the vomeronasal organ. Activation of vomeronasal receptors (V1Rs, V2Rs, or FPR-rs) in the microvillar membrane triggers a G-protein coupled signaling cascade resulting in Ca^{2+} influx and signal amplification via Ca^{2+}-activated Cl^- efflux. However, our knowledge of Ca^{2+} signaling and its function(s) in VSNs remains limited. Therefore, we investigated Ca^{2+}-activated channels in different VSN compartments, focusing on VSN somata. To identify and isolate currents elicited at the soma, we combined targeted Ca^{2+} uncaging with whole-cell patch-clamp recordings, single-cell Ca^{2+} imaging, and pharmacology. This approach revealed distinct Ca^{2+}-activated potassium and chloride currents in subsets of VSNs. Notably, individual VSN current profiles appeared heterogeneous, potentially reflecting subpopulation-specific ion channel repertoires. Together, our data extend the established concept of VSN Ca^{2+} signaling by emphasizing additional functions of Ca^{2+}-dependent channels in VSN somata.

Fri-S10-003

Stimulus induced local field oscillations in the accessory olfactory bulb

Oksana Cohen [1], Anat Kahan [1], Sebastian Mallinowski [2], Idan Steinberg [1], Marc Spehr [2], Yoram Ben-Shaul [1]
[1] The Hebrew University Faculty of Medicine, Israel Canada Medical Institute, Department of Medical Neurobiology, [2] RWTH Aachen University, Institute for Biology II, Department of Chemosensation

Local field potential (LFP) signals and oscillations are implicated in information processing in the main olfactory system, but their role in vomeronasal system (VNS) function is less understood. We recently identified prominent non-stationary oscillatory LFP patterns in the accessory olfactory bulb (AOB), that are correlated with stimulus delivery to the VNS. These theta band (5-8 Hz) patterns were found in anesthetized mice under controlled stimulus delivery, and resemble those found by other groups in awake behaving mice. We sought to understand how these patterns are related to the presentation of specific stimuli and what role they play in information processing. One challenge in the analysis of such patterns is that oscillatory episodes vary in magnitude and frequency, and are sometimes shadowed by other sources of experimental noise. By considering the spatial distribution of these oscillations, we devised a method that provides an ongoing measure of the occurrence and magnitude of these oscillatory patterns. Using this method, we show that the patterns vary in amplitude, that the amplitude depends on the identity of sensory stimuli, and that when sufficiently strong, they present as full-fledged oscillations. Notably, spiking activity of AOB neurons is correlated with particular phases of these oscillations, suggesting that these oscillatory patterns can coordinate the spiking activity of AOB output neurons to effectively activate downstream processing stages.

Fri-S10-004

Visualizing sensory responses in the accessory olfactory bulb of behaving mice

Ian Davison, Spencer Byers, Kevin Monk
Dept. of Biology, Boston University

The vomeronasal system strongly influences social behavior, but it is unclear how complex semiochemical blends are represented during natural social interactions. We addressed this question by using head-mounted 'miniscopes' to visualize sensory activity in the glomerular layer of the accessory olfactory bulb (AOB) of freely moving mice. Imaging responses in second-order projection neurons, or mitral cells, during active investigation of conspecifics revealed combinatorial activity across multiple glomeruli, with patterns overlapping substantially for different partners. Relatively few glomeruli were differentially activated by sex, strain, and/or contact site on the probe animal. Stimulus

selectivity was similar for both constrained contexts, where investigation was limited to either facial or anogenital regions, and in freely-moving social interactions. Interestingly, glomeruli selectively tuned to male and female cues were more strongly activated by facial and anogenital regions, respectively. While individual glomeruli show a wide range of selectivity, population activity readily distinguished features such as sex, although our data do not distinguish between distributed, population codes or selective 'labeled-line' pathways to downstream limbic areas. Finally, we find a mismatch between the long timecourse of sensory-driven activity, lasting tens of seconds, and rapid behavioral dynamics during investigation, where different body areas or partners can be sampled in under a second. These data suggest that the vomeronasal system modulates behavior by integrating information over extended timescales rather than mapping individual sensory events onto discrete behavioral responses. Imaging during social interactions should help expand our understanding of how the AOB encodes complex semiochemical blends to modulate behavior, including both basic biological categories like sex, and more nuanced information such as individual identity.

Fri-S10-005

Multi-sensory processing of social cues in the medial amygdala

Yoh Isogai

Sainsbury Wellcome Centre, University College London

The recognition of social cues is a major determinant for the selection of social behaviors under specific contexts. To gather social information, animals are tuned to specific multi-sensory stimuli emitted by interaction partners signifying e.g., age, sex, and hierarchy status. The dynamic nature of social interactions also means that the social cues are presented in a transient and stochastic manner. How the brain gathers and integrates different streams of multi-sensory social information, which potentially arrive with different timing, remains unclear.

As a model system to address this question, we chose to study the medial amygdala (MeA), a critical hub in the innate social behavior circuit. Previous studies demonstrated that the MeA receives strong pheromonal inputs, and that activating specific cell populations within the MeA can drive specific innate social behaviors including mating, aggression, allogrooming, and parenting. Despite this, how the MeA integrates incremental social information such as monomolecular pheromonal inputs to form an abstract social representation critical for the expression of specific behaviors remains elusive.

To this end, we developed an explantable semi-chronic recording method using Neuropixels probes (termed Re-pix) to measure the responses of the MeA neurons to a variety of social cues in awake animals, including monomolecular pheromones, pheromonal blends, volatile scents, and other stimuli including social touch. The large-scale recording of MeA neurons allowed us to chart the selectivity of single MeA neurons to different types of social stimuli. Moreover, we found that MeA neurons respond by at least two different types of kinetics and that the dynamics of neural response depends on stimulus modality and is modulated by prior social experience. Taken together, these results suggest the convergence of multi-pheromonal and multi-sensory inputs within MeA neurons with experience-dependent modulation.

Fri-S10-006

Hormonal remodeling of a parenting circuit during pregnancy

Johannes Kohl, Rachida Ammari, Francesco Monaca, Mingran Cao, Estelle Nassar, Patty Wai, Matthew Lee, Bernard Siow, Molly Strom, Nicholas del Grosso

The Francis Crick Institute, 1 Midland Rd, London, UK

Pregnancy is associated with striking behavioral adaptations such as increased food intake, elevated aggressivity, and changes to infant-directed behavior. These changes are orchestrated by the action of pregnancy hormones on the brain, but the underlying mechanisms remain largely unknown.

Here we address how parenting circuits in mice are remodeled during pregnancy. We first establish that pregnancy affects specific aspects of infant-directed behavior. These adaptations are maximal in the last trimester and outlast the transient hormonal changes of pregnancy. Next, we quantify brain-wide, pregnancy-associated volumetric changes and ovarian hormone receptor expression to identify hormonally remodeled brain areas. These unbiased screens identify the medial preoptic area (MPOA) – a key node in parenting circuits – as a promising target. Indeed, deletion of ovarian hormone receptors in the MPOA abolishes pregnancy-associated behavioral adaptations. Strikingly, this is also the case

when hormone receptors are selectively ablated in a small subset of parenting-relevant, Galanin-expressing MPOA neurons (MPOAGal neurons).
Using patch clamp recordings from acute brain slices, we surprisingly find that MPOAGal neurons undergo hormone-mediated silencing in late pregnancy. Microendoscopic calcium imaging in freely moving animals confirms that pregnancy profoundly reduces and decorrelates spontaneous MPOAGal activity. In addition, parenting-associated MPOAGal population activity is significantly sparsened in pregnancy, and pup representations segregate from representations of other social and non-social stimuli during this period, thereby increasing the discriminability of pup stimuli. This hormonally mediated adult plasticity is thus reminiscent of changes occurring during critical periods in the developing nervous system.
In summary, our work suggests that hormonal action remodels a small neuronal population to generate anticipatory behavioral changes during pregnancy.

Sat, 3 Sep 2022

08:30 - 09:30

Keynote Lecture: Anna Menini: Of mice and humans: understanding the olfactory peripheral system

Goethe Hall
Chair/s: Johannes Reisert

Sat-L4-001

Of mice and humans: understanding the peripheral olfactory system

Anna Menini
Neurobiology Sector, SISSA, International School for Advanced Studies, Trieste, Italy

My laboratory has been studying the molecular mechanisms involved in odorant transduction in amphibians and mice for many years. I will present some of our main findings related to proteins involved in the generation of the electrical signals produced after odorant binding to receptors in the cilia of olfactory sensory neurons in mice.
As COVID-19 affects the sense of smell in humans, we have recently turned our attention to the human olfactory epithelium. Human nasal tissues from biopsies of healthy individuals were provided by the group of Prof. Boscolo-Rizzo and Prof. Tirelli of the Section of Otolaryngology of the Department of Medical, Surgical and Health Sciences of the University of Trieste (Italy). In COVID-19, one mechanism causing cell death in some tissues is the formation of syncytia. Some studies showed that syncytia may be formed when SARS-CoV-2 Spike expressed at the surface of an infected cell binds to ACE2 on another cell, followed by activation of the scramblase TMEM16F (ANO6) which exposes phosphatidylserine to the external side of the membrane. To investigate if ACE2 and TMEM16F, the molecular components necessary for syncytia formation, are co-expressed in cells of the olfactory epithelium, we analysed a publicly available single-cell RNA-seq dataset from human nasal epithelium and performed immunohistochemistry in human nasal tissues from biopsies. We found that ACE2 and TMEM16F are co-expressed both at RNA and protein levels in non-neuronal supporting cells. We propose that one of the pathogenic mechanisms behind smell loss could be syncytia formation of supporting cells initiated by Spike binding to ACE2 and mediated by TMEM16F.
At present, my laboratory is obtaining electrophysiological recordings from supporting cells and olfactory sensory neurons of the human olfactory epithelium and I will report about these ongoing new results.

10:00 - 12:00

Symposium 11: Computation approaches for advancing research in the chemical senses

Goethe Hall

Chair/s: Antonella Di Pizio, Sébastien Fiorucci

Computational approaches are widely used to get insights into the chemistry and biology of chemosensation. The ECRO Special Interest Group Computational Chemosensation aims to gather researchers working in computational chemosensation, to facilitate their interaction and advance computational techniques for chemical senses, but also promote the potential of computational works to promote collaborations with experimentalists. The proposed symposium is the first initiative of the group and aims to highlight computationally guided advancements in chemosensation, ranging from machine learning based predictors, to the use of computer-aided drug design tools for ligand discovery, to the multiscale simulations of chemosensory receptors, to network analyses of proteins and signaling events. Works on both taste and smell will be presented in the symposium. We expect that bringing together computational researchers from different fields will provide stimulating and fruitful discussions about future perspectives. Moreover, during the symposium, the ECRO special interest group will be introduced to the audience.

Sat-S11-001

Neural networks learn a map of odor that achieves human-level performance at describing odor character

Emily Mayhew [1, 2], Kelsie Little [1], Matthew Andres [1], Britney Nguyen [1], Jane Parker [3], Richard Gerkin [4], Joel Mainland [1, 5]

[1] Monell Chemical Senses Center, [2] Michigan State University, [3] University of Reading, [4] Arizona State University, [5]University of Pennsylvania

Predicting olfactory perception from molecular structure is an enduring challenge in olfaction, largely because similarity in chemical structure is an unreliable predictor of perceptual similarity. Enantiomers are structurally similar, but can evoke distinct odors, while musks from very different structural classes can be perceptually similar. Neural networks show promise for resolving this issue, as they can remap traditional structural metrics into an odor space that better predicts perceptual differences. Here, we used a neural network (NN) to generate a novel map from molecular structure that preserves perceptual relationships and enables odor quality prediction of novel odorants. We found that the NN is as reliable as a human in describing odor quality: on a prospective validation set of 400 novel odorants, the NN-generated odor profile more closely matched the trained panel mean (n=15) than the median panelist. The NN embeddings outperformed both physicochemical descriptors and chemical fingerprints on other odor prediction tasks, suggesting the NN learned a generalized representation of the structure-odor relationship. This model allows us to predict the odor of any molecule and paves the way toward digitizing odors.

Sat-S11-002

Odorant binding and receptor activation deciphered at the molecular level

Matej Hladiš, Jody Pacalon, Maxence Lalis, Sébastien Fiorucci, Jérémie Topin

Université Côte d'Azur

Chemical sensations are triggered by the activation of transmembrane receptors expressed on the surface of sensory neurons which belong to the family of G-protein coupled receptors or ion channels. Their activation mechanism can be divided into two main events: the binding of the ligand to the receptor and, in the case of an agonist, the activation of the complex.

The combination of numerical approaches with experimental methods allows to decipher at the atomic scale the mechanisms of ligand binding and receptor activation. Our work reveals that agonist-induced activation of odorant receptors can be predicted. Numerical simulations identify functional molecular switches that encode agonist detection and downstream signaling mechanisms within chemical receptors.[1]

From a general perspective, establishing a relationship between the structure of a molecule and the structure of the olfactory receptors (ORs) it activates has long been a challenge. We take advantage of recent advances in representation learning and combine them with graph neural networks (GNN) to build a receptor-ligand prediction model. To the best of our knowledge, this is the first receptor ligand prediction model that takes into account an entire protein sequence. This prediction model has been evaluated on a set of more than 46,000 receptor-molecule pairs and achieves a Matthews correlation coefficient of 0.6. Thus, our protocol paves the way to decipher the combinatorial

code associated with odor perception.
[1] aL. Charlier, J. Topin, C. Ronin, S.-K. Kim, W. A. Goddard, R. Efremov, J. Golebiowski, Cellular and molecular life sciences 2012, 69, 4205-4213; bC. A. de March, J. Topin, E. Bruguera, G. Novikov, K. Ikegami, H. Matsunami, J. Golebiowski, Angewandte Chemie 2018, 130, 4644-4648; cJ. Topin, C. Bouysset, J. Pacalon, Y. Kim, M.-R. Rhyu, S. Fiorucci, J. Golebiowski, Cellular and Molecular Life Sciences 2021, 78, 7605-7615.

Sat-S11-003

Computational molecular interaction maps of signaling events within the olfactory epithelium

Federica Genovese [1], Shailendra Gupta [2], Suchi Smita [2], Dominique Fastus [2], Krishna P Singh [2], Matti Hoch [2], Olaf Wolkenhauer [2, 3], Antonella Di Pizio [3]

[1] Monell Chemical Senses Center, Philadelphia, USA, [2] Department of Systems Biology & Bioinformatics, University of Rostock, Rostock, Germany, [3] Leibniz Institute for Food Systems Biology at the Technical University of Munich, Freising, Germany

In the olfactory epithelium (OE), multiple mechanisms, like odor detection, cell regeneration, and differentiation are vulnerable to a variety of external and/or internal factors. However, the understanding of the cell-to-cell communications and molecular events associated with these mechanisms are still not fully characterized. To provide a global vision of the OE and cross-talks between its different cell types, we prepared maps related to signaling and molecular events in sustentacular cells, microvillous cells, Bowman's glands, trigeminal nerve fibers, horizontal basal cells, globose basal cells, and olfactory sensory neurons accessible via an interactive, searchable, web-based platform through MINERVA, a well-established tool used for the presentation of disease maps (https://www.sbi.uni-rostock.de/minerva/).
The molecular single-cell and interaction maps we developed will serve to conceptually visualize and analyze complex mechanisms within single cell types as well as among different cell types. The developed maps provide various entry points to the users to access the manually curated information at the cellular, process/pathway, and molecular level. The maps are designed with the aim to serve heterogeneous communities involved in olfaction including clinicians, research scientists, systems biologists, and industrial partners. In the web platform of the maps, users can identify and prioritize diagnostic/therapeutic markers associated with various olfactory diseases. For this, we developed various user-friendly plugins that help in mapping and analyzing experimental and clinical data directly onto the map. Here we provide a quick overview of manually annotated known signaling events within OE cells and highlight knowledge gaps that need further investigation.

Sat-S11-004

Structural elucidation of mammalian odorant receptors

Claire A. de March [1, 2], Jeevan Tewari [1], Ning Ma [3], Christian Billesboelle [4], Wijnand Van Der Velden [3], Nagarajan Vaidehi [3], Aashish Manglik [4], Hiroaki Matsunami [1]

[1] Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, NC, USA, [2] Unit in Biological Sciences and Biotechnologies, Nantes University, Nantes, France, [3] City of Hope, Department Computational and Quantitative Medicine, Beckman Research Institute, Duarte, CA, USA, [4] University of California San Francisco, Department of Pharmaceutical Chemistry, San Francisco, CA, USA

Odor perception is based on odorant receptors (ORs), which belong to the large family of G protein-coupled receptors and more particularly to the rhodopsin-like family, also called class A The vast majority of odorant receptors show poor cell surface expression in non-olfactory cells due to retention of the endoplasmic reticulum (ER), hindering their structural elucidation and functional study. Here, we study at the molecular level the expression mechanisms of this sub-family of G protein-coupled receptors. In this project, we use the diversity of the odorant receptor repertoire to create new optimized synthetic receptors based on their consensus sequences. Using these consensus ORs cases, we study the role of amino acids in their expression through molecular modeling, site-directed mutagenesis and flow cytometry. Their functionality is also assessed by in vitro assays. We then developed a protocol to produce and purify the most promising ORs which allow us to attempt the first structural elucidation of a mammalian OR. This research is crucial, not only to understand the strategy of our brain to perceive its olfactory environment but also to identify general mechanisms governing the function of ORs.

We thank the NIH for funding this research (CAdM K99DC01833; H.M, NV, AM R01DC020353).

Sat-S11-005

The antagonists' challenge: finding new molecules for bitter taste receptor inhibition

Fabrizio Fierro [1], Lior Peri [1], Lukas Waterloo [2], Alina Tabor-Schkade [2], Tamir Dingjan [3], Eitan Margulis [1], Herald Hübner [2], Peter Gmeiner [2], Masha Niv [1]

[1] Hebrew University of Jerusalem, Faculty of Agriculture, Rehovot, Israel, [2] Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Chemistry and Pharmacy, Erlangen, Germany, [3] Weizmann Institute of Science, Department of Biomolecular Sciences, Rehovot, Israel

Over 1000 agonists are known to activate the 25 members of the human bitter taste receptor family, with bitter taste receptor T2R14 being the most promiscuous (1) . Despite its 152 known agonists, only 3 antagonists are known, all sharing the same scaffold. Inhibiting T2Rs may help mask the undesired bitter taste of food and drugs. Due to the extra-oral expression of taste receptors, modulation of the receptor is interesting for studying extraoral roles and potential pharmaceutical applications. No experimental structure is available for any of the T2Rs, and the sequence identity with other GPCRs is very low, strongly affecting the potential of structure-based drug discovery methodologies. To address this challenge, we applied a mixed computational/experimental iterative methodology that allows for the identification of new ligands while refining the receptor structure at every step of the cycle. The initial set of ligands was employed to generate thousands of conformations of the T2R14 homology model through induced-fit docking, and, subsequently, to evaluate their performances in discriminating active ligands from decoys. Virtual screening of a multi-million library of compounds was performed using docking to the top-performing receptor conformation. Mixed structure/ligand-based approaches were also applied and potential candidates were experimentally tested. Compounds discovered in each iteration were combined with new data from cell-based screening clinical drugs and newly synthesized molecules. Overall, the number of antagonists was tripled, and their selectivity towards T2R14 was suggested by the BitterMatch computational tool (2). Over 200 new agonists have been discovered, and optimized 3D models of T2R14 were obtained.

The results stress the importance of integration of experimental and computational approaches and provide new chemical probes for inhibiting T2R14.

1. A. Di Pizio et al. Cell Mol Life Sci (2020)
2. E. Margulis et al. bioRxiv (2022)

10:00 - 12:00

Symposium 12: Modulation and integration in chemosensory processing underlying behavior

Hahn Lecture Hall

Chair/s: Daniel Muench, Katrin Vogt

Chemosensation is essential for navigating the environment, finding food sources, forming groups, or detecting mating partners. To execute the most efficient and appropriate behavior, however, animals need to process chemosensory inputs in a context dependent way. How chemosensory processing gets modulated by external and internal information (e.g. concurrent sensory stimuli or internal states) to result in an adapted behavioral response, will be the topic of this symposium. This symposium is comprised of a selection of speakers working with a diverse set of model organisms, which all show flexible behaviors towards chemosensory cues.

Sat-S12-001

State-dependent modulation of odor valence and social behavior via the main olfactory pathway

Annika Cichy [1, 5, 7], Adam Dewan [1, 6, 7], Jingji Zhang [1], Sarah Kaye [1], Tiffany Teng [1], Kassandra Blanchard [1], Paul Feinstein [3, 4], Thomas Bozza [1, 2]

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Mammalian social behaviors such as aggression are influenced by conspecific chemical cues, typically low volatility molecules that activate the vomeronasal pathway. While the main olfactory system is required for proper social behaviors, the molecular basis for how social cues are detected via the main olfactory pathway of mammals is not well-characterized. Trimethylamine is a volatile, sex-specific chemical that is enriched in adult male mouse urine and specifically activates main olfactory sensory neurons that express trace amine-associated receptor 5 (TAAR5). Here we show that trimethylamine, acting via TAAR5, elicits state-dependent attraction or aversion in male and female mice depending on neuroendocrine or social status. Genetic knockout of TAAR5 abolishes valence responses in both sexes and significantly reduces aggression-related behaviors in males, while adding trimethylamine augments aggressive behavior towards juvenile males. We further show that transgenic expression of TAAR5 specifically in olfactory sensory neurons rescues aggressive behaviors in knockout mice, despite extensive remapping of TAAR5 projections to the olfactory bulb. Our results show that state-dependent behavioral responses to a volatile social cue are mediated via the main olfactory pathway, identify a specific main olfactory input (TAAR5) as necessary for intermale aggression, and reveal that apparently innate behavioral responses are independent of patterned glomerular input to the olfactory bulb.

This work was supported by grants from NIH/NIDCD, R21DC018905 (A.C.).

Sat-S12-002

Social flexibility and olfactory processing in the desert locust

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Flexibility in social foraging behavior allows animals to maximize foraging success in nutritionally unpredictable environments. The desert locust Schistocerca gregaria exhibits one of the most extreme examples of this flexibility. Usually, solitarious locusts populate sparse landscapes at low densities and forage alone. However, under suitable conditions, mediated by an increase in density of surrounding conspecifics, locusts gradually convert into a gregarious phase. The transition to group foraging entails considerable changes in the type, quality, and quantity of sensory information available to individual animals. In addition to personally acquired evidence, gregarious locusts have access to a plethora of social information, allowing them to integrate socially derived cues on the location and quality of a food source. How is this transition mediated in terms of sensory processing? What role do social cues, such as the smell of conspecifics, play in foraging decisions? How is that modulated with change in conspecifics density? To this end, we addressed these questions by investigating the early olfactory processing of food odor cues in the presence and absence of the colony smell. We do so by widefield and confocal calcium imaging of antennal lobe projection neurons in both gregarious and solitarious locusts. We demonstrate that a simulated olfactory group context increases the overall magnitude of projection neuron activity to food odorants in gregarious animals. Yet, this social modulation is phase-dependent and does not occur in solitarious animals, suggesting it to be a potential adaptation of the olfactory system to facilitate or promote foraging in a group.

Sat-S12-003

Generating parallel representations of position and identity in the olfactory system

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Sex pheromones are key social signals in most animals. In Drosophila a dedicated olfactory channel senses a male pheromone, cis-vaccenyl acetate (cVA) that promotes female courtship while repelling males. Here we show that flies use separate cVA processing streams to extract both qualitative and positional information. We find that cVA olfactory neurons are exquisitely sensitive to concentration differences in a 5 mm range around a male fly. Second order projection neurons (PNs) detect bi-antennal differences in cVA concentration, which can reliably encode the angular position of a male. We identify an active circuit mechanism increasing left-right response differences in PNs including an interneuron performing this function by providing contralateral inhibition. At the third layer of the circuit, we find neurons with distinct response properties and sensory integration motifs. One population is selectively tuned to an approaching male with speed dependent responses. A second population responds tonically to a male fly's presence and controls female mating-decisions. A third population integrates a male taste cue with cVA, and only a simultaneous presentation of both signals promotes female mating via this pathway. Interestingly, neurons encoding speed, a positional feature, are sexually monomorphic and do not regulate sexual behavior, while neurons encoding qualitative features of male presence are sexually dimorphic and regulate female receptivity. Our results show that the olfactory system generates a range of complex percepts in discrete populations of central neurons that allow the expression of appropriate behaviors depending on context. Spatial coding is generated by integration of bilateral sensory information like the auditory system while separation of what and where pathways is reminiscent of the visual cortex.

Sat-S12-004

The short neuropeptide f regulates appetitive behavior and olfactory coding in honey bee.

Louise Bestea [1], Marco Paoli [1], Patrick Arrufat [1], Brice Ronsin [2], Julie Carcaud [3], Jean-Christophe Sandoz [3], Rodrigo Velarde [1, 4], Martin Giurfa [1, 5, 6], Gabriela de Brito Sanchez [1]

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The neuropeptide F (NPF) and its short version (sNPF) mediate food- and stress-related responses in solitary insects. In the honeybee, a social insect where food collection and defensive responses are socially regulated, only sNPF has an identified receptor. Here we increased artificially sNPF levels in honeybee foragers and studied the consequences of this manipulation in various forms of appetitive behavior. Increasing sNPF in partially fed bees turned them into the equivalent of starved animals, enhancing both their food consumption and responsiveness to appetitive gustatory and olfactory stimuli. Moreover, calcium imaging analysis of olfactory coding showed that neural activity in the antennal lobe of fed animals was reduced and could be rescued by sNPF treatment to the level of starved bees. Our results thus identify sNPF as a key modulator of hunger and food-related responses in bees, which are at the core of their foraging activities.

Sat-S12-005

The neuronal logic of how internal states control food choice

Daniel Münch, Dennis Goldschmidt, Carlos Ribeiro

Champalimaud Foundation, 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 brain of Drosophila melanogaster 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. By contrast, reproductive state acts locally to define how sensory information is translated into feeding motor output. These two states thus synergistically modulate protein-specific food intake and food choice. Finally, using a novel computational strategy, we identify driver lines that label neurons innervating state-modulated brain regions and show that the newly identified 'borboleta' region is sufficient to direct food choice towards protein-rich food. We thus 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 behaviour.

13:30 - 15:30

Symposium 13: Perturbing Chemosensation

Goethe Hall

Chair/s: Cinzia Cecchetto

Across species, chemosensation is the result of complex interactions between the environment, the sensory organs, and the neural system. As a result even minimal changes in the external or internal milieu can perturb chemosensory experience. Here we showcase a group of young, promising scientists who are uncovering the effect of different perturbations on the chemosensation of their respective model systems.

Sat-S13-001

What is the impact of climate change on the survival and chemosensation of fruit flies?

Karen Rihani [1, 3], Somasundar Arumugam [1, 3], Vignesh Venkateswaran [2, 3], Markus Knaden [2, 3], Bill Hansson [2, 3], Silke Sachse [1, 3]

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The Anthropocene era have experienced one imminent problem disrupting our ecosystem and its living organisms, climate change. Climatic changes and atmospheric pollution altered insect distributions and behaviour. Thus, pest insects expand to new crops, mosquitos spread diseases into new areas, while pollinators are decreasing in abundance. These new developments have, unfortunately, severe effects on ecological interactions, biodiversity, natural communities as well as human health.

Ozone is one of the atmospheric pollutants that exhibits increased levels in the past years and is expected to increase even further. We are therefore interested in investigating how insects, in our case vinegar flies, react and cope with elevated levels of ozone in the environment and whether this has any impact on their nervous system and in particular on sensory processing. We therefore study the olfactory preferences, activity, longevity and fecundity of flies exposed to levels of ozone normally present in polluted areas. My talk will summarize our recent findings on the impact of ozone exposure on the structure and function of the olfactory pathway of Drosophila.

Sat-S13-002

Boosting memory recall of volatile social odors with oxytocin

Renée Hartig [1, 2], David Wolf [1, 2], Wolfgang Kelsch [1, 2]

[1] Department of Psychiatry and Psychotherapy, University Medical Center, Johannes Gutenberg University, Mainz, Germany, [2] Central Institute of Mental Health, Heidelberg University, Germany

The formation of social structures relies upon the recognition of specific individuals. Recognizing familiar individuals plays an essential role, yet it remains relatively unclear how such familiarity memory is encoded in the adult brain. Social interactions are multi-sensory in nature and many species sample volatile odors emitted by conspecifics. We show here that volatile odors emitted by mice are sufficient to recognize familiar conspecifics following initial exploration. Ultra-high field awake fMRI reveals a network differentiating odors from familiar and unknowns. From this, a key relationship was identified for the processing of social orders, involving recurrent network activity between the anterior olfactory nucleus and hippocampus after appetitive social interactions (with a juvenile) and optogenetically

stimulated oxytocin release in the paraventricular nucleus of the hypothalamus. The familiarity of volatile social odors differentiated from unfamiliar odors in the olfactory bulb and striatum, overlapping with paralimbic coactivations recruited by evoked oxytocin release. Boosted oxytocin release during initial exploration produces sustained global network states with embedded strengthened familiarity memory traces. Such formation of familiarity traces requires intact oxytocin receptors in the olfactory cortex. In summary, oxytocin enables formation of distributed memory traces of learned familiarity that can be retrieved from distant chemosensory signals.

Sat-S13-003

Neuromodulation through non-invasive vagus nerve stimulation reduces wanting of a palatable chocolate drink

Lina Öztürk [1, 2], Maria Geraldine Veldhuizen [1, 3, 4]

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Vagus nerve signals from the gut to the brain carry information about nutrients and drive food reward. Such signals are disrupted by consuming large amounts of high-calorie foods, requiring greater food intake to elicit a similar neural response. Non-invasive vagus nerve stimulation (nVNS) via a branch innervating the ear is a neuromodulation tool that may affect food reward responses in humans.

In two experimental studies we examined if non-invasive vagus nerve stimulation changes the perception of palatable foods. Electrical stimulation was applied counterbalanced to either the cymba conchae (nVNS) or the ear lobe (sham) in separate test sessions. In study 1 participants (n=10, five women, on average 27.5 ± 4.0 years old) were asked to sample and rate flavored puddings with varying fat content concurrent with nVNS. Pudding samples were prepared with 0, 3.1, 6.9, and 15.6% fat weight by weight and sugar content was held constant between the four stimuli at 4.6% (w/w). We collected hedonic (dis)liking ratings and wanting rating of the food samples. In study 2 participants (n=14, 10 women, on average 29.4 +/- 6.7 years old) received nVNS before and after consumption of a palatable chocolate flavored milk (10% fat and 10% sugar w/w). We collected perceived pleasantness and wanting ratings of the drink. In study 1 we observed that concurrent nVNS increased liking ratings of low-fat stimuli by a meaningful amount from close to “neutral” to above “like slightly,” which is similar to the liking ratings that high fat puddings received ($p = .012$). In study 2 we observed that acute nVNS before consumption decreases ratings of how much participants want to consume a high-fat chocolate drink ($p = .021$).

Our results suggest that tVNS can be an effective neuromodulation tool that can help to reduce desire to consume high-calorie foods and improve liking of low-fat healthier foods in the treatment of obesity.

This study is supported by TÜBİTAK under award number 118C299.

Sat-S13-004

Viral perturbation of chemosensation: neural and perceptual insights

Elbrich M. Postma, Birgit van Dijk, Sanne Boesveldt

Sensory science and Eating behaviour group, division of Human Nutrition and Health, Wageningen University, The Netherlands

The sense of smell is important in the perception of the flavor of food and it affects several aspects of eating behavior, like appetite and food preferences, which have important implications for quality of life. Viral infections can severely impact the chemical senses. A cold or a flu can result in the loss of the sense of smell and subsequently impact eating behavior and the processing of flavor in the brain. So far, these were the most common causes of viral smell loss, but in the past 2 years, Covid-19 has emerged as a new and major viral cause for smell loss. Therefore, a large part of the population is confronted with the effects of smell loss on both perceptual and – likely - neural level. To illustrate this, we will present data from an ongoing longitudinal study on smell dysfunction in Covid-19 patients, showing the impact of changes in the sense of smell on quality of life in these patients Also, we will show how smell loss impacts eating behavior, measuring food preferences and adherence to dietary guidelines in a population of patients with smell dysfunction. Additionally, we will present data collected at the Smell and Taste Center in the Netherlands, showing the impact of smell loss due to viral infections of differences types of causes on the structure and functionality of the brain.

Sat-S13-005

Understanding the role of capsaicin in food liking and salt taste perception in individuals with smell loss

Stephanie Hunter, Pamela H. Dalton

Monell Chemical Senses Center, Philadelphia, PA 19104, United States

When people lose their sense of smell, they often find food less enjoyable and as a result alter their diet to increase flavor and eating enjoyment. One dietary alteration that is often reported is adding more salt to foods, and preferring salty foods. Over time, however, this can lead to excess salt intake and increased risk for cardiovascular disease. Among individuals with a normal sense of smell, the addition of capsaicin to reduced salt dishes has been shown to increase saltiness perception and overall flavor; whether adding capsaicin produces measurable improvements in saltiness perception and food liking has not been studied in those with smell loss. The purpose of this study was to determine 1) whether salt intake in those with smell loss differs from population averages, and 2) whether capsaicin increases flavor and salt taste intensity, and enjoyment of foods in individuals with smell loss. Individuals having confirmed partial or total smell loss for at least 12 weeks rated total flavor, taste quality, and spiciness intensity, and liking of samples with different levels of spice and/or salt. 24-hour urine samples were also collected to determine sodium intake. Preliminary findings indicate that although sodium intake is higher than recommended, those with smell loss do not consume more sodium than population averages (2741 ± 271 mg vs 3039 ± 99 mg, respectively; $p=0.3$). Adding moderate amounts of capsaicin to a reduced sodium soup increased total flavor intensity ($p=0.003$) and salt taste intensity ($p<0.001$) compared to the same soup without capsaicin, such that it was rated as flavorful and salty as a regular sodium soup with twice as much sodium. However, there were no differences in liking between the soup samples with and without capsaicin ($p>0.05$). Thus, capsaicin may help to improve flavor and increase salt taste intensity in people with smell loss, however more research is needed to understand its acceptability in the diet.

13:30 - 15:30

Symposium 14: Dynamic olfaction: linking the patterns of odour, neural activity, and behaviour across species

Hahn Lecture Hall

Chair/s: Tobias Ackels, Sebastian H Bitzenhofer, Katherine Nagel

Olfactory cues are highly dynamic, as is their processing in the brain. With this symposium, we will highlight recent work on the dynamics of natural odour stimuli, olfactory representations, and olfactory behaviour, in a variety of model systems (mouse, fish, and fly). This symposium will give an exciting and timely overview merging complementary perspectives on the dynamic aspects of olfactory processing and perception across model systems.

Sat-S14-001

Experience dependent plasticity of ongoing and odor driven activity

Emre Yaksi

Kavli Institute for Systems Neuroscience, NTNU

Ongoing neural activity has been observed across several brain regions and thought to reflect the internal state of the brain. Yet, it is not fully understood how ongoing brain activity interacts with sensory experience and shape sensory representations. Here, we show that projection neurons of the fruit fly antennal lobe exhibit spatiotemporally organized ongoing activity in the absence of odor stimulation. Upon repeated exposure to odors, we observe a gradual and long-lasting decrease in the amplitude and frequency of spontaneous calcium events, resulting in a reorganization of correlations between olfactory glomeruli during ongoing activity. Accompanying these plastic changes, we find that repeated odor experience reduces trial-to-trial variability and enhances the specificity of odor representations. Our results reveal a previously undescribed experience-dependent plasticity at peripheral levels of the fruit fly olfactory system.

Sat-S14-002

Organizational axes of structured representations of odor in the fly mushroom body

Elizabeth Hong

Division of Biology & Biological Engineering, California Institute of Technology, Pasadena, CA, USA

Understanding olfactory coding is challenging due to the complexity of chemical stimuli, which are, by nature, complex, high-dimensional, and not easily organized along any obvious coordinate systems. We investigated this problem in the Drosophila olfactory system, whose core circuit architecture is similar to that of its vertebrate analogs. Olfactory inputs are randomly expanded onto a large population of third-order, mixed layer neurons, which, in the fly, are the principal neurons of the mushroom body (MB), a major associative olfactory area in the fly brain. Using large-scale calcium imaging in defined olfactory populations, we find that MB representations of odor are sparse and structured; odor relationships are reliable and predictable across individual MBs. However, the relationships between odors are unexpectedly remapped between the input odorant receptor layer and the mushroom body layer, in a manner that deviates from the simple predictions of a sparse random expansion of olfactory inputs. We will discuss new analytical approaches towards understanding alternative organizational frameworks by which odor representations are reformatted across successive stages of olfactory processing in the fly brain.

Sat-S14-003

A canonical motion detection algorithm in olfaction and its role in turbulent odor navigation

Nirag Kadakia [1, 2], Thierry Emonet [1, 2, 3, 4], Damon Clark [1, 2, 3, 4]

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Insects navigate to odor sources by combining information from the intensity, timing, and spatial distribution of odor encounters. One key information stream is the difference in odor signals between the antennae. This bilaterally-resolved information enables gradient sensing, helping navigation in simple environments like static odor ribbons. In turbulent plumes, however, gradients are of limited use since they are hard to resolve and carry little information about the source location. Here, we have discovered a distinct role for bilateral odor sensing—detecting the direction of motion of odors. This discovery was enabled by decoupling wind from odor using spatially and temporally precise optogenetic stimulation of freely-moving Drosophila. We used stimuli previously designed for visual motion detection studies, which decompose natural stimuli landscapes into their “building blocks” of spatiotemporal correlations. Using this paradigm, we demonstrate that flies compute the direction of odor motion using a correlation-based algorithm equivalent to the Hassenstein-Reichardt correlator (HRC) proposed to describe motion detection in vision. Moreover, we replicated “olfactory illusions” providing direct evidence of correlation-based motion detection outside of vision. Finally, we combine computational modeling and virtual reality experiments to show that odor motion is a critical information stream in turbulent plumes enabling effective navigation to the source. Our work (1) reveals a critical role for bilaterality in olfaction; (2) shows that olfactory navigation exploits odor motion direction independent of wind direction; and (3) provides direct, causal evidence for analogous motion computations in olfaction and vision.

Funding provided by Swartz Foundation of Theoretical Neuroscience (USA), National Institutes of Health (USA), and National Science Foundation (USA)

Sat-S14-004

The olfactory bulb maps breathing rhythms and self-location in freely-behaving mice

Morgan Brown [1], Teresa Findley [1], Scott Sterrett [5, 6], Aldis Weible [1], Adrienne Fairhall [5, 6], James Murray [1, 3, 4], Matt Smear [1, 2]

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Odors carry useful navigational and episodic information, but no matter how many receptor genes are in an animal’s genome, there is no receptor for time or place. To optimally orient by olfactory information, brains must unify odor-driven activity with contextual representations of self-movement and -location. Studies in other sensory modalities

demonstrate that motor- and location-related signals are common in primary sensory areas. Motivated by these findings, and given the reciprocal connection between olfactory system and hippocampus, we hypothesized that the olfactory bulb encodes contextual information. To test this hypothesis, we captured the sniffing and movement of mice while recording spiking in olfactory bulb (OB), in the absence of experimenter-applied stimuli or tasks. Breathing and spiking differ between head-fixed and freely-moving states. During free movement respiration is rhythmically organized into discrete states lasting minutes, whereas these states are not apparent during head-fixation on a stationary platform. This discrete organization is likewise apparent in the "spontaneous" activity of the olfactory bulb – many individual neurons fire selectively during particular rhythmic states. In addition to these state-selective signals, we also found that allocentric position can be decoded from neuronal ensembles in OB, with comparable decoding performance to hippocampal ensembles recorded under the same conditions. Thus, even during uninstructed behavior and ambient stimuli, contextual information about state and place can be read out from the activity of the olfactory bulb. We propose that these contextual signals facilitate the incorporation of olfactory information into cognitive maps of environment and self.

Sat-S14-005

Correlating mouse head-motions with odor plume-contacts in an olfactory-guided navigation task

Mohammad Tariq [1, 2], Scott Sterrett [1, 2], Sidney Moore [2], David Perkel [3], David Gire [2]

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Although much is known about the mammalian brain olfactory structures and the physiological activity within them during passive presentations of odors in head-fixed setups, how olfactory cues shape naturalistic behaviors and their neural underpinnings in freely moving mammals remains poorly understood. One main difficulty of studying naturalistic plume-guided behaviors stemmed from the challenges associated with recreating the complex olfactory landscape that animals experience in the wild, and correlating the dynamic olfactory information with the behavior and neural processing. This is because the odor molecules emanating from a source are spread by the turbulent and chaotic motion of the air molecules, resulting in a spatiotemporally varying signal in the form of an olfactory plume. We previously reported a method (Tariq et al., 2021) to record real-time odor information during plume-tracking in mice. In addition, Findley et al., 2021 have established head-motions as a key behavioral feature for mice engaged in an odor gradient-dependent choice task. Here we combine our odor recording method with real-time head motion monitoring, using 3-axis accelerometer recordings, and posture tracking to establish correlation between plume contacts and head-motion changes. Our data show the importance of head-motions, and their plume-contacts dependence, for active sensation in an olfactory-guided navigation task. Hence, these combined results establish the naturalistic behavior of plume-tracking as a valuable experimental task to study neural encoding and decoding during a complex sensorimotor transformation in mammals.

16:00 - 16:30

Publishing your Chemosensory Research

Goethe Hall

Chair/s: Steven Munger, Alfredo Sansone

16:30 - 17:30

Keynote Lecture: Johan Lundström: Odor processing in the human olfactory bulb

Goethe Hall

Chair/s: Jessica Freiherr

Sat-L5-001

Odor processing in the human olfactory bulb

Johan N. Lundstrom

Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden, Monell Chemical Senses, Philadelphia, US

Animal studies have demonstrated that the olfactory bulb (OB) is a key node of the olfactory system and the list of olfactory tasks in which it is implicated keeps growing. However, until recently, no technique existed that allowed non-invasive measures of signal from the OB in awake and healthy humans. In this talk, I will outline the development, validation, and implementation of a new method, the electrobulbogram (EBG), that enable non-invasive measures from the human OB in healthy humans while they are processing odors. In addition, I will summarize results from our recent studies where we used the EBG method to assess the role of the human OB in forming our odor perception as well as its communication with piriform cortex. I will argue, akin to some animal models, that one of the main roles of the human OB is to sequentially process odor valence, with a temporally privileged access to negative odors. Finally, I will review our ongoing work to use the EBG measure as a potential tool for early Parkinson's disease detection.

17:30 - 18:00

Closing Remarks & Awards

Goethe Hall