PROGRAMM Friday, 29.November

9.00-9.30 **Why do we smell – from animals to humans**

Ivan Manzini, PhD, Georg-August-Universität Göttingen; imanzin@gwdg.de

9:30-10:00 **Once liked – always liked or: how do we develop odor preferences**

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10:00-10:36 Intranasal trigeminal function

Olfactory-trigeminal interaction in chemosensory perception.

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Objectives: Most odors stimulate both, the trigeminal and the olfactory system. Previous studies have presented a mutual influence of the two systems. To better understand the olfactory – trigeminal interaction, the following experiments were conducted.
Materials & methods: Psychophisical measurements in human as well as electrophysiological (EOG) and immunohistochemical experiments were conducted in rats. For stimulating the olfactory system CO2 was used and phenylethylalcohol (PEA) for olfactory activation respectively. In rats the trigeminal peptide calcitonin gene-related peptide (CGRP) was applied.
Results: CO2 markedly decreased the perceived intensity of PEA compared to PEA alone. This effect was most prominent when both stimuli were presented at the same time. In line with that, the EOG response to PEA in rats was decreased when CGRP was present. In addition trigeminal fibers in the olfactory mucosa were CGRP positive and olfactory receptor neurons expressed CGRP-receptors.
Conclusions: Data from human and animals showed a decreased olfactory response due to trigeminal activation. This effect seems to be mediated in the olfactory periphery by peptides such as CGRP.

Depicting the inner and outer nose: The representation of the nose and the nasal mucosa on the human primary somatosensory cortex (SI)

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The nose combines several important functions, such as breathing and the perception of olfactory and tactile sensations. To further understand the representation of the nose and the nasal mucosa on the primary somatosensory cortex, the non-invasive method of functional magnetic resonance imaging (fMRI) was utilized to depict the position of the nose and the nasal mucosa on the subdivisions of the human postcentral gyrus (PG), Brodman area (BA) 3b, 2 and 1. Tactile stimulation during fMRI was applied through a custom-designed, pneumatically-driven device to six stimulation sites: the alar wing of the nose, the lateral nasal mucosa, and the hand (serving as a reference area) on the left and right side of the body. We were able to discriminate individual representations for the hand as well as

the nasal mucosa and alar wing of the nose within BA 3b and 1, comparing mean activation maxima and Euclidean distances. Our results regarding the alar wing of the nose were in line with the classic sensory homunculus proposed by Penfield. We further determined an individual and bilateral representation of the nasal mucosa on the primary somatosensory cortex that is situated closer to the caudal end of the postcentral gyrus compared to the alar wing of the nose and the hand. As the primary somatosensory cortex is commonly activated during the perception of odors, these findings underline the importance of the somatosensory impact during olfactory processing, which is important for food intake, selection of mating partner, and danger signaling.
Key words: primary somatosensory cortex (SI), nasal mucosa, fMRI, somatotopy, somatosensory stimulation, homunculus, olfaction

The chemosensory path of pain

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Intranasal trigeminal sensations are important in everyday life, as they protect the airways from harmful substances. It has been shown that trigeminal sensations arise from the binding of a ligand to various sub-types of transient receptor potential (TRP) channels, but which underlying neural networks are involved in the processing of these different trigeminal inputs is still unknown. Fourteen healthy human subjects participated in this study, completing three functional magnetic resonance imaging (fMRI) scanning session during which three different trigeminal substances, activating different sub-types of chemoreceptors and evoking different sensations in the nose: CO2, menthol and cinnamaldehyde, were applied.
We identified similar functional networks responding to all three stimuli: an olfactory network, a pain network and an integrative network. The olfactory network included brain areas responsible for odor processing, such as the piriform cortex, the entorhinal cortex, the amygdala, as well as parts of the thalamus. The pain network involves the primary and secondary somatosensory cortex and the insula. The integrative network consists of brain areas, associated with multimodal integration, such as the orbitofrontal cortex, the insula and the inferior parietal lobule. Even though CO2 is perceived as odorless, stimulation with CO2 evoked activity in the olfactory network, whereas the pain network was also detected for processing menthol and cinnamaldehyde stimuli, which are usually not perceived as painful. The results of our study suggest a common central processing pathway for trigeminal information regardless the trigeminal chemoreceptor and sensation type.

10:51-11:21 **Imaging of the olfactory system – what can we see**

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11:21-12:21 Diagnostics

Clinical usefulness of time-frequency analysis of chemosensory event-related potentials.

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Background: The clinical usefulness of olfactory event-related brain potentials (OERPs) to assess olfactory function is limited by the relatively low signal-to-noise ratio of the responses identified using conventional time-domain averaging. Recently, it was shown that time-frequency analysis of the obtained EEG signals can markedly improve the signal-to-noise ratio of OERPs in healthy controls, because it enhances both phase-locked and non phase-locked EEG responses. The aim of the present study was to investigate the clinical usefulness of this approach and evaluate its feasibility in a clinical setting.
Methodology: We retrospectively analysed EEG recordings obtained from 45 patients (15 anosmic, 15 hyposmic and 15 normosmic). The responses to olfactory stimulation were analysed using conventional time-domain analysis and joint time-frequency analysis. The ability of the two methods to discriminate between anosmic, hyposmic and normosmic patients was assessed using a Receiver Operating Characteristic analysis.
Results: The discrimination performance of OERPs identified using conventional time-domain averaging was poor. In contrast, the discrimination performance of the EEG response identified in the time-frequency domain was relatively high. Furthermore, we found a significant correlation between the magnitude of this response and the psychophysical olfactory score.
Conclusion: Time-frequency analysis of the EEG responses to olfactory stimulation could be used as an effective and reliable diagnostic tool for the objective clinical evaluation of olfactory function in patients.

Chemosensory event-related brain potentials (CSERP) after monorhinal stimulation with closed contralateral nostril.

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Introduction: Leaving the flow-olfactometer the airflow passes the ipsilateral nostril and streams back via the contralateral nose because of the velopharyngeal closure. The embedded stimulus has a rectangular form and can evoke ipsilaterally olfactory or trigeminal CSERPs. In contrast, the same stimulus is not able to evoke a CSERP in the contralateral nose because the rise time is prolongated. If the contralateral nostril is closed by foam material, the air has to return through the ipsilateral nose. This could affect the rectangular shape of the stimulus preventing the development of CSERPs, probably. The goal of our study was to evaluate whether real monorhinal stimulation with closed contralateral nostril can generate ipsilateral CSERPs in association with an olfactory and, respectively, trigeminal perception.
Material and methods: 18 healthy normosmic subjects were included (3 males, 15 females; average age: 23.8 years, range 18-29 years). A flow-olfactometer OM2S was used. 2ppm

H2S and 40% CO2 were the stimulants, stimulus duration 200ms, ISI 35 s. One trial consisted of 40 randomly changing H2S and CO2 stimuli (1. trial: right nostril stimulated, left nostril closed, 2. trial: right nostril stimulated, left nostril open; 3. trial: left nostril stimulated, right nostril closed; 4.trial: left nostril stimulated, right nostril open), velopharyngeal closure, mouth breathing. 5 scalp electrodes (Fz, Cz, Pz, C3, C4), additional Fp2 recognizing blink artifacts; A1 was the reference electrode, A2 was grounded, EEG Vision Amplifier (V-Amp) recorded by Brain Vision, Gilching. Off-line analysis was performed with Vision Analyzer (Brain Vision) after EEG epoch filtering (low pass 2 Hz, high pass 70 Hz) and rejection of EEG epochs with artifacts (Fp2 >50µV automatically and visually). Latencies and amplitudes of CSERP components were measured manually and averaged. Subjects performed a tracking game to keep their attention at level high. They were asked to press a button when the stimulus was perceived. Latencies (P1, N1, P2, N2) and amplitude (N1P2) were analyzed by univariate analysis of variance (UNIANOVA, SPSS 21) with 3 factors (stimulus: H2S, CO2; stimulated nostril: right, left; contralateral nostril: closed, open). Significance level was set at p=0.05.

Results: 17 olfactory CSERPs and 16 trigeminal CSERPs could be analyzed. 1 subject did not show any CSERPs although most stimuli were perceived. One subject with trigeminal stimulation was excluded because of excessive artifacts. 93.4% of all 2880 stimuli were detected. 135 H2S stimuli and 54 CO2 stimuli were not detected. There were no differences between latencies and amplitudes (Cz/A1) related to the stimulated nostril after both stimulation modes. The latencies of P1 and N1 and the amplitude N1P2 were larger after CO2 stimulation than after H2S stimulation. The latencies of P2 and N2 were larger after H2S stimulation than after CO2 stimulation. There were no interactions between stimulated nostril and*contralateral nostril; stimulus and stimulated nostril; stimulus and contralateral nostril; stimulus and stimulated nostril and contralateral nostril.

Discussion: Most important our study confirmed that CSERPs can be induced by monorhinal stimulation even with a closed contralateral nostril. That means that the rise time of the embedded olfactory and trigeminal short stimuli was sufficient to create CSERPs and was not disturbed by the escaping air through the same nostril. The outlet of the olfactometer was placed at the nasal valve and was directed upwards the olfactory cleft. The constant air-flow with the stimuli streamed into the upper nasal passage and generated CSERPs by stimulation in the immediate vicinity of the outlet. The respiratory epithelium contains a lot of trigeminal nerve fibers here, and the olfactory pulses hit the olfactory neurons probably without being affected by any returning airflow. The backward airflow is probably guided through the middle and inferior nasal passage. This was proven by placing cotton in front of the open nostril. The cotton moved outwards below the olfactometer exit and the lower pressure above its exit sucked in the cotton.

With a closed contralateral nose it would be possible to stimulate the olfactory system strictly ipsilateral. It should be taken into account that a contralateral stimulation by the exhalation is theoretically possible when looking on the latency between both hemispheric cerebral activations. Therefore further studies strictly using monorhinal olfactory cerebral activation should be performed.

A third aspect of our results is the opportunity to evaluate the sense of smelling subjectively in cases of congenital or acquired closure of unilateral nasal exit. About 90% of the passive suprathreshold CO2 and H2S stimuli of our flow-olfactometer were detected if the contralateral nostril was closed. In a further study we would like to investigate the detection threshold of H2S and CO2, respectively, as we did in other studies with open contralateral nostrils. So far, we cannot exclude that the threshold values are the result of a mixed ipsi- and contralateral perception.

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Investigations on cerebral olfactory processing using magnetoencephalography – a pilot study

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In the past years functional magnetic resonance imaging (fMRI) has become a standard neuroimaging procedure for visualization of human olfactory processing in vivo. The main advantage of fMRI is its high spatial resolution. Unfortunately, it has only a poor ability to resolve the temporal aspect of cerebral activity. Here, magnetoencephalography (MEG) could be of advantage due to its high temporal and spatial resolution. Only a few studies used magnetoencephalography in olfactory research. In our pilot study 20 healthy subjects (10 women, 10 men, age 50–70 years) were included. Datasets were acquired on a 306-channel whole head MEG system (Elekta Neuromag) with simultaneous electroencephalography (EEG) measurement. Monorhinal olfactory stimuli were applied using an OM4b olfactometer (Burghart) using 2-phenylethanol as odorant. 4 activity peaks could be observed in the MEG and EEG data. Future studies will focus on dipole reconstruction. Here, a multimodal approach with integration of complementary neuroimaging-procedures like fMRI, MEG and EEG could be advantageous.

Magnetic source imaging of olfaction

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Recent imaging techniques show different advantages and disadvantages. The advantage of magnet encephalography (MEG) is the high time resolution in combination with source localization.
In a set of 20 healthy subjects we investigated the onset of brain activities in relation to ipsi- and contralateral stimulation with two odorants (phenylethylethanol and H2S).
Olfactory responses were identified shortly (within 150 ms) after stimulus onset in both hemispheres. Stimulation of the ipsilateral side provided earlier signals compared to contralateral stimulation in the primary olfactory cortex, hippocampus, and orbitofrontal cortex.
We suggest the MEG recording technique as a suitable tool to define the functional network of olfaction in healthy subjects and patients with olfactory dysfunction.

Clinical Study of the patients with a lateralized difference in olfactory function

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[Background] There are few studies that provide the unilateral examination in olfactory dysfunction. If the olfactory function is examined by bilateral test, olfactory dysfunction

might be missed. The aim of this study is to investigate the side differences of odor identification in patients with olfactory dysfunction and compare the unilateral dysfunction with bilateral dysfunction.
[Methods] Self-assessment of olfactory function and evaluation of olfactory function by means of a validated test were performed in 368 patients with olfactory dysfunction. A 12-item odor identification test ("Open Essence") and intravenous test was used to evaluate the bilateral olfactory functions. And Jet Stream Olfactometer was used to evaluate olfactory function separately for each nostril. Moreover we compare the unilateral dysfunction with bilateral dysfunction in their ages, sex, history and the other examinations.
[Results] The average age of these participants was 50 years (±SD 15). Men was 152, female was 216. Twenty-nine patients had more than 2 differences by olfactometer between left and right nostrils. Thirteen were post-viral infections, 11 were chronic rhino sinusitis, 4 were idiopathic and 1 was postoperative complication. Post-viral olfactory dysfunction was significantly common in patients with unilateral olfactory dysfunction. Among them, only one 26-year old lady with the post-viral olfactory dysfunction has the subjective symptoms for unilateral olfactory dysfunction. The others do not. Olfactometer score ($p < 0.05$) and a percentage of correct answers for the Open Essence ($p < 0.05$) were better in those who have the unilateral olfactory dysfunction. Visual Analogue Scale of olfactory dysfunction was not related to the unilateral olfactory dysfunction ($p=0.083$).
[Conclusion] If someone has the unilateral olfactory dysfunction, it is difficult to notice that it is unilateral, but they just notice as an olfactory dysfunction. Overall olfactory function is related to the better nostril. Future studies are needed to investigate whether side differences in patients with olfactory dysfunction are a predicator of a higher or lower risk for improving from the olfactory dysfunction.

12:21-13:09 Chemosensory function in various diseases I

Case series: From the outpatients clinic at the Dept. of ORL, Technical Univ. of Dresden, Germany

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Four cases from the Dresden Smell and Taste Outpatient clinic will be presented.

Case report: Acute changes of olfactory and gustatory function in a patient with multiple sclerosis.

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Background: The aim was to investigate a correlation between changes of taste and smell in a young patient with multiple sclerosis (MS) to the disease activity.
Methods: The Smell Discrimination Identification test (TDI score) was used for subjective olfactometry. Olfactory and trigeminal stimuli were used to generate evoked cortical potentials. Gustatory function was tested by administering a whole-mouth above-threshold test and spatial taste test using sucrose, sodium chloride (NaCl), citric acid, and quinine hydrochloride solutions.

Results: The young patient complained about an acute paresthesia of the right face and his ipsilateral hand. He also expressed a sudden loss of his smelling sense with a change in taste sensation. After 3 weeks the symptoms were reevaluated and a subjective improvement (visual analogue scale) of the smelling and gustatory function was confirmed with the TDI score. These results correlated to the clinical disease activity of multiple sclerosis.
Conclusions: The young patient was aware of his olfactory and gustatory capacity. These parameters might be useful to estimate disease activity in MS patients.

Linking dopamine and olfaction: does it make scents?

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Animal and clinical evidence suggest that dopamine (DA) plays a role in olfactory function. Transgenic mice lacking the D2 receptor exhibit severe olfactory dysfunction, and individuals with severe alterations in DA systems, such as patients with Parkinson's disease (PD) and Huntington's disease suffer from olfactory impairments. The main aim of this study was to investigate the relation between DA olfactory functions in a sample of healthy adults. Position emission tomography (PET) was used to estimate D2 receptor binding potential (D2R-BP) in brain regions involved in olfaction. The radioligands [11C]Raclopride and [11C]FLB 457 were used to estimate binding in striatal and extrastriatal regions, respectively. Fifteen participants were assessed across five different olfactory tasks: olfactory threshold, odor discrimination, episodic odor memory, as well as free and cued odor identification. The results indicated that odor discrimination proficiency was negatively correlated with D2R-BP in the left ventral striatum (r = -.58) the orbitofrontal cortex (OFC; r = -.59) and the amygdala (r =-.62). Episodic retention of odors was negatively associated with D2R-BP in the left ventral striatum (r = -.64), the amygdala (r = -.63) and the left OFC (r = -.67). Free odor identification was significantly correlated with D2R-BP (r = .58) in the right associative striatum, the anterior cingulate cortex (ACC; r = -.58) and the medial temporal lobe (MTL; r = -.75). Overall, these novel findings suggest that having lower amounts of D2 receptors in specific brain is associated with better olfactory function. It is suggested that some olfactory and cognitive functions benefit from lowered inhibition.

Olfactory bulb volume: a predictor of therapy response in depression?

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14:15-14:45 **Plasticity of the olfactory system – when and how much Regeneration can we expect?**

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14:45-15:45 Plasticity / Therapy

Effects of the MAO-B inhibitor rasagiline on olfactory function in patients with Parkinson´s disease.

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Background: Loss of olfactory function in Parkinson's disease (PD) has severe impact on the patients´ quality of life. The aim of this prospective and cross-sectional investigations was to determine whether PD patients would benefit from treatment with the MAO-B inhibitor rasagiline in terms of an improvement in their general olfactory function.
Methods: (1) Thirty-four PD patients participated in this single-center, prospective, randomized, controlled, double-blinded study. Seventeen patients were randomly assigned to rasagiline and 17 patients to placebo. Ortho- and retronasal olfactory testing and recording of event-related potentials were performed before and after 120 days of rasagiline vs. placebo intake. (2) In this cross-sectional study orthonasal olfactory function was tested in 74 PD patients with rasagiline intake and 150 PD patients without rasagiline intake.
Results: (1) When comparing olfactory score differences between baseline and after 120 days between the two groups the level of significance was not reached. Within-group differences however, proved to be significant. (2) In the cross-sectional study, olfactory function did not differ significantly between the groups with and without rasagiline intake.
Conclusion: The primary endpoint of the studies was not reached and therefore, a specific effect of rasagiline on olfactory function in PD could not be demonstrated.

The effect of acupuncture on olfactory function in patients with post-infectious smell loss.

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Background: The possibilities of therapy for patients with post-infectious olfactory dysfunction are restricted. On the basis of a study by Hauswald et al. 1998 now the effect of acupuncture on the olfactory function in patients with post-infectious olfactory dysfunction was surveyed in a randomized, single-blinded, placebo-controlled study.
Methods: 60 patients with post-infectious olfactory dysfunction were included and were assigned randomized to two groups (verum- and placebo-acupuncture). Every patient received 12 acupuncture treatments. Before and after treatment a sniffin' sticks-test was performed.
Results: Within the groups a significant improvement of the TDI-score could only be reached in the verum-group. Besides a significant difference could be shown in the TDI-difference and the discrimination-difference between the verum- and the placebo-group. The results of the threshold- and the identification-test didn't change significantly. A significant correlation could only be found between the period of the disease and the TDI-difference, not between the age as well as the starting TDI-score and the TDI-difference.
Conclusion: It could be shown, that acupuncture is an alternative possibility to treat patients with post-infectious olfactory dysfunction. The best result was achieved with a short period of disease. Old people as well as anosmics can profit by this treatment.

Olfactory training in postviral olfactory dysfunction

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Introduction: We performed a randomized, single-blind, controlled, crossover study to evaluate the effects of olfactory training (OT) on olfactory function in patients with persistent postinfectious olfactory dysfunction (PIOD) in Twelve tertiary university medical centers. Methods: Investigations were performed at three visits (baseline, after 18 weeks, and after 36 weeks), including only subjects with PIOD of <24-months duration. At each visit, participants received detailed assessment of olfactory function. Seventy subjects trained with high concentrations of four odors for 18 weeks; the other half (n574) trained with low concentrations of odors. For the following 18 weeks this regimen was switched. Results: After 18 weeks, olfactory function improved in the high-training group in 18 of 70 participants (26%), whereas only 11/74 improved in the low-training group (15%). In subjects with a duration of olfactory dysfunction of <12 months, olfactory function improved in 15/24 participants (63%) of the high-training group and in 6/31 participants (19%) of the low-training group (P5.03). Conclusions: OT improves PIOD, and the use of odors at higher concentrations is beneficial to improvement. OT is a safe procedure and appears to be particularly useful in patients who start OT within 12 months after the onset of the disorder. OT is the first successful therapy regime in patients with PIOD.

Topical corticosteroids applied with a squirt system for steroid-dependent olfactory impairment

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Objectives: To investigate whether applying topical corticosteroid with a squirt system could maintain the effect of oral corticosteroid for steroid-dependent olfactory impairment.
Methods: Patients were enrolled if they had suffered from olfactory dysfunction for more than three months, and TDI (threshold, discrimination and identification) scores in “Sniffin’ Sticks” increased by more than six points after one week of oral corticosteroid treatment. A total of 22 patients were enrolled and treated with 0.2 ml Nasacort® using the squirt system twice a day. Nasal polyps were present in eight patients. Mean Lund-Mackay score by CT scan was 11.2±4.1 (4-20).
Results: TDI scores increased from 13.1±4.2 to 26.5±5.3 with one week of oral corticosteroid treatment. One patients was lost follow-up thereafter. Nineteen patients were evaluated after one month of topical corticosteroid squirt treatment, 14 after 3 months, and 10 after 6 months. Mean TDI score was 23.2±7.1, 24.2±7.0 and 27.3±5.3 after one, three and six months of topical corticosteroid squirt treatment. The TDI scores was not significantly different from that after one week of oral corticosteroid treatment.

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Conclusion: Topical corticosteroid squirt treatment twice a day may maintain the effect of oral corticosteroid treatment in a portion of patients with steroid-dependent olfactory impairment.

Does surgery of the olfactory clefts modify the sense of smell?

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Background. The olfactory outcome after surgery of polypi in the olfactory clefts (OC) is unknown.
Objectives. 1)to investigate the relationship between clinical characteristics and the presence of the respiratory epithelial adenomatoid hamartoma (REAH) in the olfactory clefts; 2)to assess the olfactory outcome after surgery in the OC for either eosinophilic polyps (EP) or REAH in patients with ethmoidectomy for nasal polyposis (NP).
Materials and Methods: Seventy-four patients with NP having undergone nasalization procedure were enrolled in this prospective study. The olfactory clefts were systematically examined during the endoscopic surgery. Small polyps or oedematous mucosa of the OC were systematically biopsied. Moderate or big polyps in the OC were removed after ethmoidectomy. The distinction between REAH and EP relied on histopathological examinations. The olfactory function was measured with standardized “Sniffin’ Sticks” odor threshold and identification tests 1 day before and 6 weeks after surgery.
Results: There was a close relationship between the presence of REAH-OC and the duration of NP disease ($p = 0.0009$), asthma ($p = 0.004$) and previous surgery ($p = 0.0006$). Before surgery, 90.6% of patients with REAH-OC were hypo-anosmic in contrast with half of patients having EP-OC ($p = 0.0003$). Predictors of poor olfactory outcomes after surgery were long standing nasal symptoms ($p = 0.027$), history of previous surgery ($p = 0.01$) and history of previous middle turbinates resection ($p = 0.0006$). Polyp histology and surgery of the OC were not predictors of poor olfactory outcomes.
Conclusion: The resection of REAH or EP of the OC in patients with NP does not worsen but instead can improve the postoperative olfaction.

Olfactory function following fractures of the rhino-base

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15:45-16:33 Mixed Bag

Olfaction and Environment: Tsimane’ of Bolivian Rainforest Have Lower Threshold of Odor Detection Than Industrialized German People.

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Olfactory sensitivity exhibits variance between individuals. However, data regarding cross-cultural and inter-group differences are scarce. We compared thresholds of odor detection of traditional society of Tsimane' of Bolivian rainforest (n=151) and German people (n=286) using "Sniffin' Sticks" threshold subtest. Tsimane' detected n-butanol at significantly lower concentrations than Germans. In addition, the distribution of thresholds of the Tsimane' was very specific, with 25% of Tsimane' obtaining better results, and 10% of Tsimane obtaining lower results in the olfactory test than did any member of the German group. We conclude that differences in olfactory sensitivity seem to be especially salient between industrialized and non-industrialized populations inhabiting different environmental conditions. We hypothesize that the possible sources of such differences are (i) higher importance of smell in traditional populations, (ii) environmental pressures shaping olfactory abilities in these populations and (iii) the impact of pollution which impairs the sense of smell of people from industrialized countries.

The neuronal correlates of olfactory perception - an ALE meta-analysis of human functional brain imaging studies.

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Even though a lot of animal and human studies have been performed to identify the neuronal network of olfactory processing, olfaction is still among the least understood sensory modalities. Therefore we decided to perform a meta-analysis of human functional brain imaging data about olfactory stimulation to map the human neuronal correlates of olfactory stimulation with high statistical power using activation likelihood estimation (ALE). Furthermore, we were interested in results about differences between experiments with memory or rating tasks compared to experiments with passive smelling tasks, to gain more evidence about neuronal correlates of memory processing. The results of the ALE meta-analysis for olfactory stimulation confirmed the role of several already known brain regions of the olfactory network, such as the entorhinal cortex, the piriform cortex, the insula, the amygdala and the hypothalamus. Interestingly, the ALE meta-analysis of the rating and memory revealed significant activation in some brain regions so far only suspected to be responsible for olfactory memory working, such as the angular gyrus and the superior and inferior temporal gyri and also the cerebellum, which probably may play a role in cognitive olfactory processing.

Effects of topical citrate buffer on olfactory function: preliminary data

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PROGRAMM Saturday, 30.November

9:45-10:15 Taste disorders – etiology and therapy

Basile Landis, PD Dr. med, Univ. of Geneva; bnlandis@yahoo.co.uk

10:15-10:51 Taste

Results of forced-choice and non-forced-choice test procedures using the „taste strips“

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Background: A clinical test of gustatory function using impregnated „taste strip“ has been introduced by Kobal and co-workers (Mueller et al., 2003). As a non-forced-choice procedure response items include „sweet“, „sour“, „salty“, „bitter“ and „no taste“. Most clinical smell tests use forced-choice procedures. The aim of the study was to compare results of the „taste strips“ using forced-choice and non-forced-choice procedures.
Methods: The investigation included 89 subjects so far (41 females, 48 males, age 18-83, mean/SD 38.6/18.6 years). Gustatory function was assessed using both procedures in a pseudo-randomized order.
Results: The mean taste score (with standard deviation) of the forced-choice procedure was 12.5 (2.5). The non-forced-choice procedure yielded a mean taste score of 11.8 (2.6). This difference was statistically significant (95% confidence interval: 0.13-0.88, p=0.009).
Conclusion: Our results show different taste scores obtained by the two test procedures with higher results using a forced-choice paradigm.

Extension of the „taste strips“ test for the assessment of subjects with enhanced gustatory sensitivity

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Assessment of gustatory function using the „taste strips“ test is an easy and valid procedure. The aim of the study was to extend this test in order to be able to detect subjects with enhanced gustatory sensitivity (e.g., „supertaster“). Four concentrations of sweet, sour, salty and bitter taste were amended by two additional low concentrations (sweet: 0,025/0,0125 g/ml sucrose; sour: 0,027/0,015 g/ml citric acid; salty: 0,0064/0,0026 g/ml sodium chloride, bitter: 0,00015/0,00006 g/ml quinine hydrochloride). The investigation included subjects with normal gustatory function. Results of the new taste test with a maximum score of 24 will be presented and discussed.

Is the size of the cerebral cortex different in patients with burning mouth syndrome and dysgeusia as compared to healthy subjects?

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Background: Burning mouth syndrome (BMS) is a debilitating condition afflicting mainly postmenopausal women, and is often accompanied by dysgeusia. The pathophysiology of this disease is not clearly understood, but neuropathy and central mechanisms are believed to be involved. The aim of this study was to see whether the cortical thickness and density of grey matter were different in these patients as compared to healthy subjects. To the best of our knowledge, this is the first study analyzing the size and density of the grey matter of patients with these conditions.
Material and Methods: The study population consisted of 11 BMS patients, 18 dysgeusic patients and 13 healthy subjects. Gina Schlumberger collected structural MRI – images using a 1.5T scanner. These images were preprocessed with CBrain Civet (Montreal Neurological Institute, McGill University), calculating cortical thickness. To do analysis on these files the MATLAB toolbox SurfStat was used (MATLAB and Statistics Toolbox Release 2010a, The MathWorks, Inc., Natick, Massachusetts, United States). This toolbox was used to do the statistical analysis of the cortical thickness.
Results: The statistical analysis of the cortical thickness were first done with the significance level $p<0.001$, but no clusters were found. When the significance level were decreased to $p<0.005$ however, BMS subjects showed thickened areas in the superior frontal gyrus (SFG) and the cingulated gyrus (CG), and the dysgeusic subjects showed one thickened area in the SFG.
Discussion: SFG and CG are the areas seen in the cortical thickness analysis, the CG are only seen as thickened in the BMS group. There was also performed voxel – based morphometry using SPM8, and the SFG was seen as less dense in the BMS group, and both denser and less dense in the dysgeusia group (not statisticly significant, $p<0.05$). However, the fact that the grey matter in the SFG is both thickened and shown as both denser/less dense might suggest that the grey matter in the SFG is unorganized and rearranging.

10:51-11:21 **Olfactory disorders in sinonasal diseases**

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11:21-11:45 Chemosensory function in various diseases II

Olfactory function and idiopathic intracranial hypertension

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Objective: Although accumulating evidence suggests that a malfunction of the cerebrospinal fluid (CSF) system in idiopathic intracranial hypertension (IIH) may give rise to olfactory dysfunction, little objective knowledge is available at present about the olfactory capacity of patients with this condition.

Methods: Seventeen patients with IIH and 17 age and gender-matched controls were included. The extended Sniffin' Sticks procedure was used to test odor threshold (T), discrimination (D), and identification (I).
Results: Median TDI score [29 (26.5-35.5) vs. 35 (34-37), p=0.003] were reduced in IIH patients. Furthermore, Spearman correlation revealed reduced TDI values in patients with a recent clinical deterioration of IIH (r=0.66, p=0.004).
Conclusions: Our pilot study provides new evidence that olfaction is impaired in IIH patients, especially in those who have newly been diagnosed or who have experienced a recent clinical deterioration.

Smell and Taste in inflammatory bowel disease

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Objective: Inflammatory bowel disease (IBD) consists of the main clinical phenotypes Crohn's disease (CD) and ulcerative colitis (UC). To our knowledge of existing literature the olfactory function of IBD patients has not been investigated by smell tests so far. Besides suffering from weight loss, CD patients, in particular, have been shown to consume large amounts of sucrose and refined carbohydrates, whereas they consume few fruits and vegetables. Thus the objective of the study was to investigate the olfactory/gustatory functions of these patients by smell/taste tests, and to determine if disease activity or medication might influence the olfactory/gustatory functions of patients.
Patients and methods: In total, 59 IBD patients (37 CD and 22 UC patients) were studied using "Sniffin' sticks" and "taste strips" for olfactory and gustatory tests, respectively, and compared to healthy controls and published normative data.
Results: Among IBD (CD and UC) patients, the values for odor threshold, but not for odor identification or discrimination, were significantly lower than that of the normative data. Further, these patients showed lower values than the normative taste values and the control group for all tastes, except sour; 57.6% of the IBD patients were hyposmic, while 30.5% were hypogeusic. Subjective self-assessments showed that the patients were not aware of their reduced olfactory/gustatory functions. There were no relevant differences in taste and smell abilities between the CD and UC patients. Disease activity and treatment did not influence the olfactory/gustatory functions.
Conclusion: IBD (CD and UC) patients exhibited significant reductions in the olfactory and gustatory functions. Therefore, patients should be tested by smell/taste tests, in order to be adequately informed of their olfactory/gustatory functions and provided an understanding of how to overcome their limitations, and thus improve their quality of life.

12:15-12:45 **Olfaction in sleep and dreams**

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12:45-13:15 **Memory for odors**

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13:15-14:03 Work on the perception of odors and taste

Intranasal insulin decreases olfactory sensitivity in men and women

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High densities of insulin receptors are found throughout the brain in humans, including the olfactory bulb. This region situated in the frontal lobes plays an essential role for processing of odors. With this in mind, in the present study it was hypothesized that enhanced brain insulin signaling would modulate olfactory processing in humans. To this aim, a single dose of either insulin (40 IU) or placebo was administered via the nasal route to 17 subjects (7 females) with normal olfactory function. The intranasal application method is known to increase cerebrospinal fluid (CSF) levels of insulin within 30 min. Subjects' olfactory abilities were tested subsequently by means of an olfactory threshold test for the odorant n-butanol and an olfactory discrimination test. In addition, plasma glucose and serum insulin were measured before and after intranasal administration. Following intranasal insulin administration, subjects' sensitivity for the odorant n-butanol was significantly decreased in comparison to placebo. In contrast, intranasal insulin did not alter subjects' olfactory discrimination ability. While serum insulin was not changed after intranasal insulin administration, there was a small but significant drop in plasma glucose. Importantly, correlational analysis demonstrated that differences in plasma glucose between the insulin and placebo conditions were not related to respective differences in olfactory sensitivity. Taken together, these findings suggest that enhanced CSF insulin impairs olfactory sensitivity of humans for a non-food odorant. Bearing in mind that insulin acts as an anorexigenic signal in the human brain, further studies are needed to test whether intranasal insulin also impairs the ability of humans to perceive food-related odors.
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Keywords: anorexigenic effect, olfactory performance, intranasal application, metabolism

Effect of an odor that captures attention on the time of habituation?

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Natural odors sometimes contain an unpleasant and almost imperceptible component (musk in perfumes, skatol in coffee, indole in jasmine). Could it be that the "function" of this component is to capture the attention of the smeller? Grabenhorst et al (2007, 2011) showed that it was likely the effect of the indole component in the jasmine odor that captured smellers' attentions. The superior frontal gyrus [-16 18 64] was identified as the area supporting attentional-capture effect. As habituation deals with the progressive desensitization to an odor, what could be the effect of such a component on the habituation process? The direct hypothesis is that this kind of component could delay the time to habituation. To investigate this question we used an fMRI approach. 18 subjects were exposed to 60s of the JASMINE mixture, the JAS mixture that did not contain the indole, and the INDOLE component (cf Poellinger et al. 2001 for the paradigm). The scanning was performed as a 3 block design with 5 repetitions of each odor delivered for 60s. Each repetition was spaced by 90s for the subject to recover. The 60s of stimulation was divided into 4 successive timing windows (T1, T2, T3, T4). Activations due to the

JASMINE mixture were contrasted with the JAS mixture to see the effect of the INDOLE component when mixed.

Brain processing of attractive odorant added to an initially neutral mixture

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Some fragrance and perfume even if they are pleasant can contain an unpleasant odor as musk, feces or root beer. Why these components are empirically used in perfumes and more generally why naturally plants or animals incorporate these odorants in a fragrance? We suggested here to test three of these odorants that are often used in perfumery ambroxan (amber like), bacdanol (sandalwood like) and indol (feces like). Each of these odorants was included in a base mixture of 6 components with a neutral pleasantness. 27 subjects had to evaluate edibility, hedonicity, intensity of each single odorant and each mixture. They also had to discriminate the mixture added of a component from the base mixture. Then they were scanned (fMRI) while smelling the odorants and mixtures. As a major result the indol seemed to entail a specific processing. It involves putamen, amygdala, insula and frontal operculum. Although the psychophysical results showed a strong trend for a higher pleasantness of the mixture added of indol than the base mixture the specific network was supposed to process negative affects as disgust. The hypothesis is that as indol was the only odorant linked to a body odor concept (feces) and that could involve a specific network due to a cognitive or an evolutionary process. As a consequence, we can suggest that indol increase the attractiveness of the mixture which could, in our conditions, result in a higher pleasantness.

The impact of olfactory dysfunction on interoceptive awareness

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Patients with olfactory dysfunction suffer from depressive symptoms and reduced quality of life. Interoception is defined as the processing, representation and perception of the internal physical state. More precisely, this construct involves the sensation of the physiological condition of the body as well as the representation of the interior state within the context of ongoing actions and quantifies the extent of an individual´s sensitivity to these bodily signals.
This study aimed to investigate how impairment of the olfactory system influences the ability to represent one´s own internal body state. Chemosensory performance of 77 subjects was examined using the Sniffin´Sticks test battery, revealing a sample of 43 functional anosmics, 18 hyposmics and 16 healthy controls. Interoceptive sensitivity was assessed by using the Heart Beat Perception Task. Additionally, the Beck Depression Inventory as well as a sociodemographic questionnaire were completed by each subject. We obtained a correlation between odor detection threshold and interoceptive awareness, being mediated by duration of olfactory loss – the longer patients suffered from olfactory impairment, the worse the perception of bodily signals. Results of this study will significantly contribute to the basic understanding of the multifaceted effects of olfactory dysfunction.

We would like to thank our sponsors