

## Probanden mit normalem oder fehlendem Riechvermögen zeigen teilweise unerwartete Befunde bei chemosensorisch evozierten Potentialen

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Lötsch und Hummel konnten 2006 bei 48% der Hyposmiker und 30% der Normosmiker keine olfakto-chemosensorisch Ereignis bezogene Potentiale (oCSERP) während einer Phenylethylalkohol(PEA)-Reizung nachweisen. Andererseits detektierten sie bei 20% der Anosmiker oCSERP. Ziel unserer Arbeit war es, die Detektionsrate von CSERP mit einem zweiten Riechstoff, Schwefelwasserstoff ( $H_2S$ ), zu bestimmen. Außerdem sollte untersucht werden, wie die Kenntnis des Befundes der subjektiven Olfaktometrie die Entscheidung über die Erkennung von CSERP beeinflusst.

In die Studie wurden 45 Probanden zwischen 18 -75 Jahren mit altersnormalen Riechvermögen sowie 20 Anosmiker (Altersmittelwert: 55 Jahre) eingeschlossen. Zur Generierung der oCSERP wurden die rein olfaktorischen Reizstoffe Schwefelwasserstoff (6 ppm) und PEA (30%) verwendet. Trigemino-chemosensorisch Ereignis bezogene Potentiale (tCSERP) wurden mit Kohlenstoffdioxid (20-60%) erzeugt. Es wurde das Olfaktometer OM2s verwendet. Dabei wurde die Untersuchung in sechs Blöcke unterteilt. Innerhalb eines Blockes erfolgte die Reizung mit einem Reizstoff über eine Nasenseite. Ein Block enthielt jeweils 20x den gleichen Reizstoff, der immer mit einem Interstimulusintervall von 35 Sekunden für 200 ms in den Luftstrom eingebettet wurde. Danach erfolgten der Wechsel der Nasenseite und ein neuer Reizblock begann. Die Reihenfolge der drei Reizstoffe fand randomisiert statt. Die Ableitung der Hirnströme erfolgte standardgemäß mit dem EEG Vision Amplifier (V-Amp) von Brain Vision.

Bei Kenntnis des Ergebnisses der quantitativen Riechleistung konnten bei jeder der Normalpersonen mindestens ein von maximal vier oCSERP nachgewiesen werden. Ohne Kenntnis der subjektiven Riechleistung konnten bei 3 der 45 Normalpersonen (7%) kein einziges oCSERP detektiert werden. Dabei zeigten sich Unterschiede beim Auftreten von  $H_2S$ - und PEA-getriggerten oCSERP. Bei Reizung mit dem unangenehmen Reizstoff  $H_2S$  fehlten seltener (7%) oCSERP als bei Reizung mit PEA (22%).

Ein Nachweis von oCSERP gelang signifikant häufiger bei Probanden mit altersentsprechenden Riechvermögen als bei Anosmikern. Bei jeweils 11 Anosmikern (55%) konnten keine oCSERP auf eine  $H_2S$ - oder PEA-Reizung abgeleitet werden. Bei jeweils neun Anosmikern (45%) konnten wider Erwarten PEA- oder  $H_2S$ -getriggerte Potentiale dargestellt werden.

Eine Detektion von tCSERP ohne Kenntnis der Befunde der subjektiven Olfaktometrie war bei 91% der Normalpersonen und bei 85% der Anosmiker möglich. Bei Kenntnis des subjektiven Riechempfindens lag die Detektionsrate von mindestens einem tCSERP bei Normalpersonen bei 98% und bei Anosmikern bei 100%.

Die stärkeren und unangenehmen  $H_2S$ -Reize ergaben eine höhere Detektionsrate von oCSERP als PEA-Reize. In Anbetracht der Erkenntnis, dass eine hohe Applikationsrate von Reizen die Anzahl an gemittelten Daten erhöht und somit das Signal-Rausch-Verhältnis verbessert, ist in zukünftigen Studien die alleinige Nutzung von  $H_2S$  mit höherer Reizwiederholungsrate zu erwägen. Um einen subjektiven Bewertungsbias der CSERP zu vermeiden, empfiehlt sich eine EEG-Kurvenanalyse ohne Kenntnis des individuellen Riechvermögens. Nur beim Nachweis eines oCSERP ist von der Funktionsfähigkeit des Riechsystems auszugehen.

## Ortho- and retronasal olfactory function before and after rhinosurgical procedures

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Olfactory dysfunction is a common symptom in patients undergoing rhinosurgical procedures, such as Septoplasty (SP), Septumrhinoplasty (SRP) and Functional Endonasal Sinus surgery (FESS). Comparative studies of these procedures in terms of olfactory outcome however are lacking. Furthermore, this study focuses on retronasal olfactory perception in these patients. In addition, we intended to evaluate “up-to-date” PROMs, like the SNOT-20 or ETDQ7, and their relation to olfactory function. Patients were tested one day before surgery orthonasally (side separately using Sniffin´Sticks) and also retronasally (using the 27-Item Candy Smell Test). A Follow-Up was done 3 months after the rhinosurgical procedure. Preliminary data will be presented.

## Olfactory function is reduced in patients with sensorineural hearing loss

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Olfactory deficits precede neurodegenerative diseases such as M. Alzheimer and M. Parkinson. It is still unclear whether there is a correlation between hearing loss, olfactory dysfunction and impaired cognitive abilities, which was the subject of this study. Methods: One hundred subjects (age: 18 to 55 years) participated in this study. Fifty subjects (mean age: 37.9 y ± 1.6 y) had a normal symmetric hearing threshold (HT) tested by pure tone audiogram using pure tone average (PTA). Fifty subjects (mean age: 39.6 y ± 1.7 y) had an uni- or bilateral hearing loss (mean pure tone threshold right: 51.7 dB PTA5, left 55.7 dB PTA5). Olfactory function and cognitive function were tested by using a lateralized Sniffin´Sticks test examining threshold (T), discrimination (D) and identification (I) and DemTect (dementia detection test, score: 0-18). Results: Subjects with hearing loss exhibited a composite TDI score on both sides being significantly worse than subjects with normal hearing (TDI right: 26.2 vs 30.8, p= <0.001; left: 28.6 vs. 31.5, p= 0.005). Hearing impaired subjects also scored significantly worse in DemTect (14.9 vs 16.9, p= < 0.001). HT on the right side correlated significantly with discrimination (D) tests results, on the left side with discrimination on the left side only. These correlations remained significant when controlling for DemTect test results. Conclusion: We were able to show a correlation between sensorineural hearing loss, olfactory impairment and mild cognitive deficit. Thus, olfactory dysfunction and cognitive impairment in hearing impaired subjects might express a general sensorineural decline.

## Improvement of spatial and temporal resolution of functional MRI for olfactory brain regions

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Echo-planar-imaging (EPI) is a commonly used technique for BOLD (blood oxygenation level dependent) fMRI acquisition. A well-known issue in EPI is the presence of image artifacts, confounds and signal losses due to susceptibility gradients at air/tissue borders. The aim of this study is to improve image quality of EPI BOLD acquisitions in brain regions related to odor perception. The quality of the images was estimated using different indices like SNR (Signal-to-Noise Ratio) and tSNR (temporal Signal-to-Noise Ratio).

Part A: For this purpose, we compared different acquisition protocols published previously in our department. Based on the acquisition protocol currently used in our department, we created twenty different sequences by varying one parameter on time. We have modified scan plane, repetition time, echo time, flip angle and bandwidth per voxel. For this experiment we have recruited 20 healthy volunteers. All scans were performed under resting-state condition, using Siemens 3T Prisma scanner.

All anatomical and functional data was converted to BIDS (Brain Imaging Data Standard) and preprocessed with fmriprep v.1.1.6. The quality indices for the entire FOV (field of view) were calculated using mriqc v. 0.14.2. The ROI (Region of Interest) specific analysis was performed with a self-constructed pipeline, which is based on nipy python library. This pipeline allows calculation of tSNR values of each ROI separately using Harvard-Oxford-Atlas.

Part B: Based on the results from Part A we created five more sequences that are combinations of parameter with highest tSNR values from Part A. Additionally, modifications of the initial protocol using simultaneous multi-slice acquisition, 3D prospective acquisition correction and zoomed modes were included. For this experiment we have again recruited 20 healthy volunteers. The data analysis was performed as described in Part A. Our investigations show a significant difference in SNR and tSNR values depending on the parameter of the sequence. Furthermore, we have found discrepancies in the impact of the parameter on cortical and subcortical regions. In particular, flip angle of 60°-70° increase tSNR in subcortical regions up to 10-15%, compared to a flip angle of 90°. Additionally, 3D prospective acquisition reduces movement artifacts. Finally, we could show that simultaneous multi-slice acquisition allows to shorten the acquisition time, but reduces tSNR significantly.

The proper choice of parameter according to the research question of the fMRI study can improve the quality of the data. This study compares the impact of different settings of SIEMENS 3T Prisma MRI scanner on the quality of functional MRI acquisition. Additionally, we offer some recommendations for adapting EPI sequence settings depending on the research question and regions of interest.

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## Temperature and humidity do not have a significant impact on the ability to smell - a study in controlled air pressure conditions

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Verschiedene Faktoren beeinflussen das Riechvermögen. Es wurde bereits in Studien gezeigt, dass der Aufenthalt in hypobaren Bedingungen eine Reduktion des Geruchssinns zur Folge hat. Die Frage ob Temperatur und Luftfeuchtigkeit spezielle Auswirkungen auf das Geruchsempfinden haben wurde bisher noch nicht hinreichend geklärt. In dieser Studie wurde untersucht, welchen Einfluss Luftfeuchtigkeit und Temperatur auf das Geruchsempfinden haben. Dabei wurden die genannten Faktoren, unter Ausschluss von Luftdruckschwankungen, isoliert betrachtet. Die Untersuchungen fanden in einer genormten hypobaren Umgebung (950mbar, bzw. 1750ft) in einer Unterdruckkammer statt, in einer standardisierten Umgebung unabhängig von Luftdruckschwankungen. 50 Probanden durchliefen vier Untersuchungsgänge in einer pseudorandomisierten Reihenfolge. In jedem Untersuchungsgang wurden mit Hilfe der Sniffin`Sticks Testbatterie die Riechschwelle, die Diskrimination und die Identifikation von Gerüchen getestet. Folgende Situationen wurden untersucht: Kühl und trocken (20°C, 30% Luftfeuchtigkeit); Kühl und feucht (20° C, 75% Luftfeuchtigkeit); Heiß und trocken (35° C, 30% Luftfeuchtigkeit) Heiß und feucht (35° C, 75% Luftfeuchtigkeit). Es zeigte sich eine leichte Besserung der Identifikation von Düften in heißer und feuchter Umgebung, was frühere Untersuchungsergebnisse unterstützt.

## Chemosensory function in posttraumatic patients: The role of olfactory distortions

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The significance of olfactory distortions after head trauma is poorly understood. We aimed to establish chemosensory function of posttraumatic patients (PP) and analyzed whether olfactory distortions influence the degree of chemosensory impairment.

We performed a retrospective study based on 75 patients with olfactory complaints following head trauma. We assessed their chemosensory function with Sniffin` Sticks (olfaction), lateralization test (trigeminal), and taste strips (taste). Demographics, test and CT scan/MRI results were reported in a database. Data were analyzed with unpaired t-test with Welch's correction, Mann-Whitney test, and Fischer's exact test. Statistical significance was reached when  $p < 0.05$ .

Besides olfaction, taste and trigeminal function were also slightly below normal values in PP. The mean identification test score (+/-SD) was higher in the group with distortions (7.1+/-2.6;

n=34) compared to the group without (5.6+/-3.2; n=41; p<0.05). Regarding the percentage of subjects with cerebral abnormalities, gender and results of other chemosensory tests, there was no significant difference between the two groups.

We found that PP with olfactory distortions have better odor identification test scores compared to those without. A longitudinal study is needed to assess whether these symptoms may be a prognostic factor for olfactory recovery after head trauma.

### **Top-down olfactory processing in subjects with congenital and acquired anosmia**

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To investigate top-down olfactory processing in patients with congenital (CA) or idiopathic acquired anosmia (IA) in comparison to normosmia controls (NC) during expectancy and reading of odor-associated words. Fourteen CA with a life-long inability to smell, 8 IA with acquired smell loss and 16 NC with normal olfactory function were assessed for the brain response during a task of expectation and reading of words with strong olfactory associations (OW) (e.g. "Banana") and control words with little to no olfactory associations (CW) (e.g. "Chair") using functional MRI. Word stimuli were presented in blocks; odor-associated words alternated with blocks of neutral words. CA showed more activation in the occipital cortex during OW expectation, and in the OFC extending to insula during OW reading. During OW expectation brain activation patterns were different for NC, IC, or CA. It appeared that CA patients more relied on visual search routes while IA patients more used verbal and olfactory search strategies. Similarly, different patterns of activation emerged between the groups during reading of OW, especially in the area of the orbitofrontal cortex. Increased activation of the higher-order brain regions related to multisensory integration among CA patients may suggest a compensatory mechanism for processing of semantic olfactory cues.

### **Recordings of electro-olfactograms from the human olfactory epithelium in response to HLA-related PEPs**

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In many animal species, social communication and mate choice are influenced by cues encoded by the major histocompatibility complex (MHC). Here, we examined the responsiveness of the human olfactory epithelium to human leucocyte antigen (HLA) related peptide ligands (PEP).

Electro-olfactograms (EOG) in response to chemosensory stimulation were recorded in 46/52 participants (28 f, age 20-33 y) using air-dilution olfactometry. Stimuli (duration 1s, flow 7l/min) were 3 HLA-related PEPs (with only PEPs 1 and 2 thought to be active), solvent (propylene glycol, PG), a rose-like odorant (PEA) and CO<sub>2</sub>, a trigeminal stimulus. PEP 1, 2 and 3 could not be discriminated from PG. Typical responses were present in response to all stimuli; 46/52 participants exhibited an EOG. In 21/34 (61%) of the cases EOG were present to PEP 1 and 2, but not to PEP 3; in 39% of the cases subjects responded to either PEP 1 or 2 and to PEP 3. Response to one of the PEPs but not to others were seen in 10/29 for PEP 1 (34%), 4/19 for PEP 2 (21%) and 5/18 for PEP 3 (28%). In 13/34 (38%) cases responses were present to PEP 1 or 2 but not to PG, in 3/23 (13%) to PG but not to PEP 1 or 2. EOG amplitudes were larger ( $p < 0.05$ ) for PEP 2 than to PEA. If subjects responded to PEP 1, they also exhibited responses of similar amplitude to PEP 2 and 3 and PG ( $r > 0.67$ ,  $p < 0.01$ ), although this did not correlate with PEA and CO<sub>2</sub>. PEP 2 responses correlated with amplitudes to PG ( $r = 0.88$ ,  $p = 0.021$ ), but not to PEP 1 or 3, PEA or CO<sub>2</sub>. Associations of the responses with age or sex were only found for the trigeminal stimulant CO<sub>2</sub>: women had shorter response latencies than men ( $p = 0.02$ ), and the amplitude decreased with age ( $r = -0.041$ ,  $p < 0.05$ ).

EOG can be recorded in humans in response to stimulation with HLA-related PEPs. However, there was no clear difference between responses to various HLA specific PEPs when recording from isolated epithelial sites.

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### **Olfactory diary: Olfactory dysfunction during the course the day**

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Olfactory disorders (OD) have a profound effect not only on the quality of life (QOL) of affected individuals but also on their safety. Difficulties associated with OD in daily life are diverse, including those related to cooking, eating, body hygiene, safety and social life. However, there is currently no evidence, how often patients with OD are confronted with those difficulties during the course of the day. Hence there is a need to understand the distribution of these burdens in order to improve patient counselling. The aim of the present study was to follow the daily course of patients with OD and to assess (i) how many times a day (ii) at which time (iii) in which aspect of daily life patients with OD miss their sense of smell. Patients with subjective OD presenting at the Department of Otorhinolaryngology, Medical University of Vienna were prospectively included. Olfactory dysfunction was confirmed by means of the Sniffin' Sticks TDI test. Subsequently, hardcover diaries (A5) were handed out to all patients. The diary consisted of fourteen consecutive days: each page consisted of twelve rows, representing twelve hours of the day. Six columns on each page represented different aspects of daily life. Patients were instructed to mark the corresponding row/column whenever

applicable. On return of the diaries, a second olfactory test was performed by means of the Sniffin' Sticks. As the data collection has not yet been completed, the results of the first twenty diaries will be presented as preliminary results.

### **Association between self-assessment of chemosensory perception and psychophysical test results in health and disease**

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The interaction between the sense of smell, taste and the trigeminal sense contributes a major share to the human multisensory flavor perception, representing one of the most complex and important behaviors. Studies in patients with olfactory dysfunction (OD) showed that self-assessment of olfactory function seems to reflect orthonasal olfactory function quite well. However, there is currently no evidence just how self-assessment of flavor perception correlates with objective olfactory tests in patients with OD as well as healthy subjects. In the present work, we compared self-assessment of chemosensory perception smell, taste, and flavor with orthonasal olfactory test scores in patients with OD and healthy subjects, in order to determine the association between subjective and objective variables.

We retrospectively examined records of 203 patients with olfactory dysfunction and 103 healthy subjects evaluated at the Department of Otorhinolaryngology of the Medical University of Vienna. Patients demographics, reason and duration of OD, self-assessment of chemosensory perception scores as well as orthonasal olfactory test scores, by means of the TDI-Sniffin' Sticks test were noted.

A moderate correlation was found between self-assessment of smell and the TDI score ( $r_{203}=0.64$ ,  $p<0.0001$ ), weak correlation between self-assessment of flavor perception and TDI score ( $r_{203}=0.27$ ,  $p<0.0001$ ), and no linear correlation between self-assessment of taste and TDI score ( $r_{203}=0.1$ ,  $p=0.2$ ). No linear correlation was found between self-assessment of smell, taste and flavor perception and TDI scores in healthy subjects.

These data suggest that patients with olfactory dysfunction were able to judge their orthonasal olfactory function but with moderate accuracy, whereas flavor perception ratings did not reflect olfactory test scores. Further studies exploring the influence of our chemical senses on flavor perception are warranted.

### **Pepper with and without a sting: Brain processing of intranasaltrigeminal and olfactory stimuli from the same source**

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Pepper is a spice that has a sharp-smelling and tasting component-the piperine. However, pepper oil does not contain piperine. It was investigated how piperine and pepper oil differ in their perception and lateralisability. It was examined in 20 subjects using fMRT, which brain areas are activated when smelling the substances. The intensity, irritability and hedonics of the fragrances were inquired. In another session, it was tested whether the fragrances could be assigned to a nostril in one-sided presentation.

### Olfactory change detection - How precise can we guide our olfactory attention?

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Despite our very sensitive sense of smell, we rather rely on visual than on olfactory information when determining changes in the environment. The main reasons are the imprecise temporal and the spatial resolution of our olfactory system.

We developed a one-back change detection test to investigate the capacity to detect changes in the olfactory environment and their potential modulators. Participants received four odor conditions, which were presented via a computer-controlled olfactometer (2 odor qualities in 2 concentrations each). The subjects were requested to react as soon and as accurately as possible when perceiving a change of the odors. For comparison, the participants underwent the same paradigm with visual stimuli. A total of 83 healthy participants (aged 18–34 years, 50 women) were included; all of them were tested for olfactory function, the subjective importance of the sense of smell, attention, nasal airway patency, and chemical sensitivity.

All of the participants detected visual changes reliably above chance level and faster than olfactory changes. Olfactory changes were detected reliably by only less than a quarter (18%). These were characterized by high olfactory sensitivity, high scores in the importance of olfaction scale, a better nasal airway patency and low environmental sensitivity. All participants detected changes of olfactory quality more frequently than changes of olfactory concentration. Unpleasant odors were detected faster and more frequently over chance level than pleasant ones, since the unpleasant odors have a warning function for potential danger. The results suggest that (1) olfaction is imprecise in guiding environmental changes compared to vision, but still (2) the attention of the olfactory system focuses on new stimuli. This could help to explain why humans rate the importance of vision higher than the importance of olfaction.

### Modulation of cerebral activity by subliminal odors: an fMRI study

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Brain processing underpinning subliminal olfaction (i.e. odours of weak concentrations that are processed by the olfactory system but not consciously perceived) is poorly known and understood. In particular, the dynamic between subliminal olfaction and attentional processing remains unclear. Twenty-seven healthy right-handed adults were recruited under a false pretence. They experienced two odorants (pear and jacinth) both presented in a first session at weak concentrations (subliminal) and in a second session at high concentrations (supraliminal), during a functional MRI scan. Using Independent Component Analysis, four brain functional networks were identified in the weak concentration session and were not detected in the second high concentration session. These networks are not specific to olfaction and are mainly related to attentional processes. The results suggest that, instead of specific neural correlates dedicated to subliminal olfaction, exposure to subliminal odours acts as a modulator of attentional processes and associated cerebral networks. This modulation is highly dependent on the environmental context, other sensory inputs, and attention dedicated to the task at hand.

### Presence of undetected olfactory loss in the general population

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Diminished olfactory perception has implications on quality of life and health in patients. However, most of the studies looking into consequences of olfactory loss recruited patients who have already been categorized as having a dysfunctional sense of smell and sought help in an ENT clinic. We revisit these findings by reanalyzing Sniffin' Sticks normative data (Study 1) and distinguishing people with olfactory impairment from a group of subjects who all declared a normal sense of smell and enrolled for a study looking into indicators of health and well-being (Study 2). In the initial sample of 203 individuals, we found 59 to have impaired olfaction and 4 with marginal olfactory performance, not useful in daily life. However, their quality of life, cognitive abilities and health assessments were not different from subjects with a normal sense of smell. Olfactory loss certainly has a severe impact on daily life but more so in individuals who are bothered with it and decide to seek treatment. The limited-to-no olfactory perception in the fraction of people who do not complain about it or do not seek help in ENT clinics does not seem to have a major impact on their cognitive, emotional and health functioning.

## **Olfactory bulb volume changes associated with trans-sphenoidal pituitary surgery**

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The trans-sphenoidal approach is most frequently used for pituitary adenoma (PA) enucleation. However, effects of this surgery on neighboring structures have received little attention so far. In particular, no investigations on olfactory bulb (OB) anatomy after trans-sphenoidal surgery have been reported. Because impairment of olfaction has been shown in small groups following trans-sphenoidal surgery we hypothesized that the transnasal approach is likely to alter OB volume which is associated with changes of olfactory function. The study comprised 33 patients with pituitary adenoma (14 women and 19 men, mean age 50 years). Comprehensive assessment of olfactory function was conducted with the "Sniffin' Sticks" test kit. Based on magnetic resonance imaging scans OBs were measured before and approximately one year after trans-sphenoidal PA enucleation.

Owing to postoperative non-compliance and MRI artifacts partly due to drill friction complete evaluation of "Sniffin' Sticks" in term of obtaining the TDI score was possible pre- and postoperatively in 21 patients whereas OB volumes were available in 32 patients. Approximately one year after surgery olfactory function was not significantly different from baseline. However, left- and right-sided OB volume in patients treated via trans-sphenoidal surgery decreased ( $p=0.001$ ). The side of the surgical approach did not affect OB volume in a side-specific manner. Changes in odor threshold were significantly correlated to changes in right-sided OB volume ( $r=0.45$ ,  $p=0.024$ ).

Overall olfactory performance one year after surgery was not significantly different from baseline. However, changes in OB volume are associated with changes in olfactory performance and OB volumes decreased in patients.

## **The sweet smell of healthiness: How insulin resistance relates to chocolate odor sensitivity across a wide range of body weights**

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The worldwide obesity epidemic is a major health problem driven by the modern food environment. Recently, it has been shown that smell perception plays a key role in unconscious decisions for foods and is thus closely related to eating behavior. Since smell perception seems to be altered in obesity, this fact might crucially contribute to weight gain. However, the underlying mechanisms of altered olfactory perception and hedonic responses to food odors in obesity are not well understood yet. Since the olfactory system is closely linked to the endocrine system, we hypothesized that hormonal shifts in obesity might explain this relationship.

In a within-subject, repeated-measures design, we investigated sensitivity to food and non-food odor in the hungry and sated state in 75 young healthy (26 normal weight, 25 overweight, 24 obese) participants (37 women). To determine metabolic health status and hormonal reactivity in response to food intake, we assessed pre- and postprandial levels of insulin, leptin, glucose and ghrelin.

Odor sensitivity did not directly depend on body weight status/BMI or metabolic state (hungry vs. sated). However, we could show a strong negative mediating effect of insulin resistance assessed by HOMA-IR score on the relationship between BMI and olfactory sensitivity for the food odor. Post-hoc regression models revealed, that insulin resistance rather than obesity is responsible for this effect. Moreover, post-hoc analyses showed a positive relationship between BMI and olfactory sensitivity when controlling for insulin resistance. Furthermore, only individuals with high HOMA-IR exhibit a decrease in odor sensitivity after meal intake.

These findings indicate a major impact of metabolic health status on sensitivity to food odors. Our results offer an explanation for controversial findings on smell sensitivity in obesity and contribute to a better understanding of the mechanisms behind altered smell perception in obesity.

### **“Smelling is emotion” - sexual desire after olfactory loss: quantitative and qualitative reports of patients with smell disorders**

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Olfaction moderates human sexual experiences and smell disorder patients sometimes spontaneously complain about impairments in their sexual life. The aim of the present study was to systematically investigate the impact of olfactory dysfunction on sexual desire.

We compared a sample of  $n = 100$  ( $n = 52$  women; aged 23-51 years,  $M = 40.1$ ,  $SD = 8.2$ ) outpatients with olfactory disorders to a sample of  $n = 51$  age- and sex-matched healthy controls ( $n = 32$  women; aged 21-63 years,  $M = 39.2$ ,  $SD = 13.1$ ). Sexual desire was assessed with a standardized questionnaire and with two additional items asking for quantitative and qualitative change of sexual desire since the onset of olfactory loss. In addition, subjects completed standardized questions about mood (depressive / anxiety symptoms) and partnership attachment (security, dependency).

Within the smell disorder group, 26 % of the patients reported decreased sexual desire since the onset of olfactory loss. This change was predicted by depressive symptoms and olfactory function. Qualitative reports revealed for instance that the lack of attraction due to the other's body odor impedes partnership intimacy. The reported change of sexual desire was significantly related to depression and the severity of olfactory impairment but not to partnership attachment. However, in the standardized questionnaire about sexual desire we observed no differences between patients and controls.

To sum up, a considerable number of patients state sexual impairment as a concomitant complaint of olfactory dysfunction. As affected patients do typically not spontaneously report

those intimate problems, routine care settings should inform about this common side effect and explicitly ask for sexual life.

## Riechtagebuch

David T. Liu, Gerold Besser, Gunjan Sharma, Bertold Renner\*, Thomas Hummel, Christian A. Mueller

Die Prävalenz von Riechstörungen ist hoch und liegt bei 20 %. (1) Obwohl der Geruchssinn gegenüber anderen Sinnen wie dem Seh- und Hörsinn eine untergeordnete Rolle in der bewussten Wahrnehmung spielt, führen Riechstörungen nachweislich zu einer Einschränkung der Lebensqualität. (1)(2) Unterschiedliche Fragebögen werden verwendet, um die allgemeine Lebensqualität und auch Stimmungszustände zu erfragen. Der von Frasnelli und Hummel (4) ursprünglich entwickelte 'Questionnaire for Olfactory Dysfunction' (QOD) ist ein Fragebogen, welcher spezifisch den Einfluss von Riechstörungen auf das alltägliche Leben evaluiert. (3,4) Temmel et al (1) konnte zeigen, dass viele Bereiche im alltäglichen Leben von Patienten mit Riechstörungen beeinträchtigt sein können: Kochen, verminderter Appetit, persönliche Hygiene und Stimmungsschwankungen sind die am häufigsten betroffenen Bereiche. Die Frage stellt sich, welchen Tagesverlauf Riechstörungen im Leben von Patienten mit einer bekannten Riechstörung nehmen und zu welcher genauen Tageszeit Riechstörungen bemerkt werden. Dazu wird den Patienten ein Riechtagebuch mitgegeben, sowie eine täglich dreimal eine Erinnerungs-SMS verschickt. Das Ziel der vorliegenden Untersuchung ist die Erhebung der tatsächlichen Häufigkeit, mit der die Patienten mit ihrer Riechstörung konfrontiert werden und die Art sowie eine genaue tageszeitliche Zuordnung.

## Recovery of intranasal trigeminal sensitivity after sinus surgery in patients suffering from nasal polyposis

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## Top-down olfactory processing in subjects with congenital and acquired anosmia

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Olfactory loss can be acquired or inborn so that one group has olfactory experiences while the other has none. To investigate top-down olfactory processing in patients with congenital (CA) or idiopathic acquired anosmia (IA) in comparison to normosmic controls (NC) during expectancy and reading of odor-associated words. Fourteen CA with a life-long inability to

smell, 8 IA with acquired smell loss and 16 NC with normal olfactory function were assessed for the brain response during a task of expectation and reading of words with strong olfactory associations (OW) (e.g. “banana”) and control words with little to no olfactory associations (CW) (e.g. “chair”) using functional MRI. Word stimuli were presented in blocks; odor-associated words alternated with blocks of neutral words. During OW expectation brain activation patterns were different for NC, IC, or CA with CA showing more activation in the occipital cortex. It appeared that CA patients more relied on visual search routes while IA patients more used verbal and olfactory search strategies. In addition, CA patients exhibited more activation in the OFC extending to insula during OW reading. Increased activation of the higher-order brain regions related to multisensory integration among CA patients suggests a compensatory mechanism for processing of semantic olfactory cues.

### **Pleasantness of odors in children and adolescents**

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The hedonic value of odors is well examined in adults showing that various parameters are influencing the individual rating of odors such as socialization, experience and odor knowledge. The aim of this study was to examine the pleasantness of different odors in relation to odor identification ability and home country in children. Five hundred eleven children from 18 countries from five continents between an age of five and eight years underwent olfactory testing using a 17- item odor identification test and rated the pleasantness of each odor on a five-point scale. No positive correlation between correct odor identification of an odor and the pleasantness could be displayed. For most odors a higher pleasantness has been found in participants who identified these odors correctly (chocolate, biscuit, flower, lemon, peach, strawberry;  $p < 0.05$ ). Children of all countries rated sweet and fruity odors (e.g. peach, chocolate) with a high pleasantness while odors like onion and fish were labeled as less pleasant. Nevertheless, children of different continents rated the pleasantness of all odors significantly different. The results of this study show that not only the correct identification but also the home country of the children influences the hedonic value of a certain odor.

### **„Olfactory diary“: Olfactory dysfunction throughout the day**

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### **The Effect of Olfactory Training on Olfactory Bulb Volumes in Patients with Idiopathic Olfactory Loss.**

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Olfactory training (OT) enhances the olfactory function of people with and without olfactory dysfunction. Moreover, OT is associated with increased olfactory bulb volume in normosmic individuals, but not those with olfactory loss due to traumatic brain injury or infections. However, whether OT will increase olfactory bulb volume in patients with idiopathic olfactory loss remains unknown and therefore formed the aim of this study. After a minimum of six months, bi-daily OT, the olfactory function and olfactory bulb volumes of patients significantly improved compared to baseline. The findings suggest that OT may only stimulate neurophysiological changes in patients with idiopathic olfactory loss.

### Influence of smell disorders on partnership, sexuality and parenthood

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Smell disorder patients often complain about impairments in their quality of life. The aim of the present study was to investigate the impact of olfactory dysfunction on partnership, sexual desire and parenthood. We compared outpatients with olfactory disorders to a sample of healthy controls using different questionnaires about mood, partnership attachment, social network and sexual desire. Smell disorder patients reported significantly less partnership security and less partnership independency. The patients furthermore exhibited a significantly enhanced depression score and reported decreased sexual desire since the onset of olfactory loss. Patients with children experienced different limitations in parenting matters. In conclusion, it seems important to include those common side effects more into clinical practice by informing and asking about them. Further studies could specifically examine the impact of the cause of the smell disorder on different aspects of quality of life.

### Flavor Enhancement bei Patienten mit Riechstörung

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## **Influence of a nasal clip scenting on the intranasal sensitivity of patients with sinusoidal smelling disorders**

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The olfactory as well as the trigeminal sensitivity can be trained. The positive outcome of the usual active training of smelling has been tested multiple times and is undisputed. This study covers the efficiency of passive scenting of the nose via a small inhalator by the company aspUra GmbH. A peppermint and eucalyptus oil mixture was used to stimulate the nervus olfactorius along with the nervus trigeminus. 53 test candidates, who either had a sinusoidal or an idiopathic smell disorder, were included in this study. The statistic evaluation took place for resulting data of 50 participants who were put in two even groups. Two sessions took place over the course of 30 days in which the passive smell training has been completed. The ability of smelling was tested with the help of the so called Sniffin' Sticks and the trigeminal sensitivity was tested via a CO<sub>2</sub> stimulator during those sessions. There has been an additional testing of the nostril volume with an acoustic rhinometer. The subjective sensation data was registered by different numerical rating scales. The testing of all participants included show a positive effect for the smelling ability, whereby a significant improvement has only been seen for the discrimination capacity of scents ( $t = -2,2$ ;  $p = 0,03$ ). The usage of the clip generally affects the subjective sensation of smelling in a positive way. Evidence for noticeable improvements of the trigeminal sensitivity was nowhere to be found. Acoustic measured nostril units also stayed unchanged. While the passive training has a notable weaker impact than already established active forms, the training of smelling does improve the ability to smell to some extent. There is no increasing of the trigeminal sensitivity. If the application over a longer period of time or the changing of scents could have had a bigger impact remains to be seen in future studies

## **Weiterentwicklung der Schmeckstreifen: Extended Taste Strips bei Kindern**

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## **The olfactory dysfunction is associated with the degree of cognitive function in dysosmic patients with and without head trauma experience**

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Head trauma in humans can result in a large spectrum of consequences, including cognitive, affective and olfactory changes. Research in this field, however wide, often does not control for olfactory performance and if so, is focused only on comparing normosmic/hyposmic to anosmic people. At the same time, olfactory performance can be seen directly as a marker of cognitive or affective impairment. Hence, the aim of our study was to investigate whether olfactory functions correlate with the degree of cognitive function and affective state in a group of dysosmic patients with and without head trauma experience. In total, 101 participants were examined. The olfactory function was measured by means of Sniffin' Sticks, while the different aspects of cognitive performance were measured by Wisconsin Card Sorting Test (WCST), Controlled Oral Word Association (COWA), Trail Making Test (TMT), and d2 Test. Additionally, the Beck Depression Inventory (BDI) was used to gauge the severity of depression. The group of trauma patients had slightly higher level of depression and lower level of executive functioning when compared to the control group. The results also show that olfactory performance was associated to a number of cognitive functions in both groups taken together. To conclude, the obtained results indicate an association of olfactory dysfunction and the degree of cognitive function.

### **Olfaction as a moderator of parent-child bonding: New insights on the base of a HLA genotyped family cohort**

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Human parent-child bonding and kin recognition are modulated by olfactory stimuli. This modulation seems age depended: while humans are much in favor of their newborns' body odor, the enthusiasm seemingly decreases when the children get pubertal. Additionally, studies about mate choice suggest, that humans prefer the smell of an opposite sex partner who differs in terms of genetic HLA profile. We aimed to integrate those concepts by examining preferences of mother for the body odor of the own, HLA-similar and -dissimilar children over the whole period of childhood and adolescence. In a cross-sectional design, a total of 164 mothers were presented to probes of their own and four other children, aged 0 to 18 years. HLA profiling [HLA A, B, C, DR, DP, DQ] was performed for mothers and children and the estrogen and testosterone concentration was determined for all pre- to postpubertal children. Mothers preferred odors of their own offspring compared to other children for all age groups, except during puberty. During this time, body odor identification ability dropped as well. An interaction showed a negative correlation between maternal pleasantness rating and donors testosterone concentration for the own son and a positive correlation for other boys. HLA similarity had no major impact on the maternal assessment

of probes. The data suggests that familiarity, and not genetic similarity, drives body odor preference. In the light of clinical studies, we assume that infantile body odor preference is a learned mechanism which is driven by positive parenting experiences.

### **Taste of Analgesics**

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Many drugs taste bitter. This is true for analgesics, in particular for non-steroidal anti-inflammatory drugs (NSAIDs) like aspirin or diclofenac. In addition, the perception of taste is modified by NSAIDs. More than 30 excipients are used to mask or modify the taste of NSAIDs like aspirin. Thus, the patient's compliance of drug receipts and therapeutic regime is increased for young as well as elderly patients. Excipients of NSAIDs are chemically diverse but pharmaceutically inactive ingredients. However, some excipients are assumed to be involved in adverse drug reactions.

### **Ortho- and retronasal olfactory function before and after rhinosurgical procedures**

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### **In vitro regeneration of olfactory neurons**

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### **No olfactory compensation in food-related hazard detection among blind and deaf adults.**

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The current study focused on possible compensatory effects on olfactory sensitivity relevant for environmental hazard detection. We compared thresholds for detection of an unpleasant fish odor that resembled rotten fish in four groups of subjects: blind participants (n=100), sighted controls (n=100), deaf participants (n=74) and hearing controls (n=99). Overall, we observed no significant differences in smell acuity between the blind and deaf groups and

their matched control samples. However, the sensory deprived subjects assessed their sensitivity higher than control groups. The present study is yet another example of research among large samples of sensory deprived individuals that shows no evidence of olfactory compensation. This result is consistent with a growing number of studies suggesting no sensory compensation in simple, absolute sensitivity tasks.

### **Olfactory function reflects the inflammatory status in chronic rhinosinusitis**

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Olfactory dysfunction is a characteristic symptom of chronic rhinosinusitis with (CRSwNP) or without polyps (CRSsNP). This study focused on the impact on olfaction in CRS patients and effect on olfaction with corticosteroid treatment in CRS patients. Ninety-nine participants were recruited (52 women, mean age 53 years; 30 controls, 30 CRSwNP, 36 CRSsNP). Olfactory function was evaluated using the Sniffing' Sticks. Measurements were performed twice, between sessions CRS patients received systemic glucocorticosteroids. In CRS patients 29 were anosmic, 32 hyposmic, and 5 normosmic, which confirmed previous studies. Although just only odor threshold score showed no significant different between CRSwNP patients and CRSsNP patients, Odor discrimination, identification, TDI score was significantly lower in CRSwNP patients compared to CRSsNP patients. Following steroid treatment, CRSwNP patients exhibited a higher increase in odor scores compared to CRSsNP ( $p < 0.01$ ). Because olfactory function reliably reflects the inflammatory status, detailed assessment of olfactory function should receive more attention in CRS endotyping.

### **Methods for quantitatively analyzing olfactory function of patients with olfactory dysfunction by functional magnetic resonance imaging (fMRI)**

Yunpeng **Zang**, Pengfei Han, Akshita Joshi, Thomas Hummel

The diagnosis of olfactory dysfunction is mainly based on psychophysical measurements. Aim of the current study was to investigate how well functional magnetic resonance imaging (fMRI) can effectively distinguish between normosmic and patients with olfactory dysfunction. Thirty-eight participants were recruited for the study. Group 1 consisted of patients with olfactory loss ( $n=22$ , mean age= 44.3 years,  $SD=18.6$ ), and group 2 consisted of people with normal olfactory function ( $n=16$ , mean age= 49.6 years,  $SD=11.6$ ). First, olfactory functions were assessed in great detail for all participants, second, brain activation was assessed using fMRI in response to odorous stimulation. The group analysis, activated voxels response to odor stimulation from the POC and insular region presented more activations in the control group than the patient group ( $p < 0.05$ ); The individual analysis, the positive rate of

activation voxels response to odor stimulation from the POC region is much higher in normosmic (93.8%) than subjects with olfactory dysfunction (40.9%).

## **Effect of olfactory training in children and teenagers with migraine and tension-type headache**

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In this clinical trial we analyzed the effect of an olfactory training with pleasant odors in 40 children and adolescents with migraine and tension-type headache. We compared the change in pain thresholds, detection thresholds and pain questionnaires with a Control Group (40 children with migraine and Tension-type headache without Intervention). There were significant results in the change of the electrical pain threshold in the testgroup compared to the controlgroup. The olfactory training also showed a positive effect on the sleeping habits and mood of the children and teenagers.