Characterisation of odorant pathways in olfactory dysfunction

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Aim. This work investigates the functional ability of the human olfactory system to detect odorous compounds using a novel technique which:

- comprises odour stimulation with defined odour-active compounds at given concentrations using an olfactometer.
- is coupled with on-line odour detection at the nostril and olfactory cleft by means of a proton-transfer-reaction mass spectrometer (PTR-MS).
- assesses real-time sensory olfactory detection of the human subjects in relation to intra-nasal odour detection.

Introduction. Exhaled breath contains an abundance of odorous substances from manifold sources, relating to illness or disease, oral hygiene, dietary and smoking habits, and environmental exposure.

Often, a person will be unaware of odours emanating from the mouth despite constant exchange between air in the oral and nasal regions. Although this may arise due to olfactory dysfunction, mostly the lack of odour awareness is due to overexposure, i.e. the olfactory receptors are saturated with an odour and no longer register a signal to the brain.

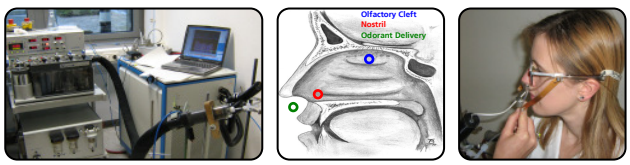
Therefore, in a clinical setting, it is often important to establish whether smell loss originates from physico-mechanical blockages of certain odorant pathways in vivo, or whether there is damage within the olfactory system, such as the receptors.

In some clinical situations a standard approach for such an assessment is to expose the patient to a particular odour of known concentration and to evaluate their response. This may be done, for example, using instrumentation such as an olfactometer.

Experiment. An olfactometer device [1] (Model OM2S, Burghart, Germany) was used in combination with a proton transfer reaction mass spectrometer (PTR-MS) [2] (model hs-FDT, Ionimed Analytik, Austria) to carry out the assessments.

Olfactometer. 2,3-butanedione (which has a buttery odour) was used as the odorant stimulus. This compound was diluted in distilled water in the chamber of the olfactometer, through which air was continually purged to establish dynamic headspace conditions. The chamber headspace gas was subsequently added to a dilution air flow (at a defined mixing ratio) and delivered to the outlet port of the olfactometer (chamber and delivery hose maintained at 40 °C) with 5 s pulses.

PTR-MS. PTR-MS enabled real-time detection of 2,3-butanedione (detected at m/z 87^+) within the nasal cavity. A medical catheter (silicone; ~20 cm length) was placed in the nose of the test subject – either at the nostril or in the olfactory cleft (see figures, below) – and the other end was connected directly to the inlet of the PTR-MS. The tubing was held in place by specially adapted glasses worn by the subject (see photo, below right).



Above left: the olfactometer (left) coupled with the PTR-MS instrument (right). The olfactometer delivery hose is connected directly to one of the two PTR-MS inlet lines, whilst the second inlet line samples in the nose. Above middle: Depiction of the nasal cavity with the PTR-MS sampling positions (at the nostril or the olfactory cleft) indicated. Above right: the test subject during a perception assessment. The olfactometer delivery tube is held at the nostril whilst the PTR-MS samples directly from within the nose.

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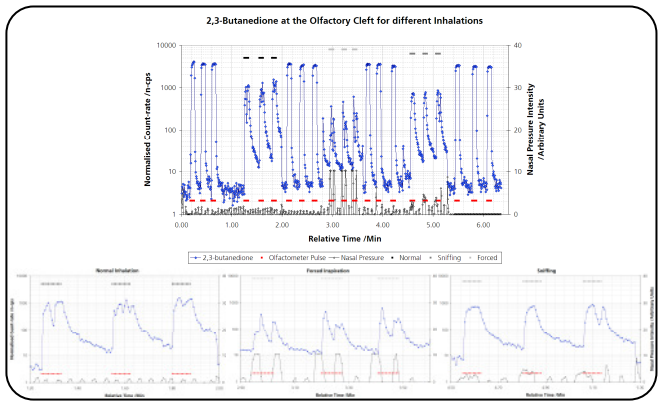
Assessment. Nasal air pressure was additionally monitored with a piezo pressure sensor (model DMU 4, Kalinsky Sensor Elektronik, Germany). The analogue output signal of this device was coupled to the PTR-MS for direct integration of these data into the 2,3-butanedione data.

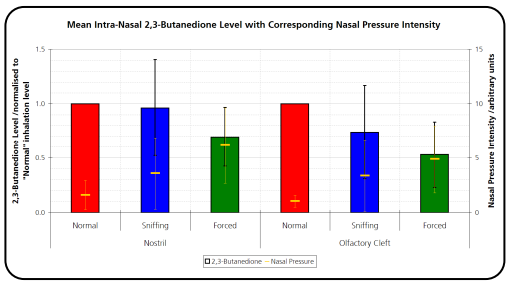
Stimuli and sampling. Pulses of 2,3-butanedione were initially measured directly from the olfactometer by the PTR-MS (in triplicate, via the second inlet line) to establish a reference level. This was necessary due to a continual decrease of the olfactometer pulses, as observed in earlier measurements (see [3]). After the reference pulse was measured, three consecutive pulses were delivered immediately in front of the subject's nose.

Both the nostril and the olfactory cleft sampling was performed in 12 subjects (6 male, 6 female, mean age 35±9). Each test subject was asked to sample the pulses using different inhalation techniques: normal inhalation, sniffing, and forced inspiration. In each case the PTR-MS monitored the 2,3-butanedione concentration at either the nostril or the olfactory cleft. Example data are shown below.



Top main: PTR-MS monitors pulses of 2,3-butanedione from the olfactometer (always in triplicate). The four sets of large pulses are reference signals directly from the olfactometer. The intermittent pulses are measured at the olfactory cleft for (from left to right) normal, forced and sniff inhalations. Bottom inserts: detailed plots of the three inhalation methods showing corresponding values from the nasal pressure sensor.

Results. Mean 2,3-butanedione levels indicated maximum intra-nasal levels during normal inhalation, with minimum levels during forced inspiration. This may result from dilution effects, whereby the odorant concentration entering the nose is much lower due to an increased volume of air. These preliminary results demonstrate the large dependence of inhalation on nasal odour concentrations.



Above: Mean 2,3-butanedione levels in the nose, at the nostril and olfactory cleft, for different inhalation modes. Mean nasal pressure is also plotted (in arbitrary units), indicating the different air-flows for normal, sniffing, and forced inhalations.

References. [1] G Kobal, Pain-related electrical potentials of the human nasal mucosa elicited by chemical stimulation, Pain 22, 151-163, (1985). **[2]** W Lindinger, A Hansel and A Jordan, Proton-transfer-reaction mass spectrometry (PTR–MS): on-line monitoring of volatile organic compounds at pptv levels, Chemical Society Reviews 27, 347-354, (1998). **[3]** J Beauchamp, J Frasnelli, A Buettner, M Scheibe, A Hansel and T Hummel, PTR-MS characterisation of an olfactometer, 4th International Conference on Proton Transfer Reaction Mass Spectrometry and its Applications, 16th-21st February 2009, Obergurgl, Austria.

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