Brain Imaging Studies of the Functional Organization of Human Olfaction

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Introduction
It is believed that sensory functions are organized in a hierarchical and parallel manner. The sense of smell differs in several aspects from other senses: odors can immediately elicit emotional evocations, they are remembered after long time and are difficult to label. This raises the question of whether olfactory stimuli may be processed differently from the other sensory stimuli. New data from brain imaging studies suggest that this is not the case and that the specific characteristics of the sense of smell can be attributed to the engagement of limbic structures at an early stage in the signal processing. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are useful for studies of olfactory functions. PET is generally preferable for limbic activations (but only in group comparisons), whereas fMRI should be used for single-subject studies.

Imaging of odorant perception
In accordance with the expectations from anatomical data both PET and fMRI studies repeatedly show an engagement of limbic structures during the passive smelling of odors. Most often, the activations cover the amygdala, piriform, orbitofrontal and insular cortex, (Zatorre et al., 1992; Williams et al., 1997; Zald and Pardo, 1997; Sobel et al., 1998, 1999) and show a right-sided predominance. Considering that the olfactory nerve projections to the brain are ipsilateral, we recently investigated whether the observed right-sided lateralization may be due to a more pronounced activation through the right nostril (Savic and Gulyas, 2000); PET measurements of rCBF were carried out during monorhinal and passive smelling of four odorants which were perceived as non-trigeminal. Independently of the activated nostril, bilateral activations were found in the amygdala and piriform cortex, anterior cingulate, in the left agranular insular cortex and the right orbitofrontal cortex. There was no significant difference in the pattern or degree of activation between the right versus left nostril stimulations. The observed bilaterality of the monorhinal olfactory processing is congruent with the reports from studies with magnetic source imaging (Kettenmann et al., 1997; Sakuma et al., 1997; Ayabe-Kanamura et al., 2002) and suggests existence of functional connections via the anterior commissure. Thus, the monorhinally presented odorants are perceived bilaterally in the brain independently on the side of presentation.

Functional organization of odorant perception
Odorants are capable to immediately elicit different evocations (hedonistic judgements, familiarity judgements) during the perception of odors, which is the most elemental level of odor processing. Indeed, Zald and Pardo (1997) found that unpleasant odors activated left orbitofrontal cortex and left amygdala significantly more than the pleasant odors. Royet et al. recently also observed that judgements of emotionally valenced stimuli compared to emotionally neutral stimuli activated left amygdala and orbitofrontal cortex. The left amygdala and orbitofrontal cortex could, thus, represent the circuits specially recruited during an automatic judgment of odor pleasantness, which possibly is more pronounced during presentations of unpleasant stimuli (Royet et al., 2000). The possibility of a parallel processing during odor perception is of particular interest in the view of the current debate on whether odors are encoded only perceptually (as stated by Engen and Ross, 1973), or also semantically. Koenig used an original olfactory priming paradigm to provide evidence for the existence of both modes (Koenig et al., 2000). The authors proposed that perceptual odor representations are stored in an olfactory pattern activation subsystem, whereas semantic odor representations are stored in an associative memory. We recently addressed this issue by comparing the pattern of cerebral activation during passive smelling of familiar and unfamiliar odors. Apart from the different rating on the VAS scale with respect to odor familiarity, the odors were rated similarly for other odor characteristics. In addition to the olfactory core regions, which were recruited during smelling of both familiar and unfamiliar odorants, smelling of familiar compounds involved networks usually attributed to semantic associations (Savic and Berglund, 2004). Thus, depending on the evocations elicited with the particular odorant, perception of odorous stimuli can involve additional areas to the core regions. This suggests that already the lowest level of conscious odor processing may be executed by distributed parallel circuits.

Imaging of higher olfactory functions
How the human brain processes the discrimination, recognition and identification of odors has only recently been systematically explored (Royer et al., 1999; Savic et al., 2000). In a series of PET studies we investigated the pattern of cerebral activation during five different olfactory tasks: Monorhinal smelling of odorless air (AS), monorhinal smelling single odors (OS), discrimination of odor intensity (OD-i), discrimination of odor quality (OD-q) and odor recognition memory (OM). Whereas activations during OS were related to AS, activations during the three odors related tasks (OD-i, OD-q and OM) were calculated using OS as the base-line. This approach enabled us to disentangle odor related from task related regions.

The olfactory functions were processed by common, as well as task-specific regions. OS activated the amygdala-piriform, orbitofrontal, insular, cingulate cortex and right thalamus. Depending on the task, different subsets of these regions were recruited along with other areas: OD-i and OD-q engaged left insula and right cerebellum. OD-q involved, in addition, the thalamus, cingulate, orbitofrontal and prefrontal cortex, the frontal operculum, the right caudate and subiculum; OM did not activate the insula, but instead, the piriform cortex; with exception for caudate and subiculum, it shared the remaining activations with the OD-q and engaged, in addition, the temporal and parietal cortex. Thus, the three olfactory tasks (OD-i, OD-q and OM) recruited also areas outside the OS-regions; some of these ‘outside OS-regions’ were shared by several tasks, whereas others were task specific. Furthermore, with the increasing complexity of the task, the activated task-associated areas were more and more remotely connected with the OS regions. For example, right cerebellum was activated by all three tasks (OD-i and
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References


