# High-Order Olfactory Projections Assessed with Positron Emission Tomography

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# IV.11. High-order Olfactory Projections Assessed with Positron Emission Tomography

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## Introduction

Throughout the nervous system, neuronal electrical activity is known to increase metabolic activity of the local tissue[1,2]. Tissue metabolic rate may be measured utilizing radiolabeled metabolic substrates or substrate analogues[3,4,5]. A direct relationship has been shown to exist between the regional cerebral metabolic rate (rCMR) of oxygen and rCBF under normal physiological circumstances[6]. In the olfactory system of the human brain, the central mechanisms of olfaction have been studied pathophysiologically, but there have been no PET studies of olfaction with physiologically normal subjects.

## Methods

The PET system (Model 931/04, CTI Inc., Knoxville, TN) was employed for all measurements[7]. Slices corresponding to the PET images were obtained using a magnetic resonance (MR) imaging system.

Five right-handed normal male volunteers between the ages of 18 and 22 were studied.

Before the start of the study, each subject was instructed to lie relaxed and comfortably on the scanning bed, to remain awake without speaking or moving, and not to change respiratory rhythm. The subject's eyes were covered with a mask to exclude light, and the room was darkened and kept noiseless for the duration of the study. Head position was adjusted so as to be parallel to the orbitomeatal line.

After inhalation for seven minutes of 15-0-labelled $CO_2$ (half life 123 s), 5-min emission scan images for control state were obtained. Then, an olfactory stimulus was presented every minute for five minutes by bolus intravenous injections of 5 ml of saline containing 4 mg Fursultiamine (Vitamin B1) until the completion of the 5-min emission scan for the stimulated state.

Obtained images for control and stimulated states were analyzed in the following manner. Global cerebral blood flow (gCBF) can vary independently of the relative rCBF distribution[8]. Since fluctuations in the measured gCBF between successive scans of the same individual occurred, measurements of rCBF changes induced by selective activation would not be accurate unless a correction was made for gCBF change. In order to exclude extracranial pixel counts, the control images were used to create templates of the brain by setting the "region of interest" on the border of the cranial cavity.

These templates were then used to mask the stimulus-minus-control subtracted images. Changes in rCBF were analyzed with these masked images.We confined our analysis to the slices which were obtained 32, 40 and 48 mm above the orbitomeatal line. These masked subtracted images were characterized by distribution parameters including the mean and standard deviation. Average counts and standard deviation of these masked images (stimulus-minus-control) were calculated and the state-dependent changes were detected by determining which pixels were more than mean + 2.58 standard deviation. These pixels correspond to the areas in which the changes due to the stimulus are statistically significant. The x and y coordinates of the locations which contain more than two continuous detected pixels were expressed as a percentage of the lateral and anteroposterior dimensions of the brain. Then, these x and y coordinates were mapped on each subject's MR image corresponding to the PET image, and anatomical locations were determined. Moreover, the x and y coordinates of all subjects corresponding to rCBF changes were mapped on the MR images of one subject.

## Results and Discussion

Table 1 shows the anatomical areas determined by mapping these pixel coordinates on each subject's MR image. High laterality of the olfactory system in response to the olfactory stimulus was observed. The right hippocampus, right parahippocampal gyrus, right cingulate gyrus and left insula consistently responded to the olfactory stimulation.

Figure 1 represents all cortical and subcortical areas mapped on the MR image of one subject. The laterality of the responses to the olfactory stimulus is more clearly shown.

Abraham et al[9] studied the effect of right temporal lobe lesions and reported that patients with righ temporal lobe lesions had difficulty in matching smells. Rausch et al [10] reported that patients with right temporal lobe excisions recalled significantly fewer odors correctly than did patients with left temporal lobe excisions. In light of the above observations, our findings that the right hippocampus and right parahippocampal gyrus are activated by olfactory stimulation become more meaningful. But Eskenazi et al[11] reported that there were no significant differences in performance between dominant and nondominant lobectomy patients. Their results differ from our findings. The degree of pleasantness or unpleasantness of the olfactory stimulus may be an important factor.

Anatomical studies have shown that the orbitofrontal cortex is a region in which pathways from various sensory areas converge[12, 13, 14, 15, 16]. Olfactory inputs can reach the orbitofrontal cortex via the mediodorsal thalamus[17], via the hypothalamus[18], or via a direct projection from the region around the prorhinal sulcus[19]. Though there is good anatomical evidence for olfactory convergence in the orbitofrontal cortex, consistent activation of the orbitofrontal cortex was not detected in our study.

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Table 1 Cortical and subcortical anatomical areas detected by paired-image subtraction method.

| Anatomical Area | Subject | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| rt. hippocampus | O | O | O | O | - |
| rt. parahippocampal gyrus | O | O | O | O | O |
| rt. cingulate gyrus ( ant. inf. ) | O | O | O | - | O |
| rt. amygdaloid body | O | - | - | - | - |
| rt. occipital gyrus | O | - | - | - | O |
| rt. gyrus semilunaris | - | O | - | - | - |
| rt. lateral occipitotemporal gyrus | - | O | - | - | - |
| rt. superior temporal gyrus | - | O | O | - | - |
| rt. lateral geniculate body | - | O | - | - | - |
| rt. middle temporal gyrus | - | O | - | O | - |
| rt. subcallosal area | - | - | O | - | - |
| rt. medial occipitotemporal gyrus | - | - | O | O | - |
| rt. head of caudate nucleus | - | - | O | - | - |
| rt. inferior frontal gyrus | - | - | - | O | - |
| rt. insula | - | - | - | O | - |
| rt. gyrus rectus | - | - | - | - | O |
| lt. frontal pole | O | - | - | O | - |
| lt. gyrus rectus | O | - | - | O | - |
| lt. insula | O | O | O | O | - |
| lt. superior temporal gyrus | O | - | - | O | - |
| lt. medial occipitotemporal gyrus | O | - | - | - | - |
| lt. lateral occipitotemporal gyrus | - | O | - | - | - |
| lt. putamen | - | O | - | - | - |
| lt. cingulate gyrus ( ant. inf. ) | - | - | O | - | - |
| lt. inferior frontal gyrus | - | - | - | O | O |

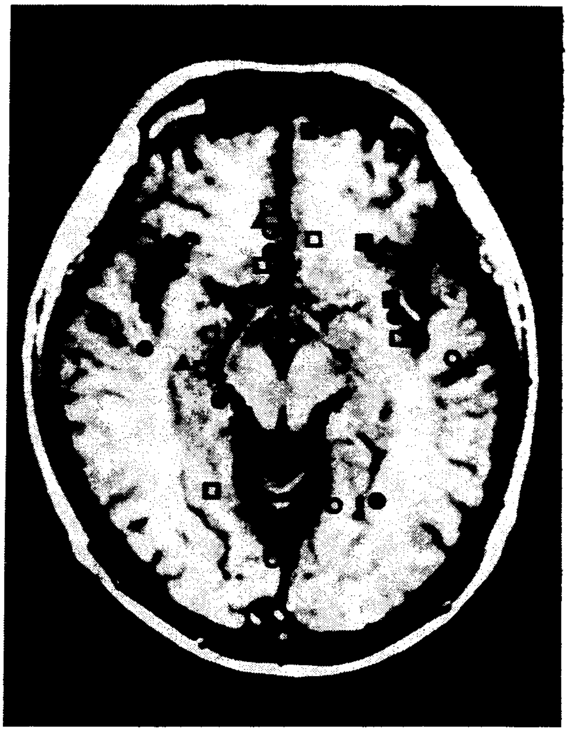

Fig. 1. Areas of activated by olfactory stimulation in five subjects mapped on the MR image of one subject. The x and y coordinates of the detected pixels are expressed as a percentage of the lateral and anteroposterior dimensions of the brain and mapped on one subject's MR image, 40 mm above the orbitomeatal line to make anatomical locations clearly distinguishable. The right hippocampus, right parahippocampal gyrus, right antero-inferior cingulate gyrus and left insula responded consistently to the olfactory stimulation.