Human cortical areas activated by odorants: A study by MEG and EEG

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1 Introduction

The olfactory projections into the cerebral cortex and their function in humans have not been revealed until recently because of the absence of appropriate measurement of human brain activities. However, recent development of brain imaging technique allows us to investigate the cerebral activities of living humans and the study of olfactory processing has already started. Zattore et al. [1] reported that by using PET, cerebral blood flow increased in the piriform cortices of both hemisphere and in the right orbitofrontal cortex after various kinds of odors were presented to human subjects. Other studies also noted the same results by using fMRI [2, 3]. Those PET and fMRI techniques strictly show the activated area of brain, however, they have the defect of low temporal resolution. By using the electrophysiological approaches, such as EEG and magnetoencephalography (MEG), it will be possible to estimate the activated areas by odor stimuli with the rigid latencies. Several studies using MEG have been reported [4-7]. But olfactory monomodal stimulation has been very difficult. Using a sophisticated olfactometer (Kobal's olfactometer) by which only olfactory sensation is caused without any other sensation, such as tactile, Kettenmann et al., reported that the region between the superior temporal plane and the parainsula cortex in both hemispheres was identified at latencies corresponding to P1 component of the olfactory evoked potentials (OEP), anterior central parts of insular cortex in dominantly left hemisphere to N1, and superior temporal sulci (STS) bilaterally to P2 [5]. In the study, these neocortical activities in each hemisphere were separately measured by 37-channnel SQUID system.

The main aim of the present study was to trace the activated cortical areas by olfactory stimulation from moment to moment by using a whole head type of SQUID system. We attempted to record olfactory evoked magnetic fields (OEMf) and OEP at the same time. Thus we investigated the activated cortical areas corresponding to the OEP responses.

2 Methods

2.1 Participants

Five healthy right handed volunteers (three women and two men, aged in their 20-30's) participated in the experiment. They were trained to breathe in only through their mouths to avoid the respiration airflow in their noses during the experiment.

2.2 Stimulation

A Kobal's type of olfactometer was used as the apparatus for olfactory stimulation. Any change of the mechanical or thermal conditions in the nostril was avoided by using this olfactometer. To achieve monomodal olfactory stimulation, the odorant pulses were presented in a constantly flowing airstream with controlled temperature (37˚C) and humidity (80%) (see Figure 1).

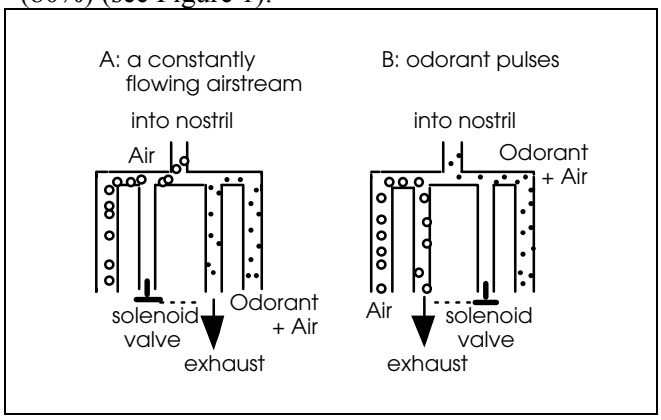

Figure 1: *Schematic drawing of the flow switching device. Any changes in flowrate were not detected by the participant when the odorant was switched on (B) or off (A).*

The odorant pulses had rise-times of less than 20 ms to 80% of maximum concentration of odor stimuli in this olfactometer. Phenylethyl alcohol (rose-like odor) with less than moderate subjective intensity was used as the odor stimulus. The duration of the stimulus was 200 ms and an interstimulus interval of 40 s was used, which was long enough to avoid olfactory adaptation. Thus it took about 20 m for one experiment.

2.3 Measurement of OEMf and OEP

OEMf were measured by using a 64-channel whole head SQUID system (CTF Systems Inc., Canada). This system has several sensors to measure the environmental magnetic noise. Thus it was possible to remove the exterior noise from the data. OEMf and OEP were recorded simultaneously. A sampling rate of 625 Hz was used. An on-line 100 Hz low-pass filter and an off-line 40 Hz low-pass filter were used for both recordings. For OEP, a high-pass filter of 0.05Hz was also used. A pre-trigger time was 400 ms and a duration of recording of 2 s was used. OEP were obtained from Cz, C3 and C4 referring to A1+A2. Each participant attended to more than two experiments for one nostril on the separate days. And so one man and two women participated in the experiment totally eight times, one woman did six times and one man did four times.

2.4 Data analysis

For data analysis, records contaminated with EOG were rejected. Data in which more than 24 among 30 trials (80%) were averaged was only used for estimation of equivalent current dipoles (ECDs). For the estimation of dipoles, MRI head shape data were used to determine the fitting sphere for each volunteer's head for source modeling. In order to have ECDs with high validity , the estimation error required less than 20% (if two dipoles were assumed for estimation). Moreover ECDs had to be stable during for a certain time (more than about 50 ms) and have suitable power. For localization of dipoles, to identify the activated areas, the location of dipoles were plotted on each volunteer's MRI and were checked whether they were on the cortical structures or not.

3 Results

3.1 OEP

Reproducible pattern of OEP were obtained within each participant. Figure 2 shows an example of OEP at Cz. The first positive peak (P1) with the latency about 360 ms, the first negative peak (N1) with the latency around 460 ms and then the second positive peak (P2) with the latency about 600 ms after stimulus onset were observed in the OEP response consisting with a previous study (5). The amplitude of P2 was the biggest among the other components in all participants. There was no clear latency difference among the locations of electrodes.

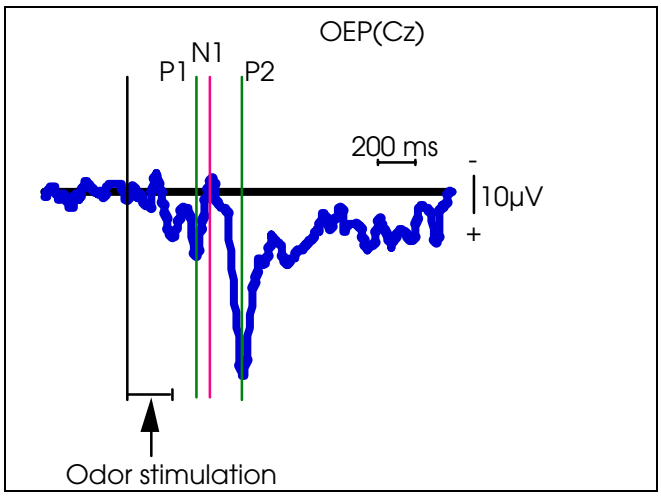

Figure 2: *An example of OEP from the vertex. The averages (SDs) of each component were; 359 (41) ms for P1, 461 (41) ms for N1, and 601 (42) ms for P2.*

3.2 OEMf

A clear change in magnetic signal intensities corresponding to each component of OEP was found. Figure 3 shows the same example as the OEP in Figure 2. The averaged magnetic signals of all of 64 channels increased corresponding to potential shift of OEP.

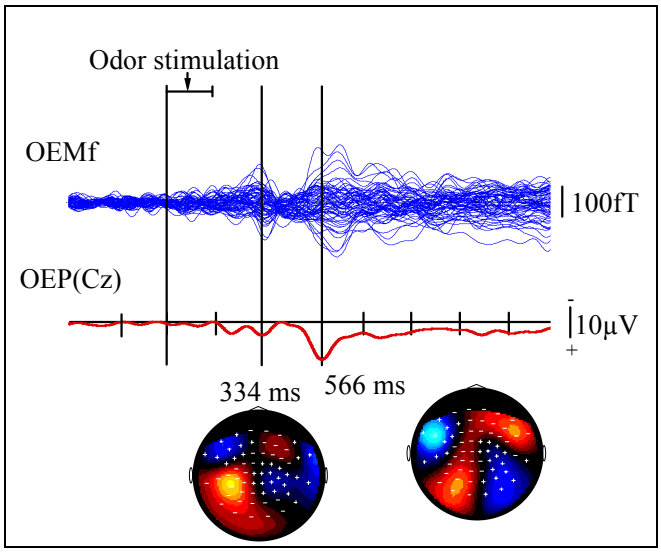

Figure 3: *An example of OEMf (superimposed MFs of 64 channels) and OEP. Iso-contour maps of P1 and P2 components.*

3.3 Estimated cortical areas

Under the necessary conditions for the estimation and localization of ECDs, one of five volunteer (sub.1) showed olfactory related activating area to P1 component of OEP, three volunteers (sub.2,

sub.4 and sub.5) showed some areas to N1 component and all of them showed some areas to P2.

Table 1: *Estimated cortical areas at latencies corresponding to P1, N1 and P2 components of OEP. (Ins.: insular cortex, Hip.: hippocampus, STS: superior temporal sulcus, tem. pl.: temporal plane, ant: anterior, mid: middle, post: posterior)*

A: left nostril stimulation

		P1		N1		P2	
Hemisphere		left	right	left	right	left	right
Sub. 1	exp.1	Ins.(ant)	Ins.(ant)			STS	Ins.(post)
	exp.2	Ins.(ant)	STS			Ins.(post)	Ins.(post)
	exp.3	Ins.(ant)	Ins.(ant)			Hip.	
	exp.4	Ins.(ant)	Ins.(ant)			STS	STS
Sub. 2	exp.1			Ins.(mid)	temp. pl.	STS	STS
	exp.2					Ins.(post)	Ins./STS
	exp.3				Ins.(mid)	Ins./STS	STS
	exp.4			Ins.(mid)		Ins./STS	temp. pl.
Sub. 3	exp.1						
	exp.2						Hip./STS
	exp.3					Ins.(post)	Ins.(post)
	exp.4					Ins.(post)	Ins.(post)
Sub. 4	exp.1			Ins.(mid)	Ins.(mid)		STS
	exp.2						STS
	exp.3				Ins.(mid)	STS	STS
Sub. 5	exp.1						
	exp.2			Ins.(mid)	Hip.	STS	STS

B: right nostril stimulation

		P1		N1		P2	
Hemisphere		left	right	left	right	left	right
Sub. 1	exp.5						
	exp.6						Ins./STS
	exp.7	Ins.(ant)	Ins.(ant)			Ins.(post)	
	exp.8	Ins.(ant)				Ins.(post)	
Sub. 2	exp.5			Ins.(mid)		STS	STS
	exp.6					STS	
	exp.7					STS	STS
	exp.8					STS	STS
Sub. 3	exp.5					Ins.(post)	STS
	exp.6					Ins./STS	Ins.(post)
	exp.7					Ins.(post)	Ins./STS
	exp.8					Ins.(post)	Ins.(post)
Sub. 4	exp.4			Ins.(mid)	Ins.(mid)	STS	STS
	exp.5			Ins.(mid)	Ins.(mid)	STS	STS
	exp.6			Ins.(mid)	Ins.(mid)		STS
Sub. 5	exp.3					Ins.(post)	Ins.(post)
	exp.4			Ins.(mid)	Ins.(mid)		

No one showed some cortical areas at latencies corresponding to every P1, N1 and P2 components of OEP. Reproducible locations of ECDs were shown within each participant and almost between participants. Table 1 shows the definit areas at latencies corresponding to P1, N1 and P2 components. Locations of olfactory activating area at latencies corresponding to P1 were almost bilaterally superior part of anterior insular cortex (see Figure 4). However, Sub.1 showed more stable and longer activation on left hemisphere than on right hemisphere under both nostril stimulation conditions. Although the orientation of ECDs at P1and P2 latencies was almost upward, it at N1 was downward. These opposite ECDs were identified at around central part of insular cortex. This area was a little bit behind to the area related to P1 component. Superior temporal sulcus (STS) and/or posterior part of insular cortex were often identified related to P2 component of OEP (see Figure 4).

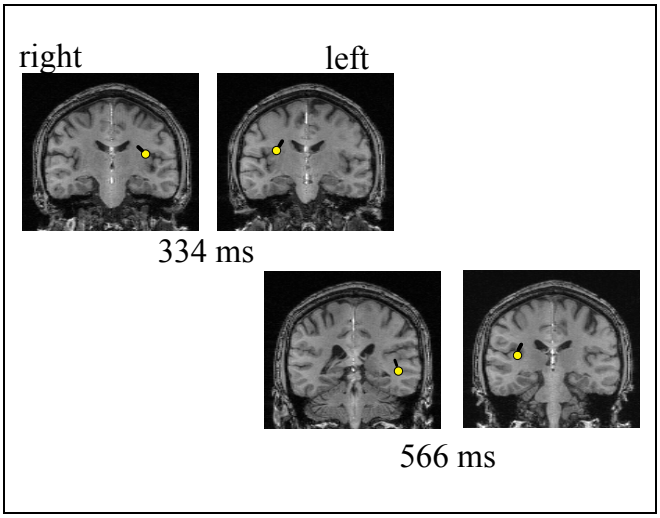

Figure 4: *An example of locations of estimated ECDs for each P1 and P2 component. This data is corresponding to it in Figure 3.*

4 Discussion

In this study, we detected the three components of EEG to olfactory stimuli. In addition the area around the anterior part of insular cortex was estimated as the activated area involved in the first positive potential in OEP. An activated area related to N1 was estimated at the central part of insula. Activation in this area was suggested to relate with odor preference by Kettenmann et al.,[5]. As in our experiment Phenylethyl alcohol was judged neutral hedonic by all volunteers, the relation between activation in this area and hedonic was not revealed. Insular cortex was generally thought to be involved in taste information processing. Kobayakawa et al., [8] suggested the implication of insula in gustation in human. The function of insular cortex which involves in both olfaction and gustation need to be investigated in further studies.

The area around the STS was estimated as related area to P2 in OEP. This P2 component seems to involve in the cognitive aspect of olfactory processing [4,5]. Besides the possible assumption is that STS would receive some information from the primary olfactory cortex via orbitofrontal cortex [9]. Thus, the temporal lobes activation would be concerned to the higher olfactory function.

Although an activation of orbito-frontal gyrus was shown by using both the PET and fMRI measurement, such activation was not found by using the MEG. The following are conceivable explanation of these results. (1) Not enough magnetic signal intensities were obtained because the orbito-frontal gyrus was located deeply to the sensor of MEG and additionaly the density of the sensors in frontal part was low. (2) The problem of the application of sphere model to estimate ECDs in this area has been pointed out.

Acknowledgements

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