Olfactory Cognitive Response Using Odorant Odd-ball Paradigm by Magnetoencephalography

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The aim of this study is to measure and analyze perception and cognition in human olfaction. In this magnetoencephalographic (MEG) study, the event-related magnetic fields were measured by a whole-cortex biomagnetometer (a 122-channel, first-order planar SQUID gradiometer which can cover the entire head of a subject). We have already reported that the response of olfactory event-related magnetic fields were obtained as a broad peak at 300-500 ms latency on bilateral frontal lobe, whose generators were located symmetrically on bilateral frontal area near the orbito-frontal sulcus. In this experiments, we applied an odd-ball paradigm to study olfactory event-related magnetic fields. Three volunteers participated in this study. The odd-ball paradigm using two kinds (amyl acetate, and isovaleric acid) of odorant pulse stimuli were applied. The subjects were instructed to count the number of rare odorant stimuli as a target.

In this odd-ball study, three responding peaks were analyzed by a **SSP** method. The first component was the trigeminal response of about 270 ms latency. The second components were olfactory responses of 350-450 ms latency which were composed from two generators estimated at the bilateral orbito-frontal regions. These latest components with latency more than 500 ms were evoked by the odorant odd-ball task only and these generators were firstly estimated on a few superior-temporal areas or near in the right and left insula regions. These late MEG components by the olfactory odd-ball paradigm suggest the activities of cognitive response of human olfaction. From these two olfactory MEG experiments and analyses, we found the perception and recognition mechanism in human olfactory system objectively.

Keywords: a 122-channel whole-cortex biomagnetometer, planar SQUID gradiometer, olfactory stimulator, olfactory event-related magnetic fields, dipole model, olfactory odd-ball paradigm, **SSP** method, olfactory perception and recognition

1.INTRODUCTION

A history of the modern technology for non-invasive human measurements starts up from the discovery of X-ray by Rentogen in 1895. Next important historical epoch was an invention of computer tomography (CT) using X-ray by EMI company in 1971. This is the origin of various graphic imaging technologies to diagnoses in medicine. X-ray imaging technology means to visualize internal organs in human body by weak rating difference of absorption and permeability to the interaction with X-ray and tissues of human body. Since this X-ray imaging, physical and chemical technologies had been applied to the fields of medical electronics, for example, functional magnetic resonance imaging (fMRI) using nuclear magnetic resonance technology and positron emission tomography (PET) using a positron created from radioisotope with an extreme short reduction rate and so on. These inverse problems are capable to resolve analytically in perfect, because these physical energies are able to be given and put into human body from the outside.

On the contrary, electrical phenomenon of inner body such as electroencephalography (EEG), electrocardiogram (ECG), and so on can not solve perfectly. They are called as ill-posed inverse problem, because these electrical phenomena are the inner signal existing in human body. Magnetoenceplahography (MEG) is also the same electrical phenomenon as EEG in human brain which was measured by using superconducting quantum interference device (SQUID). Though the response of EEG is depend on each different electric resistance of each tissue in human body, MEG is not almost depend on the electric resistance. Therefore, MEG has the more excellent nature of source localization than EEG. Functional MRI and PET are suitable to imaging the blood flow and metabolism’s change in the brain except for time resolution. The best advantage of MEG imaging is good time resolution to analyze brain response by millisecond.

A human olfactory sense has been expected to be measured by an objective method using olfactory evoked potentials [1]. Though a few studies of the olfactory evoked potentials have been tried to take responding peaks for various odorants, the characteristics of these peaks are unclear and still debatable now. Several papers of olfactory evoked potentials were reported in humans by averaging EEG using onset of an odorant stimulation.

Although olfactory-related potentials evoked by odorant pulse stimuli have been recorded from the human scalp [2-4], the neuromagnetic fields of olfactory cognitive response have not been measured yet. In the present study, we investigated olfactory event-related potentials and the neuromagnetic fields evoked by odorant pulses synchronized with the subject's respiration [3] using a whole-cortex, 122-channel SQUID neuromagnetometer (Neuromag-122™) and studied to analyze the olfactory MEG responses using an olfactory odd-ball paradigm.

The purpose of this study is to measure the human olfactory sense by MEG experiments and analyze the human's olfactory perception and cognition in non-invasively. An odd-ball paradigm has been sometimes used in visual and hearing experiments in psychological test, however has never been used in olfactory experiment. In this present olfactory experiment, we used two odors, one of which is pleasant odor and another is unpleasant odor. In general, a targeting odor in two odors is usually given at the lower stimulating rates randomly more than another non-targeting odor. In this odd-ball experimental situation, a subject had to count the number stimulated by targeting odor only. We call this targeting odor as "a rare olfactory stimulant", another as "a frequent olfactory stimulant."

We found firstly the MEG responding peak with a later component suggested as a recognition factor of targeting odor only in this present olfactory odd-ball task. This later component was not been found in non-targeting odor response. In this paper, we discuss the nature between the perception and recognition of sensing odor. We found the perception of the odor in the first experiment using one odor and the recognition of odor in the second odd-ball experiment using two odors in the human olfactory system. From the present two MEG experiments, it was suggested that we judge to recognize its nature and contents of odorants at the different regions in our brain after the perception of odor.

1.1. Research on the measurement of odorant perception

In our first MEG experiment non-magnetized control system using air-pressure valves and a respiration mask using an optical fiber sensor were applied to detect the subject's respiration. Odorant stimuli were actively given into the right or left nose cavity through a thin silicon tube using a mask attached on the subject's face by an odorant pulse synchronized with the subject's respiratory cycle.

Olfactory event-related potentials were measured by EEG and olfactory event-related magnetic fields were also measured by MEG using a 122ch whole-head neuromagnetometer. The analyses of these experimental data were done as follows.

a) To estimate the olfactory central nervous active centers.
b) Research on the dominance of human brain laterality.
c) Separation of olfactory responses from trigeminal nerve responses.

1. 2. Research on the measurement of odorant cognition

In our second experiments olfactory event-related magnetic fields were measured by an odd-ball paradigm using two odorants and these estimated signal sources were obtained in a few superior temporal regions. In this olfactory odd-ball paradigm, two odorants (pleasant odor and unpleasant one) were used at random interval, which of one is rare stimuli and another is frequent stimuli. These given rate is one by three, and a subject counted the number of frequent stimuli.

2. MATERIALS AND METHODS

Six healthy volunteers (all right-handed males) participated in the first MEG experiment. Informed consent to participate in this experiments, which was first approved by the Human's Experiment Ethics Committee and MRI Experiment Ethics Committee in the Kansai center of AIST, Japan, was obtained from all participants. Odorant pulses were administered into the subject's nostril for 300 ms through a thin silicon tube in a respiration mask using a non-magnetized olfactory stimulator.

We gave careful consideration to our experimental conditions for the olfactory adaptation. Therefore, the amount of time that passed between odorant ejections in the first olfactory experiment, which measured odorant perception and the design in the second experiment, which measured odorant cognition were especially considered as follows.

2.1 Odorant's stimulation method and experimental conditions:

In the first olfactory MEG experiment, a **"blast method"** was used and odorants were applied under the synchronization with subject's respiration. Odorant pulses were administered into the subject's nostril for 300 ms through a thin silicon tube in a respiration mask using a non-magnetized olfactory stimulator.

Amyl acetate (banana-like odor) was used at a concentration of about 1%. This odorant gas was made by the bubbling method outside the magnetically shielded room and was administered into the subject's nose at a constant flow rate of 8 l/min via air valves which were perfectly isolated magnetically. The odorant stimulus was administered into one nostril (right or left) in each session of the experiment. Delivery was synchronized with inspiration, and it was given randomly every 3-12 respirations.

In the olfactory experiments, we must always consider adaptation effects. Therefore, the ejection periods were determined as 300 milliseconds vs one odorant stimulation under the scynchronization with subject's respiration and the averaging frequency was determined as forty times under the condition of the inter stimulus interval (ISI) more than twenty seconds to avoid the olfactory adaptation of subjects.

40 evoked magnetic responses were averaged at random ISI time more than twenty seconds. Auditory responses to the sound of the air valve were avoided by using ear plugs and trials containing eye blink artifacts were rejected from the averaging process. High- and low-pass filters of 0.05 Hz and 100 Hz, respectively, were used and the sampling frequency was 400 Hz. The baseline was 100 ms before the stimulus onset, and the total sampling time was 1000 ms after the start of stimulation. A notch filter (60 Hz) and a low-pass filter (50 Hz) were applied to the averaged data.

In our second experiments, olfactory event-related magnetic fields were measured by an odd-ball paradigm to measure the odorant cognition using two odorants for three male healthy subjects (all right handed). Informed consent to participate in this study, which was approved by the Human's Experiment Ethics Committee and MRI Experiment Ethics Committee in Kansai center, AIST, Japan, was also obtained from all subjects.

We must consider adaptation effects in the second olfactory experiment, too. Therefore, ejection periods were also determined as 300 milliseconds vs one odorant stimulation and the ISI was also determined at random more than twenty seconds to avoide the olfactory adaptation of subjects.

The rare odorant stimulation (target) and the frequent odorant stimulation were given to the subject at the population rate of 1:3 at random. These estimated signal sources for rare stimulation (target) were obtained (latency: about 500-600 ms) in a few superior temporal regions for one example, insula cortex and so on.

2.2 Signal space and projection (SSP) method

A successful signal space projection (**SSP**) method was firstly performed by Ilmoniemi for separating the different components of evoked responses and spontaneous activity in brain signals as well as signals measured from the heart [5] and applied by Houtilainen et al. for the rejection of eye-blink [6]. The effective noise reduction method is one of the most important measuring techniques in olfactory neuromagnetic experiments because we must use very few summation in the acquisition of olfactory evoked sensations which have the larger adaptation effects.

We used a whole-cortex type biomagnetometer (122-channel SQUID gradiometer) in these olfactory experiments. Amyl acetate gas (1%) was administered for 300 ms into either the right or left nostril in synchronization with respiration using a mask and an optical fiber sensor. We obtained the clear olfactory responses on the both sides of forehead in all six subjects (all right-handed). This generator of olfactory magnetic fields were estimated at two regions located fairly asymmetrically near the bilateral frontal deep areas. Almost all subjects were the ipsi-lateral dominancy which the response of the same side with stimulation have become the most largest. In this research, we applied to analyze the odorant responses using principal component analysis (PCA) and this **SSP** method for the olfactory odd-ball task's data processing [7].

A set of *m* linearly independent *n*-channel magnetic fields signals,

$$\mathbf{b_1}, \mathbf{b_2}, \cdots, \mathbf{b_k}, \cdots, \mathbf{b_m} \tag{1}$$

spans an *m*-dimensional substance P of the *n*-dimensional space B of all n-channel signals. An *n*-channel signal means the set of outputs of *n* magnetic field sensors. There exists a projection operator **P** such as

$$\mathbf{Pb} \in \mathrm{P} \text{ for any } \mathbf{b} \in \mathrm{B} \tag{2}$$

P is an idempotent operator **PP** = **P**. If we have determined an orthogonal basis $\mathbf{U}_1, \cdots, . \mathbf{U}_m$,

$$\mathbf{U_J}^{\mathbf{T}}\mathbf{U_k} = \delta_{j,k} \tag{3}$$

For P we find

$$\mathbf{P} = \mathbf{UU}^{\mathbf{T}} \tag{4}$$

$$\mathbf{U} = (\mathbf{U}_1, \cdots, \mathbf{U}_m) \tag{5}$$

U is the matrix whose columns are the basis vectors. We can find the orthogonal basis to obtain a measure of the linear independence of $\mathbf{b_1}, \cdots, \mathbf{b_m}$ by the singular-value decomposition analysis (SVD) of

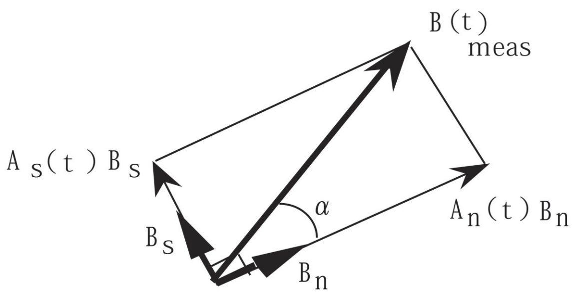

Fig. 1 Principle of signal space and projection (**SSP**) method.

$$\mathbf{B} = (\mathbf{b}_1, \mathbf{b}_2, \cdots, \mathbf{b}_m) = \mathbf{U} \wedge \mathbf{V}^{\mathbf{T}} \tag{6}$$

The orthogonal basis is given in **U** while small singular value $\wedge$ indicate linear dependence. Once **P** has been found we can multiply our measurements with either **P** or **1 − P** thereby restricting the analysis to P or its orthogonal complement substance, respectively. We denote the projection by

$$\mathbf{b}_{11} = \mathbf{P}\,\mathbf{b} \tag{7}$$

And the orthogonal complement projection by

$$\mathbf{b}_{\perp} = (\mathbf{1} - \mathbf{P})\,\mathbf{b} \tag{8}$$

Suppose that we have constructed a projection operator **P** from a set of $\mathbf{b}_1, \cdots, \mathbf{b}_m$, corresponding to a substance P. For example, using this SSP method we obtained orthogonal following vectors

$$\mathbf{B}_s \perp \mathbf{B}_n \tag{9}$$

These are shown as a linear combination equation as Fig. 1.

$$\mathbf{B}(t)_{meas} = \mathbf{A}_s(t)\mathbf{B}_s + \mathbf{A}_n(t)\mathbf{B}_n \tag{10}$$

$$\mathbf{b}_k = (\mathbf{b}_{k1}, \mathbf{b}_{k2}, \cdots, \mathbf{b}_{kn}) \tag{11}$$

2.2.1 Noise reduction on the real time MEG measurements by SSP

We have usually applied the **SSP** method to reject the circumstance magnetic noises on the real time MEG measurements. We can especially reject the noise effects of the electric current from train's electrical noise near our laboratory. These electric current noise were sometimes over more than 3000 fT/cm. We can silently detect the neuromagnetic brain responses in human by using the **SSP** on line.

2.2.2 Apply SSP method to olfactory signal processing

Next, we used the **SSP** method to analyze the real olfactory signal responses and to obtain a few current dipoles in the olfactory odd-all experimental cases [7]. We have many data of olfactory evoked magnetic response including two or three main peaks at the different latency.

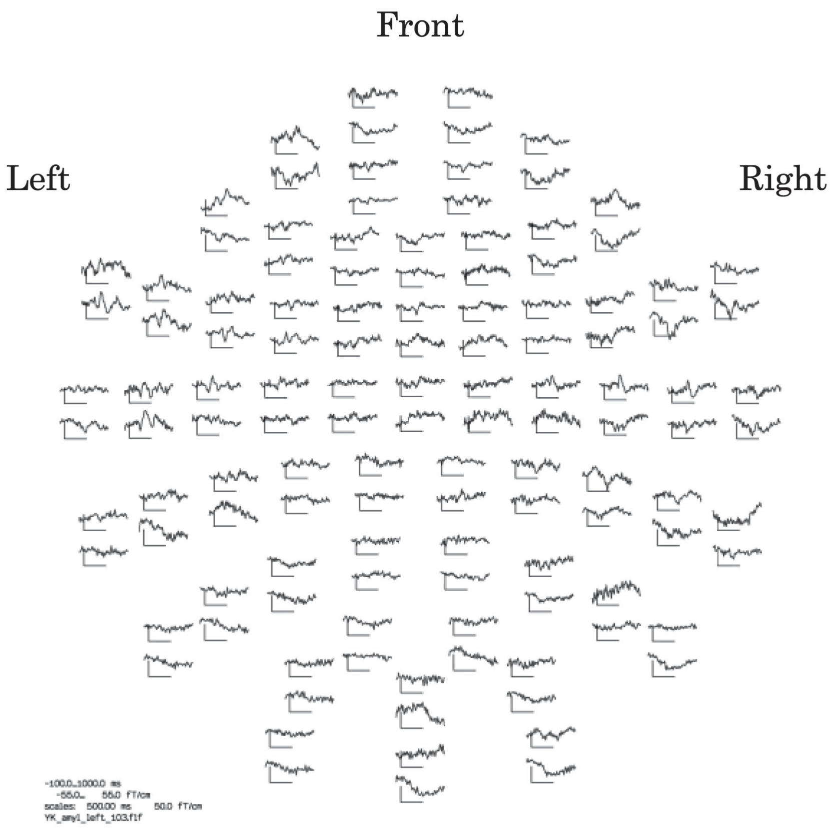

Fig. 2 Olfactory event-related magnetic fields evoked by odorant stimulation. Odorant: 1% amyl acetate. Left nose stimulation. 40 times averaging. Scale unit: 50.0 fT/cm, 500 ms.

3. RESULTS

3.1 Results of olfactory event-related experiments

Olfactory event-related magnetic fields were obtained as a fairly broad peak with 300 - 500 ms latency on both the right and left sides of the frontal lobe (Fig. 2), although the goodness of fit was not high due to noise.

MEG main response waves were sharply detected at the latency about 350 ms and these signal sources were estimated to exist as two dipoles bilaterally at the orbito-frontal lobe in the deep frontal areas in the brain. This figure shows the wave forms of the olfactory event-related magnetic fields measured by a 122-channel whole head SQUID. In these results a main peak of 300-400 ms may be considerable as the main response for the odorant (Amyl-acetate, 1% concentration).

Olfactory activation sources estimated by single dipole model

We applied single dipole model to the estimation of olfactory activation sources. This indicated that bilateral dipoles were located almost symmetrically in a fairly deep region near the frontal lobe. The goodness of fit (“g” value) was about 80%.

Estimated region of olfactory activated center :

The equivalent current dipoles were estimated by using these MEG data in the region near the deep orbito-frontal area bilaterally, differing from the trigeminal responses (estimated in the region of somatosensory area S1) obtained by the pulse stimulation of only fresh air. This result coincided with the results of olfactory physiological experiments for rhesus monkey by Takagi [8], Rolls et al. [9], and the result of human’s MRI data by Koizuka et al. [10].

Ipsi-lateral dominance of olfactory MEG responses :

In six subjects, the latency and intensity of the ipsi-lateral MEG responses were shorter and larger than those of the contra-lateral MEG responses in respectively. This shows the ipsi-lateral dominance for the latency of the response peak in five experimental sessions of the same subjects. Ipsi-lateral response is slightly bigger (a few fT/cm) than contra-lateral one. Latency of ipsi-lateral response is slightly shorter (a few ten ms) than contra-lateral one.

From the amplitude’s data of MEG peaks almost all ipsi-lateral responses for all sessions are bigger than contra-lateral one. This shows the ipsi-lateral dominance of the olfactory MEG responses. Our result of ipsi-lateral dominance did not coincide with the result of right-dominance with the PET’s data by Zatorre et al. [11], although the estimated active areas on the olfactory nervous center coincided with the orbito-frontal regions estimated by us.

Separation between olfactory response and trigeminal one :

We execute the air stimulation test as the control experiments.

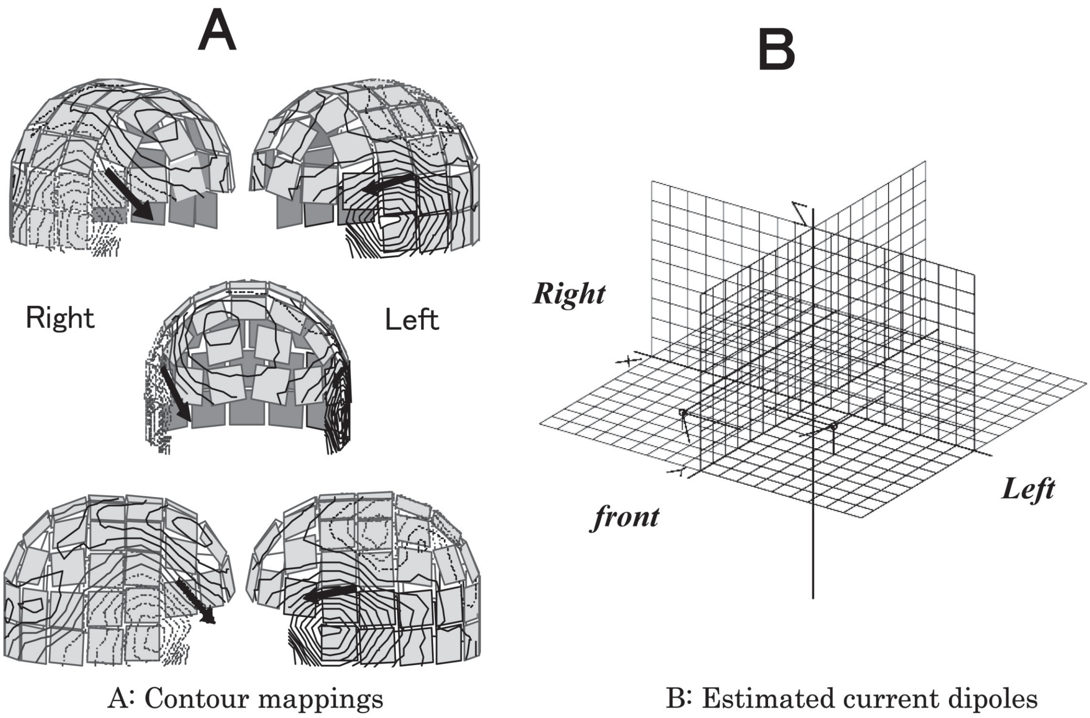

Fig. 3 Contour mappings and two equivalent current dipoles estimated from olfactory MEG responses.

Air pressure was used about 3 or 5 times of the odorant gas pressure of usual olfactory experiments. In this experimental condition the response peak of air stimulation was obtained about 270 ms and found dominantly in the contra-lateral S1 somatosensory area in the temporal region. From these results we consider that a trigeminal response was evoked by the air stimulation. This is the same tendency of olfactory evoked potentials. Figure 3 shows the summary of each activated centers in our experimental results on MRI integrations of the each estimated regions evoked by olfactory stimulation and air stimulation, respectively.

When the odorless air was stimulated into right nostril, the MEG response was obtained in the somatosensory area at the temporal lobe in the left hemisphere. In general, the MEG responses showed the contra-lateral dominancy by the air stimulation. The generators of olfactory magnetic fields were estimated to integrate the MEG data on the MRI's brain mapping at two regions located fairly asymmetrically near the bilateral orbito-frontal areas (See Fig. 3).

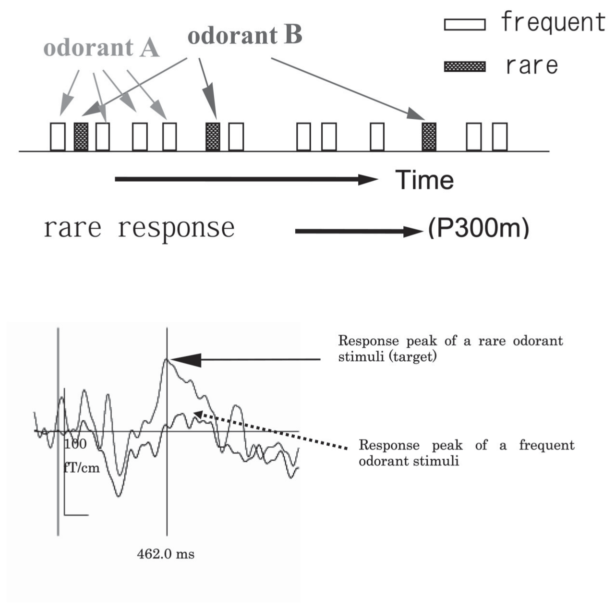

Fig. 4 Olfactory odd-ball paradigm and comparison with MEG response peak of rare and frequent odorants. Upper: Olfactory odd-ball paradigm; Lower: Comparison with rare and frequent wave.

3.2 Response of ERFs for odd-ball paradigm

In the second experiment of olfactory odd-ball paradigm MEG main response waves were also sharply detected at the latency about 350 ms and these signal sources were estimated to exist as two dipoles bilaterally at the orbito-frontal lobe in the deep frontal areas in the brain. However, in this olfactory odd-ball experiment, we obtained the more later positive components, P300 and P300m in both evoked potentials and event-related magnetic fields [12]. P300m responses of unpleasant smell for three subjects showed a different cognitive nature from pleasant one. This latency is about 500-600 ms as shown in Fig. 4. In the olfactory MEG odd-ball paradigm a few equivalent current dipoles were obtained at few different regions near the superior temporal area.

Analysis of olfactory odd-ball responses using "SSP method"

In our second olfactory experiments we obtained the more later positive components in both evoked potentials and event-related magnetic fields. This latency is about 500-600 ms. The results of the reduction of these magnetic noises using the **SSP** method gave us the remarkable improvement on the S/N ratio of the above olfactory neuromagnetic experiments [7].

Two factors of about 282.5 ms and 333.3 ms factors were extracted independently by this **SSP** method. Figure 5 shows an example of separation of two MEG components measured by olfactory odd-ball paradigm using **SSP** method (cal: 500 ms, 50 fT/cm). The upper left graph shows four example curves as original responding waves measured by the neighbouring MEG channels. We can find two peaks which have different latencies shown by two broken lines. The lower right and left graph show two each components separated independently, one of which is a peak of 282.5 ms (left graph) and another is a peak of 333.3 ms (right graph) by **SSP** method. And the upper right graph shows each complement curves obtained by the application of **SSP** method.

Figure 6 shows the all superimposition waves for 122-channel MEG responses and an example of separation analysis of three components in spatial-temporal 4-D imaging by **SSP** method for odd-ball paradigm of human olfaction. These estimated signal sources for rare stimulation (target) were obtained (latency: about 500 - 600 ms) in a few superior temporal regions for one example, insula cortex and so on. A few equivalent current dipoles were obtained at a few different superior temporal areas or near right and left insula regions. Figure 7 show two examples imagings estimated as one dipole at the superior temporal area in the case of pleasant smell and another one dipole near the insula region in the case of unpleasant smell as the targeting odors. Though a few dipoles were sometimes estimated in our present olfactory odd-ball experiment, one dipole was mainly estimated near the superior temporal area or the insula area in the case of pleasant or unpleasant smell as the targeting odor, respectively. These

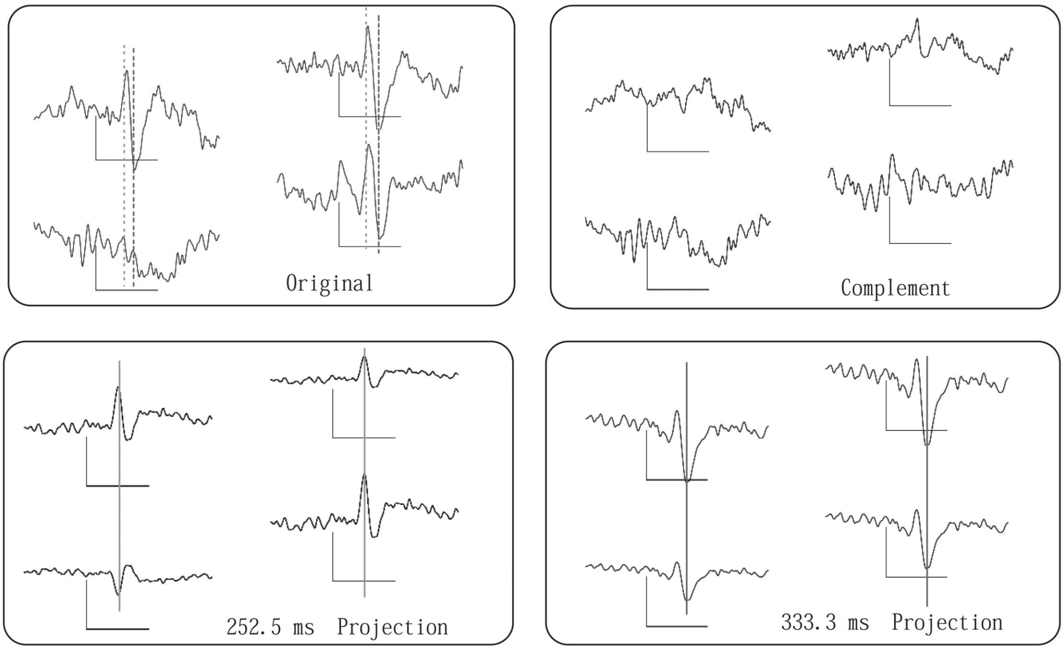

Fig. 5 An example of separation of two MEG components measured by olfactory odd-ball paradigm using **SSP** method (cal: 500 ms, 50 fT/cm). Upper-left graph: These four curves are the examples of original responding waves measured by neibouring MEG channels. We can find two peaks which have different latencies shown by two broken lines. Lower- right and left graph: We can separate two each components independently, one of which is a peak of 282.5 ms (left graph) and another is a peak of 333.3 ms (right graph) by **SSP** method. Upper-rigt graph: This graph shows each complement curves obtained by the application of **SSP** method.

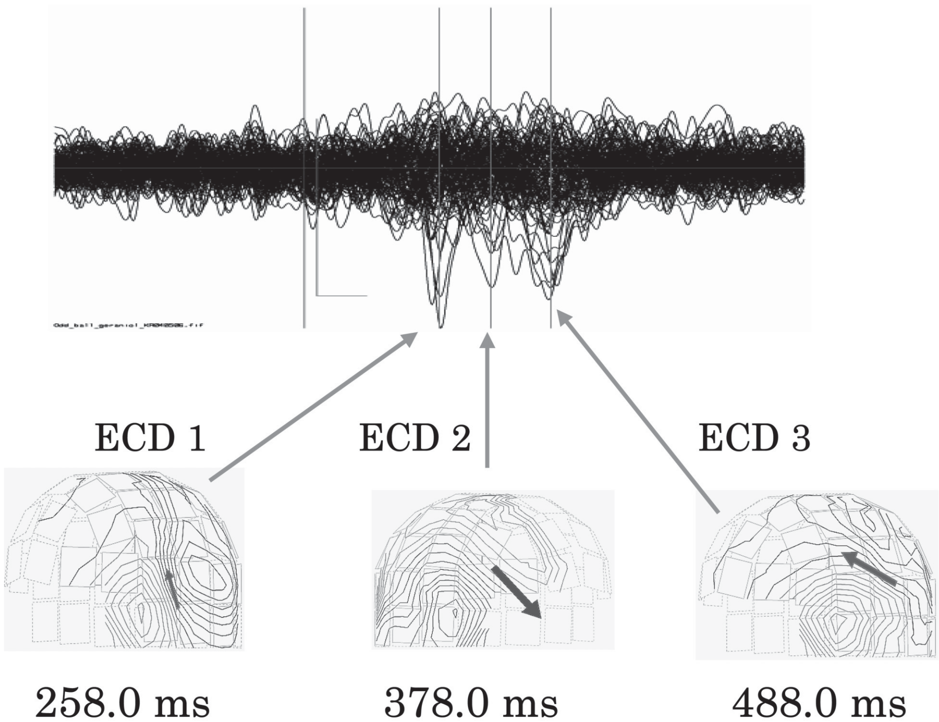

Fig. 6 An Example of the separation analysis of three components in spatio-temporal 4-Dimaging by **SSP** method for “odd-ball paradigm” of human olfaction.

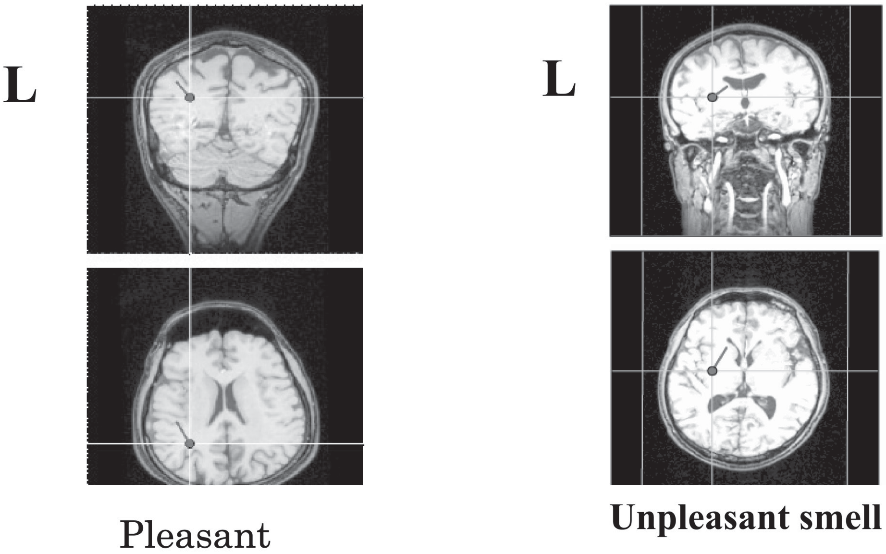

Fig. 7 Estimated dipoles of pleasant and unpleasant odorants for odd-ball MEG. The figure shows two example imagings estimated as one dipole at the superior temporal area in the case of pleasant smell and another one dipole near the insula region in the case of unpleasant smell as the targeting odors. Though a few dipoles were sometimes estimated in our present olfactory odd-ball experiment, one dipole was mainly estimated near the superior temporal area or the insula area in the case of pleasant or unpleasant smell as the targeting odor, respectively.

results suggest us to have the role of the recognition for odorant senses in these regions on the human olfaction.

Difference of laterality and annoyance nature in the olfactory cognition

In our olfactory odd-ball experiment we used two odorants (one of which is amyl acetate/pleasant odor and another is isovaleric acid/unpleasant odor). Experiments were done for two cases (Target is the case of pleasant odor and another is unpleasant one). Three subjects were tested by different one-side nose stimulation (right nose or left nose, respectively) for two case experiments. From these experiments we obtained a series of the responding data for "three subjects × two odorants (pleasant odor and unpleasant odor) × two laterality (right and left hemisphere)".

Table 1 shows the comparison for laterality of the latency of odd-ball task response [12]. In left nose stimulation the latency of pleasant odor was significantly larger than unpleasant with both hemispheres. However, in right nose stimulation the latency of left hemisphere was significantly larger than right, nevertheless annoyance of odors ($P < 0.01$, ANOVA and Fisher's PLSD test).

Figure 8 shows the annoyance nature in the olfactory cognition. The latencies of left hemisphere were significantly larger than right in subject A and B both pleasant and unpleasant odor. However, in contrast the right latencies were significantly larger than left in only subject C ($P < 0.01$, ANOVA and Fisher's PLSD test). From these results the difference of olfactory laterality suggests the difference of the cognitive nature of odorants, namely it shows the capability on the difference of olfactory cognition between pleasantness and unpleasantness.

Table 1 Comparison for laterality of the latency by the olfactory odd-ball task using two odors (pleasant, unpleasant). (subjects: n = 3, Latency: average ± SD ms). In the left nose stimulation, the latency of pleasant odor was significantly larger than unpleasant with both hemispheres. However in the right nose stimulation, the latency of left hemisphere was significantly larger than right, nevertheless annoyance of odors.

	Left nose stimulation		Right nose stimulation	
	Left	Right	Left	Right
Pleasant (amyl-acetate)	547±53	535±50	598±288	510±195
	*	*	*	
Unpleasant (isovaleric acid)	468±148	473±118	578±348	460±53

(*$P < 0.01$, ANOVA and Fisher's PLSD test)

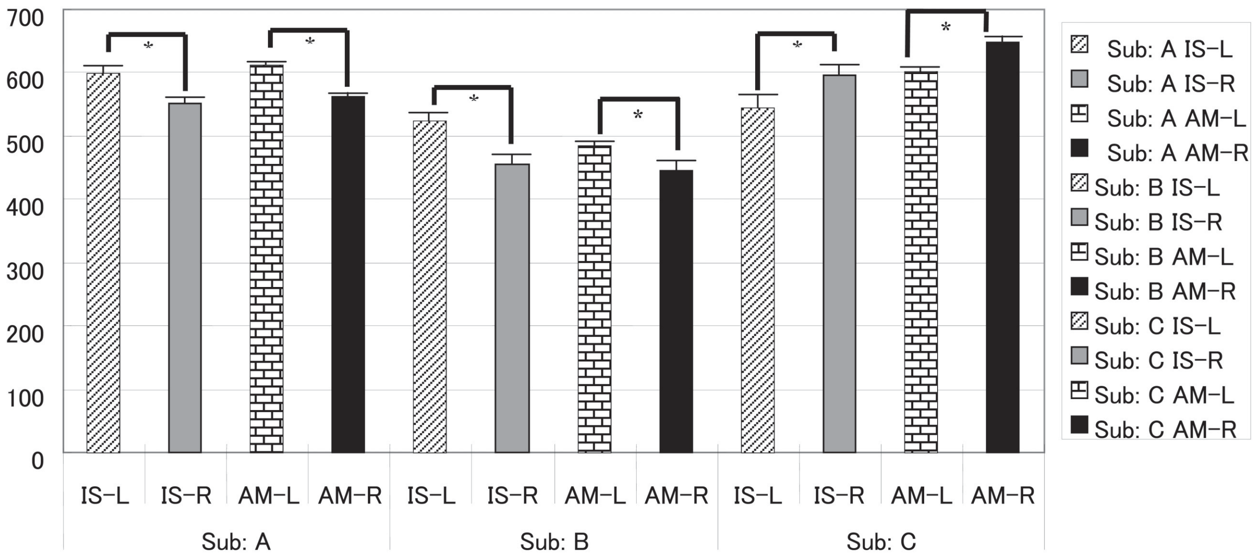

Fig. 8 Comparison of latencies among individual responses for individual subjects by the olfactory odd-ball paradigm (Subjects = 3, n = 5, Latency:average ± SD ms, *P < 0.01, ANOVA and Fisher's PLSD test). S : Isovaleric acid, AM : Amyl acetate. Hemisphere: L= left, R= right. The latencies of left hemisphere were significantly larger than right in subject, A and B both pleasant and unpleasant odor. However, in contrast the right latencies were significantly larger than left in only subject C.

4. DISCUSSION

We have previously measured olfactory-evoked potentials and event-related potentials [3, 13]. A signal source in the brain was calculated from the olfactory experimental data and we concluded that the deep frontal region was activated by odorant stimulation using topographical pattern analysis of olfactory evoked potentials. However, the electrical potentials were often distorted by the effect of differential resistance in various regions of the human brain, so we could not localize the signal source more precisely.

The response to chemosensory-evoked potentials has also been studied in humans and it has been suggested that the olfactory center is located in the superior temporal lobe [14]. The difference between this estimated region and our proposed site may be due to the following reason: (1) Differences in the type of olfactory stimulation. Kobal et al. did not apply stimulation synchronized with the subject's respiration, which we used in our olfactory experiments. Synchronization with respiration is considered to enhance the sensitivity of olfaction. (2) Differences in the method of delivery. Kobal et al. used the flow method with non-synchronized stimulation, while we used the so called **"blast method"** with very fast rising solenoid valves. This stimulation method allowed us to make possible to measure an more earlier and clear response than any other experiments. In the olfactory experiments of Kobal et al., CO_2 gas was often used, and the same response for other odorants was also obtained as with chemosensory potentials and fields [4, 15]. However, these responses may be pain-related or a trigeminal response such as a somatosensory evoked potential rather than a true olfactory response. If the responses in their experiments are assumed to be somatosensory potentials, the superior temporal area that they located would be a reasonable somatosensory nervous center. In our experiments on evoked potentials and event-related fields, olfactory responses were often more prominent on the ipsi-lateral side than the contra-lateral side at the lateral orbital sulcus in the deep frontal area and they were different from the characteristic contra-laterality of the trigeminal system [16, 17].

The results of our first MEG experiments suggest the following conclusions.

(1) Olfactory event-related magnetic fields were able to be measured clearly using a 122-channel whole-cortex neuromagnetometer.

(2) Olfactory event-related magnetic fields were obtained almost symmetrically and bilaterally near the frontal area with about 350-450 ms latency in all six subjects.

(3) Two dipoles were estimated to be located almost symmetrically on both sides of the frontal area using a single dipole model. The goodness of fit was more than 80%.

The above results suggest the existence of an olfactory area in the lateral orbital sulcus deep within the frontal lobe in the human brain, which is a site similar to that inferred on the basis of extra-cellular unit responses in the olfactory neuroscience for the rhesus monkey [7, 18].

In our present study, after the **SSP** method was applied to the noisy real experimental data, a few equivalent current dipoles (ECDs) were estimated precisely more than a usual filtering analysis with our olfactory experiments. These results suggest that **SSP** analysis is effective for many magnetic noise reduction to noisy difficult data obtained by neuromagnetic evoked responses such as olfactory experiments.

In olfactory odd-ball MEG paradigm using two kind odorants (pleasant odor and unpleasant one), a few later components were newly found near the few different regions in the superior temporal areas and near the right or left insula sulcus. These estimated signal sources for rare stimulation (target) were obtained (latency: about 500 - 600 ms). In general, the odd-ball task has been sometimes used with the psychological experiments to obtaine so called P300 peak which was defined as a “cognitive response” to the response of a cognitive human information processing [19]. We were firstly tried to apply this odd-ball task to the odorant MEG experiments measuring the olfactory cognitive responses which were considered to be different from the response of perception of odor.

From these results the difference of olfactory laterality suggests the difference of the cognitive nature of odorants, namely it shows the capability on the difference of olfactory cognition between pleasantness and unpleasantness [20]. Experiments were done for two cases (Target is the case of pleasant odor and another is unpleasant one). Three subjects were tested by different one-side nose stimulation (right nose and left nose respectively) for two case experiments. Laterality on the brain hemisphere was compared between pleasant odor and unpleasant one for the latency of the odd-ball task response, and olfactory annoyance nature was analyzed using the latency of olfactory cognitive responses.

In this paper, we discussed the nature between the perception and recognition of sensing odor. We found the perception of the odor in the first experiment using one odor and the recognition of odor in the second odd-ball experiment using two odors in the human olfactory system. From the present two MEG experiments, we judged to recognize its nature and contents of odorants at the different regions in our brain after the perception of odor. These results may suggest us the role of the processing mechanism in the perception and cognition to the annoyance of human olfaction.

5. CONCLUSIONS

The following conclusions were obtained by the present olfactory MEG experiments.

(1) Two olfactory nervous centers were found bilaterally in the deep orbito-frontal regions fairly asymmetrically in the human brain in separation with the somatosensory responses of the trigeminal puffing effects at the odorant stimulation.

(2) The capability of the ipsi-lateral dominance was suggested in human olfactory nervous system by olfactory MEG experiments.

(3) In olfactory odd-ball MEG paradigm using two odorants, a few later components were newly found at the few different regions in the superior temporal areas and near the right or left insula areas, and these results suggested us to have the role of the cognitive responses for human olfaction.

(4) A **SSP** method was applied to the data analyses in the MEG experiments of olfactory odd-ball paradigm and shown to be effective to many magnetic noise reduction for extreme noisy complex data obtained by neuromagnetic evoked responses such as difficult olfactory experiments.

(5) From the responses of laterality for the latency and the estimated dipole areas, a few differences between the first experiment using one odor and the second experiment using olfactory odd-ball task may suggest us the role of the odor processing mechanism in the perception and cognition to the annoyance of human olfaction.

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