Human Face Perception Traced By Magneto- and Electro-encephalography

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1. Abbreviations

MEG	Magnetoencephalography
EEG	Electroencephalography
fMRI	Functional magnetic resonance imaging
PET	Positron emission tomography
IT	Inferior temporal
STS	Superior temporal sulcus
SQUID	Superconducting quantum interferecne device
ECD	Equivalent current dipole
BESA	Brain electric source analysis
GOF	Goodness of fit
RV	Residual variance
1M	The first magnetic response
2M	The second magnetic response

2. Abstract

The temporal and spatial processing of face perception in normal subjects was traced by magnetoencephalography (MEG) and electroencephalography (EEG). We used 5 different visual stimuli, *face with opened eyes*, *face with closed eyes*, *eyes*, *scrambled face*, and *hand*, and they were shown in random order. Subjects were asked to count the number of *hand* stimuli. To analyze the complicated brain responses to visual stimuli, we used brain electric source analysis (BESA) as the spatio-temporal multiple source model. In MEG recording, the 1M and 2M components were identified in all subjects. The 1M was recorded to all kinds of stimuli but the 2M was recorded only to *face* and *eyes*. The 2M was recorded from the right hemisphere in all subjects, but in only 5 of 10 subjects from the left hemisphere. The mean peak latencies of the 1M and 2M were approximately 132 and 180 msec, respectively. The interpeak latency between 1M and 2M was approximately 48 msec on average but the interindividual difference was large. The 2M latency to *eyes* was significantly longer than that to *face*, and there was no significant difference of the 2M latency between *face with opened eyes* and *face with closed eyes*. The 1M was generated in the primary visual cortex in the bilateral hemispheres, and the 2M was generated in the inferior temporal cortex, around the fusiform gyrus. In the EEG recording, face-specific components, positive at the vertex and the negative at the temporal areas were clearly recorded. The EEG results were fundamentally compatible with the MEG results. The amplitude of the component recorded from the right hemisphere was significantly larger than that from the left hemisphere. These findings suggest that the fusiform gyrus plays an

important role in face perception in humans and that the right hemisphere is more dominant. Face perception takes place approximately 48 msec after the primary response to visual stimulation in the primary visual cortex, but the period of information transfer to the fusiform gyrus is variable among subjects. Detailed temporal and spatial analyses of the processing of face perception can be achieved with MEG.

3. Introduction

Face perception is considered to be one of the most important factors of daily life in animals. There are many studies concerning neural mechanisms for it, using microelectrodes in monkeys (Bruce et al., 1981; Perrett et al., 1982, 1987, 1991, 1992; Rolls, 1984; Baylis et al., 1985; Hasselmo et al., 1989; Yamane et al., 1988; Desimone, 1991; Oram and Perrett, 1992; Hietanen et al., 1992; Fujita et al., 1992; Pare et al., 1995), sheep (Kendrick and Baldwin, 1987) and humans (Ojemann et al., 1992). The face-specific neurons are found in the temporal cortex, mainly in the superior temporal sulcus (STS) and convexity of the inferior temporal (IT) cortex.

In clinical studies, prosopagnosia is usually produced by lesions in the bilateral hemispheres (Meadows, 1974; Damasio et al., 1982; Damasio, 1985), but its symptoms can also be produced by damage to the right hemisphere alone (Meadows, 1974; Whiteley and Warrington, 1977). In normal subjects, there have been various reports concerning the neural basis of the processing of face perception using electroencephalography (EEG) recorded from the scalp (Srebro, 1985; Jeffreys, 1989; Renault et al., 1989; Sommer et al., 1991; Seeck and Grusser, 1992; Hertz et al., 1994; Begleiter et al., 1995; Botzel et al., 1995; George et al., 1996; Bentin et al., 1996; Schendan et al., 1998), from the cortical surface (Allison et al., 1994a,b) or from the intracerebral regions (Halgren et al., 1994a,b; Seeck et al., 1995, 1997), and using positron emission tomography (PET) (Sergent et al., 1994; Haxby et al., 1994, 1996; Kapur et al., 1995; Courtney et al., 1996, Dolan et al., 1996) and functional magnetic resonance imaging (fMRI) (Puce et al., 1995, 1996, 1997, 1998; Clark et

al., 1996; McCarthy et al., 1997; Birbaumer et al., 1998). As in the animal studies, the importance of the STS and IT, particularly the latter, was reported. Bilateral hemispheres were activated in most reports, but a large number of studies reported the dominance of the right hemisphere (e.g., Sergent et al., 1994).

Magnetoencephalography (MEG) has the theoretical advantages of localizing brain dipoles due to reduced effects caused by cerebrospinal fluid, skull and skin, and its excellent temporal resolution is much higher than those of fMRI and PET. Therefore, the detailed temporal processing of information can be identified only by MEG and EEG. To our knowledge, there are three reports on the mechanisms of face perception using MEG (Lu et al., 1991; Sams et al., 1997; Swithenby et al., 1998). Those investigators reported the components, whose latency was about 150-170 msec, generated in the occipitotemporal and the middle temporal locations (Lu et al., 1991), and inferior occipitotemporal cortex (Sams et al., 1997; Swithenby et al., 1998). Bilateral hemispheres were activated, but the right hemisphere was dominantly activated (Sams et al., 1997; Swithenby et al., 1998). However, multiple areas including the primary visual cortex may be activated in response to face stimuli, and their activities must be temporally overlapped. To explore this concept, we used spatio-temporal multiple dipole models for analyzing MEG, and recorded EEG simultaneously. In order to investigate the specific mechanisms for eyes perception, we used not only *face with opened eyes* but also *face with closed eyes*, and only *eyes*. The objective of this study was to determine the temporal and spatial information processes of face perception in humans by MEG and EEG.

4. Subjects and Methods

We studied twelve normal volunteers (3 females, 9 males) who ranged in age from 26 to 39 years (mean age, 31.5 years) with normal or corrected visual acuity. All subjects gave informed consent to participate in the experiment, which was first approved by the Ethical Committee at our Institute. No medication was given for sedation, and the subjects were awake during the studies.

MEG was measured with 37-channel biomagnetometer (Magnes, Biomagnetic Technologies Inc., San Diego, CA). The detection coils of the biomagnetometer were arranged in a uniformly distributed array in concentric circles over a spherically concave surface. Thus, all of the sensor coils were equally sensitive to weak magnetic signals from the brain. The device was 144 mm in diameter and its radius of curvature was 122 mm. The outer coils were 72.5^0 apart. Each coil was 20 mm in diameter, and the centers of the coils were 22 mm apart. Each coil was connected to a superconducting quantum interference device (SQUID).

The probe was centered at the occipito-temporal area in the left and right hemisphere in each subject, around the T5' (left temporal area, 2cm below the T5) and the T6' (right temporal area, 2cm below the T6) based on the International 10-20 System (Fig. 1). Both positions covered the primary visual cortex, and the left and right occipito-temporal area, respectively. Each hemisphere was recorded independently.

Electroencephalography (EEG) was also recorded. Exploring electrodes were placed at the Cz (vertex), T5' and T6' position of the International 10-20 System, and the reference electrode was placed on the chin. The amplitude of each recognizable component was measured from

the baseline.

The subjects lay on their back on a bed, setting their head on the probe and looked at the stimulus on the ceiling. Responses of both MEG and EEG were recorded with a 0.1-50 Hz bandpass filter, and digitized at a sampling rate of 1,024 Hz.

We used basically the same stimuli as those described in previous reports (Allison et al., 1994; Puce et al., 1995, 1996, 1997, 1998; Bentin et al., 1996; McCarthy et al., 1997), and changed slightly for use in the MEG studies (Fig. 2). Five different categories of stimuli, (1) *face with opened eyes*, (2) *face with closed eyes*, (3) *eyes*, (4) *scrambled face*, and (5) *hand*, were used. All figures consisted of digitally scanned black and white photos. Individuals without eyeglasses were used as the faces. The photographs for *face with opened eyes* and *face with closed eyes* were taken of the same individuals in the same clothes and against the same background, and all of them were unfamiliar to subjects. To control for luminance, *scrambled face* was derived from the same component images with features rearranged so that facial components could not be identified. Consequently, the spatial frequency of *scrambled face* was the same as that of the original *face* figure.

Each category of stimuli had 60 different pictures except for *hand* (30 pictures). *Eyes* were taken from the *faces* used in this study. Two patterns were used as the stimulus in Experiment 1 and 2, respectively. Only the background of the *eyes* stimulation was different between the two patterns, to investigate brain responses to *eyes* in detail. The background was *scrambled face* in pattern 1, and a simple gray background in pattern 2. Subjects were asked to count the *hand* stimuli silently and to declare the

number after each session, to avoid the attention effects producing the P300 component and so on.

The stimulus presentation was controlled by a personal computer (IBM). The stimuli were presented by a video projector (Balcodata 3100, Barco, Belgium) set outside of the magnetically shielded room (Vacuumschmerze GmbH, Germany). The crystal liquid shutter (LUMP6, Nippon Sheet Grass, Japan) was set in front of the video projector to enable the adjustment of the stimulus onset. Stimuli were projected on the ceiling using a mirror system. The distance between the eyes and the stimuli was 150 cm. Each stimulus was 15 cm wide and 16 cm high. All stimuli subtended a visual angle of 5.7 x 6.1 degrees. The stimuli were about 72.5 cd/m^2 in brightness at the viewing point, with a background about 5.0 cd/m^2. Each stimulus was presented for 250 msec, and the interstimulus interval was randomly changed from 1,800 to 2,300 msec. Subjects were asked to look at the center of each stimulus. Stimuli of each category were delivered in a pseudorandom order. One session involved 270 pictures (60 pictures for each category except for 30 for *hand*), and their responses to two sets (540 pictures in total, 120 of each category except for 60 for *hand*) were averaged in one experiment. To avoid habituation and drowsiness, a session was divided into 6 sets, 45 stimuli in each, and the subjects had a short rest after each session, which took less than 60 min to complete.

The analysis window was 1 sec after the stimuli onset, and a pre-stimulus period (300 msec) was used as the DC baseline. We recorded MEG and EEG simultaneously at least twice on different days in each subject to confirm reproducibility.

The statistical analysis was done using the paired t-test, and $P<0.05$ was considered to be significant.

A spherical model (Sarvas, 1987) was fitted to the digitized shape of the head of each subject, and the location, orientation and amplitude of a best-fitted equivalent current dipole (ECD) were estimated at each time point every 1.95 msec. The origin of the head-based coordinate system was the midpoint between the preauricular points. The x-axis indicated the coronal plane with a positive value toward the anterior direction, the y-axis indicated the mid-sagittal plane with positive values toward the left preauricular point, and the z-axis lay on the transverse plane perpendicular to the x-y line with a positive value toward the upper side. The correlation between the recorded measurements and the values expected from the ECD estimate was calculated. This was the estimating value, in other words, of how closely the measured values corresponded to the theoretical field generated by the model and the observed field.

We also used a brain electric source analysis (BESA) (Scherg, 1995) software package (NeuroScan, Inc., McLean, VA) for the computation of theoretical source generators in a 3-layer spherical head model. The BESA was modified for the use of our 37-channel biomagnetometer. This method allows the spatio-temporal modeling of multiple simultaneous sources over defined intervals. The location and orientation of the dipoles were calculated by an iterative least-squares fit. The residual variance (%RV) indicated the percentage of data which could not be explained by the model. The goodness of fit (GOF) was expressed in % as (100 - %RV). Since the signal-to-noise (S/N) ratio of the MEG recording was much smaller than that of the EEG recording, the GOF of

the MEG was smaller than that of the EEG. GOF values larger than 85% are considered to indicate a good multiple dipole models.

Magnetic resonance imaging (MRI) was performed with a Magnex 150XT 1.5 T system (Shimadzu, Kyoto, Japan). The T1- weighted coronal, axial and sagittal images with a contiguous 1.5 mm slice thickness were used for overlays with the ECD sources detected by MEG. The same anatomical landmarks used to create the MEG head-based 3D coordinate system (the nasion and bilateral preauricular points) were visualized in the MRI images by affixing to these points high-contrast cod liver oil capsules (3 mm diameter), the short relaxation time of which provides a high-intensity signal in T1-weighted images. The common MEG and MRI anatomical landmarks allowed easy transformation of the head-based three-dimensional (3D) coordinate system (nasion and entrance of the auditory meatus of the left and right ear) used by the MEG source analysis to the MRI. The MEG source locations were converted into pixels and slice values using the MRI transformation matrix and inserted onto the corresponding MRI.

5. Results

(1) First experiment

We used the pattern 1 (*eyes* with the background of the *scrambled face*) (Fig. 2) in the first experiment.

MEG recorded from the right hemisphere and EEG waveforms in subjects 1 and 2 are shown in Figs. 3 and 4. Two components (termed 1M and 2M, the first and second magnetic response, respectively) were identified in the both cerebral hemispheres bilaterally. The 1M, whose peak latency is 131.8±13.4 msec (mean±standard deviation) to the *face with opened eyes*, was recorded to all kinds of this stimulus in all 12 subjects. Since the 2M was clearly identified in 10 of the 12 subjects from the right hemisphere (179.1±13.1 msec), we described the results of these 10 subjects. The 2M appeared to be independent of the 1M in 5 subjects as found in subject 1 (Fig. 3), and to overlap on the descending slope of the 1M in the other 5 subjects as found in subject 2 (Fig. 4), depending on the latency difference between the 1M and 2M (47.3±15.2 msec). The 2M was clearly observed in the response to the stimulation of *face with opened eyes* or *closed eyes* in all 10 subjects but the 2M was not clearly identified to the *eyes* in 7 subjects (Fig. 3). Although the 2M to *eyes* was found in only 3 subjects, it was small in amplitude (Fig. 4). There was no clear difference of latencies and amplitudes of both the 1M and 2M between *face with opened eyes* and *face with closed eyes* (Table 1, Figs. 3 and 4). The 2M was not seen in response to *scrambled face* in any subjects (Figs. 3 and 4). It seemed that the 2M-like component was found to *hand* stimulation in 3 subjects (Fig. 3), but their isocontour map and dipole location were definitely different from the 2M to *face* stimulation

(Fig. 5). Following the 2M component, some activities were identified only to *hand* stimulation due to the effects of attention (target of the oddball paradigm) (Fig. 4), but we did not analyze them in the present study.

Clear phase-reversed EEG components, negative at the T5' and T6' and positive at the Cz, were identified only for *faces with opened* and *closed eyes* in all subjects (Figs. 3 and 4) and for *eyes* in only 3 subjects (Fig. 4). In the responses to *face with opened eyes* stimulation, the latency at the T5' and T6' did not show significant difference from each other. The latencies of the positive component recorded at the Cz were significantly longer than those of the negative component recorded at the T5' and T6' ($P<0.05$), and the 2M ($P<0.01$), respectively, and those at the T5' and T6' were also longer than the 2M ($P<0.05$). These results indicated that the peak latency of the 2M was the shortest and then became significantly longer in the EEG components recorded at the T5' and T6', and the Cz, in that order (Table 1). Components to *face with closed eyes* showed similar results. To *face with opened eyes* stimulation, the amplitude of the negative component at the T6' (4.5 ± 4.3 μV) was significantly larger than that at the T5' (2.4 ± 1.8μV) ($P<0.05$) (Table 1). EEG waveforms in response to *hand* stimulation were much different from those to *face* stimulation. This finding suggested that the generating mechanisms of components in the response to *hand* stimulation were different from those for *face* stimulation.

When the probe was placed at the left hemisphere, the 1M was also recorded to all kinds of stimuli in all subjects (Fig. 6). However, the 2M was clearly identified only in 5 and 2 of the 10 subjects in response to *face*

and *eyes* stimulation, respectively. There was no clear difference of latencies and amplitudes between *face with opened eyes* and *face with closed eyes*, as found in the right hemisphere.

We first analyzed the data using a single ECD analysis. The correlation value of the ECD of the 1M was not reliably high. This was probably due to the fact that the bilateral visual cortices were activated. The ECD of the 2M to *faces* was estimated with a high correlation value at the inferior temporal cortex, probably in the fusiform gyrus (Fig. 7). However, a reliable ECD with a high correlation was estimated in only 2 subjects (subjects 1 and 4). In other 8 subjects, for example in subject 2, the isocontour maps at the peak of the 2M to *face with opened eyes* indicated multiple generators (Fig. 8), and the ECD was estimated in the deep white matter, with a low correlation value. This finding suggested that the activities in the primary visual cortices continued and affected the magnetic fields generated by the activities in the temporal area. Therefore, a multiple source model is necessary for elucidating the generator mechanisms of the 2M. The ECD of the 2M-like components to *hand* stimulation, for example in subject 1, was estimated in the strange site (deep white matter) with a low correlation value.

We then analyzed the results using the BESA. We will first describe the general strategy of our analysis method. Since the primary visual cortex in the bilateral hemispheres had to be activated to the visual stimuli used in the present study, as in response to various kinds of visual stimulation reported previously (Nakamura et al., 1997; Koyama et al., 1998; Brecelj et al., 1998), sources 1 and 2 were located in the occipital areas. When the right hemisphere was examined, source 1 and 2 was located in the right

and left hemisphere, respectively, and when the left hemisphere was examined, source 1 and 2 was located in the left and right hemisphere, respectively. Studies in monkeys and humans using fMRI, PET and MEG (see Introduction) showed that the posterior temporal area, the IT area around the fusiform gyrus and the STS were activated in response to face stimuli. Therefore, we placed source 3 in the posterior temporal area. When the right hemisphere was examined, source 3 was located in the right temporal area, and when the left hemisphere was examined, source 3 was located in the left temporal area. Additional sources were also placed, if necessary.

Figures 9 and 10 show the results of the BESA in subject 1. When the probe was located in the right hemisphere (Fig. 9), the waveforms of sources 1 and 2, being located around the primary visual cortices, seemed to correspond to the 1M component in terms of latency. Source 3 was estimated to be in the right IT area, around the fusiform gyrus. The waveform of source 3 seemed to correspond to the 2M component and was clearly independent of sources 1 and 2 in terms of latency. Source 3 was absent or very small to *eyes* and *scrambled face* stimulation. To *face with opened eyes* stimulation, the GOF was 47.1 % when only sources 1 and 2 were used. However, the GOF was much increased to 89.3 % when source 3 was added, thus this 3-dipole model was considered to be the most appropriate model. Actually, source 3 was estimated to be in the IT area in not only subject 1 but also in all other subjects. No good model including this 3-dipole model was made for *hand* stimulation. When the other source was located around the right STS, its waveform was very small in amplitude and did not contribute to the increase in GOF in any subjects.

There was no other source which contributed to making a better model. When the probe was located in the left hemisphere (Fig. 10), the results of the BESA were generally consistent with the results recorded from the right hemisphere. The source 3 located in the left IT was larger in amplitude than that in the right hemisphere (Fig. 9). However, subject 1 was an exceptional subject, since the source 3 in the left hemisphere was smaller than or almost the same as that in the right hemisphere in the other 4 subjects who showed a clear 2M in the left hemisphere.

As already described, the 1M and 2M appeared to overlap, and the single ECD model could not be applied in subject 2. Figure 11 shows the results of the BESA for the right hemisphere. Sources 1 and 2, being located in the primary visual cortex in the bilateral hemispheres, seemed to correspond to the 1M component and showed a symmetrical location. Source 3, being estimated in the right IT area, showed large waveform. Its latency was slightly but definitely longer than those of sources 1 and 2, and temporally overlapped with them. Source 3 was absent or very small to *scrambled face* stimulation. To *face with opened eyes* stimulation, the GOF was 49.1 % when only sources 1 and 2 were used. However, the GOF was much increased to 93.2 % when source 3 was added, and this 3-dipole model was thus considered to be the most appropriate model. No good model including this 3-dipole model was made for *hand* stimulation. When the other source located around the right STS was added, its waveform was very small in amplitude and did not contribute to the increase in GOF. There was no other source which contributed to make the better model. When the probe was located in the left hemisphere, sources 1 and 2 were clearly identified, but other sources were absent or

small in amplitude. These results in subject 2 suggested that after the activation of the primary visual cortex in the bilateral hemispheres, the right IT area was activated in response to *faces* and *eyes* after a short period, and its activity was temporally overlapped with activities in the primary visual cortex.

The important findings identified in the first experiment are summarized as follows;

(1) The IT areas around the fusiform gyrus are activated in response to *face* and *eyes* stimulation. This area did not respond to *scrambled face* nor *hand* stimulation. There was no significant difference of ECD location among *face with opened eyes* and *closed eyes*, and *eyes*. Activities in the STS were not clearly identified.

(2) The period between the peaks of the 1M and 2M, which probably indicated the period of information transfer from the primary visual cortex to the IT area, was about 48 msec, but the inter-individual difference was large.

The IT in the bilateral hemispheres were activated in about half of the subjects, but only the right IT was activated in the other half. The amplitudes of the EEG components recorded from the right hemisphere were significantly larger than those from the left hemisphere.

(2) Second experiment

The biggest problem of the first experiment was that the 2M to the *eyes* stimulation was not clearly recorded. We considered that the reason for this problem might be due to the inappropriate background, and then recorded MEG by changing various kinds of background for the *eyes*

stimulation in the preliminary study for the second experiment. Then we finally found that the simple gray was the good background for the *eyes* stimulation (see Fig. 2). We examined the same study as the first experiment except for changing the *eyes* stimulation in the second experiment.

Since we changed only the background of the *eyes* stimulation in the second experiment, we focused on the results of the responses to *eyes*. All 10 subjects showed clear 2M to *eyes* stimulation (Fig. 12). Table 2 shows the latencies and amplitudes of both MEG and EEG components to *face with opened eyes* and *closed eyes*, and *eyes* in the second experiment, and Table 3 shows the factors which showed the statistical significance between *eyes* stimulation and *face* stimulation. The most notable finding was that the latency of the 1M (145.6±17.5msec) and 2M (208.2± 23.0msec) to *eyes* was significantly longer than those to *face with opened* and *closed eyes* ($P<0.01$) (Tables 2 and 3, Fig. 12). From the left hemisphere, the 2M to *eyes* was recorded in all 5 subjects who showed clear 2M to *face with opened eyes* and *closed eyes* stimulation. The latency of the 2M to *eyes* was significantly longer ($P<0.01$) than those to *face* stimulation, as in the right hemisphere.

In the EEG recording, the responses to *eyes* were significantly longer than those to *faces with opened eyes* and *faces with closed eyes* ($P<0.01$) (Tables 2 and 3, Fig. 12). To *eyes* stimulation, the amplitude of the negative component at the T6' (4.4±4.4μV) was significantly larger than that at the T5' (2.3±1.7μV) ($P<0.05$) (Tables 2 and 3). This significant difference was also identified to *face with opened eyes* and *face with closed eyes*. The amplitude of the EEG components for *eyes* were larger

than those for *face* stimulation, but there was no significant difference.

We first examined the data using a single ECD analysis. Isocontour maps of *eyes* stimulation indicated multiple (at least two) generators in 8 subjects (Fig. 13). Therefore, the ECD of the 2M component to *eyes* was estimated to have a high correlation in only 2 of the 10 subjects. The ECD location to *eyes* stimulation was very close to that to *face* stimulation, around the fusiform gyrus of the right hemisphere (see Fig. 7).

The BESA results clearly indicated that the 3-dipole model (sources 1-3) was the most appropriate for *eyes* stimulation (Fig. 14), as in the first experiment (Figs. 9-11). The location of source 3 in the IT area to *eyes* stimulation showed no clear difference from those to *face with opened eyes* and *closed eyes* stimulation. The latency of source 3 to *eyes* stimulation was longer than those to *face* stimulation. Source 3 was absent or very small to *scrambled face* stimulation. To *face with opened eyes* stimulation, the GOF was 43.3 % when only sources 1 and 2 were used. However, the GOF was much increased to 86.8 % when source 3 was added. Source 3 to *scrambled face* was small in amplitude. No good model including this 3-dipole model was made for *hand* stimulation. When the other source located around the right STS was added, its waveform was very small in amplitude and did not contribute to the increase in GOF. There was no other source which contributed to make the better model, and this 3-dipole model was thus considered to be the most appropriate model. When the probe was located in the left hemisphere, results were very similar to those recorded from the right hemisphere.

6. Discussion

In the present study, two MEG components, 1M and 2M, were clearly identified. The 2M component was consistent with the previously-reported components, which were 140-170 msec in latency and generated in the inferior occipitotemporal cortex (Lu et al., 1991; Sams et al., 1997; Swithenby et al., 1998). Since the activities of the 1M and 2M were temporally overlapped, it was very difficult or impossible to estimate the generator sources by using a single-dipole model. This difficult problem was solved by using a spatio-temporal multiple dipole model, BESA. The 1M component was considered to be generated by sources in the bilateral primary visual cortices. Since the 1M was recorded in the responses to all kinds of stimulation which were shown at the center of the visual field, this result seems quite natural. The inter-peak latency between the 1M and 2M was 48 msec on average, but the interindividual difference was large, ranging from 27.4 to 71.5 msec. This finding indicates that about 48 msec is required for signals to transfer from the primary visual cortex to the visual association cortex being specific to face perception, but its speed depends on the subject. This is the first study to clarify the temporal relationship of activities between the primary visual cortex and the face-specific area (fusiform gyrus).

The fusiform gyrus is considered to be the most important area for face perception in humans. Allison et al. (1994a,b), using electrodes chronically implanted on the surface of extrastriate visual cortex in patients with drug-resistant epilepsy, found a negative potential, N200, evoked only by faces but not by the other categories of stimuli. The N200 was recorded only from small regions of the left and right fusiform

and inferior temporal gyri. Halgren et al. (1994a,b) recorded face-specific activities in patients with depth electrodes implanted for the direction of surgical treatment of drug-resistant epilepsy. They found the N130-P180-N240 components focal and polarity-inverting in the basal occipitotemporal cortex (fusiform gyus). The P180 component, probably corresponding to the N200 recorded from the cortical surface (Allison et al., 1994a,b), was evoked only by faces. PET (Sergent et al., 1994; Haxby et al., 1994, 1996; Kapur et al., 1995; Courtney et al., 1996, Dolan et al., 1996), fMRI (Puce et al., 1995, 1996, 1997, 1998; Clark et al., 1996; McCarthy et al., 1997) and MEG studies (Lu et al., 1991; Sams et al., 1997; Swithenby et al., 1998) also revealed the importance of the fusiform gyrus for face perception. For example, groups at Yale University (Puce et al., 1995, 1996, 1997, 1998; McCarthy et al., 1997) analyzed face perception using various kinds of stimulation and paradigms, mainly by fMRI. Using unfamiliar and scrambled faces, they found that the face stimuli activated portions of the midfusiform and inferior temporal gyri, including adjacent cortex within occipitotemporal sulci (Puce et al., 1995), and confirmed the good correspondence between electrophysiological and fMRI findings (Puce et al., 1997). They found that the right hemisphere was more activated to face stimulation, but the left hemisphere was more activated to the letterstrings (Puce et al., 1996). They confirmed that the face-specific processing takes place in the right fusifom gyrus (McCarthy et al., 1997). Our results are consistent with these electrophysiological and imaging studies. MEG is a very appropriate method to detect dipoles in the fusiform gyrus, since its direction is considered to be mainly tangential. In addition, MEG is very useful to detect the detailed

temporal processing of information on the order of msec. This is the greatest advantage of MEG compared with fMRI and PET.

Activities in the STS (sources 4 and 6) were small or absent in the present study. Studies of face perception using microelectrodes in monkeys (Bruce et al., 1981; Perrett et al., 1982, 1987, 1991, 1992; Rolls, 1984; Baylis et al., 1985; Hasselmo et al., 1989; Yamane et al., 1988; Desimone, 1991; Oram and Perrett, 1992; Hietanen et al., 1992; Pare et al., 1995), showed the importance of the STS area for face perception in addition to the IT area. We tried to find the activities in the bilateral STS areas, but they were small or absent. Two main possibilities for this are considered. The first possibility is that the STS area is not activated so much for face perception in humans, unlike monkeys. Studies by fMRI in humans did not find significant activities in STS (McCarthy et al., 1997). The other possibility is that the dipoles generated in the STS were mainly radially-oriented, and thus difficult to detect by MEG.

The 2M component was clearly found in all 10 of the present subjects from the right hemisphere, but in only 5 subjects from the left hemisphere. The amplitude of the EEG component at the T6' was significantly larger than that at the T5'. The dominance of the right hemisphere for face perception in humans was reported in studies using EEG (Bentin et al., 1996), fMRI (Puce et al., 1996; McCarthy et al., 1997) and MEG (Sams et al., 1996; Swithenby et al., 1998), but PET studies (Sergent et al., 1994; Haxby et al., 1994, 1996; Kapur et al., 1995; Courtney et al., 1996, Dolan et al., 1996) did not stress the interhemispheric difference. In clinical studies, prosopagnosia is usually produced by lesions in the bilateral hemispheres (Meadows, 1974; Damasio et al., 1982; Damasio, 1985), but

its symptoms can also be produced by damage to the right hemisphere alone (Meadows, 1974; Whiteley and Warrington, 1977). Meadows (1974) reported that patients with prosopagnosia nearly always have a left-upper-quadrant visual field defect, correlated with a right occipitotemporal lesion. We, therefore, suspected that the right hemisphere is dominant for face perception in humans, but that interindividual differences exist.

Eyes are considered to be the most impressive part of the face, and we analyzed the effects of eyes using *face with opened eyes*, *face with closed eyes*, and only *eyes* with different backgrounds. There was no significant difference of waveforms in terms of latency and amplitude between the *face with opened eyes* and *face with closed eyes* stimuli. It is difficult to conclude the reason for this finding, but it may indicate that neuronal activities in the fusiform gyrus for the face perception are not changed with the presence of eyes. That is, whether it is a face or not is the most important factor for the quick perception, about 150-170 msec after the stimulus, rather than the understanding of the face in detail. No clear 2M component was found to *eyes* on *scrambled face* in the first experiment, but it was clearly identified by changing the background to gray in the second experiment. This finding indicates that one of the most important factors for eyes (probably also face) perception is how they are clearly and/or easily identified. An interesting finding of the second experiment was a significantly longer latency of the 1M, 2M and 1M-2M to *eyes* stimulation than *face* stimulation, although the ECD location of the 2M to *eyes* was almost the same as that for *face* stimulation. We suspect that eyes and faces are recognized in the same area, but it takes a longer time to recognize smaller and/or less remarkable part such as *eyes*. Not only the

2M and 1M-2M but also the 1M latency was prolonged to *eyes* stimulation. Such a delay may take place in both the primary visual cortex and the IT area. Bentin et al. (1996) recently reviewed face-specific scalp-recorded EEG components in detail. They found that *eyes* elicited an N170 from the temporal electrodes which was significantly larger than that elicited by *face*. They considered that N170 may reflect the activation of an eye-sensitive region of the cortex, the mid-fusiform region anterior to the region of the inferior temporal region of the fusiform gyrus that responds to *face* stimulation eliciting the N200 (Allison et al., 1994a,b). Although we used the similar stimuli to those used by Bentin et al. (1996), some methodological differences might account for the difference of results.

In EEG recordings from the scalp, a face-specific positive component maximal around the vertex has been reported (Srebro, 1985; Jeffreys, 1989; Sommer et al., 1991; Seeck and Grusser, 1992; Hertz et al., 1994; Begleiter et al., 1995; Botzel et al., 1995; George et al., 1996; Bentin et al., 1996; Schendan et al., 1998), and we found the same component in the responses to *faces* and *eyes*. Its latency was slightly but significantly longer than those of the negative component recorded at the T5' and T6'. The latencies of the components recorded at the T5' and T6' were also slightly but significantly longer than the 2M of MEG. Therefore, we speculate that the EEG components, particularly that recorded at the Cz, may include responses to other visual factors, although face-specific responses are the major responses. MEG, rather than EEG, may be able to detect pure face-perception-specific cortical activities.

No significant 2M component was identified in the responses to the *scrambled face* stimuli. This finding supports our hypothesis that the 2M

is a face-specific response. Responses such as the 2M-like component were found to *hand* stimulation, although this was different from the face-specific component. We suspect that such responses to *hand* stimulation were a mixture of the brain responses to see the "object" and the event-related cognitive responses, because the subjects were counting the number of *hand* stimulation.

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9. Tables

Table 1 : Latency and amplitude of MEG and EEG components in the response to (1) *face with opened eyes* and (2) *face with closed eyes* in the first experiment."1M-2M" means the interpeak latency between 1M and 2M. The amplitudes of 1M and 2M were not calculated, because they partly overlapped.

(1) *Face with opened eyes*

	1M	2M	1M-2M	Cz	T5	T6
Peak latency (msec)	131.8±13.4	179.1±13.1	47.3±15.2	195.7±18.7	187.6±13.3	189.2±12.4
Amplitude (μV)	-	-	-	5.0±1.6	2.4±1.8	4.5±4.3

Latency : Cz, T5 & T6>2M($p<0.01$), Cz>T5 & T6 ($p<0.05$), Amplitude : T6>T5($p<0.05$)

(2) *Face with closed eyes*

	1M	2M	1M-2M	Cz	T5	T6
Peak latency (msec)	130.0±14.4	178.1±12.4	48.1±15.0	198.7±19.6	187.2±13.1	189.6±13.0
Amplitude (μV)	-	-	-	5.0±1.7	1.8±1.5	4.6±4.2

Latency : Cz &T6 >2M($p<0.01$), T5 >2M ($p<0.05$) , Cz>T5 & T6 ($p<0.05$), Amplitude :T6>T5($p<0.05$)

Table 2 : Latency and amplitude of MEG and EEG components in the response to (1) *face with opened eyes*, (2) *face with closed eyes* and (3) *eyes* in the second experiment.
"1M-2M" means the interpeak latency between 1M and 2M. The amplitudes of 1M and 2M were not calculated, because they partly overlapped. Note that the results in the first experiment (see text) were almost the same but not completely the same as those in the second experiment.

(1) *Face with opened eyes*

	1M	2M	1M-2M	Cz	T5	T6
Peak latency (msec)	132.2±15.2	180.0±13.9	47.8±15.7	195.9±18.9	187.9±13.5	189.4±12.5
Amplitude (μV)	-	-	-	5.1±1.7	2.3±1.7	4.4±4.4

Latency : Cz, T5 & T6>2M($p<0.01$), Cz>T5 & T6 ($p<0.05$), Amplitude : T6>T5($p<0.05$)

(2) *Face with closed eyes*

	1M	2M	1M-2M	Cz	T5	T6
Peak latency (msec)	130.3±14.5	178.6±12.2	48.2±15.1	199.7±19.9	187.3±13.2	189.8±13.2
Amplitude (μV)	-	-	-	5.1±1.8	1.8±1.6	4.7±4.5

Latency : Cz &T6 >2M($p<0.01$), T5 >2M ($p<0.05$) , Cz>T5 & T6 ($p<0.05$), Amplitude :T6>T5($p<0.05$)

(3) *Eyes*

	1M	2M	1M-2M	Cz	T5	T6
Peak latency (msec)	145.6±17.5	208.2±23.0	62.6±20.6	219.6±20.6	215.2±23.4	213.2±24.3
Amplitude (μV)	-	-	-	5.7±2.3	2.8±1.5	5.4±5.3

Latency : Cz>2M ($p<0.05$, Amplitude : T6>T5($p<0.05$)

Table 3: Factors showing significant differences between *face* and *eyes* stimulation in the second experiment.

Between *face with opened eyes* and *eyes*
1M latency (P<0.01), 2M latency (P<0.01), 1M-2M (P<0.01)
Cz latency (P<0.001), T5' latency (P<0.01), T6' latency (P<0.01)
Between *face with closed eyes* and *eyes*
1M latency (P<0.01), 2M latency (P<0.001), 1M-2M (P<0.01)
Cz latency (P<0.001), T5' latency (P<0.01), T6' latency (P<0.01)

10. Figure Legends

Fig. 1: Placement of the MEG device. This figure shows the device placement when the right hemisphere was studied. The center of the device was placed around the T6' position of the international 10-20 System. The device was placed in the symmetrical position when the left hemisphere was studied.

Fig. 2: The five categories of visual stimuli, (1) *face with opened eyes*, (2) *face with closed eyes*, (3) *eyes*, (4) *scrambled face* and (5) *hand*. *Eyes 1* (background: *scrambled face*) and *eyes 2* (background: simple gray) were used in the first and second experiment, respectively.

Fig. 3: MEG waveforms of subject 1 in response to the five categories of stimuli in the first experiment. MEG waveforms recorded from 37 channels from the right hemisphere are superimposed. Two components, 1M and 2M, were identified. The 1M was recorded to all stimuli, but the 2M was not recorded to *eyes*, *scrambled face* nor *hand*. The 2M-like component indicated by arrowhead was found to *hand* stimuli. The face-specific EEG components were also clearly identified to *face with opened eyes* and *face with closed eyes*. The EEG component at the T6' was larger than that at the T5'.

Fig. 4: MEG and EEG waveforms of subject 2 in response to the five different categories of stimuli in the first experiment in subject 2. MEG waveforms recorded from 37 channels from the right hemisphere are superimposed. Two components, 1M and 2M, were identified, but the

2M appeared to be overlapped on the descending slope of the 1M. The 1M was recorded to all stimuli, but the 2M was clearly recorded only to *face with opened eyes* and *face with closed eyes* stimulation. The 2M to *eyes* stimuli was small in amplitude. The EEG component at the T6' was larger than that at the T5', and the peak latency of the component recorded at the Cz was clearly longer than those at the T5' and T6', and the 2M peak for *face with opened eyes* and *face with closed eyes* stimulation. Some EEG components were recorded to *hand* stimulation, but that at T5' was larger than that at T6'. This finding was different from results to *face with opened eyes* and *face with closed eyes* stimulation.

Fig. 5: Isocontour maps of the 2M to *face with opened eyes*, *scrambled face* and *hand*, recorded from the right hemisphere in subject 1. Waveforms of *face with opened eyes* and *hand* stimuli were similar (Fig. 3), but their maps were quite different from each other. This finding indicated a difference of their generating mechanisms. Map of *scrambled face* stimuli indicated no meaningful component at that period. The contour step was 20 fT. The dotted lines and thin lines indicate the ingoing and outgoing flux, respectively, and the thick line indicates the zero-point line.

Fig. 6: MEG waveforms of subject 1 in response to the five categories of stimuli recorded from the left hemisphere in the first experiment. The findings were fundamentally similar to those recorded from the right hemisphere (Fig. 3).

Fig. 7: The ECD of the 2M to *face with opened eyes* recorded from the

right hemisphere was overlapped on the 2-dimensional (a) and 3-dimensional (b) MRI in subject 1. Cerebellum was removed to show the inferior temporal cortex clearly in 3-dimensional MRI (b). One ECD at the 2M peak was shown in 2-dimensional MRI(a), and ten ECDs during the 4.9 msec before and 3.9 msec after the 2M peak are plotted in 3-dimensional MRI (b). The ECDs were located in the fusiform gyrus in the right hemisphere.

Fig. 8: Isocontour maps of the 2M to *face with opened eyes* and *scrambled face* recorded from the right hemisphere in subject 2. They were complicated but map to *face with opened eyes* showed at least 2 dipoles. The contour step was 20 fT. The dotted lines and thin lines indicate the ingoing and outgoing flux, respectively, and the thick line indicates the zero-point line.

Fig. 9: Three-dipole model using BESA for responses to *face with opened eyes*, *face with closed eyes*, *eyes*, and *scrambled face*, recorded from the right hemisphere in subject 1. Sources 1 and 2 were located in the right and left primary visual cortex, respectively. Source 3 was located in the inferior temporal cortex, around the fusiform gyrus. Sources 1 and 2 corresponded to the 1M, and source 3 to the 2M. Waveform of source 3 was not clearly identified to *eyes* and *scrambled face*. This 3-dipole model was considered to be the most appropriate model. There was no other source which contributed to making a better model.

Fig. 10: Three-dipole model using BESA for responses to *face with*

opened eyes, *face with closed eyes*, *eyes*, and *scrambled face*, recorded from the left hemisphere in subject 1. Sources 1 and 2 were located in the left and right primary visual cortex, respectively. Notice that source 1 was located in the left hemisphere when the left hemisphere was examined. Source 3 was located in the left inferior temporal cortex, around the fusiform gyrus. The findings were fundamentally similar to those recorded from the right hemisphere (see Fig. 9).

Fig. 11: Three-dipole model using a BESA for responses to *face with opened eyes*, *face with closed eyes*, *eyes*, and *scrambled face*, recorded from the right hemisphere in subject 2. Since the 2M appeared to overlap on the 1M in this subject, a single ECD analysis was not applicable. Sources 1 and 2 were located in the right and left primary visual cortex, respectively. Source 3 was located in the inferior temporal cortex, around the fusiform gyrus. Sources 1 and 2 corresponded to the 1M, and source 3 to the 2M. Waveform of source 3 was not clearly identified to *eyes* and *scrambled face*. This 3-dipole model was considered to be the most appropriate model. There was no other source which contributed to a better model.

Fig. 12: MEG and EEG waveforms of subject 3 in response to the five categories of stimuli, recorded from the right hemisphere in the second experiment. MEG waveforms recorded from 37 channels are superimposed. Two components, 1M and 2M, were identified. The 1M was recorded to all stimuli, but the 2M was not recorded to *scrambled face* or *hand*. The 2M and EEG components to *eyes* which are indicated by

arrowheads were clearly longer in latency than those to *face*. The EEG components recorded at the T6' were larger than those at the T5' to *face* and *eyes* stimulation. The latency at the Cz were longer than that at T5' and T6' to *face* stimulation, but this was exceptional finding. The EEG component recorded at the Cz to *hand* stimulation was absent. This finding was much different from results to *face* and *eyes* stimulation.

Fig. 13: Isocontour maps of the 2M to *face with opened eyes* and *eyes* recorded from the right hemisphere in subject 3. They were very similar from each other, although the peak latencies were different. Both are complicated and showed at least 2 dipoles. The contour step was 20 fT. The dotted lines and thin lines indicate the ingoing and outgoing flux, respectively, and the thick line indicates the zero-point line.

Fig. 14: Three-dipole model using a BESA for the responses to *face with opened eyes*, *face with closed eyes*, *eyes*, and *scrambled face*, recorded from the right hemisphere in the second experiment in subject 3. Sources 1 and 2 were located in the right and left primary visual cortex, respectively. Source 3 was located in the inferior temporal cortex, around the fusiform gyrus. No good model was made to *hand* stimuli by this 3-dipole model. Sources 1 and 2 corresponded to the 1M, and source 3 to the 2M. Source 3 to *eyes* stimulation was clearly longer in latency than those to the *face* stimulation. Waveform of source 3 was not clearly identified to *scrambled face*. This 3-dipole model was considered to be the most appropriate model. There was no other source which contributed to a better model.

Fig.1

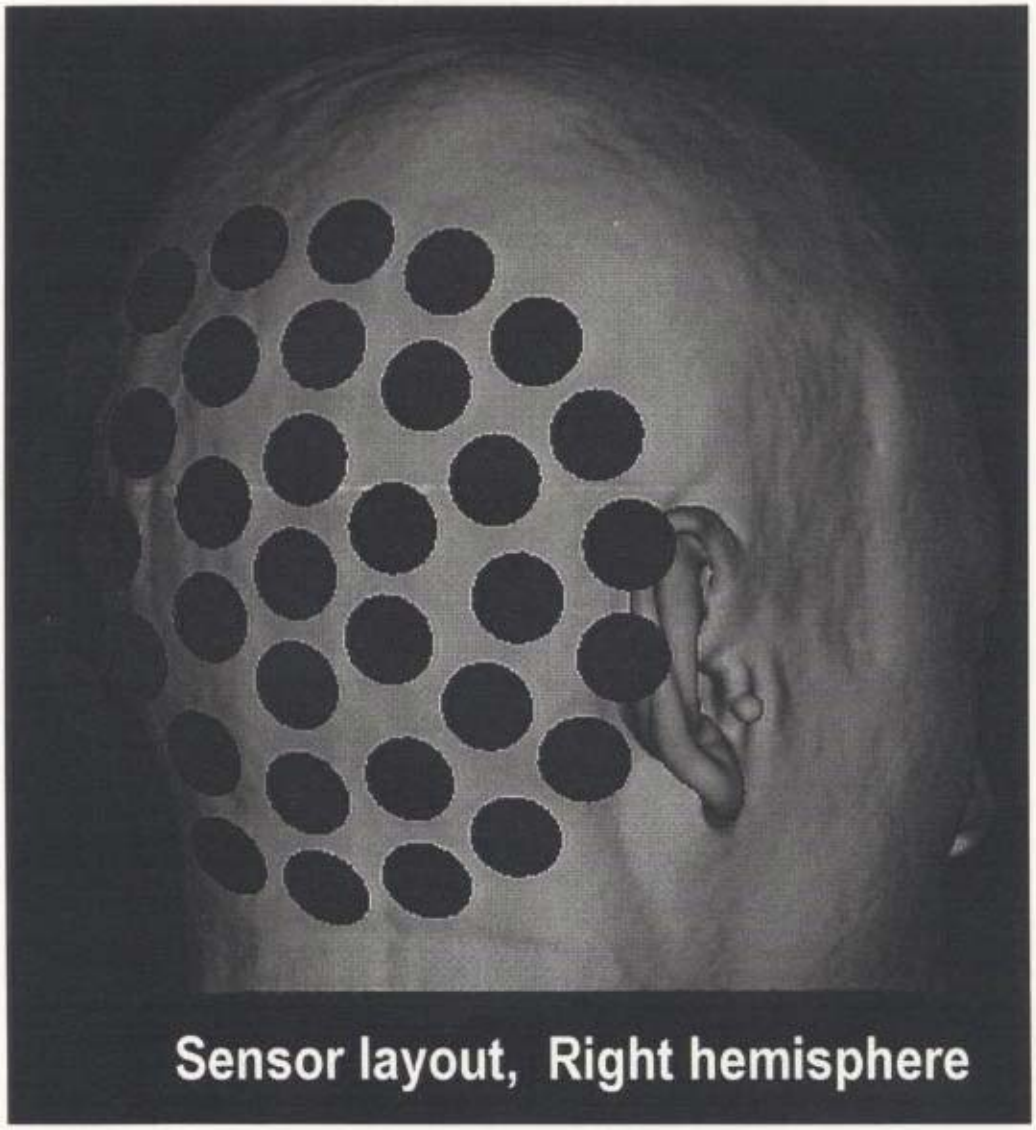


Fig.2

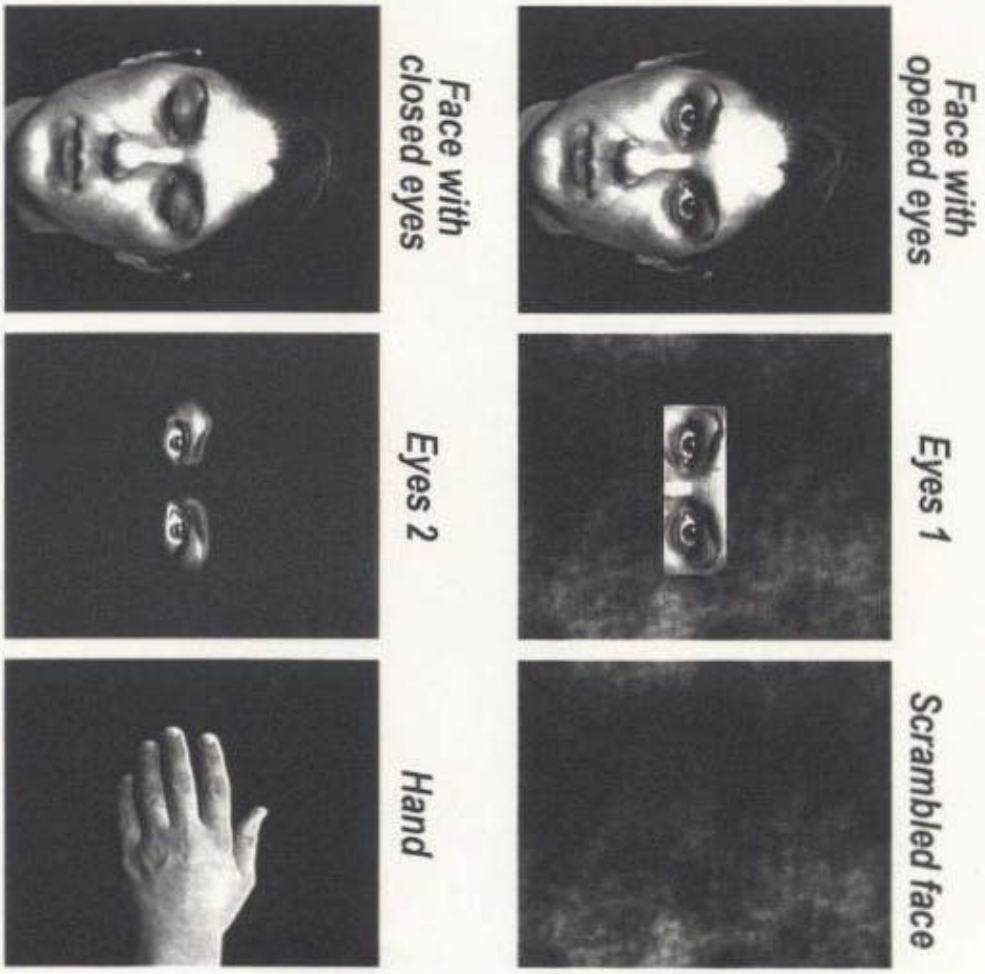

Face with opened eyes
Eyes 1
Scrambled face
Face with closed eyes
Eyes 2
Hand

Fig.3

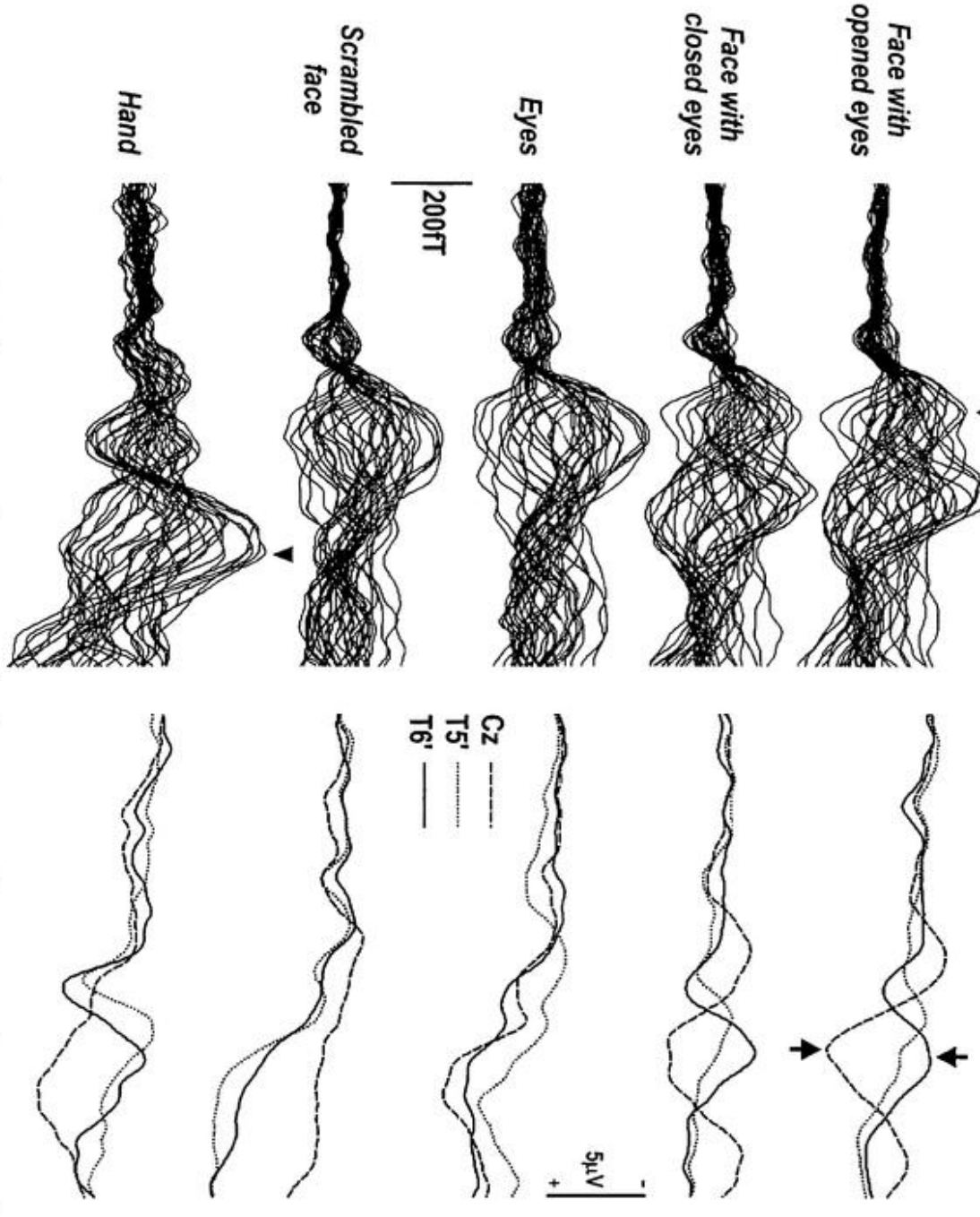

Subject 1 Right hemisphere
First experiment
1M
2M
Face with opened eyes
Face with closed eyes
Eyes
Scrambled face
Hand
200fT
Cz
T5'
T6'
5μV
0
100
200
300
msec

Fig.4

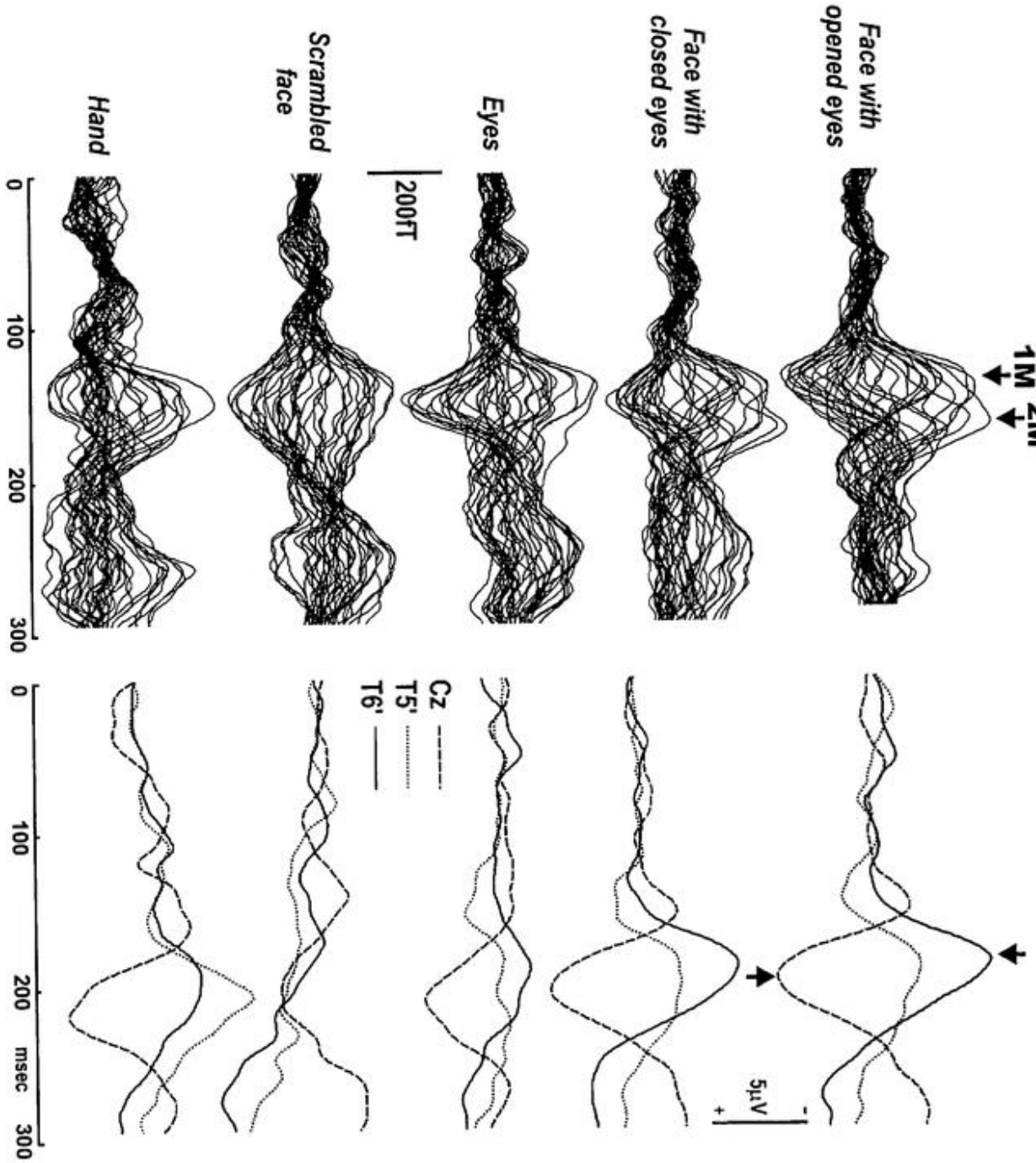

Subject 2 Right hemisphere
First experiment
1M
2M
Face with opened eyes
Face with closed eyes
Eyes
Scrambled face
Hand
200fT
5μV
Cz
T5'
T6'
0
100
200
300
msec

Fig.5

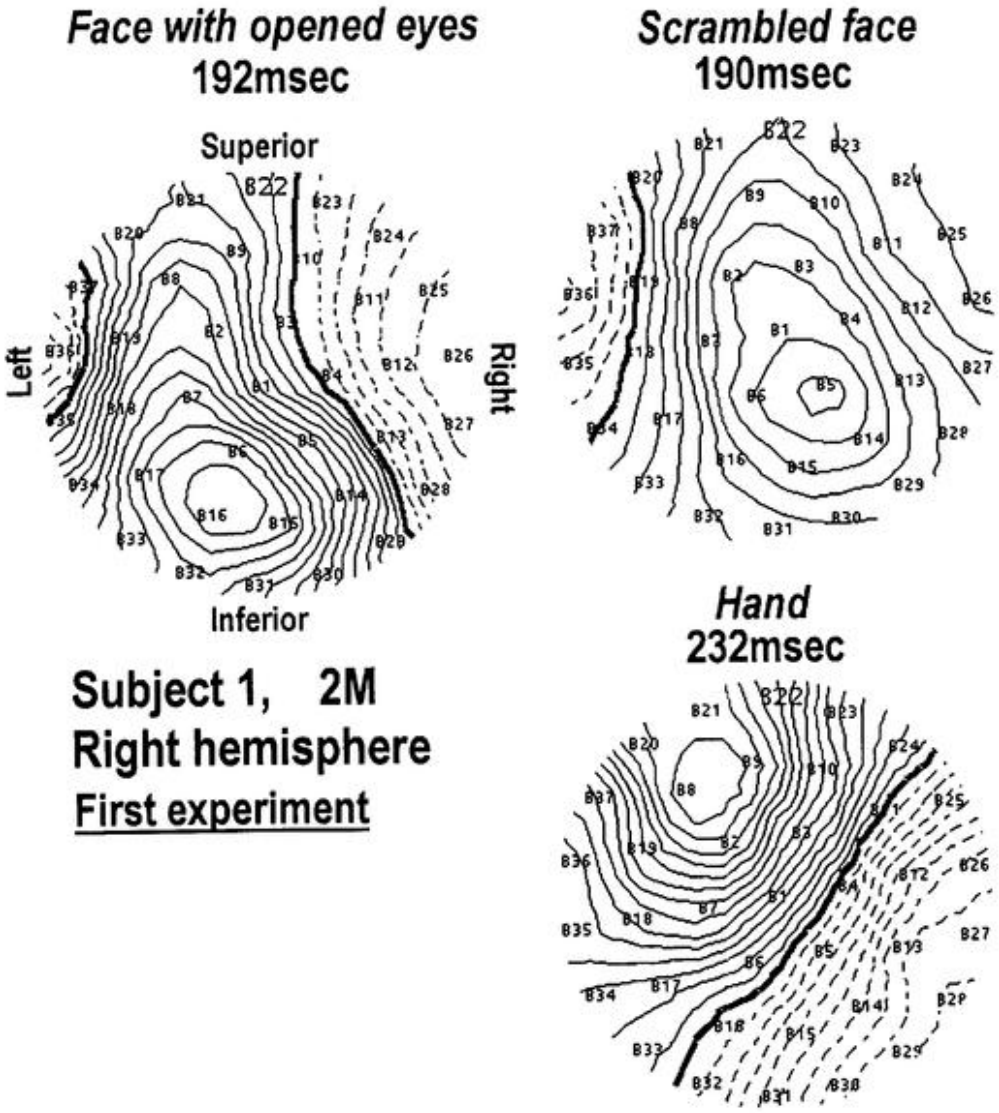
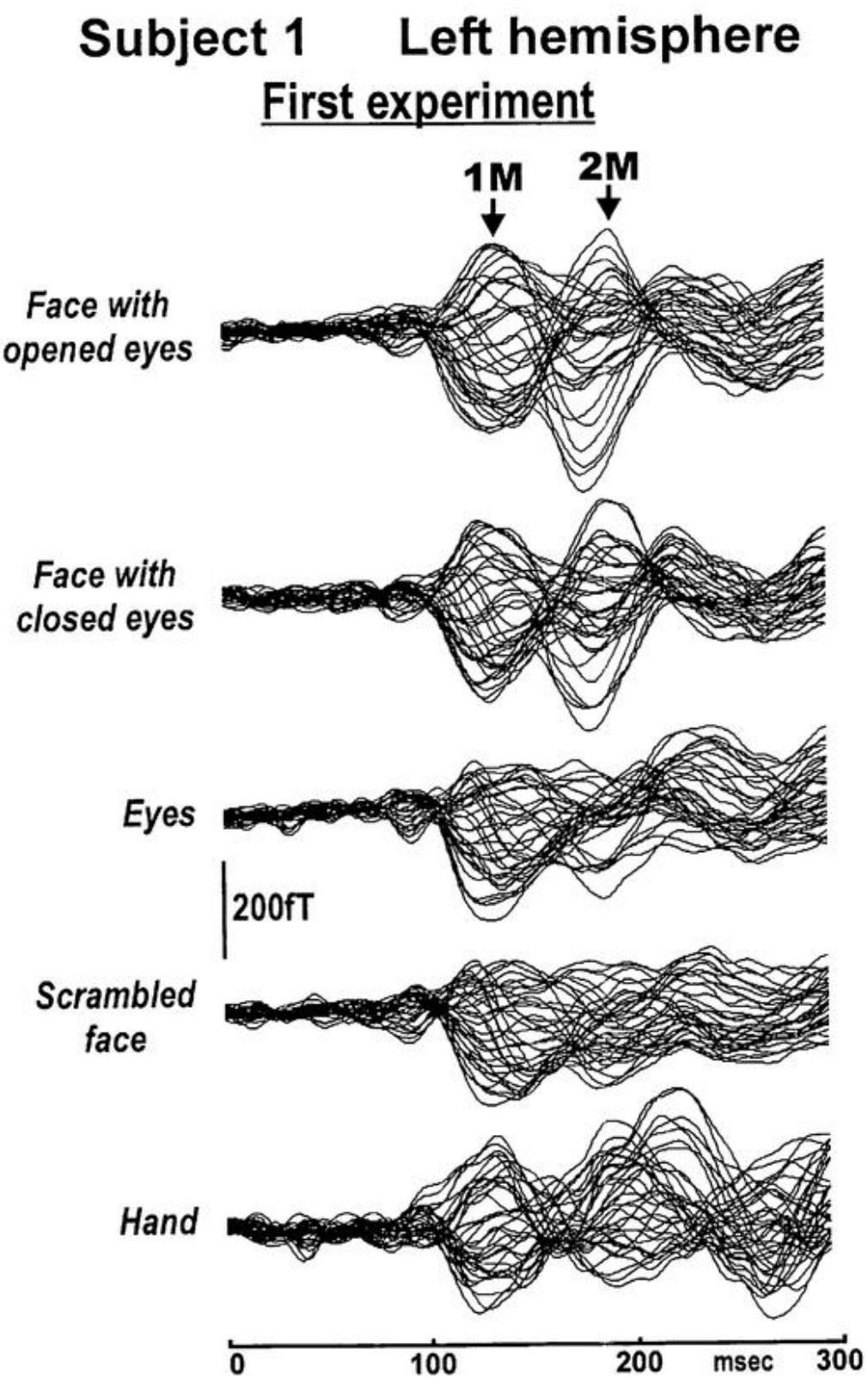

Face with opened eyes
192msec
Superior
Left
Right
Inferior
Subject 1, 2M
Right hemisphere
First experiment
Scrambled face
190msec
Hand
232msec

Fig.6


Subject 1 Left hemisphere
First experiment
1M
2M
Face with opened eyes
Face with closed eyes
Eyes
200fT
Scrambled face
Hand
0
100
200
msec
300

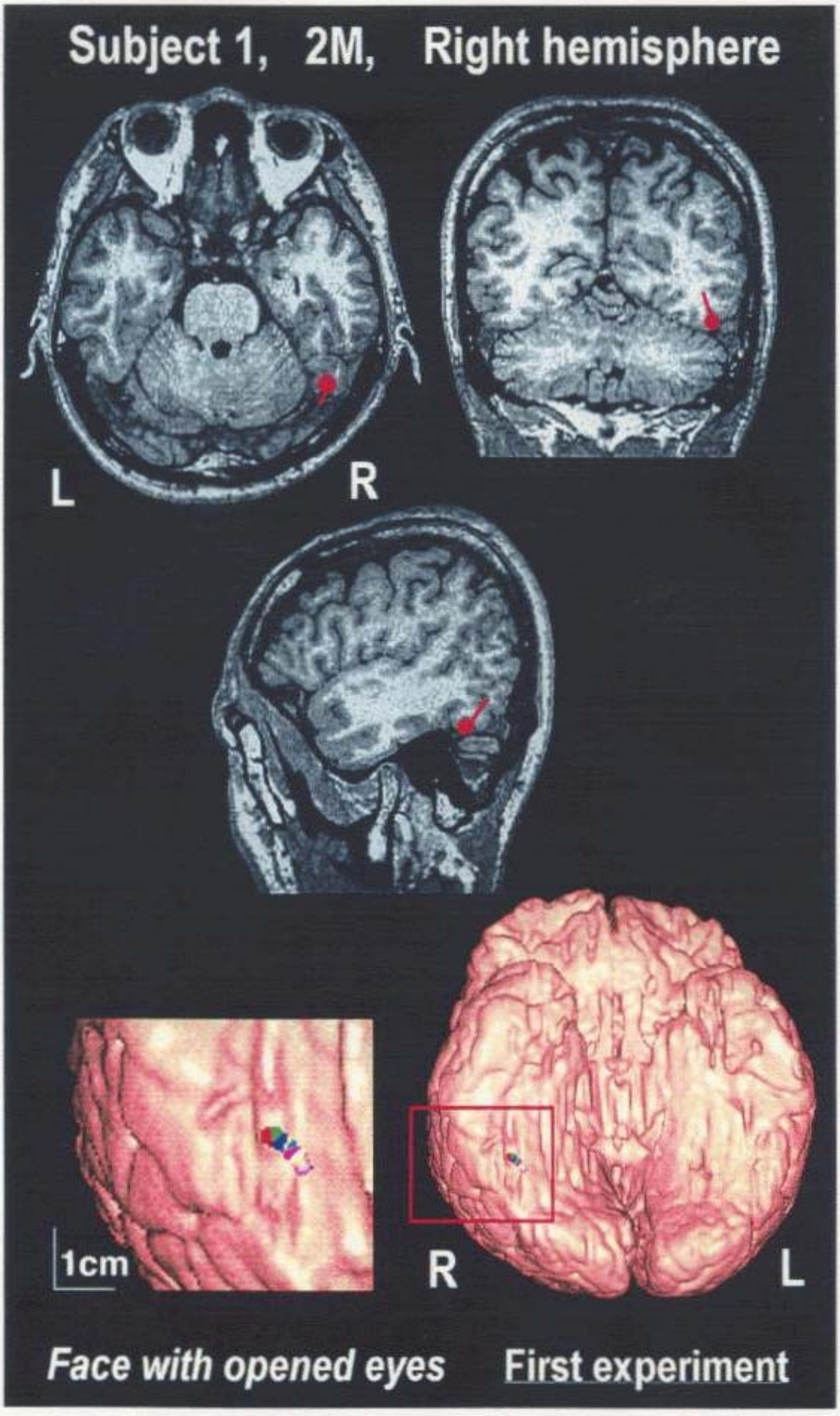

Subject 1, 2M, Right hemisphere
L
R
1cm
R
L
Face with opened eyes
First experiment

Fig.8

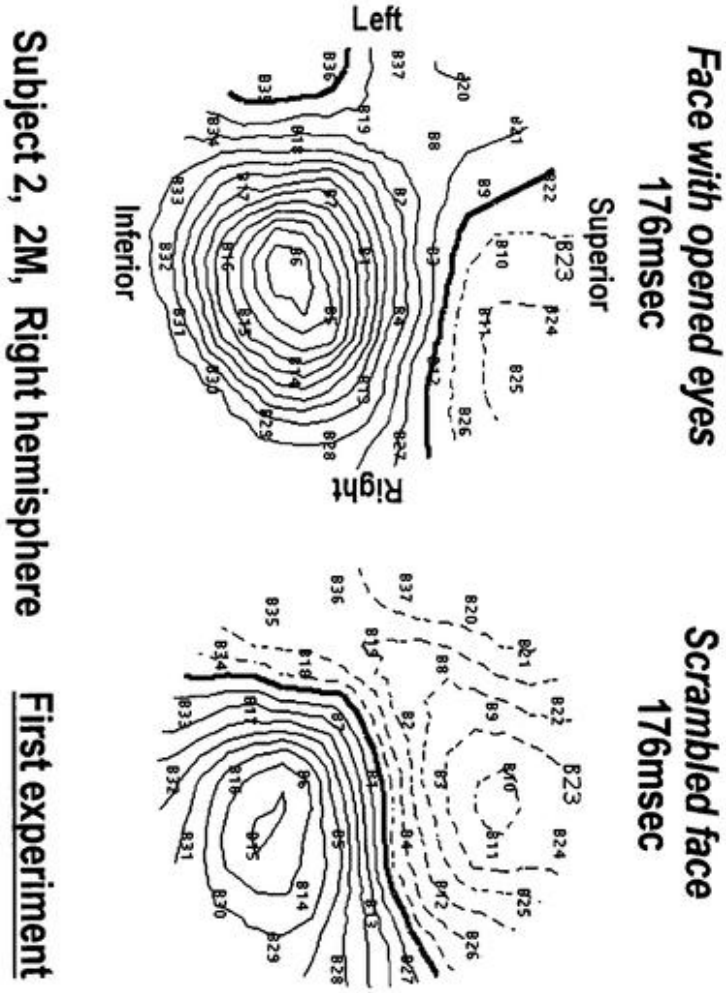

Face with opened eyes
176msec
Scrambled face
176msec
Left
Right
Superior
Inferior
Subject 2, 2M, Right hemisphere
First experiment

Fig.9

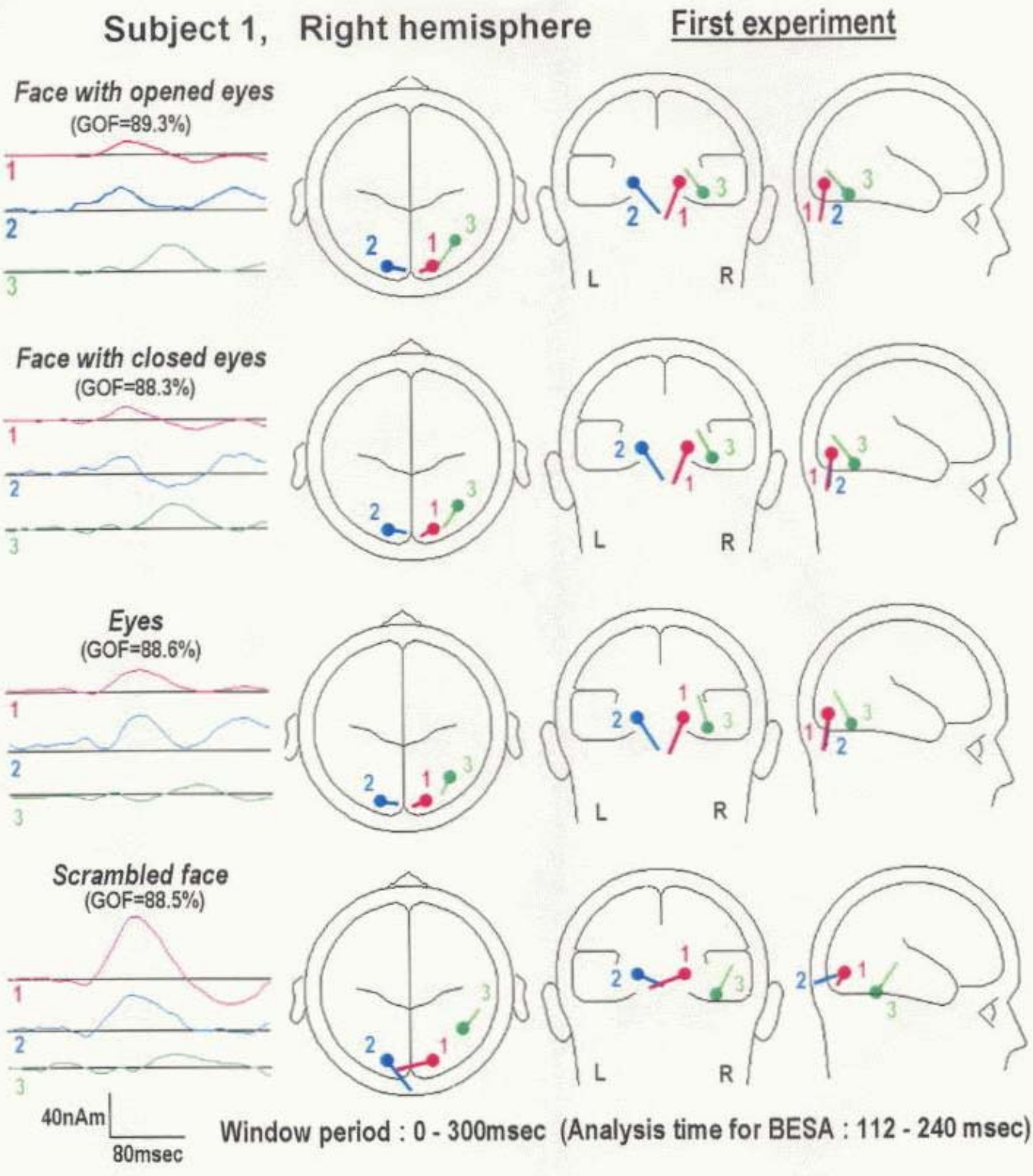

Subject 1, Right hemisphere
First experiment
Face with opened eyes
(GOF=89.3%)
Face with closed eyes
(GOF=88.3%)
Eyes
(GOF=88.6%)
Scrambled face
(GOF=88.5%)
1
2
3
L
R
40nAm
80msec
Window period : 0 - 300msec (Analysis time for BESA : 112 - 240 msec)

Fig.10

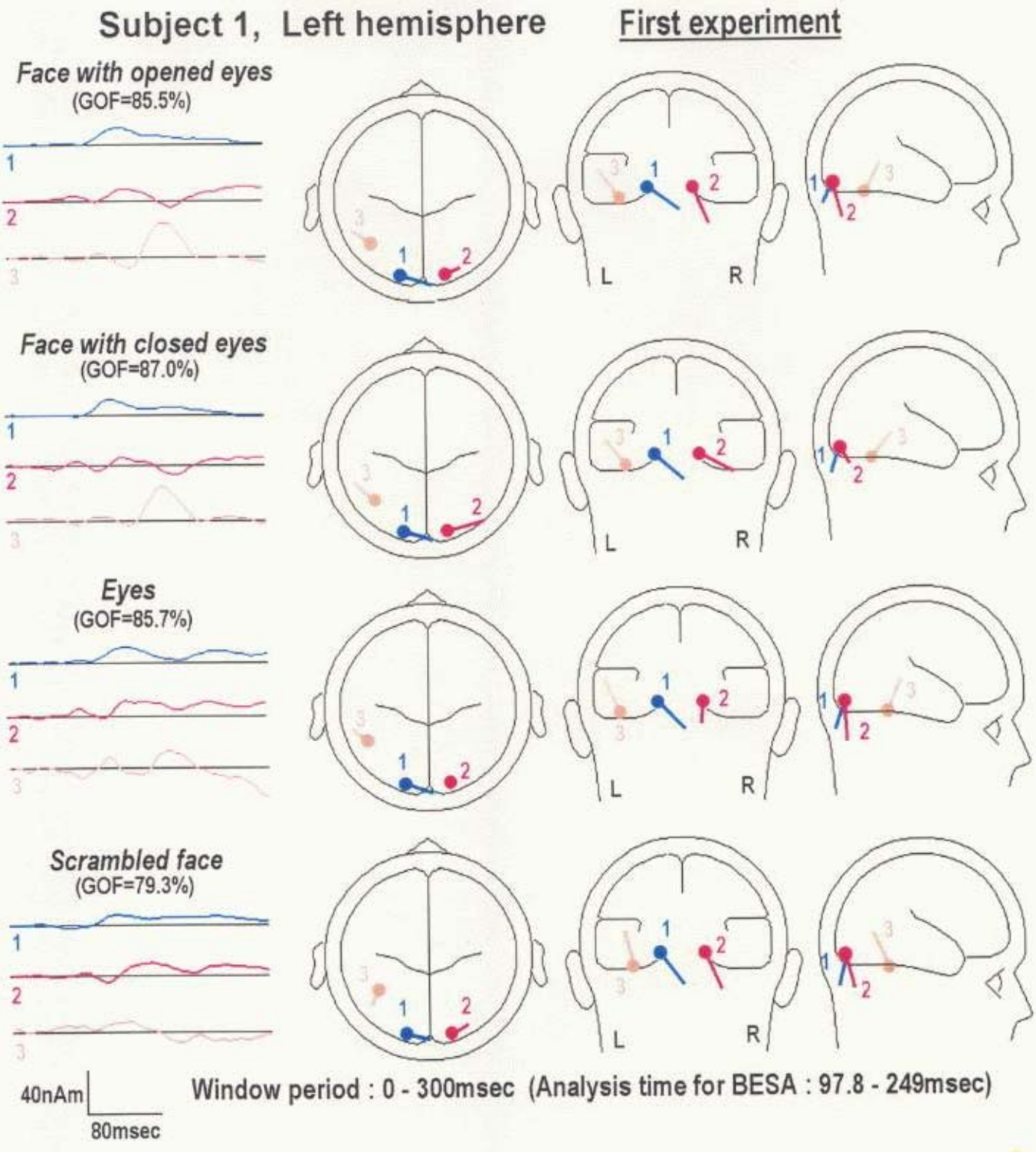

Subject 1, Left hemisphere
First experiment
Face with opened eyes
(GOF=85.5%)
Face with closed eyes
(GOF=87.0%)
Eyes
(GOF=85.7%)
Scrambled face
(GOF=79.3%)
1
2
3
L
R
40nAm
80msec
Window period : 0 - 300msec (Analysis time for BESA : 97.8 - 249msec)

Fig.11

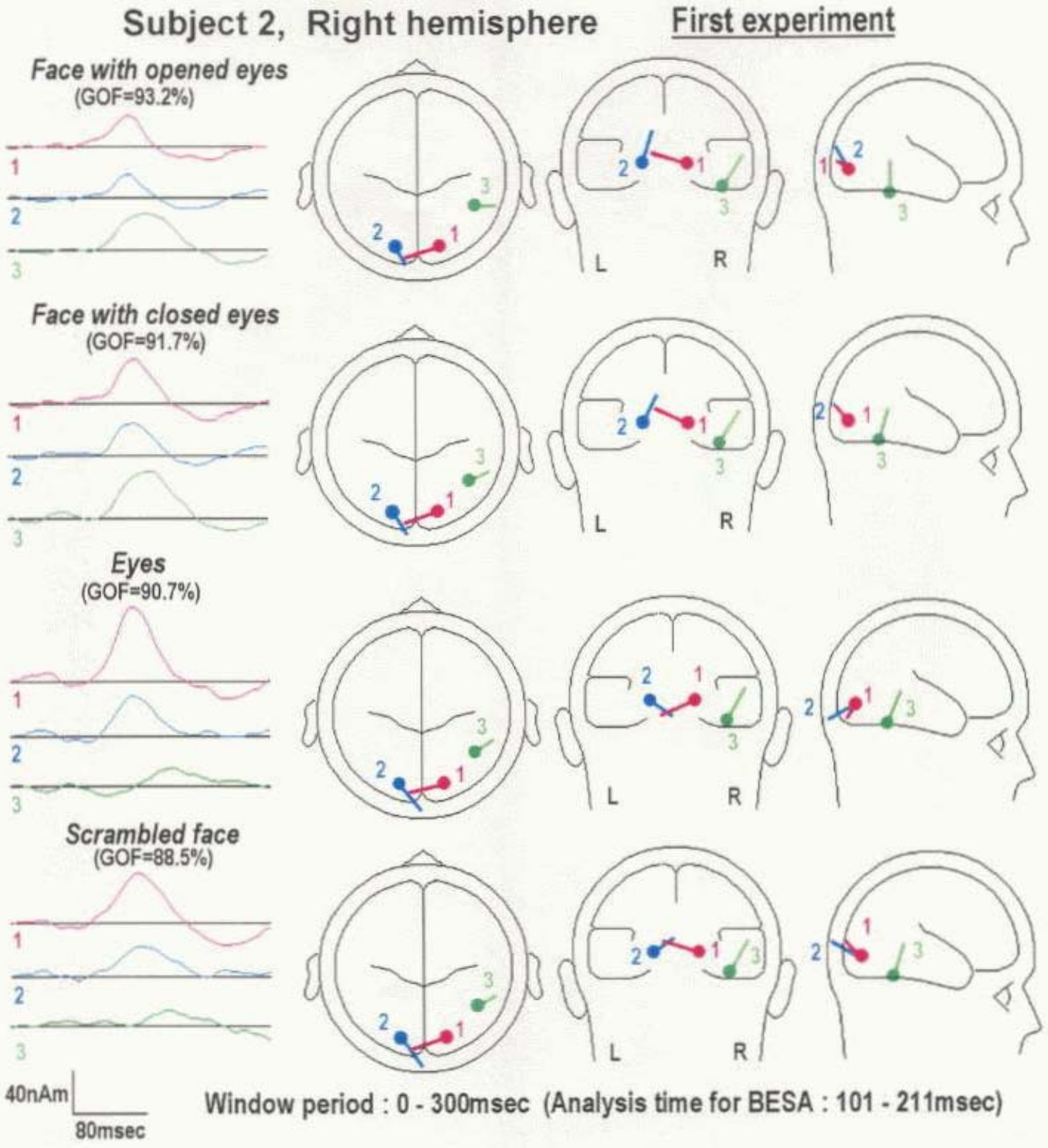

Subject 2, Right hemisphere
First experiment
Face with opened eyes
(GOF=93.2%)
Face with closed eyes
(GOF=91.7%)
Eyes
(GOF=90.7%)
Scrambled face
(GOF=88.5%)
1
2
3
L
R
40nAm
80msec
Window period : 0 - 300msec (Analysis time for BESA : 101 - 211msec)

Fig.12

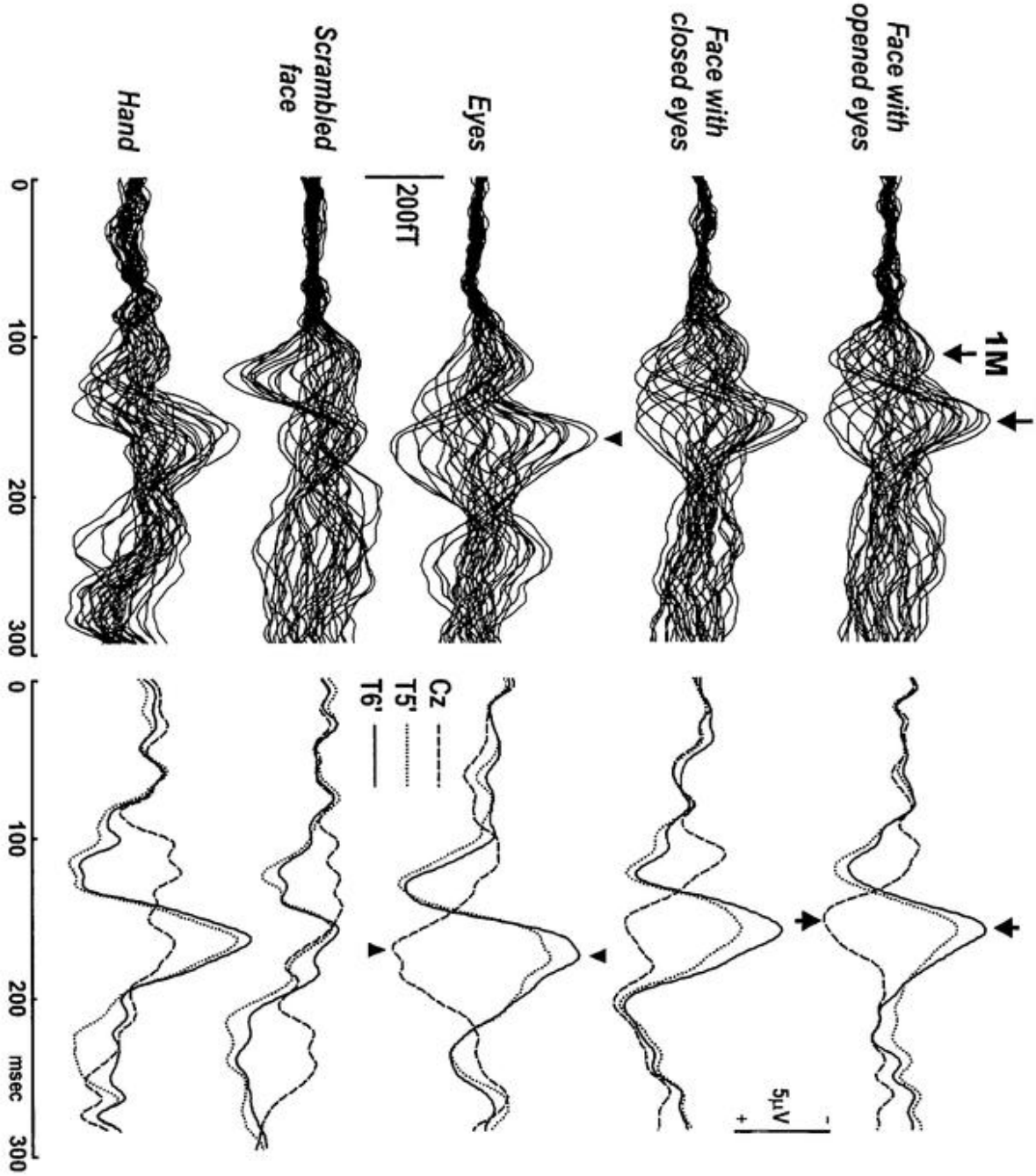

Subject 3 Right hemisphere
Second experiment
2M
1M
Face with opened eyes
Face with closed eyes
Eyes
Scrambled face
Hand
200fT
5μV
Cz
T5'
T6'
0
100
200
300
msec

Fig.13

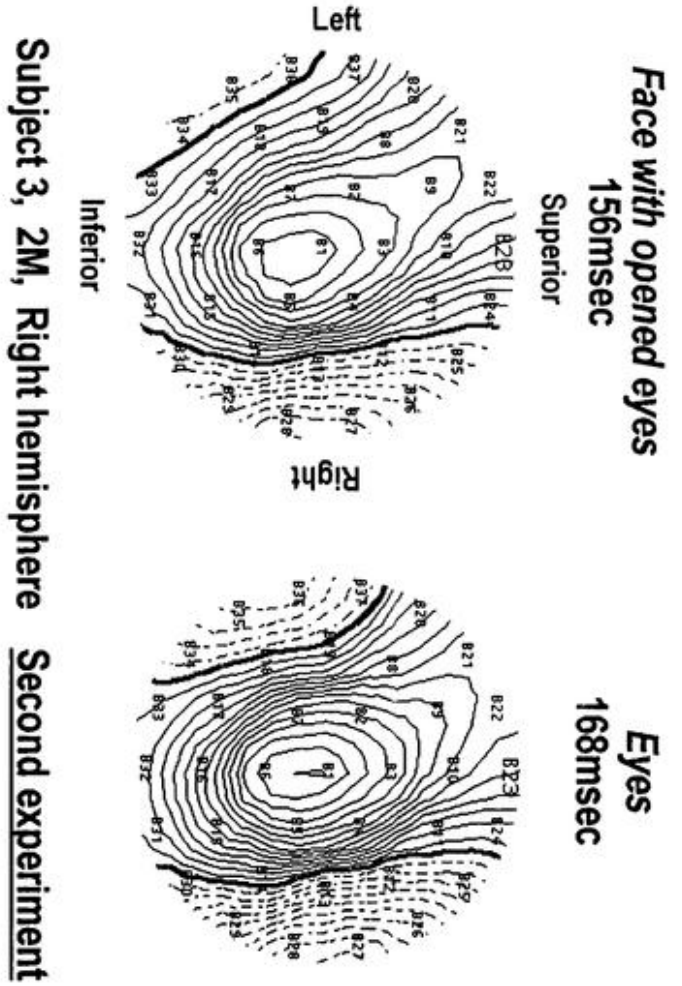
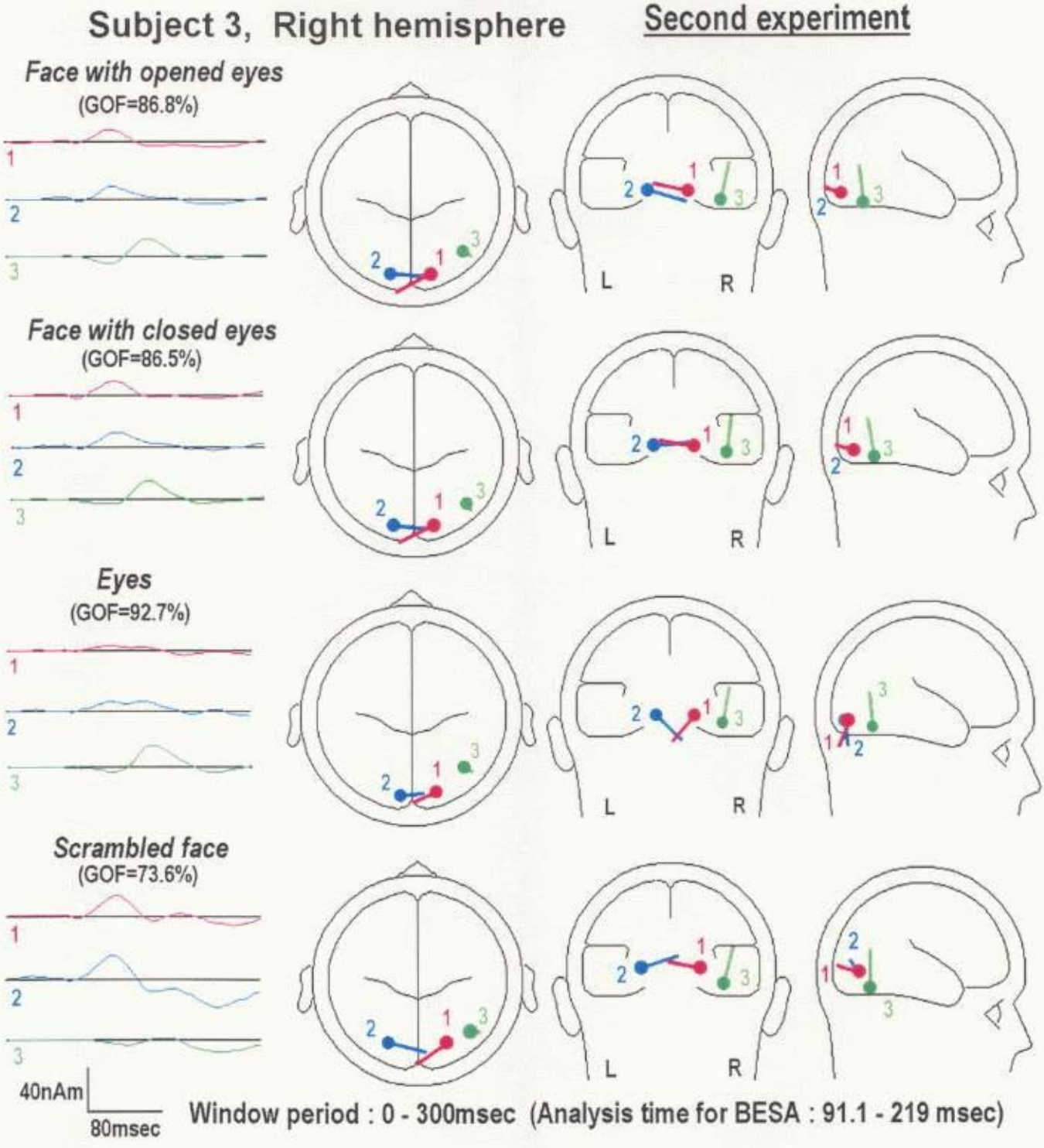

Face with opened eyes
156msec
Eyes
168msec
Left
Right
Superior
Inferior
Subject 3, 2M, Right hemisphere Second experiment

Fig.14


Subject 3, Right hemisphere
Second experiment
Face with opened eyes
(GOF=86.8%)
Face with closed eyes
(GOF=86.5%)
Eyes
(GOF=92.7%)
Scrambled face
(GOF=73.6%)
L
R
40nAm
80msec
Window period : 0 - 300msec (Analysis time for BESA : 91.1 - 219 msec)

11. Publications

1. Kakigi, R., Koyama, S., Hoshiyama, M., **Watanabe, S.**, Shimojo, M and Kitamura, Y. Gating of somatosensory evoked responses during active finger movements magnetoencephalographic studies. Journal of the Neurological Sciences, 128:195-204, 1995.
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12. Matsui, M., Kakigi, R., **Watanabe, S.** and Kuroda, Y.: Recurrent demyelinating transverse myelitis in a high titer HBs-antigen carrier. Journal of the Neurological Sciences, 139: 235-237, 1996.
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Peripheral Nervous System,1: 189-198, 1996.

14. Kakigi, R., Koyama, S., Hoshiyama, M., Kitamura, Y., Shimojo, M., **Watanabe, S.:** Pain-related brain responses following CO_2 laser stimulation: magnetoencephalographic studies. In, Visualization of Information Processing in the Human Brain (Eds. Hashimoto, I., Okada, Y. C. and Ogawa, S.), Elsevier, Amsterdam, pp. 110-120, 1996.
15. Kitamura, Y., Kakigi, R., Hoshiyama, M., Koyama, S., **Watanabe, S**. and Shimojo, M: Pain-related somatosensory evoked magnetic fields following lower limb stimulation. Journal of the Neurological Sciences, 145:187-194, 1997.
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