FACE REPRESENTATION IN THE HUMAN PRIMARY AND SECONDARY SOMATOSENSORY CORTEX

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1. Abbreviations

ECD: Equivalent current dipole
fMRI: Functional magnetic resonance imaging
GOF: Goodness of fit
MEG: Magnetoencephalography
PET: Positron emission tomography
SI: Primary somatosensory cortex
SII: Secondary somatosensory cortex
SEF: Somatosensory evoked magnetic fields
2. Abstract

To investigate the somatotopic organization of the facial skin area in the primary and secondary somatosensory cortex (SI and SII), we recorded magnetic fields evoked by air pressure–induced tactile stimulation applied to the face areas. For the SI study, we stimulated six points on the face (two points in each part of forehead, cheek and chin), lower lip and thumb. The dipole locations for SI activities were compared among eight stimulation points. The thumb area in SI was located more superior and medial to the lip area, which was consistent with Penfield’s homunculus. The face area was located between the thumb and the lip. There was no somatotopic arrangement among three parts of the face as forehead, cheek and chin (represent for three branches of the trigeminal nerve). The lips occupy a large area of the face representation in SI, whereas only a small area located between the thumb and lip areas is devoted to skin covered surfaces.

For the SII study, somatosensory evoked magnetic fields were recorded following stimulation of five body sites: the foot, lip and three facial skin points (forehead, cheek and mandibular angle point). We focused on the activities in SII and compared the dipole locations among them. There was a clear somatotopic organization in SII with the lip in the most lateral area, the foot in the most medial area and the face in the
intermediate area between the lip and the foot, closed to the lip area. However, there
was no significant difference of dipole localization in SII among the three areas of the
facial skin. The facial skin areas are considered to occupy a small area in SII with
insufficient spatial separation to differentiate each area of the facial skin.
3. Introduction

The somatosensory system mediates the processing of cutaneous, kinesthetic, visceral and noxious information; mainly consists of primary somatosensory cortex (SI), secondary somatosensory cortex (SII) and posterior parietal cortex (PPC). SI is located in the postcentral gyrus, beginning at the bottom of the central sulcus and extending posteriorly to the postcentral and intraparietal sulci. SI receives its main inputs from the sensory thalamus and has a role in the initial process of tactual functions such as encoding the type and intensity of the sensory inputs. There are four distinct areas in SI: Brodmann’s areas 3a, 3b, 1 and 2, each of which has a complete body surface map (Kaas et al., 1979). Tactile signals are processed serially through areas 3, 1 and 2. Area 3b is the first step of tactile processing for information from the skin, while area 3a is the first step for information mainly from the deep tissue (Iwamura., 1998). The cortical organization of neurons in SI was first described by Penfield and Boldrey (1937), since then many studies have clarified the somatotopic representation of the body surface in SI (Baumgartner et al., 1992; Hari et al., 1993; Kakigi et al., 1995; Hoshiyama et al., 1995, 1996; Nakamura et al., 1998; Nihashi et al., 2003). Regarding the representation of the face in SI, the face area drawn by Penfield and Boldrey (1937) is organized along
the central sulcus with the forehead in the superior-medial region adjacent to the hand area, and the chin in the inferio-lateral region. Although there are some studies reporting the locations in SI of the lip (Nakamura et al., 1998; Hoshiyama et al., 1995; Mogilner et al., 1994), tongue (Karhu et al., 1991; Altenmuller et al., 1990; Nakamura et al., 1998), oral cavity (Hari et al., 1993), and ear (Nihashi et al., 2001, 2002, 2003), there are only a few reports (Servos et al., 1999; Yang et al., 1994) on skin covered areas of the face such as the forehead, cheek and chin in humans. Interestingly, some results showed the representation of an inverted face along the central sulcus of the human brain (Servos et al., 1999; Yang et al., 1994; Pons et al., 1991), which is not consistent with the homunculus map drawn by Penfield and Boldrey (1937). In the first study, we sought to determine the topography of the whole face in SI using magnetoencephalography (MEG). MEG with a good spatial and temporal resolution is suitable to study cortical activities whose orientation is tangential to the brain surface. Since the main activities in the postcentral gyrus following somatosensory stimulation occur in the posterior wall of the central sulcus in area 3b (Kakigi et al., 2000) therefore create a tangential dipole, and MEG is suited to our purpose.

The SII area is located on the upper bank of the sylvian fissure. SII is involved in complex tactile functions and processes high-order features of the stimulus such as
attention (Burton et al., 1997; Mima et al., 1997), learning (Diamond et al., 2002), and memory (Diamond et al., 2002; Ridley and Ettinger, 1976). SII receives main inputs from area 3b. Like SI, SII has a somatotopic representation of the body. Unitary recordings in monkeys have revealed several distinct somatotopic maps of the body surface in the SII region (Burton et al., 1995; Friedman et al., 1980; Krubitzer et al., 1995; Robinson and Burton, 1980; Whitsel et al., 1969). These maps have a medio-lateral organization in which the face is represented laterally near the lip, followed in a latero-medial sequence for hand and foot representations, respectively. In humans, a somatotopic organization in the SII region has been identified by direct cortical stimulation (Penfield and Ramussen, 1950; Woolsey et al., 1979), MEG (Hari et al., 1993; Maeda et al., 1999) and functional magnetic resonance imaging (fMRI) (Del Gratta et al., 2000; Disbrow et al., 2000; Ruben et al., 2001; Iannetti et al., 2003) studies. For example, the face, hand, trunk and foot are represented in a latero-medial sequence in SII in both monkeys and humans, though the sequence is not very clear compared with that in SI, the so-called homunculus (Penfield and Ramussen, 1950). However, a map in SII of the facial skin area has not been investigated in detail. In the second study, we sought to clarify the somatotopic organization of the face in SII using MEG.
4. Methods

4.1. Experiment 1:

4.1.1. Subjects

Eleven healthy subjects, including five females and six males, participated in this study. Their age ranged from 27 to 35 (mean ± S.D: 30.0 ± 4.0) years. The study was approved in advance by the Ethical Committee of our Institute (The National Institute for Physiological Sciences), and informed consent was obtained from all the subjects.

4.1.2. Stimulation

A sensory output device, which consisted of a small balloon (1 cm in diameter) attached to the stimulation site, was used for stimulation (Figure. 1). The air pressure needed to inflate the small balloon was 0.15 MPa and induced a mechanical stimulation of 750 g/cm² at the stimulated site. A clear tactile sensation was elicited by the air pressure without a pain sensation. The air pressure, stimulus duration (50 ms), and rate
of the stimulus (2 Hz or ISI 0.5 s) were controlled by a tactile stimulator system (Nihon Kohden, Tokyo, Japan).

4.1.3. Stimulus area

We stimulated the glabrous side of the right thumb about 2 cm from the tip, the middle part of the lower lip, and six points (two points each on the forehead, cheek and chin) on the right side of the face. We defined the six points on the face as follows (see Figure. 1): (1, forehead 1) 1 cm lateral to the middle line and 3 cm superior to the eyebrow; (2, forehead 2) lateral point of the forehead region, 4 cm lateral to forehead 1; (3, nose) the top of the nose; (4, cheek) the top of the cheek-bone point; (5, chin 1) 2 cm inferior to the lower lip on the middle line; and (6, chin 2) mandibular angle point.

4.1.4. MEG recordings

Somatosensory-evoked magnetic fields (SEFs) were recorded with a 204-channel helmet-shaped planar neuromagnetometer covering the whole head (Vectorview, ELEKTA Neuromag Yo, Helsinki, Finland) (Figure. 2), which had 102 pairs of planar
gradiometers oriented orthogonally. The planar gradiometers detect the largest signal just above the source current (Hämäläinen et al., 1993). The signals were recorded with a 0.1–200 Hz bandpass filter and digitized at a sampling rate of 900 Hz. The period of analysis was from 50 ms before to 350 ms after the stimulation. The pre-stimulus period was used as the DC baseline. In each session, two points were randomly stimulated. Four sessions were conducted for each subject, three sessions for two points of each region (forehead, cheek and chin) of the face, and one session for the thumb and lip. The order of the sessions was randomized across subjects. For each stimulated point, 200 responses were averaged. White noise was simultaneously delivered during the period of stimulation at a sufficient level to mask the sound made by the air pressure stimulator.

4.1.5. Data analysis

By single equivalent current dipole (ECD) analysis, we estimated a dipole at the peak latency of a constant component around 40–50 ms following the stimulation. To select the ECD source, we first identified 3–4 channels, which detected large responses around the rolandic region (Hari and Imada, 1999), then selected 24-32 channels around
those channels with the large responses. This method has been used previously (Avikainen et al., 2002; Forss et al., 1999; Forss and Jousmäki, 1998). The subset of channels was fixed for each subject. The ECDs were estimated using the signals from these channels. The peak latency was defined by selected one channel among the subset, the channel with the biggest response amplitude. The latency point of the waveform of this channel with the biggest amplitude was defined as the peak latency. The goodness of-fit was calculated. Goodness-of-fit here refers to how well the model signal explains the original signal. In the present study, GOF was defined as:

$$g(\%) = \left[1 - \frac{\sum_{i=1}^{n} (b_i - \hat{b}_i)^2}{\sum_{i=1}^{n} b_i^2}\right] \times 100$$

where $b_1, \ldots, b_n$ are the experimental data and $\hat{b}_1, \ldots, \hat{b}_n$ are the value given by the equivalent dipole. Only the ECDs with a GOF over 85% (Avikainen et al., 2002; Forss et al., 1999; Forss and Jousmäki, 1998) were used for further analysis. The locations of dipoles were expressed with x, y and z coordinates where the x-axis indicates the mid-sagittal plane with positive values toward the right preauricular point, the y-axis indicates the coronal plane with positive values in the anterior direction, and the z-axis lies on the plane perpendicular to the x–y plane, with positive values toward the upper side (see Figure 3). The 3-D location, orientation and strength of the ECD were superimposed on MR images of each subject with the head assumed to be a sphere.
For a comparison of the ECD location among the eight stimulus points, we employed a standardized coordinate to reduce the inter-individual difference in head shape. For this purpose, we measured the maximum brain length from the y–z plane (x-axis), x–z plane (y-axis) and x–y plane (z-axis), and on MR images of each subject. The mean value for each axis among seven subjects was calculated and used as a standard. Then, the original x, y and z coordinates for ECDs of each subject were corrected using the ratio of the subject’s maximum brain length to the standard. For example, if the mean maximum length of the y axis (standard) was 100 mm, and the maximum length and original ECD value of the y-axis for subject A were 120 and 20 mm, respectively, the corrected y value of subject A was 20*100/120 = 16.7 mm. The data were expressed as the mean ± standard deviation (SD).

4.1.6. Statistical analysis

The differences in latency, dipole moment and ECD location (x, y and z values) among the eight stimulated points were assessed with a one-way analysis of variance (ANOVA). The level of statistical significance difference was set at 5% (P < 0.05).
4.2. Experiment 2

The methods of the Experiment 2 were almost the same as Experiment 1; the different points of Experiment 2 will be reported below.

4.2.1. Subject

Ten healthy subjects, 3 females and 7 males, participated in this study. Their age were ranged from 25 to 35 (mean 28.4 years).

4.2.2. Stimulation

We used the method similar to the Experiment 1. Interstimulus interval (ISI, rate of stimulus) was random from 2-4 s for this study, since the SII response is recorded with a long ISI. We stimulated the dorsal part of the right foot, lateral right part of the upper lip and 3 right facial skin points (By using a long ISI, it took a long time for recording. Therefore we stimulated only three facial skin points in this experiment); (1) the forehead, 3 cm lateral to the mid-line and 3 cm superior to the interior line of the
eyebrow; (2) the cheek, the top of the cheek-bone point; and (3) the mandibular angle point.

4.2.3. MEG recordings

The period of analysis was from 50 ms before and 250ms after the stimulation. The prestimulus period was used as the DC baseline. Two sessions were conducted for each subject, one for the foot and lip and another for the 3 facial skin points. The order of the sessions was randomized across subjects. During the recording, subjects were asked to count the number of all stimulations. Artifacts caused by blinking and large eye movements were discarded in the off-line analysis by recording electrooculograms. Sequentially, 70–100 responses were averaged for each stimulated point.

4.2.4. Data analysis

Since the field distribution of the SII activity analyzed in the present study was clearly different from that of the SI activity (Experiment 1), we considered that contribution of SI activity to evoked magnetic fields in these channels was minimum at
the peak latency of the SII activity. Therefore, we used a single dipole model to obtain ECDs in the SII area.
5. Results

5.1. Face representation in the human primary somatosensory cortex (SI)

Among 11 subjects tested, clear responses to the face stimulation could not be recorded in four, probably due to a small signal-to-noise ratio. Therefore, only results from seven subjects were used in the analyses.

5.1.1. Waveform

Although there were some earlier components, they were small in amplitude and rarely showed GOF values larger than 85%. Therefore, we chose the first consistent component for the analyses. This main deflection, occurring at a peak latency of approximately 40–50 ms, was termed M45, and had a source orientation toward the posterior regardless of the stimulus point (Figure. 4, Tables 1 and 2).

5.1.2. Latency and dipole moment
An ANOVA showed that the latency of M45 component did not differ among the eight stimulus points ($F = 0.42, P = 0.89$), but the source strength was significantly different ($F = 4.12, P = 0.0014$). The source strength tended to be larger for the thumb (23.8 nAm) or lip (23.0) than for the six facial points (7.0–15.1).

### 5.1.3. Source localization

As shown in Figure 5, the ECD for the thumb was located in the posterior wall of the central sulcus, and was medial (mean: 9.1 mm), posterior (mean: 9 mm) and superior (mean: 11.8 mm) to the ECD for lip. Results of an ANOVA for the ECD location showed no significant difference among the eight stimulus points ($P = 0.07$, 0.43, and 0.3 for the x, y and z coordinate, respectively).

Most of the ECDs for the six points on the face were located anterior, lateral and inferior to the ECD for thumb, and posterior, medial and superior to the ECD for lip (Figures 5 and 6). This meant that their locations were between the thumb and lip areas. To investigate the arrangement of representations in SI of three trigeminal branch areas, the six facial points were grouped into three subgroups (V1, V2 and V3), and the ECD location was compared among five groups (V1, V2, V3, thumb and lower lip) with a
one-way ANOVA. However, we could not find any differences (P = 0.16, 0.2, and 0.11 for the x, y and z coordinate, respectively). Next, the six facial points were grouped into medial (points 1, 3, 5) and lateral (points 2, 4, 6) areas, and the ECD location was compared among four groups (medial facial area, lateral facial area, thumb and lower lip). The results of an ANOVA showed a significant difference in the x coordinate among the four groups (P = 0.02, F = 3.6). The ECD for the thumb, the lateral facial area (3.7 mm lateral to the thumb), the medial facial area (6.7 mm lateral to the thumb), and the lip (9 mm lateral to the thumb) were arranged in this order laterally in the SI.

5.2. Face representation in the human secondary somatosensory cortex (SII)

All 10 subjects showed a clear middle-latency component, which was considered to be generated in SII. However, only results of six out of 10 subjects met our criteria for dipole localization, and were used for further analysis.

5.2.1. Waveform

Figure 8 shows the magnetic response of two subjects to the air pressure stimuli
applied to the foot, lip and three facial skin points. An early response appeared at around 40 ms following stimulation (Figure 7), were consistent with ECDs generated in SI considering the dipole location and antero-posterior direction, which were analyzed in detail in experiment 1 (Experiment 1). At a later latency around 100–150 ms, responses appeared in the bilateral hemispheres, whose ECDs were located more inferiorly than SI responses and showed a vertical orientation. A single-dipole analysis indicated that the major contributors for early and late responses were a source in the contralateral SI and sources in the upper bank of the Sylvian fissure of both hemispheres corresponding to SII, respectively. Since SII responses recorded in the hemisphere ipsilateral to the stimulation were small in amplitude with a low signal-to-noise ratio in two subjects, we focused on the SII response recorded from the hemisphere contralateral to the stimulation in the present study.

5.2.2. Latency and dipole moment

The peak latency was significantly different among the five stimulation points by a one-way ANOVA (F=5.6, P=0.0025). The peak latency for foot stimulation was longer than those following stimulation of the lip and three facial skin points (Table 3 and
Figure 8). The dipole moment of ECDs showed no significant difference among five stimulus conditions (P=0.47, Table 3). In general, all ECDs directed toward superiorly. The orientation of the ECD was not significantly different among five stimulation points (P=0.14, 0.93 and 0.9 for x, y and z axis vector).

5.2.3. Source localization

Figure 9 shows the location of ECDs following stimulation of the lip, foot and three facial skin points superimposed on the MR images in one subject. In this case, the ECDs for the foot and lip were located most medially and laterally in SII, respectively, and the ECDs for the facial skin area were located in an intermediate area close to the ECDs generated following stimulation of the lip. Table 4 shows the mean coordinates of each ECD. Figure 10 is a schematic drawing of spatial relationships of ECDs in SII following each stimulus indicating of the coordinates mean and one standard deviation of all subjects.

To certify the difference in localization of stimulus points in SII, first we compared the locations of ECDs among the five stimulus points using an ANOVA. The results showed a significant different of medio-lateral coordinate among five stimulation
groups (F=3.165, P <0.05) with the foot is most medial and the lip is most lateral, the forehead and cheek is also lateral between lip and foot (P=0.003, 0.014, and 0.037, respectively). However, there were no significant difference of the anterior–posterior and inferior–superior (P=0.64 and 0.92 for y and z values, respectively). As a second step, ECDs for the forehead, cheek and mandibular angle were grouped as ‘facial skin area’, since they were located very close to each other. We compared the ECD locations among 3 stimulation groups, the lip, foot and facial skin area using an ANOVA to determine whether there was actually a somatotopic organization of the body surface in the SII region. The results showed that the medio-lateral coordinate was significantly different among these 3 groups (F=5.83, P<0.05). The location of the ECD was most medial for foot (-42.7 mm), most lateral for lip (-54.9), and intermediate between foot and lip for facial skin area (-51.1). Although the ECD location for the facial skin area was also located between the lip and foot both for antero-posterior and infero-superior directions like for the x coordinate but the difference was not significant (P=0.41 and 0.71, respectively).

Subsequently we tried to find an orderly arrangement in SII among the 3 facial skin areas, the forehead (V1 territory of the trigeminal nerve), cheek (V2) and mandible angle point (V3) using a one-way ANOVA. The results showed no difference among 3
stimulation points (P=0.6, 0.9 and 0.52 for x, y and z coordinates, respectively).
6. Discussion

6.1. Face representation in the human primary somatosensory cortex

The study showed that the thumb’s location in SI was more superior, medial and posterior than the lower lip’s location along the central sulcus, which is consistent with the homunculus drawn by Penfield and Boldrey (1937) and other studies in humans using electrocorticography (McCarthy et al., 1993; Baumgartner et al., 1992) and MEG (Nakamura et al., 1998; Hoshiyama et al., 1996, 1995; Hari et al., 1993) as well as studies in monkeys (Nelson et al., 1998; McCarthy and Allison, 1995; Carlson et al., 1986). With regard to the spatial relationship between the thumb and lip areas in the SI, the ECDs for the facial points were located more inferior and lateral than the ECD for the thumb, and in turn, the lip area was located inferior and lateral to the six facial points, suggesting that the skin-covered areas of the face are represented between the thumb and lip in the SI, which is consistent with results of a single unit study in monkeys (Nelson et al., 1998). However, we could not find a consistent spatial arrangement of the six facial points in SI except that the lateral parts of the facial skin tended to be represented more medial than the medial parts. These results were
consistent with those of intracranial SEP studies by McCarthy and colleagues in humans (McCarthy et al., 1993) and monkeys (McCarthy and Allison, 1995), demonstrating that only a small region of SI between the thumb and upper lip areas was devoted to the upper face. Pons et al. (1991) also found in monkeys, that the cortical representations of chin and jaw were located adjacent to the hand representation. We considered that the reason we could not clearly separate the six points on the face was that the thumb and lip positions occupied a large area of the SI, and there was a relatively short distance between them. Since the thumb has an important role in prehensile function, its area in the cortex is extensive, and the facial area of SI is mostly occupied by the representation for lips as the lips have very sensitive particularity, a great mechanoreceptor density (Stöhr and Petruch, 1979), play roles in speaking and eating, and a very important part of tactile sensation. In contrast, the tactile function of the face is more modest. Therefore, it was reasonable to conclude that the remaining facial area devoted to facial skin was small. The present results showing that the source strength was significantly greater for the lip and thumb than for the six facial points are consistent with this notion. The result, however, should be interpreted with caution, because it cannot be excluded that the spatial separation of sources in the distal-proximal somatotopy was beyond the resolving capacity of MEG, or due to a large inter-individual difference. Of course, one
can clearly recognize which part of the face is stimulated in daily life. Therefore, we consider that somatotopy of the face must be present in SI, but we could not significantly separate them in the present MEG study. A relatively large inter-individual difference might be another reason for the lack of statistical significance.

In monkeys, the representation of the face in the somatosensory cortex is upside down, that is, the forehead representation is relatively inferior to the chin representation, and the cortical representations of chin and jaw are located adjacent to the hand representation (Pons et al., 1991), suggesting an inverted representation of the face in SI. Similar findings were reported in an fMRI study in humans (Servos et al., 1999). In an MEG study of two human subjects, Yang and colleagues (Yang et al., 1994) reported that ECDs for lower facial areas in the SI were located closer to those for fingers as compared to the ECDs for upper facial regions. In this study, we stimulated six points in three areas and as described above the locations of each area in the SI were not differentiated.

In monkeys, representations of medial parts of the face were located relatively posterior to those of lateral parts of the face in the SI (Nelson et al., 1998; Carlson et al., 1986; Cusick et al., 1986). In the present study, the results showed that the ECD for the medial parts of the face is located lateral to that for the lateral parts of the face. The
different pattern of medial and lateral representation of the face in the SI between humans and monkeys may result from a species difference. However, both results suggested segregated representations in the SI of the medial and lateral parts of the face.

In conclusion, our results implied that the lips occupy a large area of the facial representation in the SI, whereas only a small area located between the thumb and lips areas is devoted to the skin-covered surface of the face. This is the first study showing that the facial skin areas in the SI are located between the thumb and lower lip areas and close to each other in humans.

6.2. Face representation in the human secondary somatosensory cortex

The responses from the SII area were successfully recorded following stimulation of the facial skin points, although results in some subjects did not meet our criteria for a reliable ECD location due to a small S/N ratio, since mechanical air-puff stimulation is not sharp and strong with poor time-locking compared to electrical stimulation. The magnetic response from the SII region could be clearly differentiated from the response originating from SI by the response latency and ECD orientation. As compared with the SI response peaking around 40 ms, the SII activity had much longer response latency,
which was consistent with previous studies (Hoshiyama et al., 1996; Kakigi et al., 2000; Maeda et al., 1999). The ECD for the SII response oriented upward, which was clearly different from the ECD for SI activity with an anterior–posterior orientation (Results session of Experiment 1). In addition, the SII response was found in the bilateral hemispheres, which was in line with previous SII studies using MEG (Forss and Jousmaki, 1998; Hari et al., 1993; Hoshiyama et al., 1996; Inui et al., 2003; Kakigi et al., 1995; Maeda et al., 1999; Makela et al., 2003). The location of ECDs for SII is more lateral, inferior and posterior than that for SI (Results session of Experiment 1).

The significantly different medio-lateral locations of the ECDs for foot, lip and facial skin stimulations in the present study indicated a somatotopical organization within SII, confirming previous findings in humans (Disbrow et al., 2000; Maeda et al., 1999). Usually, the foot area of SII is located at the most medial site and the lip and face area have been reported to be located on the lateral side (Disbrow et al., 2000; Maeda et al., 1999). A similar order of somatotopic organization in SII has been identified in animals, for example, the foot area is located most caudal, near the fundus of the lateral sulcus then the hand, trunk, and face are located rostrally, respectively (Burton and Carlson, 1986; Cusick et al., 1989; Krubitz et al., 1986). Although the difference did not reach the significant level, the present results also implied the existence of an
antero-posterior and infero-superior arrangement of the body surface in SII. The present results showed that the lip was located most laterally, anteriorly and inferior, the foot was located most medially, posteriorly and superiorly and the facial skin points were located in intermediate regions close to that for lip stimulation. Such arrangements have been reported in both humans (Del Gratta et al., 2000; Disbrow et al., 2000; Hari et al., 1993; Maeda et al., 1999; Ruben et al., 2001) and monkeys (Burton and Carlson, 1986; Cusick et al., 1989; Krubitzer et al., 1986).

Although we confirmed the somatotopic arrangement in the SII region, the present study failed to find differences in location in SII of three different facial skin points. This finding was consistent with a previous fMRI study (Iannetti et al., 2003), in which activations in the SII region following stimulations of V1 and V3 regions overlapped each other. As reported in Experiment 1, the facial skin areas in SI were just between the thumb and lip areas and overlapped in a small region with no significant difference in location. The present findings in SII were consistent with those made previously in SI. That should explain why we could localize the face area in SI and SII but could not separate each part of the face. Though the lip is a part of the face but it’s function is more various compares with the facial skin as lip has an important role in speaking, sensation, eating and there are a large number of neurons responding to lip stimulation.
or lip occupies large area in both SII and SI (McCarthy et al., 1993)

Unitary recording studies in monkeys reported that neurons in SII have large, contralateral or bilateral receptive fields though some neurons do not have bilateral or ipsilateral receptive fields (Cusick and Manning, 1998; Cusick et al., 1989; Krubitzer et al., 1986; Pons et al., 1987; Robinson and Burton, 1980). Robinson and Burton (1980) reported that in monkeys, only one-third of SII neurons have bilateral or ipsilateral receptive fields. In humans, Hari et al. (1993) reported that the SEF field patterns of the ipsilateral response were not stable or changeable. This might explain why we could not record a prominent ipsilateral response at all stimulated points of some subjects.

The SII location in this study is approximately consistent with those in previous studies that used active discriminative tasks (Ledberg et al., 1995; Roland et al., 1998), while apparently more lateral to those reported in studies that used passive stimulation (Burton et al., 1993, Frot and Mauguière, 1999). Since subjects were instructed to count the number of the stimulus in this study, the present results appear to confirm that attention or discriminative tasks affect the location of active areas around Sylvian fissure (see discussions of Frot and Mauguière, 1999). These results imply that a deeper source other than SII is active simultaneously, probably the insula. Previous studies using intracranial recordings (Frot and Mauguière, 1999), PET (Ledberg et al., 1995;
Roland et al., 1998) and MEG (Inui et al., 2003) in humans as well as unitary recording studies in monkeys (Augustine, 1996; Burton et al., 1993; Friedman et al., 1980) showed that the insula is involved in tactile processing. In this study, the location of the foot response in two subjects was quite medially (x value) and the latency for foot was relatively longer compared to those of facial skin points. Therefore, it seems possible that the activity in the insula contributed to form the magnetic fields around Sylvian fissure in such cases.

In conclusion, our MEG studies indicated that neurons responding to somatosensory stimulation applied to facial skin areas in SII as well as SI were located very close to each other but clearly separated from those responding to stimulation of the lip. This finding should be redrawn after more thorough electrophysiological and neuroimaging studies.
7. General discussion and conclusion

The facial skin areas are represented in SI in a region between the thumb and the lip areas, and are represented in SII in a region between the lip and the foot areas closed to the lip area. Therefore, we could confirm somatotopic arrangements of the body surface including the face both in SI and SII by use of MEG. In SI, the medial part of the face is located more lateral than the lateral part with no somatotopic arrangement among the three branches of the trigeminal nerve, indicating that distinct segmental areas of the face have distinct representations in SI. On the other hand, we could not find any clear arrangement of the facial skin areas in SII, suggesting that the face regions in SII are located close to each other, probably overlapped in part. The results are consistent with the clearer somatotopy in SI than in SII in both monkeys (Robinson and Burton 1980; Sinclair and Burton 1993) and humans (Hari et al., 1993; Ruben et al., 2001; Iannetti et al., 2003).

Although we found a statistically significant difference in location for facial skin areas in SI, it was sometimes difficult to find a clear spatial arrangement in a single subject as compared with the very clear separation between the lip and thumb areas in SI. Since the thumb and lip have important roles in daily sensory discrimination and
speaking, respectively, they should occupy large areas in SI. By contrast, the facial skin areas occupy only a small region in SI, probably reflecting that the tactile function of the face is more modest as compared with the lip and thumb. Therefore, we consider that the spatial resolution of MEG is not high enough for detecting the precise arrangement of the facial skin areas in a very small region. In addition, a unitary recording study in monkeys (Manger et al., 1995) showed that the cortical fields responding to stimulation of different face areas have an irregular shape and lie intermingled in SI. Given similar properties for human SI neurons responding to the face stimulation, it would be expected to be very difficult to find a clear somatotopic arrangement in humans in a noninvasive study.

Neurons in SII have complex and large receptive fields reflecting its higher level in tactile processing than SI. As a result, the somatotopic organization in SII is less clear than that in SI though many previous studies in animals (Burton et al., 1995; Friedman et al., 1980; Krubitzer et al., 1995; Robinson and Burton., 1980) and humans (Hari et al., 1993; Maeda et al., 1999; Del Gratta et al., 2000; Disbrow et al., 2000; Ruben et al., 2001; Iannetti et al., 2003) found a rough somatotopy in this region. Given that the facial skin area is represented in a small region in SII like in SI, our failure to find a clear somatotopic organization in SII for the facial skin areas seems reasonable.
In conclusion, we could localize the face area both in SI and SII using MEG. Neurons responding to somatosensory stimulation applied to facial skin areas in SI as well as in SII were located very close to each other but clearly separated from those responding to stimulation of the lip. From a clinical interest, localization of the body in the cortex could be useful in surgical procedures.
7. Acknowledgement

I would like to express my deep gratitude to my professor, professor Ryusuke Kakigi for his supporting during the time I’ve been studied in the Department of Integrative Physiology, National Institute for Physiological sciences in Okazaki, for his encouragement in my studying, for giving me the opportunity so I could come to Japan for studying.

I wish to express my sincerely thankful to Dr. Koji Inui and Dr. Minoru Hoshiyama for their guidance and advice in creating the experiment; analysing the data and their invaluable contributed suggestion to writing this thesis. Without their helps, this thesis would not be accomplished.

I am grateful to Dr. Hiroki Nakata, Dr. Tuan Diep Tran for their comments and suggestions during the data processing. My thanks are also extended to Mr. Yasuyuki Takeshima and Mr. Osamu Nagata for their technical assistant.

Finally, I am greatly appreciating the kindness of all members in the Department of Integrative Physiology, National Institute for Physiological Sciences for their assistant during my time in Japan.
8. References


Binh Thi Nguyen


Nelson RJ, Sur M, Felleman DJ, Kaas JH. Representations of the body surface in


Table 1.

The mean latency, source strength and GOF value for each ECD (Experiment 1)

<table>
<thead>
<tr>
<th>Stimulation point</th>
<th>Latency (ms)</th>
<th>Source strength (Q/nAm)</th>
<th>GOF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Forehead 1</td>
<td>42.1 ± 8.2</td>
<td>15.1 ± 9.4</td>
<td>94.8 ± 3.5</td>
</tr>
<tr>
<td>(2) Forehead 2</td>
<td>43.6 ± 4.8</td>
<td>7.1 ± 5.7</td>
<td>91.8 ± 4.9</td>
</tr>
<tr>
<td>(3) Nose</td>
<td>39.8 ± 9.3</td>
<td>13.5 ± 6.4</td>
<td>95.1 ± 3.1</td>
</tr>
<tr>
<td>(4) Cheek</td>
<td>40.9 ± 9.3</td>
<td>10.5 ± 5.1</td>
<td>92.0 ± 4.3</td>
</tr>
<tr>
<td>(5) Chin 1</td>
<td>40.0 ± 8.6</td>
<td>12.5 ± 5.5</td>
<td>96.3 ± 1.9</td>
</tr>
<tr>
<td>(6) Chin 2</td>
<td>36.1 ± 10.6</td>
<td>9.3 ± 6.7</td>
<td>91.8 ± 6.5</td>
</tr>
<tr>
<td>Thumb</td>
<td>41.4 ± 5.0</td>
<td>20.9 ± 9.4</td>
<td>92.7 ± 1.4</td>
</tr>
<tr>
<td>Lower lip</td>
<td>39.3 ± 7.3</td>
<td>23.0 ± 9.2</td>
<td>95.3 ± 4.7</td>
</tr>
</tbody>
</table>

ECD, Equivalent current dipole; GOF, Goodness of fit.
Table 2. The mean ECD location of six face points, thumb and lip (Experiment 1)

<table>
<thead>
<tr>
<th>Stimulation point</th>
<th>x (mm)</th>
<th>y (mm)</th>
<th>z (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Forehead 1</td>
<td>-45.5 ± 6.5</td>
<td>25.6 ± 10</td>
<td>85.5 ± 7.0</td>
</tr>
<tr>
<td>(2) Forehead 2</td>
<td>-45.7 ± 12</td>
<td>23.0 ± 6.0</td>
<td>86.8 ± 10.4</td>
</tr>
<tr>
<td>(3) Nose</td>
<td>-51.7 ± 12</td>
<td>24.0 ± 8.0</td>
<td>85.8 ± 6.7</td>
</tr>
<tr>
<td>(4) Cheek</td>
<td>-45.0 ± 11</td>
<td>23.0 ± 8.0</td>
<td>85.0 ± 7.3</td>
</tr>
<tr>
<td>(5) Chin 1</td>
<td>-49.7 ± 6.0</td>
<td>30.5 ± 10</td>
<td>83.0 ± 7.2</td>
</tr>
<tr>
<td>(6) Chin 2</td>
<td>-40.8 ± 5.0</td>
<td>23.0 ± 5.0</td>
<td>81.0 ± 11.9</td>
</tr>
<tr>
<td>Thumb</td>
<td>-42.0 ± 8.0</td>
<td>17.0 ± 7.0</td>
<td>94.0 ± 5.3</td>
</tr>
<tr>
<td>Lower lip</td>
<td>-52.0 ± 9.0</td>
<td>26.0 ± 10</td>
<td>82.0 ± 4.0</td>
</tr>
</tbody>
</table>

The mean standardized x, y and z values (± SD) of each ECD location.

X, medio-lateral; Y, rostro-caudal; Z, dorso-ventral

To calculate the standardized x, y, z values we measured the maximum brain length from a y-z plane (x axis), x-z plane (y axis) and x-y plane (z axis) on MR image of each subject. The mean value for each axis among 7 subjects was calculated and used as a standard. Then, original x, y and z coordinate values for ECDs of each subject were
corrected by the ratio of the subject’s maximum brain length to the standard (see the methods for more details)
Table 3. The mean and standard deviation of peak latency and source strength following stimulation of the foot, lip and three face points (Experiment 2)

<table>
<thead>
<tr>
<th>Stimulation Point</th>
<th>Latency (ms)</th>
<th>Source strength (nAm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip</td>
<td>97.0 ± 11.2</td>
<td>25.0 ± 4.6</td>
</tr>
<tr>
<td>M angle</td>
<td>100.0 ± 12.5</td>
<td>17.5 ± 7.0</td>
</tr>
<tr>
<td>Cheek</td>
<td>95.8 ± 15.8</td>
<td>18.6 ± 6.0</td>
</tr>
<tr>
<td>Forehead</td>
<td>93.2 ± 13.7</td>
<td>17.1 ± 7.6</td>
</tr>
<tr>
<td>Foot</td>
<td>129.0 ± 14.9</td>
<td>25.0 ± 4.6</td>
</tr>
</tbody>
</table>
Table 4. The mean Talairach coordinates of ECD locations following stimulation of the foot, lip and three face points (Experiment 2)

<table>
<thead>
<tr>
<th>Stimulation</th>
<th>x (mm)</th>
<th>y (mm)</th>
<th>z (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip</td>
<td>-58.0 ± 6.1</td>
<td>-19.3 ± 10</td>
<td>16.7 ± 6.8</td>
</tr>
<tr>
<td>M angle</td>
<td>-51.3 ± 8.7</td>
<td>-24.1 ± 5.7</td>
<td>17.1 ± 5.6</td>
</tr>
<tr>
<td>Cheek</td>
<td>-53.8 ± 7.0</td>
<td>-25.8 ± 5.7</td>
<td>19.2 ± 4.5</td>
</tr>
<tr>
<td>Forehead</td>
<td>-56.1 ± 4.0</td>
<td>-24.1 ± 7.4</td>
<td>16.3 ± 3.4</td>
</tr>
<tr>
<td>Foot</td>
<td>-45.1 ± 7.1</td>
<td>-25.8 ± 8.6</td>
<td>19.5 ± 5.4</td>
</tr>
</tbody>
</table>

The mean standardized Talairach x, y and z values ± SD of each ECD location.

X, medio-lateral; Y, antero-posterior; Z, infero-superior
Figure legends

Figure 1. (a) Schematic drawing of the points stimulated on the face in Experiment 1; point 1: forehead 1; point 2: forehead 2; point 3: nose; point 4: cheek; point 5: chin 1; point 6: chin 2. (b) The tip of the stimulator.

Figure 2. Whole-scalp 306 channel neuromagnetometer (Elektra Neuromag Yo machine). Left: Helmet- shape with the arrangement of all sensors cover whole head. Right: MEG machine.

Figure 3. X, Y, Z coordinates system. X axis goes through LPA and RPA points, with positive direction toward the RPA. Y axis goes through Nasion point, which is a positive side of axis. Z axis is perpendicular to X and Y axis, with the positive axis is superior.

Figure 4. Evoked magnetic fields following stimulation of the thumb, lip and facial skin areas in Experiment 1. Left, SEFs following stimulation of the right thumb (black color), nose (red color) and lower lip (blue color) in subject 1. Upper panel, the head viewed from top, illustrates signals recorded by the two orthogonal gradiometers (G1 and G2) of each single sensor unit. A, B and C are selected channels over the peak response
(enlarged in the lower panel and right). Lower panel, enlargement of the upper panel's insert. Right, responses following stimulation of the eight points over the left rolandic area in subject 1. Vertical line indicates the stimulus onset.

Figure 5. Locations of the eight ECDs in subject 1 of Experiment 1. The locations of all sources are superimposed on a single axial and coronal MRI slice, with which the ECD for stimulation of the lip was estimated, to show their relative relationships. The ECD location for thumb is illustrated by a square, for lip by a triangle, and for the six points of facial skin by dots.

Figure 6. Spatial relationship of the group-mean ECD locations following stimulation of the eight points in Experiment 1. The location of each ECD is expressed by x, y and z coordinates relative to the ECD location for the thumb. (A) Medial–lateral direction (x value) and superior–inferior direction (z value); (B) medial–lateral direction (x value) and anterior–posterior direction (y value).

Figure 7. Different field distributions for activities from the primary (SI) and secondary (SII) somatosensory cortex following forehead stimulation in Experiment 2.

Figure 8. Evoked magnetic fields following stimulation of the foot, lip and three facial
skin points recorded in representative subjects in Experiment 2. Left figure: Magnetic responses recorded at all sensors produced by forehead stimulation. Sensors selected for analysis around SII are shown on a circle (A). Right figure: Enlarged waveforms of a single channel showing the largest response in the contralateral hemisphere for all stimulation points from two subjects.

**Figure 9.** ECD locations for foot, lip and three facial points superimposed on MR images in one representative subject in Experiment 2. All ECDs were overlaid on the slice on which the cheek was estimated. The ECD for lip is located most lateral, anterior and inferior, while the ECD for foot is located most medial, posterior and superior. ECDs for 3 facial skin areas are located very close to each other between the lip and foot regions, but closer to the lip region. Since the location for foot stimulation is located posterior to the sources of face. We show a coronal slice for foot. Black square for foot, pink triangle for lip, blue dot for forehead, yellow dot for cheek, navy dot for mandibular angle.

**Figure 10.** Schematic drawing of spatial relationships of ECDs for SII among each stimulation point in Experiment 2. The mean standardized Talairach coordinates of the
ECDs for foot, lip and facial points. A black square is the ECD of foot, a pink dot is the ECD of lip and small circles indicate the ECD location of each facial point (green for forehead, yellow for cheek and navy for mandibular angle). A large circle indicates their group averages. Bars indicate ± standard deviation. (A) Medio-lateral and infero-superior direction. (B) Medio-lateral and antero-posterior direction.
Figure 1
Figure 2
Figure 3
Figure 5
Figure 6
Figure 7
Figure 8
Figure 9
Figure 10
Publications

Original articles as first author


Original articles as co-author


Review articles

Kakigi R, Tran TD, Qiu Y, Wang X, Nguyen TB, Inui K, Watanabe S, Hoshiyama M. Cerebral responses following stimulation of unmyelinated C-fibers in humans: electro- and

Proceedings in International Conferences