Face Area Representation of Primary Somatosensory Cortex in Humans Identified by Whole-Head Magnetoencephalography

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Abstract: The feasibility of precise mapping was investigated noninvasively on the face component in predominantly unilateral primary somatosensory cortices (SI) in six healthy subjects. We recorded somatosensory evoked magnetic fields (SEFs) from the SI and secondary somatosensory cortices (SII) following the electrical stimulation of six skin sites: the infraorbital foramen, the angle of mouth, the upper lip, the lower lip, the mental foramen, and the mandibular angle. The median nerve at the wrist was stimulated as a standard of the map. The location of the equivalent current dipoles (ECDs) estimated from the distribution of magnetic fields was identified on MR images of the brain on each subject. The ECDs of the early components of SEF with peaks of 20–30 ms aligned along the SI in the hemisphere contralateral to the stimulation site. Late components with peaks of 80–150 ms were recorded from the bilateral hemispheres, and their ECDs were identified in the SII of the bilateral hemispheres. There was a distinct separation between the ECD locations representing discrete sites on the face and thumb in the SI of the contralateral hemisphere. Five sites of the face area in SI at the contralateral hemisphere were compatible with the conventional arrangement of homunculus in one subject. However, the remaining subjects had variations in the arrangement. The face area reorganization in the SI is possible to be related to the use-dependent cortical plasticity of the individual or to the perceptual experience by vision and proprioception. [The Japanese Journal of Physiology 54: 161–169, 2004]

Key words: somatosensory-evoked magnetic fields, magnetoencephalography, face area representation, primary somatosensory cortex, use-dependent cortical plasticity.

The face of well-known somatosensory homunculus originally described by Penfield and Boldray has long been thought to be oriented upside down along the central sulcus of the human brain [1]. The functional mapping of the human somatosensory system has commonly used invasive surgical techniques. However, a variety of neuroimaging tools have been developed that may noninvasively allow the study of human cerebral functions. Although functional magnetic resonance imaging (fMRI) has shown its power in brain research, its temporal resolution is not sufficient to clarify the sequence of activation of the brain area [2–4]. Magnetoencephalography (MEG) has excellent spatial and temporal resolution in the order of millimeter and millisecond [5, 6]. The detected sources result in a simpler field pattern more amenable to modeling as a single equivalent current dipole (ECD). Such modeling has produced highly reliable and accurate source localizations. The dipole localizations were transposed on the subject’s MRIs to resolve the anatomical locus of the individual dipoles in a given subject (e.g. Kakigi et al. [7]).

Yang and his colleagues, using MEG, recorded stimulus-evoked somatosensory magnetic fields generated by the left and right cortices in seven healthy young male and female subjects [8]. The ECD loca-
tions, which represented light pressure sensation for the tactile sites along the lower jaw and chin, lay in a group that was separate from the rest of the face. At present, the sensory map face of the monkey is established to be upside down. This arrangement positions the face upside down compared to the rest of the homunculus, which is inverted relative to the sulcal anatomy [9, 10]. Ramachandran and his colleagues reported a neural reorganization of human somatosensory cortex following the loss of a limb [11, 12]. They described a series of patients who complained of referred sensation in a phantom arm following the mechanical stimulation of their ipsilateral chin. The ECD locations of the lower jaw and chin were closer to the ECD sites representing light tactile sensation in the digits. FMRI evidence for an inverted face representation along the central sulcus in the healthy human somatosensory cortex was provided by Servos et al. [4]. On the contrary, Nakamura et al. mapped a complete homunculus in the somatosensory cortices of five normal subjects [13]. They recorded somatosensory-evoked magnetic fields (SEFs) following the electrical stimulations of 19 sites from the whole body. The ECD of the upper lip was found to be more superior than that of the lower lip in all subjects. In the study, three sites at the face region were investigated.

Thus a precise noninvasive map has been determined on the face component of somatosensory homunculus in healthy humans. The purpose of this study was to map the primary somatosensory cortex (SI) in the contralateral hemisphere corresponding to six facial sites and the thumb on the right side in six healthy male subjects by the use of a whole-head DC-SQUID neuromagnetometer with pairs of gradiometers. From the specific sensory nuclei of the thalamus, neurons carrying sensory information project in a highly specific way to the two somatic sensory areas of the cortex (SI and SII) [14]. One of the major advantages of SEF is that activities in the secondary somatosensory cortex (SII) are easily recorded [7]. The ablation of SI in animals causes deficits in position sense and in the ability to discriminate size and shape. The ablation of SII causes deficits in learning based on tactile discrimination. SI and SII process sensory information in series [14]. SII is concerned with a further elaboration of sensory data of SI [14]. Therefore the activations of SII in the bilateral hemispheres by facial electrical stimuli were also shown.

**MATERIALS AND METHODS**

Six right-handed normal subjects (males; mean age 34 years, range 22–60 years) were studied. All subjects gave written informed consent prior to the experiments. The study was approved by the Ethics Committee of our institute and was in accordance with the Declaration of Helsinki. We stimulated the following six sites of facial skin on the right side: (1) the infraorbital foramen; (2) the upper lip (2 cm lateral to the midline of the lip); (3) the angle of the mouth (1 cm lateral to the angle); (4) the lower lip (2 cm lateral to the lip midline); (5) the mental foramen; and (6) the mandibular angle. The order of the six sites was randomized. Besides the six sites of the face, the median nerve at the wrist was stimulated. A pair of silver ball electrodes embedded in resin was used for stimulation and attached to the skin of the stimulation sites. The electric stimulus was a constant current square pulse delivered at a frequency of 1 Hz. The stimulus was 0.05 ms in duration and approximately two times the strength of the sensory threshold (1–5 mA). The stimulation of the median nerve was 0.2 ms in duration, and approximately two times the sensory threshold (3–5 mA) in strength. The stimulation sites, where subjects felt movements of their own thumbs by the stimulation of the median nerve, were selected. The subjects were instructed to sit on a chair for the neuromagnetometer in a magnetically shielded room and to gaze at a spot of light illuminated on a screen placed about 1 m in front of them.

A 306 channel SQUID neuromagnetometer (Vectorview, Elekta AB) covering the whole scalp was used for recording magnetic fields from 102 points in the cerebral cortex. In this study, we measured SEFs by using 102 pairs of gradiometers. All responses were digitized at a sampling rate of 1 kHz and were bandpass-filtered at 0.1–330 Hz. In the analysis, subsequent filters at 0.1–100 Hz were used to evaluate SEF responses. The analysis window was 300 ms after the stimuli, and the DC was offset for a prestimulus period of 50 ms as the baseline. In one experiment, therefore, we stimulated the seven sites of each subject in a random order. Four hundred trials were averaged on the SEF of a stimulating site. Four head position indicator coils were attached to the scalp in the subjects, and their locations with respect to three anatomical landmarks (the bilateral preauricular points and nasion) were determined with a three-dimensional digitizer (Isotrik, Polhemus, Colchester, Vermont, USA). At the beginning of each recording session, weak currents were led into these coils, and the resulting magnetic fields were measured with the sensor array to find the head location with respect to the sensors. The information was used to align the MEG and the head MRI (1.5-T Siemens Symphony system, Erlangen, Germany) coordinate systems and
to show the source locations with respect to the anatomical structure. Isocontour maps were constructed at a time point within the analysis window from the field distribution of the cortex, using the minimum-norm estimate. To identify sources underlying the measured signals, we divided the SEFs by peak latencies, during each of which one equivalent current dipole (ECD) was first found by a least-squares search, using 30–40 channels over the response area. We then analyzed the current source by using a program supplied with the Vectorview system, including the SSP method (signal-space projection method). To obtain the higher spatial resolution of localization methods of the ECDs, we ensured sufficient reliance by the use of SSP [15]. In a spherical conductor model, these calculations resulted in determining the 3-dimensional locations, strengths, and directions of the ECDs [16]. The ECDs were then superimposed on the subject’s MRIs to show the source locations with respect to anatomical structure. We accepted only ECDs accounting for ≥80% of the field variance at selected periods for each subset of channels and confidence volume <1 cm³. Only ECDs attaining 90% of the goodness-of-fit (g%) were accepted for further analysis, in which the entire time period and all channels were taken into account when we computed the parameters of a time-varying multidipole model [17]. For this purpose, the strength of the previously found ECDs was allowed to change as a function of time, but their locations and orientations were kept fixed.

For Table 1, the peak latency of each component was measured at the maximum value of the root mean square (RMS) of the magnetic field strength recorded over the selected channels of the 204 sensors. The average field strength on the selected channels, \( a(t) \), is indicated by the following formula: \( b_i(t) \) is the measured signal on channel \( i \), \( w_i = 0 \) for ignored channels, and \( w_i = 1 \) otherwise.

\[
a(t) = \frac{\sum_{i=1}^{N} w_i b_i^2(t)}{\max \left( \sum_{i=1}^{N} w_i \right)}
\]

RESULTS

Electrically stimulated sites of facial skin are shown in Fig. 1. An example of the spatial distribution of SEFs elicited by the right mental foramen electrical stimuli in one subject is shown in Fig. 2. The SEFs were clearly identified in the regions corresponding to SI and SII in both of the hemispheres. The SEFs following stimulation of the facial sites on each right side could be successfully recorded from both of the hemispheres, as shown in Fig. 3. These traces, highlighting the largest signals, refer to channels above the contralateral hemisphere (channels 1 and 2) and the ipsilateral hemisphere (channels 3 and 4) to the right stimulated site, which were indicated as a shaded area in Fig. 2. In all subjects, we could consistently identify the early and late components within an analysis period of 300 ms in the SEF waveforms following stimulation of the six facial sites. The peak latencies

Fig. 1. Electrical stimulation sites of facial skin. We stimulated the six sites of facial skin shown in this figure and the median nerve at the wrist on the right side (not shown).

Fig. 2. An example of somatosensory evoked fields of subject 4. The traces are averages of 400 single responses following stimulations of the right mental foramen. The traces are plotted on the “flattened head,” viewed from the top, the nose pointing upward. The upper trace of each response pair illustrates the latitudinal and the lower trace the longitudinal derivatives of the radial magnetic field recorded by the 204 planar SQUID gradiometers. Each trace started 50 ms before and ended 300 ms after the stimulus onset. The shaded area shows the chosen channels for enlarged signals to stimulations of each face site in Fig. 3.
were 20 ms (M20), 40 ms (M40), 80 ms (M80), and 150 ms (M150) in the contralateral hemisphere and 40–60 ms (M40–60), 80 ms (M80), 100 ms (M100), and 150 ms (M150) in the ipsilateral hemisphere (Figs. 3 and 4 and Table 1). This is shown in an example of enlarged SEF traces (Fig. 4) elicited by stimulations of the mouth angle on the right side.

The ECDs of the M20 and the M80 components were superimposed on the MRI following the stimulations of six sites on the right side. The ECDs of the M20 components were identified along SI only in the contralateral hemisphere to the right stimulated sites in all subjects. An example in one subject is shown in Fig. 5. Reliable dipoles because of the mandibular angle stimulation were found in only two of six subjects (Fig. 5F). For this reason, the signals from the mandibular angle area might be small. We could not distinguish the ipsilateral ECDs by using the root mean square (RMS) to measure peak latency (see Table 1) or by using single-dipole analysis and multidipole analysis (not shown). The ECDs of the M80 components were identified in the bilateral hemispheres near the sylvian fissures in all subjects. An example in one subject is shown in Fig. 6 (from A1 and B1 to A6). We analyzed the M80 component by using time-varying multidipole analysis to make a model with two dipoles generated by the bilateral activation of SII. The rightmost panels (C1–C6) show the strength of ECD as a function of time. The upper two traces in each subset of C1–C6 show the strength of source 1 (SIIc) and source 2 (SIIi) of the M80 component to each stimulation. MRIs show the location and direction of two sources of the M80 component to the right stimulation of the infraorbital foramen in the same subject. These sources, 1 and 2, were situated in the contralateral (A1 to A6) and ipsilateral (B1 and A2 to A6) superior bank of the sylvian fissure, SII. These deflections were oriented more vertically in comparison with the ECDs in SI. The lowest traces in each subset of C1 to C6 illustrate the goodness-of-fit (g%) of the model calculated over all 204 gradiometers.

Detailed somatosensory receptive maps of the face in all the subjects were represented by the use of MEG. Examples of the four subjects are shown in brain images A–D in Fig. 7. We reconstructed the three-dimensional brain image by using the MRI of each subject. The central sulcus was identified by the anatomical findings of MRI or ECD locations of the M20 component in MRI slices, estimated from the distribution of magnetic field of the brain after a stimulation of the median nerve. ECD locations of the
Facial SEFs

Fig. 5. MRIs showing the location of ECD of M20 component following the stimulation of each skin site of infraorbital foramen (A), mental foramen (B), angle of mouth (C), upper lip (D), lower lip (E), and mandibular angle (F) identified in subject 4, by use of a single-dipole analysis. The M20 component of the mandibular angle was detected in two subjects. One of the ECD locations of this component for the mandibular angle is shown in Fig. 5F. The ECDs estimated from the SEF corresponding to each electrical stimulation were identified in the contralateral postcentral gyrus (SI).

Table 1. Latencies of evoked magnetic fields following face stimulations.

<table>
<thead>
<tr>
<th></th>
<th>Contralateral</th>
<th>M20</th>
<th>M40</th>
<th>M80</th>
<th>M100</th>
<th>M150</th>
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<tbody>
<tr>
<td>Infraorbital f.</td>
<td>30±4</td>
<td>46±3</td>
<td>83±2</td>
<td>114±7</td>
<td>157±8</td>
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</tr>
<tr>
<td>Upper lip</td>
<td>23±2</td>
<td>40±3</td>
<td>79±3</td>
<td>103±2</td>
<td>144±5</td>
<td></td>
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<tr>
<td>Angle of mouth</td>
<td>22±1</td>
<td>42±1</td>
<td>77±3</td>
<td>117±6</td>
<td>160±9</td>
<td></td>
</tr>
<tr>
<td>Lower lip</td>
<td>19±2</td>
<td>45±2</td>
<td>85±2</td>
<td>106±2</td>
<td>156±7</td>
<td></td>
</tr>
<tr>
<td>Mental f.</td>
<td>24±2</td>
<td>42±4</td>
<td>81±4</td>
<td>113±9</td>
<td>144±4</td>
<td></td>
</tr>
<tr>
<td>Mandibular angle</td>
<td>37±5</td>
<td>81±4</td>
<td>113±9</td>
<td>121±11</td>
<td>163±11</td>
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<thead>
<tr>
<th></th>
<th>Ipsilateral</th>
<th>M40–60</th>
<th>M80</th>
<th>M100</th>
<th>M150</th>
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<tr>
<td>Infraorbital f.</td>
<td>51±4</td>
<td>95±9</td>
<td>113±5</td>
<td>156±10</td>
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<tr>
<td>Upper lip</td>
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<td>81±5</td>
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<tr>
<td>Angle of mouth</td>
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<td>83±4</td>
<td>119±10</td>
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<tr>
<td>Lower lip</td>
<td>46±2</td>
<td>90±3</td>
<td>111±4</td>
<td>163±10</td>
<td></td>
</tr>
<tr>
<td>Mental f.</td>
<td>42±3</td>
<td>83±2</td>
<td>111±8</td>
<td>139±6</td>
<td></td>
</tr>
<tr>
<td>Mandibular angle</td>
<td>82±2</td>
<td>100±3</td>
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</table>

The averaged latencies of evoked magnetic fields following the stimulation of each face site of all subjects. The peak latency of each component was measured according to Eq. 1 (see text). The values are mean±SE, n=6. In the mandibular angle, n=2. Contralateral, contralateral side; Ipsilateral, ipsilateral side; f., foramen.
M20 component following stimulations of the six facial sites were superimposed on the 3-dimensional image. Each receptive area superimposed on the posterior bank of the central sulcus in the contralateral hemisphere was projected onto the cortical surface from six stimulated sites on the face. In one subject, each receptive area for the six stimulated sites showed Penfield’s arrangement pattern along the posterior bank of the central sulcus in the contralateral hemisphere (Fig. 7C) [1]. In the remaining subjects, variations were found in the special arrangement of their ECDs.

M80 component following the stimulation of each face site on the right side. All data were obtained from subject 4. SIIc, contralateral SII; SIIi, ipsilateral SII. Each box shows 10 nAm, 15 nAm, or 20 nAm and 10 ms. Goodness-of-fit (g [%]): each calibration bar shows 40%. Note that all the source strength of the M80 component in the two-dipole model clearly indicates the bilateral activation of SII, and the locations of these ECDs on MRI clearly differ from those of ECDs for the M20 component.

Fig. 6. MRIs showing ECDs of the M80 component following the stimulation of each face site on the right side. All data were obtained from subject 4. SIIc, contralateral SII; SIIi, ipsilateral SII. Each box shows 10 nAm, 15 nAm, or 20 nAm and 10 ms. Goodness-of-fit (g [%]): each calibration bar shows 40%. Note that all the source strength of the M80 component in the two-dipole model clearly indicates the bilateral activation of SII, and the locations of these ECDs on MRI clearly differ from those of ECDs for the M20 component.
SEFs were usually recorded following the stimulation of the median nerve at the wrist in all subjects. The ECDs of peak latency, 20–30 ms, were in the area of the thumb of the SI in the hemisphere contralateral to the stimulation. The ECD corresponding to the site on the thumb was in a region superior to the ECD locations corresponding to the sites on the face (shown by black closed circles in Fig. 7).

**DISCUSSION**

In this study, the precise map was investigated on the face component of somatosensory cortices in healthy subjects. ECDs of the early component of SEF with peaks of 20–30 ms aligned along SI alone in the hemisphere contralateral to the stimulation site (shown in Figs. 5A–F and 7A–D). In the lip area of SI, the ECD of 20 ms in SEF latency was also identified only in the hemisphere contralateral to the stimulated side [18]. A distinct separation was found between the ECDs representing sites on the face and the thumb in the SI of the contralateral hemisphere (shown in Fig. 7A–D).

In a 3-dimensional brain image constructed by use of the MRI of each subject, five sites of the face area in SI at the contralateral hemisphere were compatible with the conventional arrangement of homunculus in one subject (shown in Fig. 7C). The remaining subjects showed variations in the arrangement (three examples are shown in Fig. 7A, B, and D). The ECDs of the early component were probably generated in area 3b of the SI [7].

The ECDs with peaks of the M80 component were identified in bilateral SII (shown in Fig. 6A1–B1 and A2–A6). It has been known that SII in humans has a bilateral function. In general, the receptive fields ranked in lower–upper direction: lower lip–upper lip–thumb [7]. In their results, there were large interindividual differences [7].

The arrangement of the thalamic fibers in SI is such that the parts of the body are represented in order along the postcentral gyrus, with the legs on top and the face at the foot of the gyrus. Not only is there a detailed localization of the fibers from the various parts of the body in the central gyrus, but the size of the cortical area receiving impulses from a particular part of the body is also proportionate to the number of receptors. The cortical areas for sensation from the hand and the lower face area, including the lip, are very large [19]. The stimulation sites for this study were skin areas of the upper and lower lips and around them, primarily innervated by the infraorbital and mental nerves. The cutaneous pressure thresholds for the sites were consistently low among the face (see MATERIALS AND METHODS, Posnick et al. [20]) and approximated thresholds for the index fingertip [20]. Studies of the sensory area emphasize the very discrete nature of the point-for-point localization of peripheral areas in the cortex.

In this study, variations in the arrangements of face areas in the contralateral SI were observed in six subjects (examples are shown in Fig. 7A, B, and D). On the cortical plasticity, more recent studies suggest that...
SI processes may be modulated by context, in particular the general perceptual experience of the body provided by other senses such as vision [21]. Higher cortical regions that underlie tactile perception also provide several top-down influences that modulate perception; so the brain constructs our sense of the body instead of passively receiving peripheral inputs. Within the flexibility of the local neuronal network in SI, which ensures that the brain’s map of the body is not fixed; each neuron may have connections required to represent touch over a wide region of the body [21]. The amputation of a single digit from a monkey led to rapid changes in the SI map: Within minutes, those neurons that represented the amputated digit responded to touch on adjacent parts of the hand [22]. These wider connections must be latent, but inhibited by a dominant input from the amputated digit. These results suggest a metaphor of different parts of the body surface competing with each other to “own” cortical representation. By biasing this competition, the brain’s representation of the body can be rapidly and functionally changed [21]. Findings shown in Fig. 7A, B, and D can be explained by this mechanism. The data of Yang et al. are proximate to the findings within SI of owl monkeys, that the lower facial areas are situated closer to the fingers in comparison to the upper facial regions [8–10]. Similarly, Servos et al. showed by using fMRI that the face component of the somatosensory homunculus was actually upside down instead of upside up along the central sulcus of the healthy human brain [4]. A change of homunculus has also occurred because of the deafferentation of a limb after amputation [11, 12]. The relative short delay between amputation and phantom experience is usually less than 24 h [23]. Therefore this invasion of neuronal connections does not result from the sprouting of new connections. A more plausible explanation is that existing asleep synapses between neighboring cortical areas are unmasked after a large extent of sensory loss. Huse et al. used a protocol of asynchronous coactivation adapted from the protocol of Zepka et al. to treat upper-limb amputees having phantom limb pain [24, 25]. Somatosensory cortical representations of the face and the stump were asynchronously tactile-stimulated 60 min/d for 14 d to reverse cortical reorganization and to separate the representations of the face and the stump. After this 2-week treatment program, a reduction of phantom limb pain paralleled by segregation of the representations of the stimulated body parts was observed [24].

Training and learning induced powerful cortical reorganizational changes, which are referred to as use-or experience-dependent plasticity. Using MEG, Godde et al. investigated how a rapid reorganization of human somatosensory cortex induced by tactile stimulation leads to an improvement of spatial discrimination performance [26]. Plastic changes were induced by several hours of tactile coactivation in separated receptive fields on the right index finger. A 20% decrease in spatial two-point discrimination thresholds was accompanied by a dipole shift (by an expansion of the respective cortical representation) in a mediolateral direction along the central sulcus. The reorganization of SI induced by purely passive tactile coactivation was sufficient to improve tactile discrimination performance without training, attention, or reinforcement [26]. For this type of plasticity, the importance of synchronicity of cortical neuronal activity is imposed.

The face areas shown above in the sensory homunculus of humans receive large impulses from the parts of the lip associated with speech and other oral functions. In this manner, the subjects produce constantly expressional differences on their faces, depending on life and social environments. The crucial stimulus parameters associated with use must be hypothesized to support the thought as a result of purely passive tactile coactivation. The face area reorganization of SI as shown in Fig. 7A, B, and D is possible to be involved in the latent local wider connection and use-dependent cortex plasticity of the individual. Other reasons may also exist. For example, such an interindividual difference may be inborn or innate characteristics, or a limitation of spatial resolution of MEG might cause such a large interindividual difference. The inborn or innate characteristics associated with such an interindividual difference may be contributed by proprioceptive inputs. The analogous context effects of noninformative vision on proprioception and motor control have also been reported. The neural mechanism underlying this influence could involve multimodal representations in the parietal cortex biasing local networks within SI. The sense of touch embodies both the exteroceptive and the proprioceptive functions within a single sensory system. The interaction among such inputs of touch, proprioception, and vision (described above) would seem essential to produce a single coherent sense of our own body, as opposed to a series of fractionated and independent sensory maps [21].
REFERENCES