Differentiation of receptive fields in the sensory cortex following stimulation of various nerves of the lower limb in humans: a magnetoencephalographic study

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The authors investigated magnetoencephalography following stimulation of the posterior tibial (PT) and sural (SU) nerves at the ankle, the peroneal nerve (PE) at the knee, and the femoral nerve (FE) overlying the inguinal ligament in seven normal subjects (14 limbs) and confirmed its usefulness in clarifying the detailed differentiation of the receptive fields in the lower limb area of the primary sensory cortex in humans. The results were summarized as follows: 1) the equivalent current dipoles (ECDs) estimated by the magnetic fields following stimulation of the PT and SU were located very close to each other, along the interhemispheric fissure in all 14 limbs. They were directed horizontally to the hemisphere ipsilateral to the stimulated nerve. 2) The ECD following stimulation of the PE was clearly different from that seen in the other nerves, in terms of the location and/or direction, in all 14 limbs. The ECDs of 14 limbs were classified into two types according to the distance of ECD location between PT and PE; Type 1 (> 1 cm, nine limbs) and Type 2 (< 1 cm, five limbs). The ECD following PE stimulation was located on the crown of the postcentral gyrus or at the edge of the interhemispheric fissure in Type 1 and was close to the ECDs following PT and SU stimulation along the interhemispheric fissure in Type 2. 3) The ECD following FE stimulation was located along the interhemispheric fissure in all 14 limbs as for PT and SU. Its location was slightly but significantly higher than that of PT and SU in Type 1 and was close to ECDs following PT and SU stimulation in Type 2. The present findings indicated that approximately 65% (nine of 14) of the limbs showed the particular receptive fields compatible with the homunculus. Large inter- and the intraindividual (left–right) differences found in the present study indicated a significant anatomical variation in the area of the lower limb in the sensory cortex of humans.

KEY WORDS • somatosensory evoked potential • magnetoencephalography • posterior tibial nerve • sural nerve • peroneal nerve • femoral nerve

Receptive fields of the lower limb in the primary sensory cortex in humans are located in the bank along the interhemispheric fissure and the crown of the postcentral gyrus. The homunculus that Penfield and Rasmussen reported is well known, but inter- and intraindividual (left–right) differences may be present. In comparison with the somatosensory evoked potentials (SEPs) following stimulation of the upper limb, the generating mechanisms and generator sources of SEPs following stimulation of the lower limb have not been elucidated in detail, mainly due to anatomical problems. There have been several reports of scalp topography of SEPs following stimulation of the lower limb. Most responses are largest near the foot area of the primary sensory cortex following stimulation of any nerves of the lower limb, but the detailed locations of their generator sources could not be clarified by using SEPs. Compared with electroencephalograms (EEGs), magnetoencephalograms (MEGs) have several theoretical advantages in localizing brain dipoles because of fewer effects from cerebrospinal fluid, skull, and skin. Therefore, the objective of this study was to clarify the differentiation of the receptive fields of various nerves of the lower limb for a reappraisal of the homunculus by recording MEGs. To our knowledge, this is the first noninvasive study to show the detailed receptive fields in the lower limb area of the primary sensory cortex in humans.

Clinical Material and Methods

Study Population

Seven normal volunteers (two women and five men) with a mean age of 32 years (range 28–41 years) and a mean height of 168 cm (range 151–178 cm) were studied. Informed consent was obtained from all participants prior to the study.
Intensity and Location of Stimulus

The electrical stimulus was a constant-voltage square-wave pulse delivered transcutaneously to four nerves of each lower limb unilaterally: the posterior tibial nerve (PT) at the ankle, the peroneal nerve (PE) at the knee, and the femoral nerve (FE) overlying the inguinal ligament, at a rate of 1 pulse per second. Therefore, somatosensory-evoked fields (SEFs) were recorded following stimulation of eight different nerves in each volunteer and the differences among these measurements were examined in 14 limbs of seven volunteers. The stimulus was monophasic and its intensity for the PT, PE, and FE stimulation was decided individually to obtain sufficient stimulus strength to produce a definite movement of the corresponding muscles. The intensity of the SU stimulation was matched to give a sensation as strong as that of the PT stimulation. The stimulus duration was 3 msec. The recordings were made in a magnetically shielded room with the participants seated with their eyes open.

Biomagnetometer Arrangement and Analysis Time

The SEFs were measured with dual 37-channel biomagnetometers (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. Each device was 144 mm in diameter and its radius was 20 mm in diameter and the distance between the centers of each coil was 22 mm. Each coil was connected to a superconducting quantum interference device.

The biomagnetometers were centered around the vertex (Cz in the International 10–20 System) in each participant. Responses were filtered by a 0.1- to 200-Hz bandpass and digitized at a sampling rate of 1024 Hz. The analysis time was 100 msec before and 400 msec after the stimulus, and...
Receptive fields to lower limb stimulation

### TABLE 3
Amplitude of each recognizable component to each nerve stimulation in the lower limbs of seven normal volunteers

<table>
<thead>
<tr>
<th>Nerve Stimulated</th>
<th>Lt Limb (7 humans)</th>
<th>Rt Limb (7 humans)</th>
<th>Total (14 limbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>posterior tibial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>361.4 ± 106.0</td>
<td>318.6 ± 82.7</td>
<td>340.0 ± 94.0</td>
</tr>
<tr>
<td>2M</td>
<td>230.0 ± 71.9</td>
<td>203.6 ± 64.3</td>
<td>216.8 ± 67.0</td>
</tr>
<tr>
<td>3M</td>
<td>215.0 ± 81.7</td>
<td>235.6 ± 77.0</td>
<td>234.3 ± 78.7</td>
</tr>
<tr>
<td>4M</td>
<td>317.1 ± 114.7</td>
<td>253.6 ± 143.1</td>
<td>285.4 ± 128.9</td>
</tr>
<tr>
<td>sural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>215.7 ± 44.9</td>
<td>210.0 ± 81.4</td>
<td>212.9 ± 63.2</td>
</tr>
<tr>
<td>2M</td>
<td>190.7 ± 127.1</td>
<td>232.1 ± 66.7</td>
<td>211.4 ± 99.9</td>
</tr>
<tr>
<td>3M</td>
<td>179.3 ± 34.5</td>
<td>165.0 ± 42.5</td>
<td>172.1 ± 37.9</td>
</tr>
<tr>
<td>4M</td>
<td>202.1 ± 71.0</td>
<td>197.9 ± 81.7</td>
<td>200.0 ± 73.6</td>
</tr>
</tbody>
</table>

| femoral          |                   |                   |                 |
| 1M               | 167.9 ± 62.8      | 160.0 ± 68.8      | 163.9 ± 63.4    |
| 2M               | 195.7 ± 95.0      | 218.6 ± 104.3     | 207.1 ± 96.6    |
| 3M               | 188.6 ± 90.0      | 156.4 ± 33.3      | 172.5 ± 67.1    |
| 4M               | 199.3 ± 47.6      | 205.0 ± 48.1      | 202.1 ± 46.1    |

| peroneal         |                   |                   |                 |
| 1M               | 133.6 ± 54.8      | 158.6 ± 58.6      | 146.1 ± 56.0    |
| 2M               | 141.4 ± 71.7      | 177.1 ± 74.2      | 159.3 ± 72.5    |
| 3M               | 152.1 ± 50.9      | 140.0 ± 61.1      | 146.1 ± 54.4    |
| 4M               | 190.7 ± 91.5      | 203.6 ± 55.1      | 197.1 ± 72.9    |

* Measures are given as mean ± standard deviation. Abbreviation: M = magnetic field.

The mean prestimulus period was subtracted to compensate for the DC offsets. An average of 200 or 300 trials comprised each session, and at least two averages were obtained to ensure reproducibility.

### Correlation and Goodness of Fit

A spherical model was fitted to the digitized head shape of each subject, and the location (x, y, and z positions), orientation, and amplitude of a best-fitting single equivalent current dipole (ECD) was estimated for each time point. 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. Correlation and goodness of fit were calculated. The value of the former was the correlation between recorded measurements and the values expected from the ECD estimate. It was a report of how closely the measured values corresponded to the theoretically expected values. Correlations between the theoretical field generated by the model and the observed field were used to estimate the goodness of fit of the model parameters. To ensure a strict criterion for dipole fitting, only estimates with a correlation and/or goodness of fit above 0.98 were analyzed.

### Statistical Analysis

Statistical analysis of the difference of the latency and amplitude and ECD location of each component was performed by a paired t-test, and a probability of less than 0.02 was considered to be significant. As all components of SEFs showed polarity reversal, the amplitude of each component was measured by adding the maximum amplitude of the outgoing and ingoing magnetic fields.

### Magnetic resonance (MR) images

Magnetic resonance (MR) images were obtained using a 1.0 tesla system. Coronal and axial T$_1$-weighted images were obtained.
TABLE 6  
Distance of ECDs between each nerve stimulation in Type 1 and Type 2 limbs of seven normal volunteers*†

<table>
<thead>
<tr>
<th>Nerve Stimulated†</th>
<th>Type 1 (9 limbs)</th>
<th>Type 2 (5 limbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT → SU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>0.98 ± 0.52</td>
<td>1.10 ± 0.71</td>
</tr>
<tr>
<td>2M</td>
<td>1.32 ± 0.64</td>
<td>1.33 ± 0.82</td>
</tr>
<tr>
<td>3M</td>
<td>1.97 ± 0.57</td>
<td>1.51 ± 0.82</td>
</tr>
<tr>
<td>4M</td>
<td>1.32 ± 0.78</td>
<td>1.64 ± 0.58</td>
</tr>
<tr>
<td>PT → PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>0.75 ± 0.53</td>
<td>1.43 ± 0.63</td>
</tr>
<tr>
<td>2M</td>
<td>1.58 ± 0.88</td>
<td>2.34 ± 1.46</td>
</tr>
<tr>
<td>3M</td>
<td>1.60 ± 1.07</td>
<td>2.35 ± 0.52</td>
</tr>
<tr>
<td>4M</td>
<td>1.47 ± 1.94</td>
<td>2.44 ± 0.97</td>
</tr>
<tr>
<td>SU → PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>1.12 ± 0.48</td>
<td>1.47 ± 0.75</td>
</tr>
<tr>
<td>2M</td>
<td>1.82 ± 0.58</td>
<td>1.63 ± 0.34</td>
</tr>
<tr>
<td>3M</td>
<td>2.15 ± 0.29</td>
<td>2.08 ± 0.62</td>
</tr>
<tr>
<td>4M</td>
<td>1.44 ± 0.50</td>
<td>2.36 ± 0.44</td>
</tr>
<tr>
<td>SU → FE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>1.93 ± 0.45</td>
<td>1.35 ± 0.84</td>
</tr>
<tr>
<td>2M</td>
<td>1.98 ± 0.59</td>
<td>2.25 ± 0.60</td>
</tr>
<tr>
<td>3M</td>
<td>1.34 ± 0.96</td>
<td>2.22 ± 0.73</td>
</tr>
<tr>
<td>4M</td>
<td>1.85 ± 0.81</td>
<td>1.87 ± 0.65</td>
</tr>
<tr>
<td>PE → FE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1M</td>
<td>1.39 ± 0.54</td>
<td>1.64 ± 0.89</td>
</tr>
<tr>
<td>2M</td>
<td>1.65 ± 1.18</td>
<td>2.59 ± 0.67</td>
</tr>
<tr>
<td>3M</td>
<td>1.75 ± 1.25</td>
<td>3.18 ± 1.19</td>
</tr>
<tr>
<td>4M</td>
<td>1.45 ± 0.95</td>
<td>3.00 ± 0.71</td>
</tr>
</tbody>
</table>

* ECDs = equivalent current dipoles; FE = femoral; M = magnetic field; PE = peroneal; PT = posterior tibial; SU = sural.
† A significant difference was found by paired t-test in Type 1 nerves (ECD distance > 1 cm) between the following. In 1M: PT → SU and PT → FE, p < 0.01; PT → SU and SU → FE, p < 0.01; PT → PE and PT → FE, p < 0.01; PT → PE and SU → FE, p < 0.01; PT → PE and SU → PE, p < 0.01. In 2M: PT → SU and SU → FE, p < 0.01; PT → SU and SU → PE, p < 0.01; SU → PE and SU → FE, p < 0.01; SU → PE and SU → FE, p < 0.01. In 3M: PT → SU and SU → FE, p < 0.01; PT → SU and SU → PE, p < 0.01. In 4M: PT → SU and SU → PE, p < 0.001. No significant difference was found in Type 2 nerves (ECD distance < 1 cm).  

with a contiguous 3-mm slice thickness were used for overlays with ECD sources determined by magnetoencephalography. The nasion and bilateral preauricular points were visualized on MR images by placement of high-contrast cod liver oil capsules that were 3 mm in diameter.

Results

Deflections less than 100 msec in latency that were recorded following stimulation of each nerve were generally similar in waveform, but the peak latency was different, mainly due to the difference in the stimulus site and stimulated fibers. Therefore, we named each recognizable component 1M, 2M, 3M, and 4M for the first, second, third and fourth magnetic field, respectively (Fig. 1); their peak latency was approximately 37, 47, 58, and 76 msec, respectively, after PT stimulation. As described in detail previously,10 independent minor deflection, with a latency approximately 3 msec longer than the 1M, was also clearly identified in approximately half of the participants. They were marked in Fig. 1 by an asterisk in the waveform following stimulation of PT and SU. However, to avoid confusion, only major deflections were analyzed in the present study.

Peak Latency of 1M

The peak latency of the initial component, 1M, was the shortest following FE stimulation, then latencies were prolonged following PE, PT and SU stimulation, respectively (Table 1). Differences in peak latencies among each of the eight nerve stimulations were statistically significant (Table 2). The amplitude of the 1M was the largest after PT stimulation; it was reduced following SU, PE, and FE stimulation, respectively. The difference in amplitude was significantly larger between PT stimulation and others (p < 0.001) (Tables 3 and 4). The amplitude of the 1M after SU stimulation was also significantly larger than that following FE stimulation. The difference in the 1M amplitude between PE and FE stimulation was not significant.
Receptive fields to lower limb stimulation

**Peak Latencies of 2M, 3M, and 4M**

The peak latencies and amplitudes of the 2M, 3M, and 4M components showed the same tendency; however the interindividual difference was large (Tables 1 and 3) and the statistical significance was gradually reduced (Tables 2 and 4). There was a small left–right difference in the peak latency and amplitude (Tables 1 and 3).

**Estimated ECDs**

The ECD of each deflection was estimated to be every 0.96 msec. The estimated ECD overlapped on MR imaging. All estimated ECDs of the 1M, 2M, 3M, and 4M components following each nerve stimulation were located on the hemisphere contralateral to the stimulated limbs. However, the location of the ECD in the late-latency components, particularly 3M and 4M, was variable and outside the primary sensory cortex in studies of some limbs. This finding was probably due to the mixture of activities in various areas for such later components. In addition, we determined the differentiation of receptive fields following stimulation of various nerves. Therefore, we focused on the results of the 1M component in the present study.

The ECD following the PT, SU, and PE stimulation was located along the interhemispheric fissure in all 14 limbs. By contrast, the location of ECD after the FE stimulation was variable; it was found on the crown of the postcentral gyrus, at the edge of the interhemispheric fissure or along the interhemispheric fissure. The distance of the ECD location of each component between each nerve was calculated (Table 5). The ECD location after PT stimulation was very close to that following SU and PE stimulation; the mean difference was approximately 1 cm. The difference of ECD location between FE stimulation and the three other nerve stimulations was relatively large. For example, the mean of the distance of ECD between FE and SU was 1.71 cm, approximately 0.7 cm longer than that between PT and SU (p < 0.001). By considering the isocontour map and the distance of ECD of the 1M following each nerve stimulation, we classified the results of tests of 14 limbs into two types (Table 6).

**Results for Type 1**

In Type 1 (nine limbs), the distance of ECD between FE and PT stimulation was longer than 1 cm. The ECDs of the PT and SU stimulation were close to each other, but that of the FE stimulation was clearly isolated. The distance of ECDs between PT and FE was significantly (p < 0.01) longer than that between PT and SU in Type 1 (Table 6). The ECD after PE stimulation was along the interhemispheric fissure in all 14 limbs as for PT and SU, but its location was higher to some degree than that of PT and SU in Type 1. The isocontour maps following PT, SU, and PE stimulation were similar, in terms of the position of the maximal point of the ingoing and outgoing flux and the zero-point line, but that following the FE stimulation was much different (Fig. 2). The ECD of the FE was positioned on the crown of the postcentral gyrus or at the edge of the interhemispheric fissure and was directed posteriorly and inferiorly (Fig. 3). By contrast, the direction of the ECDs following stimulation of the other three nerves located along the interhemispheric fissure was mainly...
dotted line and the thin line indicate the ingoing and outgoing flux, respectively. The dotted line and the thin line indicate the ingoing and outgoing flux, respectively. The center of the map was around the vertex (Cz of the International 10–20 System). Magnetic fields following posterior tibial and sural nerve stimulation were similar. However, those following peroneal and femoral nerve stimulation were very different from those following stimulation of the posterior tibial and sural nerves. Notice the inverted magnetic fields between peroneal and femoral nerve stimulation. A = anterior; L = left; P = posterior; R = right.

horizontal to the hemisphere, ipsilateral to the stimulated nerve (Fig. 3). The distance of the ECD between PT and PE stimulation was variable; for example it was sometimes small (as shown in Fig. 3), but the distance of the ECDs between PE and FE was significantly shorter (p < 0.01) than that between PT and FE in Type 1 (Table 6).

Results for Type 2

In Type 2 (five limbs), the distance of the ECD between FE and PT stimulation was less than 1 cm, and the ECDs of each nerve stimulation were located relatively close to each other. Therefore, no significant difference in the distance of the ECD was identified in Type 2. However, the direction of the ECDs of the FE and PE was different from that of PT and SU in five and two limbs, respectively. This difference was clearly recognized on the isocontour map (Fig. 4) and the axial plane of the MR image (Fig. 5).

With regard to the intraindividual (left–right) difference, Type 1 was found in two volunteers after each limb stimulation, and the remaining five participants showed Type 1 after one limb stimulation and Type 2 after stimulation of the other limb.

These findings are summarized as follows: 1) the magnetic fields caused by stimulation of PT and SU were similar in the results of all 14 limbs; 2) the location of the ECDs following PE stimulation was between that of PT and SU and that of FE in Type 1, and the direction of the ECD after PE stimulation was clearly different from that of PT and SU in two limbs of Type 2; 3) the ECD after FE stimulation was clearly different from that of others, in terms of the location and/or direction, in the results of tests of all 14 limbs; and 4) inter- and intraindividual differences were frequently identified.

Discussion

Unlike the hand area of the primary sensory cortex, the area of the lower limb in primary sensory cortex is located mainly in the bank along the interhemispheric fissure and the crown of the postcentral gyrus. Therefore, it is very difficult to determine the receptive fields following separate stimulation of various nerves of the lower limb using noninvasive studies, which consist mainly of averaged EEG (SEP) recordings. When SEPs are recorded after stimulation of PT, the initial main response (the P37 corresponding to the 1M in the present study) appeared to be recorded in the hemisphere ipsilateral to the stimulated nerve, because the generator dipole was directed horizontally to that hemisphere. This particular finding is called “paradoxical lateralization,” a term that complicates its interpretation.

The receptive fields have been examined by analyzing the scalp topography of SEPs. Wang, et al.,25 and Matsubara, et al.,15 reported that the scalp topography of SEPs after FE stimulation was different from that following PT stimulation. Wang, et al.,22 studied mapping after FE stimulation in 10 volunteers and found that the initial component was maximal on the midline in all participants. Its scalp distribution was clearly contralateral in six and restricted to the midline or slightly ipsilateral in four participants. In other words, SEPs following stimulation of FE generally did not show the paradoxical lateralization. However, even using such a method, it was impossible to determine the generator site in detail from the EEG recording. Therefore, the MEG recording shown in the present study was very useful in solving this important problem. The SEFs have been analyzed following lower limb stimulation,3,5,6,10,13,16 but they have been studied only after stimulation of nerves at the ankle. Therefore, this is the first systematic report on the differentiation of the receptive fields of the lower limb area of the primary sensory cortex by stimulation of many nerves at various sites.

The middle-latency deflections 2M, 3M, and 4M, were considered to be generated in the primary sensory cortex like the 1M, but the location and direction of their ECDs were relatively variable and unstable as compared with those of the 1M, probably because of the effects of activity from surrounding areas. Therefore, we will primarily discuss the 1M.

The ECDs following stimulation of PT and the SU at the ankle were estimated to be located around the middle of the bank of the interhemispheric fissure contralateral to the stimulated nerve and to be fundamentally directed to the hemisphere ipsilateral to the stimulated nerve. The
paradoxical lateralization can be clearly accounted for by
the position and direction of the ECDs of these nerves.
The present finding was generally compatible with previ-
ous studies.3,6,10,13 The mean difference of the ECD posi-
tion between the PT and SU was approximately 1 cm.
Therefore, the receptive fields for these two nerves were
considered to be very close or overlapping. Huttunen, et
al.,6 reported that the mean difference in ECD location of
those two nerves was 1.1 cm, which was very similar to
our present findings.
The ECD location following stimulation of the PE at
the knee was between that following PT and SU stimula-
tion and that following FE stimulation in Type 1. This
finding might indicate that the fields receptive to the ankle
and knee stimulation were clearly separated in such limbs
as shown in the homunculus. In Type 2, ECDs were close
to those following stimulation of PT and SU at the ankle,
but their direction was apparently different from that of
PT and SU in two limbs. The results in these two limbs
might indicate the independence of the receptive fields to
PE. The amplitude of SEFs following PE stimulation was
smaller than that of the PT, although its motor threshold
was much lower than that of the latter. This finding may
have been due to a large movement of the leg produced by
stimulation of the PE, because such movements caused
reduction in amplitude of the cortical responses, named
“gating” effects.19
The ECD following FE stimulation was located on the
crown of the postcentral gyrus or at the edge of the inter-
hemispheric fissure in nine of the 14 limbs studied (Type
1), and the distance between ECD locations of FE and
other nerves was significantly large. This indicated that
differentiation of the receptive fields in the area of the
lower limb of the sensory cortex was compatible with
the homunculus in approximately 65% (nine of 15) of
the limbs. The ECD following FE stimulation was located
along the interhemispheric fissure in five other limbs.
However, even when the FE was close to the ECD fol-
lowing stimulation of the other nerves, its direction was
apparently different from theirs. This finding indicated the
definite independence of the receptive fields following FE
stimulation and could account for the fact that EEG map-
ning following FE stimulation was largely different from
stimulation of the other nerves at the ankle.15,22

Conclusions
Magnetoencephalography was a very useful noninva-
sive method for detecting the differentiation of the recep-
tive fields of the lower limb in the primary sensory cortex
in humans. The present findings indicate that approxi-
mately 65% of the limbs show the particular receptive
fields compatible with the homunculus. Even in the other
35%, the magnetic fields showed an apparent differentia-
tion following stimulation of the PE and/or FE from those
following the PT and SU. Interindividual and intraindi-
vidual differences were recognized. This is probably due
to the anatomical variation of the area of the lower limb in
the primary sensory cortex in humans.

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