
Handedness and asymmetry of hand representation in human motor cortex was determined in left- and right-handed people with whole-head magnetoencephalography. Different movements were found to be represented by spatially segregated dipolar sources in primary motor cortex. The spatial arrangement of neuronal sources for digit and wrist movements was nonsomatotopic and varied greatly between subjects. As an estimator of hand area size in primary motor cortex, we determined the smallest cuboid volume enclosing the five dipole sources within the left and right hemisphere of each subject. Interhemispheric comparison revealed a significant increase of this volume in primary motor cortex opposite the preferred hand. This asymmetry was due to a greater spatial segregation of neuronal dipole generators subserving different hand and finger actions in the dominant hemisphere. Mean Euclidean distances between dipole sources for different movements were 10.7 ± 3.5 mm in the dominant and 9.4 ± 3.5 mm in the nondominant hemisphere (mean ± SD; P = 0.01, two-tailed t-test). The expansion of hand representation in primary motor cortex could not simply be attributed to a greater number of pyramidal cells devoted to each particular movement as inferred from current source amplitudes. The degree of hemispheric asymmetry of hand area size in the primary motor cortex was correlated highly with the asymmetry of hand performance in a standardized handedness test (r = –0.76, P < 0.01). These results demonstrate for the first time a biological correlate of handedness in human motor cortex. The expansion of hand motor cortex in the dominant hemisphere may provide extra space for the cortical encoding of a greater motor skill repertoire of the preferred hand.

INTRODUCTION

Hand preference is the most prominent behavioral indicator for hemispheric specialization in humans. About 90% of humans are right-handed and therefore left-hemisphere dominant for manual skills. The neurobiological correlate of handedness, however, is still a matter of debate. Some investigators have attributed handedness to a possible hemispheric asymmetry of cortical association areas controlling the cognitive-motor requirements of skilled movements (Haaland and Harington 1996). Others have argued that hand preference should be reflected by functional or structural asymmetries of the primary motor cortex and descending pathways (Amunts et al. 1996; Nathan et al. 1990; White et al. 1997). But conclusive evidence has not been found for either view. Recent studies have revealed conflicting results about structural hemispheric differences at the level of primary motor cortex and pyramidal tract (Amunts et al. 1996; Nathan et al. 1990; White et al. 1997). The failure to detect consistent anatomic asymmetries in these studies may be due to the lack of historical information about handedness in postmortem studies and the inaccuracy of delineating hand function in these structures based on anatomic landmarks.

Functional neuroimaging techniques now exist to measure the cortical representation of skilled movements noninvasively with high spatial accuracy. Here we report in vivo measurements of hand movement representation in left- and right-handed subjects using whole-head magnetoencephalography (MEG). We assessed possible functional asymmetries of primary motor cortex in the context of individual hand preference and performance.

METHODS

Movement-related neuromagnetic fields were recorded with the 122-channel Neuromag MEG system in 10 healthy, male subjects (5 right-handed subjects, age: 34.0 ± 6.1 yr; 5 left-handed subjects, age: 28.2 ± 2.5 yr) for five simple finger and hand movements: flexion of the distal phalanx of the thumb, index finger abduction, index finger extension, little finger abduction, and wrist flexion. All subjects showed consistent hand preference in everyday activities as assessed by a handedness questionnaire (Witelson 1989) and compatible asymmetry of hand performance in a standardized hand dominance test (Jäncke 1996). Surface electromyograms (EMG) of the musculi extensor indicis (ei), interosseus dorsalis 1 (id1), flexor pollicis longus (fpl), abductor digitii minimi (adm), and flexor carpi ulnaris (fcu), vertical electrooculogram (EOG), and neuromagnetic activity (band-pass 0.01–100 Hz, sample rate 512 Hz) were recorded simultaneously. The subjects were seated inside a magnetically shielded room in a nonmagnetic chair with both forearms supported by an armrest. For index abduction, index flexion, thumb flexion, and little finger abduction both hands were resting on the volar side with all fingers outstretched on the arm support. For wrist flexions, both hands were supinated and lying on the dorsal side with all fingers passively flexed and the forearm fully supported. These positions ensured a minimal muscular effort for maintaining hand posture throughout a trial. Subjects were instructed to perform brisk isolated movements from complete relaxation approximately once every 4 s, alternating between hands. No pacing signal was provided. Subjects were free in choosing the starting hand. Feedback about performance based on surface EMG was given during a short initial training period. By visual inspection, the examiner moreover controlled for involuntary cocontractions of other limb parts and corrected motor performance during the training period if necessary. Each subject participated in three recording sessions on different days during a 3-wk period in which the sequence of the five movement conditions was randomized. During each recording session, a total of 100–120 movements was collected for each hand and condition. We made sure that each subject kept the hand posture constant for the individual move-
For source localization, a spherical head model was fitted to the individual magnetic resonance image (MRI; Siemens-Magnetom 1.5 Tesla, T1–3D-Flash sequence) after alignment of the MRI and MEG coordinate system based on fiducial point markers. Software tools provided by Neuromag were used for the segmentation of MR images and computation of three-dimensional surface renderings.

To quantify hemispheric asymmetries in the spatial extent of hand representation in primary motor cortex, we computed the smallest cuboid volume containing all contralateral dipole sources of the investigated movements in either hemisphere. Each side of the cuboid was defined by the maximal Euclidean distance between dipole sources within each spatial direction of the MEG coordinate system. A hemispheric asymmetry index (R/L) then was calculated for each subject expressing the proportional difference of hand area volume in the left (L) and right hemisphere (R). Negative values indicate left and positive values indicate right hemisphere dominance.

In a second analytic approach, we also investigated the functional activation of ipsilateral motor cortex to determine the degree of hemispheric asymmetry of motor output activity during unilateral hand movements. The contribution of ipsilateral motor cortex activity to each movement was investigated using the following approach: after calculating the optimal source locations for the contralateral motor field separately for left and right hand performance, as outlined above, both dipole sources were introduced into a time-varying two-dipole model. The movement evoked fields then were reanalyzed including the full set of 122 MEG channels to determine the time course of ipsi- and contralateral source activity. From the activation curves, we computed the time point and amplitude of contralateral peak activity (C) and the maximal amplitude of ipsilateral source activity (I) in a time window of ±20 ms around the contralateral maximum. The asymmetry of motor cortex activation was quantified for each movement by means of a hemispheric asymmetry index (I/C + I). This index varies between 0 for perfectly symmetrical and 1 for strictly unilateral motor cortex activation.

For a review of the standard MEG methods used in the present study, see Hämmäläinen et al. (1993).

RESULTS

The analysis of the surface MEG records for all movements did not reveal any significant effect of dominant versus nondominant hand performance on the parameters EMG burst duration (P = 0.11, two-tailed t-test), EMG interburst duration (P = 0.64, two-tailed t-test), and the area under the curve (AUC) (P = 0.22, two-tailed t-test) in left- and right-handed subjects. These EMG parameters approximately correspond to the kinematic parameters movement time, repetition rate, and contraction force. Table 1 summarizes the results. It therefore was concluded that any hemispheric asymmetries observed in the further analysis were unlikely to be caused by differences in motor performance.

So-called “mirror movements” (simultaneous cocontractions of the nonactive hand) only were observed in one left-handed subject in <5% of all analyzed movements. Mirror movements were therefore not further analyzed quantitatively.

Only in few recordings did dipolar activity emerge over ipsilateral motor cortex (Fig. 2). In most cases, ipsilateral source activity as predicted by the two-dipole model was within the noise level of the recording. The average dipole moment in contralateral motor cortex was 18.4 ± 8.4 nA·m and in ipsilateral motor cortex 6.4 ± 5.0 nA·m. Left- and

FIG. 1. A: movement-related averaged activity exhibits a typical slow magnetic field shift over the contralateral hemisphere culminating in the motor field (MF) before electromyographic (EMG) onset. A typical trace recorded from a left central magnetocencephalographic (MEG) sensor during repetitive right index finger extensions is shown along with the rectified and averaged EMG. B: MF is characterized by a strong dipolar field pattern (contour plot on the left) with a current source in primary motor cortex (brain surface reconstruction on the right).
TABLE 1. Summary of motor parameters

<table>
<thead>
<tr>
<th>Movement Type and Muscle</th>
<th>Burst Duration, s</th>
<th>Interburst Duration, s</th>
<th>Area Under the Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominant hand adm</td>
<td>0.61 ± 0.27</td>
<td>4.36 ± 1.26</td>
<td>0.83 ± 0.40</td>
</tr>
<tr>
<td>ei</td>
<td>0.36 ± 0.14</td>
<td>4.73 ± 1.40</td>
<td>0.34 ± 0.20</td>
</tr>
<tr>
<td>fcu</td>
<td>0.42 ± 0.14</td>
<td>4.96 ± 1.83</td>
<td>0.52 ± 0.22</td>
</tr>
<tr>
<td>fpl</td>
<td>0.32 ± 0.17</td>
<td>4.88 ± 1.52</td>
<td>0.32 ± 0.16</td>
</tr>
<tr>
<td>idl</td>
<td>0.76 ± 0.96</td>
<td>4.46 ± 1.46</td>
<td>1.10 ± 0.51</td>
</tr>
<tr>
<td>Nondominant hand adm</td>
<td>0.57 ± 0.23</td>
<td>4.60 ± 1.22</td>
<td>0.82 ± 0.31</td>
</tr>
<tr>
<td>ei</td>
<td>0.32 ± 0.13</td>
<td>4.71 ± 1.11</td>
<td>0.26 ± 0.14</td>
</tr>
<tr>
<td>fcu</td>
<td>0.42 ± 0.20</td>
<td>4.94 ± 1.56</td>
<td>0.56 ± 0.30</td>
</tr>
<tr>
<td>fpl</td>
<td>0.28 ± 0.14</td>
<td>5.13 ± 1.61</td>
<td>0.31 ± 0.14</td>
</tr>
<tr>
<td>idl</td>
<td>0.52 ± 0.27</td>
<td>4.66 ± 1.36</td>
<td>0.88 ± 0.40</td>
</tr>
</tbody>
</table>

This table summarizes the motor performance parameters obtained from surface electromyographic analysis separated by movement type and muscle: adm (m. abductor digiti minimi), little finger abduction; ei (m. extensor indicis), index extension; fcu (m. flexor carpi ulnaris), wrist flexion; fpl (m. flexor pollicis longus), thumb flexion; and idl (m. interosseus dorsalis 1), index abduction. Values are means ± SD.

right handed subjects did not differ significantly in the hemispheric asymmetry of motor cortical output during unilateral movements as determined by the hemispheric asymmetry index of the dipole moment ($P = 0.73$; two-tailed t-test). Pooled data of both groups, however, revealed a statistical tendency for a stronger activation of ipsilateral motor cortex during movements of the nonpreferred hand (mean asymmetry index $0.49 ± 0.24$) than during movements of the preferred hand (mean asymmetry index $0.54 ± 0.26$; $P = 0.09$; two-tailed t-test).

For each subject, we reconstructed the topographic organization of hand and finger movement representation in primary motor cortex by projecting equivalent current dipole sources of contralateral motor output activity into the individual high resolution magnetic resonance scans of the brain. Motor output maps had a low intraindividual variability in repeated measurements with an SE < 1.5 mm in each spatial direction. Figure 3 shows typical examples of hand motor representation in a right-handed (RH) and a left-handed (LH) subject. These cases illustrate the three characteristic features of motor output organization in M1 that were observed in all subjects. 1) Different digit and wrist movements were represented by spatially segregated neuronal sources in primary motor cortex. Across subjects 87% of all interdipole distances in the nondominant hemisphere and 89% in the dominant hemisphere were significant (95% lower confidence limit of the Euclidean interdipole distance > 0 in repeated measurements). 2) The spatial arrangement of neu-

FIG. 2. Examples of the time course of ipsilateral and contralateral motor cortex activation during the abduction of the right little finger (adm) in 2 right-handed subjects. A: ipsilateral motor cortex activity is apparent in this subject by a weaker dipolar field pattern over the ipsilateral hemisphere. Ipsilateral field pattern appears slightly asymmetric due to the interaction with coinciding activation of the other hemisphere. Time course of the ipsilateral dipole moment is roughly parallel to the contralateral source. A gray bar underlying the activation curves indicates the time window of ±50 ms around the contralateral source maximum, which we used to determine the maximal ipsilateral source activity. B: in the majority of recordings, however, no dipolar field pattern emerged over the ipsilateral hemisphere as demonstrated in this case. Goodness of fit of the 2-dipole model is displayed as a function of time in the lowest chart.
FIG. 3. Equivalent current dipole sources of motor output activity for different hand and finger movements are superimposed onto magnetic resonance image reconstructions of the cerebral cortex of a left- (LH) and right-handed (RH) subject. To better visualize source locations in primary motor cortex, the parietal cortex was removed exposing the posterior bank of precentral gyrus, which normally is buried within the central sulcus. All dipole sources fall into the hand area of primary motor cortex, which is anatomically characterized by a typical knob-like protrusion of the precentral gyrus in the depth of the central sulcus just dorsal to the intersection of the superior frontal sulcus and the precentral sulcus (Yousry et al. 1995). Spatial arrangement of neural sources for digit and wrist movements is nonsomatotopic. Even sources for different movements of the same finger (index extension and index abduction) are significantly separated. Topographic organization of motor output maps varies greatly between both subjects but shows some similarity across hemispheres of each individual. In the right-handed subject, sources of hand and finger movements cover a larger area of cortex in left than in right hemisphere. This asymmetry is reversed in the left-handed subject.

Dipole moment indicates the total strength of cortical polarization, which is proportional to the number of synchronously active pyramidal cells (Lu and Williamson 1991). Comparison of left- and right-handed subjects revealed a significant increase in the size of the hand area in primary motor cortex opposite to the preferred hand. (Fig. 4A). This expansion was due to larger intersource distances in the dominant hemisphere. Mean Euclidean distances between dipole sources for different movements were 10.7 ± 3.5 mm in the dominant and 9.4 ± 3.5 mm in the nondominant hemisphere (P = 0.01, two-tailed t-test). On the basis of the hemispheric asymmetry of hand motor representation in M1, handedness could be correctly predicted for each individual in the present sample (Fig. 4B). Moreover, the degree of hemispheric asymmetry of hand area size in primary motor cortex was correlated significantly (r = −0.76; P < 0.01) with the asymmetry of hand performance in a standardized handedness test (Fig. 4B).

Equivalent current dipole sources reflect the center of gravity of a synchronously active neuronal population. The center of gravity of a neuronal population may shift when a larger cortical surface is being activated. To test this hypothesis, we compared magnetic source amplitudes of contralateral motor output activity in both hemispheres. Given a constant direction of the equivalent current dipole, the dipole moment indicates the total strength of cortical polarization, which is proportional to the number of synchronously active pyramidal cells (Lu and Williamson 1991). Mean dipole moments in the present experiment were 17.5 ± 8.8 nA · m) in the dominant and 19.0 ± 9.7 nA · m) of left- and right-handed subjects (P = 0.15, 2-tailed t-test). Assuming a similar degree of neuronal synchronicity and cellular architecture in both motor cortices of an individual, one may conclude that each particular movement is represented by approximately the same number of pyramidal cells within each hemisphere. This result indicates that the observed larger intersource distances in the dominant hemisphere indeed must be related to a greater spatial segregation of the neuronal clusters representing the investigated elementary movements.

DISCUSSION

Handedness in our study is related to a different topographical organization of movement representation in the dominant and nondominant hemisphere. Our results confirm the nonsomatotopic representation of hand and finger movements in primary motor cortex of human (Sanes et al. 1995) and nonhuman primates (Humphrey 1986; Kwan et al. 1978;
source with a radius of $\sim 8$ mm. Given the observed intersource distances in the present study and the limited number of movements investigated, a significant degree of overlap must indeed be assumed. From a bird’s eye perspective as taken by MEG, our finding of topographically organized neuronal clusters in M1 subserving different hand and finger actions supports the concept of a functional grouping of different muscle representations at a cortical site into synergies that make kinesiological sense (Humphrey 1986; Nudo et al. 1992). In such an arrangement, an overlap of different movement representations would be economical by sharing muscle representations that are used as common elements in different synergies.

Our finding of an enlarged hand representation in motor cortex opposite to the preferred hand is in agreement with previous studies using transcranial magnetic stimulation in humans. Triggs et al. (1994) described a lateralization of motor cortex excitability, which correlated with handedness. Wassermann et al. (1992) investigated the cortical topography of the abductor pollicis brevis muscle using focal magnetic stimulation with a figure-eight-shaped coil and found a larger area of representation in the dominant hemisphere.

A more complete picture of hemispheric differences of motor cortical output maps was obtained by intracortical microstimulation in nonhuman primates (Nudo et al. 1992). Nudo et al. related—in complete agreement with our findings in human subjects—that individual distal forelimb representations in monkeys were highly idiosyncratic but that the representational topography varied less between hemispheres of each animal. Forelimb representation opposite to the preferred hand of the monkey was generally larger in total area and boundary length.

It is reasonable to assume that the expansion of hand motor cortex in the dominant hemisphere provides the neural substrate for a more efficient processing of motor output to the preferred hand. Higher efficiency can be achieved through an increase in the total number of elements in a neural assembly and by a tighter intraregional connectivity.

In agreement with this concept, motor output maps opposite to the preferred hand of the squirrel monkey were not only expanded but also showed a higher degree of fragmentation and spatial complexity (Nudo et al. 1992). Such an increase in spatial complexity may allow for better interaction between neuronal clusters at a cortical site representing muscles that are used in close temporal contiguity. The behavioral consequence of such improved interaction may be a more refined motor skill repertoire of the preferred hand.

In a previous study with functional magnetic resonance imaging (fMRI) Kim et al. (1993) described a hemispheric asymmetry in the functional activation of the human motor cortex during contralateral and ipsilateral finger movements. Whereas right motor cortex was activated mostly during contralateral movements, the left motor cortex was activated substantially during ipsilateral movements in left-handed subjects and even more so in right-handed subjects. These results could not be replicated in the present study using neuromagnetic recordings. We found that in both left- and right-handed subjects the contralateral motor cortex activation was clearly dominant over the ipsilateral motor cortex activation. There was no
significant difference in the degree of ipsilateral motor cortex activity during left- or right-hand movements. Pooled data of both handedness groups revealed a tendency for a stronger contribution of ipsilateral motor cortex to movements of the nonpreferred hand. This finding rather indicates a differential effect of hand preference on the hemispheric asymmetry of motor cortical output than of the hemisphere per se. One may speculate about methodological differences between both studies. While the motor field in MEG most likely reflects the synchronous discharges of pyramidal cells during corticospinal outflow from motor cortex, fMRI provides an indirect measure of neuronal activity and integrates due to its limited time resolution over motor cortical outflow and reafferent activity.

Our study demonstrates that individual variability in hand motor performance covaries with features of hand movement representation in primary motor cortex. It does not explain, however, the mechanism underlying this asymmetry. A short- and long-term plasticity of sensorimotor cortical representations in relation to motor learning and training has been demonstrated in several previous studies (Karni et al. 1995; Pascual-Leone et al. 1994). This use-dependent plasticity has been attributed to changes in cortical excitability through the unmasking of preexisting, but unused, synaptic connections (Pascual-Leone et al. 1994). In contrast, in the present study hand representations in motor cortex were expanded due to a shift in the centers of cortical activation. This finding rather indicates an underlying structural asymmetry such as described by a recent in vivo morphometry study, which found a larger surface of dorsolateral motor representations in the dominant hemisphere of left- and right-handed subjects (Amunts et al. 1996).

It has been suggested that handedness may be determined genetically (Carter-Saltzman 1980). Motor asymmetries already can be observed in neonates, and handedness as defined by preference and performance scores is measurable in children as young as 3 yr (Annett 1970). Recently, twin studies revealed the significance of genetic contributions to individual differences in motor skill acquisition. Both, motor performance and rate of learning of a rotatory pursuit task hand area were found to be highly heritable (Fox et al. 1996). The contribution of environmental factors to the development of hand preference and underlying brain asymmetries thus may be limited. We therefore would like to suggest that the functional asymmetry of hand movement representation in motor cortex, that we have reported here, is more likely a prerequisite than a consequence of handedness.

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