NeuroImage **11,** 697–707 (2000)
doi:10.1006/nimg.2000.0579, available online at http://www.idealibrary.com on IDEAL®

Supplementary Motor Area Activation Preceding Voluntary Movement Is Detectable with a Whole-Scalp Magnetoencephalography System

M. Erdler,* R. Beisteiner,* D. Mayer,* T. Kaindl,* V. Edward,* C. Windischberger,† G. Lindinger,* and L. Deecke*

**Department of Clinical Neurology, General Hospital and University of Vienna and Ludwig Boltzmann Institute for Functional Brain Topography, A-1090 Vienna, Austria; and †NMR-Group–Institute for Medical Physics, University of Vienna, Vienna, Austria*

Received September 3, 1999

Despite the fact that the knowledge about the structure and the function of the supplementary motor area (SMA) is steadily increasing, the role of the SMA in the human brain, e.g., the contribution of the SMA to the Bereitschaftspotential, still remains unclear and controversial. The goal of this study was to contribute further to this discussion by taking advantage of the increased spatial information of a whole-scalp magnetoencephalography (MEG) system enabling us to record the magnetic equivalent of the Bereitschaftspotential 1, the Bereitschaftsfeld 1 (BF 1) or readiness field 1. Five subjects performed a complex, and one subject a simple, finger-tapping task. It was possible to record the BF 1 for all subjects. The first appearance of the BF 1 was in the range of −1.9 to −1.7 s prior to movement onset, except for the subject performing the simple task (−1 s). Analysis of the development of the magnetic field distribution and the channel waveforms showed the beginning of the Bereitschaftsfeld 2 (BF 2) or readiness field 2 at about −0.5 s prior to movement onset. In the time range of BF 1, dipole source analysis localized the source in the SMA only, whereas dipole source analysis containing also the time range of BF 2 resulted in dipole models, including dipoles in the primary motor area. In summary, with a whole-head MEG system, it was possible for the first time to detect SMA activity in healthy subjects with MEG. © 2000 Academic Press

Key Words: **supplementary motor area; magnetoencephalography; Bereitschaftsfeld; readiness field; motor cortex; voluntary movement.**

INTRODUCTION

After the discovery of the readiness potential (Bereitschaftspotential, BP) (Kornhuber and Deecke, 1964, 1965) and the classification of brain potentials preceding voluntary movement into readiness potential, premotion positivity, and motor potential (Deecke *et al.*, 1969, 1976), it became obvious that the vertex maximum of the BP cannot be explained by potentials from both primary motor cortices (MI). Rather, the vertex BP must have its own generator independent of the MI area, the best candidate being the supplementary motor area (SMA; Deecke and Kornhuber, 1978), which was first described by Vogt and Vogt (1919) in the monkey and by Foerster (1936) in humans.

Subsequently, many authors investigated the structure and the function of the SMA with different methods. SMA activity during voluntary hand movement has been shown using regional cerebral blood flow (rCBF) measurements with the gamma camera (Lassen *et al.*, 1978a, b), and using positron emission tomography (PET) (Roland *et al.*, 1980). Referring to these results, some authors have stated that the SMA functions as a "supramotor area" for programming and execution of voluntary movements (Orgogozo and Larsen, 1979; Roland *et al.*, 1980; Goldberg, 1985). However, in view of electrophysiological recordings, the term "premotor area" appears to be sufficient (Deecke, 1987, 1990). On the basis of movement-related electrical potentials, SMA was proposed as the major source of the BP, as well as the region of the brain where functions such as will or intention to move are represented (Barrett *et al.*, 1986; Kornhuber *et al.*, 1989). The finding that performance of bilateral hand movements is impaired in patients with unilateral SMA lesion, and related work, supported the notion that the SMA functions bilaterally and is involved in organizing the timing and coordination of sequential movement (Dick *et al.*, 1986; Deecke *et al.*, 1987; Deecke, 1990; Lang *et al.*, 1991; Deiber *et al.*, 1991; Grafton *et al.*, 1993).

Discussion has also been centered around the question of whether serial or parallel processing of SMA and MI has to be assumed. It has been suggested that the early Bereitschaftspotential (BP 1) reflects preparatory activity of the SMA prior to voluntary movement (Deecke and Kornhuber, 1978; Lang *et al.*, 1991; Knösche *et al.*, 1996) and the late component of the Bereitschaftspotential (also termed NS′) reflects acti-

1053-8119/00 $35.00

vation of the MI following the onset of SMA activity (Barrett *et al.*, 1986). Recently, a sequential order of activity in the SMA preceding activity of MI has also been shown by functional magnetic resonance imaging (fMRI) (Atlas *et al.*, 1996; Wildgruber *et al.*, 1997). In contrast, single-cell recordings have found activation onsets ranging from −2000 ms to the onset of movement within both SMA and MI at the single-cell level (Neafsey *et al.*, 1978; Okana and Tanji, 1987; Thaler *et al.*, 1988).

The conclusion that the SMA is necessary for the organization of upcoming movements in complex motor sequences, especially when they are retrieved from memory, was made when high-frequency repetitive transcranial magnetic stimulation (rTMS) was applied to explore SMA (Gerloff *et al.*, 1997). These data are consistent with the assumption of serial processing between SMA and MI.

Furthermore, the contralateral SMA seems to contribute somewhat more to the initiation of a movement than the ipsilateral one (Deecke, 1987; Ikeda *et al.*, 1992), and it has been shown that SMA activity correlates with movement complexity (Neshige *et al.*, 1988; Lang *et al.*, 1990; Simonetta *et al.*, 1991; Kitamura *et al.*, 1993; Shibasaki *et al.*, 1993). These studies suggest that the SMA is significantly more activated in programming and executing complicated motor performances than in executing simple movements.

Both techniques, PET and fMRI, are able to demonstrate movement-correlated SMA activation (Rao *et al.*, 1993; Boecker *et al.*, 1994; Weiller *et al.*, 1996; Jenkins *et al.*, 1997; Wessel *et al.*, 1997; Atlas *et al.*, 1996; Wildgruber *et al.*, 1997).

On the other hand, some authors have failed to find evidence of SMA activation prior to voluntary movement (Cheyne and Weinberg, 1989, in the MEG; Bötzel *et al.*, 1993; Boecker *et al.*, 1994; Nagamine *et al.*, 1996, when using dipole source analysis). Possible explanations for this failure are that the contribution from the SMA may be too small to be detected from the scalp, that two tangentially oriented dipoles opposing each other may weaken the detectable field (Lang *et al.*, 1991), or that the movement paradigms used were not sufficiently complex. Also, when AC recordings with long time constants rather than DC recordings are used in EEG, SMA activity may escape detection. Despite the fact that so many studies have been performed in the past and the knowledge about the structure and the function of the SMA is steadily increasing, the role of the SMA in the human brain still remains unclear and continues to promote the discussion.

The goal of this study, therefore, was to contribute further to this discussion by taking advantage of an extended area of single sampling of a whole-scalp magnetoencephalography system enabling us to record the magnetic equivalent of the Bereitschaftspotential 1.

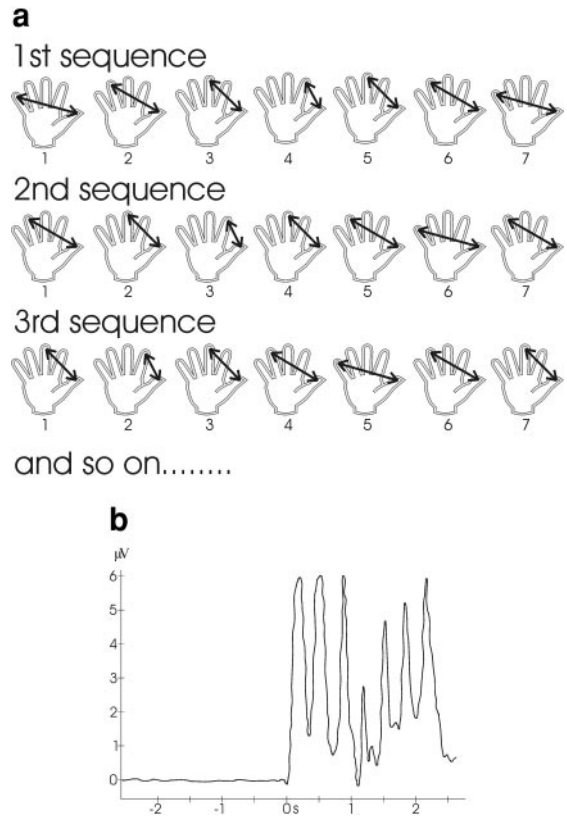

FIG. 1. (a) Paradigm: Subjects had to perform a sequential tapping of the right thumb against the tips of the other fingers. The first sequence was started by tapping against the fifth finger, the second by tapping against the fourth finger, the third by tapping against the third finger, the fourth by tapping against the second finger, the fifth by tapping against the fifth finger, and so on. Note that the sequence always began and ended with the same finger. (b) The time course of the averaged rectified EMG of S4 is shown with the seven taps of the thumb against the tips of the other fingers for one sequence of movement.

MATERIAL AND METHODS

Subjects

Six healthy males with a mean age of 28 years (range 22 to 32 years) participated in the experiment. All were right-handed as measured using a modified Oldfield (1971) Inventory. All subjects gave informed written consent and the study was approved by the Ethical Committee of the University of Vienna. Subjects were paid ATS 350 for participation in the study.

Paradigm

Five of the six subjects performed a sequential tapping of the right thumb against the tips of the other four fingers in the following order: starting the movement by tapping against the fifth finger, then the fourth, third, second, third, fourth, and back to the fifth again (see Fig. 1a). Figure 1b shows the time course of the rectified EMG of the finger-tapping task of subject

4 (S4) with its seven taps. Subjects had to execute the movements and sequences as fast as possible and were asked to be attentive and concentrate on the precise performance of the movement to avoid the movement becoming automatic. After a self-determined pause of at least 5 s, subjects had to start the next trial, but this time beginning with the fourth finger. Each subsequent trial then began with the next finger in the sequence. According to Fig. 1a, the sequence always began and ended with the same finger. Subjects performed a minimum of 300 of such movements split into three blocks with 100 trials each. One of the six subjects (S6) performed a simple single tapping of one finger of the right hand at irregular intervals not shorter than 5 s also 300 times.

Data Acquisition

Data were recorded with a whole-scalp MEG system featuring 143 channels (CTF, Inc., Port Coquitlam, Canada) located in a magnetically shielded room using a software third-order gradiometer (orders of gradiometer can be selected even offline). The noise level of the system is <10 fT rms/$\sqrt{}$Hz. Detection coils are first-order axial gradiometers with a coil diameter of 2 cm and a baseline of 5 cm. The distance from sensor coils to room temperature helmet surface is 1.7 cm. Channels are distributed over the whole cortex with an approximate separation between sensors of 3.2 cm. A sample rate of 125 Hz, a low-pass filter of 40 Hz, and a recording time of 5 s with 2.5 s pretrigger time were used. EMG was recorded from two surface electrodes overlying the abductor pollicis muscle. The onset of the rectified EMG was used as a trigger. Head localization was done before and after each run with a motion tolerance of 0.3 cm, using electrodes over the nasion and the two preauricular points as references.

To avoid artifacts due to head movements the subject's head was wrapped up with a gauze bandage in order to fix the head perfectly into the dewar. Subjects sat in a comfortable chair and were requested not to move during recording and to fix their gaze on a cross in front of them. Subjects were monitored during acquisition via a video camera. In addition, MR images were obtained for all subjects (except S3). These were T1-weighted images showing high anatomic resolution.

Data Processing

After acquisition, data from every trial were visually examined for artifacts such as drifts, muscle activity, eye movements, or head movements. Such artifact-contaminated data were excluded from further analysis. The mean number of remaining artifact-free trials in one dataset was 230 (range 179–270). These artifact-free trials were subsequently averaged for each subject. The baseline period was determined from -2.5 to -2 s. The field distribution of every subject was then examined in 8-ms steps for magnetic fields originating from SMA. The time range in which such a field was recognized was recorded. The onset of the Bereitschaftsfeld 1 (BF 1) and the subdivision into the early component BF 1 and the late component BF 2 was determined both by estimating the development of the field distribution and by exploring the signal time course of selected channels with the largest signal changes located over the activated area (Fig. 4). For every subject, different dipole models were then computed for different time windows of the epoch. Localization of equivalent current dipoles was performed using a least-squares fitting algorithm. Sources were fitted spatiotemporally. One-dipole models, two-dipole models, and three-dipole models were calculated according to "best fit" criteria. These criteria included the physiologic dipole position, judgment of the time course of the source activity of the SMA dipole, whether the source was active over the whole period of fitting, and the error being acceptably low.

After calculation of a chosen dipole model, the time courses of the strengths of the SMA dipole and, for the case of multiple dipole models, also for the MI dipoles were examined for the selected time period.

The computed spherical head models, together with the calculated dipoles, were superimposed on anatomical MRIs (except for S3). For S3, the judgment about the position of the dipoles was formed qualitatively on the basis of their relative position inside the spherical head model. For the central dipole localization no gross deviations from a realistic head model are to be expected.

RESULTS

The first appearance of the bipolar field of the SMA was in the range of -1.9 to -1.7 s prior to movement onset for subjects 1–5 (see Table 1). Figures 2 and 3a show the field distributions over the time course for two of the subjects (S1 and S5). Figure 3b shows the averaged waveforms of each channel for S5. Figure 4 shows superimposed waveforms of representative channels, one of each subject. At these selected channels waveforms with large amplitudes were found.

Table 1 gives a brief overview of the results. The time epochs for dipole calculations were always chosen on the basis of the temporal development of magnetic fields arising from SMA and MI. After dipole positions were calculated over a selected time period, the time courses of the SMA dipole and, for multiple-dipole models, the MI dipoles were examined. In all subjects and in all calculated dipole models the SMA dipole moments increased with time and had their maximum immediately before the onset of movement (see Fig. 5).

Concerning individual results, the best solution for S1 was a three-dipole model fitted in the time range from -1 to 0 s (onset of movement). Figure 2 shows the

TABLE 1

Subject No. and dipole model	Beginning of BF prior to movement onset (s) BF 1	BF 2	Time epoch for the dipole model (s)	Error in %
1	−1.9	−0.7		
3-dipole model			−1 to 0	8.5
2	−1.8	−0.5		
1-dipole model			−1.5 to −0.5	13
2-dipole model			−1 to 0	11.6
3-dipole model			−1.8 to −0.3	16
3	−1.7	−0.6		
1-dipole model			−1.7 to −0.6	18
4	−1.9	−0.5		
3-dipole model			−1.2 to 0	18
5	−1.7	−0.5		
2-dipole model			−1.7 to −1	10.9
3-dipole model			−0.6 to 0	13
6	−1.0	−0.5		
3-dipole model			−1 to 0	10.8

Note. The different dipole models chosen for each subject, the time epoch in which this model was calculated, and the residual error are shown. The time points of BF 1 and BF 2 onset are also given for each subject.

field distribution over the time course, Fig. 5 the dipole localization in the spherical head model together with the waveforms of the source activities of the SMA dipole and the two MI dipoles and the time course of the total error. Figure 7a shows the overlay of the dipoles of the anatomical MRI. The two lateral dipoles represent the two MI motor areas and the dipole located over the anterior–posterior median line represents the SMA.

For S2, three different dipole models for different time epochs were established. For the one-dipole model a time period from −1.5 to −0.5 s prior to movement was selected because activity of SMA in the field maps was clearly visible at −1.5 s, while at −0.5 s activity of MI became more dominant. A two-dipole model was calculated in the time period from −1 s to the onset of movement. Further, a three-dipole model was calculated over the period from −1.8 s (the beginning of SMA activity) to −0.3 s to test SMA dipole stability. Since the dipoles over MI were active only in the later portion of this time range, the resulting error was a little higher than for the one- and the two-dipole models. The variance in the localization of the SMA dipole is very small, i.e., in the range of millimeters (Table 2). Figure 6 shows the dipole localization for these three

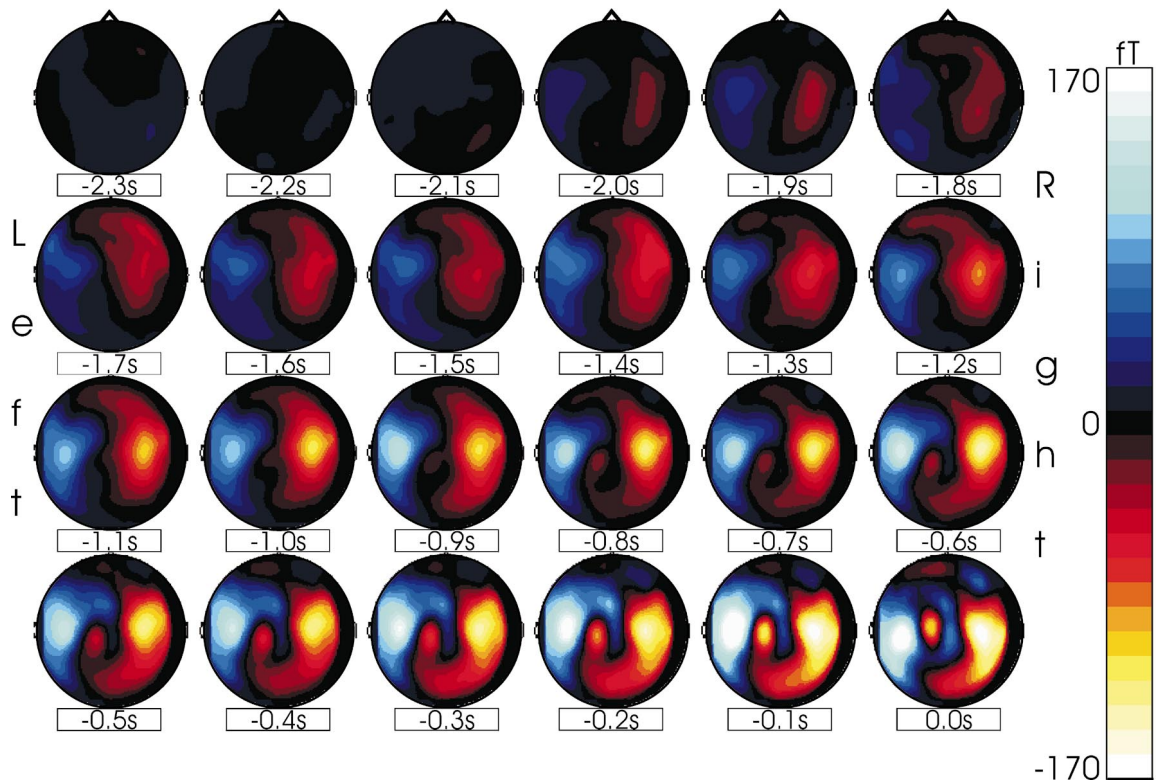

FIG. 2. The development of the field distribution for S1 is shown in steps of 10 ms. Each map shows the field distribution at an indicated time point. The blue field represents the magnetic flux coming out of the head and the red field represents the magnetic flux entering the head. The definite field arising from the SMA is seen first at −1.9 s (a weak field at −2.0 s), the definite field arising from the contralateral MI at −700 ms prior to movement onset (again, a weak field a little bit earlier). The color scale on the right side displays the strength of the magnetic field in fT. It can be seen that the magnetic field strength increases with time until movement onset.

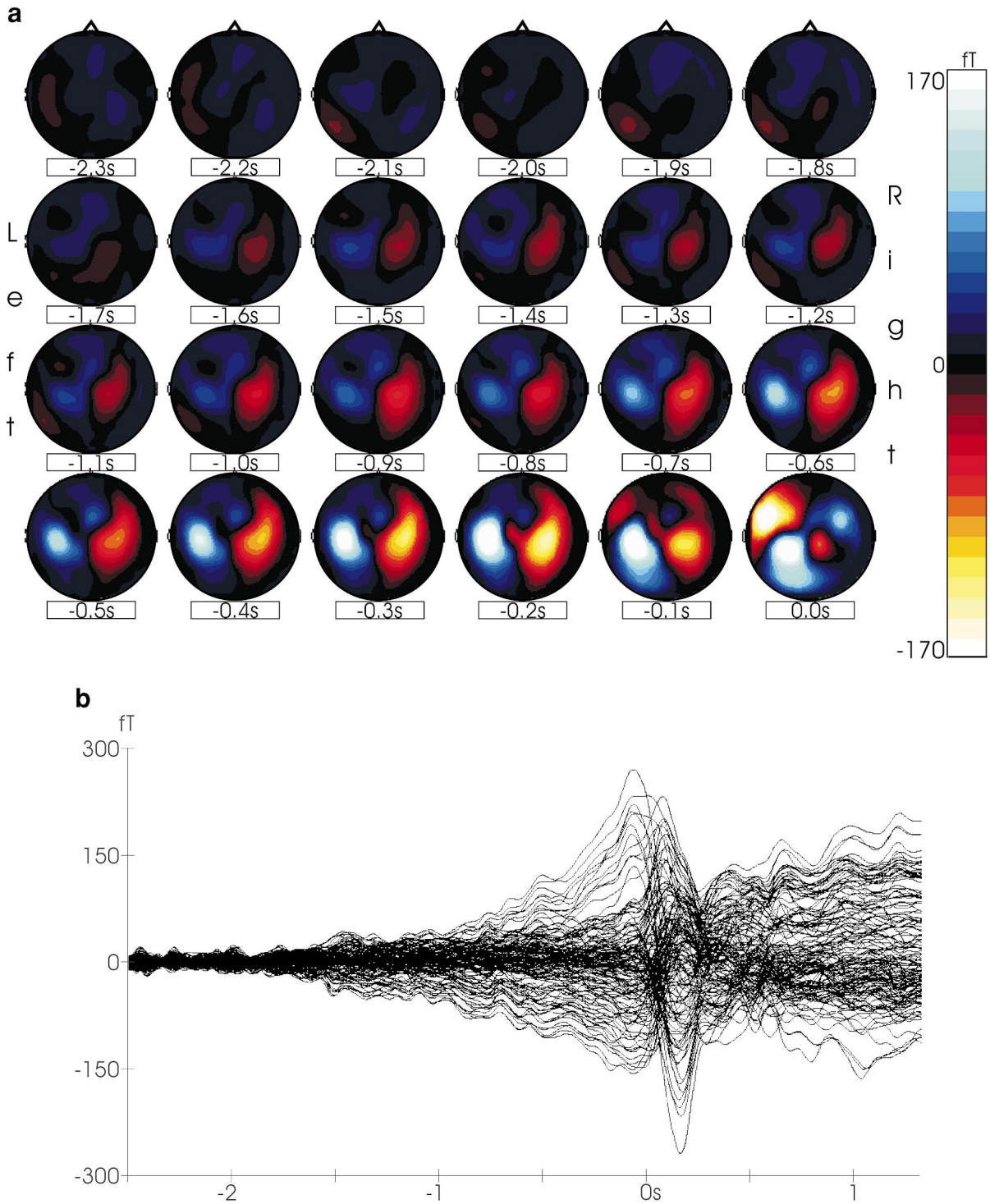

FIG. 3. (a) The development of the magnetic field distribution for S5 in the same setting as in Fig. 2. Activation of the SMA starts at about −1.7 s, activation of MI at about −500 ms prior to movement onset. (b) The averaged waveforms of all channels of S5 are shown. The baseline setting was from −2.5 to −2 s, a low-pass filter of 40 Hz and no high pass filter was used. 270 trials were averaged. The good SNR can clearly be seen.

different dipole models and Fig. 7a the overlay of the three-dipole model on the individual MRI.

The best result for S3 was achieved with a one-dipole model calculated in the period from −1.7 to −0.6 s. This dipole was clearly located in the contralateral SMA.

The best solution for S4 was found in a three-dipole model, one SMA dipole and the contra- and ipsilateral

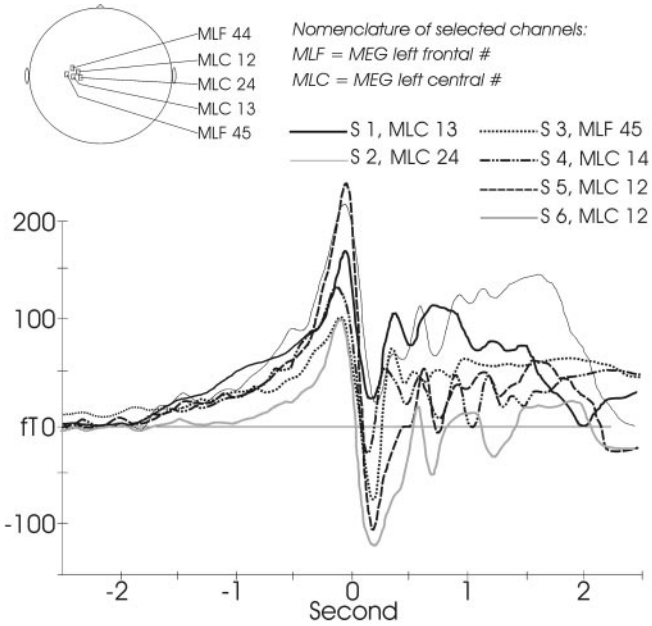

FIG. 4. Waveforms of representative channels, one of each subject, are shown. The localization of these channels over the scalp are shown at the top. At these channels waveforms with large amplitudes were found.

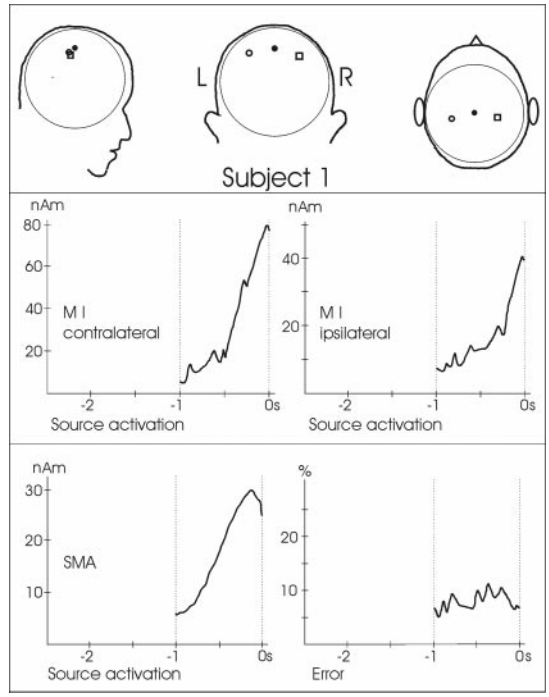

FIG. 5. The upper row shows the dipole localization for S1: the filled circle represents the SMA dipole, the hollow circle the dipole of the contralateral MI, and the hollow square the dipole of the ipsilateral MI. The curves of the source activation for the contralateral MI, the ipsilateral MI, and the SMA dipole and the error are shown within the time window (in s on the abscissa) in which the dipole model was calculated. The strengths of the dipoles are given in nA on the axis of ordinates (the percentage of error for the error course). Note that the courses of the source activation of the two MI dipoles are getting steeper at the beginning of BF 2.

MI dipoles, computed over the time range from −1.2 s to the onset of movement. The overlay on the MRI is shown in Fig. 7a.

The first of two different dipole models fitted for S5 was calculated in the time epoch between −1.7 and −1 s prior to movement onset. Only in this subject was it possible to fit a dipole in both the contralateral and the ipsilateral SMA for the specified time range. At the beginning of BF 1 (at −1.7 s) the dipole moment for the contralateral dipole was stronger, having a moment of 2.4 nA compared with the ipsilateral dipole moment of 1.65 nA. This difference in dipole moments, strongest on the contralateral side, remained over the whole period of the BF until the onset of movement. The second stable dipole model for this subject was a three-dipole model fitted in the time range from −0.6 to 0 s. The localization of the dipoles of the two-dipole and the three-dipole model are shown on an overlay on the individual MRI in Fig. 7b.

Finally, S6 was performing the simple single-finger tapping. In the time range from −1 to 0 s a three-dipole model was established with two dipoles in the two primary motor areas and one dipole in the contralateral SMA (Fig. 7b). While for S1–5 SMA activity started between −1.9 and −1.7 s prior to movement onset on average, SMA activity began at −1 s prior to movement onset in S6.

The localization and orientation of SMA dipoles of all subjects are shown in Fig. 8.

DISCUSSION

As a main result the present study showed the possibility of detecting SMA activity in healthy subjects with magnetoencephalography for the first time.

With our first MEG recordings (Deecke *et al.*, 1982, 1983; Cheyne *et al.*, 1990, 1991; Kristeva *et al.*, 1991) only BF 2, the late component of the readiness field, was detected with one-channel or oligochannel MEG systems, and the dipoles were localized in the MI area, distributed in a somatotopic homuncular pattern

TABLE 2

Dipole model	Anterior–posterior axis in mm	Mediolateral axis in mm	Craniocaudal axis in mm
1-dipole model	34.5	2.5	73
2-dipole model	36.7	2	72.9
3-dipole model	34.5	2.5	73

Note. The coordinates of the SMA dipole for the three calculated dipole models of subject 2 are given in all three dimensions. Note the very small variance of the localization of the SMA dipole for the different dipole models, i.e., in the range of mm and thus indicating the accuracy and reliability of the measured data and the analysis.

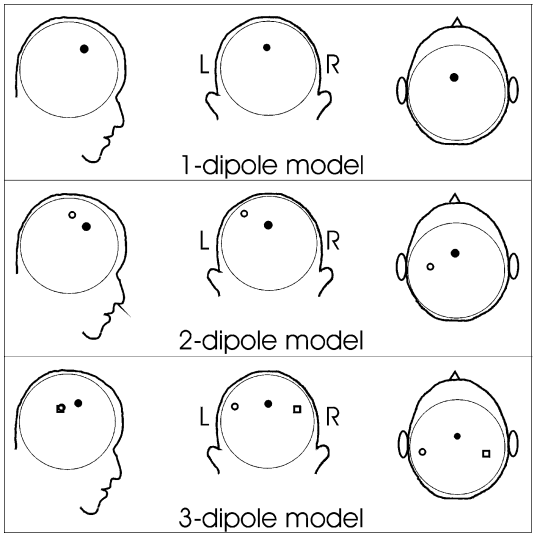

FIG. 6. The localization of the dipoles for three different dipole models (1-dipole, 2-dipole, and 3-dipole model) calculated for S2 are shown. The filled circle represents the SMA dipole, the hollow circle the dipole of the contralateral MI, and the hollow square the dipole of the ipsilateral MI. The different dipole models were calculated in different time epochs (see Table 1). Note the stable position of the SMA dipole for all dipole models (for coordinates of the SMA dipole see Table 2).

(Cheyne *et al.*, 1991). Following this observation, dipole source analysis was applied to the BF by other investigators. Some presented dipole models did not include a SMA source at all (Bötzel *et al.*, 1993; Böcker *et al.*, 1994) or the SMA source was said to not contribute to the premovement negativity (Toro *et al.*, 1993). There may be many reasons for these failures to record BF 1 or find an adequate SMA source.

One explanation given was that both SMAs are always active even preceding unilateral movement (the BP 1 is symmetrical). The two opposing SMA dipoles therefore may cancel one another to a large extent in the MEG (cancellation hypothesis). One solution to this problem was to investigate a patient with a unilateral SMA lesion (Lang *et al.*, 1991).

While the above-mentioned dipole source analyses in healthy subjects failed to find significant activity of the SMA prior to movement onset, intracranial recordings (of Ikeda *et al.*, 1992, and of Rektor *et al.*, 1994) showed SMA activity preceding voluntary movement, confirming the opinion that the SMA participates in BP generation (Deecke and Lang, 1996). It therefore seemed very likely that the reported absence of the SMA contribution to the BF in dipole source analyses was due to methodological failures and problems, such as an insufficient and inaccurate separation of SMA and MI activity. Such failures were possibly due to the fact that SMA and MI sources were grouped together into one source by the source model used (Boetzel *et al.*, 1993). This problem was solved with an improved method for separating MI and SMA activity with EEG data (Praamstra *et al.*, 1996).

To optimize the SNR, the measurements for the present study were done at night when the environmental noise from street cars, etc., was reduced to a minimum. Also head fixation by use of gauze bandage wrapping contributed to SNR improvement. The good SNR that was achieved can be seen in Fig. 3b.

The selection of movement type is also a very important issue when studying SMA activity. Involvement of the SMA in processing complex movements is well supported. A larger amplitude of the slow negative electrical activity over the SMA during execution of complex movements compared with simple ones has been demonstrated (Lang *et al.*, 1989), as well as an increase in rCBF of the SMA while performing various complex movements (Orgogozo and Larsen, 1979). Similar results were achieved by comparing a simple finger-opposition task with a complex sequential finger-opposition task (Shibasaki *et al.*, 1993) and a simple compared with a complex finger-tapping task (Rao *et al.*, 1993). The latter authors showed that this finding is also valid for both self-paced and metronome-paced movements. Stimulating the SMA with rTMS caused errors in the most complex task only and not in more simple movement sequences. Thus it was concluded that the SMA is more active and more critically involved in processing complex sequences than simpler ones (Gerloff *et al.*, 1997).

Investigating the neural activation of cells in the SMA in trained monkeys in a visually guided motor task and a memory guided motor task (Mushiake *et al.*, 1991) showed that more than half of the SMA neurons were preferentially or exclusively active before and during the memorized motor task. In the visually guided task, however, neurons in the premotor area were more active. In a subsequent study, it was similarly found that a majority of SMA neurons were preferentially active when the sequence of the movement was generated on the basis of memory (Tanji and Shima, 1994). The task selected for the present study, including a complex sequential movement which was trained before the recording and then executed on the basis of memory, takes these previous findings into account. Thus it is most likely that performing such a task involves strong activation of the SMA.

We measured one subject with a simple single tapping task of the fifth finger. As reported under Results, it was possible to detect contralateral SMA activity in this subject, but activity of the SMA began distinctly later than in the other subjects performing the more complex task. However, it is not possible to draw too many conclusions from the data of just one subject.

Concerning the data analysis approach selected, the principal idea was to select individual dipole models for each individual subject. The basis of this selection was first the development of the field distribution over the

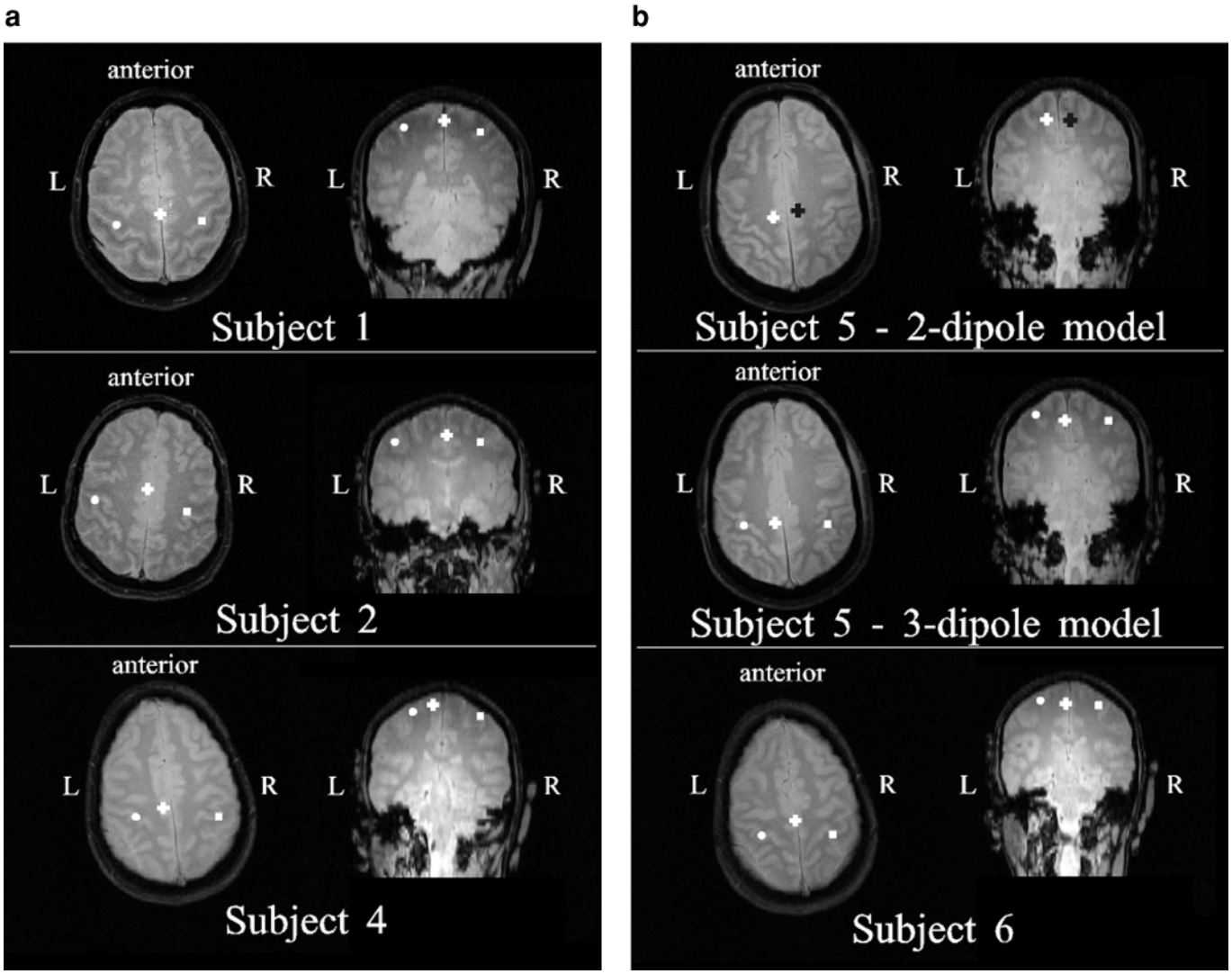

FIG. 7. (a) Overlays of 3-dipole models on axial and coronal anatomical MRIs are shown for S1, S2, and S4. The cross represents the SMA dipole, the circle the contralateral MI dipole, and the square the ipsilateral MI dipole. Dipoles are visualized through different MRI slices. L, left; R, right. (b) For S5 two different dipole models are overlaid on an axial and coronal MRI. The upper row shows the overlay of the 2-dipole model, the white cross representing the contralateral SMA and the black cross the ipsilateral SMA. The middle row shows the 3-dipole model for S5 and the bottom row the 3-dipole model for S6, the cross representing the SMA dipole, the circle the contralateral MI dipole, and the square the ipsilateral MI dipole. Dipoles are visualized through different MRI slices. L, left; R, right.

whole recording time (Figs. 2 and 3a) and second the course of channel waveforms over the area of the two generators of the BF, namely SMA and MI (Fig. 4). The subdivision of the BF into the early BF 1 component and the late BF 2 component (see also Table 1) was determined in the following way: we estimated the development of the field distribution and explored a number of selected channels located over the activated areas. With such knowledge of the individual onsets of SMA and MI activities, adequate dipole models were selected. One of the problems when calculating dipole models including SMA and MI dipoles is the weakness of the SMA field compared with the strength of the fields arising from MI. This problem could be solved by thorough selection of the chosen dipole models in individual time ranges. The detailed processing and analysis and the way in which individual problems occurring in individual dipole models were handled are described under Material and Methods and Results. It is important to mention that all dipole models had to fulfill the "best fit" criteria, including physiologic dipole positions, judgment of the time courses of the source activities of the SMA dipole and MI dipoles, whether the source was active over the whole period of calculation, and an acceptably low error.

Figure 8 shows that the SMA dipoles always tend to be oriented anterior when fitting models with one SMA dipole, whereas both the contralateral and the ipsilat-

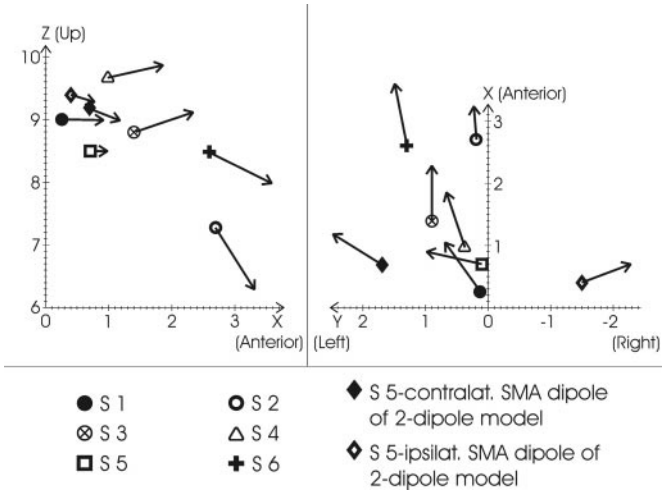

FIG. 8. The relative localization and the orientation of SMA dipoles of all subjects are shown within a common coordinate system. In addition, for S5 the two separated SMA dipoles of the 2-dipole model are shown (x, anterior; y, left; z, up).

eral SMA dipole in S5 are more laterally oriented. Having in mind that two SMA sources exist, the question occurs why it was mostly possible to fit only one SMA dipole with this specific orientation. Dipoles that are organized in a quadrupole manner with strictly antiparallel orientation and identical dipole moments cancel each other with far field measurements like MEG (Dumitru and King, 1993). Any imbalance of the two antiparallel dipole moments of the quadrupole should result in a detectable magnetic field with a resulting dipole with a strict lateral orientation. A deviation of the antiparallel orientation of the two dipoles would also lead to an incomplete cancellation of the dipoles and thus to a detectable magnetic field. It may be assumed that the two SMA dipoles are not organized in a perfect symmetric manner, with differences in dipole strengths and at least small angles between dipoles. On the basis of this model it may be proposed that the anterior-oriented dipole is the result of an imbalanced quadrupole. Since a separation of the contralateral and ipsilateral SMA dipole was only possible in S5, it seems that the two SMA sources usually may lay too close together to be successfully separated, especially when they have a slight antiparallel orientation (Lütkenhöner, 1998). Another obvious reason for the posteroanterior direction of the SMA dipole is that the activated area also includes a fissure within the interhemispheric surface. Thus the dipoles of opposite direction on the inner surfaces facing each other would cancel each other, whereas the posteroanterior currents in the fissure would add up.

The question whether SMA activity operates upstream of or in parallel with MI activity in the planning and execution of voluntary movement has been and still is a controversy. A sequential order of activity in the SMA preceding activity of MI has been confirmed by electrophysiological recordings, as well as by fMRI (Kornhuber and Deecke, 1965; Deecke and Kornhuber, 1978; Barrett *et al.*, 1986; Lang *et al.*, 1991; Knösche *et al.*, 1996; Atlas *et al.*, 1996; Wildgruber *et al.*, 1997). In contrast, single-cell recordings have found activation onsets ranging from −2000 ms to the onset of movement within SMA and MI at the single-cell level (Neafsey *et al.*, 1978; Okana and Tanji, 1987; Thaler *et al.*, 1988), but also show that the percentage of cells that are activated earlier than 500 ms in advance of voluntary movements is many times higher in the SMA (and in the anterior cingulate gyrus) than in any other part of the cortex related to motor preparation and execution. This notion fits very well with the findings of the present study, as well as with those of some previous studies.

The time point of about 500 ms (Table 1) prior to the onset of movement represents approximately the transition period between BF 1 and BF 2. The analysis and selected dipole models showed that only SMA sources could be localized in the time range from the beginning of the BF until BF 2 onset. From −500 ms until movement onset, sources in the SMA as well as in both primary motor cortices could be detected.

It is important to note that this result is not in contrast, but in good accordance, with the above-mentioned single-cell recordings, which are of course a much more sensitive method. With noninvasive functional brain imaging methods, it seems to be possible now to detect even very weak signals when using adequate methodological approaches.

ACKNOWLEDGMENTS

This work was supported by the Austrian Fonds zur Förderung der Wissenschaftlichen Forschung (FWF; Projects, P11437-MED and P12451-MED) and the Human Frontier Science Program.

REFERENCES

Atlas, S. W., Howard, R. S., Maldjian, J., Alsop, D., Detre, J. A., Listerud, J., D'Esposito, M., Judy, K. D., Zager, E., and Stecker, M. 1996. Functional magnetic resonance imaging of regional brain activity in patients with intracerebral gliomas: Findings and implications for clinical management. *Neurosurgery* **38:**329–338.

Barrett, G., Shibasaki, H., and Neshige, R. 1986. Cortical potentials preceding voluntary movement: Evidence for three periods of preparation in man. *Electroencephalogr. Clin. Neurophysiol.* **63:**327–339.

Boecker, H., Kleinschmidt, A., Requardt, M., Hanicke, W., Merboldt, K. D., and Frahm, J. 1994. Functional cooperativity of human cortical motor areas during self-paced simple finger movements. A high-resolution MRI study. *Brain* **117:**1231–1239.

Bötzel, K., Plendl, H., Paulus, W., and Scherg, M. 1993. Bereitschaftspotential: Is there a contribution of the supplementary motor area? *Electroencephalogr. Clin. Neurophysiol.* **89:**187–196.

Cheyne, D., and Weinberg, H. 1989. Neuromagnetic fields accompanying unilateral finger movements: Pre-movement and movement-evoked fields. *Exp. Brain Res.* **78:**604–612.

Cheyne, D., Kristeva, R., Lang, W., Lindinger, G., and Deecke, L. 1990. Neuromagnetic localisation of sensorimotor cortex sources associated with voluntary movements in humans. In *Advances in Biomagnetism* (S. J. Williamson, M. Hoke, and M. Kotani, Eds.), pp. 79–93. Plenum, New York.

Cheyne, D., Kristeva, R., and Deecke, L. 1991. Homuncular organization of human motor cortex as indicated by neuromagnetic recordings. *Neurosci. Lett.* **122:**17–20.

Deecke, L. 1987. Bereitschaftspotential as an indicator of movement preparation in supplementary motor area and motor cortex. In *Motor Areas of the Cerebral Cortex* (R. Porter, Ed.), pp. 231–250. Wiley, Chichester.

Deecke, L. 1990. Electrophysiological correlates of movement initiation. *Rev. Neurol.* **146:**612–619.

Deecke, L., Scheid, P., and Kornhuber, H. H. 1969. Distribution of readiness potential: Pre-motion positivity and motor potentials of the human cerebral cortex preceding voluntary finger movements. *Exp. Brain Res.* **7:**158–168.

Deecke, L., Grözinger, B., and Kornhuber, H. H. 1976. Voluntary finger movement in man: Cerebral potentials and theory. *Biol. Cybernet.* **23:**99–119.

Deecke, L., and Kornhuber, H. H. 1978. An electrical sign of participation of the mesial "supplementary" motor cortex in human voluntary finger movements. *Brain Res.* **159:**473–476.

Deecke, L., Weinberg, H., and Brickett, P. 1982. Magnetic fields of the human brain accompanying voluntary movement: Bereitschaftsmagnetfeld. *Exp. Brain Res.* **48:**144–148.

Deecke, L., Boschert, J., and Brickett, P. 1983. Magnetic fields of the human brain (Bereitschaftsmagnetfeld) preceding voluntary foot and toe movements. *Exp. Brain Res.* **52:**81–86.

Deecke, L., Lang, W., Heller, H. J., Hufnagl, M., and Kornhuber, H. H. 1987. Bereitschaftspotential in patients with unilateral lesions of the supplementary motor area. *J. Neurol. Neurosurg. Psychiaty* **50:**1430–1434.

Deecke, L., and Lang, W. 1996. Generation of movement-related potentials and fields in the supplementary sensorimotor area and the primary motor area. In *Supplementary Sensorimotor Area—Advances in Neurology* (H. O. Lüders, Ed.), Vol. 70, pp. 127–146. Lippincott/Raven, Philadelphia.

Deiber, M. P., Passingham, R. E., Colebatch, J. G., Friston, K. J., Nixon, P. D., and Frackowiak, R. S. J. 1991. Cortical areas and the selection of movement: A study with positron emission tomography. *Exp. Brain Res.* **84:393–402.**

Dick, J. P. R., Benecke, R., Rothwell, J. C., Day, B. L., and Marsden, C. D. 1986. Simple and complex movements in a patient with infarction of the right supplementary motor area. *Movement Disord.* **1:**255–266.

Dumitru, D., and King, J. C. 1993. Far-field potential production by quadrupole generators in cylindrical volume conductors. *Electroencephalogr. Clin. Neurophysiol.* **88:**421–431.

Foerster, O. 1936. Motorische Felder und Bahnen. In *Handbuch der Neurologie VI* (O. Bumke and O. Grosshirn, Eds.). Springer-Verlag, Berlin.

Gerloff, C., Corwell, B., Chen, R., Hallett, M., and Cohen, L. G. 1997. Stimulation over the human supplementary motor area interferes with the organization of future elements in complex motor sequences. *Brain* **120:**1587–1602.

Goldberg, G. 1985. Supplementary motor area structure and function: Review and hypotheses. *Behav. Brain Sci.* **8:**567–615.

Grafton, S. T., Woods, R. P., and Mazziota, J. C. 1993. Within-arm somatotopy in human motor areas determined by positron emission tomography imaging of cerebral blood flow. *Exp. Brain Res.* **95:**172–176.

Ikeda, A., Lüders, H. O., Burgess, R. C., and Shibasaki, H. 1992. Movement-related potentials recorded from supplementary motor area and primary motor area. *Brain* **115:**1017–1043.

Jenkins, I. H., Passingham, R. E., and Brooks, D. J. 1997. The effect of movement frequency on cerebral activation: A positron emission tomography study. *J. Neurol. Sci.* **151:**195–205.

Kitamura, L., Shibasaki, H., and Kondo, T. A. 1993. Cortical slow potential is larger before an isolated movement of a single finger than simultaneous movements of two fingers. *Electroencephalogr. Clin. Neurophysiol.* **86:**252–259.

Knösche, T., Praamstra, P., Stegeman, D., and Peters, M. 1996. Linear estimation discriminates midline sources and a motor cortex contribution to the readiness potential. *Electroencephalogr. Clin. Neurophysiol.* **99:**183–190.

Kornhuber, H. H., and Deecke, L. 1964. Hirnpotentialänderungen beim Menschen vor und nach Willkürbewegungen, dargestellt mit Magnetbandspeicherung und Rückwärtsanalyse. *Pflügers Arch.* **281:**R52.

Kornhuber, H. H., and Deecke, L. 1965. Hirnpotentialänderungen bei Willkürbewegungen und passiven Bewegungen des Menschen: Bereitschaftspotential und reafferente Potentiale. *Pflügers Arch.* **284:**1–17.

Kornhuber, H. H., Deecke, L., Lang, W., Lang, M., and Kornhuber, A. 1989. Will, volitional action, attention and cerebral potentials in man: Bereitschaftspotential, performance-related potentials, directed attention potential, EEG spectrum changes. In *Volitional Action* (W. Hershberger, Ed.), pp. 107–168. Elsevier, Amsterdam.

Kristeva, R., Cheyne, D., and Deecke, L. 1991. Neuromagnetic fields accompanying unilateral and bilateral voluntary movements: Topography and analysis of cortical sources. *Electroencephalogr. Clin. Neurophysiol.* **81:**284–298.

Lang, W., Zilch, O., Koska, C., Lindinger, G., and Deecke, L. 1989. Negative cortical DC shifts preceding and accompanying simple and complex sequential movements. *Exp. Brain Res.* **74:**99–104.

Lang, W., Obrig, H., Lindinger, G., Cheyne, D., and Deecke, L. 1990. Supplementary motor area activation while tapping bimanually different rhythms in musicians. *Exp. Brain Res.* **79:**504–514.

Lang, W., Cheyne, D., Kristeva, R., Beisteiner, R., Lindinger, G., and Deecke, L. 1991. Three dimensional localization of SMA activity preceding voluntary movement. A study of electric and magnetic fields in a patient with infarction of the right supplementary motor area. *Exp. Brain Res.* **87:**688–695.

Lassen, N. A., Ingvar, D. H., and Skinhøj, E. 1978a. Brain function and blood flow. *Sci. Am.* **239:**50–59.

Lassen, N. A., Larsen, B., and Orgogozo, J. M. 1978b. Cortical localizations seen by the dynamic gamma-camera: A new approach in neuropsychology. *Encephale* **4:**233–249.

Lütkenhöner, B. 1998. Dipole separability in a neuromagnetic source analysis. *IEEE Trans. Biomed. Eng.* **45:**572–581.

Mushiake, H., Inase, M., and Tanji, J. 1991. Neuronal activity in the primate premotor, supplementary, and precentral motor cortex during visually and internally determined sequential movements. *J. Neurophysiol.* **66:**705–718.

Nagamine, T., Kajola, M., Salmelin, R., Shibasaki, H., and Hari, R. 1996. Movement-related slow cortical magnetic fields and changes of spontaneous MEG- and EEG-brain rhythmus. *Electroencephalogr. Clin. Neurophysiol.* **99:**274–286.

Neafsy, E. J., Hull, C. D., and Buchwald, N. A. 1978. Preparation for movement in the cat. I. Unit activity in the cerebral cortex. *Electroencephalogr. Clin. Neurophysiol.* **44:**706–713.

Neshige, R., Lüders, H., and Shibasaki, H. 1988. Recording of movement-related potentials from scalp and cortex in man. *Brain* **111:** 719–736.

Okana, K., and Tanji, J. 1987. Neuronal activities in the primate motor fields in the agranular frontal cortex preceding visually triggered and self-paced movement. *Exp. Brain Res.* **66:**155–166.

Oldfield, R. C. 1971. The assessment and analysis of handedness: The Edingburgh Inventory. *Neurophysiology* **9:**97–113.

Orgogozo, J. M., and Larsen, B. 1979. Activation of the SMA during voluntary movements in man suggests it works as a supramotor area. *Science* **206:**847–850.

Praamstra, P., Stegeman, D. F., Horstink, M. W. I. M., and Cools, A. R. 1996. Dipole source analysis suggests selective modulation of the supplementary motor area contribution to the readiness potential. *Electroencephalogr. Clin. Neurophysiol.* **98:**468–477.

Rao, S. M., Binder, J. R., Bandettini, P. A., Hammeke, T. A., Yetkin, F. Z., Jesmanowicz, A., Lisk, M. S., Morris, G. L., Mueller, M. D., Estkowski, R. T. R., Wong, E. C., Haughton, M. D., and Hyde, J. S. 1993. Functional magnetic resonance imaging of complex human movements. *Neurology* **43:**2311–2318.

Rektor, I., Feve, A., Buser, P., Bathien, N., and Lamarche, M. 1994. Intracerebral recordings of movement related readiness potential: An exploration in epileptic patients. *Electroencephalogr. Clin. Neurophysiol.* **90:**273–283.

Roland, P. E., Larsen, B., Lassen, N. A., and Skinhoj, E. 1980. Supplementary motor area and other cortical areas in organization of voluntary movements in man. *J. Neurophysiol.* **43:**118–136.

Shibasaki, H., Sadato, N., Lyshkow, H., Yonekura, Y., Honda, M., Nagamine, T., Suwazono, S., Magata, Y., Ikeda, A., Miyazaki, M., Fukuyama, H., Asato, R., and Konishi, J. 1993. Both primary motor cortex and supplementary motor area play an important role in complex finger movement. *Brain* **116:**1387–1398.

Simonetta, M., Clanet, M., and Rascol, O. 1991. Bereitschaftspotential in a simple movement or in a motor sequence starting with the same simple movement. *Electroencephalogr. Clin. Neurophysiol.* **81:**129–134.

Tanji, J., and Shima, K. 1994. Role for supplementary motor area cells in planning several movements ahead. *Nature* **371:**413–416.

Thaler, D. E., Rolls, E. T., and Passingham, R. E. 1988. Neuronal activity of the supplementary motor area (SMA) during internally and externally triggered wrist movement. *Neurosci. Lett.* **93:**264–269.

Toro, C., Matsumoto, J., Deuschl, G., Roth, B. J., and Hallett, M. 1993. Source analysis of scalp-recorded movement-related electrical potentials. *Electroencephalogr. Clin. Neurophysiol.* **86:**167–175.

Vogt, C., and Vogt, O. 1919. Allgemeinere Ergebnisse unserer Hirnforschung. IV. Die physiologische Bedeutung der architektonischen Rindenfelderung auf Grund neuer Rindenreizungen. *J. Psychol. Neurol.* **25:**339.

Weiller, C., Jüptner, M., Fellows, S., Rijntjes, M., Leonhardt, G., Kiebel, S., Müller, S., Diener, H. C., and Thilmann, A. F. 1996. Brain representation of active and passive movements. *NeuroImage* **4:**105–110.

Wessel, K., Zeffiro, T., Toro, C., and Hallett, M. 1997. Self-paced versus metronome-paced finger movements. *J. Neuroimag.* **7:**145–151.

Wildgruber, D., Erb, M., Klose, U., and Grodd, M. 1997. Sequential activation of supplementary motor area and primary motor cortex during self-paced finger movement in human evaluated by functional MRI. *Neurosci. Lett.* **227:**161–164.