

G. Dirnberger · M. Reumann · W. Endl
G. Lindinger · W. Lang · J.C. Rothwell

Dissociation of motor preparation from memory and attentional processes using movement-related cortical potentials

Received: 27 October 1999 / Accepted: 16 June 2000 / Published online: 6 September 2000
© Springer-Verlag 2000

Abstract The EEG activity preceding self-paced voluntary movements (movement-related cortical potential, MRCP) is smaller if subjects make the same movement each time (regular task) compared with when different movements are made each time (random task). To test whether extra activity in the random task is due to increased motor preparation needed to switch between different movements, or to memory/attentional processes needed to select movements randomly, we compared regular and random movements with an additional alternating task. This alternating task required subjects to make different movements each time as in the random task, but since the task was very simple, the memory/attentional load was similar to that in the regular task. The MRCP was equally large over motor areas in both random and alternating tasks, suggesting that the extra activity over sensorimotor areas reflected processes involved in motor preparation rather than memory/attention. We speculate that, in the regular task, some part of the instructions for the previous movement remains intact, reducing the amount of preparation needed for the next repetition. Thus the MRCP is smaller than in the alternating and random tasks. Although the MRCPs in alternating and random tasks were similar over the motor areas, the random task had more activity than the alternating task in contralateral frontal areas. This part of the MRCP may therefore be related to memory/attentional processes required to randomize the sequence of movements. We conclude that the MRCP contains dissociable components related to motor preparation and memory/attention.

Key words Event-related potentials · Readiness potential · Directed spatial attention · Dorsolateral prefrontal cortex · Premotor cortex · Supplementary motor area

Introduction

The movement-related cortical potential (MRCP) is a widespread EEG potential that precedes voluntary movements and is caused by neural processes involved preparing and executing the commands to move. Because the potential is small in relation to the ongoing background EEG activity, several movements are made, and the potential averaged with respect to the onset of each.

In several previous studies, MRCPs have been recorded while subjects move a hand-held joystick either up, down or to the left or right, or performed other kinds of 'freely selected' random movements (Praagstra et al. 1995; Touge et al. 1995; Dirnberger et al. 1998). If the same movement is made on each occasion, then the MRCPs are smaller than if different movements are made each time, particularly for activity recorded from electrodes around the frontocentral areas of the scalp. Concurrent positron emission tomography (PET) activation studies (Deiber et al. 1991; Playford et al. 1992) suggest that the extra brain activation in the random task comes from the region of the supplementary motor area (SMA), lateral premotor cortex, and dorsolateral frontal regions. This is consistent with the lack of effect of task type on the MRCPs in patients with Parkinson's disease, in whom SMA activation seems to be impaired (Touge et al. 1995; Playford et al. 1992).

The question we wish to address here is the nature of the extra premovement activity in freely selected random versus regular (repetitive) movements. The tasks differ in two main ways. The first concerns what we term 'motor preparation'. This may include facilitatory processes that prepare areas of the motor system to receive forthcoming commands. In the repeated task it is conceivable that some part of this facilitatory activity could remain in

G. Dirnberger (✉) · M. Reumann · W. Endl · G. Lindinger
W. Lang
University Department of Neurology,
University of Vienna, AKH Wien,
Währinger Gürtel 18–20, 1090 Vienna, Austria
e-mail: georg.dirnberger@akh-wien.ac.at
Tel.: +43 1 40400 6346, Fax: +43 1 40400 3141

G. Dirnberger · J.C. Rothwell
Medical Research Council,
Human Movement & Balance Unit, Institute of Neurology,
23 Queen Square, London WC1N 3BG, UK

place between trials, and reduce the activity time-locked to each movement. This benefit would not be available in the random task, and therefore the premovement EEG signal would be larger than in the regular task. In addition, 'motor preparation' may also include inhibitory processes which might be needed in tasks that require one movement to be followed by a different one. These inhibitory processes might erase any trace of activation related to a non-identical previous movement before, or at the same time as, a new one is prepared. Neurophysiological studies have shown that prior to onset of movement there are changes in discharge of cells at all levels of the motor system from spinal cord to primary, premotor and supplementary motor cortex (Ikeda et al. 1992, 1995; Rektor et al. 1994). We use the term 'motor preparation' to cover all of this activity, whether excitatory or inhibitory.

The second difference between tasks concerns 'memory/attentional processes'. In this we include non-motor processes that are needed in the random task but not in the regular task. For example, in the random task, subjects need to decide which movement to make on every trial, whereas no decision is needed if the movements are regular. This decision process involves checking the memory of past movements and testing the 'randomness' of the selection. In addition the subject may have to shift attention to a different part of the body in order to make the random movements (for example it might be important to check that the limb is in the correct place to produce the movement). This would not be necessary in the regular task. Again, the reduced involvement of memory and attention related processes might contribute to the smaller EEG potential in regular movements.

The present experiments were designed to tease apart these mechanisms of memory/attention and motor preparation. To do this we employed a third task in addition to the random and regular movements studied previously. This was an alternating task in which subjects had to alternate between two different movements on each trial. This task had components common to both the regular and random task. It was similar to the regular task in that the movement to be made on each trial was always pre-specified, so that the memory and monitoring component of the task was very small. It also resembled the random task in that each movement was different from the previous one, so that the amount of motor preparation should have been similar in both cases. We can therefore predict that if the increase in the MRCP in the random versus regular task is due mostly to a change in motor preparation, then the alternating task will also have a large MRCP. Alternatively if the increase in MRCP from regular to random is due to memory/attentional processes, the MRCP in alternating movements should resemble that in the regular movements. Finally, by looking at the EEG activity at different electrode sites on the scalp, we may be able to obtain some spatial information about which parts of the brain are involved in memory/attentional processes and motor preparation.

Materials and methods

Subjects

Sixteen subjects (eight males) aged 19–27 years (mean 23.9 years, SD 2.5 years) participated in the study. All were right handed (Oldfield 1971) and had no history of psychiatric or neurological disease. Written informed consent was obtained from each subject in accordance with the guidelines approved by the University of Vienna.

Design

Subjects made self-paced flexion movements with the index or middle finger of their left or right hand by pressing one out of four response buttons.

There were three conditions, alternating, random or regular: In the alternating mode, subjects pressed the left index finger response button on the first trial, the right index finger response button on the second trial, etc., in an alternating fashion. This condition was examined for the index fingers only. In the random mode, subjects had to press down any one of the four buttons corresponding to left or right index or middle fingers, with the instruction to avoid repetitive sequences of more than two button presses of the same type. In the regular mode, subjects had to press down a particular predetermined button repetitively across trials. There were two types of series in the regular mode, one series performed exclusively with the right index finger and one series performed exclusively with the left index finger.

Subjects had to perform a series of 70 button presses 8 different times, 2 of which were in the alternating mode, 4 of which were in the random mode and 2 of which were in the regular mode. Half the subjects started with a series of freely selected random movements and half the subjects started with a series of alternating or regular movements. Performance of a random mode condition was always followed by the performance of an alternating or regular mode condition, and vice versa. The order of performance of the series in the alternating and regular mode was altered across subjects so that each condition was executed equally often under each serial position.

Procedure

Subjects were comfortably seated with their arms supported by padded armrests. At the end of the left and right armrests were two buttons placed at a distance so that they could be reached comfortably by the subjects with the index or middle fingers. The inter-button distance on each side was 2.5 cm. Subjects were instructed always to rest all four fingers on the appropriate buttons. Before starting the task, and during its execution, subjects had to fixate on a point straight ahead in order to minimize eye movements. At the end of each sequence subjects were instructed via the intercom about the type of movement (alternating, random, or regular mode) and, in the latter case, the finger (left or right index finger) they should use in the next block. Subjects were required to make brisk flexion movements irregularly but no earlier than 5.0 s after the previous movement. They were instructed neither to count nor to maintain any other rhythmic activity during the entire session. The average intermovement interval of the subjects was about 8–9 s. An average of about ten movements in each series was not included in further analysis because their intermovement intervals were too short.

The total time taken to complete the tasks was about 1.5 h. Task performance was video-monitored. In between the blocks, subjects were allowed to have a break. They had two breaks of approximately 10 min in the course of testing. The randomness of each subject's movements during the random blocks was tested by calculating the randomization index according to Evans (1978). This score ranges from 0.0 to 1.0, with higher values indicating poorer randomization.

Recording of MRCPs

EEG activity was recorded unipolarly using Ag/AgCl electrodes from the sites F3, Fz, F4, C5, C3, C1, Cz, C2, C4, C6, P3, Pz and P4 (electrode position according to the extended international 10–20 system; Chatrian et al. 1985), referenced to linked mastoids. In addition, horizontal and vertical electrooculogram (EOG) (electrode positions: above and below the left eye and adjacent to the outer canthus of each eye) and electromyogram (EMG) from left and right musculus flexor digitorum superficialis were recorded. Electrodes were attached on the carefully cleaned skin by collodion, and their impedance was kept below 3 k Ω . Electrical activity was recorded using a PC-supported 64-channel DC amplifier system (Lindinger 1990) with the following settings:

- EEG: DC mode, frequency band DC to 100 Hz
- EOG: DC mode, frequency band DC to 41 Hz
- EMG: AC mode, frequency band 0.1–300 Hz

EEG, EOG and the EMG envelope were digitized online at a rate of 250 Hz and stored for subsequent analysis. The EEG was corrected for minor eye blink artefacts using an automatic blink correction. All trials with artefacts remaining after this procedure were rejected from further analysis. For each trial, the EEG was averaged in reference to movement onset.

The period used for statistical analysis started 2000 ms prior to movement onset and lasted till movement onset, with a baseline calculated from 3250 ms before movement onset. In what follows, the term ‘MRCP’ is used for all parts of the premovement potential.

Data analysis

Means were calculated for each condition and each finger separately, e.g. alternating left index finger movements. Only index finger movements were included in the final analysis. For each block, the mean amplitude of the EEG at each electrode was calculated for four time intervals or epochs prior to movement. Each of the four epochs lasted 500 ms. The earliest premovement epoch started 2000 ms before movement, followed by three consecutive epochs starting at 1500 ms, 1000 ms, and 500 ms before movement onset, respectively. The three earlier epochs were selected to test for effects that may build up during the initial phases of the potential but would not necessarily be present through the entire early MRCP. The latest epoch was chosen because it corresponds to the NS’ (Barrett et al. 1986), a strongly lateralized component of the MRCP immediately prior to movement onset.

A repeated measures analysis of variance (ANOVA) was carried out for each epoch separately, with mode of movement selection (alternating, random, or regular), side of movement (left vs right) and electrode (F3, Fz, F4, C5, C3, C1, Cz, C2, C4, C6, P3, Pz, P4) as the within-subject factors. Where appropriate, Greenhouse-Geisser (1959) corrected univariate F -values are reported. Interactions with the factor electrode were re-calculated with normalized data (McCarthy and Wood 1985). Interactions with the factor electrode are always reported using F -values derived from this second analysis. Only significant main or interaction effects are reported. For all statistical comparisons, the level of significance was set to $P \leq 0.05$.

To investigate any lateralized effects of the mode of movement selection over pairs of homologous electrodes (F3/F4, C5/C6, C3/C4, C1/C2, and P3/P4), the lateralized readiness potential (LRP) was calculated using the following formula (de Jong et al. 1988):

$$\text{LRP} = (\text{Electrode}_{\text{odd}} - \text{Electrode}_{\text{even}})_{\text{left hand}} - (\text{Electrode}_{\text{odd}} - \text{Electrode}_{\text{even}})_{\text{right hand}}$$

First, the voltage difference between homologous electrodes was computed separately for each mode of movement selection and movements to the left and to the right. In the second step, for each mode of movement selection separately, the value for right hand

movements was subtracted from the corresponding value for left hand movements. For the resulting score, the bigger the LRP, the greater the degree of lateralization towards the contralateral side. The LRP was subject to a separate statistical analysis focussed on lateralized effects of the mode of movement selection.

Results

Behavioural data

The randomization index for the random movements ranged from 0.54 to 0.69 (mean \pm SD 0.62 \pm 0.04). The mean number of trials that reached the criteria for further analysis was 60 \pm 8 for the alternating condition, 62 \pm 11

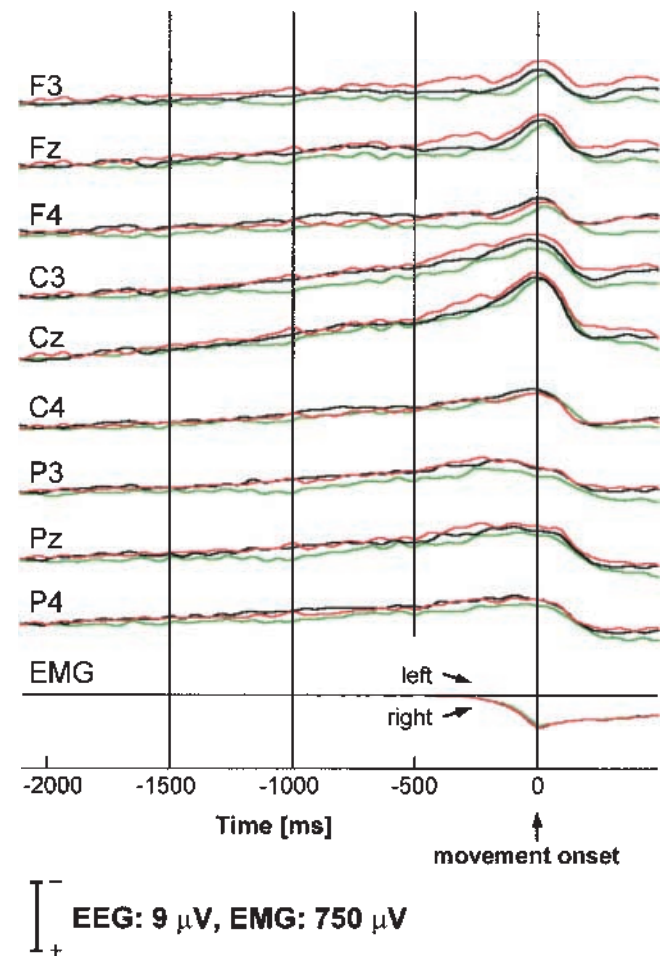


Fig. 1 Grand average of the movement-related cortical potentials (MRCPs) preceding regular (green line), alternating (black line) and random (red line) movements with the right index finger. Only waveforms of the most relevant electrodes are shown. Electrooculographic activity (not shown) was minimal and not significantly different for any of the three conditions. The zero mark on the time axis is aligned with movement onset. Traces of left and right electromyogram (EMG) of forearm flexors are superimposed on each other, indicating that all three conditions had an equivalent level of muscle activity of the right arm and that for none of the conditions was there any accompanying muscle activity of the left arm. The vertical lines show the time intervals that were used in the statistical analysis

Table 1 Comparison of the amplitude of the movement-related cortical potentials (MRCPs) preceding regular, alternating, and random movements using repeated measures analysis of variance (ANOVA), separately for the four subsequent premovement epochs. The degrees of freedom (*df*) and *F* ratio are presented as ac-

tual values, whereas the *P* value is that associated with the conservative *df* after the Greenhouse-Geisser (1959) correction. The four premovement epochs are defined in relation to movement onset. All significant main and interaction effects are given

	<i>df</i> (<i>n1,n2</i>)	ANOVA terms							
		Epoch -2000 ms to -1500 ms		Epoch -1500 ms to -1000 ms		Epoch -1000 ms to -500 ms		Epoch -500 ms to 0 ms	
		<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>	<i>F</i>	<i>P</i>
Main effects									
Mode (regular vs alternating vs random)	2, 30	5.53	<0.01	6.22	<0.01	6.10	<0.01	4.58	<0.05
Electrode	12, 180	16.65	<0.01	19.08	<0.01	25.35	<0.01	29.13	<0.01
Interaction effects									
Electrode × Side of Movement	12, 180	5.03	<0.01	7.13	<0.01	16.12	<0.01	20.90	<0.01
Mode × Electrode × Side of Movement	24, 360			1.71	<0.05	2.39	<0.01	1.79	<0.05

for the random condition, and 57±11 for the regular condition. This difference in the number of trials per condition was not significant ($F_{(2,30)}=2.23$, NS), nor was there any other significant main or interaction effect. The higher number of index finger movements for the random mode condition was explained by the fact that subjects made slightly more left (76±12) and right (78±10) index than middle finger movements in the random as compared to the regular or alternating condition (70 index finger movements for either side).

Movement-related cortical potentials

Figure 1 shows the grand average MRCPs across all subjects for movements with the right index finger in the alternating, in the random and in the regular mode separately. For all three conditions, the average negativity slowly increases from about 2 s prior to movement onset, with a steeper rise (NS; Barrett et al. 1986) in the last 500 ms before movement onset. After movement onset, the potential rapidly returns to near baseline. The term MRCP is used here for all parts of the premovement potential.

The general shape of the potential is the same for the alternating, the random and the regular condition. However, alternating and random movements are in general associated with larger MRCPs than regular movements, particularly at contralateral electrodes C1 and C3. The difference appears to begin about 2 s before and increases until movement onset. The EMG recordings show that the average right arm muscle activity is equal for all three types of movement. The lack of any left side EMG activity indicates that for none of the three conditions was there accompanying muscle activity in the other hand.

Statistical analysis (see Table 1) showed that the main effect of Mode resulted from the amplitude of the MRCPs being higher for alternating than regular movements during all epochs ($F_{(1,15)}=7.92, 9.92, 8.46, 5.50$ respectively; $P<0.05, P<0.01, P<0.05, P<0.05$). The amplitude was also increased for random compared with regular movements from -1500 ms before movement onset onwards ($F_{(1,15)}=6.33, 7.23, 8.39$ respectively; all $P<0.05$), whereas there was no significant difference between the alternating and the random condition ($F_{(1,15)}<3.75, 1.16, 1.70, 0.06$; all NS). The main effect of Electrode resulted from the MRCP amplitude having its highest peak at the central electrode Cz. There was no significant main effect of the side of movement. The interaction Electrode × Side of Movement was associated with a higher MRCP amplitude contralaterally to the side of movement.

The significant three-way interaction Mode × Side of Movement × Electrode occurred because the type of movement (Mode) altered the amount by which MRCPs were lateralized over lateral, but not midline frontal and central, electrodes. This interaction was further analyzed into two steps. First, we limited our attention to the lateral electrodes C1, C2, C3, and C4 because in our previous study of random versus regular movements (Dirnberger et al. 1998) we found a lateralized effect in the same region. In a second step, we tested whether there were further effects at the remaining electrodes for either random versus alternating or alternating versus regular movements.

When the number of electrodes entered into statistical analysis was reduced to electrodes C1, C2, C3, and C4, the interaction Mode × Side of Movement × Electrode was still significant for all three epochs ($F_{(6,90)}=4.57, 5.96, 4.47$ respectively; all $P<0.01$) and was more pronounced for electrodes C3 and C4 ($F_{(2,30)}=8.40, 14.59$,

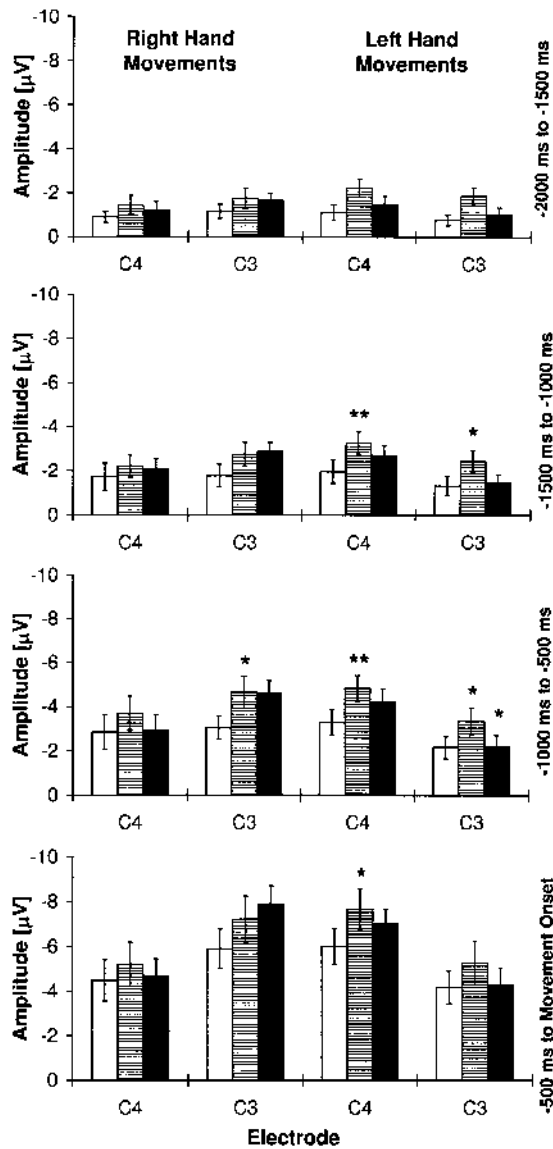


Fig. 2 Mean amplitude of the movement-related cortical potentials (MRCPs) for left and right hand movements in the regular (white boxes), alternating (hatched boxes) and random (black boxes) movements at the lateral electrodes C3 and C4 for each of the four epochs. MRCP amplitudes of movements performed in the random condition were compared to amplitudes of movements performed in the alternating condition, and MRCP amplitudes of movements performed in the alternating condition were compared to amplitudes of movements performed in the regular condition. This shows increased contralateral negativity over sensorimotor areas during alternating as compared to regular movements which is not further increased in the random task. Increased ipsilateral negativity occurs during alternating movements only. Error bars indicate standard error (paired samples *t*-tests: * $P < 0.05$, ** $P < 0.01$)

12.27 respectively; all $P < 0.01$) than for electrodes C1 and C2 ($F_{(2,30)} = 3.03, 4.13, 2.93$ respectively; $P = 0.06, P < 0.05, P = 0.07$). For the central electrodes, when we pursued the interaction Mode \times Side of Movement \times Electrode further we limited our attention to the C3/C4 electrode pair since the changes here were larger than

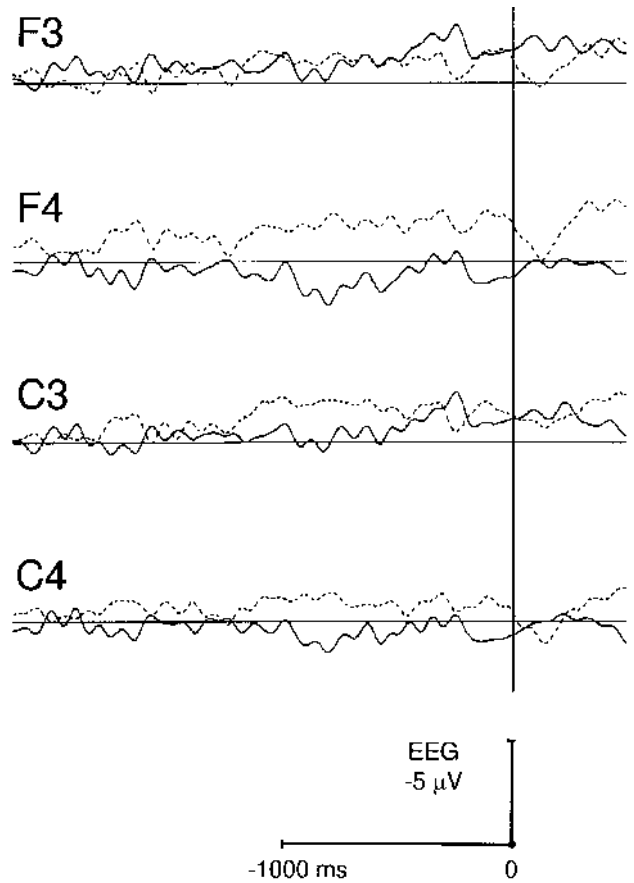
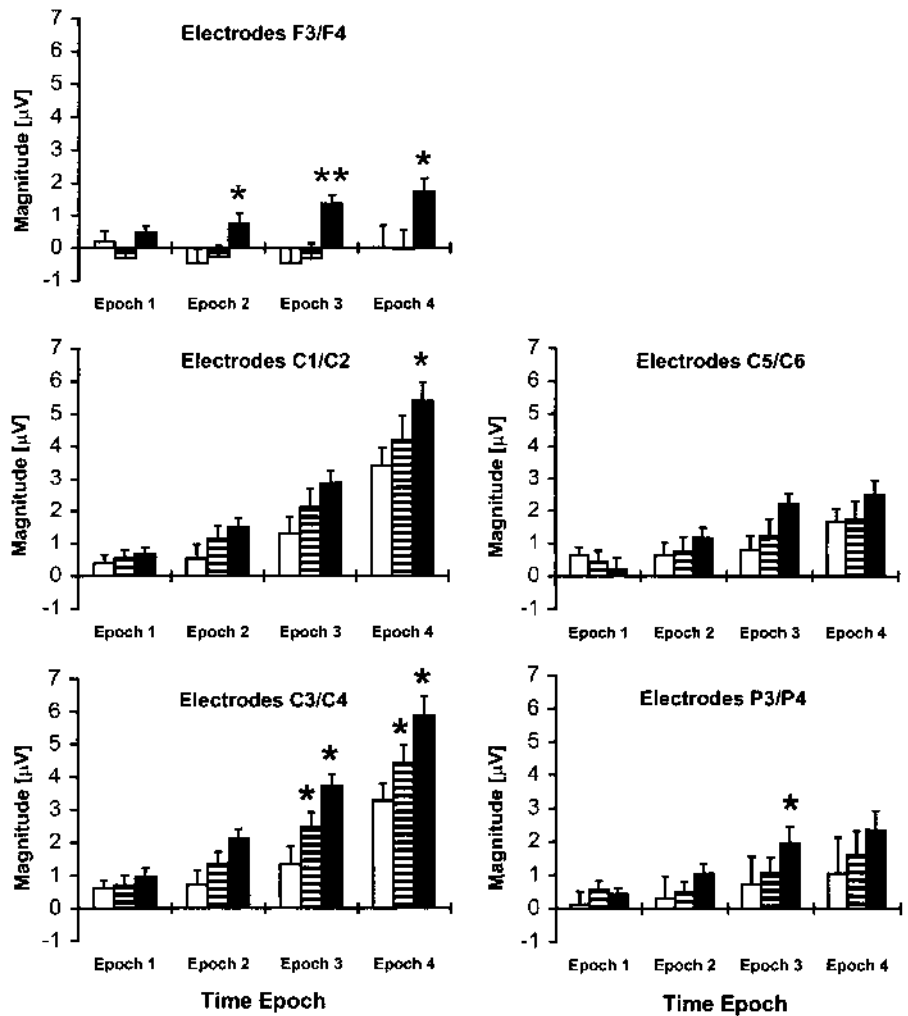


Fig. 3 Comparison of the waveforms at lateral central (C3, C4) and frontal (F3, F4) electrodes for movements with the right index finger. The difference waveform of alternating minus regular movements (broken line) is compared to the difference waveform of random minus alternating movements (solid line). Negative waveforms for alternating or random movements show additional negativity for these compared to the regular or alternating tasks, and positive waveforms for alternating or random movements show reduced negativity for these compared to the regular or alternating tasks. The zero mark on the time axis indicates movement onset

those at C1/C2. We found a lateralized effect of ‘mode’ at the C3/C4 electrodes for alternating compared to the regular movements, starting -1000 ms before movement onset (for the intervals -1000 to -500 and -500 to 0 ms, $F_{(1,15)} = 4.56, 6.10$ respectively; $P = 0.05, P < 0.05$). For random compared to alternating movements, a lateralized effect of ‘mode’ was present from -1500 ms before movement onset till movement onset (for the intervals -1500 to -1000 ; from -1000 to -500 ; and from -500 to 0 ms, $F_{(1,15)} = 4.20, 8.49, 4.67$ respectively; all $P < 0.05$).

Post hoc tests showed that the MRCP was larger over the contralateral central electrode sites (C3 for right sided and C4 for left sided movements) during movements in the alternating compared to movements in the regular task, but did not further increase for movements in the random compared to movements in the alternating task. This contralateral effect of ‘mode’ was significant for alternating movements with the left and right hand in

Fig. 4 Schematic representation of the time course of the lateralized readiness potential (LRP) through all four epochs for regular (white boxes), alternating (hatched boxes), and random (black boxes) movements. Electrode pairs (F3/F4, C1/C2, C3/C4, C5/C6, P3/P4) are indicated above each set of histograms. Alternating movements were compared to regular movements, and random movements were compared to alternating movements. In comparison to regular movements, alternating movements have a larger LRP at pairs C1/C2 and C3/C4 that is further increased in the random condition. Only random movements were found to be associated with a significantly increased magnitude of the LRP at pair F3/F4 (epochs: Epoch 1 –2000 ms to –1500 ms before movement onset, Epoch 2 –1500 ms to –1000 ms before movement onset, Epoch 3 –1000 ms to –500 ms before movement onset, Epoch 4 –500 ms to movement onset). Error bars indicate standard error (paired samples *t*-tests: * $P < 0.05$, ** $P < 0.01$)



some, but not all, of the premovement epochs (right hand movements for the interval from –1000 to –500 ms: paired *t*-test $t_{(1,15)}=2.58$, $P < 0.05$; left hand movements for the interval from –1500 ms to movement onset: paired *t*-test $t_{(1,15)}=3.63$, 3.58 , 2.65 , $P < 0.01$, $P < 0.01$, $P < 0.05$). In alternating compared to random and regular movements, the MRCP also was larger in central leads ipsilateral to the side of movement. This was significant for some of the premovement epochs of left but not right hand movements (alternating compared to regular left hand movements for the interval from –1500 to –500 ms: paired *t*-test $t_{(1,15)}=2.09$, 2.30 , all $P < 0.05$; alternating compared to random left hand movements for the interval from –1000 to –500 ms: paired *t*-test $t_{(1,15)}=2.44$, $P < 0.05$). Figure 2 illustrates these ipsilateral and contralateral effects of mode at central electrodes.

For the remaining nine electrodes F3, Fz, F4, C5, Cz, C6, P3, Pz, and P4, the interaction Mode \times Side of Movement \times Electrode was significant for the epoch from –1000 ms to –500 ms before movement onset ($F_{(16,240)}=1.76$; $P < 0.05$). This was explained by a significant effect for electrodes F3 and F4 ($F_{(2,30)}=5.77$; $P < 0.01$) but not for the other seven electrodes

($F_{(12,180)}=1.44$; NS) during this interval. The effect at the frontal electrodes F3 and F4 was significant for random compared to alternating ($F_{(1,15)}=9.43$, $P < 0.05$) but not alternating compared to regular ($F_{(1,15)} < 1$) movements. This was explained by reduced negativity over the ipsilateral frontal electrode (F4 for right sided and F3 for left sided movements) and a tendency for increased negativity over the contralateral frontal electrode prior to random movements. However, this effect was significant only for movements with the right hand (paired *t*-test $t_{(1,15)}=2.30$, $P < 0.05$). Figure 3 illustrates this effect of a differential increase in negativity at contralateral frontal electrodes prior to random movements and compares these findings to those at central electrodes.

The frontal effect was seen more clearly by calculating the lateralized readiness potential (LRP) separately for each pair of lateral electrodes (Fig. 4). At central and parietal sites, this potential is always positive and increases continuously across the three conditions from the earliest (–2000 ms to –1500 ms before movement onset) to the latest (–500 ms before movement onset to movement onset) epoch. Activity at pairs C1/C2 and C3/C4 is larger during the alternating task as compared with the

regular condition (results for pair C3/C4 for the interval from -1000 ms to movement onset: paired t -test $t_{(1,15)}=2.61, 2.21$, all $P<0.05$) and shows a further increase for the random compared with the alternating task (results for pair C3/C4 for the interval from -1000 ms to movement onset: paired t -test $t_{(1,15)}=2.87, 2.80$, all $P<0.05$). This effect at the central electrodes extends to parietal sites in the interval from -1000 to -500 ms (paired t -test $t_{(1,15)}=2.12, P=0.05$). The smaller LRP during alternating than random movements for the central electrodes is due to the larger ipsilateral activity in the alternating compared with the random task. This makes the difference between hemispheres (the LRP) smaller than in the random task. The pattern at the frontal electrodes F3/F4 is different. Here, the LRP does not increase in magnitude for regular and alternating movements. A positive LRP is seen only in random movements indicating increased contralateral frontal activity in later epochs (for the interval from -1500 ms to movement onset: paired t -test $t_{(1,15)}=2.07, 2.98, 2.34, P<0.05, P<0.01, P<0.05$).

The increase in the magnitude of the LRP was significant at pair C3/C4 for *both* alternating compared to regular movements and random compared to alternating movements, the latter also at pair C1/C2. A significant increase in lateralized frontal activity at pair F3/F4 was found for random compared to alternating movements *only*.

Discussion

In the present experiments subjects made three types of self-paced movements using the fingers of each hand. In the regular condition, they repeatedly moved the index finger of one hand. In the alternating condition, they moved first the left index, then the right, then the left, etc. In the random condition, subjects chose freely between movements of the index and middle finger of either hand. For all three tasks, MRCPs were averaged only for the index finger movements, with separate averages made for left and right hand. The design of the experiment meant that the same number of index finger movements was averaged for each task. EMG recordings showed that the average muscle activity was the same for all types of movement and that in no case were both hands ever active simultaneously.

The results show that: (1) MRCPs over sensorimotor areas were larger for both the alternating and random conditions than in the regular task. This effect was distributed asymmetrically over the scalp, and was particularly prominent over contralateral areas. (2) The increased activity over sensorimotor areas persisted through virtually the whole time course of the MRCP. (3) Compared with either the regular or alternating condition, movements made in the random condition were accompanied by extra activity in contralateral frontal leads.

Motor preparation versus memory/attentional processes

Several previous studies have noted that MRCPs are larger before freely chosen compared with regular movements (Praamstra et al. 1995; Touge et al. 1995; Dirnberger et al. 1998). However, in no case did the experiments test whether the differences between tasks were due to differences in the amount of activity involved in preparing motor structures for commands related to the forthcoming movement (motor preparation), or differences in memory related and attentional processes. Indeed, the implication in many of these studies was that the extra cognitive load (attention and memory) in the random task was the most important reason for the large MRCPs.

The present experiments tried to distinguish between different forms of preparatory brain activity by introducing the alternating task. As we argued in the 'Introduction', both this task and the random task involve a similar amount of switching from one movement to another and may therefore involve a similar amount of preparatory activity in motor structures. However, they differ in that the load on memory/attentional processes is less in the alternating than in the random task. Our hypothesis is that patterns in the MRCPs that are common to both the alternating and the random task but differentiate these tasks from the regular one can be attributed to the higher demands on motor preparation, rather than attention/memory. Effects that can only be seen in the random task but not in the regular or the alternating task are presumably related to attention/memory processes.

Location of extra activity related to motor preparation

MRCPs in both the alternating and the random tasks were larger than in the regular task. Following the reasoning above, this is likely to be related to the extra demands on motor preparation in the former tasks. The main increases involved frontocentral midline leads, as well as lateral central leads contralateral to the side of movement. Both effects have been reported in previous studies, particularly in those involving movements switching between the two hands (Praamstra et al. 1995; Touge et al. 1995; Dirnberger et al. 1998). The question is which structures are responsible for generating activity that is additional to that seen in the regular task.

The structures responsible for generating this extra activity are probably similar to those which are responsible for the regular MRCP itself (Praamstra et al. 1996) including central motor areas such as the SMA and cingulate cortices, with additional activity in sensorimotor and premotor cortex. It is consistent with the fact that MRCPs increase in random movements was much less prominent in patients with Parkinson's disease in whom SMA function is known to be compromised (Jahanshahi et al. 1995; Touge et al. 1995). We conclude that the extra activity needed to prepare motor instructions for al-

ternating and freely chosen random movements takes place in contralateral sensorimotor/premotor cortex as well as midline motor areas. The former areas may dominate EEG activity in the lateral central leads, whilst the latter may dominate in midline leads. Since increases in electrical activity can be seen in both areas even at the very onset of the MRCP, we presume that (1) these processes (which are additional to those needed for the regular task) begin at up to 2 s prior to onset of movement, and (2) that preparation occurs in parallel in both regions, rather than beginning in the midline and then spreading to lateral motor areas.

Facilitatory and inhibitory processes in motor preparation

The question is what is the nature of this extra motor preparation? A clue may come from comparing the alternating and regular tasks. In both cases, subjects know exactly what movement to make next; the only difference is that the movements change in the alternating task, but not in the regular task. The extra EEG activity in the alternating task must therefore come from processes involved in cancelling one movement and starting a new one. In essence we speculate that, in regular trials, some trace of the activity needed to produce the next movement persists between trials and reduces the amount of preparation needed for the next trial. This option is not available for either alternating or random movements. When a different movement is made on each trial, any persisting memory of the previous movement must be erased, and a full preparation completed for the subsequent movement. This extra preparation in motor structures presumably leads to the increased MRCP at central electrodes seen in these tasks.

The implication is that the preparation for movement involves inhibition as well as facilitation. Indeed, it is well known clinically that lesions of motor areas can produce both positive and negative motor signs. For example, damage to SMA and adjacent areas can lead to a reduction in self-initiated movements (Laplaine et al. 1977; Goldberg et al. 1981; Lang et al. 1991), but also to the alien limb sign or mirror movements (Brinkman 1984; Chan and Ross 1988; McNabb et al. 1988; Gasquoine 1993). The same might be true for the lateralized effect of 'mode', where any increase in the amplitude of the MRCPs also might result from inhibitory as well as excitatory processes. There are hints from animal and MRCP studies that both inhibitory and excitatory processes can produce similar electric potentials (Kalaska and Crammond 1995; Terada et al. 1995; Rothwell et al. 1998).

Therefore, it might well be possible that part of the extra midline negativity during the alternating and the random task can be attributed to enhanced inhibitory SMA activation, as well as facilitatory SMA activation. The process of inhibition may also account for another detail of the present results: a tendency for there to be more activity in ipsilateral central leads in the alternating

than in the regular and free choice tasks. In the alternating task, subsequent movements are always on opposite sides of the body. If we assume that activity related to cancellation of instructions for the previous movement is contralateral to that movement, then it will show up in the hemisphere ipsilateral to the next movement. The effect would not show up so well in the random movements since in that task there was not the requirement to switch movements from one hand to the other on every trial. In that task some movements could switch from index to middle finger of the same hand, in which case inhibitory and facilitatory motor preparation for the next movement would occur in the same hemisphere.

As we found the nature of the preceding movement to affect the amplitude of the MRCP, our findings might have some implications on the choice of blocked, alternating, or randomized designs in future MRCP studies.

Extra frontal activity in the random task

The random task involved extra activity in contralateral frontal leads that was not seen in either the alternating or regular conditions. In the absence of detailed modelling we can only speculate on the possible origin of this activity. It might result either from activity under the electrode itself, for example in the area of the dorsolateral prefrontal cortex, or it could be projected activity from a distant dipole. Candidate sources for the latter would be the SMA, projecting a dipole perpendicular to the inter-hemispheric fissure, or the motor or lateral premotor cortex, projecting perpendicular to the central sulcus. However, projected activity does not seem very likely. PET studies of free choice movements have shown slightly larger SMA activity contralateral to movement (Playford et al. 1992). According to studies by Lang et al. (1991), this should lead to a dipole with an ipsilateral frontal negativity rather than the contralateral one observed here. A dipole in the contralateral motor area is conceivable, although it would have to be quite separate from the source of the central negativity itself. The time course of the frontal activity was quite different to that over central leads throughout the entire length of the MRCP, and for all conditions examined.

The most likely explanation is that the extra activity results from local cortical discharge under the frontal electrode in the region of the DLPFC. Its function would be related to the additional requirement in the random task for subjects to choose the nature of the next movement. This is consistent with several studies that have shown that the DLPFC is involved in processes such as memory and attention that would be needed to perform this task. For example, lesions of the DLPFC lead to motor neglect and impaired initiation of movements contralateral to the lesion (Watson et al. 1978; Laplaine and Degos 1983; Daffner et al. 1990; Heilman et al. 1995), and PET activation studies have shown increased blood flow in the DLPFC in random versus regular movements

(Deiber et al. 1991; Playford et al. 1992). Increased flow in this region is also seen when subjects pay attention while they perform a prelearned sequence of movements compared with when they perform the sequence automatically (Jueptner et al. 1997).

Several previous studies have emphasized the importance of DLPFC in 'attention to action' (Passingham 1996). Such attention to action allows subjects to reflect on and to manipulate possible responses in the hand. It might also involve attention to somatosensory input or efference copy, as activity in the DLPFC is enhanced during directed attention towards somatosensory stimulation (Pardo et al. 1991). We suggest that lateralized activation of the contralateral DLPFC may be associated with unidirectional exploratory-motor attention in healthy normal subjects. Disorders of this system might be the basis for exploratory-motor neglect.

Conclusion

The present experiments show that, compared with regular movements, much of the extra EEG activity seen in alternating and freely chosen random tasks is caused by activity in motor structures related to the details of the next movement to be made. This difference is evident throughout the whole of the 2-s period of the MRCP, and we speculate that some of the effect may involve erasing any trace of activity related to the previous movement as well as preparing fully for the next movement. Higher level, cognitive aspects of the tasks also play a role in the random condition where extra activity detected over the contralateral frontal cortex may be related to the increased cognitive requirements of the random task.

References

- Barrett G, Shibasaki H, Neshige R (1986) Cortical potentials preceding voluntary movement: evidence for three periods of preparation in man. *Electroencephalogr Clin Neurophysiol* 63: 327–339
- Brinkman C (1984) Supplementary motor area of the monkey's cerebral cortex: short- and long-term deficits after unilateral ablation and the effects of subsequent callosal section. *J Neurosci* 4:918–929
- Chan J, Ross E (1988) Left-handed mirror writing following right anterior cerebral artery infarction: evidence of nonmirror transformation of motor programs by right supplementary motor area. *Neurology* 38:59–63
- Chatrjian GE, Lettich E, Nelson PL (1985) Ten percent electrode system for topographic studies of spontaneous and evoked EEG activities. *Am J EEG Technol* 25:83–92
- Daffner KR, Ahern GL, Weintraub S, Mesulam M (1990) Dissociated neglect behavior following sequential strokes in the right hemisphere. *Ann Neurol* 28:97–101
- de Jong R, Wierda M, Mulder G, Mulder LJ (1988) Use of partial stimulus information in response processing. *J Exp Psychol Hum Percept Perform* 14:682–692
- Deiber MP, Passingham RE, Colebatch JG, Friston KJ, Nixon PD, Frackowiak RS (1991) Cortical areas and the selection of movement: a study with positron emission tomography. *Exp Brain Res* 84:393–402
- Dirnberger G, Fickel U, Lindinger G, Lang W, Jahanshahi M (1998) The mode of movement selection: movement-related cortical potentials prior to freely selected and repetitive movements. *Exp Brain Res* 120:263–272
- Evans JF (1978) Monitoring attention deployment by random number generation: an index to measure subjective randomness. *Bull Psychonomic Soc* 12:35–38
- Gasquoine PG (1993) Alien hand sign. *J Clin Exp Neuropsychol* 15:653–667
- Goldberg G, Mayer NH, Togliola JU (1981) Medial frontal cortex infarction and the alien hand sign. *Arch Neurol* 38:683–686
- Greenhouse SW, Geisser S (1959) On methods in the analysis of profile data. *Psychometrika* 14:95–112
- Heilman KM, Valenstein E, Day A, Watson R (1995) Frontal lobe neglect in monkeys. *Neurology* 45:1205–1210
- Ikeda A, Shibasaki H (1992) Invasive recording of movement-related cortical potentials in humans. *J Clin Neurophysiol* 9: 509–520
- Ikeda A, Luders HO, Shibasaki H, Collura TF, Burgess RC, Morris HH 3rd, Hamano T (1995) Movement-related potentials associated with bilateral simultaneous and unilateral movements recorded from human supplementary motor area. *Electroencephalogr Clin Neurophysiol* 95:323–334
- Jahanshahi M, Jenkins IH, Brown RG, Marsden CD, Passingham RE, Brooks DJ (1995) Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. *Brain* 118:913–933
- Jueptner M, Stephan K, Frith CD, Brooks D, Frackowiak RSJ, Passingham RE (1997) Anatomy of motor learning. I. Frontal cortex and attention to action. *J Neurophysiol* 77: 1313–1324
- Kalaska JF, Crammond DJ (1995) Deciding not to GO: neuronal correlates of response selection in a GO/NOGO task in primate premotor and parietal cortex. *Cereb Cortex* 5:410–428
- Lang W, Cheyne D, Kristeva R, Beisteiner R, Lindinger G, 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
- Laplane D, Degos JD (1983) Motor neglect. *J Neurol Neurosurg Psychiatr* 46:152–158
- Laplane D, Talairach J, Meininger V, Bancaud J, Orgogozo JM (1977) Clinical consequences of corticectomies involving the supplementary motor area in man. *J Neurol Sci* 34:310–314
- Lindinger G (1990) Cortical DC-shifts: methods of computer aided acquisition and processing in neurology. Thesis, Technical University of Vienna, Austria
- McCarthy G, Wood CC (1985) Scalp distribution of event-related potentials: an ambiguity associated with analysis of variance models. *Electroencephalogr Clin Neurophysiol* 69:218–233
- McNabb AW, Carroll WM, Mastaglia FL (1988) "Alien hand" and loss of bimanual coordination after dominant anterior cerebral artery territory infarction. *J Neurol Neurosurg Psychiatr* 51: 218–222
- Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9:97–113
- Pardo JV, Fox PT, Raichle ME (1991) Localization of a human system for sustained attention by positron emission tomography. *Nature* 349:61–64
- Passingham RE (1996) Attention to action. *Philos Trans R Soc Lond Biol* 351:1473–1479
- Playford ED, Jenkins IH, Passingham RE, Nutt J; Frackowiak RS, Brooks DJ (1992) Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study. *Ann Neurol* 32:151–161
- Praamstra P, Stegeman DF, Horstink MW, Brunia CH, Cools AR (1995) Movement-related potentials preceding voluntary movement are modulated by the mode of movement selection. *Exp Brain Res* 103:429–439

- Praamstra P, Stegeman DF, Horstink MW, Cools AR (1996) Dipole source analysis suggests selective modulation of the supplementary motor area contribution to the readiness potential. *Electroencephalogr Clin Neurophysiol* 98:468–477
- Rektor I, Fève A, Buser P, Bathien N, Lamarche M (1994) Intracerebral recording of movement related readiness potentials: an exploration in epileptic patients. *Electroencephalogr Clin Neurophysiol* 90:273–283
- Rothwell JC, Higuchi K, Obeso JA (1998) The offset cortical potential: an electrical correlate of movement inhibition in man. *Mov Disord* 13:330–335
- Terada K, Ikeda A, Nagamine T, Shibasaki H (1995) Movement-related cortical potentials associated with voluntary muscle relaxation. *Electroencephalogr Clin Neurophysiol* 95:335–345
- Touge T, Werhahn KJ, Rothwell JC, Marsden CD (1995) Movement-related cortical potentials preceding repetitive and random-choice hand movements in Parkinson's disease. *Ann Neurol* 37:791–799
- Watson RT, Miller B, Heilman KM (1978) Nonsensory neglect. *Ann Neurol* 3:505–508