Movement-related potentials in Parkinson’s disease
Motor imagery and movement preparation

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Summary
Movement-related potentials (MRPs) associated with voluntary movements reflect cortical activity associated with processes of movement preparation and movement execution. Early-stage pre-movement activity is reduced in amplitude in Parkinson’s disease. However, it is unclear whether this neurophysiological deficit relates to preparatory or execution-related activity, since previous studies have not been able to separate different functional components of MRPs. Motor imagery is thought to involve mainly processes of movement preparation, with reduced involvement of end-stage movement execution-related processes. Therefore, MRP components relating to movement preparation and execution may be examined separately by comparing MRPs associated with imagined and actual movements. In this study, MRPs were recorded from 14 subjects with Parkinson’s disease and 10 age-matched control subjects while they performed a sequential button-pressing task, and while they imagined performance of the same task. Early-stage pre-movement activity was present in both Parkinson’s disease patients and control subjects when they imagined movement, but was reduced in amplitude compared with that for actual movement. Movement execution-related components, arising predominantly from the primary motor cortex, were relatively unaffected in Parkinson’s disease subjects. However, motor preparatory processes, probably involving the supplementary motor area, were reduced in amplitude overall and abnormally prolonged, indicating impaired termination following the motor response. Further, this impaired termination of preparatory-phase activity was observed only in patients with more severe parkinsonian symptoms, and not in early-stage Parkinson’s disease.

Keywords: Parkinson’s disease; movement preparation; supplementary motor area

Abbreviations: MRP = movement-related potential; SMA = supplementary motor area

Introduction
The neural control of voluntary movement involves complex interactions between cortical and subcortical areas which are difficult to examine non-invasively in the human brain. Cortical activity associated with movement preparation and execution can be detected at the scalp surface by averaging EEG activity to reveal MRPs occurring before and during voluntary movement. However, it is difficult to separate functional components of MRPs relating to different stages of the motor control process since they generally overlap in time.

Despite this difficulty, two major components can be distinguished in MRPs associated with voluntary movement. A late component, consisting of a rapidly increasing negative potential, begins within 500 ms prior to movement. This late component is thought to reflect activity associated with movement execution, arising predominantly from the contralateral primary motor cortex, since its localization appears to follow the somatotopic organization of the primary motor cortex, varying from lateral sources for finger movement to medial sources for foot movement (Boschert et al., 1983; Brunia and van den Bosche, 1984; Brunia et al., 1985).

The early component of the MRP consists of a more slowly increasing negative potential, usually beginning between 1 and 2 s prior to movement. This early component is bilaterally symmetrical across the scalp with a maximal amplitude recorded at the vertex (position Cz), but generally shows a wide-spread distribution across the scalp.

The early MRP component is generally considered to reflect activity associated with processes of movement preparation.
However, there is much debate regarding the source of this activity. Studies of single-cell activity in monkeys have identified neurons which show increased preparatory or ‘set-related’ activity, often beginning several seconds prior to movement onset (Wise and Kurata, 1989; Romo and Schultz, 1992; Tanji and Shima, 1994). Such neurons are found in the highest proportion within the SMA (Tanji, 1985; Alexander and Crutcher, 1990; Riehle and Requin, 1995), but they are also found within primary motor cortex (Tanji, 1985; Alexander and Crutcher, 1990) and somatosensory and parietal areas (Riehle et al., 1994; Riehle and Requin, 1995). In humans, intracranial recordings from within premotor and sensorimotor areas show that both the SMA and primary motor cortex contribute to early-stage pre-movement activity (Neshige et al., 1988; Ikeda et al., 1992; Rektor et al., 1994). Studies of MRPs using dipole-source-analysis methods have shown mixed results, with some supporting sources located within the SMA and primary motor cortex (Toro et al., 1993; Tarra, 1994; Praamstra et al., 1996b), but others supporting sources located mainly within primary motor cortex only (Bötzel et al., 1993; Böckler et al., 1994). Studies of magnetoencephalography initially failed to localize pre-movement activity within the SMA (Cheyne and Weinberg, 1989; Kristeva et al., 1991), since bilateral SMA activity may have caused current-source dipoles of opposite directions to cancel at the scalp surface (Cheyne and Weinberg, 1989). A subsequent study of a patient with a unilateral SMA lesion found pre-movement activity within the intact SMA, beginning ~1.2 s prior to movement (Lang et al., 1991). Similarly, modulations of magnetoencephalographic activity along the central sulcus, indicating increased activation of primary motor cortex, may begin up to 1 s prior to movement onset (Salminen et al., 1995). It is therefore clear that several areas, particularly the SMA and primary motor cortex, may contribute to early-stage pre-movement activity. In this study, however, we are more concerned with the neurophysiology of this activity in relation to processes of movement preparation, rather than its precise anatomical location.

There is considerable evidence that the SMA plays a major role in movement preparation and planning (for review, see Cunnington et al., 1996a). The SMA is more involved in internally determined rather than externally cued movements. This has been shown both by studies of cerebral blood flow in humans (Deiber et al., 1991) and single-cell recordings in monkeys (Mushiake et al., 1991; Romo and Schultz, 1992). Similarly, the SMA is more involved in complex and sequential movements rather than simple repetitive movements (Roland et al., 1980; Rao et al., 1993; Shibasaki et al., 1993). Such complex sequential movements and non-externally cued movements require a greater degree of internal planning and preparation for their organization. Therefore, the SMA has been suggested to play an important role in the internal organization of voluntary movement, establishing motor programs or time-ordered motor commands (Orgogozo and Larsen, 1979; Roland et al., 1980), and transforming intention into the specification of action (Goldberg, 1985).

Such a role of the SMA is also supported by clinical studies of the motor deficits associated with Parkinson’s disease. Input to the SMA arises predominantly from the globus pallidus of the basal ganglia, via the ventral lateral thalamus (Schell and Strick, 1984; Tokuno et al., 1992; Hoover and Strick, 1993), and Parkinson’s disease involves a loss of dopaminergic neurons of the substantia nigra pars compacta, severely disrupting basal ganglia function (Marsden, 1990). Therefore, deficits in SMA function would be expected in Parkinson’s disease since its major input from the basal ganglia is impaired. In accord with the proposed functions of the SMA, parkinsonian patients show particular motor deficits in the absence of external cues, i.e. when movements must be internally determined (Jones et al., 1992; Georgiou et al., 1993, 1994), and in the performance of complex and sequential movements involving simultaneous control of multiple joints (Benecke et al., 1986) or the organization of submovements into motor sequences (Benecke et al., 1987; Harrington and Haaaland, 1991).

Neurophysiological studies have shown particular deficits in SMA activity associated with Parkinson’s disease. Studies of cerebral blood flow show that activity within the SMA and putamen during movement is significantly reduced in parkinsonian compared with healthy control subjects (Playford et al., 1992, 1993). However, this impairment is improved following treatment with apomorphine (Jenkins et al., 1992; Rascol et al., 1992) and levodopa (Rascol et al., 1994) which both act to increase dopamine levels in the striatum, improving basal ganglia function. Similarly, pre-movement activity associated with the early MRP component is significantly reduced in amplitude in parkinsonian subjects compared with healthy controls (D Leeke et al., 1977; Shibasaki et al., 1978; Simpson and Khurabi, 1987; Dick et al., 1989; Cunnington et al., 1995), and this deficit in the amplitude of the early component is improved with levodopa treatment (Dick et al., 1987). Further, in a direct comparison of activity measured by cerebral blood flow and MRP methods, Jahanshahi et al. (1995) showed that the lower amplitude of the early MRP component in parkinsonian subjects was associated with underactivation of the SMA. The consistency of results between these two methods therefore provides further evidence that the SMA indeed contributes to early-stage preparatory activity of the MRP.

More recently, it has been reported that MRPs for parkinsonian subjects show a prolonged peak, indicating impairment in the termination of pre-movement activity following movement onset (Cunnington et al., 1995; Harasko-van der Meer et al., 1996). This deficit is also apparent in MRP traces of other studies, but has not as such been reported (D Leeke et al., 1977; Dick et al., 1989). Such a deficit is difficult to examine and interpret since the termination phases of activity associated with early and late MRP components, which overlap around the time of movement onset, are difficult to separate. In our previous study (Cunnington et al., 1995), we suggested that this prolonged activity represented impairment in the termination of early component preparatory
activity, since movement durations did not differ between parkinsonian and control subjects, and so movement-execution components were unlikely to have differed between the groups. However, our interpretation could not be conclusively supported since it was not possible to separate early and late MRP components.

It may be possible to examine MRP components relating to movement preparation and execution separately by recording MRPs associated with imagined movements. Motor imagery is claimed to involve the same processes of motor preparation as actual movements, but without the end-stage processes related to movement execution (Jeannerod, 1994; Decety, 1996). Imagined and executed movements both result in autonomic activation involving increased heart rate and respiration (Decety et al., 1991, 1993). Such autonomic changes usually occur immediately before movement onset, and are therefore related to the preparation for action (Jeannerod, 1994). Both imagined and executed movements therefore involve similar vegetative preparatory processes. Further, imagined and executed movements have the same temporal characteristics (Decety and Michel, 1989; Sirigu et al., 1996), while in patients with hemi-Parkinson’s disease, both imagined and executed movements are similarly slowed on the affected side, compared with the unaffected side (Dominey et al., 1995).

Similar neurophysiological processes also appear to underlie both movement preparation and motor imagery. Studies of cerebral blood flow have consistently shown that imagined movements involve strong activation of the SMA, as with movement execution, but little if any activation of primary motor cortex (Roland et al., 1980; Decety et al., 1988; Rao et al., 1993). Similarly, Stephan et al. (1995) found little difference in activation of the SMA and lateral premotor cortex during motor imagery compared with movement execution, but found reduced activation of the contralateral primary motor cortex during motor imagery. Stephan et al. (1995) also examined an additional condition of movement preparation, which showed further reduced activation of medial (SMA) and lateral premotor areas compared with motor imagery. However, since there was no resting condition examined, it was not known whether the movement preparation condition involved any significant activation of SMA and premotor areas (as would be expected), nor whether primary motor cortex activity contributed to either movement preparation or motor imagery conditions. More recently, Roth et al. (1996) reported that the primary motor cortex is involved in motor imagery, although its level of activation was only 30% of that found for movement execution, while the level of SMA activity did not differ significantly between imagined and executed movements. Similarly, Beisteiner et al. (1995) showed a lateralized topography of MRPs localized to contralateral primary sensorimotor areas during motor imagery, but with significantly reduced amplitudes during imagery compared with actual movement execution. Therefore, these studies indicate that the SMA shows similar activation for both imagined and executed movements; however, the primary motor cortex, while still involved in motor imagery, shows greatly reduced activation compared with movement execution. Crammond (1997) tentatively suggests that the low levels of activation of primary motor areas during motor imagery may be the ‘neuronal correlate of the motor efference copy’.

Motor imagery also involves activation of additional prefrontal areas, including dorsolateral prefrontal and anterior cingulate areas (Decety et al., 1988; Ceballos-Baumann et al., 1994; Stephan et al., 1995). These areas are also activated during actual movement performance and are therefore suggested to reflect task-specific cognitive processes possibly associated with attention and memory (Jeannerod, 1994; Decety, 1996).

Our recent study of MRPs associated with motor imagery showed that the early MRP component did not differ in amplitude or temporal and topographic characteristics during imagined movements compared with actually performed movements. However, the late MRP component was significantly reduced in amplitude for imagined movements (Cunnington et al., 1996b). Consistent with previous studies, these results suggest that both imagined and executed movements involve similar early-phase motor preparatory processes, but involve reduced activity of primary motor cortex which is normally associated with movement execution-related processes.

The aim of this study was therefore to separate MRP components relating to movement execution from other contributing components by recording MRPs associated with motor imagery, and thereby to examine the precise nature of any deficits in preparatory and execution-related activity associated with basal ganglia dysfunction in Parkinson’s disease. As is common in studies of cerebral blood flow, activity relating to individual functional processes was found by comparing (subtracting) results during conditions in which specific task components were progressively removed. Subjects performed three experimental conditions: (i) performing a sequential button-pressing task in response to external cues; (ii) imagining performance of the same task in response to the same cues; and (iii) watching and focussing attention on the same sequence of external cues, but without imagining movement. A sequential movement task similar to the one we have used previously (Cunnington et al., 1995, 1996b) was chosen, since MRPs show the greatest amplitude for sequential rather than simultaneous or simple movements (Benecke et al., 1985; Lang et al., 1989; Simonetta et al., 1991; Kitamura et al., 1993). As subjects made no overt responses during imagined movements, it was essential to provide external cues to which MRPs could be time-locked. Such cues may result in cognitive potentials relating to anticipation or expectancy, such as the contingent negative variation (Walter et al., 1964). Therefore, this was controlled in the third condition which was designed to involve only extraneous components common to all tasks. The performed-movement task should involve additional components relating...
Table 1 Clinical data for Parkinson’s disease subjects

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Duration of PD (years)</th>
<th>Webster rating</th>
<th>Hoehn and Yahr stage</th>
<th>Medication*</th>
<th>Dose (mg/day)</th>
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<td>Madopar</td>
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*Generic names for medication: Sinemet = levodopa/carbidopa; Sinemet CR = controlled release levodopa/carbidopa; Madopar = levodopa/benserazide; Eldepryl = selegiline hydrochloride; Permax = pergolide mesylate; PD = Parkinson’s disease.

...to movement preparation and execution, while the imagined-movement task should involve reduced movement execution-related activity of primary motor cortex. By subtracting between conditions, components relating predominantly to movement preparation and execution may therefore be separated and examined in detail.

**Method**

**Subjects**

Subjects consisted of 14 patients with Parkinson’s disease (mean age $\pm$ SD = 67.6 $\pm$ 10.5 years) and 10 healthy control subjects of the same age range (64.0 $\pm$ 8.9 years). All subjects were male and were right handed. Parkinson’s disease patients were assessed according to the Webster scale (mean severity 10.5 $\pm$ 4.9) and Hoehn and Yahr stage of disease (mean stage 2.1 $\pm$ 0.9). Webster ratings were significantly correlated with age, $r = 0.67, P < 0.01$, and Webster and Hoehn and Yahr ratings were also highly correlated, $r = 0.89, P < 0.01$. Patients remained on their normal medication throughout the study (see Table 1 for clinical details). All subjects were without previous history of head injury, stroke or other neurological disturbance, were not clinically depressed, and were screened for dementia using the Short Test of Mental Status (Kokmen et al., 1987). Informed consent was obtained from each subject in accordance with the declaration of Helsinki, and all experimental work was carried out under the approval of the Kingston Centre Research and Ethics Committees.

**Procedure**

Subjects performed experiments using a tapping board, consisting of a box containing two parallel rows of 10 buttons, one above the other (Fig. 1). Light emitting diodes underneath each button provided both temporal and spatial cues, and were initially illuminated along a particular pathway, consisting of 10 alternating top and bottom row buttons (see Fig. 1). During experimental trials, lights were progressively extinguished from right to left at a constant rate of one every 4 s. Three experimental conditions were examined.
**Performed movements**

Subjects were required to hold down each illuminated button (starting from the right), until the light underneath was extinguished (always a period of 4 s), then to move as quickly as possible to press the next illuminated button in the sequence.

**Imagined movements**

Subjects were instructed to focus on the last illuminated button to the right and imagine their finger pressing the button. When the light underneath was extinguished (after 4 s), subjects imagined moving their finger to press the next illuminated button in the sequence, without actually performing the movement.

**Watching cues**

Subjects simply focussed on the last illuminated button to the right and, when the light underneath was extinguished (after 4 s), they focussed on the next illuminated button in the sequence. Subjects were instructed not to imagine any finger movement, and only to move their eyes to follow the progressive extinction of lights along the sequence.

For all conditions, subjects were explicitly instructed to try to anticipate extinction of the light cue, so that when the cue was given they were ready to respond. A previous study has shown that the amplitude of the early MRP component is dependent upon the internal generation of responses (Cunnington et al., 1995). Therefore, subjects were always instructed to concentrate on anticipating the cue and thereby internally generating responses, even though an external timing cue was provided. The external cue was nonetheless necessary to provide a constant time point with which MRPs to covert responses could be determined.

Conditions were always performed in the above order, with all subjects performing movement first. Our previous study has shown that the early MRP component for imagined movement is of larger amplitude when subjects have prior practice at performing a movement before imagining it (Cunnington et al., 1996b).

Movement-related potentials were recorded using an Amlab workstation (AMLAB International, Sydney, Australia) which performed digital on-line processing and averaging of EEG and EMG activity. The EEG was recorded from silver/silver chloride surface electrodes, with recording electrodes placed at positions C3, Cz and C4 (10–20 system), referenced bilaterally to electrodes over both mastoids, and with a ground electrode on the forehead. EMG activity associated with upper limb movement was recorded from two silver/silver chloride surface electrodes placed over the biceps brachii muscle of the right arm. Electrode impedances were always kept <5 kΩ.

The EEG was amplified using isolated AC amplifiers with a long time constant (gain 20 000 V/V, time constant 25 000 ms), digitized at 100 Hz, and filtered at 20 Hz (low-pass). The EMG was amplified at a gain of 10 000 V/V (time constant 97 ms), digitized at 100 Hz, and filtered at 48 Hz (low-pass). The EEG and EMG potentials were averaged over 4-s sweeps, time-locked to the extinction of light cues on the tapping board, over the period from 3 s before the cue to 1 s after it. An artefact-rejection system disabled the averager for any sweeps in which the recorded EEG potential deviated by >150 µV peak-to-peak. Consequently, sweeps containing artefacts from vertical eye movements, blinks and large EMG responses from neck and jaw muscles were rejected from the mean. At least 100 sweeps were averaged in each condition for each subject. Averaged potentials were calibrated to µV units and corrected to a baseline calculated as the average potential over the first 1000 ms of the trace.

Extraneous components of MRPs associated with the task, such as the anticipation of forthcoming cues, horizontal eye movements associated with following the lights along the board and visual evoked potentials associated with extinction of the light cues, were further controlled by examining the condition of watching cues. Horizontal eye movements associated with the task would be minimal since consecutive buttons on the board subtend a visual angle of 1.5°, and we have previously found no contribution of electro-oculographic activity to MRPs for the same movement execution task (Cunnington et al., 1995). Similarly, our previous study using the same motor-imagery task showed no difference between MRPs for the watching-cues condition compared with a fixation condition in which no eye movements were made. Therefore, horizontal eye movements between responses did not contribute to recorded MRPs (Cunnington et al., 1996b). In this study, the effect of any such eye movements has been controlled by examining the watching cues condition which is identical in every physical way to the imagined-movement condition.

MRPs for the watching-cues condition would therefore involve only extraneous components, while MRPs for the imagined-movement condition would involve additional components relating to the planning and preparation of the forthcoming response. Therefore, to separate the MRP component relating only to movement preparation, MRPs for the watching-cues condition were subtracted from those for the imagined-movement condition. Similarly, MRPs for the performed-movement condition would involve additional components relating to movement execution. Therefore, to separate the component relating to movement execution alone, MRPs for the imagined-movement condition were subtracted from those for the performed-movement condition.

Characteristics of averaged potentials and subtracted functional components for each subject in each condition were quantified by the following measures.

**Early-component onset-time**

This concerns the time prior to the cue when the early component of the potential began to increase in negativity.
(Cunnington et al., 1995, 1996b). Using iterative curve-fitting software (Marquardt-Levenberg algorithm), the potential over the period from 3000 to 500 ms prior to the cue was fitted with two linear segments representing: (i) baseline activity prior to the MRP onset; and (ii) the increasing potential of the early component of the MRP. The point of intersection of the two segments represented the early-component onset-time.

**Early slope**
This is the average slope of the potential over the period from 1500 to 500 ms prior to the cue, calculated by linear regression. Activity over this time interval reflects the increase in neural activity associated with the early component of the MRP, since our previous studies have shown the early component to begin at position Cz >1500 ms prior to the cue for this task (Cunnington et al., 1995, 1996b).

**Peak amplitude**
The maximum amplitude of the potential occurring near the time of the cue. This reflects the combined activity of early and late components of the MRP which overlap around the time of movement onset. Previous studies have examined both peak and late component amplitudes of MRPs (Dick et al., 1989; Jahanshahi et al., 1995). However, since the late component amplitude is derived from the difference between peak and early component amplitudes it is somewhat redundant. In our previous study, the peak amplitude measure was sufficiently reliable to show significant differences between imagined and executed movements (Cunnington et al., 1996b). Our measure of the peak amplitude is arithmetically different from the peak amplitude of group mean MRPs. Peak amplitudes for individual MRP traces vary in time, and as a consequence are partly averaged out when combined into group mean MRPs. Therefore, this measure of peak amplitude may appear quite different from the peak amplitudes in mean MRPs, since it is measured from individual traces before averaging group data.

**Peak time**
This is the time, relative to movement, at which MRPs reached peak amplitude.

**Post-peak slope**
This is the average slope of the potential from the time of the peak to 300 ms after the peak. This reflects the rate of decrease in activity associated with the termination of pre-movement activity reflected in the MRP (Cunnington et al., 1995).

Measures of the post-peak slope were not analysed for the experimental conditions of performed movement and imagined movement, since the termination of both pre-movement and execution-related activity overlap following the peak, making interpretation difficult. The post-peak slope was therefore measured only for the subtracted functional MRP components in which these confounding factors were separated.

Potentials recorded only at position Cz were analysed for comparison between conditions and between subject groups, since the greatest amplitude pre-movement activity is consistently recorded from position Cz (Cunnington et al., 1995). Lateralized differences in potentials across the scalp were subsequently analysed by comparing potentials recorded at positions C3 (left hemisphere) and C4 (right hemisphere). All measures were analysed by ANOVA (analysis of variance) (mixed factorial with unweighted means) and t tests where appropriate.

**Results**
Mean MRPs for performed-movement, imagined-movement, and watching-cues conditions are shown for control subjects in Fig. 2 and for Parkinson’s disease subjects in Fig. 3. As can be seen, a pre-movement rise in activity was clearly present in both subject groups for both performed- and imagined-movement conditions, but not for the watching-cues condition. However, the amplitude of MRPs was greatly reduced for Parkinson’s disease subjects. EMG responses also clearly show activation of biceps muscles during movements in both control and Parkinson’s disease subjects, but no significant muscle activation when they imagined movement or watched cues.

Measures of the early slope and peak amplitude of these potentials are shown in Figs 4 and 5, respectively. As can be seen, the early slope and peak amplitude were always greatest in potentials recorded from position Cz. Single-sample t tests showed a significant level of early slope (significantly different from zero) in both subject groups during both performed and imagined movements (P < 0.001), but no significant early slope during cue watching alone (P > 0.05). Therefore, since the watching cues condition did not involve any significant level of activity associated with the early component of the MRP, it was not included in subsequent analyses.

As can be seen in Figs 4 and 5, both the early slope and peak amplitude are greater for control subjects than for Parkinson’s disease subjects, and are also both greater for the performed-movement condition than the imagined-movement condition. These differences were analysed by two-way ANOVA, showing significant differences between subject groups both for the early slope [F(1,22) = 20.32, P < 0.001], and peak amplitude [F(1,22) = 4.44, P < 0.05], and significant differences between conditions for both the early slope [F(1,22) = 17.65, P < 0.001], and peak amplitude [F(1,22) = 66.64, P < 0.001], but no significant interactions between subject groups and conditions for the early slope [F(1,22) = 0.93, P > 0.05], or for the peak amplitude [F(1,22) = 0.56, P > 0.05]. Recorded MRPs therefore
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showed both a greater increase in activity over the early component and greater overall peak amplitude for control subjects than Parkinson’s disease subjects, and when subjects were performing movements rather than imagining movements.

Lateralized differences in MRPs across the scalp were also examined by comparing early slopes and peak amplitudes of potentials recorded from lateral positions C3 (left) and C4 (right). As can be seen in Fig. 4, the early slope appears to be relatively symmetrical, with little difference between positions C3 and C4 for both subject groups over all conditions. This was supported by three-way ANOVA showing no significant difference between lateral recording sites \( F(1,22) = 0.39, P > 0.05 \), nor any significant two- or three-way interactions between the recording site and subject groups or conditions \( (P > 0.05) \).

Similarly, as shown in Fig. 5, the peak amplitude appears to be symmetrical for the imagined-movement condition, with little difference between C3 and C4 recording sites. However, for the performed-movement condition, the peak amplitude appears to be lateralized to the left side, with a greater amplitude at position C3. Accordingly, three-way ANOVA showed a significant interaction between recording sites and conditions \( F(1,22) = 18.17, P < 0.001 \), which was due to a significant difference between lateral recording sites for the performed-movement condition \( F(1,22) = 27.92, P < 0.001 \), but not for the imagined-movement condition \( F(1,22) = 0.44, P > 0.05 \).

Therefore, the early components of recorded MRPs were bilaterally symmetrical across the scalp for both subject groups, both during performed and imagined movements. The peak amplitude was found to be similarly symmetrical for the imagined-movement condition, but was significantly lateralized to the left hemisphere in both subject groups during actual movements.

Early-component onset-times and peak times of MRPs were also examined. Mean onset times for MRPs at position Cz did not significantly differ between Parkinson’s disease (mean 1.64 ± 0.54 s prior to movement) and control subjects (mean 1.70 ± 0.49 s) \( F(1,22) = 0.12, P > 0.05 \), and did not significantly differ between conditions of performing (mean 1.62 ± 0.48 s) and imagined movement (mean 1.71 ± 0.56 s) \( F(1,22) = 0.33, P > 0.05 \), nor was there any significant interaction between subject groups and conditions \( F(1,22) = 0.30, P > 0.05 \). Further, there were no significant lateralized differences in onset times between recording sites C3 and C4 \( F(1,22) = 0.16, P > 0.05 \), nor any significant interactions involving the recording site \( (P > 0.05) \). Early-component onset-times were therefore consistent across subject groups, conditions, and recording sites.

Peak times of MRPs also showed no significant difference between Parkinson’s disease (mean 75 ± 195 ms prior to
Fig. 3 Mean MRPs for Parkinson's disease subjects, recorded from scalp positions C3, Cz and C4, for conditions of performing movement, imagined-movement and watching cues. Potentials are shown from 3 s before the cue to 1 s after it, with the dotted line marking the time of the cue.

Fig. 4 Means and standard errors of the early slope of MRPs across scalp locations for control and Parkinson's disease subjects.

Fig. 5 Means and standard errors of the peak amplitude of MRPs across scalp locations for control and Parkinson's disease subjects.
movement) and control subjects (mean 109 ± 187 ms prior to movement) \(F(1,22) = 0.41, P > 0.05\). However, the peak time was significantly earlier for the imagined-movement condition (mean 191 ± 160 ms prior to movement) than for the performed-movement condition (mean 13 ± 165 ms after movement onset) \(F(1,22) = 22.22, P < 0.001\). This was consistent for both parkinsonian and control subjects, since there was no significant interaction between subject groups and conditions \(F(1,22) = 0.02, P > 0.05\). An examination of lateralized differences in MRP peak times showed no significant difference between C3 and C4 recording sites \(F(1,22) = 0.01, P > 0.05\), nor any significant interactions involving recording site \(P > 0.05\). Peak times were therefore consistent across subject groups and recording sites, but were significantly earlier during imagined-movements than during performed movements.

Figure 6 shows mean MRP components relating only to movement execution, found by subtracting MRPs for imagined-movements from MRPs for performed movements. As can be seen, there appears to be very little difference in execution-related components between control and Parkinson’s disease subjects, both in terms of amplitudes and temporal profiles. Accordingly, independent \(t\) tests showed no significant differences in potentials at Cz between control and Parkinson’s disease subjects for measures of early slope \([t(22) = 1.85, P > 0.05]\), peak amplitude \([t(22) = 0.37, P > 0.05]\), nor post-peak slope \([t(22) = 0.14, P > 0.05]\).

Lateralized differences in the execution-related components across the scalp were also examined. Both the early slope and peak amplitude were greater in potentials at position C3 (means 2.32 μV/s and 8.42 μV, respectively) than C4 (means 1.49 μV/s and 5.68 μV, respectively). Consequently, two-way ANOVA showed significant differences between lateral recording sites for both the early slope \(F(1,22) = 7.05, P < 0.05\), and peak amplitude \(F(1,22) = 24.22, P < 0.001\), but no significant differences between subject groups, or interactions between recording sites and subject groups \(P > 0.05\).

Therefore, MRP components relating to movement execution alone were found to be lateralized to the left hemisphere, with both a greater early slope and peak amplitude at position C3 than at C4. Further, this lateralization, as well as overall measures of early slope, peak amplitude and post-peak slope, did not differ significantly between controls and Parkinson’s disease subjects.

Mean MRP components relating to movement preparation only, found by subtracting MRPs for watching cues from MRPs for imagined movements, are shown in Fig. 7. An examination of individual MRP traces revealed that some parkinsonian subjects showed an apparent prolonged peak of activity around the time of the cue. Therefore, correlations were performed between measures of the post-peak slope and clinical measures for Parkinson’s disease subjects. The post-peak slope was negatively correlated with both age \((r = -0.57, P < 0.05)\), and severity as measured on the Webster scale \((r = -0.53, P < 0.05)\), indicating that older and more severe Parkinson’s disease subjects showed a reduced post-peak slope of the MRP compared with younger and less severely affected patients.

In order to examine this relationship between MRPs and clinical status, Parkinson’s disease subjects were subdivided into groups of early-stage (five subjects with Webster rating <10) and later-stage disease (nine subjects with Webster rating of ≥10). Compared with the later-stage group, the early-stage group were significantly younger (mean ages 69.2 ± 4.8 and 54.6 ± 6.2 years, respectively) \([t(12) = 4.95, P < 0.001]\), rated significantly lower on the Webster scale (mean severity 13.4 ± 3.2 and 5.2 ± 1.9, respectively) \([t(12) = 5.25, P < 0.001]\), and were also significantly younger \((r = 0.42, P > 0.05)\), indicating that differences in the post-peak slope between early and later-stage Parkinson’s disease subjects were unlikely to be due to ageing per se.

Mean MRPs relating to movement preparation alone for each subject group are shown in Fig. 7. As can be seen, MRPs appear to be reduced in amplitude for both early- and later-stage Parkinson’s disease subjects compared with controls. Also, MRPs appear to be terminated sharply at the time of the cue, returning rapidly to the baseline level, for control and early-stage patients, but not for later-stage Parkinson’s disease subjects. These differences are reflected in measurement of the early slope, peak amplitude, and post-peak slope (Fig. 8). As can be seen, both Parkinson’s disease groups showed a reduced early slope compared with control subjects. Independent \(t\)-tests showed that the early slope was significantly greater for control subjects compared with
both early-stage \( t(13) = 2.37, P < 0.05 \) and later-stage Parkinson’s disease subjects \( t(17) = 2.29, P < 0.05 \), and there was no significant difference between Parkinson’s disease groups \( t(12) = 0.12, P > 0.05 \). Measures of the peak amplitude followed the same pattern, with both early and later-stage patients showing a reduced peak amplitude compared with controls. However, differences between groups were not significant for this measure \( (P > 0.05) \).

Measures of the post-peak slope, however, were reduced only for later-stage Parkinson’s disease subjects (Fig. 8). Independent \( t \) tests showed that the post-peak slope was significantly reduced (indicating a less steep slope) for later-stage compared with early-stage Parkinson’s disease subjects \( t(12) = 2.64, P < 0.05 \), and compared with controls \( t(17) = 3.28, P < 0.01 \), and early-stage patients did not differ significantly from controls \( t(13) = 0.41, P > 0.05 \). Even when the post-peak slope was corrected for differences in amplitudes between groups (i.e. by dividing the post-peak slope by the peak amplitude), later-stage patients still showed a significantly reduced post-peak slope compared with early-stage patients \( t(12) = 2.83, P < 0.05 \), and compared with control subjects \( t(17) = 2.15, P < 0.05 \). Therefore, while the early component of the MRP was significantly reduced in amplitude for both Parkinson’s disease groups, the more severely affected later-stage patients also showed a significantly reduced post-peak slope of the MRP following the cue which was not simply related to differences in MRP amplitudes between the groups.

Lateralized differences in MRPs across the scalp were also assessed, comparing early slopes and peak amplitudes from lateral recording sites C3 and C4. Two-way ANOVA showed no significant differences between lateral recording sites for either the early slope \( F(1,22) = 1.31, P > 0.05 \), or peak amplitude \( F(1,22) = 0.33, P > 0.05 \), nor any significant interactions between recording sites and subject groups for either measure \( (P > 0.05) \), indicating that the early slope and peak amplitude were both symmetrically distributed across the scalp for all subject groups.

**Discussion**

Movement-related potentials associated both with actual and imagined movement showed increasing pre-movement activity beginning ~1.7 s prior to the cue. For the performed-movement condition, recorded MRPs were consistent with those reported previously. The early slope, reflecting motor preparatory processes, was symmetrically distributed across the scalp and maximal over position Cz. The peak amplitude, however, reflecting later components of the MRP occurring around the time of movement onset, was significantly lateralized to the left side, with a greater amplitude at position C3 than C4. Therefore, this later component probably reflects
increasing activity of the left-side primary motor cortex associated with the execution of right-side finger movement (Boschert et al., 1983; Brunia et al., 1984; Deecke et al., 1987).

MRPs were also reduced in amplitude for Parkinson’s disease subjects compared with their age-matched controls. This is consistent with previous studies which show that the early MRP component to be reduced in amplitude in Parkinson’s disease (Deecke et al., 1977; Shibasaki et al., 1978; Simpson and Khuraibet, 1987; Dick et al., 1989; Jahanshahi et al., 1995), and is consistent with studies of cerebral blood flow which show reduced SMA activation during movement in Parkinson’s disease (Jenkins et al., 1992; Playford et al., 1992, 1993; Jahanshahi et al., 1995).

Movement-related potentials for imagined movements also showed increasing early-component activity for both Parkinson’s disease and control subjects. This early component activity was not related to actual movement, since EMG responses showed no sign of muscle activation at the time of the imagined movement response. Similarly, increased activity was not likely to reflect cognitive potentials such as the contingent negative variation, relating only to anticipation of the forthcoming cue and response, since no such pre-cue activity was observed for the watching cues condition which involved the same anticipation of the cue, as well as similar eye movements and visual evoked-potentials. Therefore, increased activity observed prior to imagined movements was probably related directly to the imagined movement response itself.

The early slope of the MRP associated with imagined movement was bilaterally symmetrical across the scalp and maximal at position Cz, and therefore showed the same pattern as the early component of MRPs associated with movement performance. The latter component, reflected in measurement of the peak amplitude, was also found to be symmetrical across the scalp for imagined movements, suggesting the absence of lateralized activity related to movement execution which would normally arise mainly from the primary motor cortex. Although previous studies have found lateralized activity during imagined movement (Beisteiner et al., 1995) and reduced but still detectable activation of primary motor cortex during motor imagery (Roth et al., 1996), our results suggest that imagined movement involves little primary motor cortex activity, which would normally be associated with movement execution.

The MRP component presumed to reflect movement execution alone, found by subtracting MRPs relating to imagined movement from those relating to movement performance, was significantly lateralized toward the left side for both the early slope and peak amplitude. Execution-related components should arise predominantly from the left-side primary motor cortex, since most other components of the potential should have been removed by subtraction. Accordingly, observed potentials were significantly lateralized towards the left side over both early and late stages, further indicating that they do indeed reflect predominantly movement execution-related processes arising mainly from the left primary motor cortex.

These results, showing a significantly lateralized component over the early stage of the MRP, support previous claims that the primary motor cortex may contribute to pre-movement activity (Neshige et al., 1988; Botzel et al., 1993; Böcker et al., 1994). However, as shown in Fig. 6, this lateralized pre-movement activity appears to begin significantly later than the bilaterally symmetrical early component activity occurring prior to movement performance (Figs 2 and 3). These results are in accord with single-cell studies which show that neurons within primary motor cortex do contribute to pre-movement activity. However, a far greater proportion of preparatory neurons are found within the SMA (Tanji, 1985; Alexander and Crutcher, 1990) and neurons within primary motor cortex are more active in close temporal association with movement execution (Tanji and Shima, 1994). It therefore appears that the primary motor cortex does contribute to pre-movement activity observed in MRPs, although it may begin later than other sources of bilateral preparatory activity probably involving the SMA.

Activity relating to movement execution alone did not differ significantly between Parkinson’s disease subjects and their age-matched controls, indicating that Parkinson’s disease patients show little deficit in movement execution-related processes. Similarly, studies of cerebral blood flow have shown that, although activation is reduced in the SMA in Parkinson’s disease, patients show no deficit in primary motor cortex activation during movement (Playford et al., 1992, 1993). These results may also relate to movement performance studies which show that simple movements are largely unaffected in Parkinson’s disease. However, patients show particular deficits for more complex movements which require simultaneous control of multiple joints (Benecke et al., 1986) and the organization of submovements into sequences (Benecke et al., 1987; Harrington and Haaland, 1991). These more complex movements require a greater degree of higher-order organization and involve the SMA to a greater extent (Cunnington et al., 1996a). Parkinson’s disease subjects may therefore be expected to show the greatest deficit in higher-order movement planning or preparatory processes, while the end-stage execution-related processes are relatively unaffected.

The MRP component presumed to reflect movement preparation alone, found by subtracting MRPs for the watching cues condition from MRPs for imagining movement, was found to be bilaterally symmetrical during both early and late stages. Although previous studies have reported lateralized activity of a preparatory nature (Praamstra et al., 1996b) and have found lateralized activity associated with motor imagery (Beisteiner et al., 1995), our results show preparatory activity to be primarily symmetrical and show early-stage lateralized activity to be associated more with movement execution for this task.

Both early-stage and later-stage Parkinson’s disease
subjects showed a significantly reduced amplitude of the MRP related to movement preparatory processes. This is consistent with previous reports, as stated above, that the early component of MRPs, reflecting mainly preparatory processes, is reduced in amplitude in Parkinson’s disease (Deecke et al., 1977; Shibasaki et al., 1978; Simpson and Khuriabiet, 1987; Dick et al., 1989), and that Parkinson’s disease subjects show reduced activation of the SMA during movement (Playford et al., 1992, 1993). Therefore, as would be expected, activity relating to movement preparatory processes was reduced in Parkinson’s disease subjects.

Later-stage Parkinson’s disease patients also showed a significantly reduced or less steep slope of the potential following the cue which was independent of overall differences in amplitudes between the groups. This deficit was correlated both with age and severity of Parkinson’s disease, such that the younger and less severe patients showed no deficit compared with controls. As is usually the case with Parkinson’s disease patients, age, severity and progression of disease were all highly inter-related, such that older patients were generally at a later stage of disease and more severely affected than younger patients. Issues of ageing and clinical status could therefore not be examined separately. However, the post-peak slope showed no correlation with age for control subjects, suggesting that slope of the MRP following the cue is not affected by ageing independent of Parkinson’s disease, but is more likely to be related to disease progression and severity which, in turn, are correlated with age.

The reduced slope of the potential following the cue probably indicates impairment in the termination of early component preparatory activity at the time of the cue in more advanced Parkinson’s disease. Such a deficit in the termination of activity at movement onset has been suggested by previous MRP studies (Cunnington et al., 1995; Harasko-van der Meer et al., 1996) and is apparent, but not reported, in MRP traces of other studies (Deecke et al., 1977; Dick et al., 1989). However, these previous studies could not separate preparatory and execution phase activity which overlaps at the time of movement. Therefore, no firm conclusions could be made regarding the precise nature of this neurophysiological deficit in Parkinson’s disease. By separating functional MRP components, it appears that preparatory-phase activity is abnormally prolonged in Parkinson’s disease, possibly indicating impaired termination of SMA activity following movement onset.

This interpretation is also supported by animal studies which have examined the activity of SMA neurons directly. Single-cell recordings from within the SMA in monkeys have shown that sustained neuronal activity is normally terminated sharply upon movement onset (Romo and Schultz, 1992; Watts and Mandir, 1992). However, when monkeys are rendered parkinsonian following treatment with MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), which selectively destroys nigrostriatal dopaminergic neurons, SMA neurons show no abrupt termination of activity, and continue firing throughout the task (Watts and Mandir, 1992). Impaired termination of SMA activity may therefore be associated with impaired basal ganglia function, as in Parkinson’s disease.

It has been suggested that the basal ganglia may provide the signal for the termination of sustained pre-movement activity within the SMA (Iansek et al., 1995; Cunnington et al., 1996a). Single-cell recordings from the globus pallidus of monkeys have revealed a phasic neuronal discharge associated with predictable and well-learnt movements (Brotchie et al., 1991). This discharge usually occurs 200–300 ms prior to the end of a sustained hold period, and it appears to ‘predict’ the initiation of the next movement within a sequence, even when its time is varied (although several trials of learning are required). It was suggested that this phasic discharge was appropriately timed to act as an internal cue to terminate sustained pre-movement activity in the SMA (Brotchie et al., 1991). Therefore, with impaired basal ganglia function, as in Parkinson’s disease or MPTP treated monkeys, this internal cue would be disrupted, resulting in a deficit in the termination of SMA activity at the time of movement onset.

In the current study, we have found support for this mode of interaction between the basal ganglia and SMA in humans. Parkinson’s disease subjects, with impaired basal ganglia output, showed a deficit in the termination of pre-movement preparatory-phase activity, probably reflecting prolonged activity involving the SMA. Further, parkinsonian patients showed a reduced amplitude of preparatory-phase activity prior to movement, while lateralized execution-related processes, involving mainly the primary motor cortex, were largely unaffected by Parkinson’s disease. Such neurophysiological deficits in preparatory-stage activity may underlie difficulties in movement performance associated with Parkinson’s disease, particularly for more complex and sequential movements which rely to a greater extent on higher-order planning and preparatory processes for their organization.

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