Involvement of human thalamus in the preparation of self-paced movement

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Summary
Cortical areas participating in the preparation of voluntary movements have been studied extensively. There is emerging evidence that subcortical structures, particularly the basal ganglia, also contribute to movement preparation. The thalamus is connected to both the basal ganglia and the cerebellar pathways, but its role in movement preparation has not been studied extensively in humans. We studied seven patients who underwent deep brain stimulation (DBS) electrode implantation in the thalamus for treatment of tremor (six patients) and myoclonus–dystonia (one patient). We recorded from the DBS contacts and scalp simultaneously, while patients performed self-paced wrist extension movements. Postsurgical MRI was used for precise localization of the DBS contacts in six patients. Back-averaging of the scalp recordings showed a slow negative movement-related potential (MRP) in all patients (onset 1846 ± 189 ms prior to electromyography onset), whereas DBS electrode recordings showed pre-movement MRP in five out of seven patients. The thalamic MRP preceded both contralateral and ipsilateral wrist movements. There was no significant difference between the onset time of thalamic MRP (−2116 ± 607 ms) and cortical MRP. Neither the scalp nor the thalamus showed pre-movement potentials with passive wrist extensions in two patients. In four patients with postoperative MRI who had thalamic MRP, the maximum amplitude or phase reversal occurred at contacts located in the ventral lateral nucleus. Frequency analysis was performed in the five patients with thalamic MRP. The medial frontocentral scalp contacts and the thalamic contacts with maximum MRP amplitude showed two discrete frequency bands in the α (mean peak 9 Hz) and β (mean peak 17 Hz) range. Both frequency bands showed pre-movement event-related desynchronization (ERD). In the grand average, α and β ERD in the scalp and β ERD in the thalamus began 2.5–2.8 s prior to the onset of movement. However, the thalamic α ERD began considerably later, at 1.2 s before EMG onset. The β band showed cortico-thalamic coherence from the beginning of the baseline period until ~0.5 s before the onset of movement. There was no cortico-thalamic coherence in the α band.

Our findings suggest that the cerebellar thalamus is involved early in the process of movement preparation. Different cortico-subcortical circuits may mediate α and β oscillations. During movement preparation, the motor thalamus and the supplementary motor area predominantly interact in the β band.

Keywords: ventrolateral nucleus of the thalamus; pre-movement potential; event-related desynchronization; coherence; cerebellar pathway

Abbreviations: BP = Bereitschaftspotential; DBS = deep brain stimulation; ECoG = electrocorticography; EMG = electromyography; ERD = event-related desynchronization; ERS = event-related synchronization; M1 = primary motor cortex; M-D = myoclonus–dystonia; MEG = magnetoencephalography; MRP = movement-related potential; S1 = primary sensory cortex; SMA = supplementary motor area; STN = subthalamic nucleus; Vim = nucleus ventralis intermedius of the thalamus; VL = ventral lateral nucleus of the thalamus; Vop = nucleus ventralis oralis posterior of the thalamus.


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Introduction

Cortical activity preceding voluntary movements is well described with both neurophysiological (Kornhuber and Deecke, 1965; Jahanshahi et al., 1995) and imaging techniques (Jahanshahi et al., 1995; Richter et al., 1997; Wildgruber et al., 1997). Back-averaging of scalp EEG recorded with monopolar montage in normal subjects shows a slow, negative movement-related potential (MRP) preceding the onset of self-paced movements by 1–2 s (Barrett et al., 1986). High resolution scalp EEG recordings (Cui et al., 1999) and whole scalp magnetoencephalography (MEG) (Erdler et al., 2000) suggest that preparation of self-paced movement in humans involves the supplementary motor area (SMA), pre-SMA, primary motor cortex (M1) and the anterior cingulate cortex. Involvement of these cortical areas was confirmed by recording with subdural electrodes (Ikeda et al., 1992, 1995).

Back-averaging techniques rely on signals that are time locked and phase locked to an event. However, certain events can block EEG rhythms which may be time locked but not phase locked (Berger, 1929). Reductions in amplitude of specific frequency bands preceding and during voluntary movement were described in the human scalp EEG (Gastaut et al., 1952) and electrocorticogram (ECoG) (Jasper and Penfield, 1949). These changes were later assessed with digital recordings and off-line frequency analysis of EEG (Pfurtscheller and Lopes da Silva, 1999) and MEG signals (Salmelin et al., 1995a, b). The amplitude decrement or block of a frequency band related to an event is termed event-related desynchronization (ERD), whereas the amplitude increment is termed event-related synchronization (ERS) (van Burik et al., 1999).

Scalp recording in humans showed that ERD in the α (8–13 Hz, including the θ rhythm) (Pfurtscheller and Aranibar, 1979; Pfurtscheller, 1992; Derambure et al., 1993a) and β (14–30 Hz) bands (Pfurtscheller, 1981; Toro et al., 1994; Stancak and Pfurtscheller, 1996) starts ~2 s before the onset of movement (Pfurtscheller and Lopes de Silva, 1999). EEG (Pfurtscheller and Berghold, 1989; Stancak et al., 2000) and MEG studies (Salmelin et al., 1995a; Erdler et al., 2000; Kaiser et al., 2000) showed that changes in the cortical oscillatory activity involve the SMA and both contralateral and ipsilateral sensorimotor areas.

Coherence is a measure of the correlation of two signals in the frequency domain. It assesses the same frequency in coupled regions within each trial and the variation of frequency and amplitude across trials. Similar phase difference and amplitude across trials result in high coherence. Values range from 1, which corresponds to a perfect correlation, to 0, that represents random oscillations. Coherence analysis may reveal the functional connection between two neural structures (Sklar et al., 1972; Thatcher et al., 1986). In humans, coherence between the scalp and the subthalamic nucleus (STN) (Brown et al., 2001; Marsden et al., 2001; Cassidy et al., 2002), GPi (Brown et al., 2001; Cassidy et al., 2002) and thalamic contacts (Marsden et al., 2000) has been reported. The thalamus showed coherence with the cortex and muscle activity during rest and sustained movement (Marsden et al., 2000). However, thalamocortical coherence during movement preparation has not been studied.

Cortical and subcortical changes related to movement were also studied with imaging techniques. PET studies showed increased regional cerebral blood flow preceding voluntary movements in the cerebellum, the basal ganglia and the thalamus, in addition to SMA, sensorimotor, motor and cingulate cortex (Wessel et al., 1994, 1997; Jahanshahi et al., 1995; Deiber et al., 1996). Similar results were obtained in functional magnetic resonance studies (Cunnington et al., 2002). However, imaging studies have limited time resolution and there may be a contribution from post-movement activity.

We recently reported that MRP preceding self-paced movement could be recorded in the STN in patients who underwent deep brain electrode implantation for Parkinson’s disease, suggesting that the cortico-basal ganglia–thalamocortical circuit participates in movement preparation (Paradiso et al., 2003). Deep brain stimulation (DBS) of the ventral lateral nucleus of the thalamus (VL) (Ilinsky and Kultas-Ilinsky, 2001), which is mainly comprised of the nuclei ventralis intermedius (Vim) and ventralis oralis posterior (Vop) according to Hassler’s nomenclature for human thalamic nuclei (Hassler, 1959), is an established treatment for tremor (Schaumberg et al., 2000; Koller et al., 2001). The VL is related to the cerebellar system. It receives the dentato-thalamic pathway and projects mainly to M1 (Nolte, 1993; Kelly and Strick, 2003). While the cerebellar pathways play a major role during movement, their role in movement preparation is not well understood. Monkeys with cerebellar hemispherectomy showed impaired slow cortical potentials preceding self-paced movements (Sasaki et al., 1979), suggesting that cerebellar pathways are active in movement preparation. In humans, scalp MRP changes in patients with cerebellar stroke (Gerloff et al., 1996), infarct of the mesial tegmentum of the midbrain (Ikeda et al., 1994), progressive myoclonic ataxia (Shibasaki et al., 1986), and Benedikt’s syndrome and Vim thalamotomy (Shibasaki et al., 1977) also suggest that the cerebellar circuit participates in movement preparation.

The aim of the present study was to assess the role of the cerebello-dentato-thalamocortical pathway in the preparation of self-paced movement. In patients with tremor and myoclonus, we simultaneously recorded from DBS contacts surgically placed in the VL and from scalp electrodes while the patients performed a self-paced movement. Thalamic and cortical changes preceding movement were assessed with MRP and frequency analysis, and thalamo-cortical coherence was estimated.

Patients and methods

We studied seven patients (mean age ± SD 48 ± 21 years) who had implanted DBS electrodes in the VL for treatment of
tremor or myoclonus–dystonia (M-D). Their main clinical features are shown in Table 1. Patients were taking their usual medications at the time of the study. Patient 2 had head trauma as a consequence of a traffic accident 11 years earlier. Imaging studies showed right frontal contusion and diffuse axonal injury that resulted in left hemiplegia, right hemiparesis and progressive right arm postural and intention tremor. Patients with tremor had unilateral DBS electrodes, four in the left thalamus and two in the right thalamus, whereas the patient with M-D had bilateral implantation. The DBS electrodes were targeted to the anterior aspect of the VL using MRI-guided stereotaxy and intraoperative micro-electrode recordings based on the VL response to kinaesthetic stimuli (Krack et al., 2002). All patients provided written informed consent and the study was approved by the University Health Network Research Ethics Board.

The experimental procedure has been described previously (Paradiso et al., 2003). In brief, the study was performed during the first week after surgical implantation, when the leads were still externalized. Seated in a comfortable armchair and looking at a fixation point placed 3 m in front of them, the patients were asked to make brisk, self-paced unilateral wrist extension followed by passive flexion approximately once every 5–10 s. Two recording sessions lasting at least 10 min each were performed on each side. We studied the movement of both right and left wrists in five patients and only the hand movement contralateral to the thalamic electrode in two patients (Table 2). Passive wrist extension was studied with one of the authors extending the wrist every 5–10 s in two patients.

The quadripolar DBS electrodes (Medtronic model 3387) contain four contacts numbered 0–3, with contact 0 being the closest to the tip. The contacts are 1.3 mm in diameter, 1.5 mm in length and spaced 1.5 mm apart. The scalp EEG was recorded with silver–silver chloride electrodes placed at Fp1, Fp2, Fz, Cz, C3 and C4 according to the International 10–20 System. Eye movements were assessed with the frontal-polar electrodes. Linked ear electrodes were utilized as reference. The impedance was 5 kΩ or less for all electrodes. The EMG of the active extensor carpi radialis muscle was recorded with surface electrodes. For the passive movement study, an accelerometer was placed on the dorsal aspect of the hand. SynAmp amplifiers (NeuroScan Laboratories, El Paso, TX) were used for all recordings. The sampling rate was 2.5 kHz. Filters were set at 0.05–70 Hz for scalp and DBS electrodes, 30–500 Hz for EMG and 10–30 Hz for the accelerometer.

Off-line analysis was carried out with Scan 4.1 software (NeuroScan Laboratories). DBS recordings were transformed into a bipolar montage between two consecutive contacts. The scalp electrodes remained referenced to linked ears for the MRP analysis, whereas for the frequency domain analysis a transformed bipolar montage of Fz–Cz was used. Epochs

### Table 1 Characteristics of patients studied

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Disease</th>
<th>Medications and doses (mg/day)</th>
<th>Side of VL electrodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>F</td>
<td>Myoclonus–dystonia</td>
<td>Clonazepam 1.5, valproate 1000</td>
<td>Bilateral</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>M</td>
<td>Post-traumatic tremor</td>
<td>Carbamazepine 100</td>
<td>Left</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>F</td>
<td>Multiple sclerosis</td>
<td>Baclofen 40</td>
<td>Left</td>
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<tr>
<td>4</td>
<td>65</td>
<td>M</td>
<td>Essential tremor</td>
<td>Propranolol 120</td>
<td>Left</td>
</tr>
<tr>
<td>5</td>
<td>63</td>
<td>M</td>
<td>Essential tremor</td>
<td>Clonazepam 2</td>
<td>Left</td>
</tr>
<tr>
<td>6</td>
<td>45</td>
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<td>Essential tremor</td>
<td>No medication</td>
<td>Right</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>M</td>
<td>Essential tremor</td>
<td>No medication</td>
<td>Right</td>
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</table>

### Table 2 Scalp MRP onset time and details of thalamic MRP

<table>
<thead>
<tr>
<th>Patient</th>
<th>Scalp MRP Movement side</th>
<th>Onset (ms)</th>
<th>Thalamic MRP TH Onset (ms)</th>
<th>Contralateral Amplitude (µV)</th>
<th>Contact</th>
<th>Ipsilateral Onset (ms)</th>
<th>Amplitude (µV)</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R</td>
<td>1725</td>
<td>R</td>
<td>N/R</td>
<td>2−</td>
<td>N/R</td>
<td>1330</td>
<td>2.4</td>
</tr>
<tr>
<td>2</td>
<td>R</td>
<td>1900</td>
<td>L</td>
<td>2034</td>
<td>2</td>
<td>N/S</td>
<td>1710</td>
<td>3.5</td>
</tr>
<tr>
<td>3</td>
<td>R</td>
<td>1790</td>
<td>L</td>
<td>N/R</td>
<td>2</td>
<td>N/R</td>
<td>1950</td>
<td>3.5</td>
</tr>
<tr>
<td>4</td>
<td>R</td>
<td>1690</td>
<td>L</td>
<td>1590</td>
<td>2+</td>
<td>N/S</td>
<td>2270</td>
<td>9.7</td>
</tr>
<tr>
<td>5</td>
<td>L</td>
<td>1950</td>
<td>L</td>
<td>N/R</td>
<td>2</td>
<td>N/S</td>
<td>2660</td>
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<tr>
<td>6</td>
<td>R</td>
<td>1770</td>
<td>L</td>
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<td>7.5</td>
<td>2+</td>
<td>2370</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Onset refers to the time before EMG onset. Scalp MRP onset precedes left or right wrist extension. Thalamic recordings are contralateral or ipsilateral to the wrist extension. Contact refers to the contact with maximum amplitude. TH = thalamus; MRP = movement-related potential; R = right side; L = left side; N/R = no response; N/S = not studied; + = positive polarity; − = negative polarity.
starting 4 s before and ending 1 s after the EMG onset were created for all subsequent analyses. Epochs with eye movement or recording artefacts were rejected.

For MRP analysis, at least 30 selected epochs were then averaged. The mean and SD of the baseline period (4000–3000 ms before onset of movement) for the averaged waveform was calculated. Criteria for considering waves as MRP were: (i) amplitude >1 μV and >3 SD of the baseline; and (ii) duration >500 ms. The MRP amplitude was the maximum deflection between the MRP onset and the EMG onset. Potentials with onset before time 0 have negative values.

The recordings from five patients with thalamus MRPs were assessed for frequency analysis. The left thalamus was studied in patient 1, who had bilateral DBS electrodes. Contralateral hand movements were analysed using the Fz–Cz electrodes and the pair of contacts with maximum MRP amplitude. The Fz–Cz montage was chosen because it has fewer artefacts due to surgical dressing, exit wounds, oedema and muscle activity compared with C3 and C4 contacts. The first step was to use fast Fourier transform to examine the frequency content of the entire epochs between 2 and 50 Hz. ERD/ERS was then studied between 8 and 12 Hz for the α band and between 14 and 30 Hz for the β band. In order to obtain a stable reference interval, the baseline period was extended between 4000 and 2500 ms before the onset of movement. Bins of 125 ms were created and the relative bandpower of each bin was expressed as a percentage of the bandpower of the reference interval. In addition, the time varying cumulative sum (cusum) of the ERD was computed. Changes greater than mean ± 3 SD of the baseline period were considered significant. The onset of ERD was defined as the time of last crossing of the baseline in the cusum plots.

Coherence between Fz–Cz and the thalamus was analysed with complex demodulation using Brain Electrical Source Analysis (BESA) 5.0 software (MEGIS Software GmbH, Munich, Germany), using the same epochs as in ERD/ERS measurement. The frequency resolution was 2 Hz and data were sampled every 25 ms. Coherence was studied over the frequency range of 2–50 Hz.

Postoperative contact localization

Brain MRI was obtained in all patients, except patient 7, during the first week after surgery. The positions of the contacts were identified using a novel high resolution T2-weighted fast spin echo sequence designed to reduce magnetic susceptibility artefacts and noise. This method has been used to determine the position of electrodes implanted in the STN (Paradiso et al., 2003) and has been described in detail elsewhere (Saint-Cyr et al., 2002). Briefly, the DBS electrodes were visualized in each of the three planes. The three-dimensional location of the electrode tip relative to the anterior and posterior commissure line, the mid-commissural point and the midline was first determined. Measurement data were normalized to an intercommissural distance of 23 mm and the position of the electrodes was plotted onto a sagittal plane, 20 mm from the midline, according to the atlas of Schaltenbrand and Wahren (1977). Individual differences in the size and location of the thalamic nuclei were corrected by correlating MRI measurements to intra-operative neurophysiological mapping data. The position of each contact was then calculated according to the known dimensions of the DBS electrode and the angle of implantation.

Results

Scalp recordings

A pre-movement potential or Bereitschaftspotential (BP) preceding wrist self-paced extension was recorded in all studied sides, except on the left side movement of patient 3, who had multiple sclerosis (Table 2). We were not able to distinguish between different subcomponents of BP (Barrett et al., 1986), probably due to variations in the response, related to the relative small number of epochs that we recorded. At the Cz contact, the BP onset latency was 1846 ± 189 ms (range 1584–2270) and its amplitude was 9.2 ± 5.1 μV (range 3–15.9).

DBS recordings

Most patients showed pre-movement potentials on the monopolar recordings with the DBS contacts referenced to linked ears. Their shape and latency were similar in all four contacts. Moreover, these pre-movement potentials had similar shape and onset time compared with the cortical MRP, but had reversed polarity (Fig. 1).

![Fig. 1 Monopolar scalp and thalamic MRP recordings. Averaged responses from 77 self-paced left wrist extension movements in patient 5. The recording is referenced to linked ears. Cz is the scalp electrode placed at the vertex. For thalamic electrodes, L refers to left, and 0–3 refers to the quadripolar electrode contacts. The lowest trace shows the averaged rectified EMG activity of the right extensor carpi radialis muscle. The cortical and thalamus MRP (BP) had similar onset (left marker) at ~1.8 s prior to EMG onset (right marker), but had opposite polarity with negative potentials in the scalp electrodes and positive potentials in the thalamic electrodes. The waveform is similar in all thalamic contacts.](https://academic.oup.com/brain/article-abstract/127/12/2717/335114)
After bipolar transformation, MRPs were recorded from the DBS electrodes in five of the seven patients, and on nine of the 14 sides studied (Table 2). No potential could be recorded from one patient with post-traumatic tremor (patient 2) and from another patient with essential tremor (patient 4). In these two patients, only right hand movements were studied because of fatigue and drowsiness at the time of the study. MRPs were absent in the thalamus of one side in patient 1, with M-D, and in patient 3, with multiple sclerosis, who had no cortical BP with hand movements of the same side. The recorded MRP was a slow wave, either positive or negative, present with both contralateral (five of eight recordings) and ipsilateral (four of six recordings) hand movements. The onset time of the MRP was $1919 \pm 6452$ ms (range 1590–2660) for contralateral hand movements and $2363 \pm 759$ ms (range 1330–3094) for the ipsilateral wrist extensions, with no significant difference between both sides. Moreover, the onset time of the thalamic MRP was not significantly different from that of scalp-recorded MRP ($P = 0.21$, unpaired t-test). The amplitude of the thalamic MRP was $4.4 \pm 2.9 \mu V$ (range 2–7.5) for contralateral movements and $4.7 \pm 3.4 \mu V$ (range 2.4–9.7) for ipsilateral wrist extensions. The maximum amplitude was always recorded in the central electrodes, contact 2 on six sides and contact 1 on three sides. There was phase reversal between adjacent pairs of contacts in four recordings and the potential could be a positive or a negative wave. Figure 2 shows an example of scalp and thalamic MRPs recorded from one patient (patient 5), and Fig. 3 shows the thalamic MRPs with maximum amplitude from five patients.

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Passive wrist extension was studied in two subjects. Post-movement potentials were present in scalp and DBS contacts, but no pre-movement potential was recorded (Fig. 4).

**Localization of contacts with phase reversal or MRP maximum amplitude**

Postoperative MRI was obtained in six subjects, four of whom had MRP (Fig. 5). In the patients in whom MRP were
recorded preceding both contralateral and ipsilateral hand movement, the maximum MRP amplitude was recorded from the same contact (Table 2). Right wrist extension in patient 5 was preceded by a left thalamic MRP with phase reversal and maximum amplitude in contact 1, as shown in Fig. 2, and contact 1 was located in the VL as shown in Fig. 3A (black dot with number 5). The contact with maximum MRP amplitude was localized at the limit between the ventralis anterior (VA) and VL nuclei of the left thalamus in patient 1 (ipsilateral and contralateral movement), at the limit between the reticular thalamus and the lateral aspect of VL in patient 3 (contralateral movement), and in the VL in patients 5 (ipsilateral and contralateral movement) and 6 (ipsilateral and contralateral movement). Regarding the patients in whom MRP could not be recorded, patient 2 had contacts 0, 1 and 2 in the ventral part of the VL. Patient 4 had the electrode below

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**Fig. 5** Location of thalamic contacts with maximum pre-movement potential amplitude. (A) Sagittal plot corresponding to the Schaltenbrand and Wahren atlas plate, 14.5 mm lateral to the midline. The contour line represents the limit of the non-reticular thalamus and the dotted line represents the limit of the reticular thalamus. The thick solid line delimits the VL. The vertical axis indicates the dorsal–ventral distance from the anterior commissure–posterior commissure (AC–PC) line, with dorsal being the upper side. The horizontal axis indicates the anterior–posterior distance from the mid commissural point (MCP). Anterior is to the left side (negative values). The black dots depict the contacts with maximum amplitude for contralateral MRP. The numbers in the black dots correspond to the patient numbers shown in Tables 1 and 2. (B) The contralateral MRP data in (A) are plotted in the coronal plane at a distance of 7 mm posterior to the MCP. The vertical axis indicates the dorsal–ventral distance from the AC–PC lines, with dorsal being the upper side. The horizontal axis indicates the distance lateral to the midline. Solid lines delimit the upper and lower borders of the thalamus, as interpolated from the sagittal plates of the Schaltenbrand and Wahren atlas. The vertical dotted lines denote the most lateral plate representing the VL. (C) A plot similar to (A) showing ipsilateral MRP. (D) The ipsilateral MRP data in (C) plotted in the coronal plane.
the inferior border of the thalamus with contacts situated in the zona incerta and the reticular thalamus. Patient 1, who had bilateral DBS electrodes and MRP recorded from left thalamus, had three contacts in the right VL.

**Frequency analysis**

Figure 6 shows the frequency spectrum of the entire epoch for the scalp and thalamic leads in patient 5, which consists of two discrete peaks. Similar results were obtained in the other patients. The first peak was in the range of the α band and was present in the scalp in all five patients (mean 9.5 Hz, range 8.2–10.6) and in the thalamus in four patients (mean 9.4 Hz, range 8.1–11.1). The second peak, in the low β band, was present in the Fz–Cz derivation in all patients (mean 16.6 Hz, range 14.5–18.4) and in the thalamus in four patients (mean 16.5 Hz, range 14.0–20.1). The α peak covered a narrow band ranging between 7 and 12 Hz, whereas the β peak consisted of a broader band with range between 12 and 29 Hz. The frequency bands used for the analysis of α and β ERD/ERS, therefore, covered most of the frequency peaks recorded in the patients.

**Event-related desynchronization**

Figure 7 shows the results of the ERD analysis from patient 5. α and β ERD in the Fz–Cz electrodes became significant ~1 s prior to movement initiation. In the thalamus, α ERD reached significance only a few milliseconds before movement onset, whereas the thalamic β ERD became significant at ~1.7 s. Pre-movement desynchronization in the α band was significant in three patients in the scalp and in three patients in the thalamic contacts, whereas ERD in the β band was significant in four patients in the scalp and in all five patients in the thalamic recordings. The grand average showed ERD in both the α and β bands in the scalp and in the thalamus (Fig. 8).

Figure 9 shows the ERD cusum results from patient 5. ERD onset was ~2.5 s in the α and β bands in the scalp, and ~1.8 and ~2.0 s in the α and β bands in the thalamus. Significant changes were seen in the cusum of the α band in the Fz–Cz contact of four patients and in the thalamic contacts of all the patients, whereas the changes in β cusum were present in the cortical and thalamic recordings of all patients. Table 3 shows the onset times of α and β ERD in the cortical and thalamic contacts of the five patients. The grand average of the cusums showed significant changes in α and β bands both in the cortex and in the thalamus (Fig. 10). ERD onset time was ~2.5 s for scalp α and β bands. In the thalamus, β ERD onset time was ~2.7 s, whereas the α ERD onset time occurred much later, at ~1.2 s.

**Coherence between cortex and thalamus**

The findings in patient 5 are shown in Fig. 11. Four of the five patients showed coherence at the β band with a peak at ~20 Hz. They showed coherence in the β band from the beginning of the epochs, at 4 s before the onset of movement. The coherence diminished ~0.5 s before movement initiation. No patient showed coherence in the α band. The grand average of the five patients showed similar features (Fig. 12).

**Discussion**

Five of seven patients performing self-paced wrist extension showed MRP recorded from bipolar DBS contacts implanted in the thalamus. The MRP was a slow wave, preceding the onset of movement by 1.5–3 s. It was present with both ipsilateral and contralateral hand movements. The time of onset of the DBS MRP was not significantly different from the time of onset of the cortical BP. Frequency analysis showed discrete frequency peaks in the α and low β bands of the scalp Fz–Cz derivation and in the thalamic contacts with maximal MRP amplitude. Both bands showed ERD preceding movement. Cortical–thalamic coherence was apparent only for the β band. It was present during the baseline period and was reduced ~0.5 s prior to movement onset.

Using a monopolar montage, we recorded a slow positive potential mirroring the scalp negative BP from all DBS contacts (Fig. 1). The same finding has been reported in a previous study using monopolar recording from the human thalamic VL during stereotactic surgery (Baba et al., 1976). MRPs with similar characteristics have also been recorded from electrodes implanted in the posterothalamic nucleus of the thalamus (Rektor et al., 2001c), pallidum and caudate (Rektor et al., 2001b), putamen (Rektor et al., 2001a) and STN (Paradiso et al., 2003). Moreover, a reversed contingent negative variation potential was also recorded from the VL and even from the subcortical white matter in patients performing externally
Fig. 7  Cortical and thalamic ERD in patient 5. Cortex refers to midfrontal central contacts, and thalamus to contacts 1–2 of the quadripolar electrode implanted on the left side. The patient performed right wrist extensions. The abscissa denotes time in seconds, where 0 refers to movement onset, and the ordinate denotes ERD percentage with respect to the mean value of the reference interval. The dotted lines correspond to 3 SD of the reference interval. Scalp recordings show increasing ERD that became significant at \(~1\) s before the onset of movement, in both \(\alpha\) and \(\beta\) bands. Thalamic contacts show increasing ERD that reached significance a few milliseconds before movement onset in the \(\alpha\) band and \(1.7\) s prior to movement onset in the \(\beta\) band.

Fig. 8  Grand average of cortical and thalamic ERD from five patients. Cortex refers to midfrontal central contacts, and thalamus to the pair of contacts of the quadripolar electrode with maximum MRP amplitude. Electrodes were implanted in either the right or left thalamus and the patient performed contralateral wrist extensions. The abscissa denotes time in seconds, where 0 represents movement onset, and the ordinate denotes ERD percentage with respect to the mean value of the reference interval. The dotted lines correspond to 3 SD of the reference interval. Significant pre-movement ERD is present in cortex and thalamus for both \(\alpha\) and \(\beta\) bands.
cued movements (Tsubokawa and Moriyasu, 1978). Therefore, these waves may represent a far field potential arising from a structure between the intracerebral recording contacts and the scalp leads. Volume conduction with DBS scalp montages has been illustrated recently in patients with epilepsy, in whom cortical spikes recorded from DBS contacts with monopolar montage could lead to the erroneous conclusion that the spike originated in subcortical structures (Wennberg and Lozano, 2003). Therefore, we used a bipolar montage between two consecutive contacts of the DBS electrode in the main analysis of this study. This montage is apt for recording local field potentials between adjacent contacts with their centre to centre separation of only 3 mm. The findings of MRPs in the STN (Paradiso et al., 2003) and the cerebellar thalamus are consistent with the hypothesis that subcortical structures may contribute to the cortical BP (Rektor, 2002).

Our study has several limitations. The underlying pathology and the conditions of the patients studied immediately after surgery probably affected our results. No potential could be recorded from scalp or DBS electrodes with left hand movements in patient 3 who had multiple sclerosis, probably due to lesions in multiple sites. Similarly, patient 2 had a diffuse post-traumatic axonal injury that may have been responsible for the absent response. Although abnormalities of pre-movement potential have not been reported in essential tremor, previous studies showed a decrease in VL neuronal firing rate (Lenz et al., 2002), longer reaction time and slower movement velocity (Montgomery et al., 2000) in essential tremor patients that may have influenced our recordings. The pre-movement potential could also have been influenced by postoperative oedema and the low number of epochs collected in some subjects due to drowsiness and fatigue, which may have adversely affected the signal to noise ratio. Nevertheless, we were able to record potentials

![Fig. 9 Cusums of cortical and thalamic ERD in patient 5. This figure represents the cusums of the ERD shown in Fig. 7. Cortex refers to mid frontocentral contacts, and thalamus to contacts 1–2 of the quadripolar electrode implanted on the left side. The patient performed right wrist extensions. The abscissa denotes time in seconds, where 0 represents movement onset, and the ordinate denotes ERD csum in arbitrary units (a.u.). The dotted lines correspond to 3 SD of the reference interval. The arrows show the onset time of ERD. In the cortex, α and β ERD start 2.5 s prior to movement. In the thalamus, the onset time of α ERD is 1.8 s and of β ERD is 2.0 s before movement initiation.](https://academic.oup.com/brain/article-abstract/127/12/2717/335114)

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Scalp and thalamic α and β ERD onset times</th>
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<tr>
<td>Patient</td>
<td>Movement side</td>
</tr>
<tr>
<td></td>
<td>α band onset (ms)</td>
</tr>
<tr>
<td>1</td>
<td>R</td>
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<td>3</td>
<td>R</td>
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<td>5</td>
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Onset refers to the time before EMG onset. Scalp and thalamic ERD onset precedes left or right wrist extension. Contacts refers to the pair of thalamic contacts in the side contralateral to movement. ERD = event-related desynchronization, R = right side, L = left side, N/S = no significant ERD.
preceding self-paced movements from the scalp and from the thalamus in most patients.

Motor preparatory activity in the thalamus has been studied in animals to a limited extent. Microelectrode recordings from the cat VL–VA nuclear complex during externally triggered movements showed that changes in neuronal firing preceded the movement by >500 ms (Neafsey et al., 1978). Similarly, in the monkey VL, changes in neuronal firing occurred ~100 ms

**Fig. 10** Grand average of cusums of cortical and thalamic ERD in five patients. This figure represents the cusums of the ERD grand average shown in Fig. 8. Cortex refers to midfrontal central contacts, and thalamus to the pair of contacts of the quadripolar electrode with maximum MRP amplitude. Electrodes were implanted in either the right or left thalamus and the patients performed contralateral wrist extensions. The abscissa denotes time in seconds, where 0 represents movement onset, and the ordinate denotes ERD cumum in arbitrary units (a.u). The dotted lines correspond to 3 SD of the reference interval. The arrows show the onset time of ERD. In the cortex, ERD in the α and β bands began 2.5 s prior to movement. In the thalamus, onset time of ERD was 1.2 s before movement onset in the α band and 2.7 s before movement onset in the β band.

**Fig. 11** Temporal representation of coherence between cortex and thalamus in patient 5. This figure represents coherence analysis between the scalp mid frontocentral contacts and thalamic contacts 1–2 of the quadripolar electrode implanted on the left side, in patient 5. Frequency spectra and ERD of this patient in the same contacts are depicted in Figs 6, 7 and 9. The abscissa denotes time in seconds, where the red marker at 0 represents movement onset, and the ordinate denotes frequency. The colour-graded scale represents coherence values. Coherence in the β range, centred at ~22 Hz, was present from the start of the epoch and diminished ~0.5 s before the movement onset. There was no coherence in the α frequency band.
prior to movement (Evarts, 1971; Strick, 1976; Fortier et al., 1989). Another study found increased neuronal activity in both the basal ganglia and the cerebellar receiving areas of the primate motor thalamus ~300 ms before movement onset for both visually triggered and internally generated limb movements (Rebert, 1972; van Donkelaar et al., 1999). However, most animal studies assessed firing rate changes of single neurons during externally triggered movements. Therefore, the earlier occurrence of thalamic field potentials in our patients may be related to differences in the experimental paradigms used.

In humans, routine intra-operative neurophysiological recording frequently identified VL neurons that change their firing rate with voluntary movement (Raeva, 1986; Lenz et al., 1990). Crowell et al. (1968) studied patients with Parkinson’s disease and writer’s cramp, and found both an increase and a decrease in neuronal firing rate in the VL before and during voluntary movements of the contralateral or ipsilateral limb. Other studies have found that the spike activity of VL neurons in Parkinson’s disease patients increased significantly 0.5–1 s before the onset of voluntary movement (Raeva et al., 1999) and that changes in firing rate occurred ~300 ms before the initiation of externally triggered movements (Kropotov et al., 1992). Increased thalamic unit firing preceding voluntary movement was also observed in a study on internally and externally generated sequential movements (MacMillan et al., 2003). Thus, previous studies have found changes in the firing rate of VL neurons before voluntary movement, but most studies used externally triggered or sequential movement rather than the self-paced movement we studied.

Most human studies used micro- or semi-microelectrodes that recorded from either single neurons or a small number of neurons. Since the change in firing rate was highly variable among different units, the overall thalamic changes were difficult to estimate. In contrast, we used macroelectrode recordings, and the local field potentials that we recorded reflect synchronous activation of a population of adjacent neurons, with spatial recruitment playing a direct role in the amplitude of the MRP. There was phase reversal between adjacent pairs of contacts in the VL in four recordings, suggesting that the potential originates from a local field source within the VL or neighbouring tracts and neurons. A slight difference in the location of the thalamic electrode contacts with respect to the source of the local field potential may account for some recordings with no phase reversal.

Previous human VL recordings (Crowell et al., 1968; Hongell et al., 1973; Raeva et al., 1999) used Walker’s classification of the primate thalamus, that includes areas receiving both pallidal and cerebellar projections (Walker, 1977).
In the sensorimotor cortex, β oscillations react somatotopically to movements (Jasper et al., 1949; Arroyo et al., 1993; Salmelin and Hari, 1994). Blocking or desynchronization correlates with attention-related cortical activation and increased neuronal excitability (Gastaut et al., 1952; Pfurtscheller, 1981; Pfurtscheller and Bergold, 1989; Derambure et al., 1993b). However, the precise functional significance of ERD/ERS of α and β rhythms remains unsolved. It was suggested that, in the cortical convexity, the α activity is predominantly generated in the post-central somatosensory and the β rhythm arises mainly from the pre-Rolandic motor area (Jasper et al., 1949; Pfurtscheller and Neuper, 1994; Salmelin et al., 1995b). However, intracerebral (Szurhaj et al., 2003) and ECoG studies (Crone et al., 1998) found overlapping α and β ERD in different areas of the brain.

Intracerebral recordings in humans showed α and β ERD in the putamen (Sochurkova and Rektor, 2003) and the STN (Cassidy et al., 2002; Kuhn et al., 2004) preceding voluntary movements. In the cerebellar thalamus, it was reported that oscillatory activity between 8 and 27 Hz is coherent with sensorimotor cortex oscillations both at rest and during sustained muscle contraction (Marsden et al., 2000). However, ERD in the thalamus has not been assessed previously. Our findings indicate that α and β oscillations are present in the cerebellar thalamus and they desynchronize before the onset of movement. The onset time of β ERD was ~2.5 s before EMG onset for both the mid frontocentral contacts over the SMA and the thalamus. In contrast, α ERD started >1 s later in the thalamus compared with the mid frontocentral cortex. Moreover, the thalamic and mid frontocentral α oscillations showed no coherence. This is consistent with the suggestion that areas related to motor activity are involved in the generation of β rhythms (Jasper et al., 1949; Salmelin et al., 1994; Crone et al., 1998) and the α rhythm could be related to the somatosensory areas. β oscillations of the SMA and thalamus are coherent in the baseline period, a finding consistent with previously reported thalamo-cortical coherence at rest (Marsden et al., 2000). Coherence continued during most of the β ERD period but diminished at ~0.5 s before the onset of movement. Therefore, the cerebellar thalamus interacts with the SMA in the β band during the resting state and the early stage of movement preparation. These findings also suggest that different subcortical circuits mediate α and β oscillations and the cerebellar thalamus and the SMA interact in the β band during movement preparation. The reduction in SMA–thalamic coherence in the β band close to movement onset may be due to the cerebello-thalamo-cortical interactions shifting to other cortical areas such as the M1 (Neshige et al., 1988a, b).

Because of the close anatomical relationship between the nucleus VA and the VL, we cannot rule out local field potentials arising from this neighbouring nucleus. Patient 1, for instance, had the contact with maximum MRP located in the limit of these two nuclei (Fig. 5). The VA is part of the cortico-basal ganglia–cortical loop (Parent and Hazrati,
1995). Moreover, there is overlap in the input to the anterior VL between pallidal and cerebellar afferents (Sakai et al., 1996) and in the input to the posterior VL between cerebellar and spinothalamic afferents (Ilinsky and Kultas-Ilinsky, 2002). In a previous study, we recorded pre-movement potentials from the STN, supporting the role of the basal ganglia circuit in movement preparation (Paradiso et al., 2003). The STN MRP occurred with a similar time frame as the MRP recorded in the thalamus, raising the possibility that thalamic MRP may represent activation of the thalamic segment of the basal ganglia circuit. However, the bulk of the VL neurons are related to the cerebello-cortical pathways (Aumann, 2002), and most of the contacts with phase reversal or maximum MRP amplitude were inside the VL (Fig. 3). Therefore, our findings suggest that the cerebellar thalamus is active before the initiation of self-paced movements. This activity arises early during movement preparation and occurs in parallel with cortical and basal ganglia activation.

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