

## PAPER

# Cerebral motor control in patients with gliomas around the central sulcus studied with spatially filtered magnetoencephalography

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**Objective:** Application of spatially filtered magnetoencephalography (MEG) to investigate changes in the mechanism of cerebral motor control in patients with tumours around the central sulcus.

**Methods:** MEG records were made during a repetitive hand grasping task in six patients with gliomas around the central sulcus and in four control subjects. Power decreases in the  $\alpha$  (8–13 Hz),  $\beta$  (13–30 Hz), and low  $\gamma$  bands (30–50 Hz) during the motor tasks (event related desynchronisation, ERD) were analysed statistically with synthetic aperture magnetometry. The tomography of ERD was superimposed on the individual's magnetic resonance image.

**Results:**  $\beta$  ERD was consistently localised to the contralateral primary sensorimotor cortex (MI/SI) in control subjects, whereas the  $\alpha$  and low  $\gamma$  ERD showed considerable intersubject variability.  $\beta$  ERD in patients during non-affected side hand movement was also localised to the contralateral MI/SI, but exclusively to the ipsilateral hemisphere during affected side hand movement.

**Conclusions:** The altered pattern of ERD in the patient group during affected side hand movement suggests recruitment of diverse motor areas, especially the ipsilateral MI/SI, which may be required for the effective movement of the affected hand.

Initial impairment of motor function after ischaemic or traumatic/surgical insults often recovers to a certain degree with intensive physiotherapy. In slowly progressive tumours, impairment of motor function does not become apparent until a certain area of the motor cortex is involved.<sup>1</sup> Clinical observations of patients suggest that functional remodelling in the brain is taking place during recovery from the acute insult or during the gradual growth of the tumour. For surgical treatment of tumours involving the motor areas, elucidation of this remodelling is of great importance for presurgical planning and for programming effective rehabilitation after initial treatment.

Various different studies with positron emission tomography (PET)<sup>2,3</sup> and functional magnetic resonance imaging (fMRI)<sup>4–6</sup> in patients with diverse lesions affecting cerebral motor control have shown altered activation patterns in the motor areas. Those studies mainly depict haemodynamic changes generated during the motor task. High resolution electroencephalography<sup>7</sup> was capable of capturing neural activation directly, but the results were only demonstrable on gross topography.

Magnetoencephalography (MEG) has been employed to demonstrate neural activation directly with enhanced spatial resolution. Using a currently available signal processing technique—synthetic aperture magnetometry (SAM)—multiple simultaneously active sources became subjects for the analysis.<sup>8</sup> Combined with statistical comparison of the power of each source,<sup>9</sup> a differential study between two arbitrarily chosen states became possible, which is much easier to do than the time locked motor task.<sup>10–11</sup>

A power decrease in background brain activity during a motor task was first demonstrated in EEG studies and was termed “event related desynchronisation” (ERD).<sup>12</sup> This was evident in the primary sensorimotor area and was considered to be a representation of the active cortex during the motor task.<sup>13–14</sup> In the present study, ERD on  $\alpha$ ,  $\beta$ , and low  $\gamma$  bands

during a grasping task was studied in patients with intrinsic brain tumours around the central sulcus.

## METHODS

### Subjects

Six patients (ranging in age from 36 to 60 years) with gliomas around the central sulcus and six control subjects (age range 33 to 47 years) gave their informed consent for the experimental procedures and participated in the MEG study. Five patients and all control subjects were right handed and one was left handed according to the modified Oldfield's inventory.<sup>15</sup> Four patients had a tumour in their dominant hemisphere. Clinical data on the patients are given in table 1. Subject 1 was studied at one month after tumour removal while he was gradually recovering from his right sided weakness (from 3/5 immediately after surgery to 4/5 at the time of MEG recording, assessed by manual muscle testing). Subject 5 had a five months history of fine movement disorder before the study. Others had experienced no motor complications, and all were capable of carrying out the motor task.

### Motor task and data acquisition

A helmet shaped 64 channel SQUID array (NeuroSQUID Model 100, CTF Systems Inc, Port Coquitlam, Canada) was used for MEG data acquisition. Details of the motor task have been described previously.<sup>10</sup> In brief, subjects were instructed to undertake a trial consisting of six sessions of repetitive hand grasping (not a tonic sustained grasp) of either hand

**Abbreviations:** ERD, event related desynchronisation; fMRI, functional magnetic resonance imaging; MEG, magnetoencephalography; MI, primary motor cortex; MI/SI, sensorimotor cortex; PET, positron emission tomography; SAM, synthetic aperture magnetometry; SI, primary sensory cortex

**Table 1** Clinical data on the patients in the study

Patient No	Sex/age (years)	Handedness	Diagnosis/tumour location	Symptom
1	Male/57	Right	Glioblastoma/L superior frontal-cingulate gyrus	R weakness (4/5 according to MMT, one month after tumour removal), seizure
2	Male/36	Right	Astrocytoma/R superior frontal gyrus	No neurological deficit (diagnosed incidentally)
3	Male/49	Right	Oligoastrocytoma/R pre- and post-central gyrus	Psychomotor seizure
4	Male/38	Right	Astrocytoma/L precentral gyrus	Seizure
5	Female/51	Right	Glioblastoma/L postcentral gyrus	R weakness (five months' history of fine movement disorder), seizure
6	Male/60	Left	Glioblastoma/R postcentral gyrus	Dysaesthesia in left thumb

L, left; MMT, manual muscle testing; R, right.

for 10 seconds after 10 seconds of rest, keeping their eyes closed. The beginning and end of the movement was signalled to the subject by the investigator. Movements were monitored on video throughout the recording. All subjects practised the task before data acquisition to learn to grasp the hand appropriately without excessive movement of the forearm. The grasping rate was about 2 Hz, and absence of apparent mirror movement was confirmed on EMG or on inspection. The MEG data were acquired on trigger at the very end of the 10 seconds of grasping with a 625 Hz sampling rate and on-line low pass filtering of 200 Hz. Individual anatomical MRI datasets were acquired using 1.5 T imaging systems (Magnetom Impact, Siemens, Erlangen, Germany). For all measurements, fiducial skin markers were placed on the subject's nasion and at bilateral preauricular points to establish common coordinate systems for MRI and MEG for subsequent superimposition of the MEG results on the individual magnetic resonance images.

**MEG analysis**

Detail of the SAM algorithm have been described previously.<sup>8, 16, 17</sup> SAM is a spatial filtering technique based on the adaptive beamformer theory. It estimates source activity at each selected voxel within the region of interest.<sup>18</sup> A volumetric image of root mean squared source activity in  $\alpha$ ,  $\beta$ , and low  $\gamma$  bands with 2 mm voxel resolution is generated for

time intervals of -20 to -15 and -5 to 0 seconds relative to trigger onset as control and active states, respectively. The statistical imaging is computed subsequently by comparing the power of both states on a single voxel basis using the Student *t* test. Only voxels displaying peak signal changes within each trial are displayed on the individual magnetic resonance images. Images with a peak *t* value less than 2.5 or ERD distributed evenly over the hemisphere were excluded. To investigate the left-right difference in the basic rhythm, the raw MEG data in the control state were fast Fourier transformed. The  $\beta$  band power values of channels covering the sensorimotor cortex in both hemispheres were superimposed and compared.

**Direct cortical stimulation**

In two subjects, cerebral cortex adjacent to the lesion was stimulated at the time of surgery. The stimulation was conducted with the patient awake. A bipolar probe with a current of 10 mV at 50 Hz was used. The motor responses were confirmed either on inspection by the trained investigator or by patient's self report.

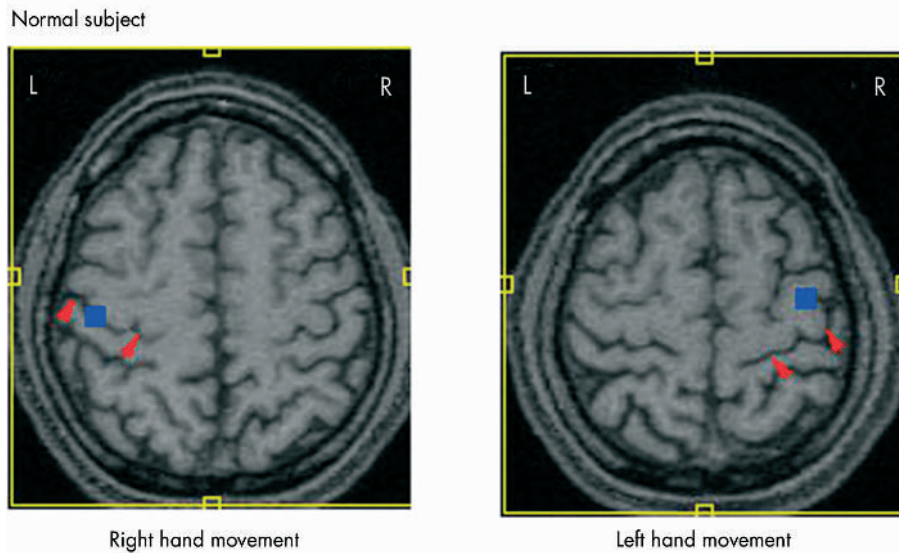
**RESULTS**

Monitoring of the movement during the recording revealed an almost congruent grasping rate of about 2 Hz in both the control group and the patient group, except for subject 5 who

**Table 2** Areas displaying most significant power changes in the  $\alpha$ ,  $\beta$ , and low  $\gamma$  bands during each motor task in the normal subjects (n = 4)

Side of movement		Number of trials / <i>t</i> maximum of each trial		
		$\alpha$ (8-13 Hz)	$\beta$ (13-30 Hz)	Low $\gamma$ (30-50 Hz)
Dominant hand movement	Contralateral MI/SI	1/5.65	3/2.89 to 4.45	3/2.56 to 3.50
	Contralateral superior parietal lobule			1/2.56
	Ipsilateral MI/SI	1/2.9	1/3.0	
	Ipsilateral superior parietal lobule	2/2.92 to 3.6	1/2.89	
	Ipsilateral inferior parietal lobule			1/2.73
Non-dominant hand movement	Contralateral MI/SI	1/2.93	4/2.85 to 4.99	3/2.7 to 3.60
	Contralateral superior parietal lobule	1/2.93	1/2.85	
	Contralateral inferior parietal lobule	1/4.0	1/4.05	
	Contralateral frontal operculum		1/2.85	
	Ipsilateral MI/SI	1/5.01	2/2.85 to 4.99	1/3.56
	Ipsilateral superior parietal lobule	1/5.01		
	Ipsilateral occipital lobe	1/4.22		
	Ipsilateral superior temporal gyrus	1/2.93		

MI/SI, sensorimotor cortex.



**Figure 1** Voxels displaying most significant event related desynchronisation (ERD) in the  $\beta$  band (13–30 Hz) during right and left hand grasping in a control subject are displayed in blue superimposed on the subjects' anatomical magnetic resonance image. Arrowheads indicate the central sulcus. Note the ERD on the contralateral sensorimotor cortex in the control subject.

had weak motor palsy resulting in a decreased grasping rate of about 1 Hz.

### Control subjects

Two subjects' results were excluded from the analysis as the voxels with the highest  $t$  value were distributed evenly over the entire hemisphere. In the other four subjects, the  $t$  value ranged from 2.56 to 5.65 (table 2). A consistent ERD in the sensorimotor cortex (MI/SI) contralateral to the hand movement was observed in the  $\beta$  band (fig 1) except in one subject, who showed ipsilateral SI activity during dominant hand grasping. Those ERD were almost congruent with the "knob"<sup>19</sup> or "omega shaped structure"<sup>20</sup> which is considered to be the hand representative area. Additional  $\beta$  ERD was observed on the ipsilateral superior parietal lobule during dominant hand movement (one subject) and on the ipsilateral MI/SI (two subjects), the contralateral inferior parietal lobule (one subject), and the superior parietal lobule and frontal operculum (one subject) during non-dominant hand movement (fig 2).

Low gamma ERD was observed in the contralateral MI/SI during dominant and non-dominant hand movement (three subjects). In contrast,  $\alpha$  ERD was observed over diverse regions of both cerebral hemispheres.

### Patients

Four patients had  $\gamma$  ERDs with  $t$  values less than 2.5 and were excluded from subsequent analysis. In other frequency bands, the  $t$  value ranged from 2.54 to 6.78 (table 3). For hand movement on the non-affected side, the  $\beta$  ERD was observed on contralateral MI/SI and in the inferior parietal lobule (three and four subjects, respectively). For hand movement on the affected side the  $\beta$  ERD was observed on ipsilateral MI/SI lateral to the assumed hand representative area, in the lateral premotor area, and in the inferior parietal lobule (four, two, and one subjects, respectively) (figs 3 and 4).

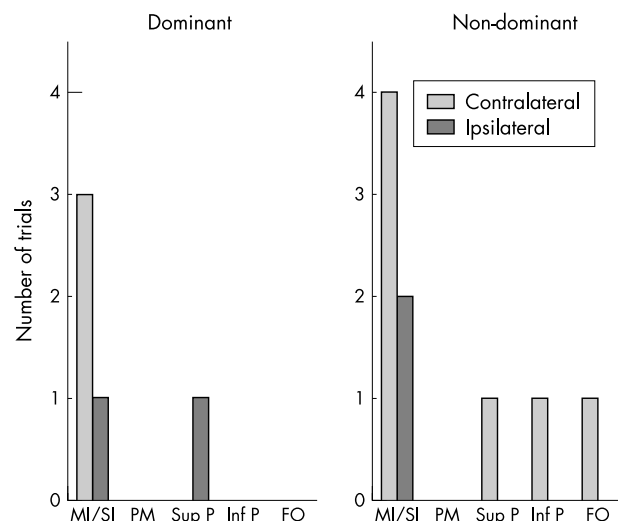
The low  $\gamma$  ERD was observed in the contralateral MI/SI and the premotor area during non-affected hand movement (two subjects each) and in the ipsilateral MI/SI during affected hand movement (three subjects). The  $\alpha$  ERD was observed in diverse regions without any strong consistency.

### $\beta$ Band power

Left–right difference in  $\beta$  band power in the resting state was negligible in the control subjects (figs 5 and 6). In the patient group, attenuation of the  $\beta$  band power was evident, especially in the sensors covering the central region in the affected hemisphere (statistically significant for sensors 23, 24, 33, and 34 by two tailed Student  $t$  test (fig 6)).

### Cortical stimulation

In both subjects studied, weak muscular contractions in the contralateral upper extremity were elicited with the stimulation of the cerebral cortex adjacent to the lesion around the central sulcus.



**Figure 2** Number of trials showing  $\beta$  event related desynchronisation (ERD) on motor areas for control subjects during dominant hand movement (left) and non-dominant hand movement (right). FO, frontal operculum; Inf P, inferior parietal lobule; MI/SI, sensorimotor area; PM, premotor area; Sup P, superior parietal lobule.

**Table 3** Areas showing the most significant power changes in the  $\alpha$ ,  $\beta$ , and low  $\gamma$  bands during each motor task (n=6 patients)

Side of movement		Number of trials / t maximum of each trial		
		$\alpha$ (8–13 Hz)	$\beta$ (13–30 Hz)	Low $\gamma$ (30–50 Hz)
Non-affected side hand movement	Contralateral MI/SI	1/6.78	3/3.4 to 3.95	2/2.4 to 3.26
	Contralateral lateral premotor area			2/2.4 to 3.26
	Contralateral inferior parietal lobule	3/3.61 to 6.2	4/3.95 to 5.06	
	Contralateral superior temporal gyrus			1/3.35
	Ipsilateral superior parietal lobule	1/4.27		
	Ipsilateral inferior parietal lobule	1/5.46		
	Ipsilateral SI			1/3.35
Affected side hand movement	Contralateral prefrontal area			1/2.9
	Contralateral occipital lobe	2/5.2 to 5.86		
	Contralateral cerebellar hemisphere	1/3.88		
	Ipsilateral MI/SI	1/5.2	4/3.07 to 4.8	3/2.54 to 4.75
	Ipsilateral lateral premotor area	1/4.2	2/2.9 to 4.5	
	Ipsilateral inferior parietal lobule	1/3.94	1/3.5	
	Ipsilateral occipital lobe	1/3.88		

MI/SI, sensorimotor cortex; SI, sensory cortex.

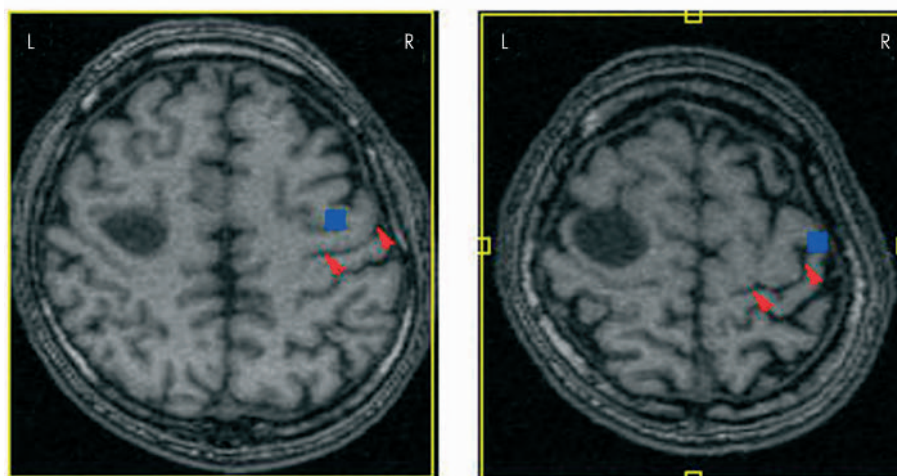
**DISCUSSION**

In control subjects, the  $\beta$  ERD was consistently observed in the contralateral MI/SI adjacent to the so called “knob” or “omega shaped structure”,<sup>19, 20</sup> as in previous studies.<sup>10, 14</sup> In contrast, the  $\alpha$  ERD showed considerable intersubject variability. Compared with the previous studies,<sup>21</sup> the task employed in the present one was repetitive grasping over a fixed time interval; this was not time locked, so both the planning and the execution and proprioceptive feedback phases of each movement were included in the analysis. This, and the broad classical frequency width applied for each band being analysed, may thus have blurred the phase and frequency specific ERD and resulted in the lack of consistent  $\alpha$  ERD. This may also explain why movement related synchronisation in the low  $\gamma$  band<sup>22</sup> was only observed in five of 12 trials. The low  $\gamma$  ERD was also less concentrated in

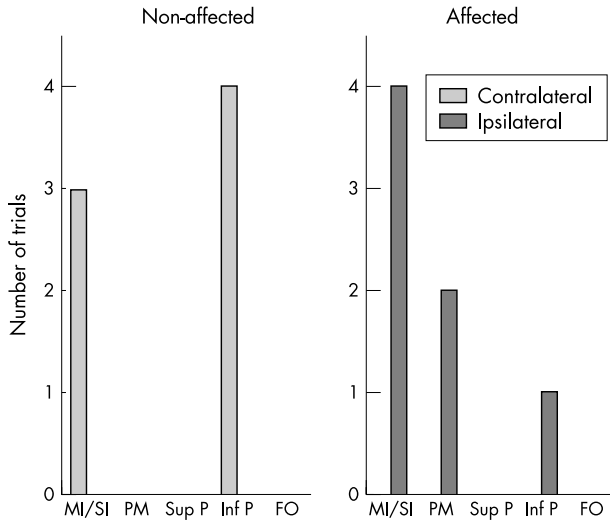
primary motor areas, appeared to be less constrained to the primary hand representation area, and showed less contralateral dominance. Based on a clearer localisation in the control group, our subsequent analysis therefore concentrated on the  $\beta$  band ERD.

The most prominent finding in our study was the lack of  $\beta$  ERD in the MI/SI contralateral to the hand movement on the affected side in the patients (figs 2 and 4). This does not necessarily mean a lack of activity in the MI/SI, as ERD is a reflection of the modulation on basic rhythm by a motor event. Thus if the basic rhythm were suppressed in the resting state owing to the presence of the tumour and the surrounding oedema, the ERD would not become apparent. The  $\beta$  band power attenuation in sensors on the affected side in the resting state, in comparison with the non-affected side (as shown in figs 5 and 6), would provide evidence for the

Patient 4: right hand movement



**Figure 3**  $\beta$  Band event related desynchronisation (ERD) in patient 4 during right hand grasping. Arrowheads indicate the central sulcus. Note the exclusive ipsilateral multiple ERDs in the patients during the affected side hand movement.



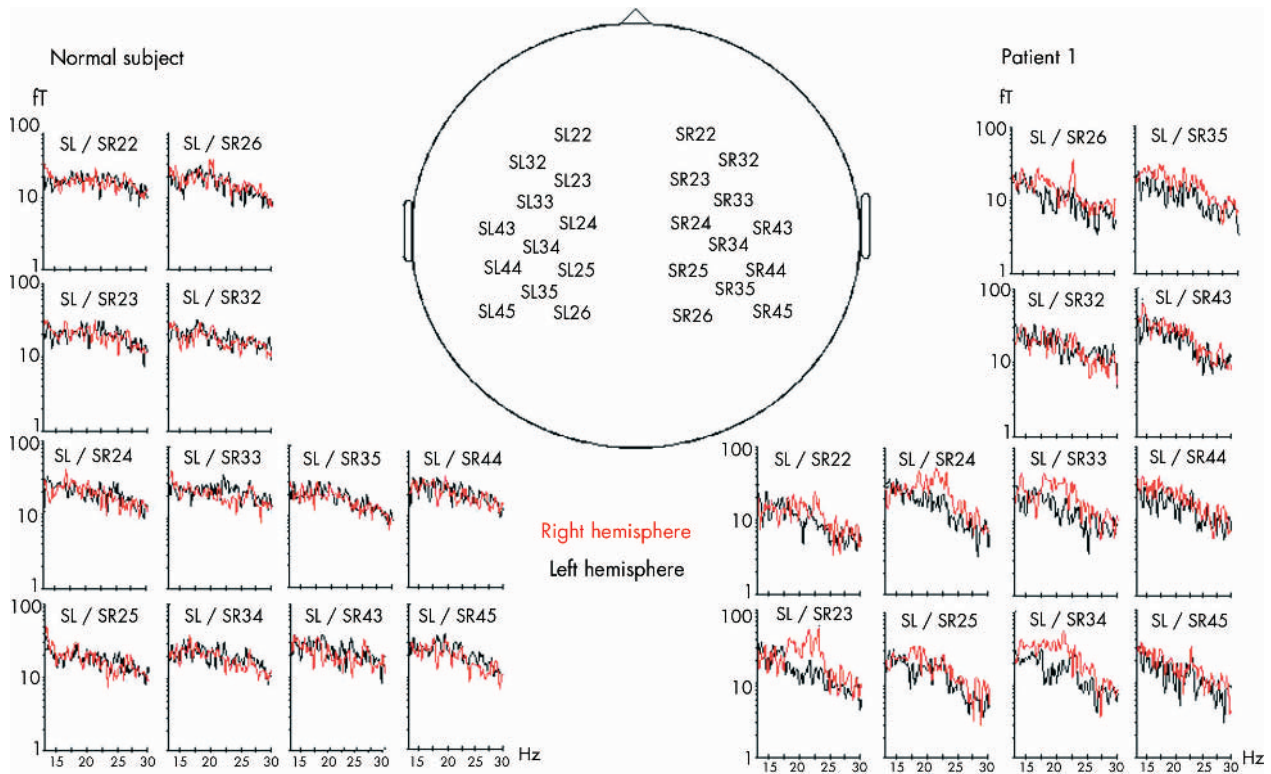
**Figure 4** Number of trials showing beta band event related desynchronisation (ERD) in motor areas for patients during non-affected hand movement (left) and affected hand movement (right). Note the exclusive ipsilateral sensorimotor area ERD for affected side movement. FO, frontal operculum; Inf P, inferior parietal lobule; MI/SI, sensorimotor area; PM, premotor area; Sup P, superior parietal lobule.

basic rhythm alteration in the tumour bearing hemisphere, making the above mentioned hypothesis plausible. Nevertheless, the ipsilateral ERD during affected hand movement would suggest that considerable mobilisation of the ipsilateral motor areas is mandatory to maintain appropriate motor function. This suggests that the affected motor cortex does not function fully in the normal range even

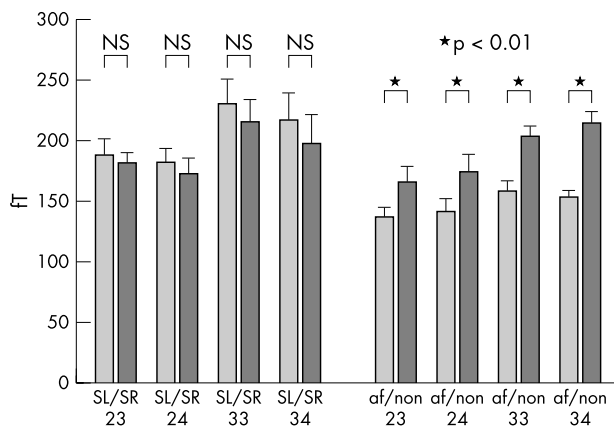
at the stage when the motor impairment is not apparent at all, as was the case in most of the patients studied. The fact that ipsilateral ERD was also observed in subjects in whom intraoperative cortical stimulation showed motor responses around the contralateral motor area suggests that one strategy preferentially employed by the brain in the early stage of motor impairment is recruitment of diverse motor areas, especially the ipsilateral MI/SI.

Another striking feature was the inferior parietal cortex ERD in four of six patients during non-affected hand movement. As this region is considered to become active during motor attention,<sup>23</sup> the results suggest that more attention was needed in those patients. That is likely to have been the case as the task employed was repetitive grasping, which probably requires repeated disengagement and switching of the focus of motor attention from one movement to another. Inferior parietal cortex ERD might also have been present in the contralateral hemisphere during affected side movement, but for the same reason that the ERD of MI/SI does not become apparent owing to the reduced basic beta band power, this ERD might also have been masked. Whether this is the result of any form of motor plasticity is not clear and would need further exploration.

MEG depicts neuronal activity directly, with superior temporal and spatial resolution.<sup>24</sup> Recording of the motor related field, however, is based on time locked motor tasks,<sup>25, 26</sup> which require practice to obtain a consistent result, even in control subjects. Such complex tasks for the patient would result in high intertrial variability, as various aspects of a motor movement—for example, rate and strength of a movement—would affect the result considerably.<sup>27, 28</sup> As the application of SAM source analysis does not require identification of peak amplitudes in the averaged response for discrete movements and dipole modelling, arbitrarily



**Figure 5** Superimposition of the beta band power during resting stage in the sensors covering the central region in a control subject (left) and patient 1 (right). Signal power changes in sensors over the right and left hemispheres are indicated in red and black, respectively. Note the basic power attenuation in sensors 23, 24, 25, 33, 34, and 35 covering left (affected side) central region in patient 1.



**Figure 6** Bar graph indicating  $\beta$  band power (ft) of representative channels covering the sensorimotor cortex for normal subjects and for the patient group. Values are means, error bars = SD. Note the significant difference between channels over the affected and non-affected hemispheres in the patient group. Though some differences between left and right channels in the normal subjects were demonstrated, these were not statistically significant. af, channels over the affected hemisphere; non, channels over the non-affected hemisphere; SL, MEG sensors on left hemisphere; SR, MEG sensors on right hemisphere.

paced tasks such as repetitive grasping are applicable. The grasping task employed in this study was simple, so little effect of differences in the rate and strength of movement could be expected on the activation pattern. All subjects were instructed to grasp the hand weakly at a constant rate, which was confirmed on the monitor during the recording. Thus differences in the appearance of each motor movement could not be accounted for the differences between the control and patient groups. Finally, based on our previous studies of movement related ERD,<sup>10</sup> in the current study, we included voxels displaying an ERD with a pseudo  $t$  value of 2.5 or greater. However, the use of the SAM pseudo  $t$  score<sup>29</sup> makes direct statistical comparisons between experimental conditions and subject groups difficult and remains an area for further development.

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