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Preservation of motor programs in paraplegics as demonstrated by attempted and imagined foot movements

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Execution and imagination of movement activate distinct neural circuits, partially overlapping in premotor and parietal areas, basal ganglia and cerebellum. Can long-term deafferented/deefferented patients still differentiate attempted from imagined movements? The attempted execution and motor imagery network of foot movements have been investigated in nine chronic complete spinal cord-injured (SCI) patients using fMRI. Thorough behavioral assessment showed that these patients were able to differentiate between attempted execution and motor imagery. Supporting the outcome of the behavioral assessment, fMRI disclosed specific patterns of activation for movement attempt and for motor imagery. Compared with motor execution data of healthy controls, movement attempt in SCI patients revealed reduced primary motor cortex activation at the group level, although activation was found in all single subjects with a high variability. Further comparisons with healthy subjects revealed that during attempt and motor imagery, SCI patients show enhanced activation and recruitment of additional regions in the parietal lobe and cerebellum that are important in sensorimotor integration. These findings reflect central plastic changes due to altered input and output and suggest that SCI patients may require additional cognitive resources to perform these tasks that may be one and the same phenomenon, or two versions of the same phenomenon, with quantitative differences between the two. Nevertheless, the retained integrity of movement attempt and motor imagery networks in SCI patients demonstrates that chronic paraplegics can still dispose of the full motor programs for foot movements and that therefore, attempted and imagined movements should be integrated in rehabilitative strategies.

Keywords: Spinal cord injury; Attempt to move; Motor imagery; Functional MRI

Introduction

The human motor system generates accurate movements, which are centrally stored and can be modified and retrieved under various conditions. The complexity of the processes involved in any motor action has led to the concept that the central nervous system contains internal models representing these processes and optimizing motor control (Kawato, 1999; Wolpert and Ghahramani, 2000). Among these models, forward models predict the relationship between issued motor commands and the resulting changes in the sensorimotor system, monitored by the reafferent sensory inflow which supplies information about the state of the body. In this context, patients with complete spinal cord injury (SCI) provide a unique human model for studying the effects of deafferentation on motor control, and on the sensorimotor system in general.

We have recently used functional magnetic resonance imaging (fMRI) to investigate the activation patterns during motor imagery in chronic SCI patients (Alkadhi et al., 2005). This study provided evidence that in this patient group motor imagery still engages the central machinery of movements as suggested by Jeannerod (1995). Studies in healthy subjects revealed that internal simulation of a movement induces similar physiological reactions as its execution (Decety and Jeannerod, 1995; Jeannerod and Decety, 1995). A number of imaging studies disclosed functional circuits shared by both movement execution and imagination (Jackson et al., 2001; Lafleur et al., 2002), although subtle differences in the localization of activation foci between the two tasks have also been reported (Stephan et al., 1995; Gerardin et al., 2000; Hanakawa et al., 2003; Nair et al., 2003).

While it is generally accepted that "overt" or executed motor behavior and "covert" or simulated behavior are intimately related (Jeannerod, 2001), the ability to physically execute a movement is not necessarily required for its mental performance. This is well recognized in patients with hemiplegia who are still able after a cerebrovascular insult to mentally move their limbs, even after years of disuse (Johnson, 2000; Johnson-Frey, 2004). In a case

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study using fMRI, a woman with congenitally absent limbs was able to cortically command movements of her phantom limbs, suggesting that body parts that have never been physically developed can be represented in sensory and motor cortical areas (Brugger et al., 2000). In the investigation of Alkadhi et al. (2005), paraplegic patients mentally moving their paralyzed feet strongly activated brain areas corresponding to both the execution network, including the primary sensorimotor cortex, and the imagery network described in healthy subjects.

In complete SCI patients, both intended overt movements and covert movements remain without obvious motor responses. Therefore, only attempted (MA) and imagined (MI) movements can be compared. The ability of SCI patients to distinguish between attempted and imagined movements has up to now not been assessed behaviorally and only a few imaging studies have investigated brain activity in these patients during attempted and imagined movements of the disconnected body parts (Sabbah et al., 2002; Cramer et al., 2005). These investigations with heterogeneous patient groups reported reduced activation in primary and secondary cortical motor regions for both MA and MI, thus being at odd with our previous experience (Alkadhi et al., 2005).

To address this issue, we undertook further neuroimaging investigations in a homogeneous group of chronic paraplegics, all after at least two years post injury, with complete SCI lesions ascertained by standardized neurophysiological methods. We consider this time interval as a chronic state and thus, appropriate to investigate the influence of long-term deafferentation on attempting to move the feet and generating mental images of the same movement. In addition, the ability of the patients to perform MI and MA and to distinguish between the two was quantitatively assessed. We expected that in SCI patients able to distinguish between MI and MA these two tasks will generate distinct brain activation patterns.

Material and methods

Subjects

Nine paraplegic patients were recruited from the outpatient clinic of our institution (3 females and 6 males; mean age 35 years, SD 6). The Edinburgh Handedness Inventory revealed clear right hand dominance for all subjects. Table 1 gives the age, sex, etiology of the SCI, the level of complete motor deficit, and the time since SCI. For the nine patients, the mean period following traumatic SCI was 9 years (range 2–20 years). All had clinically complete motor SCI between Th3 and L3, as assessed with the impairment scale of the American Spinal Injury Association (ASIA; Maynard et al., 1997), transcranial magnetic stimulation (TMS), and somatosensory evoked potentials (SSEP; Curt and Dietz, 1999). All subjects had repeated clinical examinations and SSEP of the posterior tibial nerves and MEP (motor evoked potentials) of the anterior tibial muscles. The measures were performed at the outpatient clinic and were repeated within 6 months to assure the completeness of SCI. Only one subject (S4) reported some clinical sensation (light touch) at the sacral dermatomes but had complete paralysis of the lower limbs and the SSEP and MEP were completely abolished. Twelve age-matched healthy right-handed volunteers (5 females and 7 males; mean age 29 years, SD 3.7) were recruited as controls.

None of the participants had suffered a brain lesion or had a history of neurological or psychiatric illness. Informed consent was obtained from all subjects and they were reimbursed for their participation in the study. The experimental protocol was approved by the Ethics Committee of the Balgrist University Hospital of Zurich, Switzerland.

Assessment of movement attempt and execution

The motor task studied in the fMRI experiments consisted of repetitive alternating dorsal and plantar flexion of the right foot (30°–0°–45°) at a self-paced rhythm of approximate of 0.5 Hz. The ability to attempt moving the foot (motor attempt, MA) was assessed as follows. The perceived intensity and frequency of attempted movements was rated in a structured interview on phantom sensations, which had been developed for evaluating phantom body phenomena, paresthesia and movement sensations in SCI patients. Of particular relevance was rating the intensity of the feeling to move the right foot and the frequency of spontaneous attempts in daily life. Answers were noted as qualitative descriptors and both the phenomena's frequency and intensity were individually rated

Table 1
Individual clinical and behavioral data for the SCI patients with means

Subject	Level of complete motor impairment/ASIA[a]	Age/Sex[b]	Time since injury (years)	Vividness of kinesthetic motor imagery (VQIM)[c]	Ability for attempted movement intensity[d]	Ability for attempted movement frequency[d]
S1	Th6/A	40/M	7	54	3	3
S2	L1/A	28/M	11	33	4	4
S3	Th5/A	42/M	20	24	5	5
S4	L3/B	29/M	2	26	6	6
S5	Th3/A	38/M	5	106	4	1
S6	Th6/A	29/F	11	25	5	4
S7	Th9/A	27/M	13	31	3	2
S8	Th8/A	41/F	9	34	5	5
S9	Th11/A	39/F	10	24	5	3
Group mean		34.8	9.8	39.7	4.5	3.6
SD		6.3	5.1	26.6	3.6	1.7

[a] ASIA impairment scale: A: no sensory or motor function is preserved; B: sensory is preserved below the level, but not motor.
[b] M: male; F: female.
[c] Kinesthetic MI assessed with Vividness of Motor Imagery Questionnaire (VQIM), range 1–5 (1: high, 5: low imagination, range of 24–120, with the best score at 24).
[d] Ability of attempt to move the right foot with intensity of the feeling (1: very weak; 6: very high) and frequency of spontaneous attempt in daily life (1: very rare; 6: very often).

using a 6-point scale (see Table 1). The verbal instruction for MA in SCI patients was: "*Try* to *move your right foot up and down at an approximate speed of 0.5 Hz*". Correct performance was controlled using an adapted version of the controllability of motor imagery (CMI) described by Naito et al. (2002). With eyes closed, the subjects were required to try moving their right foot as described above and, on command, to promptly give a verbal description of the foot position (flexed or extended). In healthy volunteers, attempt to move was not required as the MA task is difficult to perform without generating isometric muscle contractions. Instead, they had to execute the foot movement (motor execution, ME). Following instruction, the ability of the controls to move their right foot up and down was visually verified.

Assessment of motor imagery

The ability of the subjects to perform MI was assessed with the Vividness of Motor Imagery Questionnaire (VMIQ; Isaac et al., 1986). The VMIQ consists of 24 items specific to movement. It refers to the visual imagery of the movement and to the imagery of movement kinaesthetic sensations. The interesting feature of this questionnaire is that each item refers to two imagery perspectives; the 'internal' or first person perspective and the 'external' or third person perspective. Responders were required to imagine each item both with respect to themselves (first person, kineasthetic sensation) and with respect to someone else (third person, visualisation). For each item, participants were asked to indicate the vividness of an imagined movement on a 5-point scale: 1 (excellent imagination of the movement performance as lively as actual performance), 2 (a good capacity to imagine movement performance), 3 (moderate capacity to imagine the performance of a movement), 4 (a vague or unclear image) or 5 (no image at all). This questionnaire has a possible range of 24–120 for both, first and third person imagination, with the best score at 24. The lower the score, the more vivid the imagery.

To achieve consistent performance of MI in both groups and avoid muscle activity in the healthy subjects, all were trained with eyes closed in the first person motor imagery to mentally move their right foot (dorsal and plantar flexion) outside of the scanner. The instruction for MI in both controls and SCI patients was "*Imagine yourself performing the same foot movement without actually executing it*". To control for proper task performance, the CMI was applied here as in the MA task (see above, Naito et al., 2002). The training was continued up to the point where subjects could fulfill the requirements of the CMI and felt comfortable with the task.

Experimental protocol

The brain activation patterns underlying execution and imagination of foot movements were investigated with fMRI. Experimental conditions were presented in a fixed-order sequence consisting of attempted (SCI patients) or overt (controls) movements followed by motor imagery. The eyes were kept closed in both conditions. Each experimental condition was administered in a standard block design consisting of three 21-s periods of baseline alternating with three 21-s periods of motor task. For the ME/MA condition, the baseline was rest, for the MI condition the baseline condition consisted of silent automatic upwards counting starting from number six. This rest condition was chosen to make a clear distinction between the mental motor task and the rest condition (i.e. to ensure that subjects stopped imagery). Starting with six avoids the tendency of subjects to imagine counting with their fingers. All execution and imagery tasks were self-paced at a rate of approximately 0.5 Hz. The beginning and end of each activation period were signalled with verbal commands "go" and "stop" for ME and MA and "go" and "six" for MI, transmitted over the MR scanner's intercom system. Correct task performance during data acquisition was visually controlled, with the observer monitoring of any movements or apparent change in the resting state of the non-moving limbs, and verifying performance of the ME task by the controls. No overt movements were observed during the MI task in healthy controls, or during MI or MA by the SCI patients.

Scanning procedure

Blood oxygenation level-dependent (BOLD) sensitive fMRI was carried on a 1.5 T whole body scanner equipped with a standard 6-channel head coil using a single-shot, gradient-echo, echo-planar imaging (EPI) sequence (TE = 55 ms, TR = 3000 ms, flip angle 90°). For each task, 126 time points were acquired consisting of 30 contiguous, axial slices (resolution $5 \times 3.4 \times 3.4$ mm^3) covering the entire brain. A T1-weighted whole-brain anatomical reference volume data with an isotropic spatial resolution of 1.2 mm was also acquired with a 3D spoiled, gradient-echo sequence (TE (echo time) = 9 ms, TR (repetition time) = 50 ms).

Imaging analysis

Image analysis was performed using SPM99 (Welcome Department of Cognitive Neurology, London, http://fil.ion.ucl.ac.uk/spm) under MATLAB 6.1 (Mathworks Inc., Natiek, MA, USA). The first two volumes of each fMRI time series were discarded. For each subject, all remaining EPI volumes were realigned to the tenth volume of the first time series. A mean image was then created and the anatomical image was co-registered with this mean image. After co-registration, the structural image was spatially normalized into the reference system of a representative brain template (Montreal Neurological Institute, MNI) using an affine and nonlinear transformation. The normalization parameters were subsequently applied to the functional images. Finally, the EPI images were resampled to a voxel size of $3 \times 3 \times 3$ mm^3 and smoothed with a Gaussian kernel of 10 mm full-width at half-maximum (FWHM). The statistical analysis was performed at two levels in the context of the General Linear Model. Each single condition was modeled using a delayed boxcar function convolved with the hemodynamic response function. This data analysis was performed on a subject-by-subject basis to identify the general network involved in the tasks by comparing the activation with the rest condition.

Group analyses were performed according to the random effects procedure, using the single subject contrast images as input (Friston et al., 1996). Four group-wise parametric maps were generated using a one-sample *t*-test as ME and MI of foot movements in healthy subjects and as MA and MI of foot in the SCI patients. Additionally for the second level analysis four contrasts were defined: (i) MA in SCI patients compared with ME in healthy controls; (ii) MI in SCI compared with MI in healthy controls; (iii) ME compared with MI in healthy controls; and (iv) MA compared with MI in SCI patients.

Region of interest analysis

To analyze the acquired data a region of interest (ROI) approach was used. Based on the known functional neuroanatomy of the

human sensorimotor system (Jackson et al., 2001; Lafleur et al., 2002), the following ROIs were defined for both hemispheres: precentral and postcentral gyrus, paracentral lobule, supplementary motor area (SMA), cingulate motor area (CMA), frontal operculum, superior and inferior parietal regions, thalamus, basal ganglia and cerebellum. The anatomical ROIs were defined according to the automated anatomic atlas (Tzourio-Mazoyer et al., 2002). For each activated cluster, the volume of activation and the maximal signal intensity were determined and the localization in MNI coordinates was obtained using the "WFU-Pickatlas", a web-based interactive program which provides the coordinates of a specified ROI after implementation of small volume correction (Maldjian et al., 2003). The chosen threshold was set at $p<0.01$ because of the relatively weak activation expected for foot movements as already described in other fMRI investigations (Dobkin et al., 2004; MacIntosh et al., 2004).

Results

Behavioral data

In the structured interview, all SCI subjects claimed to be able to attempt moving their foot and to differentiate between attempted and internally simulated movements. The ability to perform both tasks was further confirmed by the test for controllability of motor imagery (CMI; Naito et al., 2002) since all subjects were able to indicate the posture of their foot during both tasks. The patients were able to rate the intensity of their feeling during attempted movements on the 6-point scale, as well as the frequency of spontaneous daily performance (Table 1). The intensity was described as medium to very high during task performance (mean 4.5, SD 3.6, range from 3 to 6). In contrast, the daily performance was lower (mean 3.6, SD 1.7, range from 3 to 6). The intensity and frequency of task performance were significantly correlated ($r=0.77$, $p<0.05$). In the Vividness of Motor Imagery Questionnaire (VMIQ), the performance of the SCI patients did not significantly differ from that of the healthy controls (mean 39.7, SD 26.6 and 44.3, SD 16.3, respectively).

fMRI study

Motor execution (ME) in healthy controls and movement attempt (MA) in SCI patients

In the controls, dorsal and plantar flexion of the right foot activated the left primary sensorimotor cortex (M1/S1) and bilaterally mesial (SMA, pre-SMA, CMA, CMAr), dorsal premotor (PMd) and ventral premotor (PMv) areas. Further, left-sided activation was observed in the superior (SP) and inferior (IP) parietal lobules, in thalamus, posterior putamen, and in anterior cerebellum (Table 2; Fig. 1).

When the SCI patients attempted to move their foot, the pattern of activated regions was very similar to that found in the controls during execution. In addition, new significant clusters were found bilaterally in the prefrontal (PF) and SP cortex, in the right PMv region and the posterior putamen (Table 2).

The single-subject analysis revealed activation in the primary motor cortex in all 9 SCI patients (Table 3). In this analysis, a considerable variation in volumes and *t*-values was found in the primary motor and somatosensory (S1) foot representations of the SCI patients during MA. Fig. 2 displays for the individual subjects the activation maxima in the foot motor region. The greater scatter of the individual SCI data is most probably responsible for the smaller activation extent and intensity found in the group analysis for the patients during MA compared to ME in healthy subjects. Fig. 2 also displays the activation maxima of each subject in PMv, SP, and IP with some scatter in all three regions.

Motor imagery (MI) in healthy controls and SCI patients

During imagined movements the healthy subjects activated the left PMd, the mesial PM areas, and the PMv cortex bilaterally. Significant bilateral clusters were also found in the PF and IP cortex and a contralateral one in the anterior putamen (Fig. 3; Table 2). BOLD signal changes in the left primary motor and S1 cortex was significant in only 3 of the 12 subjects (Table 3) and did not reach significance in the group.

The main findings in SCI patients during MI were large activated clusters in IP and PF cortex, as well as in thalamus, anterior putamen and pallidum bilaterally (Table 2). Other activated areas included the mesial and ventral PM cortex, similar to the control group. The majority of the subjects (7 out of 9) however, had activation in the primary motor cortex (Table 3).

Contrast between movement attempt (MA) in SCI and execution (ME) in healthy

The contrast between MA in SCI patients and ME in healthy volunteers revealed an overlap of many regions activated in both groups. However, MA produced more activation than ME in several regions: left PMv and putamen resp. pallidum, and bilaterally in SP and IP lobules, PF cortex and cerebellum (Table 4; Fig. 1). In contrast, no significant differences were found when ME in healthy controls were compared to MA in the SCI patients.

In the single-subject analysis, although considerable variation in extent and intensity was found in the primary motor and S1 foot representations of the SCI patients for MA, the differences with the ME values in healthy subjects did not reach the significance level (*t*-test, resp. *F*-test for the standard deviations).

Contrast between MI in SCI patients and in healthy controls

To find out whether MI in paraplegia activates the same regions as MI in healthy controls and to the same degree, a contrast between patients and controls was performed. This contrast mainly revealed the presence of bilaterally activated clusters in the IP and PF cortex of the SCI patients (Table 4; Fig. 3). Activation was greater in the SCI patients in all regions activated by MI, except for SP and secondary somatosensory (S2) cortex (Table 4). Bilateral stronger activation was also disclosed in the thalamus and putamen/pallidum. The opposite contrast, i.e. between MI in healthy and MI in SCI, did not disclose any increased or additional activation.

Contrast between MI and ME in healthy controls and MA and MI in SCI patients

The results of the second level analysis between ME and MI in control subjects are listed in Table 4. Stronger activation during ME was shown in the left primary motor and S1 cortex and in most regions activated by execution. Motor imagery induced stronger activation than ME only in the left PF cortex. This contrast is therefore not listed in Table 4.

In the SCI patients, MA produced more activation than MI in many regions: left primary motor cortex, bilateral CMA and SMA, and in the right hemisphere PMv, SP and IP, and PF cortex, as well as in subcortical regions shown for MA (Table 4). Conversely, the comparison between MI and MA only revealed three clear foci in

Table 2
Coordinates (in MNI standard brain space) of significant cluster maxima, *t*-values, and volumes in the ROI group analysis for executed, attempted, and imagined movements versus baseline in healthy controls and SCI patients (threshold $p<0.01$, corrected)

Functional ROI		Movement execution healthy					Movement attempt SCI					Motor imagery healthy					Motor imagery SCI				
		x	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)
M1	Left	−6	−36	60	11.51	266	−12	−33	60	9.75	95										
S1	Left	−15	−39	75	5.55	26	−30	−45	66	3.26	8										
S2	Left	−57	−21	18	4.77	42	−60	−21	15	9.75	35						−63	−21	30	4.05	9
SMA	Left	−9	−18	57	7.91	300	3	−21	57	6.88	124	−18	−6	66	3.08	5					
Pre-SMA	Right	0	0	48	10.62	241						6	6	51	4.19	40					
	Left																−9	18	45	3.26	14
CMA	Left	−6	−30	48	5.22	29	−12	−36	54	8.74	77										
CMAr	Right	0	0	45	12.18	229						6	9	39	3.55	21					
	Left						−3	−3	42	5.47	105						−6	0	36	6.63	47
PMd	Right	45	−3	48	7.68	51															
	Left	−36	−3	57	7.98	72						−36	−6	54	3.31	8					
PMv	Right	60	9	9	8.92	157	51	3	0	4.77	67	60	15	−3	3.87	13	42	3	30	4.41	14
	Left	−57	3	6	8.85	161	−45	3	9	8.76	193	−48	3	0	5.01	35	−48	6	33	5.62	161
SP	Right						15	−63	66	5.26	37										
	Left	−27	−48	69	5.39	69	−30	−63	57	7.55	165						−30	−51	69	4.66	5
IP	Right	66	−27	30	7.03	170	54	−30	24	6.56	111	54	−30	24	3.94	18	66	−33	33	6.65	216
	Left	−54	−36	27	9.28	239	−57	−39	39	5.15	319	−60	−33	24	3.34	7	−54	−48	30	10.47	527
PF	Right						42	39	3	3.8	20	30	33	−15	5.12	11	54	42	0	8.40	148
	Left						−51	15	30	4.14	8	−45	15	−6	5.69	235	−54	30	9	6.73	471
TH	Right																24	0	3	3.96	48
	Left	−9	−18	−3	8.80	106	−21	−15	6	5.81	101						−21	−12	3	3.37	13
PU/PA	Right						30	−15	6	4.56	77						−30	9	3	7.85	18
	Left	−30	−15	6	6.46	87	−30	−21	3	9.66	129	−24	−6	−6	8.09	17	−21	−3	0	4.33	51
CB	Right	27	−42	−27	7.26	99	9	−45	−18	20.86	553										
	Left	−33	−57	−30	6.41	44	−18	−72	−24	7	146										
	Right						27	−45	−45	7.71	10										
	Left	−30	−54	−45	4.81	14	−9	−84	−27	6.11	7										

L=left, R=right, L/R=bilateral; ROI, region of interest; M1, primary motor cortex; S1, primary somatosensory cortex; S2, secondary somatosensory cortex; SMA, supplementary motor area; CMA, cingulate motor area; PMd, premotor dorsal cortex; PMv premotor ventral cortex; SP, superior parietal cortex; IP, inferior parietal cortex; PF, prefrontal cortex; TH, thalamus; PU/PA, putamen/pallidum; CB, cerebellum.

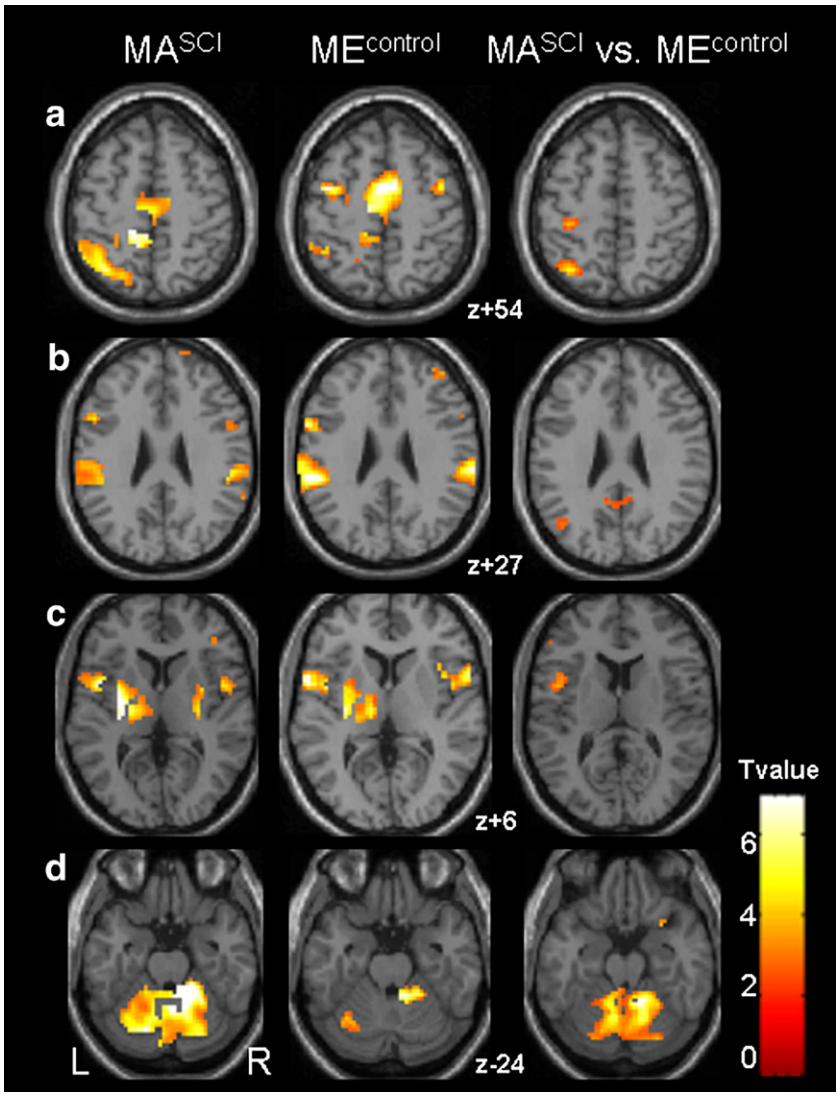

Fig. 1. Activation patterns (group analysis) in SCI patients and controls displayed on mean anatomic T1-weighted images. *Left column*: movement attempt (MA) in SCI patients. *Middle column*: movement execution (ME) in controls. *Right column*: contrasts between movement attempt in SCI patients (MA) and movement execution in controls (ME). (a) central region, superior and inferior parietal areas (SP and IP); (b) IP area, premotor ventral (PMv) and prefrontal cortex (PF); (c) premotor ventral (PMv), putamen/pallidum, thalamus; (d) cerebellum. Coordinates of significant regions listed in Tables 2 and 4.

the left hemisphere: one in left PMd and two maxima in the parietal cortex, one in the SP and the other in the IP lobules.

Correlation of behavioural data and fMRI data

For the SCI patients correlation coefficients were computed between the quantitative aspects of the BOLD signal in all ROIs (max *t*-values and volumes of activation) and the clinical and behavioral data of the individual subjects (number of disconnected segments, time since injury, VMIQ scores, intensity and frequency in the 6-point rating scale for MA). No correlation coefficient reached the significance level, neither for MA nor for MI.

Discussion

The present study assessed the ability of chronic SCI patients to internally distinguish between attempted and imagined movements of their paralyzed feet and how these differ from executed and simulated movements in healthy controls. Four main findings summarize our results. First, the behavioural data clearly demonstrate that chronic complete SCI patients retain their ability to subjectively differentiate between the executive features required for MA and the cognitive ones necessary for MI. Secondly, this behavioural finding was confirmed by fMRI data revealing distinctly differential patterns of activation for the two conditions. Moreover, when SCI patients attempted to move their paralyzed foot the same network was recruited as when healthy subjects actually executed the foot movement. The same was true for the internal simulation of the movements, which activated the regions previously described for MI in healthy subjects and also seen in the controls of the present study. Third, our study confirms that during MA, cortical motor areas, in particular the primary sensorimotor cortex, are functionality preserved in SCI patients, though with reduced activation due to a long period of disconnection. Finally, the enhanced activation in most secondary motor areas and the additional recruitment of prefrontal and parietal areas both during MA and MI in SCI patients suggests that the paraplegic condition

Table 3
Frequency of single subject activation in specified ROIs

Functional ROI	Execution controls $N=10$	Movement attempt SCI $N=9$	Motor imagery controls $N=10$	Motor imagery SCI $N=9$
M1	10/–	9/–	3./–	7/–
S1	10/5	6/4	3/–	3/1
S2	9/5	6/4	3/3	5/3
SMA	10	7	5	8
CMA	10	7	5	7
PMd	8/7	5/4	5/2	3/2
PMv	8/7	5/4	5/5	5/7
SP	9/5	9/7	7/1	4/3
IP	6/4	6/4	7/6	9/9
PU/PA	4/0	3/2	–/–	–/–
CB	9/4	8/7	4/3	3/3

Number contralateral/Number ipsilateral. Abbreviations: see Table 2.

may require an increase in attention allocation to perform the tasks and/or have induced some adaptive changes in the functional networks involved.

Movement attempt in SCI patients

Few neuroimaging studies have addressed MA in chronic spinal cord-injured patients (Sabbah et al., 2002; Cramer et al., 2005; Halder et al., 2006; Fallani et al., 2007). The most recent fMRI investigation (Cramer et al., 2005) reported an activation pattern during MA similar to that observed during execution in healthy controls, though with decreased volumes in most cortical regions examined. The present study replicated this activation pattern however, with the exception of the primary motor cortex, equivalent or greater BOLD activation was found in all other areas, as well as recruitment of several additional regions (PMv, SP, IP, and PF cortex). In addition, in the present investigation, the basal ganglia were always activated, in the healthy subjects as well as in the chronic SCI patients. This is in contrast with Cramer et al. (2005) who reported a significant BOLD signal in the pallidum only for their SCI population and who interpreted this finding as the emergence of pathological activation. Differences in experimental designs most likely account for the discrepancy between these findings. In the study by Cramer et al. (2005), attempted movement was initiated by a video of the target motion shown before and during the fMRI session, and the foot task used in their investigation, an attempt to crush a displayed object every 3 s, was more complex than our self initiated, simple, repetitive dorsal and plantar foot flexion. Furthermore, healthy subjects in their study performed also a movement attempt task, which is difficult to perform without isometric muscle contractions, as opposed to the simple motor execution used in our study.

The fact that no significant differences in BOLD signal between MA in the SCI patients and ME in healthy controls were found in primary sensorimotor and PM mesial cortex, supports our assumption that these are two corresponding conditions, which can be contrasted with each other, despite the fact that attempt to move can only be indirectly controlled through behavioural tests, as the movements are not visible. The similarity between the network activated in SCI patients during MA and the execution network of healthy subjects additionally provides the neural and thus "visible" evidence for task performance. In fact, this finding in chronic paraplegics, who were all neurophysiologically tested for completeness of the disconnection, reveals their retained potential to initiate and control foot movements, even after a long period of non-use, as suggested by the behavioural assessment. Persistence of motor networks in long-term deafferented subjects has also been reported in amputees who showed fast recovery of sensory motor functions following reafferentation. fMRI studies in these subjects revealed following hand-grafting a reversal of cortical reorganization to a normal activation pattern (Giraux et al., 2001; Neugroschl et al., 2005). Consistent with results of earlier investigations (Lacourse et al., 1999; Halder et al., 2006) in the group analysis, the activation in the primary motor cortex during MA was reduced as compared to ME of healthy controls, but this did not reach the significance level. At the single subject level however, the size and intensity of signal changes in the primary motor cortex did not differ significantly

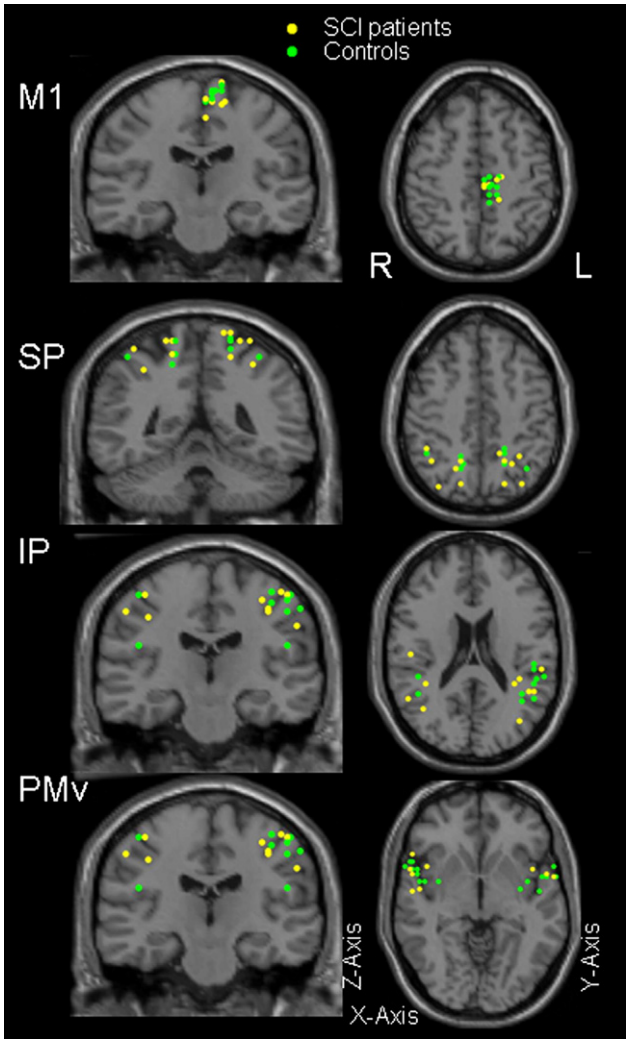

Fig. 2. Local maxima of the single-subject activations for movement attempt in SCI patients and execution in controls after normalization for primary motor cortex (M1), superior parietal cortex (SP), inferior parietal cortex (IP), premotor ventral (PMv). *Yellow*: SCI patients. *Green*: controls. *Left column*: *x*, *y* coordinates projected onto a coronal section of a representative MNI standard brain through the most anterior local maxima. *Right column*: *x*, *z* coordinates projected onto a transverse section through the most inferior local maxima. Note that the general scatter is partially because several higher and lower sections have been projected onto one single section.

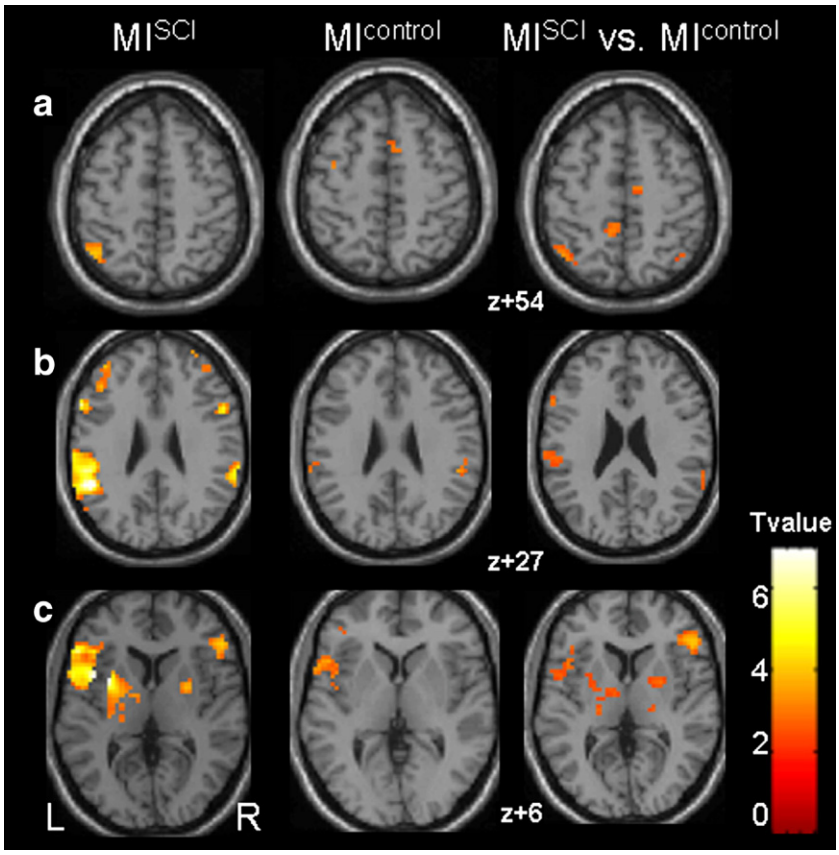

Fig. 3. Activation patterns (group analysis) in SCI patients and controls displayed on mean anatomic T1-weighted images. *Left column*: motor imagery in SCI patients (MI^{SCI}). *Middle column*: motor imagery in controls ($MI^{control}$). *Right column*: contrasts between motor imagery in SCI patients (MI^{SCI}) and in controls ($MI^{control}$). (a) central region, superior and inferior parietal areas (SP and IP); (b) IP area, premotor ventral (PMv) and prefrontal cortex (PF); (c) premotor ventral (PMv), putamen/pallidum, thalamus. Coordinates of significant regions listed in Tables 2 and 4.

when controls and patients were compared, suggesting that the smaller cluster observed in the SCI patients at group level was probably due to the scatter of the individual data during the averaging process. In spite of the electrophysiological assessed interruption of the sensory afferent pathway from the periphery, a small BOLD signal has been observed in the postcentral region confirming our earlier findings of a primary somatosensory (S1) foot representation recruitment in complete SCI patients (Alkadhi et al., 2005). This postcentral activation can be attributed to an efference copy of the ongoing movement in sensory regions (Holst and Mittelstaedt, 1950). A recent fMRI investigation with ischemic nerve block on the lower limb also disclosed activation in S1 giving further support to this hypothesis (Christensen et al., 2007).

Two present findings suggest that MA is a more demanding task than ME. First, both the additionally activated focus in the PF cortex and the activation enhancement in the parietal lobe suggest the existence of a stronger cognitive component during MA. This may reflect the intense attention allocation required from the chronic SCI patients to perform a considered easy over-learned task (Allen et al., 1997; Rowe et al., 2002; Rushworth et al., 2003). Second, the comparison between attempted and performed foot task revealed stronger activity specific for MA in the parietal cortex, in cerebellar regions, and in the putamen. One cannot exclude that the chronic paraplegic condition has also induced adaptive changes in these key structures yielding sensorimotor transformations and movement guidance (Catalan et al., 1998; Allen et al., 2005). The scattered activation seen in the individual activation in the SCI individual data in parietal and premotor regions also points to the presence of adaptive changes. Recent EEG data strongly suggest modifications in connectivity between cortical regions during MA in SCI patients compared to healthy subjects (Fallani et al., 2007).

Motor imagery in SCI patients

In our earlier study (Alkadhi et al., 2005), SCI patients were asked to mentally move their right foot. This instruction led to enhanced activation of an extensive network of brain areas comprising regions activated both during motor imagery and during execution in healthy controls (Lafleur et al., 2002). In the present investigation, MI in SCI patients recruited areas that were spatially more restricted to frontal, mesial and premotor ventral cortex, parietal regions, thalamus and striatum. These are regions that normally activate during MI in healthy subjects (Gerardin et al., 2000). Compared to our former study where the primary motor cortex was significantly activated during MI, activation in the present study was inconsistently observed in the individual subjects, in accordance with previous investigations using similar tasks (Porro et al., 1996; Gerardin et al., 2000). In contrast, during MA, the primary motor cortex was consistently activated, though at a reduced intensity. These fMRI findings clearly confirmed the results in the behavioral assessments namely that the SCI patients were performing distinct MA and MI tasks.

Table 4
Coordinates (in MNI standard brain space) of significant cluster maxima, *t*-values, and volumes for the contrasts in healthy controls and SCI patients (threshold $p<0.01$, corrected)

Functional ROI		Controls ME vs. MI					SCI MA vs. MI					SCI MI vs. MA					SCI MA vs. ME controls					SCI MI vs. controls MI				
		x	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)	*x*	*y*	*z*	Max. *t* value	Volume (voxel)
M1	Left	−3	−36	60	10.87	262	−12	−33	60	7.34	111															
S1	Right	18	−45	75	5.07	40																				
	Left	−15	−39	75	6.05	29																				
SMA	Bilat	9	−15	66	10.97	501	6	−24	57	5.94	45											12	−12	54	3.26	5
CMA	Bilat	−3	−36	51	6.00	53	−12	−36	54	6.63	70															
CMAr	Bilat	−3	0	39	11.82	169																−6	0	39	3.26	12
PMd	Right	15	−21	66	5.56	12																				
	Left	−15	−15	69	3.63	13						−39	−27	60	3.76	9										
PMv	Right	45	−30	18	6.61	41	51	12	27	5.24	37											54	12	30	2.91	10
	Left	−48	−27	18	8.14	46											−45	3	12	3.75	56	−45	12	6	2.99	22
SP	Right						15	−72	51	3.99	24						30	−60	63	3.75	12					
	Left	−18	−42	63	5.46	41						−42	−30	63	5.38	85	−30	−63	57	4.92	62					
IP	Right	63	−24	18	7.98	152	42	−63	27	4.86	88						39	−72	36	3.41	30	63	−45	33	3.67	91
	Left	−51	−27	18	8.14	100						−57	−24	48	5.26	19	−36	−63	54	4.13	17	−60	−51	33	3.53	109
	Right	45	−42	54	3.64	23	42	−48	45	4.38	23															
	Left	−39	−51	60	6.1	5											−42	−72	36	3.37	42	−42	−60	54	3.44	30
PF	Right						42	42	18	5.88	112						30	12	−21	3.84	6	51	30	6	4.08	152
	Left																−30	45	−15	3.97	39	−36	33	39	3.80	41
TH	Right																					21	−21	9	3.02	7
	Left	−21	−24	6	3.83	14	−21	−24	−3	4.94	21											−9	−6	9	3.1	18
PU/PA	Right																					21	−3	−6	3.3	81
	Left	−30	−12	6	5.03	46	−27	−15	6	6.85	48						−30	−6	−6	3.47	29	−27	6	3	3.14	53
CB	Right	15	−42	−24	8.22	81	9	−45	−21	6.21	96						12	−48	−21	7.92	384	21	−45	−27	3.01	9
	Left	−36	−57	−39	7.09	98	−15	−48	−15	4.27	24						−9	−63	−24	6.34	314					
	Right	27	−69	−27	4.21	17											27	−45	−45	4.36	14	9	−57	−15	3.01	11
	Left	−24	−36	−30	3.73	10	−12	−84	−27	3.86	43						−30	−81	−33	4.43	43					

Abbreviations: see Table 2.

Prefrontal and parietal areas showed enhanced activation during MI in the SCI patients when compared to the control group. This increased activity confirms our previous findings (Alkadhi et al., 2005), but is not in line with those of Cramer and colleagues (2005) who, in a similar contrast, did not observe significant changes in these regions. In their study, the only cortical area showing increased activation during MI was the superior temporal gyrus, a region important for the visual perception of biological motion, which never activated in our investigation. These conflicting findings between the two studies can be attributed to differences in the experimental protocols used. Videos of the required complex movement were shown in their study with the instruction to imagine movement completion, which may have induced unconscious strategies leading to 3rd person motor imagery. As recently demonstrated, kinesthetic (1st person) and visual (3rd person) motor imagery are supported by different neural networks (Solodkin et al., 2004). In our experiment, no visual stimuli were presented and the subjects with eyes closed were specifically instructed and trained to prevent developing a strategy leading to visualization of their limb. Accordingly, activation in visual regions was not observed during attempted or imagined movements.

Central motor control in paraplegia

The present investigation indicates that in chronic paraplegic patients the central programs for execution of foot movements and their internal simulation remain preserved, activating several common regions and, in addition, other distinct ones specific to either task. MA and MI in a status of chronic deafferentation and deefferentation are complex tasks, which recruit cortical regions involved in higher cognitive processes. Despite every effort in this study to distinguish between the two tasks, taking into consideration the single subjects' activations, as well as their contrasts, we cannot completely rule out the likelihood of a contamination of either task by the other. This possibility may explain the activation of the PF cortex during MA and the large number of SCI patients who had some activation in the primary motor cortex during MI. These two tasks may be one and the same phenomenon, or two versions of the same phenomenon, with quantitative differences between the two.

How the control of virtual foot movements can be preserved after a prolonged period of complete disconnection? In patients with chronic hemiplegia, the ability to construct internal action representations of the upper limbs can be robust even after years of limb non-use (Johnson-Frey, 2004). The process of matching the final position of one's limbs with an intended movement is achieved through a comparison process between the predicted sensory consequences of the action and the actual sensory feedback (Desmurget and Grafton, 2000; Wolpert and Ghahramani, 2000). Since peripheral cutaneous and proprioceptive afferents of the lower limbs are unavailable in complete SCI patients, this process can be accomplished solely by means of stored motor programs and the resulting stream of motor commands with their sensory signals generated through corollary discharge (Blakemore and Sirigu, 2003). The additional fact that the SCI patients have continuous daily visual control of their body may also play a role in maintaining an internal representation of their limbs through a continuous updating by simply looking at them (Wolpert et al., 1998). These speculations are supported by the retained integrity of the internal action representation in our patients as revealed by both the structured interview and the fMRI data.

It has been suggested that parietal areas constitute the neural substrate for the storage of visual and kinaesthetic limb postures, which are subsequently mapped onto corresponding motor regions (Sirigu et al., 1996). Damage to the parietal cortex leads to the inability both of maintaining an internal representation of the body (Wolpert et al., 1998) and of internal movement simulation (Sirigu et al., 1996). These findings indicate that the parietal cortex is a key structure in sensorimotor integration and, together with its interactions with the cerebellum, plays an important role in acquisition and recall of skilled movements (Allen et al., 1997; Shadmehr and Holcomb, 1997; Andersen and Buneo, 2003; Blakemore and Sirigu, 2003). The enhanced parietal and cerebellar activations observed in chronic SCI patients during MA and MI in our study suggests that some adaptive changes have occurred in these regions. The absence of sensory input may have modified the functionality of these areas in order to maintain an intact body representation and organize motor plans accordingly.

Clinical significance

The present study demonstrates in chronic paraplegics the retained functionality of neuronal networks that in healthy subjects are responsible for dorsal and plantar flexions of the foot and their internal simulation. This finding may have important clinical value when considering new treatment approaches aiming at functional recovery following spinal cord damage. If reconnection of the brain to the paralyzed limbs through the spinal cord is successful, according to our present data, the still functional motor programs should allow a certain degree of motor control. It further provides the principal physiological requirements for the development of a brain–computer interface device that uses intention-driven neuronal activity to be converted into a control signal that enables useful tasks (Hochberg et al., 2006). The apparent integrity of MI in SCI patients and the resemblance of their MA network with the ME network of healthy subjects suggest that the paraplegics still dispose of the full motor programs for overt and covert foot movements. Recent reports provide convincing evidence that mental practice based on motor imagery might be beneficial for learning new movements and/or strengthening memorized ones (Jackson et al., 2003; Lacourse et al., 2005; Cramer et al., 2007). We therefore suggest that MA and MI may be useful adjuncts to traditional rehabilitation strategies for improving motor functions after spinal cord injury particularly for incomplete patients with residual motor functions.

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References

Alkadhi, H., Brugger, P., Boendermaker, S.H., Crelier, G., Curt, A., Hepp-Reymond, M.C., Kollias, S.S., 2005. What disconnection tells about motor imagery: evidence from paraplegic patients. Cereb. Cortex 15, 131–140.

Allen, G., Buxton, R.B., Wong, E.C., Courchesne, E., 1997. Attentional activation of the cerebellum independent of motor involvement. Science 275, 1940–1943.

Allen, G., McColl, R., Barnard, H., Ringe, W.K., Fleckenstein, J., Cullum,

C.M., 2005. Magnetic resonance imaging of cerebellar–prefrontal and cerebellar–parietal functional connectivity. NeuroImage 28, 39–48.
Andersen, R.A., Buneo, C.A., 2003. Sensorimotor integration in posterior parietal cortex. Adv. Neurol. 93, 159–177.
Blakemore, S.J., Sirigu, A., 2003. Action prediction in the cerebellum and in the parietal lobe. Exp. Brain Res. 153, 239–245.
Brugger, P., Kollias, S.S., Muri, R.M., Crelier, G., Hepp-Reymond, M.C., Regard, M., 2000. Beyond remembering: phantom sensations of congenitally absent limbs. Proc. Natl. Acad. Sci. U. S. A. 97, 6167–6172.
Catalan, M.J., Honda, M., Weeks, R.A., Cohen, L.G., Hallett, M., 1998. The functional neuroanatomy of simple and complex sequential finger movements: a PET study. Brain 121, 253–264.
Christensen, M.S., Lundbye-Jensen, J., Geertsen, S.S., Petersen, T.H., Paulson, O.B., Nielsen, J.B., 2007. Premotor cortex modulates somatosensory cortex during voluntary movements without proprioceptive feedback. Nat. Neurosci. 10, 417–419.
Cramer, S.C., Lastra, L., Lacourse, M.G., Cohen, M.J., 2005. Brain motor system function after chronic, complete spinal cord injury. Brain 128, 2941–2950.
Cramer, S.C., Orr, E.L., Cohen, M.J., Lacourse, M.G., 2007. Effects of motor imagery training after chronic, complete spinal cord injury. Exp. Brain Res. 177, 233–242.
Curt, A., Dietz, V., 1999. Electrophysiological recordings in patients with spinal cord injury: significance for predicting outcome. Spinal Cord 37, 157–165.
Decety, J., Jeannerod, M., 1995. Mentally simulated movements in virtual reality: does Fitts's law hold in motor imagery? Behav. Brain Res. 72, 127–134.
Desmurget, M., Grafton, S., 2000. Forward modeling allows feedback control for fast reaching movements. Trends Cogn. Sci. 4, 423–431.
Dobkin, B.H., Firestine, A., West, M., Saremi, K., Woods, R., 2004. Ankle dorsiflexion as an fMRI paradigm to assay motor control for walking during rehabilitation. NeuroImage 23, 370–381.
Fallani, F.D., Astolfi, L., Cincotti, F., Mattia, D., Marciani, M.G., Salinari, S., Kurths, J., Gao, S., Cichocki, A., Colosimo, A., Babiloni, F., 2007. Cortical functional connectivity networks in normal and spinal cord injured patients: evaluation by graph analysis. Hum. Brain Mapp. (Electronic publication ahead of print).
Friston, K.J., Holmes, A., Poline, J.B., Price, C.J., Frith, C.D., 1996. Detecting activations in PET and fMRI: levels of inference and power. NeuroImage 4, 223–235.
Gerardin, E., Sirigu, A., Lehericy, S., Poline, J.B., Gaymard, B., Marsault, C., Agid, Y., Le Bihan, D., 2000. Partially overlapping neural networks for real and imagined hand movements. Cereb. Cortex 10, 1093–1104.
Giraux, P., Sirigu, A., Schneider, F., Dubernard, J.M., 2001. Cortical reorganization in motor cortex after graft of both hands. Nat. Neurosci. 4, 691–692.
Halder, P., Curt, A., Brem, S., Lang-Dullenkopf, A., Bucher, K., Kollias, S., Brandeis, D., 2006. Preserved aspects of cortical foot control in paraplegia. NeuroImage 31, 692–698.
Hanakawa, T., Immisch, I., Toma, K., Dimyan, M.A., Van Gelderen, P., Hallett, M., 2003. Functional properties of brain areas associated with motor execution and imagery. J. Neurophysiol. 89, 989–1002.
Hochberg, L.R., Serruya, M.D., Friehs, G.M., Mukand, J.A., Saleh, M., Caplan, A.H., Branner, A., Chen, D., Penn, R.D., Donoghue, J.P., 2006. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature 442, 164–171.
Holst, E.v., Mittelstaedt, H., 1950. Das Reafferenzprincip (Wechselwirkungen zwischen Zentralnervensystem und Periferie). Naturwissenschaft 37, 464–476.
Isaac, A., Marks, D.F., Russel, D.G., 1986. An instrument for assessing imagery of movements: the Vividness of Movements Imagery Questionnaire (VMIQ). J. Ment. Imag. 10, 23–30.
Jackson, P.L., Lafleur, M.F., Malouin, F., Richards, C., Doyon, J., 2001. Potential role of mental practice using motor imagery in neurologic rehabilitation. Arch. Phys. Med. Rehabil. 82, 1133–1141.
Jackson, P.L., Lafleur, M.F., Malouin, F., Richards, C.L., Doyon, J., 2003. Functional cerebral reorganization following motor sequence learning through mental practice with motor imagery. NeuroImage 20, 1171–1180.
Jeannerod, M., 1995. Mental imagery in the motor context. Neuropsychologia 33, 1419–1432.
Jeannerod, M., 2001. Neural simulation of action: a unifying mechanism for motor cognition. NeuroImage 14, S103–S109.
Jeannerod, M., Decety, J., 1995. Mental motor imagery: a window into the representational stages of action. Curr. Opin. Neurobiol. 5, 727–732.
Johnson, S.H., 2000. Imagining the impossible: intact motor representations in hemiplegics. NeuroReport 11, 729–732.
Johnson-Frey, S.H., 2004. Stimulation through simulation? Motor imagery and functional reorganization in hemiplegic stroke patients. Brain Cogn. 55, 328–331.
Kawato, M., 1999. Internal models for motor control and trajectory planning. Curr. Opin. Neurobiol. 9, 718–727.
Lacourse, M.G., Cohen, M.J., Lawrence, K.E., Romero, D.H., 1999. Cortical potentials during imagined movements in individuals with chronic spinal cord injuries. Behav. Brain Res. 104, 73–88.
Lacourse, M.G., Orr, E.L., Cramer, S.C., Cohen, M.J., 2005. Brain activation during execution and motor imagery of novel and skilled sequential hand movements. NeuroImage 27, 505–519.
Lafleur, M.F., Jackson, P.L., Malouin, F., Richards, C.L., Evans, A.C., Doyon, J., 2002. Motor learning produces parallel dynamic functional changes during the execution and imagination of sequential foot movements. NeuroImage 16, 142–157.
MacIntosh, B.J., Mraz, R., Baker, N., Tam, F., Staines, W.R., Graham, S.J., 2004. Optimizing the experimental design for ankle dorsiflexion fMRI. NeuroImage 22, 1619–1627.
Maldjian, J.A., Laurienti, P.J., Kraft, R.A., Burdette, J.H., 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. NeuroImage 19, 1233–1239.
Maynard Jr., F.M., Bracken, M.B., Creasey, G., Ditunno Jr., J.F., Donovan, W.H., Ducker, T.B., Garber, S.L., Marino, R.J., Stover, S.L., Tator, C.H., Waters, R.L., Wilberger, J.E., Young, W., 1997. International standards for neurological and functional classification of spinal cord injury. American Spinal Injury Association. Spinal Cord 35, 266–274.
Nair, D.G., Purcott, K.L., Fuchs, A., Steinberg, F., Kelso, J.A., 2003. Cortical and cerebellar activity of the human brain during imagined and executed unimanual and bimanual action sequences: a functional MRI study. Brain Res. Cogn. Brain Res. 15, 250–260.
Naito, E., Kochiyama, T., Kitada, R., Nakamura, S., Matsumura, M., Yonekura, Y., Sadato, N., 2002. Internally simulated movement sensations during motor imagery activate cortical motor areas and the cerebellum. J. Neurosci. 22, 3683–3691.
Neugroschl, C., Denolin, V., Schuind, F., Van Holder, C., David, P., Balériaux, D., Metens, T., 2005. Functional MRI activation of somatosensory and motor cortices in a hand-grafted patient with early clinical sensorimotor recovery. Eur. Radiol. 15, 1806–1814.
Porro, C.A., Francescato, M.P., Cettolo, V., Diamond, M.E., Baraldi, P., Zuiani, C., Bazzocchi, M., di Prampero, P.E., 1996. Primary motor and sensory cortex activation during motor performance and motor imagery: a functional magnetic resonance imaging study. J. Neurosci. 16, 7688–7698.
Rowe, J., Friston, K., Frackowiak, R., Passingham, R., 2002. Attention to action: specific modulation of corticocortical interactions in humans. NeuroImage 17, 988–998.
Rushworth, M.F., Johansen-Berg, H., Gobel, S.M., Devlin, J.T., 2003. The left parietal and premotor cortices: motor attention and selection. NeuroImage 20 (Suppl 1), S89–S100.
Sabbah, P., de, S.S., Leveque, C., Gay, S., Pfefer, F., Nioche, C., Sarrazin, J.L., Barouti, H., Tadie, M., Cordoliani, Y.S., 2002. Sensorimotor cortical activity in patients with complete spinal cord injury: a functional magnetic resonance imaging study. J. Neurotrauma 19, 53–60.
Shadmehr, R., Holcomb, H.H., 1997. Neural correlates of motor memory consolidation. Science 277, 821–825.
Sirigu, A., Duhamel, J.R., Cohen, L., Pillon, B., Dubois, B., Agid, Y., 1996.

The mental representation of hand movements after parietal cortex damage. Science 273, 1564–1568.

Solodkin, A., Hlustik, P., Chen, E.E., Small, S.L., 2004. Fine modulation in network activation during motor execution and motor imagery. Cereb. Cortex 14, 1246–1255.

Stephan, K.M., Fink, G.R., Passingham, R.E., Silbersweig, D., Ceballos-Baumann, A.O., Frith, C.D., Frackowiak, R.S., 1995. Functional anatomy of the mental representation of upper extremity movements in healthy subjects. J. Neurophysiol. 73, 373–386.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage 15, 273–289.

Wolpert, D.M., Ghahramani, Z., 2000. Computational principles of movement neuroscience. Nat. Neurosci. 3, 1212–1217 (Suppl).

Wolpert, D.M., Goodbody, S.J., Husain, M., 1998. Maintaining internal representations: the role of the human superior parietal lobe. Nat. Neurosci. 1, 529–533.