Motor execution and imagination networks in post-stroke dystonia

Stéphane Lehéricy,[1,2,CA] Emmanuel Gerardin,[2,5] Jean-Baptiste Poline,[1] Sabine Meunier,[3] Pierre-Francois Van de Moortele,[1] Denis Le Bihan[1] and Marie Vidailhet[4]

[1]Service Hospitalier Frédéric Joliot, CEA, Orsay; [2]INSERM U610; [3]Service de Médecine Physique et Réadaptation, Hôpital de la Salpêtrière, Paris and [4]INSERM U289, Hôpital de la Salpêtrière; Department of Neurology, Hôpital Saint Antoine, Paris; [5]Department of Neuroradiology, CHU Rouen; France

[CA]Corresponding Author: stephane.lehericy@psl.ap-hop-paris.fr

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Reorganization of motor execution and imagination networks was studied in six patients with unilateral dystonia secondary to a subcortical stroke and compared with seven control subjects using fMRI. Patients performed imagined and real auditory-cued hand movements. Movements of the dystonic hand resulted in overactivity in bilateral motor, premotor, and prefrontal cortex, insula, precuneus, and cerebellum, in parietal areas and the striatum contralateral to the lesion. Movements of the unaffected hand resulted in overactivity in bilateral preSMA, prefrontal, and parietal areas, insula and cerebellum, the ipsilateral premotor cortex and the contralateral striatum to the lesion. Mental representation of movements with each hand resulted in overactivity in bilateral parietal, premotor and prefrontal areas. These results suggest that execution and mental representation of movement are altered in these patients. *NeuroReport* 15:1887–1890 © 2004 Lippincott Williams & Wilkins.

Key words: Dystonia; Stroke; Functional magnetic resonance imaging; Basal ganglia; Motor system

INTRODUCTION

Dystonia is characterized by involuntary sustained muscle contractions causing prolonged twisting and repetitive movements or abnormal postures of the affected body part(s) [1]. Secondary post-stroke dystonia are attributed to lesions of the basal ganglia, the thalamus, and the mesencephalon [2]. Previous PET activation studies have shown overactivity in lateral premotor (PM) and prefrontal (PF) areas in patients with primary dystonia during movement execution whereas activity in the primary motor cortex (MC) and caudal supplementary motor area (SMA) was lowered [3,4]. There is only one report of patients with secondary dystonia, which showed overactivity in PM and PF areas, similarly to patients with primary dystonia and also overactivity in the MC. In primary dystonia, cortical activation pattern associated with imagination of movement was not altered [5], suggesting that motor networks are altered only during movement execution.

In this study, patients with unilateral dystonia secondary to a stroke in the basal ganglia and the thalamus were examined during execution and mental representation of hand movements.

SUBJECTS AND METHODS

Subjects: Six patients with unilateral dystonia secondary to a well-defined infarct in the striato-pallidal complex or the thalamus were studied at 3 T (Table 1). Patients were compared with 7 age-matched right-handed healthy volunteers (three males and four females, mean age 38.7 ± 17.9 years, range 20–70) with no history of neurological or psychiatric disease. They gave informed consent. The local Ethics Committee approved the experiment.

Tasks: Subjects performed the following tasks paced at 0.5 Hz by an auditory stimulus. First, execution of a simple (simultaneous flexion/extension of the fingers) or complex movement (selective flexion/extension of the index and the little finger). Second, imagination of the same hand movements. Third, rest, when subjects were asked to stay motionless and relax. Subjects were trained for about 30 min before scanning until they were capable of performing the task. Patients were videotaped and assessed clinically. Each condition was randomized across 8 runs. Resting period alternated with each of the experimental conditions. Four runs composed of 12 epochs of 20 s were performed with each hand. Task switching instructions were presented orally. The ability of each subject to perform mental imagery was assessed by means of a motor imagery questionnaire. Good imagery abilities scored 8–32 and poor imagery abilities scored 33–56. Control subjects had good imagery abilities (visual imagery (mean ± s.d.) 15 ± 8.3, range 8–29; kinesthetic imagery 13.9 ± 5.1, range 8–22).

Functional imaging: Twenty-four 5 mm axial slices were obtained with a gradient echo EPI sequence, using BOLD

Table I. Clinical features of the patients.

Patient/sex/handedness	1/F/R	2/F/R	3/M/R	4/F/L	5/M/R	6/F/R
Age at onset of stroke	23	26	28	21	42	52
Initial signs	L hemiparesia, hemianesthesia	L hemiparesia, hemianesthesia	L hemiparesia, dysarthria	L hemiparesia, hemianesthesia	L hemiparesia, hemianesthesia	L hemiparesia, hemianesthesia
Delay of improvement	1 year	8 months	6–8 months	<2 hours	2 years	2 months
Delay of AIM onset	15 years	4 years	1 year	<6 months	2 years	1 year
Duration of AIM	19 years	5 years	4 years	14 years	15 years	4 years
Dystonia	pronation of arm, flexion arm and fingers	flexion of toes, extension of big toe and fifth finger	writer's cramp micrographia, slowness	extension of arm and forearm, claw-like flexion of the fingers	flexion of the fingers, "main creuse"	extension of the fingers
Other signs	arm hypoesthesia	absent	absent	R pyramidal syndrome	hemianesthesia, hyperpathia, pseudo-athétoid movements	hemianesthesia, mild cerebellar syndrome, 4 Hz*, rare myoclonus
Topography of lesion	R lent. nucleus	R lent. nucleus	R lent. nucleus	R lent. nucleus	R post-lat thalamus	R thalamus
Cause of the stroke	multiple arteries thrombosis	cardiac embolism	cardiac embolism	unknown	heamatoma	unknown

lent., lenticular; F, female; L, left; M, male; R, right; *rest, postural and action tremor.

contrast (TR/TE/flip angle=5000 ms/40 ms/90°, matrix 64×64, field of view $220 \times 220\,mm^2$). Fifty-two brain volumes were acquired for each run. The first four volumes of each run were discarded to reach signal equilibrium. Three-dimensional T1-weighted anatomical images were also acquired.

Statistical analysis: Data analysis was performed with SPM 99 (Wellcome Department of Cognitive Neurology, London). Images were normalized (MNI template) such that all lesions were right-sided, using a method previously described in lesioned brain [6]. In normalized images, the Talairach coordinates of the primary motor hand area, calculated at mid-distance along the supero-inferior and transverse axis in normalized brains did not differ between patients and controls (patients: left hemisphere -37 ± 4, -27 ± 1, 55 ± 2; right 36 ± 3, -26 ± 2, 54 ± 2; controls: left -38 ± 3, -25 ± 3, 56 ± 2; right 37 ± 5, -26 ± 3, 56 ± 2, $p > 0.05$). Functional scans were corrected for subject motion and smoothed with a Gaussian spatial filter to a final smoothness of 10 mm. Data from each run were modeled using the general linear model. Analyses were performed using random effect analysis. Z maps were first thresholded at $p < 0.01$. In these maps, activated clusters were considered significant at $p < 0.05$, corrected for multiple comparison.

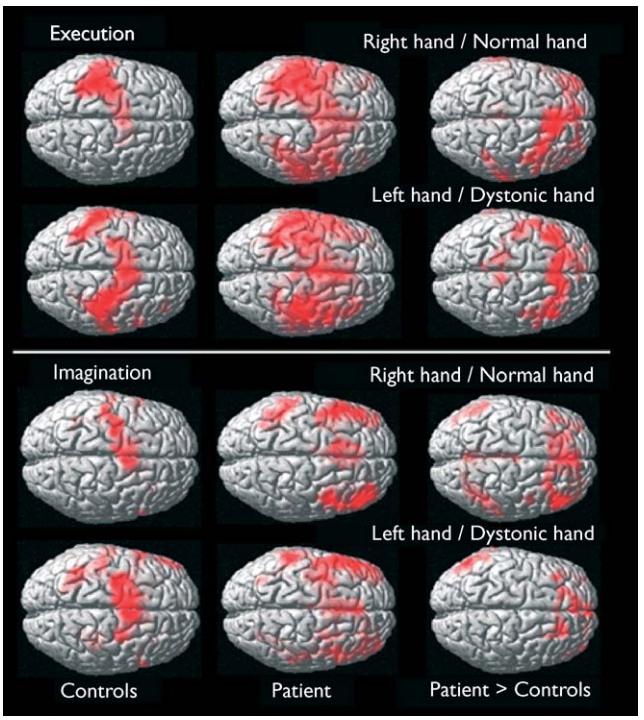

Fig. 1. Activation maps. Areas activated in controls (left column) and patients (middle column) during movement execution (execution compared with rest), and imagination (imagination compared with rest) for each hand. Right column: Areas more activated in patients than in controls for the same contrasts. Activated clusters are displayed on a three dimensional template viewed from above ($p < 0.05$ corrected for multiple comparison).

RESULTS

Motor performances: Motor performances of the patients were slow on the dystonic side, mainly for complex movements with slow flexion/extension of the index and the little finger and more tonic flexion of the third and forth fingers. Some degree of dystonic posture persisted in addition to the voluntary movement but did not alter the voluntary movement. Movements were limited to the hand without overflow to forearm muscles or contralateral limb. Movements were normal on the non-affected side without diffusion of synkinesias on the dystonic side. All patients were capable of performing the movements without errors at the slow frequency of 0.5 Hz after the training period. As for control subjects, no visible movement was detected in patients during the imagination periods. All six patients had good imagery abilities, comprised within control range (visual imagery=16.7 ± 8.1, range 8–24; kinesthetic imagery=19.7 ± 4.6, range 17–25, $p > 0.05$).

Within-group comparison (Fig. 1): In control subjects, for each hand, activation during movement execution

Table 2. Talairach coordinates of cluster maxima more activated in patients than in control subjects for the contrasts Execution compared with rest in patients *vs* execution compared with rest in control subjects (Execution) and Imagination compared with rest in patients versus imagination compared with rest in control subjects (Imagination).

Patients > Controls		Execution								Imagination							
		Right hand				Left hand				Right hand				Left hand			
Anatomic Areas (Brodmann area)	Hemisphere	X	Y	Z	Tscore	X	Y	Z	Tscore	X	Y	Z	Tscore	X	Y	Z	Tscore
Frontal cortex																	
Primary sensorimotor area BA4	R					9	−30	72	7.38								
	L					−45	−15	54	4.12								
PM BA6	R	30	18	60	4.65	45	−3	51	5.11	45	3	48	4.89				
	L					−54	3	42	4.07								
pre SMA	R	12	30	51	5.07	9	21	60	5.34	6	33	51	4.90				
	L	−12	27	39	2.99	−12	30	54	4.94					−9	30	57	3.69
SMA	R									0	−15	60	4.57				
BA8	R	21	54	42	3.88	33	24	42	3.87	27	18	45	4.92	27	33	42	3.92
	L	−36	42	42	3.41	−39	24	48	6.87					−39	27	48	3.55
BA9/46	R	54	9	36	4.13	45	21	39	4.46	48	36	18	7.46				
	L	−54	42	24	3.14	−39	18	33	3.78	−51	24	42	4.97				
BA10	R	39	60	18	3.33					36	54	21	3.53	24	57	6	3.2
	L	−42	51	15	3.71	−24	57	12	3.29	−36	45	18	4.10	−33	54	0	4.56
BA45/47	R	51	24	−3	3.61					39	30	−12	4.69				
	L	−48	24	0	5.60	−51	12	−3	4.36	−50	21	−12	3.9				
Medial prefrontal	R									6	51	36	5.45	3	51	42	4.14
	L	−12	51	12	3.67									−12	48	42	4.23
Orbitomedial frontal cortex	R	9	39	−6	2.94					12	42	−15	3.57	33	39	−15	4.09
	L	−15	36	−6	3.58									−18	42	−15	3.66
Anterior cingulate cortex	R					3	27	36	3.64								
Parietal cortex																	
Secondary sensory area (SII)	R	54	−39	30	3.41												
	L	−57	−21	15	4.17	−47	−27	15	4.58								
Inferior parietal area. BA39/40	R	42	−45	57	3.78					36	−66	39	6.28				
	L	−42	−63	30	4.77	−42	−63	39	4.76	−57	−45	33	4.14	−48	−63	30	5.59
Posterior cingulate gyrus	R	9	−48	27	3.29												
	L	−9	−27	42	4.26					−3	−30	36	4.02				
Precuneus						0	−72	60	3.50	3	−63	48	5.31				
Other cortical areas																	
Posterior temporal	L	−72	−33	0	4.21	−66	−45	6	4.72					−66	−45	3	3.38
Anterior temporal lobe	R													39	18	−27	3.19
	L													−45	0	−21	4.54
Insula	R	33	15	3	4.86	33	21	−12	4.09								
	L	−33	21	9	3.37	−45	21	0	3.82					−33	−21	−12	3.29
Subcortical areas																	
Caudate nucleus	L	−21	12	21	3.50	−18	24	3	3.95								
Putamen	L	−18	21	3	3.34	−21	9	15	3.81								
Cerebellum	R	12	−72	−27	3.44	12	−78	−21	4.49								
	L	−15	−69	−27	3.47	−15	−75	−21	4.28								

BA, Brodmann area; L, left; R, right; SMA, supplementary motor area. Activated clusters were significant at $p < 0.05$ corrected for multiple comparisons. Left hand is the dystonic hand.

compared with rest was found in the sensorimotor cortex (SMC), secondary sensory areas (SII) and inferior parietal areas, medial and lateral PM cortex, putamen, thalamus, and cerebellum. Activation predominated in the hemisphere contralateral to the moving hand. During movement imagination, activation was observed in similar areas with less SMC and more PF cortex activation. There was no difference between complex and simple movements.

Compared with control subjects, prefrontal and parietal activation during movement execution was larger in patients, involving bilateral associative areas. The anterior putamen and the thalamus were activated during both hand movements. Activation was absent in the right posterior putamen (lesion location). Compared with control subjects, activation during movement imagination compared with rest was larger in the frontal and parietal lobes, and the caudate nuclei.

Between-group comparison (Table 2, Fig. 1): When execution was compared with rest in patients and in control subjects, no area was more activated in control subjects for either hand. Using the unaffected (right) hand, patients activated more bilateral preSMA, PF cortex, SII and inferior parietal areas, posterior cingulate cortex, insula and cerebellum, the right PM cortex, and the left striatum and posterior temporal lobe. Using the dystonic (left) hand, patients activated more bilateral MC, PM, preSMA, and PF cortex, anterior insula, precuneus, and cerebellum, the left SII, inferior parietal areas, posterior temporal lobe, anterior striatum, and the right anterior cingulate cortex.

When comparing imagination with rest in patients and in control subjects, no area was more activated in control subjects for both hands. Using the unaffected (right) hand, patients activated more the right PM, preSMA and SMA,

BA8, and medial orbitofrontal cortex, the left posterior cingulate gyrus, and bilateral PF cortex, inferior parietal cortex and precuneus. Using the dystonic (left) hand, patients activated more the left preSMA, inferior parietal cortex and insula, and bilateral PF cortex, orbitomedial frontal cortex and temporal lobes.

DISCUSSION

During movement execution, there was a relative increase in motor, premotor, and prefrontal activity in patients and no areas of decreased activity. Overactivity in PM and PF areas was in line with previous studies in patients with unilateral symptomatic dystonia [7] and primary dystonia [3,8], and may thus be a common feature of both types of dystonia. Several explanations have been proposed to explain this increased frontal activity, including abnormal basal ganglia outflow [3,7], increased mental effort necessary for patients to perform the movements or to suppress abnormal muscular contractions, or a deficit of intracortical inhibition evidenced in patients with primary dystonia [9].

In contrast, patients with primary dystonia usually presented underactivity in the SMC [3,4,10,11], and thus SMC overactivity found in the present study may be a characteristic of post-stroke dystonia [7]. Alternatively, SMC overactivity may be associated with the performance of dystonic movements during scanning irrespective of the origin of dystonia [7,12]. Altered functioning of the cerebellum is in agreement with previous imaging reports in patients after stroke [7] and in those with primary dystonia [13].

Frontal overactivity was also reported in previous studies of post-stroke patients who recovered without dystonic posture [14], suggesting that enhanced frontal activity may be part of the normal recovery process and may not be specific to dystonia. Thus, abnormal neuronal mechanisms resulting in dystonia may be more complex than under or overactivity. Other abnormalities have been reported in patients with primary dystonia, including altered firing pattern, reduced selectivity of sensorimotor neurons and altered processing of peripheral sensory inputs in the GPi [15], and altered finger representation in S1 [16]. Similar aberrant plastic changes may develop over time in post-stroke patients resulting in dystonic recovery of the paretic limb.

In the present study, altered activation was observed in parietal and premotor areas during movement imagination. Both areas have been associated with mental representation of movement [17]. Post-stroke dystonic patients presented clinical and functional signs of parietal dysfunction (Table 1). Parietal dysfunction in these patients may represent the substrate of altered mental representation of movement and may contribute to the abnormal processing of sensory inputs reported in these patients [18]. Lastly, frontal overactivity during movement imagination can not be related to increased mental effort necessary to perform the movements as no movement was performed.

CONCLUSIONS

This study suggests that both execution and mental representation of movement are altered in patients with post-stroke dystonia.

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