

Brain Cortical Activation during Guitar-Induced Hand Dystonia Studied by Functional MRI

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Focal hand dystonia in musicians is a strongly task-related movement disorder. Typically, symptoms become apparent only when players execute specific overpracticed skilled exercises on their instrument. We therefore examined five guitarists with functional MRI during dystonic symptom provocation by means of an adapted guitar inside the magnet. The activation patterns obtained in comparable nondystonic guitarists and in the study patients when performing normal-hand exercise served as references. A 1.5-T system equipped with echo-speed gradients and single-shot echoplanar imaging software was used. Data acquisition was centered on the cortical motor system encompassed in eight contiguous slices. Dystonic musicians compared with both control situations showed a significantly larger activation of the contralateral primary sensorimotor cortex that contrasted with a conspicuous bilateral underactivation of premotor areas. Our results coincide with studies of other dystonia types in that they show an abnormal recruitment of cortical areas involved in the control of voluntary movement. However, they do suggest that the primary sensorimotor cortex, rather than being underactive in idiopathic dystonic patients, may be overactive when tested during full expression of the task-induced movement disorder. © 2000 Academic Press

INTRODUCTION

Focal hand dystonia is often associated with occupational activities requiring repetitive hand movements (Chen and Hallett, 1998). Professional musicians are at risk to develop this type of motor disorder involving loss of control in individual finger movements and leading, not infrequently, to professional disability. Guitarists may develop dystonia either in their left hand, affecting rapid forceful finger posturing, or in their right hand, interfering with fine alternating finger

movements (Elbert *et al.*, 1998; Wilson *et al.*, 1993; Lederman, 1994; Bejjani *et al.*, 1996; Jankovic and Shale, 1989; Hochberg *et al.*, 1983).

Although the association with specific activities is clear, the pathophysiology of focal hand dystonia is only partially understood. The principal characteristic of dystonic movement is the overflow of motor output that produces an intense, extensive, and prolonged muscular activity (Cohen and Hallett, 1988; Berardelli *et al.*, 1998). Deficient inhibition is a basic underlying defect in dystonia occurring at different levels of the nervous system (Rothwell *et al.*, 1988; Valls-Solé and Hallett, 1995), including the cortex, which is particularly hyperexcitable (Berardelli *et al.*, 1998; Hallett, 1998a; Bressman, 1998). Nevertheless, not all the altered cortical responses are exacerbated in dystonic patients. Functional imaging studies have shown both overactivity and underactivity, depending on the dystonia type assessed, the anatomical region studied, and the testing condition adopted (Tempel and Perlmuter, 1993; Feiwell *et al.*, 1999; Eidelberg *et al.*, 1998; Ceballos-Baumann *et al.*, 1995a,b, 1997; Playford *et al.*, 1998; Ibañez *et al.*, 1996, 1999; Obergren *et al.*, 1998). Although imaging data coincide in demonstrating an abnormal cortical activation in dystonia, they rarely provide direct evidence of the primary motor output overflow suggested by electrophysiological research (Berardelli *et al.*, 1998).

To further explore the cortical function disturbances occurring in different dystonic processes, a tailored assessment of patients in the dystonia-inducing situation could be useful, particularly in musicians whose disorder may be extremely task-specific. A pianist showing, for example, a dystonic extension of the third finger while playing trills may well show proper coordination when carrying out the same alternating movement on a computer keyboard. There is a conspicuous lack of functional imaging data obtained from musicians during instrument-induced focal dystonia.

TABLE 1
Clinical Characteristics of Guitarists with Hand Dystonia

Pt	Sex	Age (yr)	Years of practice	Dystonic hand	Specific complaint	Testing exercise
1	M	27	10	Left	Dystonic extension of finger 3 in forced flexion of the other fingers	Chromatic scale
2	M	46	22	Right	Unable to control flexion of finger 3	Arpeggio (fingers 1, 2, and 3)
3	F	24	12	Right	Finger tremor in attempts to flex fingers 3 and 4	Arpeggio (fingers 1, 2, 3, and 4)
4	M	50	40	Right	Unable to control flexion of finger 2	Arpeggio (fingers 1, 4, 3, and 2)
5	M	33	22	Left	Dystonic impediment to flexion of fingers 4 and 5	Chromatic scale

We conducted a functional MRI (fMRI) study aimed at assessing guitarists with occupational hand dystonia during their guitar-induced specific motor alteration. A guitar was adapted to the magnetic environment and spatial constraints of the MRI system and the musicians were specially trained to play the specific dystonia-inducing exercises inside the magnet. Our functional assessment was focused on the cortical motor system, using an echoplanar eight-slice acquisition method.

MATERIALS AND METHODS

Subjects

We studied five guitarists with focal, task-specific hand dystonia. In all cases, the only neurological alteration involved a single-hand guitar-induced movement disorder that met the criteria proposed by Wilson *et al.* (1993) to define musicians' occupational cramp. In each case, symptoms were sufficiently severe to interrupt the subject's professional career. All five guitarists were right-handed as determined by The Edinburgh Inventory of handedness (Oldfield, 1971). Neurological symptoms involved left hand in two cases and right hand in the remaining three. Table 1 specifies gender, age, instrument experience, and the specific movement complaint. Characteristically in our patients, left-hand dystonia was associated with an evident involuntary extension of one or more fingers in attempts to fret the strings during scale exercises. Right-hand dystonia involved uncontrolled flexion of individual fingers that disrupted the rapid succession required for plucking during arpeggio exercises.

In each patient a personal and family medical history was recorded and they all underwent a comprehensive clinical and neurological evaluation to rule out other causes of dystonia. Routine electrophysiological studies of the peripheral nervous system, cranial computed tomography, standard cranial and cervical MRI, and blood levels of uric acid, copper, and ceruloplasmin were within normal limits in each case.

Three additional guitarists served as control subjects in this study. They were all right-handed men of ages

within the range of studied patients (37, 37, and 33 years) and with comparable experience (21, 30, and 21 years of practice). Each of the three subjects carried out both left-hand (scale) and right-hand (arpeggio) exercises. Thus, a total of six reference fMRI studies were used to control the five patients assessed. Written informed consent was obtained from all participating musicians and the study was approved by the Institutional Review Boards.

Tasks and Testing Procedures

All the tasks involved the use of a specially built musical instrument. A six-string classical guitar neck was constructed by a professional guitar-maker using nonferromagnetic material and reproducing real guitar dimensions, texture, and string tension. The guitar's body was not included due to space constraints inside the magnet.

The test was based on the performance of a guitar exercise capable of reproducing the patient's dystonia. In each case, the task involved unilateral repetitive self-paced sequences of hand movements. In the two patients with left-hand dystonia, the adopted guitar exercise was the left-hand finger movement sequence that is used to play a chromatic scale. This task requires forced finger flexion with a rapid change of the finger flexion pattern. The three patients with right-hand dystonia were required to execute with their right hand the particular arpeggio exercise that most consistently induced the dystonic disorder (see Table 1). Guitar arpeggios involve the rapid succession of fine and notably isolated finger movements. Single scale and arpeggio sequences were successively repeated during testing with no external cues.

Each patient was instructed to invest motivation, precise muscle tension, and the specific timing features that maximally engaged the abnormal movement while sustaining the abnormal condition for the entire 30-s testing periods. A prolonged training session outside the MRI system was completed to ensure that the task would be performed with these requirements. Subsequently, patients were trained inside the scanner, where they were specifically instructed to avoid

head movement during fMRI acquisitions. Two soft holders allowed us to fix each subject's head with minimal comfort reduction (Pujol *et al.*, 1998).

Additionally, patients were required to carry out the dystonia-inducing task using their normal hand. In this case, patients were instructed to perform the repetitive scales or arpeggios at a rate similar to that of the functionally altered hand. As the execution of arpeggios with the left hand and scales with the right hand are not usual exercises for a guitarist, all patients rehearsed these tasks for at least 2 h. Therefore, this control condition was a fully learned complex task to compare with the overlearned task that produced focal hand dystonia.

Control musicians performed both the chromatic scale with the left hand and a particular arpeggio (fingers 1, 2, 3, and 4) with the right hand to complete the total of six control studies. Instructions and training in these subjects were identical to those of patients, except the search for dystonia-engaging strategies, which was not applicable.

Functional MRI

The fMRI examination was carried out using a 1.5-T Signa system (GE Medical Systems, Milwaukee, WI) equipped with echo-speed gradients and single-shot echoplanar imaging software. The functional sequence consisted of gradient recalled acquisition in the steady state (TR 3000 ms, TE 50 ms, pulse angle 90°) with a 96×64 -pixel matrix (interpolated to 128×128 pixels when reconstructed), within a field of view of 24 cm, with a section thickness of 5 mm and an interslice space of 2 mm. Eight interleaved slices, parallel to the anterior–posterior commissure line, were obtained for each functional sequence to cover the upper cortical motor system from the brain vertex to the frontal operculum. The functional time series consisted of 60 consecutive images acquired in 3 min, in which 30-s periods of rest and activation were alternated using an ABABAB epoch succession.

Functional sequences were analyzed using an auxiliary workstation (SPARCstation 20; Sun Microsystems, Mountain View, CA) and specific image analysis software (FuncTool; GE Medical Systems, Buc, France). Statistical parametric maps were obtained using Student's *t* statistics and adopting previously described procedures (Pujol *et al.*, 1998, 1999). Activation images were displayed in pseudocolor, scaled according to significance, and superimposed on corresponding anatomical images.

The activation threshold was empirically assessed as in a previous report (Pujol *et al.*, 1999) performing a new experiment adapted to the current fMRI technique. A total of 100 stimulus-lacking (identical procedures, but with no task) four-slice functional sequences were acquired in control subjects. Prior to image anal-

ysis, head motion was finely detected in each image series by using a cine display method. The largest head displacement was identified and then measured in millimeters. Series showing head displacements of 1.5 mm or over were rejected and replaced by additionally acquired sequences. The analysis of the finally resulting 400 functional (*t* test) images produced, within the brain contour, only eight (2%) clusters greater than 4 pixels ($3.75 \times 3.75 \text{ mm}^2$) below the *P* value of 0.0001. Thus, by considering functional changes above this cluster size at this significance level, the probability of including task-unrelated activations is low. An activation threshold reference is provided in Fig. 1A.

This simple method is able to control the main sources of false positive results in fMRI studies (McCarthy *et al.*, 1996), as is the case with statistically probable activations, head motion (displacements beyond 1.5 mm in our study) and physiological noise (e.g., arterial brain pulsation or respiration changes unrelated to task). Inspection of the eight image series that produced functional changes above the established threshold revealed that the changes corresponded to signal oscillations unrelated to motion and suggested a coupling with physiological events in motor and visual areas. Therefore, pseudoactivations existed, but the risk of their occurrence was empirically measured.

Activation Analysis

Each subject performed the assigned tasks twice. The first trial was the main fMRI assessment, while the second trial served as a reserve. Sequences were checked for head motion before study analysis. They were rejected when head displacement exceeded 1.5 mm and were replaced by reserve functional trials. A trial replacement was necessary in 5 of the 20 sequences acquired in dystonic musicians and in 2 of the 12 sequences acquired in control musicians.

fMRI results are presented as the description of the activation patterns obtained in reference musicians and in dystonic patients, by considering only the brain regions that show activations consistent across subjects. The number of activated pixels in specific brain regions was registered and the activation area was calculated in square millimeters. Additionally, the brain area was measured in each slice and a global score was computed in each subject using the sum of all the measurements. The "superior premotor cortex" was defined as the brain region that surrounds the caudal half of the superior frontal sulcus and the precentral sulcus at this level. The posterior supplementary motor area (supplementary motor area proper) was the region medial to this superior premotor cortex at both sides of the interhemispheric fissure. Functional changes around the central sulcus represented primary sensorimotor cortex activation.

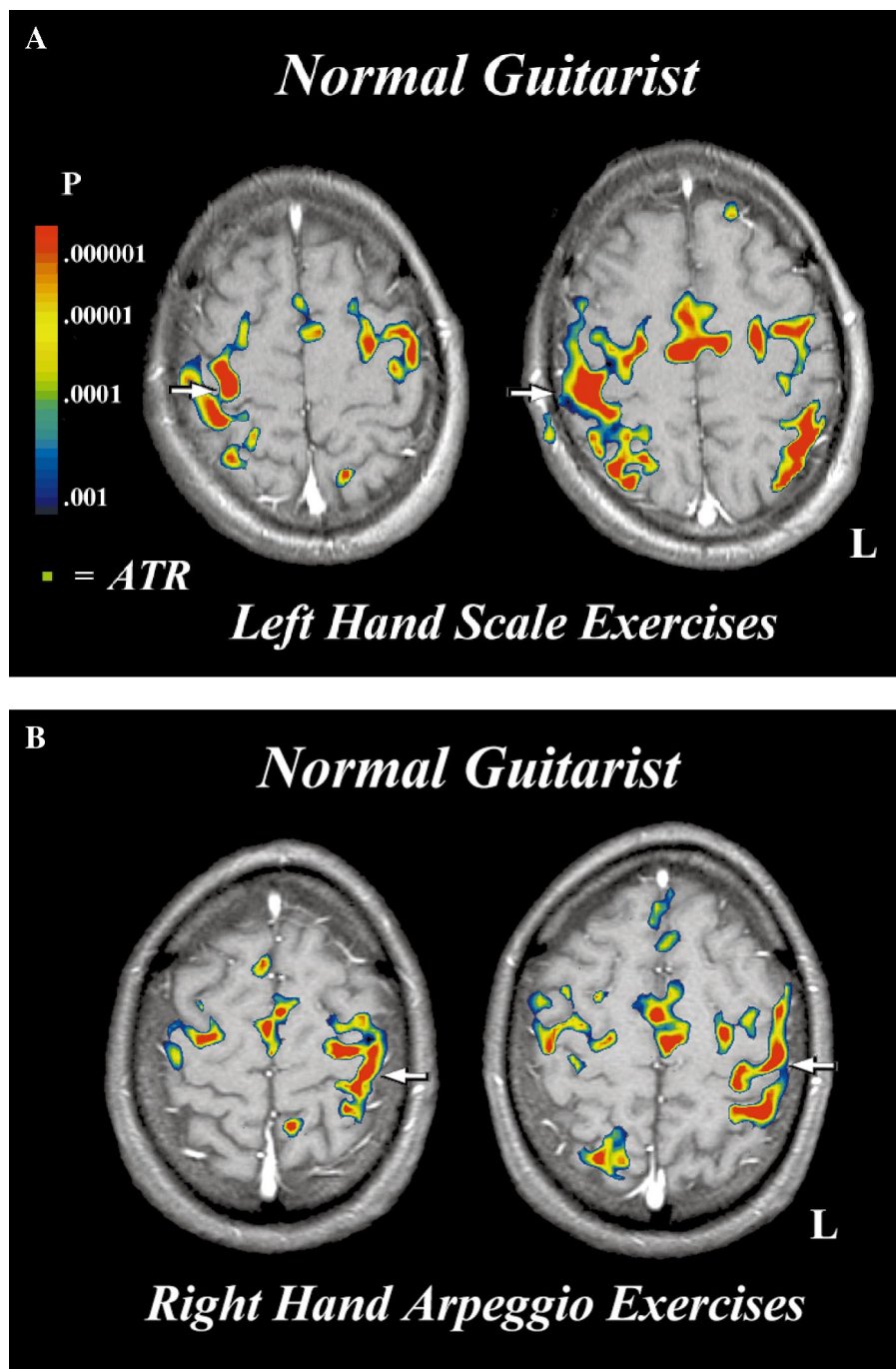


FIG. 1. The normal activation pattern observed in control guitarists during left-hand scale (A) and right-hand arpeggio (B) exercises. Two continuous slices (superior to inferior) centered at the upper cortical motor system are provided in each case. Both tasks consistently activated the contralateral primary sensorimotor cortex (arrows), the supplementary motor area and bilateral premotor and parietal regions. A reference color scale of t image P values is provided (A). ATR denotes the activation threshold reference ($3.75 \times 3.75 \text{ mm}^2$ pixel cluster at 0.0001 P value). L indicates left hemisphere in all figures.

In the Talairach and Tournoux (1988) reference atlas, the considered premotor and supplementary motor regions are located at the z level +45 to +65 mm, which involves three slices in our study. The superior

premotor region in each hemisphere has a maximum length of 30 mm in axis x and 25 mm in axis y and the supplementary motor area a maximum x of 15 mm and y of 25 mm. The right and left primary sensorimotor

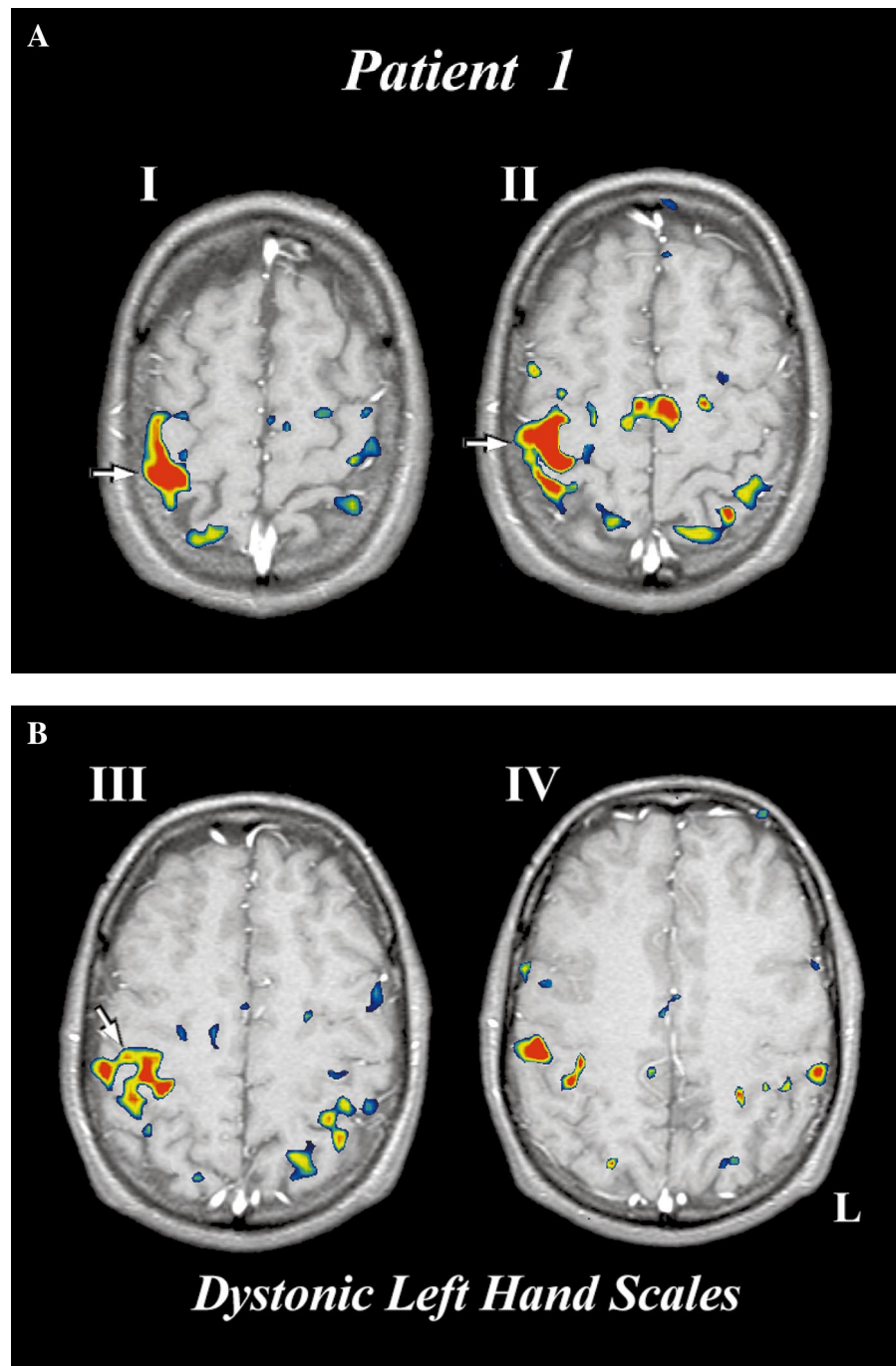


FIG. 2. fMRI images obtained in patient 1 during left-hand scale exercises illustrating the activation pattern of guitarists' focal hand dystonia in our study. Outstanding changes in the primary sensorimotor cortex (arrows) contrast with a notably poor premotor activation in these four continuous superior-to-inferior slices (I to IV) that encompass the cortical hand motor system. Significant activity was additionally found in the posterior supplementary motor area and the parietal lobe.

cortex regions considered extend from +40 to +65 mm in axis z (four slices) and do not exceed 30 mm in axis x and 25 mm in axis y.

A "premotor-to-sensorimotor ratio" resulted from dividing the number of activated pixels obtained in the

superior premotor cortex region bilaterally by the pixel count in contralateral primary sensorimotor cortex. Similarly, a "supplementary motor-to-sensorimotor ratio" was obtained by dividing the activated pixels in the supplementary motor area by those obtained in primary

sensorimotor cortex. All the measurements were performed by a single researcher, blind to all subjects' data.

Univariate analysis of variance (ANOVA) was used to compare activation areas and ratios between dystonic and reference musicians. To control the possible effect of brain size on between-group differences, this analysis was also performed using brain area (global score) as a covariate in the case of direct (nonnormalized by ratios) activation areas. Repeated-measure ANOVA was used in comparisons between the dystonic and the nondystonic trials in patients. Two-tailed *P* values are provided in each case and the level of significance was set at $P < 0.05$.

RESULTS

Task Performance

Task performance speed was similar in control and dystonic musicians, although accuracy was substantially lower in patients. This was a direct consequence of task instructions, as patients were required to perform the exercises with the usual playing speed to fully engage the specific dystonic posturing. In all patients and control subjects the average time for scale sequences (including both ascending and descending phases) was within the range of 2.5 to 3.5 s and for arpeggios within 1 to 2 s.

After image acquisition, all patients reported having successfully reproduced their specific alteration. Objectively, during scanning, patient 1 showed a constant dystonic extension of finger left 3 when he flexed the other fingers in the chromatic scales. Similarly, patient 5's disturbances when fretting the string with fingers left 4 or 5 were obvious and involved defective pressure or inaccurate finger position in 55% of scale sequences.

During arpeggios, patient 2's failure to reach the corresponding string with finger right 3 due to excessive finger flexion was observed in 30% of performed movement sequences. In patient 3, a slight but continuous tremor of fingers right 3 and 4 was observed in each fMRI activation period. In patient 4, abnormal flexion of finger right 2 was milder and could not be objectively verified during scanning, as the patient's specific alteration was only evident during audible playing.

Functional MRI Activation Results

In the normal reference guitarists, left-hand scales and right-hand arpeggios practiced inside the scanner produced a consistent fMRI pattern, which was notably homogeneous across both tasks and subjects. In each scale and arpeggio trial, contralateral activation of the primary sensorimotor cortex and bilateral activation of the superior premotor cortex, the supplementary motor area, and the posterior parietal lobe were observed

(Fig. 1). Functional changes in the inferior premotor cortex (at the inferior frontal sulcus level) and the opercular-insular region were also detected, although activation in these regions was less evident and was not invariably present (occurring in only three of six and four of six trials, respectively).

In the dystonic musicians during dystonia-inducing guitar exercises, a notably different pattern of brain cortical activation was obtained (Figs. 2, 3, and 4). Activation of the primary sensorimotor cortex was the outstanding finding in each case in both left-hand scales and right-hand arpeggios, mostly due to a marked decrease of the activation in premotor areas, but also as a result of a net increase in primary sensorimotor cortex. Mean $\pm$ SD activation area in the defined premotor region was $850 \pm 192 \text{ mm}^2$ in control subjects and $377 \pm 198 \text{ mm}^2$ in patients ($F = 16.1$; $P = 0.003$), while mean activation area in the primary sensorimotor cortex was $488 \pm 201 \text{ mm}^2$ in controls and $765 \pm 150 \text{ mm}^2$ in patients ($F = 6.4$; $P = 0.032$). Comparable results were obtained after adjusting for the effect of brain area ($F = 12.0$, $P = 0.009$ in the case of the premotor region and $F = 7.7$, $P = 0.024$ in the case of the primary cortex).

The premotor-to-sensorimotor activation ratio numerically summarizes this main study finding. In control musicians, this ratio was 1.9 ± 0.5 , whereas in dystonic musicians it was 0.5 ± 0.3 . Group differences were significant at ($F = 29.4$; $P < 0.001$). However, despite the significance of the overall differences, the amount of premotor activation varied across dystonic musicians (see figures). Premotor cortex activation was relevant in patients 4 and 5. The former was the patient with the mildest clinical alteration, while the latter presented a more severe movement disorder. In general, we were unable to find a clear association between the clinical severity of the dystonia and the fMRI alterations observed.

The extent of the supplementary motor area activation produced during the guitar-induced dystonic movements was also variable. Three of the five patients showed changes above our activation threshold, whereas the remaining two did not. Group differences were less evident than in the case of premotor cortex activation. Mean activation area in this region was $421 \pm 260 \text{ mm}^2$ in control subjects and $198 \pm 139 \text{ mm}^2$ in dystonic patients ($F = 2.9$ and $P = 0.121$ in direct comparison and $F = 0.9$ and $P = 0.381$ after adjusting for brain area). The supplementary motor-to-sensorimotor ratio was 0.8 ± 0.4 in controls and 0.3 ± 0.2 in patients ($F = 6.7$; $P = 0.029$).

As in the normal guitarists, guitar exercises in the dystonic patients produced activity behind the postcentral sulcus in the parietal lobe. In addition, task-related functional changes were also observed at inferior brain levels (inferior premotor cortex and opercular-

insular region) in patients. Again, we failed to find consistent results in these brain regions.

Abnormal versus Normal Hand Comparison in Dystonic Musicians

Scales and arpeggios executed with the patient's normal hand produced an activation pattern close to that observed in control musicians, showing an evident premotor and supplementary motor activation. Thus, premotor-to-sensorimotor activation ratio in nondystonic hand exercises in dystonic musicians was also significantly larger than during guitar-induced dystonia (1.7 ± 0.3 versus 0.5 ± 0.3 ; $F = 30.3$; $P = 0.005$). In the case of supplementary motor-to-sensorimotor ratio, however, the differences (0.5 ± 0.1 versus 0.3 ± 0.2) did not reach a significant level ($F = 3.0$; $P = 0.158$). Figure 4 shows fMRI comparative results of dystonic versus normal hand in two examples. These subjects were the patients showing the largest premotor activation during dystonia. Note that nondystonic movements, even in these cases, produced more premotor activation.

DISCUSSION

This study was aimed at reproducing task-specific hand dystonia during fMRI acquisition in our patients. Guitarists used a real guitar neck inside the scanner and a tailored guitar exercise that specifically triggered the abnormal hand movement. Sufficient rehearsal was allowed to ensure that each patient's problem would appear during testing and fMRI was obtained only in this situation. Therefore, the cortical activation pattern described is a direct expression of the brain function disturbances that underlie our professional guitarists' specific movement disorders.

Increased primary sensorimotor cortex activation contralateral to the dystonic hand was a consistent finding in dystonia-producing left-hand scale and right-hand arpeggio exercises. However, premotor activation was notably reduced with respect to reference musicians and to the normal hand trials in each patient. Therefore, a shift from premotor to primary sensorimotor activation was detected in the guitarists engaged in their specific motor disorder. In other words, the complex hand movements necessary to produce scales and arpeggios normally involve widespread bilateral cortical regions, even in expert professional musicians such as those who acted as controls in this study. Nonetheless, the dystonic execution of the same movements was associated with a more focal activation around the central sulcus, thus suggesting an abnormal recruitment of the cortical areas involved in motor control.

A similar conclusion of impaired cortical activation was drawn by Ceballos-Baumann *et al.* (1995a), although these authors demonstrated a pattern that was

the reverse of our findings. Indeed, they found overactivity of the premotor and prefrontal regions and a defective activation of the primary sensorimotor cortex during arm movement in idiopathic torsion dystonia. At first glance, it seems that our results do not harmonize with consolidated PET data (Ceballos-Baumann *et al.*, 1995a; Playford *et al.*, 1998). Nevertheless, in our opinion these opposed brain activation patterns refer to the same cortical functional alteration studied during a different testing condition.

In early PET studies, the testing stimulus was a motor task involving paced joystick movements in freely chosen directions with the right hand (Ceballos-Baumann *et al.*, 1995a,b; Playford *et al.*, 1998). Movement performance was only mildly altered in this condition, in which the patient's goal was the successful achievement of the required movement. Successful strategies here were those attempting to avoid any engagement of dystonic-related motor patterns. It is a possibility that the poor primary sensorimotor cortex activation in the studies of Ceballos-Baumann *et al.* was a consequence of the patients' strategy used to circumvent dystonia, in which overactivity of premotor and prefrontal regions represents a conscious attempt to try and suppress the unwanted movements (Brooks, 1995). Our study did not favor conscious strategies to avoid dystonia. Thus, the results of both studies may be interpreted as revealing primary sensorimotor cortex functional alteration. PET findings may express abnormally poor use of the primary areas and our fMRI results may reflect a task-interfering overactivation.

In another PET study from the same research group (Ceballos-Baumann *et al.*, 1997), paced stereotyped writing of a word was used as a task. This task produced mild dystonic posturing during scanning. In this case, defective primary motor cortex activation was again demonstrated. Nevertheless, primary sensory cortex activation was enhanced instead of reduced and overactivity of premotor and prefrontal areas was less conspicuous than in the studies using freely selected joystick movements as a paradigm. Moreover, Ibañez *et al.* (1999) recently found in patients with writer's cramp significantly poor activation in the sensorimotor cortex during sustained hand contraction, but poor activation in premotor cortex during writing. They suggested that dysfunction of the premotor cortical network is compatible with a loss of inhibition during the generation of motor commands. The possibility exists that these testing conditions are midway between early joystick PET studies and our testing using an adapted guitar.

The study of Odergren *et al.* (1998) gives strong support to this suggestion. These authors initially observed a relatively poor primary motor cortex activation during writing in patients with writer's cramp compared with matched control subjects. Interestingly, as the duration of the writing period increased, a pro-

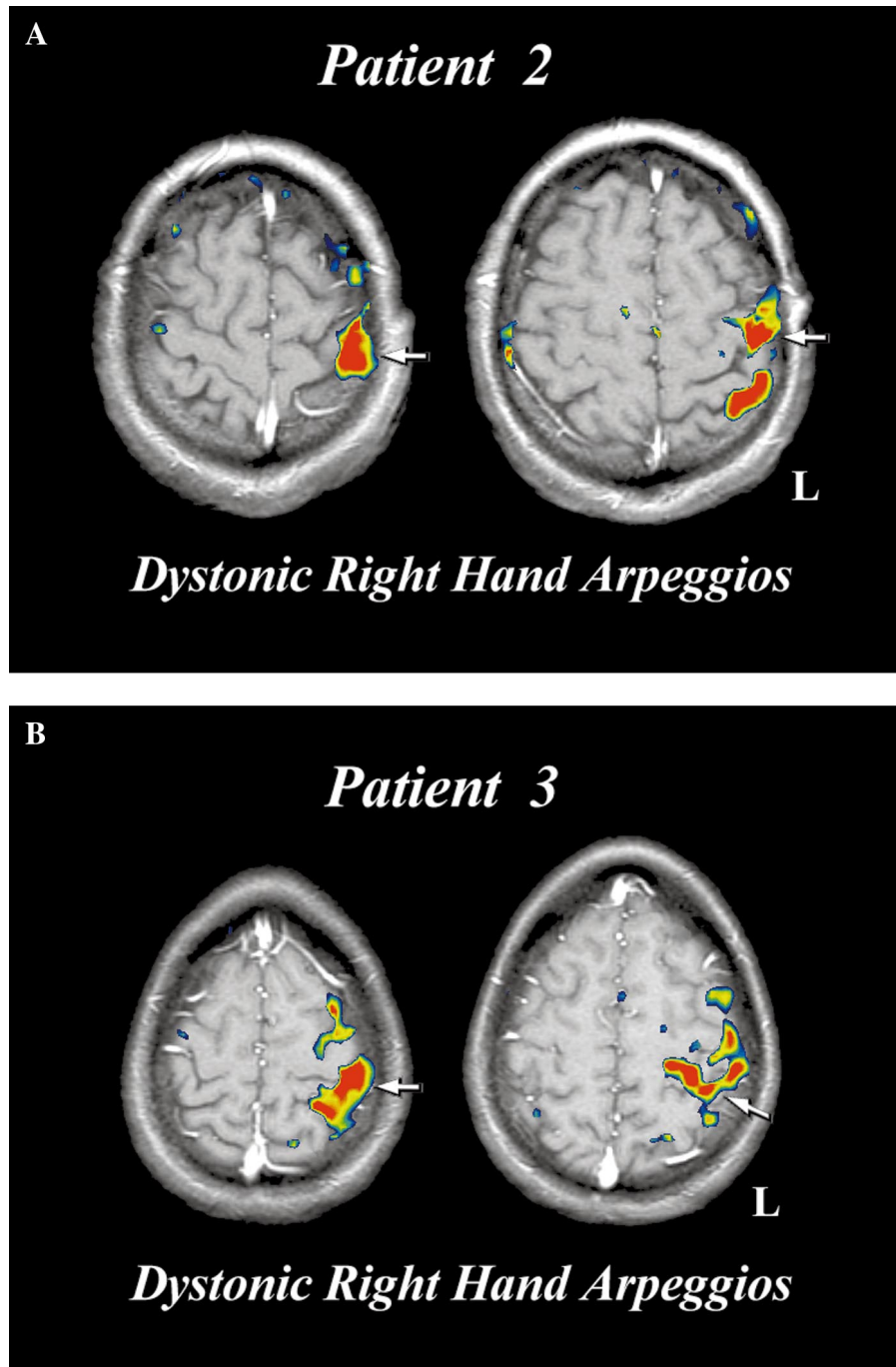


FIG. 3. Functional changes observed in patients 2 and 3 (A and B) during dystonic right-hand arpeggio exercises. Note again predominance of the activation in the contralateral primary sensorimotor cortex (arrows).

gressively abnormal increased activity in primary sensorimotor cortex was observed, correlating with the duration of writing and also with perceived difficulty and signs of dystonia. This study largely suggests that primary sensorimotor cortex has a dual behavior in tasks involving movements of the affected hand. A defective activation during nondystonic movements may shift to an overactivation when a dystonia-inducing task triggers latent unsuppressed activity.

Neurophysiological data further support the possibility of dual behavior of the primary sensorimotor cortex in patients with focal dystonia. There are signs of deficient motor cortex activation in movement-related cortical potentials in patients with writer's cramp (Deuschl *et al.*, 1995). On the other hand, impaired cortical inhibition (Ridding *et al.*, 1995; Chen *et al.*, 1997; Siebner *et al.*, 1999) and enhanced cortical motor excitability (Ikoma *et al.*, 1996) have consistently been

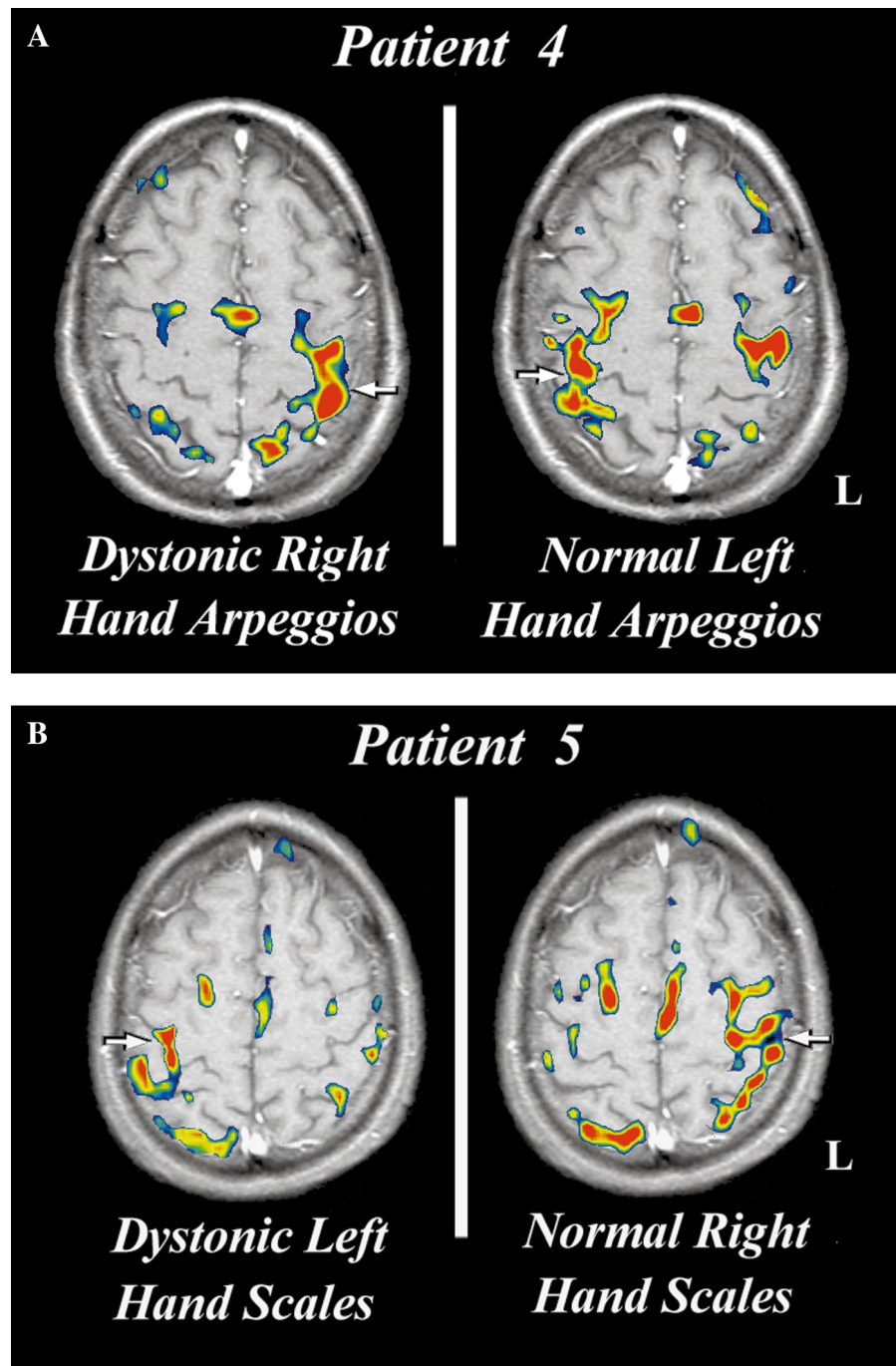


FIG. 4. Functional results from patient 4 and patient 5. Activity around the central sulcus (arrows) during the dystonia-inducing task (left sides in A and B) was less dominant in these cases due to a notable premotor activation (patient 4) and a poor sensorimotor activation (patient 5). Note, however, the increase of premotor cortex activation when the same task was performed using the normal hand.

demonstrated in transcranial magnetic stimulation studies. Thus, a specific form of testing may be prone to detect underactivity of cortical inhibitory neurons, while other situations may better emphasize the activity overflow that occurs during dystonic movements (Hallett, 1998a).

The origin of the well-documented primary sensorimotor cortex derangement is still unclear for most dys-

tonia forms. In occupational cramp, typically occurring after many hours of daily practice of stereotyped exercises, dynamic mechanisms have been postulated (Chen and Hallett, 1998). Repetitive motions induce relevant plasticity changes in the primary sensorimotor cortex. Indeed, cortical motor output is enhanced during the learning of sequential finger movements (Pascual-Leone *et al.*, 1994) and the activation area is

enlarged when a sequence has been overlearned (Karni *et al.*, 1995). Animal research suggests that the cortical remodeling associated with learning may finally degrade the topography of cortical hand representation and lead to a motor disorder in forced circumstances (Chen and Hallett, 1998; Byl *et al.*, 1996; Wang *et al.*, 1995). Furthermore, altered finger cortical representation has already been reported in musicians with focal hand dystonia in two recent independent studies using different techniques to map the somatosensory cortex (Elbert *et al.*, 1998; Bara-Jimenez *et al.*, 1998). Thus, abnormal plasticity appears as a firm candidate in favoring the development of task-related hand dystonia. Learning-induced dedifferentiation of cortical schemes is one proposed form of abnormal plasticity (Byl *et al.*, 1996), which could be more probable in predisposed persons showing primary or secondary impairment of basal ganglia inhibitory influences upon the cortex (Hallett, 1998b).

Certainly there is a need to examine larger series of patients before drawing definitive conclusions. Our results should be referred to the specific type of dystonia studied and are not necessarily applicable to other forms. It is likely that clinically different dystonic disorders show different cortical alteration patterns. Interestingly, acquired hemidystonic patients with structural lesions of the basal ganglia or thalamus showed a pattern of overactivity that involved both premotor and primary sensorimotor cortices during paced joystick movements (Ceballos-Baumann *et al.*, 1995b). Moreover, Ikoma *et al.* (1996) noticed differences between musicians with occupational cramp and patients suffering from writer's cramp with regard to altered responses to transcranial magnetic stimulation.

Likewise, precise details of the task may largely determine the activation pattern obtained and some differences between studies. We would stress the relevance in our study of the specific instruction given to patients whereby they should attempt to engage the dystonia as opposed to resisting it. Another important aspect is the fact that the difference between PET and fMRI in terms of sensitivity, particularly in detecting activations in nonprimary brain regions, is not completely known. Therefore, a different sensitivity between both techniques in the detection of premotor and primary motor activation could also explain some study discrepancies.

A technical limitation of our study is the relatively reduced field of view used in our fMRI, as only eight slices were acquired in each trial to cover the upper cortical motor system. Odergren *et al.* (1998) observed relevant changes in the cerebellum, a structure not included in our assessment, in patients with writer's cramp while writing. Similarly, abnormal activity was previously observed in basal ganglia in patients with idiopathic dystonia (Eidelberg *et al.*, 1998; Ceballos-Baumann *et al.*, 1995a; Playford *et al.*, 1998). Our

functional sequences included only the superior part of the basal ganglia. We did not observe consistent findings at this level. Nevertheless, a more comprehensive anatomical assessment would be necessary to ascertain the participation of the entire motor system in guitar-induced dystonic movements.

In conclusion, we have described a functional cortical pattern that directly correlates with guitar-induced hand dystonia in professional musicians. Our results coincide with studies of other dystonia types in showing an abnormal recruitment of cortical areas involved in the control of voluntary movement. The results do, however, suggest that the usually poorly responding primary sensorimotor cortex in idiopathic dystonic patients may be overactive when tested during full expression of task-induced movement disorder.

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