Selective impairment of hand mental rotation in patients with focal hand dystonia

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Mental rotation of body parts determines activation of cortical and subcortical systems involved in motor planning and execution, such as motor and premotor areas and basal ganglia. These structures are severely impaired in several movement disorders, including dystonia. Writer’s cramp is the most common form of focal hand dystonia. This study investigates whether patients affected by writer’s cramp present with difficulties in tasks involving mental rotation of body parts and whether any impairments are specific to the affected hand or generalized to other body parts. For this purpose we tested 15 patients with right writer’s cramp (aged 21–68 years, 8 women) and 15 healthy control subjects (10 women, age and education matched). Stimuli consisted of realistic photographs of hands and feet presented on a computer monitor in different orientations with respect to the upright canonical orientation. In each trial, subjects gave a laterality judgement by reporting verbally whether the presented body part was left or right. Two main results of the study are, firstly, writer’s cramp patients are slower than controls in mentally rotating hands [F (1,28) = 5.4; P = 0.028] but not feet, and secondly, the pattern of response times to stimuli at various orientations suggests that the mental motor imagery of controls and patients reflects the type of processes and mechanisms called into play during actual execution of the same movements. In particular, increased difficulty in rotating right-sided stimuli at 120° and left-sided stimuli at 240° would suggest that mental rotation of body parts reflects the anatomical constraints of real hand movements. In conclusion, patients with writer’s cramp presented mental rotation deficits specific to the hand. Importantly, deficits were present during mental rotation of both the right (affected) and the left (unaffected) hand, thus suggesting that the observed alterations may be independent and even exist prior to overt manifestations of dystonia.

Keywords: mental rotation; focal hand dystonia; hand; basal ganglia; body schema

Abbreviations: RT = response time

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Introduction

Mental rotation is the ability to imagine how an object would look if rotated away from the orientation in which it actually appears (Thayer et al, 2001). Psychophysical studies in healthy individuals suggest that mental rotation of body parts is carried out by simulating the actual movement of the very same body part (Parsons, 1994). More specifically, subjects compare the stimulus to a mental representation of their own body parts throughout visuo-spatial and motor integration. The mental simulation of real perceptual-motor behaviours could be considered a sort of internal or cognitive analogue of actual movements (Duncombe et al., 1994), useful for movement planning and prediction. Cortical neural networks including posterior parietal (areas 5 and 7) and visual cortex, premotor and supplementary motor areas and primary motor cortex are activated during mental rotation of objects and body parts (Bonda et al., 1995; Parsons et al., 1995; Kosslyn et al., 1998; Ganis et al., 2000).

Research in humans has demonstrated that during mental rotation tasks subcortical structures such as the basal ganglia are also activated (Alivisatos and Petrides, 1997). Since basal
ganglia and motor cortices are known to be involved in motor planning and execution, their activation during mental rotation suggests that actual and mentally simulated movements share largely overlapping cerebral structures.

Dystonia, a neurological syndrome characterized by sustained muscular contractions that cause repetitive movements and abnormal postures, appears linked to basal ganglia dysfunction. These motor disturbances may affect many body parts (generalized) or involve a single body region (focal), such as the hand, the neck and the eyes. Writer’s cramp is the most common form of focal hand dystonia (Bressman, 1998; Fahn et al., 1998; Hallett, 1998). Neuropsychological and neuroimaging studies show an impairment of motor planning and execution of hand movements in writer’s cramp (Deuschl et al., 1995; Van der Kamp et al., 1995; Odergren et al., 1998).

It is still not known, however, whether dystonia is associated with an altered ability to mentally rotate body parts.

In this study we investigated whether patients affected by writer’s cramp present with difficulties in a mental rotation task of the hand and whether this impairment is specific to the dystonic hand or is also found when non-affected body parts are mentally rotated.

**Methods**

We tested 15 patients affected by writer’s cramp in their dominant right hand (8 women) and 15 healthy subjects (10 women) matched for age (mean 41.3 years, range 21–65) and education (mean 11.4 years of schooling, range 5–18). Duration of patients’ disease ranged from 1 to 20 years. Severity of motor impairment was evaluated by using the Burke–Fahn–Marsden movement and disability scale (Burke et al., 1985). Biochemical, computed tomography and magnetic resonance imaging examinations were normal, thus suggesting that dystonia was idiopathic. Biochemical tests were based on blood and urine analyses. In the blood we analysed copper and ceruloplasmin levels, calcium and liver function, CK level, α-fetoprotein, immunoglobulins, lactate and pyruvate, blood count and film for acanthocytes, and blood amino acids. In the urine we analysed urinary amino acids, urinary copper excretion and urinary organic acids. Eleven patients were untreated; the remaining four patients had received treatment with botulinum toxin until 6 months before the study. Additional demographic and clinical information on the patient group is provided in Table 1.

All subjects gave their written informed consent after the non-therapeutic nature of the experimental tests was explained to them. Before testing, all subjects were naive about the aims of the experiment. The procedures were approved by the Local Ethics Committee. The test was carried out in a quiet room at a temperature of 20–23°C. Subjects were seated in front of a computer screen with their hands out of sight on their laps. The experiment was programmed using the E-Prime Beta software running on a PC. Stimuli consisted of realistic photos of hands or feet presented on the computer screen. Left and right hands (and feet) were mirror images of each other. Stimuli were located ~9.3 cm along the widest axis, which corresponded to ~8° of horizontal visual angle with participants’ viewing distance of 50 cm. Images of hands (and feet) could be presented in four views (back in picture plane, palm in picture plane, side from little finger and side from thumb) and six angular orientations (upright stimuli with fingers or toes pointing upwards had a rotation angle of 0°; five clockwise rotations of upright stimuli, namely 60, 120, 180, 240 and 300°, were used). Views and orientation of the experimental stimuli are represented in Fig. 1A and B, respectively.

A total of 96 photographs of hands and 96 of feet were presented in two separate blocks. After each stimulus presentation, subjects had to report verbally whether the presented hand (or foot) was the right or the left one. Stimuli remained on the screen until subjects responded; their responses were recorded by a microphone positioned in front of the computer screen. The microphone recorded reaction time, and the experimenter recorded response accuracy. The sequence of position, orientation and side of hands and feet was randomized within and between subjects. Half of the participants first performed the task of mentally rotating hands before feet. The opposite sequence was used with the other half.

**Table 1** Patients’ demographic and clinical information

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Education (years)</th>
<th>Diagnosis</th>
<th>Severity score</th>
<th>Duration of Symptoms (years)</th>
<th>Therapy††</th>
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<tbody>
<tr>
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<td>3</td>
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<tr>
<td>5</td>
<td>M</td>
<td>46</td>
<td>13</td>
<td>SC</td>
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</tr>
<tr>
<td>6</td>
<td>M</td>
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</tr>
<tr>
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<td>M</td>
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<td>13</td>
<td>DC</td>
<td>12</td>
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<td>8</td>
<td>F</td>
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<td>M</td>
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<td>18</td>
<td>SC</td>
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</table>

††All these four patients were treated with botulinum toxin until 6 months before the study.
Response time (RT) was defined as the time between the appearance of the stimulus on the computer screen and the onset of the subject’s verbal response. Trials in which subjects did not speak loudly enough to trigger the voice box were eliminated prior to the analysis (2.5%). Trials in which RTs were 3 or more standard deviations above the mean for each cell (defined by stimulus type and side) were also eliminated prior to the analysis (1.6%). These trials were not associated with the most difficult rotation angles; indeed, the percentage of removed trials did not correlate with the degree of stimulus orientation (Spearman correlation, $P = 0.266$). Only RTs to trials in which the correct response was made were considered.

Five patients (numbers 1, 2, 4, 5, and 9 in Table 1) were also tested by recording surface EMG activity from the flexor and extensor carpi radialis (FCR and ECR) muscles of the affected side. These two muscles were chosen because they are typically most severely involved in focal hand dystonia (Marsden and Sheehy, 1990). Subjects were seated in front of a computer screen with their arms comfortably lying on a cushion positioned on their laps. We recorded muscle activity for 15 min before the task and for another 15 min while patients executed the task. This procedure allowed us to control for any EMG activity induced by the execution of the mental rotation task. This activity may in principle be more likely in the writer’s cramp subjects.

RT and accuracy were analysed by means of two different analysis of variances (ANOVAs) with repeated measures. Since RT and accuracy are separate measures of patients’ performance, no correction for multiple ANOVAs was made. Each ANOVA had one between-subjects factor: Group (writer’s cramps versus control subjects), and three within-subjects factors: Stimulus type (hands and feet), Stimulus side (left and right) and Stimulus orientation ($0^\circ$, $60^\circ$, $120^\circ$, $180^\circ$, $240^\circ$ and $300^\circ$). Post hoc comparisons were carried out by means of HSD Tukey Test.

**Fig. 1 Schematic representation of the experimental stimuli in (A) four different views (back, thumb, palm and little finger), and (B) six orientations ($0^\circ$, $60^\circ$, $120^\circ$, $180^\circ$, $240^\circ$ and $300^\circ$). Left stimuli were mirror images of right stimuli.**

**Results**

Figure 2 represents mental rotation reaction times contingent upon orientation of the stimuli in the two experimental groups.

The analysis of variance on RTs (mean observed power $0.68 \pm 0.43$, computed averaging the observed power value for each factor; level of significance: $P = 0.05$) showed the significance of the main effect Group [$F(1,28) = 3.4$; $P = 0.028$]. This effect was due to faster mental rotation time in controls (1240.2 ms) than writer’s cramp patients.
The significant effect of Stimulus side \( F(1,28) = 38.8; \ P < 0.001 \) was due to the fact that subjects were faster in mentally rotating the right (1327.8 ms) than the left stimuli (1452.5 ms).

The insignificance of the Stimulus type \( F(1,28) = 0.4; \ P = 0.542 \) indicates that the time requested for mentally rotating hands and feet was comparable. Interestingly, however, the Group \( \times \) Stimulus type interaction reached significance \( F(1,28) = 4.2; \ P = 0.049 \). Post hoc comparisons showed that patients were significantly slower than controls in mentally rotating hands (\( P < 0.001 \)), but not feet (\( P = 0.121 \)). The insignificance of the triple interaction Group \( \times \) Stimulus type \( \times \) Stimulus side \( F(1,28) = 0.1; \ P = 0.729 \) indicates that longer RTs in rotating hands found in writer’s cramp patients with respect to controls was comparable for left and right hands.

The factor Stimulus orientation was significant \( F(5,140) = 16.2; \ P < 0.001 \) insofar as RTs were higher when stimuli had an orientation of 180° (1603.8 ms) than in the other five orientations (0° = 1285.2 ms; 60° = 1320.9 ms; 120° = 1428.2 ms; 240° = 1416.8 ms; 300° = 1283.8 ms). Moreover, RTs were significantly higher at 120° with respect to 0, 60 and 300°, and at 240° with respect to 60 and 300°.

The Stimulus side \( \times \) Stimulus orientation interaction was significant \( F(5,140) = 5.9; \ P < 0.001 \). Post hoc comparisons showed that mental rotation of right-sided stimuli required longer RTs at 120° than at 0°, 240° and 300° (\( P < 0.047 \)), and 180° than at 0°, 60°, 240° and 300° (\( P < 0.003 \)); in a similar vein, mental rotation of left-sided stimuli implies longer RTs at 180° than at all the other stimulus orientations (\( P < 0.026 \)), and at 240° than at 0°, 60° and 300° (\( P < 0.011 \)). The triple interaction Stimulus type \( \times \) Stimulus side \( \times \) Stimulus orientation was significant \( F(5,140) = 6.9; \ P < 0.001 \).

Post hoc comparisons showed that right hand was more difficult to rotate at 120 and 180° than at 0°, 240° and 300° (\( P < 0.002 \)); left hand was more difficult at 180° and 240° than at 0, 60, 120 and 300° (\( P < 0.001 \)); right foot was more difficult to rotate at 120° than at 0° and at 180° than at 0, 60° and 300° (\( P < 0.020 \); left foot was more difficult to rotate at 180° than at all the other stimulus orientations (\( P < 0.020 \)).

Finally, the interaction Group \( \times \) Stimulus type \( \times \) Stimulus side \( \times \) Stimulus orientation was significant \( F(5,140) = 4.4; \ P = 0.001 \). Post hoc comparisons showed that writer’s cramp patients were slower than control subjects when rotating the right hand at all the stimulus orientations (\( P < 0.007 \) and when rotating the left hand at 0, 180, 240 and 300° (\( P < 0.002 \)). In contrast, during mental rotation of feet the only significant difference contingent upon stimulus orientation between controls and patients was observed for right stimuli at orientation 180° (\( P = 0.05 \)). The difference between writer’s
control subjects and patients with writer’s cramp at the remaining orientations was as follows: right foot: 0°: $P = 0.16$; 60°: $P = 0.51$; 120°: $P = 0.88$; 240°: $P = 0.11$; 300°: $P = 0.09$; left foot: 0°: $P = 0.07$; 60°: $P = 0.16$; 120°: $P = 0.13$; 180°: $P = 0.41$; 240°: $P = 0.47$; 300°: $P = 0.87$.

To further assess whether the patients’ slower performance in mental rotation of hands was due to a specific mental rotation impairment rather than to a more general impairment in stimuli identification, we calculated the mean difference between the two groups for each degree of stimulus orientation. Figure 3 shows an increased patient–control difference at longer mental rotation distances (mainly at 180° orientation). Figure 3 shows an increased patient–control difference between the two groups for each degree of stimulus orientation. This result suggests that the RTs pattern reflects a genuine rotation rather than a stimulus identification deficit.

Accuracy was high and, as attested by the absence of any significant effect in the ANOVA, comparable in both groups (Table 2).

It is worth noting that the comparable accuracy in the two groups suggests that the longer RTs during mental rotation of hands found in patients with focal hand dystonia cannot be explained in terms of a speed-accuracy trade-off.

EMG recording from FCR and ECR muscles of the affected arm in five patients showed no muscle activation before or during the mental rotation task. This result suggests that the body-part related differences in the performance of focal hand dystonia patients were not related to peripheral factors. It is worth noting that performance in the hand mental rotation task of the five patients in whom EMG was recorded showed the same pattern as that of the entire group of patients with dystonia. Mean mental rotation time for the left hand was as follows: 0° = 1453.5 ms; 60° = 1160.8 ms; 120° = 1226.5 ms; 180° = 1560.0 ms; 240° = 1552.9 ms; and 300° = 1690.6 ms. Mean mental rotation time for each degree of orientation when rotating the right hand was as follows: 0° = 1269.8 ms; 60° = 1094.8 ms; 120° = 1521.9 ms; 180° = 1632.2 ms; 240° = 1408.0 ms; and 300° = 1241.4 ms. Also in these patients, accuracy followed the pattern found in the large group of focal hand dystonia patients.

Fig. 3 Mean RT differences between dystonic patients and controls for each stimulus orientation in the hands mental rotation task. This difference has been computed by averaging RTs to left and right hands.

**Table 2** Mean percent accuracy and standard errors in the two groups for the two body parts (hand and foot), laterality (left and right) of the stimuli and stimulus orientations (0°, 60°, 120°, 180°, 240° and 300°)

<table>
<thead>
<tr>
<th></th>
<th>Hand</th>
<th>Foot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0°</td>
<td>60°</td>
</tr>
<tr>
<td>Patients with writer’s cramp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>85.0%</td>
<td>90.8%</td>
</tr>
<tr>
<td></td>
<td>(4.2)</td>
<td>(2.7)</td>
</tr>
<tr>
<td>Right</td>
<td>85.0%</td>
<td>83.3%</td>
</tr>
<tr>
<td></td>
<td>(3.4)</td>
<td>(5.0)</td>
</tr>
<tr>
<td>Control subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>90.8%</td>
<td>95.0%</td>
</tr>
<tr>
<td></td>
<td>(2.4)</td>
<td>(2.1)</td>
</tr>
<tr>
<td>Right</td>
<td>89.2%</td>
<td>82.5%</td>
</tr>
<tr>
<td></td>
<td>(4.0)</td>
<td>(4.0)</td>
</tr>
</tbody>
</table>
Discussion

The mental rotation of body parts is a cognitive task in which subjects imagine moving their body parts from their actual posture into that of the stimulus. This ability requires the integrity of specific cortical-subcortical motor structures (motor and premotor areas and basal ganglia) and sensory systems (somatosensory and visual) (Kosslyn et al., 1998; Vingerhoets et al., 2002; Wolbers et al., 2003; de Lange et al., 2005). Mental rotation engages an anatomically interconnected system implicated in the integration of sensory information with motor actions. Sensory–motor integration is dysfunctional in patients with writer’s cramp (Ibanez et al., 1999; Tinazzi et al., 2000; Abbruzzese et al., 2001). For instance, EEG studies in patients with writer’s cramp have revealed a reduced amplitude of the movement-related cortical potential attributed to alterations in the activity of the primary motor and supplementary motor areas (Deuschl et al., 1995; Van der Kamp et al., 1995). A recent TMS study demonstrated that the motor cortical excitability preceding a voluntary movement is abnormally modulated in dystonia (Gilio et al., 2003).

The present study shows a clear impairment of mental rotation of hands but not feet in patients with idiopathic writer’s cramp. Two main results of the study should be emphasized. First, writer’s cramp patients are slower than controls in mentally rotating hands but not feet. Second, the pattern of RTs at the different orientations of the stimuli suggests that in both controls and patients mental motor imagery reflects the type of processes and mechanisms called into play during actual execution of the same movements. In particular, the higher difficulty in rotating right-sided stimuli at 120° and left-sided stimuli at 240° would suggest that mental rotation of body parts reflects the anatomical constraints of real hand movements. Indeed, these two orientation positions would probably be reached with higher difficulty (with respect to the other positions except 180°) during actual execution because of biomechanical constraints. Moreover, in keeping with previous studies (Parsons, 1994) the 180° orientation was the most difficult orientation for both left- and right-sided stimuli insofar as it implies the longest rotation distance.

Functional neuroimaging studies have documented changes in the activity of primary motor cortex and prefrontal motor areas in patients with focal hand dystonia during passive vibrotactile stimulation of the hand (Tempel and Perlmuter, 1993), freely selected movements with a joystick (Ceballos-Baumann et al., 1995), writing a stereotyped word (Ibanez et al., 1999) and during full expression of a task-induced movement disorder (Odergren et al., 1998; Pujol et al., 2000). These findings may be consistent with the observed impairment of mental rotation in our patients, since real and mentally simulated movements rely upon largely overlapping motor networks. Thus, the abnormality in mental simulation of real perceptual-motor behaviours could be considered as a cognitive analogue of the real movement disorder.

Several lines of evidence suggest that somatosensory areas are also dysfunctional in focal hand dystonia. Magnetoencephalography studies (Bara-Jimenez et al., 1998; Elbert et al., 1998) have reported neural changes in the primary somatosensory cortex representing the most trained fingers in writer’s cramp. Recent psychophysical studies have shown an impairment of somatosensory spatial (Bara-Jimenez et al., 2000a; Molloy et al., 2003) and temporal (Tinazzi et al., 1999, 2002; Bara-Jimenez et al., 2000b; Sanger et al., 2001; Aghio et al., 2003; Fiorio et al., 2003) discrimination, which has been related to a dysfunction of the primary somatosensory area and higher order parietal areas (5 and 7). Since all of these areas are activated by mental rotation tasks, our patients’ impaired performance might also be due to the dysfunction of these areas (Kosslyn et al., 1998; Ganis et al., 2000). Therefore, abnormalities in both motor and somatosensory structures could explain the mental task impairment observed in writer’s cramp. Although it is known that the visual system is strongly involved in mental rotation tasks, we do not believe that it affected our patients’ performance because integration of visual information is intact in patients with writer’s cramp (Fiorio et al., 2003).

Mental rotation has been previously assessed in patients with Parkinson’s disease, a condition in which, like in idiopathic dystonia, the basal ganglia circuit is dysfunctional (Duncombe et al., 1994; Dominey et al., 1995; Lee et al., 1998). Results were controversial in that some studies reported that parkinsonian patients were slower than controls when required to rotate both objects and body parts (hands and feet) (Dominey et al., 1995; Lee et al., 1998); however, normal performance was also reported in similar experimental conditions (Duncombe et al., 1994). We extended the research on Parkinson’s disease patients by exploring mental rotation of body parts in focal hand dystonia and evaluating whether or not the possible deficit in mental rotation abilities specifically involved symptomatic body parts. To ensure that performance was not worsened by difficulty in executing the real movements, but was rather a measure of the mental representation of those movements, our subjects reported their answers verbally, without pressing a key as in previous studies. In dystonic patients, the mental rotation impairment was observed for hands but not for feet. This suggests that in writer’s cramp, unlike Parkinson’s disease, the mental rotation ability is strictly linked to the affected body part. This observation suggests that in focal hand dystonia mentally transforming the body parts is dependent on mechanisms at least in part common to the task of actually rotating the very same body part. Differences in the pathophysiology of Parkinson’s disease and dystonia could account for the different impairment of mental rotation in the two diseases.

Since our subjects performed the mental rotation tasks by using vocal responses, their performance should not be influenced by peripheral factors, such as unwanted muscular activity of the dystonic hand and arm during the experimental task. Moreover, simple and dystonic cramps are associated with...
muscular activity only during writing or other manual tasks, but not at rest (Marsden and Sheehy, 1990; Berardelli et al., 1998). However, it is in principle possible that involuntary muscular contractions might be elicited by the mental effort of rotating body parts. Were this the case, the selective impairment of patients with focal hand dystonia in the mental rotation of hands might be due to peripheral rather than central factors. This possibility is ruled out by the absence of EMG activity of forearm muscles on the dystonic side during the mental rotation task, at least in the five patients tested with EMG recordings. Thus, we suggest that the pattern of results found in our patients may be best explained by the notion that actual and imagined movements share largely overlapping neural substrates.

Longer reaction times were observed for hand and foot orientations (180°) in which actual movements would be more difficult. It may be even more interesting to emphasize the higher difficulty in rotating right-sided stimuli at 120° and left-sided stimuli at 240° insofar as this would suggest that mental rotation of body parts may reflect the anatomical constraints of real hand movements. This result is in keeping with previous studies showing that reaction times are longer for mental rotation of stimuli corresponding to body part positions that would actually be difficult to maintain (Parsons, 1994; Thayer et al., 2001; Petit et al., 2003). Recent studies have shown that body schema alterations bring about performance alterations in hand laterality tasks. Patients suffering from chronic arm pain, for example, showed slower RTs for mental rotation of the affected than the unaffected limb, suggesting that a brain representation of the body might be influenced by peripheral factors such as pain (Schwoebel et al., 2001). Similar results were obtained in patients with complex regional pain syndrome (CRPS) who presented with a specific impairment in mental rotation of the affected hand. Interestingly, the deficit was related to the pain that would be evoked by executing the movement and to symptom duration (Moseley, 2004). Analysis of mental rotation of body parts in upper limb amputees demonstrated that judging the laterality of body parts was more difficult in patients with amputation of the dominant than the non-dominant limb (Nico et al., 2004). These results support our findings that the motor impairment of patients with dystonia could cause an alteration in the representation of specific body parts. It is worth noting that our patients showed slow RTs also when rotating the unaffected hand. This observation suggests that the difficulties in mental rotation do not strictly depend on a peripheral motor impairment but may be due to an alteration of hand representation. This is in keeping with our previous study showing deficits in the temporal processing of tactile and visuo-tactile stimuli, both on the affected and non-affected hand in writer’s cramp patients (Fiorio et al., 2003). In addition, neuroimaging and electrophysiological studies in focal hand dystonia have shown that sensorimotor structures may be affected bilaterally despite unilateral clinical manifestations (Stoessl et al., 1986; Tempel and Perlmutter, 1993; Ridding et al., 1995; Meunier et al., 2001).

Abnormalities occurring in the unaffected (personal or peripersonal) space may indicate susceptibility to developing focal hand dystonia in the clinically normal hand. Indeed, it is known that over time some writer’s cramp patients who learn to write with the opposite hand develop a similar focal dystonia in the non-dominant hand (Marsden and Sheehy, 1990). In a similar vein, slowness of mental rotation of the unaffected hand may suggest that the observed alterations are not the mere consequence of abnormal movements and postures, but may be independent and may have existed prior to overt manifestations of dystonia. In conclusion, the present study shows for the first time that mental rotation of the hand is impaired in patients with writer’s cramp and suggests that the cognitive representation of hand movements may also be altered in focal hand dystonia.

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References


