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

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Summary
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 in which symptoms manifest mainly during writing. The present study aims to investigate 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 10 patients with right writer’s cramp and 10 healthy control subjects. Stimuli consisted of realistic photographs of different views of hands and feet presented on a computer monitor in different orientations with respect to the upright canonical orientation. On each trial, subjects gave a laterality judgement, that is, they reported verbally whether the presented body part was left or right. Patients with writer’s cramp presented mental rotation deficits specific to the hand, that is, the body part affected by the motor disturbances. Importantly, deficits were present during mental rotation of both the right and the left unaffected hand, thus suggesting that the observed alterations may be independent and even exist prior to overt manifestations of dystonia.

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

Abbreviations: ANOVA = analyses of variance; CRPS = complex regional pain syndrome; ECR = extensor carpi radialis; EMG = electromyography; FCR = flexor carpi radialis; RT = response time

Received August 4, 2004. Revised December 29, 2004. Accepted January 5, 2005

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), most often the hand. Writer’s cramp is the most common form of focal hand dystonia (Bressman, 1998; Fahn et al., 1998; Hallett, 1998). Neurophysiological 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 10 patients affected by writer’s cramp in their dominant right hand (5 women) and 10 healthy subjects (8 women) matched for age (mean 36.9 years, range 24–65) and education (mean 14.0 years of schooling, range 5–18).

Duration of patients’ disease ranged from 5 to 12 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. Seven patients were untreated; the remaining three 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 Ethical 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 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 approximately 9.3 cm along the widest axis, which corresponded to about 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.

Response time (RT) was defined as the time between the appearance of the stimulus on the computer screen and the onset of the subjects’ verbal response. Trials in which subjects did not speak loudly enough to trigger the voice box were eliminated prior to analysis (2.3%). Trials in which RTs were three or more standard deviations above the mean for each cell (defined by stimulus type and side) were also eliminated prior to analysis (2.0%). 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, \( P = 0.234 \)).

Only RTs to trials in which the correct response was made were considered. RTs for correct trials were used to compute rotation speed (defined as the ratio between a given rotation angle and RTs at the same angle). This dynamic index (computed in degrees/s) seems to be optimal for estimating mental rotation processes (Wohlschlager and Wohlschlager, 1998; Wohlschlager, 2001; Petit et al., 2003).

Five patients (number 1, 2, 4, 5, 9 in Table 1) were also tested by recording surface electromyographic (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

### 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>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>32</td>
<td>13</td>
<td>SC</td>
<td>6</td>
<td>6</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>45</td>
<td>11</td>
<td>DC</td>
<td>12</td>
<td>20</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
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<td>5</td>
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<td>37</td>
<td>13</td>
<td>SC</td>
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<tr>
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<td>M</td>
<td>46</td>
<td>13</td>
<td>SC</td>
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<td>No</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>31</td>
<td>18</td>
<td>DC</td>
<td>3</td>
<td>11</td>
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</tr>
<tr>
<td>7</td>
<td>M</td>
<td>32</td>
<td>13</td>
<td>DC</td>
<td>12</td>
<td>8</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>47</td>
<td>9</td>
<td>DC</td>
<td>7</td>
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</tr>
<tr>
<td>9</td>
<td>M</td>
<td>47</td>
<td>18</td>
<td>SC</td>
<td>3</td>
<td>5</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>41</td>
<td>13</td>
<td>SC</td>
<td>4</td>
<td>10</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*SC = simple writer’s cramp, DC = dystonic cramp. **Burke–Fahn–Marsden movement and disability scale. †Years from disease onset. ††All 3 patients were treated with botulinum toxin until 6 months before the study.
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.

Rotation speed and accuracy were analysed by means of two different analyses of variance (ANOVAs) with repeated measures. Each ANOVA had one between-subjects factor: Group (writer’s cramps versus control subjects), and two within-subjects factors: Stimulus type (hands and feet) and Stimulus side (left and right).

Results
Mental rotation speed of the two experimental groups is reported in Fig. 2. Its inspection suggests three main results. First, writer’s cramp patients seem to be slower than controls in mentally rotating hands. Second, patients’ hand mental rotation seems to be comparable for the right (affected by dystonia) and left (unaffected) side. Third, in control subjects, mental rotation speed seems to be higher for the right (dominant) than for the left side of both hand and foot stimuli.

These observations were confirmed by the analysis of variance (mean observed power 0.60; level of significance: $P = 0.05$). The significance of the main effect Group [$F_{(1,18)} = 5.8; P = 0.027$] was due to controls’ faster mental rotation speed (162°/s) than writer’s cramp patients (123°/s). The significant effect of Stimulus side [$F_{(1,18)} = 33.5; P < 0.001$] was due to the fact that subjects were faster in mentally rotating the right (150°/s) than the left stimuli (135°/s). The Group $\times$ Stimulus

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

Fig. 2 Mean values and standard deviations of mental rotation speed in writer’s cramp (black circles) and control subjects (white squares) for the two types of stimuli (hands and feet) and laterality (right and left).
type interaction was also significant \( F(1,18) = 4.4; P = 0.049 \). Post hoc comparisons (carried out by using \( t \)-tests and Bonferroni correction) showed that patients were significantly slower than controls in mentally rotating hands \( (P = 0.010) \) but not feet \( (P = 0.240) \). The triple interaction Group × Stimulus type × Stimulus side was also significant \( F(1,18) = 4.6; P = 0.046 \). Patients were slower than control subjects both when rotating the right \( (P = 0.005) \) and the left hand \( (P = 0.021) \); in contrast, the performance of the two groups was not significantly different during mental rotation of right \( (P = 0.139) \) or left \( (P = 0.123) \) feet. Moreover, while control subjects were faster in mentally rotating right-sided (their dominant side) than left-sided hands \( (P < 0.001) \) and feet \( (P = 0.006) \), patients showed a right-side advantage only when rotating feet \( (P = 0.001) \). No other effects or interactions were significant. Figure 3 shows that mental rotation speed and easiness of the task contingent upon orientation of the stimuli were correlated (Spearman: \( r = 0.99; P < 0.001 \)) in both controls and patients. This suggests that mental rotation of body parts reflects the anatomical constraints of real hand/foot movements.

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

Table 2  Mean percent accuracy and standard deviation in the two groups for the two body parts (hand and foot) and laterality (left and right) of the stimuli

<table>
<thead>
<tr>
<th></th>
<th>Hand</th>
<th></th>
<th>Foot</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Patients with writer’s cramp</td>
<td>85.0% (8.4)</td>
<td>85.0% (9.9)</td>
<td>84.0% (7.8)</td>
<td>87.5% (8.7)</td>
</tr>
<tr>
<td>Control subjects</td>
<td>88.3% (10.1)</td>
<td>85.4% (9.3)</td>
<td>85.2% (10.7)</td>
<td>81.5% (12.0)</td>
</tr>
</tbody>
</table>

It is worth noting that the comparable accuracy in the two groups means that rotation speed effects cannot be explained in terms of a speed–accuracy tradeoff.

EMG recording from FCR and ECR muscles of the affected arm in five patients showed no unwanted activation before or during the mental rotation task. This result suggests that the observed body-part-related differences in the performance of focal hand dystonia patients was not related to peripheral factors. It is worth noting that performance in the hand mental rotation task was comparable in the five patients in whom EMG was recorded and in the entire group of patients with dystonia. Mean mental rotation speed
for each degree of orientation when rotating the right hand was as follows: \(60^\circ = 57^\circ/s; 120^\circ = 83^\circ/s; 180^\circ = 130^\circ/s; 240^\circ = 215^\circ/s; 300^\circ = 257^\circ/s\) (Spearman: \(r = 1.0; P < 0.001\)). Mean mental rotation speed for the left hand was as follows: \(60^\circ = 263^\circ/s; 120^\circ = 198^\circ/s; 180^\circ = 124^\circ/s; 240^\circ = 86^\circ/s; 300^\circ = 40^\circ/s\) (Spearman: \(r = -1.0; P < 0.001\)).

Discussion

This study assessed the speed and accuracy of mental rotation of hands and feet in writer’s cramp patients. 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 (somatic-sensory and visual). The results of the present study demonstrate a clear impairment of mental rotation speed in patients with idiopathic writer’s cramp. 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 potential 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). Moreover, 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 in writer’s cramp (Tempel and Perlmutter, 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 share largely overlapping motor structures. Thus, this 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; Aglioti et al., 2003; Fiorio et al., 2003) discrimination, which has been related to a dysfunction of the primary somatosensory area and associative parietal areas (5 and 7). Since all of these areas are activated by a mental rotation task, our patients’ impaired performance might also be due to 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 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 unwanted 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. Thus, the pattern of results found in our patients can be best explained by the notion that actual and imagined movements share largely overlapping neural substrates.

To control whether subjects performed the task by mentally simulating the rotational movement of the real corresponding body part, we correlated rotation speed and angle of stimulus orientation. The significant correlation suggests that the strategy used by the subjects during the task was the mental simulation of the movement of their own rotated body part. Indeed, faster mental rotation was observed for hand and foot orientations in which actual movements would be more difficult because of anatomical constraints. This result is in line 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 hand, 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 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 dominant than 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.

References


