

## Mental rotation and working memory in musicians' dystonia

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Word count (abstract/text): 204/3031

Figure/Table/References: 3/0/27

Running title: Mental rotation in musicians' dystonia

Keywords: musician, focal hand, dystonia, mental rotation, action observation

Funding: none

Conflict of interest related to the current work: none

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## 1 **Abstract**

2 Background: Mental rotation of body parts engages cortical-subcortical areas that are  
3 actually involved in the execution of a movement. Musicians' dystonia is a type of focal  
4 hand dystonia that is grouped together with writer's cramp under the rubric of  
5 "occupation dystonia", but it is unclear to which extent these two disorders share  
6 common pathophysiological mechanisms. Previous research has demonstrated patients  
7 with writer's cramp to have deficits in mental rotation of body parts. It is unknown  
8 whether patients with musicians' dystonia would display similar deficits, reinforcing the  
9 concept of shared pathophysiology.

10 Methods: Eight patients with musicians' dystonia and eight healthy musicians matched  
11 for age, gender and musical education, performed a number of tasks assessing mental  
12 rotation of body parts and objects as well as verbal and spatial working memories  
13 abilities.

14 Results: There were no differences between patients and healthy musicians as to  
15 accuracy and reaction times in any of the tasks.

16 Conclusions: Patients with musicians' dystonia have intact abilities in mentally rotating  
17 body parts, suggesting that this disorder relies on a highly selective disruption of  
18 movement planning and execution that manifests only upon playing a specific  
19 instrument. We further demonstrated that mental rotation of body parts and objects  
20 engages, at least partially, different cognitive networks.

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1 Motor imagery is defined as the mental process by which an individual rehearses or  
2 simulates a given action [1]. Motor imagery engages brain areas that are also active  
3 during the observation and/or execution of actions such as the sensorimotor cortices  
4 and basal ganglia [2-4]. One paradigm to evaluate motor imagery is the mental rotation  
5 of body parts (BMR). Namely, subjects have to imagine how a body part would look if  
6 rotated away from the orientation in which it actually appears [1]. This likely occurs via  
7 the integration of visual, proprioceptive and motor information and BMR can be deemed  
8 a cognitive analogue of an actual action [5], as also supported by the fact that longer  
9 rotation times are usually observed for stimuli orientations that would actually be  
10 difficult to maintain [6]. However, it is conceivable that BMR engages a wider cognitive  
11 network, which also deals with problem solving and decision-making. In fact, to  
12 mentally rotate a body part, one most likely creates a mental representation that is  
13 continuously updated as it rotates [7,8]. This process is consistent with current models  
14 of working memory (WM) [9], in which a central executive can access and manipulate  
15 information retained in dissociable buffers for visuospatial and sensori-motor  
16 information and determine, for instance, if the body part will be rotated clockwise or  
17 not. One study supporting this notion found a significant association between higher  
18 rotational ability for objects and lower reaction times (RT) in a task of spatial WM  
19 (SWM) [10]. Yet, it is not entirely clear to which extent BMR, object MR (OMR), and  
20 scene MR, share common cognitive mechanisms [11].

21 Musicians' dystonia (MD) is a type of focal, task-specific, hand dystonia affecting as  
22 many as 1 in 200 musicians during their career and often resulting in the termination of  
23 professional performance [12]. The pathophysiology of MD is not entirely clear [12].  
24 There are many clinical and pathophysiological similarities between MD and other types  
25 of task-specific, focal dystonia such as writer's cramp (WC), so that MD and WC are

1 usually grouped together under the umbrella of “occupational dystonia”, based on the  
2 suggestion that over-training can induce maladaptive plasticity and results in dystonia  
3 [12-13]. In this context, previous research using MR paradigms has shown that patients  
4 with WC have deficits in BMR, which are selective to the hands, as compared to healthy  
5 controls, suggesting a close link between the impairment of motor planning/execution  
6 (at least as assessed by MR) and the manifestation of dystonia [14]. It is, however,  
7 unknown whether subjects with MD would display similar deficits with this paradigm,  
8 reinforcing the concept of shared pathophysiology between these two disorders.

9 In the current study we therefore aimed to explore this topic using the MR paradigm in  
10 MD. Specifically we assessed BMR for hands, feet and hemi-faces. As a control task, we  
11 used a task of OMR, in which a letter was presented in its canonical or mirror-reversed  
12 form. Moreover, we further evaluated WM abilities in MD to explore if they are indeed  
13 associated with MR performances for body parts and/or objects.

## 14 **2. Methods**

### 15 **2.1 Subjects**

16 Eight patients with MD and eight healthy professional musicians with similar age  
17 ( $53.5 \pm 8.3$  vs  $54.5 \pm 12.8$ ,  $p > 0.05$ ), gender (6M/2F vs 5M/3F,  $p > 0.05$ ) and musical  
18 education ( $40.9 \pm 13.1$  vs  $42.8 \pm 8.9$ ,  $p > 0.05$ ) were enrolled in the current study. All  
19 subjects but 3 (2 among patients and 1 among healthy musicians) were right-handed,  
20 ( $p > 0.05$ ). MD patients were either not receiving any treatment ( $n=3$ ) or were assessed  
21 at least four months after the last set of botulinum toxin ( $n=5$ ). The study was approved  
22 by the Local Ethics Committee and all subjects gave their written informed consent.

### 23 **2.2 Procedure**

24 The test was carried out in a quiet room. Subjects were seated in front of a computer  
25 screen (15 inches) with their non-dominant hand out of sight on their laps. The

1 dominant hand was used to press the answer key (right/left arrow keys for right-  
2 handed subjects and z/c keys for left-handed subjects) on an international US-keyboard,  
3 as described below. All tasks were programmed using MatLab 2013b.

#### 4 *2.2.1 Mental rotation paradigm*

5 The mental rotation paradigm was adapted from previous studies in focal dystonia [14-  
6 15]. Specifically, subjects were presented with realistic photos of left or right hands, feet  
7 and hemi-faces. The three different types of stimuli were chosen to explore whether  
8 abnormalities were present only in the affected (dystonic) body regions (e.g., hands)  
9 compared to non-affected ones (e.g., feet and hemi-faces). All three stimuli were  
10 presented in eight angular orientations (AO; e.g., 0, 45, 90, 135, 180, 225, 270 and 315  
11 degrees) and subjects had to report the laterality of the presented stimuli (e.g., right or  
12 left) by pressing the corresponding key on a keyboard.

13 Subjects were instructed to respond to each stimulus accurately and as quickly as  
14 possible. Response accuracy (RA) and reaction time (RT) were recorded. Each stimulus  
15 was presented until subjects responded (for a maximum of 5 seconds, after which the  
16 response was discarded), and was followed by inter-trial interval of 2 seconds. For each  
17 stimulus, six different trials were presented for a total of 96 pictures, randomly  
18 presented (6 trials x 8 angular orientations x 2 sides). Hands, feet, and hemi-faces tasks  
19 were performed separately in three different blocks. A control task of OMR was also  
20 developed following the same structure as described above. Namely, a letter ("F") was  
21 presented in eight angular orientations and subjects had to indicate whether the  
22 displayed alphanumeric character was in its normal or mirror-reversed orientation.  
23 Patients were instructed that MR was permitted only in the bi-dimensional plane and  
24 performed a free trial (4 items) for each block to get confident with the tasks. Figure 1A-  
25 D provides an example of different probes. Subjects randomly performed the four tasks

1 and were allowed to rest for a few minutes after completion of each.

### 2 *2.2.2 Working memory tasks*

3 The two tasks for SWM and verbal WM (VWM) were adapted from previous studies [10].  
4 Specifically, for the SWM task a 4x4 grid of 16 squares displaying 4 different letters,  
5 randomly located within the grid, was presented for 5 seconds (encoding phase).  
6 Subjects were instructed to remember only the locations of the letters and to ignore  
7 their identities. Following the 5s encoding phase, a fixation cross was displayed for 1  
8 second, and then the grid was again presented, this time displaying only a single probe  
9 letter (retrieval phase). The probe letter was always different from those presented in  
10 the encoding phase, in terms of identity. For each grid to be memorized there were four  
11 probe trials and each probe trial was presented for 2 seconds with a 1 second interval  
12 between each presentation (figure 1E). Within this 2 seconds window, participants were  
13 required to indicate whether or not the location of the probe letter had been occupied in  
14 the original grid by pressing a key on the keyboard. Subjects were instructed to respond  
15 accurately and as quickly as possible. On average 50% of probes were true and 50%  
16 were false and any particular block of trials may have had 0 to 4 true probes.  
17 Participants completed a total of 60 grids and thus were presented with a total of 240  
18 probe items. RA and RT were recorded.

19 The parameters for the VWM task were the same as in the SWM task, with the exception  
20 that subjects were requested to remember only the identities of the letters and to ignore  
21 their locations during the encoding phase. Also in this task, probe items were always  
22 incongruent with the items presented in the encoding phase (e.g., probe items were  
23 always in different locations than those presented in the encoding phase).

### 24 *2.3 Statistical analyses*

25 Descriptive statistics (t-test and Fisher's test) were performed as appropriate. Normal

1 distribution of data was checked by means of the Shapiro-Wilk test and Greenhouse-  
2 Geisser correction was used, when necessary, to correct for nonsphericity (e.g.,  
3 Mauchly's test  $<0.05$ ). Thus, RA and RT were analysed by means of two different  
4 analyses of variances (ANOVA). Only RTs to trials in which the correct response was  
5 made were considered. For each angular orientation, the averaged RT was entered in  
6 the analyses, as in previous works [14,15]. For MR results, each ANOVA had one  
7 between-subjects factor (group – e.g., MD versus healthy musicians) and three within-  
8 subjects factors: Stimulus type (hands, feet, hemi-faces and letters), stimulus side (left  
9 and right) and stimulus angular orientation (0, 45, 90, 135, 180, 225, 270 and 315  
10 degrees). Additional analyses were performed to explore whether, within each MR task,  
11 there was a learning effect across the trials. Thus, the *trial number* factor was added to  
12 the ANOVA analyses, either discarding the *AO* factor (e.g., to explore a learning effect  
13 from trial 1 to 96, regardless of the *AO*) or considering the *AO* factor (e.g., to explore a  
14 learning effect from trial 1 to 6 for each *AO*).

15 Similarly, ANOVA analysis exploring WM abilities had one between-subjects factor  
16 (group – e.g., MD versus healthy musicians) and one within-subjects factor (stimulus  
17 type –e.g. spatial vs verbal). Correlation analysis was performed in order to explore  
18 possible associations between MR and WM abilities and was carried out with the  
19 Spearman's test with Bonferroni's correction for multiple comparisons.

20

### 21 **3. Results**

#### 22 *3.1 Mental rotation paradigm*

23 There were no differences as to RA between the two groups in any of the four tasks.  
24 Mean percent accuracy showed that the 180° stimulus was the most difficult orientation  
25 for both left- and right-hand for both groups (supplementary table 1). The same trend

1 was observed for feet, hemi-faces, and letters (supplementary table 1). Figure 2  
2 represents mental rotation RTs contingent upon orientation of the stimuli in the two  
3 experimental groups. The analysis of variance on RTs showed no significance of the  
4 factor *group*, *stimulus side*, *stimulus orientation* or their interaction. Also, there was no  
5 significance of the factor “stimulus type”, indicating that the time requested for mentally  
6 rotating hands, feet, hemi-face and letters was comparable, despite a non-significant  
7 trend ( $p=0.06$ , see figure 2 where it is appreciable that for both groups the RT for  
8 rotating the feet was higher than the time requested to rotate other stimuli).

9 Additional analyses to explore a learning effect within each MR task, showed a general  
10 significant effect of the *trial number* factor ( $p<0.05$ ) with no difference between the  
11 groups. However, this was no longer significant when analyzing different AOs  
12 separately, (as an example, supplementary figure 1 shows RTs for trial 1 vs 6, upon  
13 different AO, in the MR of the right hand; other negative data not shown but available  
14 upon request).

### 15 *3.2 Working memory tasks*

16 There was no difference as to RA in any of the two WM tasks, between the two  
17 experimental groups (figure 3). Furthermore, analysis of variance on RTs failed to  
18 identify any significance as to the factor “group” in both SWM and VWM tasks (figure 3)

### 19 *3.3 Correlations between mental rotation and working memory tasks*

20 Considering the two groups as a whole, a significant correlation was found between the  
21 RT of the OMR task and the RT of the SWM task ( $r=0.696$ ;  $p=0.002$ ). Moreover, for each  
22 MR task but the feet rotation task, RA and RT were negatively correlated (for all,  $r > -$   
23  $0.531$  and  $p<0.03$ ), suggestive of a speed-accuracy tradeoff.

## 24 **4. Discussion**

25 The present study shows that patients with MD have intact abilities to mentally rotate



1 body parts as well as objects. Moreover, we demonstrated a correlation between SWM  
2 abilities and OMR, but not with BMR, in both healthy musicians and MD.

3 BMR is a cognitive task that requires the integrity of a cortical-subcortical network  
4 involved in the integration of sensory (somatosensory and visual) afferents with motor  
5 actions (motor and premotor areas and basal ganglia) [1-4]. Given that the  
6 pathophysiology of dystonia is suggested to affect sensori-motor integration [16], one  
7 would have expected MD patients to exhibit deficits in such a task. Similar research  
8 conducted in other forms of focal, task-specific dystonia, has in fact shown that patients  
9 with WC have an impairment of BMR, which is selective for the hands, at least as  
10 indicated by longer RT [14]. Interestingly, the authors found that such an abnormality  
11 was not only present in the affected (dystonic) hand, but also in the contralateral one  
12 [14], suggesting that the observed alterations were not merely consequential to the  
13 abnormal movements/postures, but existed prior to overt motor manifestations and  
14 might indeed contribute to the development of dystonia. Therefore, the key question  
15 remains as to why patients with these two types of task-specific, focal dystonia of the  
16 hand should behave differently using MR paradigms.

17 The first consideration that should be made is about the task-specificity of these two  
18 entities. A large body of work has in fact demonstrated that MD is highly specific for a  
19 certain type of task, which is not just playing music in general, but playing music with a  
20 certain instrument and not another one [12,17,18]. This reinforces the notion that MD is  
21 a strict task-specific dystonia and therefore (sensori)motor abilities other than playing  
22 music could be unaffected. In theory, the same argument could be raised for WC.  
23 However, additional evidence exists that the abnormalities seen in WC might be grosser  
24 than in MD. In fact, although WC is largely considered a task-specific dystonia, with  
25 careful assessment a more pervasive, if mild, motor control disorder can be

1 demonstrated [19]. Moreover, whereas musicians spend many hours per day on  
2 practice, WC patients have usually a history of average hand use [20], suggesting that  
3 the pre-existing abnormalities in the latter could be severer than in MD and bring on  
4 dystonic symptoms upon the execution of relatively simple and less-skilled actions. In  
5 line with this hypothesis, Ibanez et al. found WC patients to have deficient activation of  
6 such areas as prefrontal cortex and basal ganglia (e.g., areas that are seemingly involved  
7 in BMR as well) compared to healthy controls, also when performing non-writing tasks  
8 as tapping or maintaining a sustained wrist contraction [21]. Interestingly, these  
9 abnormalities were bilateral [21], in keeping with the observation that BMR is  
10 bilaterally altered in WC [14]. These lines of evidence would suggest that BMR  
11 abnormalities in WC are related to a more deranged sensori-motor network, whereas  
12 MD relies on a highly-selective disruption of a motor output that is contingent to playing  
13 a particular instrument but not to other motor tasks, thus accounting for the negative  
14 results observed here. Although this speculation cannot be directly made based on the  
15 current study (as we did not include patients with WC), it could be also argued that  
16 musical training can possibly enhance such cognitive processes involved in MR [22], so  
17 that direct comparisons between these two disorders would not be reliable. To avoid  
18 any artificial results owing to the musical training we in fact collected a group of healthy  
19 professional musicians to serve as controls. Studies directly comparing MD and WC are  
20 very scarce. Yet, preliminary evidence suggests that MD and WC might indeed have  
21 different electrophysiological abnormalities at the cortical level, supporting our  
22 argument [20].

23 Another factor that should be taken into account is about the possible body location-  
24 specificity of MD. For such a highly selective disorder as MD, it might appear that the  
25 definition of “affected hand” is rather unspecific. Indeed, patients with MD show motor

1 deficits that are limited to one or few fingers (most commonly among the first three  
2 ones) [12,17,18]. This might raise the question as to whether MR paradigms based on  
3 rotation of single fingers could identify subtler abnormalities in MD that are  
4 somatotopically congruent with the affected (dystonic) fingers. This speculation stems  
5 for the evidence that BMR is impaired in WC only for the hands [14]. However, MR  
6 paradigms have been used in other dystonia groups, including cervical dystonia [15] and  
7 generalized dystonia with *TOR1A* (DYT1) mutations [23]. Although a certain degree of  
8 MR impairment was observed in these populations, these were not somatotopically  
9 congruent with the affected body parts [15,23]. Thus, the relationship between the  
10 cognitive correlated of MR deficits and the development of dystonia needs to be  
11 clarified.

12 Finally, we demonstrated a correlation between SWM and rotational abilities for objects.  
13 Another study found the same and further demonstrated an association between OMR,  
14 SWM and the event-related P300 on electroencephalography (EEG) [10]. Despite the  
15 limited spatial resolution of the EEG, converging evidence would locate the posterior  
16 P300 generators in the same areas (temporal and parietal cortices) [24,25] that activate  
17 when mentally rotating an object [4,26]. This further suggests that BMR and OMR rely,  
18 at least partially, on different mechanisms. Whereas OMR would be linked to visuo-  
19 spatial abilities more in general, BMR seems to be largely dependent on the sensori-  
20 motor network subserving the actual preparation and execution of movements. In line  
21 with this view and in keeping with previous studies [1,5,6,14], we found that longer RT  
22 were required for the 180° orientation stimuli, corresponding to body part positions  
23 that would be actually difficult to maintain. This effect, despite being non-significant,  
24 was stronger for the feet, which are in fact the body parts where the *real* possible  
25 rotation is most restricted. Our results, arguing for a dissociation between the cognitive

1 mechanisms underlying BMR and OMR abilities, are supported by a recent *activation*  
2 *likelihood estimation* meta-analysis [27]. Thus, it was showed that bodily stimuli induce  
3 a bilateral sensorimotor activation as compared to non-bodily-related stimuli that  
4 instead lead to a posterior, right lateralized, activation [27]. Moreover, the networks  
5 subserving such abilities seem to be wide and involve many cortical areas that also deal  
6 with problem solving and decision-making [27]. In this regard, we acknowledge that our  
7 study is limited by the lack of an extensive neuropsychological battery.  
8 Moreover, given the small sample size, our results should be considered preliminary.  
9 Yet, they would suggest that patients with MD do not have deficits in mentally rotating  
10 body parts, implying that this disorder relies on a highly selective disruption of  
11 movement planning and execution than manifests (at least in the majority of cases) only  
12 upon playing a specific instrument. This would support a dissociation between the  
13 clinical sub-phenotypes grouped under “occupational dystonia”. Our results further  
14 suggest that mental rotation of body parts and objects engages different cognitive  
15 networks. In this context, it will be interesting to explore whether an interaction  
16 between these two cognitive processes take place, for instance showing patients with  
17 MD body parts while playing an instrument.

18

### 19 **Figure caption**

20 Figure 1. A-D: Examples of different probes used in the mental rotation tasks. E:  
21 Graphical description of the spatial working memory task.

22 Figure 2. Reaction time profiles at different stimulus orientations in musician dystonia  
23 (red squares) and control subjects (blue squares) for hands, feet, hemi-faces and letters  
24 (D). Panels on the left represent left-sided stimuli (mirror-reversed for the letter task).

25 Error bars indicate standard deviation.

1 Figure 3. Mean response accuracy (left panel) and reaction times (right panel) for both  
2 tasks of working memory in musicians' dystonia (blue bars) and healthy musicians (red  
3 bars). Error bars indicate standard deviation.

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