Mental rotation and working memory in musicians' dystonia

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Abstract

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

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

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

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

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

Musicians' dystonia (MD) is a type of focal, task-specific, hand dystonia affecting as many as 1 in 200 musicians during their career and often resulting in the termination of professional performance [12]. The pathophysiology of MD is not entirely clear [12]. There are many clinical and pathophysiological similarities between MD and other types of task-specific, focal dystonia such as writer's cramp (WC), so that MD and WC are usually grouped together under the umbrella of "occupational dystonia", based on the suggestion that over-training can induce maladaptive plasticity and results in dystonia [12-13]. In this context, previous research using MR paradigms has shown that patients with WC have deficits in BMR, which are selective to the hands, as compared to healthy controls, suggesting a close link between the impairment of motor planning/execution (at least as assessed by MR) and the manifestation of dystonia [14]. It is, however, unknown whether subjects with MD would display similar deficits with this paradigm, reinforcing the concept of shared pathophysiology between these two disorders.

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

2. Methods

2.1 Subjects

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

2.2 Procedure

The test was carried out in a quiet room. Subjects were seated in front of a computer screen (15 inches) with their non-dominant hand out of sight on their laps. The dominant hand was used to press the answer key (right/left arrow keys for right-handed subjects and z/c keys for left-handed subjects) on an international US-keyboard, as described below. All tasks were programmed using MatLab 2013b.

2.2.1 Mental rotation paradigm

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

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

2.2.2 Working memory tasks

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

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

2.3 Statistical analyses

Descriptive statistics (t-test and Fisher's test) were performed as appropriate. Normal distribution of data was checked by means of the Shapiro-Wilk test and Greenhouse–Geisser correction was used, when necessary, to correct for nonsphericity (e.g., Mauchly's test <0.05). Thus, RA and RT were analysed by means of two different analyses of variances (ANOVA). Only RTs to trials in which the correct response was made were considered. For each angular orientation, the averaged RT was entered in the analyses, as in previous works [14,15]. For MR results, each ANOVA had one between-subjects factor (group – e.g., MD versus healthy musicians) and three within-subjects factors: Stimulus type (hands, feet, hemi-faces and letters), stimulus side (left and right) and stimulus angular orientation (0, 45, 90, 135, 180, 225, 270 and 315 degrees). Additional analyses were performed to explore whether, within each MR task, there was a learning effect across the trials. Thus, the *trial number* factor was added to the ANOVA analyses, either discarding the *AO* factor (e.g., to explore a learning effect from trial 1 to 96, regardless of the AO) or considering the *AO* factor (e.g., to explore a learning effect from trial 1 to 6 for each AO).

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

3. Results

3.1 Mental rotation paradigm

There were no differences as to RA between the two groups in any of the four tasks. Mean percent accuracy showed that the 180° stimulus was the most difficult orientation for both left- and right-hand for both groups (supplementary table 1). The same trend was observed for feet, hemi-faces, and letters (supplementary table 1). Figure 2 represents mental rotation RTs contingent upon orientation of the stimuli in the two experimental groups. The analysis of variance on RTs showed no significance of the factor *group*, *stimulus side*, *stimulus orientation* or their interaction. Also, there was no significance of the factor "stimulus type", indicating that the time requested for mentally rotating hands, feet, hemi-face and letters was comparable, despite a non-significant trend ($p=0.06$, see figure 2 where it is appreciable that for both groups the RT for rotating the feet was higher than the time requested to rotate other stimuli).

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

3.2 Working memory tasks

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

3.3 Correlations between mental rotation and working memory tasks

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

4. Discussion

The present study shows that patients with MD have intact abilities to mentally rotate body parts as well as objects. Moreover, we demonstrated a correlation between SWM abilities and OMR, but not with BMR, in both healthy musicians and MD.

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

The first consideration that should be made is about the task-specificity of these two entities. A large body of work has in fact demonstrated that MD is highly specific for a certain type of task, which is not just playing music in general, but playing music with a certain instrument and not another one [12,17,18]. This reinforces the notion that MD is a strict task-specific dystonia and therefore (sensori)motor abilities other than playing music could be unaffected. In theory, the same argument could be raised for WC. However, additional evidence exists that the abnormalities seen in WC might be grosser than in MD. In fact, although WC is largely considered a task-specific dystonia, with careful assessment a more pervasive, if mild, motor control disorder can be demonstrated [19]. Moreover, whereas musicians spend many hours per day on practice, WC patients have usually a history of average hand use [20], suggesting that the pre-existing abnormalities in the latter could be severer than in MD and bring on dystonic symptoms upon the execution of relatively simple and less-skilled actions. In line with this hypothesis, Ibanez et al. found WC patients to have deficient activation of such areas as prefrontal cortex and basal ganglia (e.g., areas that are seemingly involved in BMR as well) compared to healthy controls, also when performing non-writing tasks as tapping or maintaining a sustained wrist contraction [21]. Interestingly, these abnormalities were bilateral [21], in keeping with the observation that BMR is bilaterally altered in WC [14]. These lines of evidence would suggest that BMR abnormalities in WC are related to a more deranged sensori-motor network, whereas MD relies on a highly-selective disruption of a motor output that is contingent to playing a particular instrument but not to other motor tasks, thus accounting for the negative results observed here. Although this speculation cannot be directly made based on the current study (as we did not include patients with WC), it could be also argued that musical training can possibly enhance such cognitive processes involved in MR [22], so that direct comparisons between these two disorders would not be reliable. To avoid any artificial results owing to the musical training we in fact collected a group of healthy professional musicians to serve as controls. Studies directly comparing MD and WC are very scarce. Yet, preliminary evidence suggests that MD and WC might indeed have different electrophysiological abnormalities at the cortical level, supporting our argument [20].

Another factor that should be taken into account is about the possible body location-specificity of MD. For such a highly selective disorder as MD, it might appear that the definition of “affected hand” is rather unspecific. Indeed, patients with MD show motor deficits that are limited to one or few fingers (most commonly among the first three ones) [12,17,18]. This might raise the question as to whether MR paradigms based on rotation of single fingers could identify subtler abnormalities in MD that are somatotopically congruent with the affected (dystonic) fingers. This speculation stems for the evidence that BMR is impaired in WC only for the hands [14]. However, MR paradigms have been used in other dystonia groups, including cervical dystonia [15] and generalized dystonia with *TOR1A* (DYT1) mutations [23]. Although a certain degree of MR impairment was observed in these populations, these were not somatotopically congruent with the affected body parts [15,23]. Thus, the relationship between the cognitive correlated of MR deficits and the development of dystonia needs to be clarified.

Finally, we demonstrated a correlation between SWM and rotational abilities for objects. Another study found the same and further demonstrated an association between OMR, SWM and the event-related P300 on electroencephalography (EEG) [10]. Despite the limited spatial resolution of the EEG, converging evidence would locate the posterior P300 generators in the same areas (temporal and parietal cortices) [24,25] that activate when mentally rotating an object [4,26]. This further suggests that BMR and OMR rely, at least partially, on different mechanisms. Whereas OMR would be linked to visuo-spatial abilities more in general, BMR seems to be largely dependent on the sensori-motor network subserving the actual preparation and execution of movements. In line with this view and in keeping with previous studies [1,5,6,14], we found that longer RT were required for the 180^{o} orientation stimuli, corresponding to body part positions that would be actually difficult to maintain. This effect, despite being non-significant, was stronger for the feet, which are in fact the body parts where the *real* possible rotation is most restricted. Our results, arguing for a dissociation between the cognitive mechanisms underlying BMR and OMR abilities, are supported by a recent *activation likelihood estimation* meta-analysis [27]. Thus, it was showed that bodily stimuli induce a bilateral sensorimotor activation as compared to non-bodily-related stimuli that instead lead to a posterior, right lateralized, activation [27]. Moreover, the networks subserving such abilities seem to be wide and involve many cortical areas that also deal with problem solving and decision-making [27]. In this regard, we acknowledge that our study is limited by the lack of an extensive neuropsychological battery.

Moreover, given the small sample size, our results should be considered preliminary. Yet, they would suggest that patients with MD do not have deficits in mentally rotating body parts, implying that this disorder relies on a highly selective disruption of movement planning and execution than manifests (at least in the majority of cases) only upon playing a specific instrument. This would support a dissociation between the clinical sub-phenotypes grouped under "occupational dystonia". Our results further suggest that mental rotation of body parts and objects engages different cognitive networks. In this context, it will be interesting to explore whether an interaction between these two cognitive processes take place, for instance showing patients with MD body parts while playing an instrument.

Figure caption

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

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

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

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