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ORIGINAL COMMUNICATION

Spatial and egocentric mental rotation in patients with cervical dystonia

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Abstract
Mental rotation has attracted the interest of cognitive research on dystonia, but at the moment, contrasting data are available on whether this complex cognitive ability is impaired in the disorder. Here, we assessed spatial and egocentric mental rotation in patients with cervical dystonia (CD). Patients with CD and healthy controls were required to perform a letter rotation task (spatial mental rotation) and to judge laterality of front-facing and back-facing human images (egocentric mental rotation). CD patients were selectively impaired on letter rotation, whereas they did not differ from controls when judging laterality of both front-facing and back-facing bodies. These findings support the view according to which neural circuits involved in spatial processing are dysfunctional in CD.

Keywords Cervical dystonia · Mental rotation · Mental transformation · Spatial abilities

Introduction

Cervical dystonia (CD) is characterized by involuntary contractions of neck muscles leading to a wide variety of abnormal head and neck postures [1], as head and neck twist (torticollis), or bending forward (anterocollis), backward (retrocollis), or sideways (laterocollis). Although CD is the most common form of idiopathic focal dystonia, the pathophysiology of the abnormal head postures is still unclear [2, 3].

Several data supported the view that despite the motor conceptualization of CD, sensory systems and higher-level cognitive abilities are also affected. In particular, CD patients have difficulties on different spatial tasks as localization of visual, auditory, or tactile stimuli [4–6], line bisection [7], straight-ahead pointing [8], and spatial memory [9].

Mental rotation is another complex spatial ability that has attracted the interest of research on cognitive functioning in patients with different forms of dystonia [10–15]. Literature on mental rotation has traditionally distinguished spatial (object-based) mental transformation [16] and egocentric mental transformation [17]. Spatial transformations are imagined rotations of objects relative to the spatial reference frame of the environment and have been classically assessed by tasks requiring participants to judge whether pairs of three-dimensional images differing in spatial orientation were the same or different or whether two-dimensional rotated objects, as letters or numbers, faced normally or were mirror-reversed [16, 18]. Egocentric transformations are, instead, imagined rotations or translations of one's point-of-view relative to the reference and have been usually studied through tasks requiring subjects to make left–right judgments on pictures of human bodies presented at varying orientations [17, 19]. To solve this task, participants have to mentally simulate moving themselves into the position of the human figure (egocentric transformation) [17, 19], analogously to mental rotation tasks requiring simulation of hands' movements [20].

Past behavioral studies on mental rotation in CD patients reported no significant, or only marginally significant,

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differences between patients and controls on the Ratcliff Figures test [21], a paper-and-pencil mental rotation task requiring participants to decide whether the black hand of a manikin drawing, presented in either an upright or an inverted position, was on the manikin's right or left sides [11, 14]. More recently, Fiorio et al. [10] used a computerized mental rotation task requiring patients with CD to mentally rotate images of the affected (neck) and unaffected (hands and feet) body parts, and images of a car; results showed a deficit of CD patients in mental rotation of stimuli representing head, hand, and foot, whereas no deficit was found in mental rotation of the non-corporeal objects. However, in a study searching for the most discriminative test to separate patients with CD and healthy controls, Kägi et al. [12] demonstrated that mental rotation tasks requiring to mentally transform corporeal stimuli (head, hand, and foot), as in Fiorio et al.'s study [10], were not suitable to separate patients from controls, since no between-group difference was found in behavioral performance.

Together, inconsistent results are available on mental rotation in dystonia, and in particular on CD. One possible reason could be found in the complex nature of mental rotation, since different kinds of stimuli and experimental tasks can recruit distinctive cognitive strategies, thus preventing to clarify whether this cognitive ability is impaired in CD and whether a distinction can be made between the two main types, i.e., spatial vs. egocentric, of mental rotation.

In the present study, we selected two classical and well-validated mental rotation tasks [18, 19] allowing to directly compare spatial and egocentric mental transformation in CD. Indeed, patients and healthy controls were asked to perform an object-based transformation task requiring mental rotation of letters [19] and a body rotation task requiring laterality judgments on a human image [18]. By these means, we could test whether a generalized mental transformation deficit was present in CD or whether a dissociation between spatial vs. egocentric mental rotation could be found in the syndrome.

Material and methods

Participants

Twenty-one (13 females and 8 males; mean age = 56.5 years, SD = 10.8, range 34–75 years; mean education = 14.7, SD = 2.5, range 11–18 years) consecutive outpatients with idiopathic and isolated cervical dystonia [1] were recruited for this study at the Department of Neurosciences, Reproductive Sciences and Odontostomatology of University of Naples "Federico II" from 2016 to 2017. All patients were responsive to treatment with botulinum toxin injections administered every 3 or 4 months. Idiopathic or isolated CD was diagnosed on clinical basis; brain MRI or CT scan was occasionally performed to exclude secondary cases. All patients showed head and neck abnormal postures with cervical rotation and/or tilting; extension and flexion of the neck could also be present. None of the patients had a strict retrocollis or anterocollis, and thus, patients were distinguished in two phenotypes depending on the prevailing dystonic position: laterocollis, when patients mainly showed neck tilting to the shoulder; and rotatocollis when rotation of head and neck was more evident than other postural abnormalities. Detailed demographic and clinical features of each CD patient are reported in Table 1.

Twenty-one right-handed healthy subjects (12 females and 9 males) matched to patient group for age (mean = 56.6 years, SD = 10.6, range 35–74 years) and education (mean = 14.7, SD = 2.5, range 11–18 years) took part in the experiment as controls.

For both groups, exclusion criteria were the following: (1) diagnosis of Parkinson disease or any other neurologic or psychiatric disorder; (2) clinically evident dementia or major depression; (3) general intellectual impairment, defined by an age- and education-adjusted score on the Italian version of the MOCA < 15.5 [22].

The study was approved by the Local Committee and was conducted in accordance with the ethical standards of the Helsinki Declaration. Informed consent was obtained from all participants after the nature of the study was explained to them.

Experimental tasks

CD patients and healthy controls underwent letter rotation and body rotation tasks. In particular, patients were administered the two tasks just before receiving the periodic injection of botulinum toxin, and thus, the effect of the last injection (at least 3 months before) had worn off and the motor symptoms were evident.

In the *letter rotation task*, participants were required to judge whether a capital letter (R) presented on a computer screen was in the canonical or mirror-reversed form [18]. Stimuli consisted of line drawings depicting letters in canonical or mirror-reversed form, and presented in four spatial orientations: 0°, 90°, 180°, and 270° in clockwise direction (Fig. 1).

In the *body rotation task*, participants were required left–right judgments on a human image whose left hand or right hand was marked to appear as wearing a black glove, after having imagined themselves in the figure's body position [19]. Stimuli consisted of line drawings depicting body images facing toward (front-facing) or away (back-facing) from the observer, whose right hand or left hand was marked in black. As in the letter rotation task, bodies

Table 1 Demographic and clinical features of the CD group

Phenotype (L = laterocollis; R = rotatocollis)	Age	Sex (M = male; F = female)	TSUI score	Tremor (Y = yes; N = no)	Side of the deviation (l = left; r = right)	Disease duration (years)
L	60	M	10	Y	l	2
L	65	F	11	N	r	3
L	57	M	12	Y	l	25
R	56	F	7	N	l	15
R	56	F	6	Y	r	40
L	67	F	9	N	l	6
R	59	F	5	N	l	11
R	75	F	6	N	l	6
L	58	F	9	N	r	9
R	56	M	7	N	r	15
L	67	F	5	N	l	12
L	73	M	3	Y	r	15
L	52	M	4	N	r	2
L	46	F	8	N	r	3
L	48	F	9	N	l	3
L	40	M	8	N	r	3
L	34	F	7	Y	r	1
R	53	M	14	N	r	3
L	42	M	5	N	l	3
R	53	F	5	Y	l	1
L	70	F	4	N	l	2

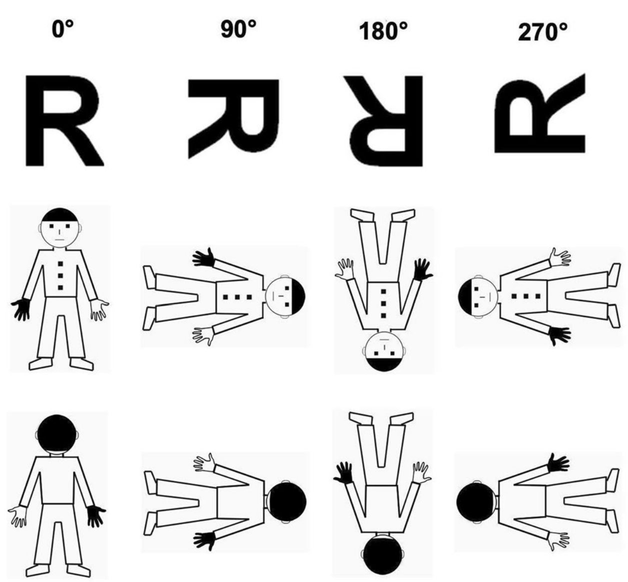

Fig. 1 Instances of stimuli used in the mental rotation tasks: letter rotation (first row), body rotation (front-facing: second row; back-facing: third row), in the four spatial orientations: 0°, 90°, 180°, and 270° (schematic human figures with their left hand marked in black, and letters in the mirror-reversed form are not reported here)

were presented in four spatial orientations (0°, 90°, 180°, and 270° in clockwise direction) (Fig. 1).

Both letter and body rotation tasks consisted of 48 trials: in the letter rotation task, six trials were presented for each combination of type of stimulus (canonical or mirror-reversed) and spatial orientation; in the body rotation (both front-facing and back-facing views), six trials were presented for each combination of hand laterality (left or right) and spatial orientation. Trials were randomized within each task, which was divided into two blocks, with a 3-min pause allowed between the two blocks. Each trial started with a fixation point (1000 ms) at the center of the monitor, and then followed by stimulus (letter or body image) that remained on view until response completion. Patients and controls gave their responses by pressing one of two centrally located keys (B and H keys on QWERTY keyboard) with their index and middle fingers of the dominant hand, while placing the other in a comfortable position, palm down next to the keyboard. The stimulus–response association for each task was counterbalanced across participants.

Before starting each task, eight practice trials were given; if a wrong response was provided, feedback appeared on the monitor screen and the trial was repeated. Experimental session started only if the participants provided at least six consecutive correct responses. Participants were encouraged to respond as correctly as possible.

Stimulus presentation and data collection were controlled by a PC using Cedrus SuperLab v.4. Testing was conducted in a quiet room and in a single session that lasted about 20 min; the order of the two tasks was counterbalanced across participants.

Results

Raw data are available upon request (massimiliano.conson@unicampania.it).

Letter rotation

A two-way mixed-design ANOVA was performed on accuracy, with spatial orientation (0°, 90°, 180°, and 270°) as within-subject factors, and with group (CD patients and healthy subjects) as a between-subject factor. Results showed a significant main effect of stimulus orientation, $F(3,120) = 25.345$, $p = 0.0001$, $\eta^2_p = 0.388$, with the classical bell-shaped pattern of response; Bonferroni corrected post hoc comparisons showed that accuracy was significantly higher at 0° (mean = 0.96, SEM = 0.01) with respect to all the other orientations (all $p = 0.001$), it progressively decreased at both 90° (mean = 0.83, SEM = 0.03) and 270° (mean = 0.85, SEM = 0.03) without differences between the two orientations ($p > 0.05$), and finally, it significantly dropped at 180° (mean = 0.67, SEM = 0.04) with respect to all the other orientations (all $p = 0.0001$). Moreover, we found a significant main effect of group, $F(1,40) = 9.290$, $p = 0.004$, $\eta^2_p = 0.188$, with lower accuracy of CD patients (mean = 0.76, SEM = 0.03) than controls (mean = 0.89, SEM = 0.03), whereas the interaction between spatial orientation and group only showed a trend towards significance, $F(3,120) = 2.376$, $p = 0.073$, $\eta^2_p = 0.056$ (Fig. 2).

Body rotation

A three-way mixed-design ANOVA was performed, with stimulus view (front-facing or back-facing) and spatial orientation (0°, 90°, 180°, or 270°) as within-subject factors, and with group (CD patients or controls) as a between-subject factor. Results showed a significant effect of spatial orientation; Bonferroni corrected post hoc comparisons showed that accuracy was significantly lower at 180° (mean = 0.82, SEM = 0.03) with respect to 90° (mean = 0.90, SEM = 0.02; $p = 0.001$) and 270° orientations (mean = 0.89, SEM = 0.03; $p = 0.031$), but not with respect to 0° orientation (mean = 0.87, SEM = 0.04; $p > 0.05$). Moreover, there was a significant interaction between view and spatial orientation, $F(3,120) = 6.337$, $p = 0.002$, $\eta^2_p = 0.137$, showing a different influence of stimulus orientation on accuracy depending on the perspective of the body image; indeed, in the front-facing view, Bonferroni corrected post hoc comparisons did not show significant differences among the four spatial orientations (0°: mean = 0.86, SEM = 0.04; 90°: mean = 0.91, SEM = 0.02; 180°: mean = 0.87, SEM = 0.03; 270: mean = 0.83, SEM = 0.04; all $p > 0.05$); in the back-facing view, Bonferroni corrected post hoc comparisons showed that accuracy was significantly higher for 270° stimuli (mean = 0.94, SEM = 0.02) with respect to all the other orientations (0°: mean = 0.87, SEM = 0.03; 90°: mean = 0.88, SEM = 0.03; 180: mean = 0.77, SEM = 0.04; all $p < 0.039$), with a significant difference also between 90° and 180° orientations ($p = 0.024$). All remaining main effects and interactions were not significant ($p > 0.05$). Remarkably, the accuracy profile of CD patients and controls was almost

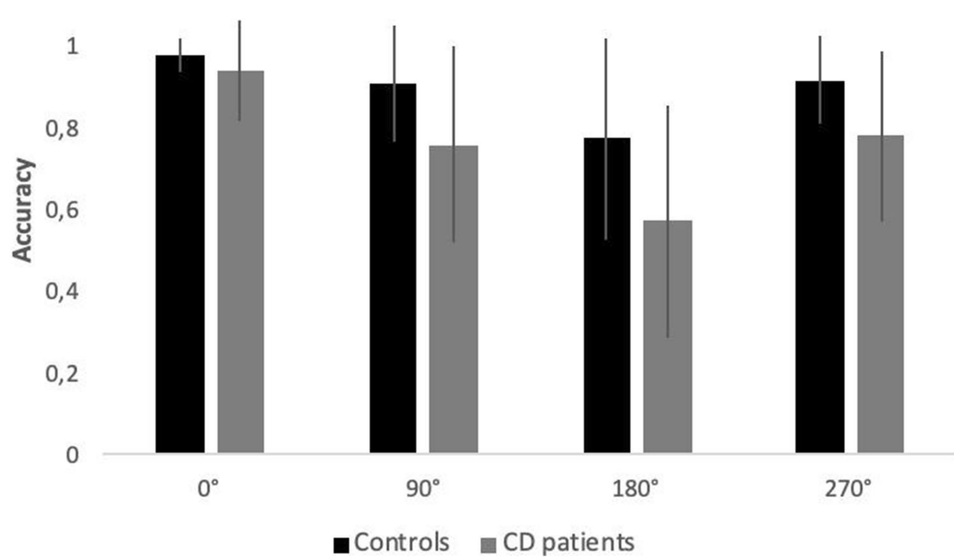

Fig. 2 Mean accuracy (bars are SD) on letter rotation as a function of stimulus orientation, separately in CD patients and controls

similar across all combinations of stimulus view and orientation (Fig. 3).

Correlations of mental rotation performance with disease severity and duration

In the patient group, the correlations between severity (TSUI score) and duration of the disease with performance on the letter and body rotation tasks were not significant (Spearman correlation, all $p > 0.05$).

Analysis on CD phenotypes

An in-depth between-group comparison was performed taking into account the phenotype of CD. We, thus, compared the two phenotype groups (laterocollis: $n = 14$; rotatocollis: $n = 7$) with the control group on the total accuracy on two mental rotation tasks. Because of the small and the different size of the two subsamples of the patient group, statistical analysis was performed by means of non-parametric methods (Mann–Whitney U test). The two phenotype groups did not differ for demographics, disease severity and duration, while comparisons on mental rotation tasks confirmed data reported above (Table 2). More precisely, results showed that, on letter rotation, accuracy of both phenotype groups was lower than controls, although the comparison between laterocollis group and controls reached the significance, while the comparison between rotatocollis group and controls was only marginally significant; the difference between the two phenotypes was not statistically significant. Between-group comparisons on body rotation never revealed statistically significant differences.

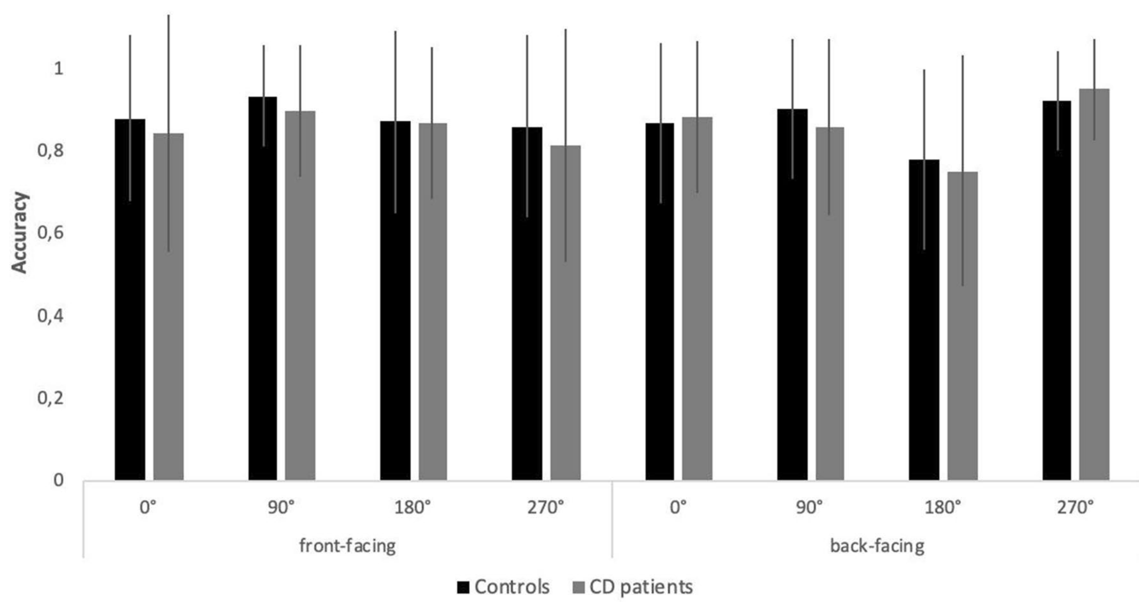

Fig. 3 Mean accuracy (bars are SD) on body rotation as a function of stimulus orientation and view (front-facing and back-facing), separately in CD patients and controls

Table 2 Demographics, disease severity (TSUI) and duration of the two CD phenotypes, total accuracy in letter and body rotation tasks, and summary of between-group statistical comparisons (laterocollis, L; rotatocollis, R; controls, C)

	L group ($n=14$)	R group ($n=7$)	C group ($n=21$)	L vs. R	L vs. C	R vs. C
Age	55 ± 11.7	58 ± 9.2		$U=43.5$, $p=0.68$		
Education	10.8 ± 4.4	11.3 ± 4.2		$U=44.5$, $p=0.73$		
TSUI	7.4 ± 2.8	7.1 ± 3.1		$U=43$, $p=0.65$		
Disease duration	6.4 ± 6.8	13 ± 13.1		$U=31.5$, $p=0.18$		
Letter rotation	0.76 ± 0.16	0.78 ± 0.18	0.89 ± 0.11	$U=48$, $p=0.94$	$U=71$, $p=0.01$	$U=39$, $p=0.06$
Body rotation	0.85 ± 0.18	0.87 ± 0.11	0.88 ± 0.12	$U=47.5$, $p=0.91$	$U=136$, $p=0.71$	$U=68.5$, $p=0.79$

Discussion

Results demonstrated a specific difficulty of CD patients in mentally rotating letters while leaving spared mental rotation of body images presented both in front-facing and back-facing views.

Mentally rotating bi- or three-dimensional objects implies the so-called spatial (object-based) transformation referring to imagined rotations or translations of objects relative to the spatial reference frame of the environment, whereas mental rotation of body or body parts implies the so-called egocentric transformation referring to imagined movements of one's own body or body parts toward the visual stimulus [16–20].

In a seminal neuroimaging study, Zacks et al. [19] presented participants with front-facing or back-facing human figures with one outstretched arm; to judge which arm was outstretched (i.e., left–right judgment), participants imagined themselves in the position of the figure. Hence, this body rotation seems to imply some sort of "rotation of the self", and thus consisting in an egocentric transformation. However, other authors suggested that body rotation can also be accomplished by resorting to an object-based, spatial transformation not related to self-body representation, thus undermining the idea that body rotation actually represents an egocentric transformation [23]. The present results showing that letter rotation can be specifically impaired in CD might provide support to the view according to which object-based and body mental rotation could be related to different cognitive processes.

Although several neuropsychological studies investigated mental rotation abilities in CD patients, available results are contrasting. In particular on a simplified, paper-and-pencil, version of the body rotation task no significant, or marginally significant, differences have been found between patients with CD and controls [11, 14]. On a computerized version of the mental rotation of body parts and objects, CD patients were found to be impaired on mental rotation of head, hand, and feet while being able to rotate the image of a car [10]. However, impaired mental rotation of corporeal stimuli [10] was not confirmed by a recent study by Kägi et al. [12], underscoring that mental rotation of body parts does not allow to discriminate between CD patients and controls. Here, we employed object-based and body rotation tasks that have been widely used in the classical literature on mental rotation and have been proved to be a reliable measure of this cognitive ability [17–19]. By this means, we could highlight that spatial rather than egocentric transformation was defective in CD patients, consistent with data demonstrating difficulties in different aspects of spatial processing in this clinical population [4–9]. In particular, it has been suggested that spatial deficits in CD could be related to the dysfunctional activity of a circuit involving the associative parietal cortex, the cerebellum, and subcortical structures [4, 5, 7, 24]. Recent neurophysiological models of dystonia underline the key role of cerebellum within the so-called neural integration model combining visual and proprioceptive information to control head movements [25]. Clinical neuropsychology and cognitive neuroscience literature demonstrated the pivotal role of parietal cortex and cerebellum in spatial mental rotation [26–29]. Interestingly moreover, some classical studies on mental rotation demonstrated that manipulating head position in healthy persons significantly affect mental rotation of letters and numbers [30, 31]. Our results nicely fit these findings, thus providing support to the view that complex neural circuits involved in spatial processing are implied in neuropsychological symptoms of CD.

From a clinical point-of-view, the present results would be consistent with data suggesting that mental rotation of corporeal stimuli (body or body parts) cannot represent an appropriate task to differentiate CD patients from controls [12], and allow to make a step forward suggesting that a suitable way to comprehensively assess cognition in movement disorders could also include testing object-based mental rotation, for instance using letter rotation.

As a limitation of the study, we have to underline the heterogeneous composition of the patient group, especially with respect to age and disease of duration. Indeed, although our analysis on correlations of performance with disease severity and duration and on differences between CD phenotypes did not revealed significant results, the present data need to be replicated in future research on a more homogeneous group. Notwithstanding this limitation, the present findings could be of interest to improve characterization of the complex clinical picture of CD. Indeed, although most of the subjects with CD have persistent benefits from botulinum toxin injections over years [32], there is still a group of patients, responsive to the treatment and with a low degree of disease severity, who complains deep discomfort from dystonia [33, 34]. Such a poor association between clinical presentation and severity perception of the disease is still unclear. We could speculate that the spatial deficits found in the present study could be part of a complex cognitive pattern contributing to the subjective feeling of discomfort produced by dystonia. In this respect, our study might contribute to debate on the pathophysiology of CD by elucidating the neuropsychological functioning of the disorder. Further investigations are needed to relate cognition, quality of life, and severity of the disease in patient with CD.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical standard The study was approved by the Local Committee and was conducted in accordance with the ethical standards of the Helsinki Declaration. Informed consent was obtained from all participants after the nature of the study was explained to them.

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