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### ► To cite this version:

Julie Di Marco, Marine Lunven, Patrice Revol, Laure Christophe, Sophie Jacquin-Courtois, et al.. Regression of left hyperschematia after prism adaptation: A single case study. *Cortex*, 2019, 119, pp.128 - 140. 10.1016/j.cortex.2019.04.002 . hal-03484620

**HAL Id: hal-03484620**

**<https://hal.science/hal-03484620>**

Submitted on 20 Dec 2021

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## Regression of left hyperschematia after prism adaptation: a single case study

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1 Abstract

2

3 Prism adaptation (PA) is a promising treatment in the rehabilitation of post-stroke cognitive  
4 disorders such as unilateral spatial neglect or constructional deficits. Right brain damage can  
5 bring about another representational spatial disorder, termed «hyperschematia», and defined  
6 by a left-sided disproportionate expansion of drawings by copy and from memory, and by an  
7 overestimation of left lateral extent when a leftward movement is required. This case study  
8 aimed at evaluating the effect of PA induced by prismatic lenses creating a shift to the left on  
9 hyperschematia signs. A 63-year-old woman with left hyperschematia, consecutive to a right  
10 fronto-temporo-parietal hematoma, was exposed to a leftward optical deviation produced by  
11 prismatic lenses. An anatomical MRI studied topography of the brain lesion; the patient's  
12 lesion was then mapped onto tractography reconstructions of white matter pathways. Results  
13 showed that PA significantly reduced the left-sided expansion of drawing by copy and from  
14 memory, and the overestimation of left lateral extent, immediately after prism removal and 4  
15 days later, indicating a persistent long lasting cognitive effect. MRI showed a right hemisphere  
16 disconnection of the posterior and long segments of the arcuate fasciculus, and of the inferior  
17 longitudinal and fronto-occipital fasciculi. Overall, these findings suggest that: i) PA is effective  
18 also in hyperschematia by re-orientating spatial attention towards the right side of space,  
19 with a relative rightward PA-induced unbalance, and re-setting the spatial representation to  
20 the left side of space, contralateral to the side of the lesion; ii) the left misrepresentation of  
21 lateral extent may be related to a disconnection between visual coordinates and attentional  
22 networks to the frontal lobe.

23

24 Key words: hyperschematia, prism adaptation, space representation, bottom-up.

25

## 1. Introduction

Prism adaptation (PA) is one of the most widely used and studied rehabilitation methods on a large range of spatial neglect manifestations, including visual neglect (Pisella et al., 2006; Rossetti et al., 1998), somatosensory and haptic neglect (Dijkerman et al., 2003), tactile extinction (Maravita et al., 2003), hearing biases (Pochopien & Fahle, 2017), representational neglect, numerical representations (Rode et al., 2001; Rossetti et al., 2004), and everyday activities like writing or wheelchair driving (Jacquin-Courtois et al., 2008). The logic underlying the utilization of PA to improve deficits such as spatial neglect consists in taking advantage of the systematic leftward shift of visuomotor and proprioceptive responses induced during an active exposure to a rightward optical deviation of the visual field. PA reorients behavior of neglect patients toward the neglected side and produces a reduction of their deficits. These effects have also been reported for neglect symptoms involving no visual or manual components, such as representational neglect (Rode et al., 2001) suggesting that the effects of PA extend to higher-level, supramodal representations of space (Jacquin-Courtois et al., 2013).

The common ground permitting to explain the improvement of neglect symptoms remains debated. One possible candidate is the realignment of the visuo-motor space through adaptation, which would lead to the simultaneous enlargement and shift of the visuo-attentional space (Redding et al., 2005; Redding & Wallace, 2006; Rode et al., 2001; Rossetti et al., 2004). In case of left spatial neglect, which associates a shift and a restriction of the attentional field toward the ipsilesional side, such mechanism of action would stimulate the regression of visuo-perceptive and visuo-motor symptoms (see review in Barrett et al., 2012; Rossetti et al., 2015). The reorientation of exogenous and endogenous attentional components toward the pathological side may contribute to reduction of left-sided behavioural bias, and a more symmetrical construction of 2D or 3D allocentric and egocentric space representation. In representational neglect, such as neglect for the left side of an imagined map of France (Rode et al., 2001; Rossetti et al., 2004), PA would increase the capacity to find the topographic location. The re-orientation of the attentional bias towards the left side of imagined space after PA may favour the building up of a more symmetrical representation of space, and the access to topographic information in relation to that part of

1 space, as if the positive effects of PA on processes involved in spatial localization ('where')  
2 facilitate the recall of semantic knowledge ('what') (Glize et al., 2017; Rode et al., 2004;  
3 2010).

4 PA may also temporarily improve constructional deficits (Rode et al., 2006a), and  
5 navigation and representation in virtual reality (Glize et al., 2017) in right brain-damaged  
6 patients with left neglect, and postural imbalance in patients with left hemiparesis (Hugues et  
7 al., 2015; Tilikete et al., 2001). PA may also reduce pathologic pain in the Complex Regional  
8 Pain Syndrome (CRPS) (Bultitude & Rafal, 2010; Christophe et al., 2016; Sumitani et al., 2007).  
9 Effects such as those on constructional abilities, independent of neglect, and on the CRPS  
10 indicate that the effects of PA may be not confined to deficits of spatial attention and  
11 representation contralateral to the side of the cerebral lesion, such as in the case of unilateral  
12 spatial neglect (Bultitude et al., 2017; Legrain et al., 2012; Moseley et al., 2013).

13 In this study, we investigated the effects of PA on a representational spatial disorder  
14 consecutive to a right brain damage, such as hyperschematia (Rode et al. 2006b, 2008, 2014).  
15 Right-brain-damaged patients with left hyperschematia exhibit a left-sided disproportionate  
16 expansion of drawings, both by copying and from memory, contralateral to the side of the  
17 hemispheric lesion. In a series of 7 right-brain damaged patients with left hyperschematia,  
18 this symptom-complex also included an overestimation of left lateral extent, when a leftward  
19 movement was required, an unawareness of the disorder, and no unilateral spatial neglect; a  
20 perceptual underestimation of the lateral extent of objects located in the left hand-side of  
21 space was not a deficit present in all patients. This left-sided space expansion can be  
22 interpreted in terms of a lateral leftward distortion of the representation of extra-personal  
23 space, with a leftward anisometric expansion (relaxation) of the spatial medium.

24 Hence, the present study aimed at assessing this hypothesis, namely: whether PA can  
25 reduce the left-sided disproportionate expansion of drawings, both by copying and from  
26 memory, contralateral to the side of the hemispheric lesion, and the disproportionate  
27 overestimation of left lateral extent, when a leftward movement is required in a patient with  
28 left hyperschematia. We reasoned that, since left unilateral spatial neglect is ameliorated by  
29 adaptation to prisms deviating the visual scene rightward, with leftward aftereffect, in the  
30 case of a disproportionate leftward relaxation of the spatial medium, such as that taking place

1 in left hyperschematia, where patients «expand», rather than «neglect», the left side of  
2 space, the appropriate adaptation was the one to prisms deviating the visual scene leftward,  
3 with rightward aftereffect.

4 This reverse orientation of prisms is also described for rehabilitation of right neglect in  
5 case of left-brain damaged patients. PA could temporarily improve right personal neglect  
6 (Facchin et al., 2017). But even if patients adapted to prisms, rightward aftereffect was  
7 reduced compared with right-brain-damaged patients (Magnani et al., 2011; Ronchi et al.,  
8 2018), underlying the role of the left hemisphere in mediating effect of PA.

9

10 In the seven right brain-damaged patients with left hyperschematia reported by Rode  
11 and coworkers (2006b, 2008, 2014) evidence for a disproportionate expansion of the  
12 representation of the left side of space was provided using the tasks of drawing objects (a  
13 daisy) from memory and by copy, judging the lateral extent of two horizontal rectangles  
14 (perceptual matching), and reproducing in the leftward and in the rightward direction  
15 (namely, starting respectively from the leftward and the rightward endpoints of a line, aligned  
16 with the mid-sagittal plane of the participant's body) the lateral extent of horizontally  
17 presented lines (line extension task). All patients with left hyperschematia showed evidence  
18 for a disproportionate leftward expansion in the drawing tasks. Conversely, in the perceptual  
19 matching task, while four patients exhibited a relative underestimation of the lateral extent of  
20 the leftward rectangle (with scores being significantly different than the average of controls in  
21 three patients) this was not the case for three patients, with one such patient exhibiting if  
22 anything a significant underestimation of the rightward rectangle, as compared with control  
23 participants. Overall, these findings suggest that the perceptual underestimation of the  
24 leftward extension of objects is not likely to be a crucial mechanism underlying the  
25 hyperschematic deficit in drawing (Rode et al., 2014). Finally, in the line extension task, group  
26 analyses show in patients significant leftward, but not rightward, hyperextension, in  
27 comparison with control participants. Based on this evidence, the effects of PA on drawing,  
28 perceptual matching and line extension tasks were assessed in patient FV.

29

## 2. Case report

A 63-year-old right-handed woman (FV), with a middle school level (BTEC First Diploma), with a history of arterial hypertension and essential thrombocythemia, was admitted to a neurological unit for the sudden onset of left hemiparesis, left homonymous hemianopia, and left spatial neglect, consecutive to a right fronto-temporo-parietal haematoma. One month after stroke onset, the patient showed no left-sided motor or somatosensory deficits, including tactile and proprioceptive sensation, and no tactile extinction to double simultaneous stimulation (see Bisiach & Faglioni, 1974). There were neither motor nor ideational apraxia, nor underutilization of the left-sided limbs. There were no dexterity disorders. However a left lower quadrantanopia remained, with the patient being aware of her visual deficit. Visual acuity was normal (10/10). The patient was alert and cooperative, and showed an auditory extinction at a clinical exam, but no left spatial neglect. In a line cancellation test the patient crossed out 40/40 lines (Albert, 1973). In a star cancellation test the patient crossed out 55/56 targets, with one omission in the left side of the display (Wilson et al., 1987). In a letter cancellation task (Diller et al., 1974), the patient crossed out 51/53 targets in the left-hand side, and 48/51 targets in the right-hand side of the sheet. In a line bisection task (Schenkenberg et al., 1980) the patient scored +0.4%, within the normal range (mean -0.7%, S.D.  $\pm 2.46$ , range -4.3 - +2.9), see Rode et al., 2006b. The patient was able to read correctly short and long words, numbers, sentences, and passages of text, presented on an A4 sheet, with the center of the stimulus being aligned with the midsagittal plane of the patient's trunk. The patient did not show constructional apraxia in drawing figures such as a cube, a house, and a pyramid, both by copy, and from memory (table 1). However, in drawing by copy, and from memory, the patient showed no evidence of spatial neglect but produced symmetrical objects (a fir tree, a Christmas fir tree, a butterfly, a daisy) disproportionately larger on the left-hand side (Figure 1), and was unaware of this deficit, as the 7 right-brain-damaged patients reported by Rode et al. (2014).

The experimental procedure was applied 1 month post-onset of their stroke. Consent of patient was obtained.

Control (C) data were provided by six right-handed neurologically unimpaired participants [three females; mean age: 54.8 years (range 34–78); mean years of schooling: 12 (range 9–18)] from previous studies (Rode et al., 2006b, 2008).

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Insert here Table 1

Insert here Figure 1

### 3. Experimental study

#### 3.1 Tests

The effectiveness of PA on hyperschematia was tested with four different tasks.

##### *3.1.1 Drawing from memory*

FV was required to draw from memory a daisy, on a 21 x 29.7 cm sheet of paper, placed in front of her, with the centre of the sheet being aligned with the midsagittal plane of her body. No model was provided, and no further specific instructions were given. The drawing was repeated in three sessions: prior to prism exposure (pre-test), on prism removal (post-test) and 4 days later (late-test). Six trials were given. FV showed no difficulties in executing the task, and drew the pistil and the right-sided petals first. In order to measure the area and the number of petals of the left-hand and of the right-hand sides, each drawn daisy was divided into two sides by a vertical line passing through the centre of its pistil. Petals divided into approximately equal parts by the vertical line were not considered in counting the number of drawn petals. The areas of the two sides of each drawing were computed by a Leica imaging system and Quantimet 500 software. For the left- and right-sided areas of each drawing, a laterality index score (LI) was computed:  $(\text{left-sided area} - \text{right-sided area}) / (\text{left-sided area} + \text{right-sided area}) \times 100$ . A positive value of this LI indicated a greater left-sided area, a negative LI a greater right-sided area. A similar laterality index score was computed for the number of petals (PLI).

##### *3.1.2 Drawing by copy*

FV was asked to draw a daisy by copy. The drawing was repeated in three sessions: prior to prism exposure (pre-test), on prism removal (post-test) and 4 days later (late-test). This test



1 differed from the previous one in that a symmetric daisy model was provided. The model was  
2 printed in the centre of a 21 x 29.7 cm sheet. Six trials were given. The data were analyzed as  
3 in the drawing from memory study, computing the LI and PLI scores.

4 Both tasks were performed at four time-points: two pre-tests at day -4 and day prior to  
5 prism exposure, and two post-tests after intervention upon prism removal (0 h post-test), and  
6 at 4 days thereafter (late-test).

### 1                    3.1.3 *Perceptual matching task*

2  
3 This task assessed the patient's ability to judge the lateral extent of two rectangles. The task  
4 was repeated in two sessions: prior to prism exposure (pre-test) and after prism removal  
5 (post-test). The stimuli were pairs of black rectangles 15 mm high. Twenty-five pairs of  
6 rectangles were presented in a pseudorandom series, in order to measure the point of  
7 subjective equality between patterns placed in the left and in the right visual half-spaces. The  
8 distance between the right-hand side of the left-sided rectangle, and the left-hand side of the  
9 right-sided rectangle was 8 cm. The centre of this distance was aligned with the midsagittal  
10 plane of the patient's body. In each pair, the length of one rectangle was fixed (8 cm), the  
11 length of the other varied from 6.4 cm to 9.6 cm, in four 8 mm steps. In five trials the two  
12 rectangles were equal in length (8 cm). In ten trials the right-sided rectangle was longer than  
13 the left-sided segment, in ten trials vice-versa. The subject's task on each trial was to report  
14 verbally which was the longer out of the two rectangles. The scoring procedure of (Milner et  
15 al., 1993) was used. Each error on a given trial was scored a value of  $n \pm 1$ , where  $n$  was the  
16 number of steps by which the patterns' lengths differed on that trial. Rightward errors (i.e.,  
17 the right-sided rectangle judged as longer, when the left-sided rectangle was longer), were  
18 given a positive score. Leftward errors (i.e., the left-sided rectangle judged as longer, when  
19 the right-sided rectangle was longer) were given a negative score. Using this scoring method,  
20 an identical pair of stimuli ( $n = 0$ ) yielded a score of either +1 (rightward error), or -1  
21 (leftward error). The larger was the difference in length between the two rectangles, the  
22 greater the error score. The task was performed at two time-points pre-test at day prior to  
23 prism exposure, and post-test after intervention upon prism removal.

### 24 25                    3.1.4 *Line extension task*

26  
27 The patient' task was to reproduce the length of a horizontal black line in two conditions. In  
28 the leftward movement condition, the line was placed in the right-hand side of the sheet,  
29 with its left end being aligned with the midsagittal plane of the body of the participant, who  
30 received instructions to reproduce the perceived length of the segment with a leftward  
31 extension. In the rightward movement condition, the line was placed in the left-hand side of  
32 the sheet, with its right end being aligned with the midsagittal plane of the body of the

1 participant, who received instructions to reproduce the perceived length of the segment with  
2 a rightward extension. The stimuli were horizontal black lines, 1 mm in width, with three line  
3 lengths (4, 6, and 8 cm). Each black line was printed on an A4 sheet. In each movement  
4 condition, 24 lines were presented, eight per each length, in a random fixed order, for a total  
5 of 48 lines. The length of the segment drawn by each subject on each trial was measured to  
6 the nearest mm. For the extension of each line drawing, a Laterality Index score (LI) was  
7 computed: (i) leftward extension (leftward extended length minus length of the right-sided  
8 line/leftward extended length plus length of the right-sided line  $\times$  100); (ii) rightward  
9 extension (rightward extended length minus length of the left-sided line/rightward extended  
10 length plus length of the left-sided line  $\times$  100). A positive value of the LI indicated  
11 overextension, a negative value underextension. The mean LIs were calculated for the two  
12 conditions. The task was performed at two time-points pre-test at day prior to prism  
13 exposure, and post-test after intervention upon prism removal.

14

### 15 3.2 Prism adaptation procedure

16

17 FV was exposed to a leftward optical deviation produced by prismatic lenses. Glacier goggles  
18 (Julbo<sup>®</sup>, Lyon, France) were fitted with wide-field, point-to-point wedge lenses creating an  
19 optical shift of 10° ([www.optiquePeter.com](http://www.optiquePeter.com), Lyon, France), affording wide binocular vision.  
20 The exposure period consisted in 50 pointing responses to visual targets presented 10° to the  
21 right or to the left of the objective body midline. During the prism exposure, FV was asked to  
22 point at a fast but comfortable speed; the participant could see the target, the second half of  
23 her pointing trajectory and her terminal error. The patient's head was kept aligned with the  
24 body's sagittal axis by a chin-rest and controlled by the investigator (GR). During prism  
25 exposure, the terminal errors of each movement were captured by means of the thimble and  
26 converted into degrees of angular error with regard to the target. The total duration of this  
27 exposure was about 3 min.

28

### 29 3.3 Open loop pointing task

30

31 The after-effects of PA were evaluated by means of open loop pointing (OLP) in the direction  
32 of a visual target (n = 10), prior to prism exposure (pre-test), and on prism removal (post-

1 test). OLP accuracy measurement was carried out by asking FV to point with her right hand in  
2 darkness to a target. A luminous visual target was aligned with FV's sagittal axis. The  
3 instruction given to FV was to place her right hand at the target drip-line, as precisely as  
4 possible but without time constraint, the goal being to distance herself from the pointing  
5 conditions employed during exposure, with the aim of obtaining measurements of sensory-  
6 motor aftereffects. Pointing was measured using a contractor attached to a thimble threaded  
7 into the index finger, atop a table covered with iso-resistant carbon paper on which two  
8 electrodes were applied, thereby delimiting a section at an angle of 50° and a depth of 70 cm  
9 centered at the starting position near the torso. A direct 5 V current was generated between  
10 the electrodes. When the finger touched the surface of the table, tension between the  
11 thimble contact point and the reference electrode was measured as in a potentiometer.  
12 Tension measurement enabled us to calculate the angular position in relation to the objective  
13 sagittal axis, and this position could then be converted into degrees and conventionally signed  
14 (negative on the left, positive on the right). Measurement precision was estimated at 0.5  
15 degrees (see details in Rode et al., 2015).

16

17 Insert here Figure 2

18

### 19 3.4 Statistical analyses

20 In the drawings tasks (by memory or by copy) the patient's LI, and PLI scores were compared  
21 through different sessions using a one-way repeated measure ANOVA with scores as depend  
22 variables and sessions as independent one. Planned comparisons were performed to assess  
23 patient's performances across sessions. Then patient's scores were compared against the  
24 mean score of control data set (Rode et al., 2006b) by t-tests (Crawford & Garthwaite, 2002;  
25 Crawford & Howell, 1998) for each session, with scores of controls being considered as the  
26 standard. Student t-test was used to compare the patient's performance in pre-test and post-  
27 test for the line extension task, as well as for Open Loop Pointing and Perceptual matching.

## 28 4 Neuroimaging

29

### 30 4.1 Imaging data acquisition

31

1 Six months post-onset, topography of the brain lesion was studied by an anatomical MRI and  
2 diffusion weighted imaging (DWI), in order to objectify the different white matter tracts  
3 impaired.

4 A sequence of Diffusion Weighted Imaging (DWI) with 32 diffusion with a b-value of 800 sec  
5  $\text{mm}^{-2}$  and one volume with no diffusion gradient were acquired on a 3T Ingenia Philips  
6 medical system equipped with a 16-channel head coil (Philips Medical Systems, Erlangen, The  
7 Netherlands). The acquisition sequence was fully optimized for tractography, providing  
8 isotropic resolution ( $2 \times 2 \times 2 \text{ mm}$ ) and coverage of the whole brain. A three-dimensional axial  
9 Gadolinium-enhanced T1 weighted covering the whole head was also acquired (160 slices,  
10 voxel resolution =  $0.5 \times 0.5 \times 1 \text{ mm}$ , TE = 5.1, TR = 9.7).

11

#### 12 4.2 *Atlas-based analysis of disconnection*

13

14 Lesion mask of the patient was first drawn on the native 3D T1 images by using the MRICroN  
15 software (Rorden et al., 2007). Registrations of the patient's T1 MRI were performed using  
16 BCBtoolkit (<http://www.toolkit.bcblab.com>, (Foulon et al., 2018). We used the  
17 enantiomorphic approach (Nachev et al., 2008). During spatial normalization, the mask of the  
18 lesion was replaced symmetrically by the healthy tissue of the contralateral hemisphere. T1  
19 images were registered to the template (MNI152) using affine and diffeomorphic  
20 deformations (Avants et al., 2011; Klein et al., 2009). Finally, patient's lesion was manually  
21 drawn a second time on the normalized images.

22

23 The patient's lesion was mapped onto tractography reconstructions of white matter pathways  
24 obtained from a group of healthy controls (Rojkova et al., 2016). Severity of the disconnection  
25 was obtained by measuring the probability of the tract to be disconnected (Thiebaut de  
26 Schotten et al., 2014), using Tractotron software as part of the BCBtoolkit (Foulon et al.,  
27 2018). In tracts with a minimum probability of 50% to be disconnected, we quantified the  
28 severity of the disconnection by measuring the proportion of the tract to be disconnected  
29 (Dalla Barba et al., 2018).

30

### 1           4.3     *Disconnectome map approach*

2  
3     A second approach was chosen to identify brain areas deafferented by the lesion using a  
4     disconnectome map approach using BCBtoolkit. This approach uses a set of 10 healthy  
5     controls (Rojkova et al., 2016) diffusion weighted imaging datasets to track fibers passing  
6     through the lesion of the patient. We registered the patient’s lesion in the MNI152 space to  
7     each healthy control native space in order to use it as a seed for the tractography. We created  
8     percentage overlap maps by adding the normalized visitation maps from each subject at each  
9     point in the MNI space. Results were projected in a 3D rendering, using MRICron.

### 10 11           4.4     *Tractography*

12  
13     We reconstructed fasciculi identified in our previous analysis (atlas-based analysis) in order to  
14     confirm disconnections in the patient. In the first step, we corrected simultaneously diffusion  
15     datasets for motion and geometrical distortions using ExploreDTI  
16     (<http://www.exploredti.com>, (Leemans & Jones, 2009). The tensor model was fitted to the  
17     data using the Levenberg-Marquardt non-linear regression (Marquardt, 1963). Whole-brain  
18     tractography was performed using Euler integration, that propagates from voxel to voxel  
19     following a step size of 1 mm, and an angle threshold less than 45° (Dell’Acqua et al., 2013).  
20     We excluded from the tractography voxel showing an FA value inferior to 0.2 (Jones, 2004).  
21     This preprocessing was performed using Startrack (<http://www.natbrainlab.co.uk>). The whole  
22     brain tractography was imported to “TrackVis” software (<http://www.trackvis.org>, (Wedeen  
23     et al., 2008). ROIs were manually drawn on cerebral regions considered as an obligatory  
24     trajectory for tracts of interest (Catani & Thiebaut de Schotten, 2008).

1 5 Results

2

3 5.1 Open Loop pointing task

4

5 In pre-test, the mean OLP value was  $+0.98^\circ$  (SD: 1.38). In post-test, the mean OLP value was  
6  $+9.86^\circ$  (SD: 2.71), reflecting a significant sensori-motor after-effect directed toward the right  
7 side induced by PA [ $t(1;18) = 9.6, p < 0.001$ ].

8

9 Insert here Table 2

10

11 5.2 Drawing from memory

12

13 One-Way ANOVA performed on patient's LI, and PLI scores were significant ( $F(3,21)=6.58,$   
14  $p < 0.01$  and  $F(3,21)=4.42, p < 0.05$  respectively) revealing that patient behaved differently  
15 across session. In two pre-tests, the mean LIs were  $+11.74$  (S.D.  $\pm 9.27$ ) in Pre-test 1, and  $+6.4$   
16 (S.D.  $\pm 6.35$ ) in Pre-test 2; (planned comparison  $F(1,21)=1.14, p=0.30$ ), meaning larger left-  
17 sided drawn areas; the mean PLIs were respectively  $+9.77$  (S.D.  $\pm 7.64$ ) in Pre-test 1, and  $+0.87$   
18 (S.D.  $\pm 7.98$ ) in Pre-test 2; (planned comparison  $F(1,21)=1.24, p=0.28$ ). A t-test comparing the  
19 scores of the patient with the control data ( $-4.87$ ; S.D.  $\pm 1.34$  for the LI, and  $-2.39$ ; S.D.  $\pm 4.04$   
20 for the PLI), showed a significant difference for both the LI ( $t = 11.76, p < 0.001$ , for Pre-test 1;  
21  $t=7.83, p < 0.001$ , for Pre-test 2), and the PLI in the first Pre test only ( $t = 2.79, p < 0.05$ , for Pre-  
22 test 1;  $t=0.75, p=0.24$ , for Pre-test 2). In post-test, the mean LI was significantly reduced ( $-$   
23  $8.94$ , S.D.  $\pm 13.42$ , planned comparison with Pre-test 1  $F(1,21)=17.13, p < 0.001$ , and Pre-test 2  
24  $F(1,21)=8.74, p < 0.001$ ), showing a regression of left hyperschemata after prism adaptation,  
25 with a significant lowest number of left petals (PLI=  $-12.28$ , S.D.  $\pm 14.49$ , planned comparison  
26 with Pre-test 1  $F(1,21)=12.93, p < 0.001$ , and Pre-test 2  $F(1,21)=5.33, p < 0.05$ ). In late test, the  
27 mean LI and PLI were respectively  $-1.90$  (S.D.  $\pm 4.22$ ) and  $-4.61$  (S.D.  $\pm 8.04$ ) and significantly  
28 reduced compared with the Pre-test 1 only (planned comparison  $F(1,21)=7.56, p < 0.05$  for LI  
29 and  $F(1,21)=4.46, p < 0.05$  for PLI). Comparison of control data, and patient's performance  
30 immediately after prism adaptation (post-test), revealed a significant difference for LI ( $t=$   
31  $2.28, p < 0.05$ ), and PLI ( $t= 2.27, p < 0.05$ ). As figure 3A shows, this statistical difference was due  
32 to a greater right-sided area and a greater number of petals in the right side of the drawings,

1 meaning a reduction of left hyperschematia after PA. Comparison of mean scores, before  
2 (pre-test) and 4 days later (late-test) failed to revealed any significant difference for LI ( $t=$   
3 2.00,  $p=0.06$ ) and PLI ( $t= 0.51$ ,  $p=0.31$ ), showing that the patient behaved as control  
4 participants, as well as a persistent reduction of the left hyperschematia up to 96 h after PA  
5 (Figure 3A).

### 6 5.3 Drawing by copy

7  
8 One-Way ANOVA performed on patient's LI and PLI scores were significant ( $F(3,21)=3.42$ ,  
9  $p<0.05$ , and  $F(3,21)=4.03$ ,  $p<0.05$  respectively) showing that patient behaved differently  
10 across session. In two pre-tests, the mean LIs were +15.29 (S.D.  $\pm 6.78$ ) in Pre-test 1, and  
11 +11.94 (S.D.  $\pm 14.12$ ) in Pre-test 2; (planned comparison  $F(1,21)=0.28$ ,  $p=0.60$ ), meaning larger  
12 left-sided drawn areas, as for the drawing from memory. In pre-tests, mean PLIs were +12.52  
13 (S.D.  $\pm 9.29$ ) in Pre-test 1, and +7.2 (S.D.  $\pm 14.56$ ) in Pre-test 2 (planned comparison  
14  $F(1,21)=0.87$ ,  $p=0.39$ ). A t-test comparing the scores of the patient with the control data (-  
15 3.94, S.D.  $\pm 3.18$  for the LI; -4.43, S.D.  $\pm 8.17$  for the PLI), showed significant differences for  
16 both the LI ( $t= 5.59$ ,  $p < 0.01$ , for Pre-test 1;  $t= 4.62$ ,  $p < 0.01$ , for Pre-test 2), and the PLI only in  
17 the first Pre-test ( $t= 1.93$ ,  $p < 0.05$ , for Pre-test 1;  $t= 1.32$ ,  $p=0.12$  for Pre-test 2). In post-test,  
18 the mean LI was significantly reduced +0.99 (S.D.  $\pm 10.83$ ) compared with Pre-test 1 only  
19 (planned comparison  $F(1,24)=6.09$ ,  $p < 0.05$ ), and did not differ from controls ( $t= 1.48$ ,  $p=0.11$ ),  
20 showing a regression of left hyperschematia after prism adaptation with a significantly lowest  
21 number of left petals (PLI= -6.70 SD.  $\pm 12.16$ ; planned comparison with Pre-test 1  
22  $F(1,24)=10.42$ ,  $p < 0.001$  and Pre-test 2  $F(1,24)=5.14$ ,  $p < 0.05$ ) compared with controls ( $t = 0.26$ ,  
23  $p=0.40$ ), as for the drawing from memory. In late test, the mean LI was +3.80 (S.D.  $\pm 9.85$ ), and  
24 was not different from Pre-test sessions (planned comparison with Pre-test 1  $F(1,24)=3.21$ ,  
25  $p=0.09$ , and Pre-test 2  $F(1,24)=1.53$ ,  $p=0.23$ ). The mean PLI was -0.34 (S.D.  $\pm 8.95$ ) and was  
26 significantly different only for Pre-test 1 (planned comparison with Pre-test 1  $F(1,24)=5.08$ ,  
27  $p < 0.05$  and Pre-test 2  $F(1,24)=1.66$ ,  $p=0.21$ , see Figure 3B).

28  
29 Insert here Figure 3

30

31 Comparison of control data, and patient's performance revealed a significant difference for LI



1 (t= 2.26, p<0.05), but not for PLI (t= 0.46, p=0.33). So, four days after prismatic adaptation the  
2 patient copied a daisy with a significantly larger right-sided area, compared with controls, but  
3 with similar numbers of petals on the right side, suggesting some evidence of a persistent  
4 reduction of the left hyperschematia after PA, as for the drawing from memory test. The  
5 persistent after-effect of PA on left hyperschematia can be illustrated by the drawings of  
6 butterfly from memory before and after PA (see Figure 4).

7 Insert here Figure 4

#### 9 5.4 Perceptual matching task

10  
11 In pre-test, the score was +0.80 (S.D.  $\pm 1.24$ ), and similar to the mean score of the control  
12 group (+0.91, S.D.  $\pm 0.11$ ). In post-test, the score was (+0.85, S.D.  $\pm 1.29$ ). Comparison by t-test  
13 of scores before and after prism removal showed no significant difference (t= 0.13, p=0.85).

#### 14 5.5 Line extension task

15  
16 In pre-test, the mean leftward extension LIs were respectively +8.57 (S.D.  $\pm 3.21$ ) for 4 cm,  
17 +4.02 (S.D.  $\pm 3.25$ ) for 6 cm and +3.94 (S.D.  $\pm 4.93$ ) for 8 cm lines. The mean rightward  
18 extension LIs were respectively +2.73 (S.D.  $\pm 5.08$ ) for 4 cm, -1.27 (S.D.  $\pm 2.77$ ) for 6 cm and -  
19 0.66 (S.D.  $\pm 8.95$ ) for 8 cm lines. The patient showed a leftward overextension for the three  
20 lines. The performance of FV was similar to those of previously reported patients (Rode et al.,  
21 2006, 2008, 2014). Comparison of LIs before and after prism removal showed a significant  
22 increase of the mean rightward extension LIs for the three lines lengths: +10.12 (S.D.  $\pm 4.83$ )  
23 for 4 cm (t=2.98, p<0.05), +6.75 (S.D.  $\pm 4.48$ ) for 6 cm (t=4.09, p<0.01), and +7.13 (S.D.  $\pm 4.40$ )  
24 for 8 cm lines (t=2.21, p<0.05). There was no significant difference of the mean leftward  
25 extension LIs for two lines lengths: LI= +9.73 (S.D.  $\pm 6.17$ ) for 4 cm (t=0.47, p=0.65), and LI=  
26 +6.01 (S.D.  $\pm 3.90$ ) for 6 cm (t=1.07, p=0.31), and a significant difference for the 8 cm lines -  
27 5.85 (S.D.  $\pm 3.43$ ; t=4.61, p<0.001). Results showed that PA brought about a rightward  
28 overextension for the three lines, associated to a reduction of the leftward overextension for  
29 the longest line (8 cm), with no such effect on the 4 and 6 cm lines (see Figure 5).

30  
31 Insert here Figure 5

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5 Anatomical correlates

3D T1 images showed that the lesion involved mostly the right temporo-parietal white matter, the occipital (Brodmann areas BA 17, 18, 19, 41, 42), and temporal (BA 20, 21, 22, 37) cortices, and both the angular and supramarginal gyri (BA 39, 40) of the inferior parietal lobule (Figure 6A).

The atlas-based analysis of disconnection revealed that the lesion damaged 25% of the optic radiations, 17% of the post and 16% of the long segments of the arcuate fasciculus, 11% of the inferior longitudinal fasciculus and 10% the inferior fronto-occipital fasciculus. The lesion damaged less than 5% of all other tracts.

The disconnectome map approach showed the high probability of deafferentation of the inferior parietal lobule and of the temporal lobe (Figure 6B).

We conducted a tractography analysis to confirm the disconnection of previously identified fasciculi using the atlas-based approach. Results demonstrated in our patient a disconnection of the posterior and long segments of the arcuate fasciculus, of the inferior longitudinal and fronto-occipital fasciculi and of optic radiations, in the right hemisphere. Posterior inter-hemispheric connections were comparatively preserved (Figure 6C).

Insert here Figure 6

6 Discussion

The aim of the present study was to assess whether PA can reduce the left-sided disproportionate expansion of drawings, both by copying and from memory, contralateral to the side of the hemispheric lesion, and the overestimation of left lateral extent, when a leftward movement is required in a patient with left hyperschematia, and without left unilateral visual neglect.

6.1 Hyperschematia

Before prism exposure, FV exhibited a left spatial hyperschematia characterized by a

1 disproportionate leftward expansion of drawings (with the addition of leftward details), both  
2 by copy and from memory, overestimation of lateral extent, when a leftward movement was  
3 required, but without perceptual underestimation of left-sided extent. As for the previous  
4 seven cases reported patients by Rode et al., (2006b, 2014), the disorder was not associated  
5 to a left visual neglect, but FV still suffered from a left auditory extinction, a deficit that may  
6 occur independent of visuo-spatial neglect (Brozzoli et al., 2006; de Renzi et al., 1984). Lastly,  
7 as for the previous cases (Rode et al., 2006b, 2008, 2014) , FV was not aware of her behaviour  
8 in the drawing and line extension tasks. Since hyperschematia, and unawareness of it were  
9 associated to a right hemispheric lesion, such an unawareness may be considered under the  
10 rubric of anosognosia (see Mograbi & Morris, 2018) for components of the neglect,  
11 specifically for the productive manifestation of “hyperschematia” (Vallar & Bolognini, 2014).

12 After the period of prismatic adaption to a leftward shift of the visual environment (10°),  
13 towards which FV exhibited a disproportionate expansion of spatial representation and  
14 attention in a number of visuo-motor tasks, the patient showed a significant after-effect  
15 directed to the opposite side (right), as measured by the OLP task (mean amount: 8,88°). This  
16 after-effect was associated to a dramatic reduction of the left-sided disproportionate  
17 expansion of drawings, and added leftward details both in drawing from memory and by copy  
18 tasks. These modifications remained unchanged four days later, meaning a persistent  
19 cognitive effect on the spatial disorder affecting size representation of objects in extra-  
20 personal space, along the horizontal dimension. One can speculate that the realignment of  
21 the visuo-motor space through PA therefore leads to the building up of more symmetrical  
22 representation of object space. In line with recent findings (Lunven et al., 2018), effects of PA  
23 on space representation may be supported by intact inter-hemispheric connections.

24 Patient FV did not show a disproportionate perceptual underestimation of leftward extension.  
25 This finding is in line with evidence from previously reported patients with leftward  
26 hyperschematia, who may or may not show such biases, that, accordingly, do not represent a  
27 core mechanism of the disorder (Rode et al., 2014). FV’s preserved performance in the task of  
28 estimation of perceptual extent was not modulated by PA. This result may be considered with  
29 reference to the evidence from studies in neurologically unimpaired participants, showing  
30 directional effects of PA in a task broadly similar to the present one, namely the Landmark

1 task. Such effects mimic unilateral spatial neglect (Nijboer et al., 2010; Striemer & Danckert,  
2 2010). Here, we do not find a modulation of a preserved performance, in a task assessing  
3 perceptual biases largely unrelated to hyperschematia (Rode et al., 2014), by PA in a brain-  
4 damaged patient. Seen in this perspective, these negative findings corroborate the conclusion  
5 that the mere perceptual underestimation of leftward extent in the visual modality is not a  
6 mechanisms of hyperschematia, where the disordered representation of the left hand-side of  
7 space may also involve action components for leftward movements, and is not confined to  
8 the visual modality [see Patient #1 of Rode et al. (2006b), who showed a leftward expansion  
9 in drawing a daisy also in blindfolded conditions]. Future research using the present  
10 perceptual matching task may further investigate the effects of PA in neurologically  
11 unimpaired participants, although this is outside the aims of the present study.

12 Finally, in the line extension task, the significant effects of PA on FV's leftward overextension  
13 were confined to the longest, 8 cm, segment, while the average scores for the 6 and 4 cm  
14 segments were, if anything, increased, although not significantly, further indicating that the  
15 leftward overextension for these segments was not affected by PA. These findings may be  
16 tentatively considered in the context of a result, showing that, at least in the line extension  
17 task, FV's performance is not made symmetrical by PA, but a rightward hyperextension is  
18 produced. The tentative possibility may be then entertained that, in the case of the shortest  
19 segments, where an extension in a part of space closer to the midline, and then to the right  
20 hand side of space, is required, the spatial representation of extent is not normalized, with a  
21 residual leftward (for 6 and 4 cm segments), and a rightward hyperextension involving all  
22 segments, brought about by PA.

23 The hypothesis of a realignment of the visuo-motor space induced by PA has been proposed  
24 in order to explain the reversibility after PA of the manifestations of the syndrome of  
25 unilateral neglect, affecting the extrapersonal and imaginal spaces. In the case of left spatial  
26 neglect (Vallar & Bolognini, 2014; Vallar & Calzolari, 2018), this realignment may involve the  
27 simultaneous enlargement and reorientation of attentional components toward the  
28 neglected side, contributing to the reduction of the right-sided behavioural bias, and resulting  
29 in the construction of more symmetrical 2D and 3D allocentric and egocentric space  
30 representations (see Figure 1D). In the case of left hyperschematia (Rode et al., 2006b, 2014;

1 Vallar & Rode, 2009), as shown by the present study, the realignment of visuomotor space  
2 may conversely involve a reduction of the disproportionately leftward expanded visuo-  
3 attentional space, with a more symmetrical orientation of voluntary attention toward either  
4 side of space (Nijboer et al., 2008), contributing to a reduction of the left-sided  
5 disproportionate expansion of drawings, and of the relevant spatial medium, ultimately  
6 resulting in a more symmetrical construction of 2D or 3D allocentric and egocentric space  
7 representations.

## 8 6.2 Imaging

9  
10 In FV, the lesion involved mostly the right temporo-parietal white matter, the occipital  
11 (Brodmann areas BA 17, 18, 19, 41, 42), and the temporal cortices (BA 20, 21, 22, 37), and the  
12 inferior parietal lobule [angular and supramarginal gyri (BA 39, 40)], as for the previous seven  
13 cases reported patients by (Rode et al., 2006b, 2014): accordingly, these cerebral regions  
14 could support the processes involved in the representation of lateral extent. The patient  
15 exhibited a disconnection between right attentional fronto-parietal networks, and the ventral  
16 visual stream and a relative preservation of posterior callosal connections. The ILF and the  
17 IFOF play an important role in spatial processing, executive function and attention (Urbanski  
18 et al., 2008). Left misrepresentation of lateral extent may be related to a disconnection  
19 between visual coordinates and attentional networks to the frontal lobe, brought about by  
20 damage to these two fasciculi. By its role in “multimodal integration”, the IFOF plays an  
21 important role for the perception of visuo-spatial information, and in the planning of visually-  
22 guided movement (Aralasmak et al., 2006). Extending a line also requires participants to  
23 orient attention to the leftward movement of the pencil and to continuously monitor their  
24 spatially oriented movement (Perri et al., 2000). The temporo-parietal junction, which is  
25 damaged in patient FV, is involved in shifting or maintaining spatial attention and  
26 representation, in association with activity in the dorsolateral prefrontal cortex (Corbetta &  
27 Shulman, 2002; Fan et al., 2005). In patient FV, the disconnection between right attentional  
28 fronto-parietal networks may bring about an alteration in an internally driven intentional  
29 system in the contralateral left side of space, resulting in the left-sided disproportionate  
30 expansion of drawings and the hyperextension of lines, when a leftward movement is  
31 required without any interruption by an external stimulus (Kim et al., 2016).

1 The pattern of white matter damage of patient FV is also compatible with an interpretation of  
2 the disorder of size perception of left space in terms of a compensation mechanism of the left  
3 visual neglect presented in the acute phase by the patient, based on the integrity of posterior  
4 callosal connections and of the second and of the first branch of the SLF (Lunven et al., 2015;  
5 Thiebaut de Schotten et al., 2014). In order to compensate for the alteration of space  
6 representation and attention, disproportionately biased rightwards, an excessive leftward  
7 extension with a comparatively reduced rightward extension of the spatial medium may take  
8 place. This hypothesis could challenge the previously proposed explanation of  
9 hyperschematia: a disordered representation of extrapersonal space, possibly involving a  
10 contralesional relaxation of the spatial medium; a deficit which does not arise at the level of  
11 retinotopic coordinate frames and considered as a distinct spatial disorder, which could  
12 nevertheless co-occur with neglect following right brain damage (Rode et al., 2006b). It may  
13 be relevant to note here that all reported patients with left hyperschematia had shown left  
14 visuo-spatial neglect in the acute and subacute post-stroke phase (Rode et al., 2014). Be as it  
15 may, the present single case study shows that PA with rightward aftereffects reduces the  
16 leftward hyperschematic behavior.

17

### 18 6.3 Conclusion

19

20 PA appears then to be effective in disorders of spatial representation and attention,  
21 featuring a contralateral deficit, such as unilateral spatial neglect: under these conditions, the  
22 appropriate direction of the after-effects is towards the neglected side of space, since the  
23 spatial representation of the neglected side is to be enhanced, and attention oriented  
24 towards it. A similar directional approach holds for the CRPS (Christophe et al., 2016; Sumitani  
25 et al., 2007).

26 With the limitations intrinsic to a single case observation, performed in early post-  
27 stroke stage, that needs replication (Vallar, 1999), the present study shows that PA is also  
28 effective in disorders of spatial representation and attention brought about by unilateral right  
29 brain-damage, such as hyperschematia, featuring instead a disproportionately expanded  
30 representation of the side of space contralateral to the side of the lesion: under these  
31 conditions, the appropriate direction of the aftereffects is in a direction opposite to the  
32 disproportionately expanded side of space, since such a “hyper-representation” needs to be

1 diminished. In both conditions, PA would operate re-setting more symmetrically the  
2 orientation of spatial attention, and the spatial representation of both sides of space.

3

4 Declarations of interest: none

5 Funding. G.V. was supported in part by Ricerca Corrente Grants from the IRCCS istituto  
6 Auxologico Italiano.

7

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46

47

1 **Captions to Figures**

2

3 **Figure 1.**

4 Examples of drawings a daisy from memory (LI=+9,46; PLI=0) (**1A**), and by copy (LI=+44,3;  
5 PLI=+23,8) (**1B**), a Christmas tree (LI=+10,4) (**1C**), and a house and trees (Gainotti et al., 1972)  
6 (**1D**), by copy. In copying multiple-object arrays (1D), patient FV drew greater left-hand sides  
7 of objects, also when they were located in the right hand-side of the model, indicating the  
8 involvement of allocentric reference frames. LI: Laterality Index Score. PLI: Petal Laterality  
9 Index Score.

10

11 **Figure 2.**

12 Description and time course of the experimental procedure. PA: Prism Adaptation; PMT:  
13 Perceptual Matching Test; LET: Line Extension Task; OLP: Open Loop Pointing task.

14

15 **Figure 3.**

16 Scores for daisy drawing from memory (**A**) and by copy (**B**) in patient FV and in six control  
17 participants. Mean Laterality Index scores, LIs (SEM), for drawn areas and mean Petal LIs (PLIs,  
18 SEM) of patient FV, prior to PA (pre-test), immediately after PA (post-test), and after a delay  
19 of about 96 h following PA (late-test).

20

21 **Figure 4.**

22 Effect of PA on drawing of an object (a butterfly) in patient FV, prior to PA (LI=+18),  
23 immediately after PA (LI=+3,21), and after a delay of 4 days following PA (LI=-1,97).

24

25 **Figure 5.**

26 Line extension task: mean (SEM) laterality indexes (LIs) of patient FV for rightward, and  
27 leftward (L, R) extended lines, by line length (4, 6, and 8 cm), prior to PA and immediately  
28 after PA.

29

30 **Figure 6.**

31 Lesion analysis of patient FV. Reconstruction of patient's brain lesion (**6A**); brain areas  
32 identified by the disconnectome maps analysis (**6B**) and tractography of the white matter

- 1 connections (orange: Inferior Fronto-occipital Fasciculus, blue: Inferior Longitudinal
- 2 Fasciculus, green: Optic radiations, red: Arcuate Fasciculus) (**6C**).
- 3
- 4

## 1 Tables

---

Patient FV	
Age, years / gender	63 / female
Laterality	Right-handed
Stroke localisation	Right fronto-temporo-parietal haematoma
Neurological exam	Lower left quadrantanopia and left auditory extinction, no motor or somatosensory deficit
Line cancellation test (Albert)	40/40
Star cancellation test (Wilson)	55/56 (one omission in the left side)
Letter cancellation task (Diller)	51/53 (2 omissions in the left side), 48/51 (3 omissions in the right side)
Line bisection task (Schenkenberg et al., 1980)	+0.4% (normal range -4.3--2.9, mean -0.7%, SD $\pm 2.46$ )
MOCA test (Nasreddine et al., 2005)	20/30
Other cognitive disorders	Dysexecutive syndrome (dysfunction of sustained and divided attention, cognitive inflexibility) anosognosia, no constructional apraxia, no memory disorder.
FIM	126/126

---

2

3 **Table 1.** Neuropsychological and neurological profile of patient FV.

4

5

1

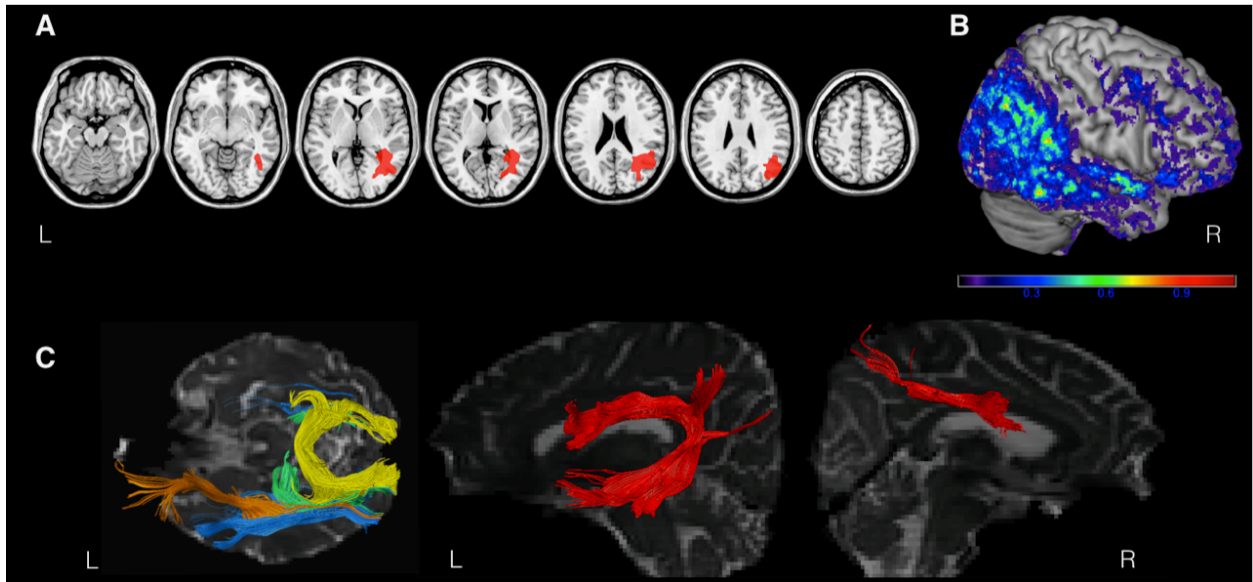
	Pre-test 1 (Day-4)	Pre-test 2 (before PA)	Post-test (after prism removal)	Late-test (Day+4)	Controls (n=6)
<i>Drawing from memory</i>					
LI score	11.74 <sup>#</sup> (9.27)	6.4 <sup>#</sup> (6.35)	-8.94 <sup>#</sup> (13.42)	-1.9 (4.22)	-4.87 (SD±1.34, range -7.08 to -3.57)
PLI score	9.77 <sup>#</sup> (7.64)	0.87 (7.98)	-12.28 <sup>#</sup> (14.49)	-4.61 (8.04)	-2.39 (SD±4.04, range -8.13 to +3.89)
<i>Drawing by copy</i>					
LI score	15.29 <sup>#</sup> (6.78)	11.94 <sup>#</sup> (14.12)	0.99 (10.83)	3.8 <sup>#</sup> (9.85)	-3.94 (SD±3.18, range -0.81 to -8.28)
PLI score	12.52(9.29)	7.2 (14.56)	-6.7 (12.16)	-0.34 (8.95)	-4.43 (SD±8.17, range 0 to -20.8)
<i>Perceptual matching task (LI)</i>		0.8 (1.24)	0.85 (1.29)		+0.905 (SD±0.11, range +0.81 to +1.07)
<i>Line extension task</i>					
Leftward LI (4cm)		8.57 (3.21)	9.73 (6.17)		
Leftward LI (6 cm)		4.02 (3.25)	6.01 (3.9)		
Leftward LI (8 cm)		3.94 (4.93)	-5.85 (3.43)		
Rightward LI (4 cm)		2.73 (5.08)	10.12 (4.83)		
Rightward LI (6 cm)		-1.27 (2.77)	6.75 (4.48)		
Rightward LI (8 cm)		-0.66 (8.95)	7.13 (4.4)		
<i>After-effect measurements</i>					
OLP		0.98 (1.38)	9.86 (2.71)		

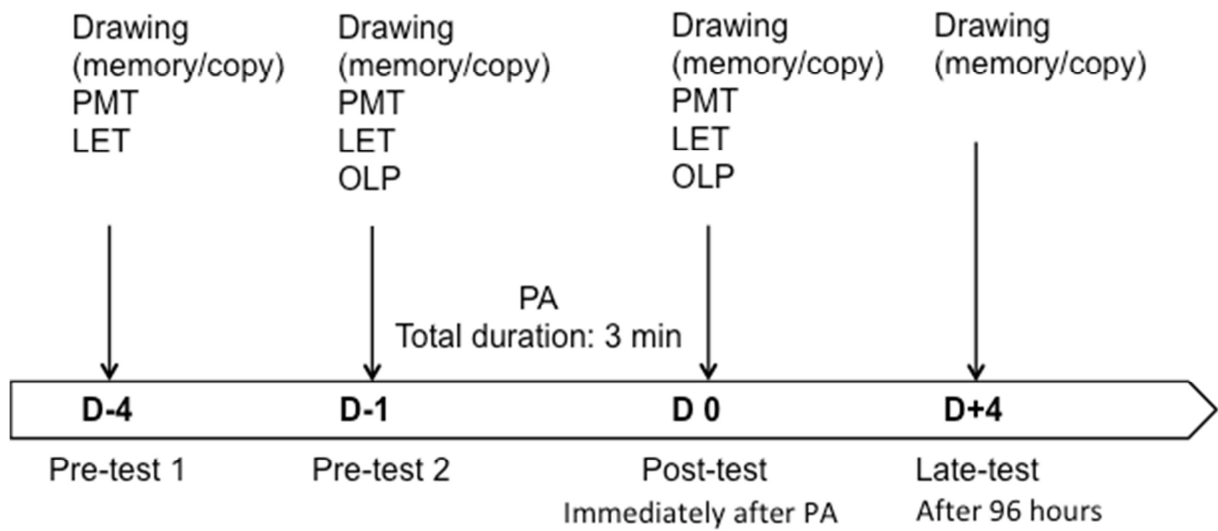
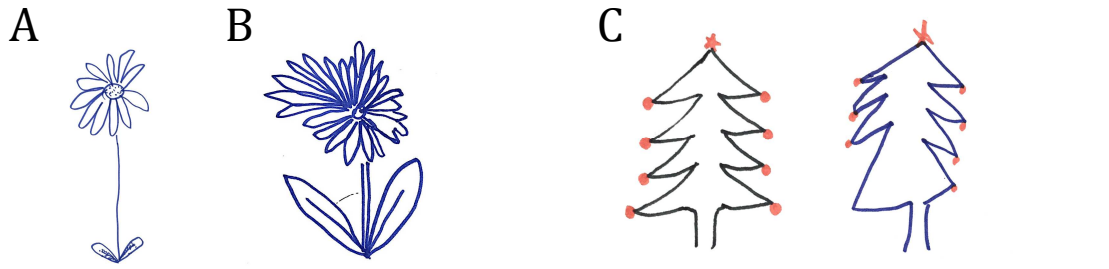
2

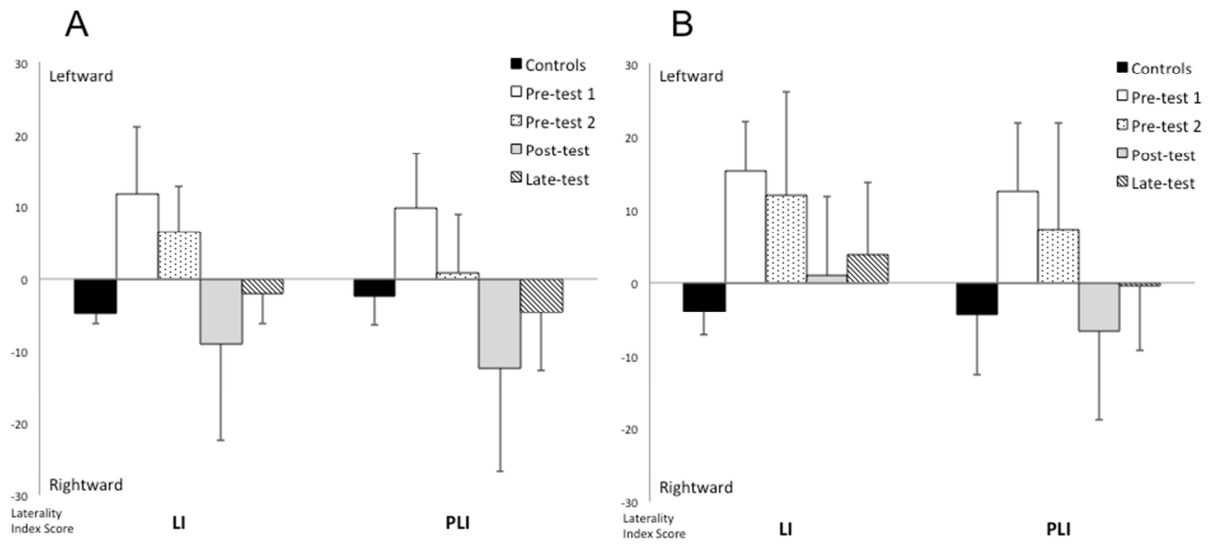
3 **Table 2.** Mean (SD) values of the four different tasks testing the effectiveness of PA. After-  
4 effects of PA were evaluated by means (SD) of open loop pointing task (OLP).

5 <sup>#</sup>FV's scores significantly different from controls data.

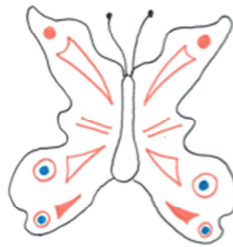








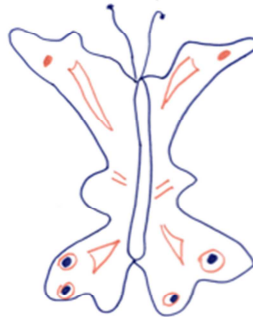
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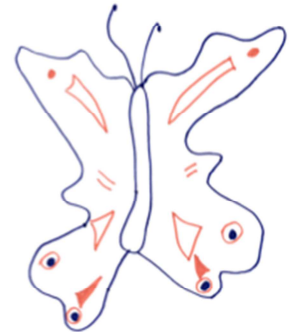
Pre-test

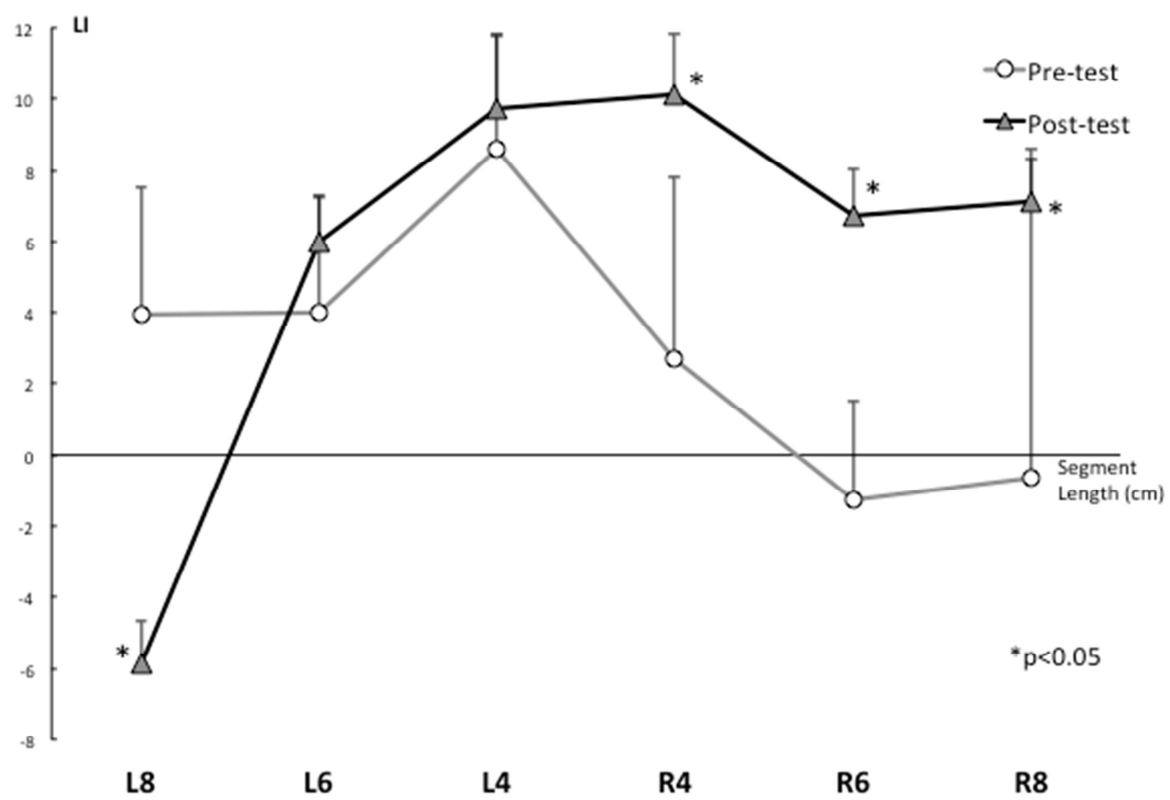


Post-test



Late-test





## **CRedit author statement**

**Julie Di Marco:** Investigation, Writing- Original draft, Writing- Reviewing and Editing

**Marine Lunven :** Software, Writing- Original draft, Writing- Reviewing and Editing

**Patrice Revol :** Methodology, Formal analysis

**Laure Christophe :** Investigation, Visualization

**Sophie Jacquin-Courtois :** Investigation, validation

**Giuseppe Vallar :** Writing- Original draft, Writing- Reviewing and Editing, Validation

**Gilles Rode :** Conceptualization, Investigation, Writing- Original draft, Writing- Reviewing and Editing, Supervision