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The Asymmetrical Effect of Leftward and Rightward Prisms on Intact Visuospatial Cognition

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Abstract

Rightward prismatic adaptation (RPA) can reduce neglect symptoms in patients whereas adaptation to leftward deviating prisms (LPA) can induce neglect-like behavior in healthy subjects. One influential anatomo-functional model of PA postulates that it inhibits activity of the posterior parietal cortex (PPC) contralateral to the prismatic deviation. By hypo-activating the PPC and thus eventually acting on interhemispheric balance, both LPA and RPA could possibly affect visuospatial perception in healthy subjects, however, such behavioral modulation has seldom been reported after RPA. In the light of recent evidence showing that LPA-induced visuospatial shift need time to develop we hypothesised that RPA might induce significant changes in visuospatial cognition on a longer time scale. We thus assessed the Landmark task, as well as sensorimotor aftereffects, several times over eight hours after a single session of either LPA or RPA. In agreement with previous reports, sensorimotor effects were symmetrical and long-lasting, with both LPA and RPA inducing shifts of comparable amplitudes in the direction opposite to the deviation that lasted up to 8 hours. Visuospatial cognition assessed by Landmark performance, was also significantly modulated for up to 8 hours, but only after LPA. Interestingly, the timing and direction of this modulation differed according to participants' baseline bias. An initial leftward bias led to a rapid, but short-lasting rightward shift, whereas an initial rightward bias led to a slower-developing and longer-lasting leftward shift. These findings shed new light on a so-far relatively overlooked feature of spatial cognition that may interact with the effect of PA: the state of the visuospatial system prior to PA should be taken into account when attempting to understand

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and modulate visuospatial cognition in healthy and brain-damaged populations. This highlights the need for refining current models of PA's mechanisms of action.

Keywords

Line bisection; pseudoneglect; visuospatial cognition; plasticity; prism adaptation

1. Introduction

Hemispheric rivalry is a widely acknowledged model of the orientation of spatial attention. Its main tenet is that spatial attention results from the balancing of two competitive and contralaterally-directed hemispheric vectors whose weights depend on the activation level of each hemisphere (Kinsbourne, 1977). According to this theory, neglect results from the breakdown of interhemispheric equilibrium, an idea that has gathered increasing support over time as it can explain both spontaneous (Corbetta et al., 2005) and stimulation-induced neglect recovery (Oliveri et al., 2001; Brighina et al., 2003; Koch et al., 2008; Sparing et al., 2009). The rivalry theory also accounts for visuospatial orienting biases in healthy subjects and their modulation by single-pulse transcranial magnetic stimulation (TMS) (Szczepanski and Kastner, 2013). One of the most promising treatments for neglect to date is rightward prismatic adaptation (RPA) (Farnè et al., 2002; Luauté et al., 2006; Serino et al., 2009; Nijboer et al., 2011; Kerkhoff and Schenk, 2012; Newport and Schenk, 2012; Jacquin-Courtois et al., 2013), which alters the activation level of both hemispheres (Saj et al., 2013).

One of the most influential anatomo-functional models of the effects of PA hypothesizes that both RPA and leftward prismatic adaptation (LPA) modulate the activity of the contralateral posterior parietal cortex (PPC) via bottom up signals from the cerebellum ipsilateral to the prismatic deviation (Pisella et al., 2005; Newport and Schenk, 2012), which in turn possibly acts upon (healthy or pathological) interhemispheric equilibrium (Pisella et al., 2006; Striemer and Danckert, 2010; Newport and Schenk, 2012). This model provides a compelling theoretical framework for understanding the mechanism of action of PA because it evokes the same mechanism to explain both RPA's therapeutic effects in neglect (Rossetti et al., 1998) and the induction of rightward (neglect-like) biases following LPA in healthy subjects (Colent et al., 2000). For example, RPA would ameliorate neglect symptoms by inhibiting the left PPC and decreasing its pathological hyperactivity caused by the right hemisphere lesion (Koch et al. 2008), while in healthy subjects LPA would simulate neglect-like behavior by inhibiting the right PPC (Pisella, Rode, Farnè, Tilikete, & Rossetti, 2006). In the context of inter-hemispheric rivalry, rather than right hemisphere specialization for visuo-spatial cognition (Kinsbourne, 1977; Szczepanski and Kastner, 2013), this model would predict that both LPA *and* RPA should produce opposite effects on visuospatial cognition in healthy subjects. The published data, however, are in sharp contrast with this, as reports of significant changes in visuospatial cognition after RPA in healthy subjects are so rare that RPA has become the gold-standard control for the effects of LPA. Indeed, most studies showing a significant visuospatial modulation following LPA report no behavioral modulation after RPA (Colent et al., 2000; Michel et al., 2003; Loftus et al., 2009; Bultitude et al., 2013; Reed and Dassonville, 2014; Schintu et al., 2014). The two studies that have

reported RPA-induced visuospatial behavioral modulations found it either in the unexpected direction (Berberovic and Mattingley, 2003), or in only the sub-population displaying a rightward bias before PA (Goedert et al., 2010), typically smaller than that displaying a leftward bias (pseudoneglect, see Jewell and McCourt, 2000 for a review).

In addition to the participants' initial visuospatial bias, time might also be important for modulating visuospatial behaviour. In a previous study, we measured both the Landmark task and the sensorimotor aftereffect of PA every five minutes for 40 minutes after a single PA session. We observed that, compared with the sensorimotor aftereffect, the visuospatial shift induced by LPA (no shift was observed after RPA) needed some time to fully develop and fluctuated across time (Schintu et al., 2014). If these fluctuations result from the perturbation of the balance of competitive, contralaterally-directed hemispheric vectors, then RPA might also perturb this balance and induce significant changes in visuospatial cognition in healthy subjects. RPA's visuospatial effects might require more time than those of LPA, due to asymmetries in interhemispheric inhibition between the parietal cortices (Koch et al., 2011). Here we investigated this possibility by examining over 8 hours the aftereffects induced by a single session of left or right PA in healthy subjects who had either a leftward or rightward bias on the landmark task prior to PA.

2. Materials and Methods

2.1. Participants

Eighty-one healthy volunteers participated in the study. Participants were assigned to either the LPA (n=40, 23 females, mean age = 24.47 standard error of the mean (SEM) = 0.63) or RPA group (n=40, 26 females, mean age = 23.6 SEM = 0.52; one participant was excluded and his data were not analyzed as he did not comply with the instructions). Participants were classified on the basis of their leftward (-) or rightward (+) bias at baseline, thus giving rise to 4 subgroups: LPA- (N=25), LPA+ (N=15), RPA- (N=30) and RPA+ (N=10). All participants had normal or corrected-to-normal vision and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). They gave informed consent and were paid for their participation in the experiment. The study was approved by the local ethics committee and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki (World Medical Association, 2013).

2.2. Procedure

The experiment consisted of seven blocks: one before and six after PA. The first block occurred before PA and the post adaptation blocks were administered 2 minutes, 1, 2, 4, 6, and 8 hours (T0 to T8) after PA. Between each block participants were free to do whatever they chose (such as writing, reading, sleeping...etc.).

Each experimental block included four different tasks which measured four different parameters:

- Landmark (LM) – visuospatial shift;
- Open-loop pointing (OL) – sensorimotor shift;

- Straight-ahead pointing (SA) – proprioceptive shift;
- Visual judgment (VJ) – visual shift.

The four tasks were presented in one of two sequences and participants were randomly assigned to one of the two sequences (Sequence A: SA - VJ - LM – OL; Sequence B: OL - SA - VJ- LM). Based upon the previous study from our group showing that the visuospatial shift was not significant until 5 minutes after LPA (Schintu et al., 2014), the Landmark task was always the third or fourth task in the sequence such that it started between 5 and 10 minutes after the onset of the block. Care was taken to ensure that each experimental block started at the correct time after PA, but since response times during each task varied slightly across participants (and for a given participant across blocks), block duration ranged between 10 and 12 minutes. For each task the block before adaptation provided a baseline measurement which was then compared with each of the six post-adaptation blocks.

2.3. Apparatus

The same experimental setup was used throughout the whole experiment (baseline measurement, prism adaptation, and post-adaptation measurements). Participants were comfortably seated with their head positioned on a chinrest in front of a horizontal board that measured the landing position of the finger during the open-loop and straight-ahead pointing tasks with an accuracy of 1 degree (similar to that used in Rossetti et al., 1998), and on which three target dots (8 mm diameter) were positioned at 0, -10 and +10 degrees from their body midline approximately 57 cm from their nasion. During both the open-loop and straight-ahead pointing tasks and the adaptation procedure, participants rested their left hand on their left thigh and pointed with their right index finger perpendicular to the board while wearing a thimble-mounted sensor which permitted the position of the index finger to be measured in angular degrees from the mid-sagittal axis. The right index finger's (unseen) starting position was marked by a home-pad close to the chest aligned with the body's mid-sagittal axis. Participants were instructed to point at a fast but comfortable speed during the PA procedure, and as uniformly as possible throughout the experiment in terms of speed and distance from their chest. During the visual judgment and Landmark tasks a computer screen (22 inches, resolution 1680×1050, refresh rate 60 HZ) was positioned 35 cm from the eyes with its center aligned with the mid-sagittal axis. During these tasks, participants placed their hands on their lap beneath the table.

2.4. Prism adaptation

Participants were fitted with prismatic goggles that deviated their visual field by 15 degrees either leftward or rightward. They were seated in front of the board described above and performed a total of 150 verbally-instructed pointing movements with their right index finger towards the right (+10°) and left (-10°) targets in a pseudorandom order. Before pointing they placed their right index finger on the starting position. Participants could not see their hand when it was at the starting position, nor during the first third of the pointing movement. They were instructed to point with the index finger perpendicular to the board, to execute a one-shot movement at a fast but comfortable speed, and to return their hand to the starting position when instructed by the experimenter. After 150 pointing movements the

prismatic goggles were removed and performance on the four tasks mentioned above and described in detail below was measured six times.

2.5. Experimental tasks

2.5.1. Landmark to measure visuospatial shift—The Landmark task (a modified version of the Landmark task Milner et al., 1992) was used to measure the visuospatial shift induced by PA. We chose the Landmark task because the original work by Colent and colleagues (2000) showed that line bisection judgment in healthy subjects can be modified by LEFT prisms only as measured by the Landmark task (no manual line bisection) which quantifies the perceptual rather than the motor component of the visuospatial bias (Milner et al., 1992). The Landmark task consisted of a series of pre-bisected lines that were displayed centrally on the computer screen. Participants were instructed to fully inspect each pre-bisected line and judge whether the mark (transector) was closer to the left or right end of the line. In this two-alternative forced-choice paradigm participants answered by pressing the pedal under their left foot if the transector was perceived as being closer to the left end and under their right foot if they thought it was closer to the right end. Response by pedals was chosen to limit the use of the right hand, which was used to adapt to the prisms, since any feedback from that hand could contribute to de-adaptation. They were instructed to respond accurately and quickly. Prior to the baseline measure at least ten practice trials were given to ensure that participants properly understood the instructions and were confident answering with the pedals. The stimuli were white lines (350 mm × ~2 mm) and were displayed on a black screen positioned 35 cm from the eyes. Lines were transected at the true center and at 2, 4, 6, 8, and 10 mm toward the left and right of the true center. Each of the 11 different pre-bisected lines was presented six times in a random order, yielding a total of 66 trials, which took approximately three minutes to complete. Each pre-bisected line was displayed for a maximum of five seconds or until a response was made, and was then replaced by a black-and-white patterned mask which stayed on the screen for one second before the next pre-bisected line was displayed. Presentation software (Neurobehavioral Systems, Inc., USA) was used to generate the stimuli, record responses, and control the timing of stimulus presentation throughout the task. For each participant, the percentage of 'right' responses was plotted as a function of the position of the transector. These data were then fitted with a sigmoid function and the value on the x-axis corresponding to the point at which the participant responded 'right' 50% of the time was taken as the point of subjective equality (PSE). PSE values smaller than 0 (i.e. negative values) indicated the presence of pseudoneglect, which is the tendency to perceive the center of the line leftward of the true center (i.e. perceiving the transector mark closer to the right end of the line and thus implying an overestimation of the left segment). PSE values larger than 0 (i.e. positive value) indicated the presence of a right bias, which is the tendency to perceive the center of the line rightward of the true center (i.e. perceiving the transector mark closer to the left end of the line and thus implying an overestimation of the right segment).

2.5.2. Open-loop pointing to measure sensorimotor shift—The open-loop pointing task was used to measure the sensorimotor shift induced by PA. Participants performed six pointing movements to the central target (0°) without visual feedback. Before each of the six pointing movements participants were instructed to look at the central target (0°), close their

eyes, point to the target with their right index finger while keeping their eyes closed, and then return their hand to the starting position. The delay between participants closing their eyes and pointing to the central target ranged between 1 and 2 seconds. To ensure that participants had no visual feedback regarding either their movement or their landing position, vision of the arm and hand was occluded before movement onset. The sensorimotor shift was measured as the average distance (of the six pointing movements) between the landing position and the central target.

2.5.3. Straight-ahead pointing to measure proprioceptive shift—The straight-ahead pointing task was used to measure the proprioceptive shift induced by PA. Participants performed six pointing movements to their perceived midline. Before each movement they were verbally instructed to close their eyes and imagine a line splitting their body in half, to project this line onto the board in front of them, to point to the line while keeping their eyes closed, and then return their hand to the starting position. As for the open-loop task described above, the delay between participants closing their eyes and pointing was always between 1 and 2 seconds, and vision of the arm and hand was occluded before movement onset. The proprioceptive shift was measured as the average distance (of the six pointing movements) between the landing position and the true midline.

2.5.4. Visual judgment of body midline to measure visual shift—A novel visual judgment task was used to measure the visual shift induced by PA. Participants had to judge whether a white dot (0.3° of diameter) that appeared on the computer screen was on the right or left side of their body's midline. In this two-alternative forced-choice paradigm the experimenter recorded the participant's verbal responses. The dot was displayed on a black screen positioned 35 cm from the eyes in total darkness and remained on the screen until a response was made. We used a simple staircase method with adaptive step size of the horizontal dot position, and the step size gradually decreased during the course of the experiment based on the participant's responses. At the beginning of the experiment the first stimulus was positioned within a range of 40 degrees centered on the participant's midsagittal axis: between -20° (to the left) and $+20^\circ$ (to the right). The left/right side of the dot's initial position was alternated across blocks to avoid biases related to the starting position. After each response, the horizontal space was split in half, and the half space that included the positive response was selected for the next stimulus presentation. The iterative process ended when the difference between the two values (maximum and minimum) was smaller than the step resolution (0.6°). Each measurement, for each time point, was the average of six staircase procedures. Presentation software (Neurobehavioral Systems, Inc, USA) was used to generate the stimuli, record responses, and control the timing of stimulus presentation throughout the task. This task took approximately 5 minutes to complete.

2.5.5 Statistics—Statistical analyses were carried out using the software IBM SPSS Statistics 20 with significance set at .05 (two-tailed). All data are presented as mean with the standard error of the mean (SEM) in parentheses. When sphericity was violated Greenhouse-Geisser corrected values are reported. Each of the four measures indexing sensorimotor (OL, SA, VJ) and visuospatial (LM) effects of PA was submitted to a repeated measure ANOVA with Time (7 levels) as a within-subject factor, and PA Direction (LPA or RPA) and

Bias at Baseline (+ = rightward; - = leftward) as a between-subject factors. By including Time as a factor and not as a continuous variable we could test non-linear effects over time, which are the main focus of the subsequent analyses. Since we were interested in comparing each post-adaptation session to the baseline for a given direction of PA, planned comparisons (two-tailed, paired t-tests, Bonferroni corrected) were carried out independently for each PA direction. Effect sizes are reported as Cohen's d or partial eta squared.

3. RESULTS

3.1. Visuospatial shift

Figure 1 shows the average PSE for each of the seven Landmark task sessions for both the LPA (left panel) and RPA (right panel) groups, with participants separated according to bias at baseline.

The repeated measures ANOVA on the PSE data revealed a significant main effect of Time [$F(4.104, 311.903) = 3.212, p = .012, \eta^2_p = .041$], a main effect of Bias at Baseline [$F(1,76) = 20.53, p < .001, \eta^2_p = .213$], a Time by Bias at Baseline interaction [$F(4.104, 311.903) = 5.126, p < .001, \eta^2_p = .063$], and a Time by PA Direction by Bias at Baseline interaction [$F(4.104, 311.903) = 3.405, p = .009, \eta^2_p = .043$]. No other main effects or interactions were significant.

The triple interaction was followed-up by two repeated measures ANOVAs for each prism direction with Time (7) and Bias at Baseline (2) as within-subject factors. The RPA group showed only a main effect of Bias at Baseline [$F(1,38) = 10.71, p < .002, \eta^2_p = .220$], with no main effect of Time ($p = .077$), nor a Time by Bias at Baseline interaction ($p = .336$). The LPA group showed a main effect of Time [$F(3.803, 144.500) = 3.759, p = .007, \eta^2_p = .090$], a main effect of Bias at Baseline [$F(1,38) = 9.710, p < .003, \eta^2_p = .204$], and a Time by Bias at Baseline interaction [$F(3.803, 144.500) = 8.163, p < .001, \eta^2_p = .177$]. Bonferroni-corrected t-tests revealed that, compared to baseline, the line bisection judgments in the LPA- group were significantly shifted rightward at T0 ($p = .006$, Cohen's $d = 0.35$) ($p > .05$ at all other timings), whereas in the LPA+ group the line bisection judgments were significantly shifted leftward at T1 ($p = .024$, Cohen's $d = 0.55$), T2 ($p = .006$, Cohen's $d = 0.55$), T4 ($p = .024$, Cohen's $d = 0.55$), T6 ($p = .006$, Cohen's $d = 0.55$) and T8 ($p = .048$, Cohen's $d = 0.72$), with the leftward tendency being already visible at T0 ($p = .078$, Cohen's $d = 0.28$).

The one-way Anova comparing the baseline measurement having PA direction and Bias at Baseline as a between-subject factors showed only the main effect of Bias at Baseline due to the classification (i.e., by design), [$F(1,76) = 74.157, p < .001, \eta^2_p = .494$], importantly the main effect of PA direction ($p = .137$) and the PA direction by Bias at Baseline interaction ($p = .079$) were not significant.

Finally, since age has been related to the presence (LPA -) or absence (LPA +) of pseudoneglect (Schmitz and Peigneux, 2011) we compared age across the four sub-groups and the one-way ANOVA on participant age revealed no significant differences between subgroups [$F(3,79) = 1.104, p = .353, \eta^2_p = .042$].

3.2. Sensorimotor shift

Figure 2A shows the average landing position for the seven open-loop pointing task sessions. The repeated measures ANOVA on these data revealed a main effect of PA Direction [$F(1, 76) = 171.689, p < .001, \eta^2_p = .693$], and a Time by PA Direction interaction [$F(3.542, 296.156) = 124.388, p < .001, \eta^2_p = .621$]. No other main effects or interactions were significant. Bonferroni-corrected t-tests revealed that for both groups (LPA and RPA) all six post-adaptation sessions differed significantly from the baseline measurement (all p s $< .001$, all d s > 0.71).

To assess whether there was any correlation between an individual participant's shift in PSE (post-adaptation – pre-adaptation) and the amplitude of their sensorimotor aftereffect (shift in open-loop pointing error), we computed six (one per post-adaptation block) separate Pearson product moment correlations between the absolute values of the two shifts. None of these correlations were significant (all r s $\leq .106$, all p s $\geq .359$).

To check whether participants were adapted to comparable levels, a repeated measures ANOVA was performed on the absolute value of the sensorimotor shift (post-adaptation – pre-adaptation) with Time (6 levels) as a within-subject factor, and PA Direction (LPA or RPA) and Bias at Baseline (+ or –) as between-subject factors. This revealed a main effect of Time only [$F(3.282, 294.447) = 127.263, p < .001$] (all other p s $\geq .161$), meaning that there was no difference in the amount of adaptation across groups or subgroups.

3.3. Proprioceptive shift

Figure 2B shows the average landing position for the seven straight-ahead pointing task sessions. The repeated measures ANOVA on these data revealed a main effect of PA Direction [$F(1, 76) = 51.021, p < .001, \eta^2_p = .402$], and a Time by PA Direction interaction [$F(3.785, 287.648) = 42.687, p < .001, \eta^2_p = .360$]. No other main effects or interactions were significant. Bonferroni corrected t-tests revealed that straight ahead pointing was significantly shifted rightward at all post-adaptation task sessions in the LPA group (p s $\leq .002$, all d s > 0.35) and leftward at all post-adaptation task sessions in the RPA group (p s $\leq .006$, all d s > 0.54), with the exception of T8 ($p = .078$, Cohen's $d = 0.24$).

3.4. Visual shift

The repeated measures ANOVA on the visual shift data revealed no main effects or interactions (all other p s $> .05$).

4. Discussion

Previous studies reported that LPA induces a significant rightward shift in the Landmark task (e.g. Colent et al., 2000; Schintu et al., 2014). In line with this finding, we observed, as compared to baseline, a significant *rightward* shift in midline perception 5-to-10 minutes following LPA (at T0) in the subgroup of participants with a leftward bias (pseudoneglect) at baseline. The subgroup of participants with a rightward bias at baseline displayed, a significant *leftward* shift in midline perception after LPA, which lasted until the last tested time point (i.e. 8 hours after adaptation). In contrast, and regardless of the participants' bias

at baseline, RPA did not affect visuospatial judgments. The asymmetrical effect of PA on visuospatial cognition is even more compelling considering that, at the sensorimotor level, both LPA and RPA induced significant and comparable sensorimotor shifts independent of the visuospatial bias exhibited at baseline. Hatada et al. (2006) previously showed that a single session of PA (with a potentiated procedure) induced sensorimotor aftereffects that were still present on the seventh day after adaptation. Our results, however, are the first to show that sensorimotor effects can last for up to 8 hours after a regular, single session of PA. Interestingly, in the same experiment, the visual shift induced by the potentiated PA procedure lasted only 2 hours, suggesting that the absence of a visual shift in our data might be because our single-session, non-potentiated, adaptation procedure might not have been strong enough to elicit a shift and/or that our task was not sensitive enough.

Waiting longer does not reveal visuospatial shifts after RPA

The present results do not support the hypothesis that RPA may affect interhemispheric balance, and hence visuospatial judgments, on a different time-scale compared with LPA. Instead, it adds to the previously reported null results regarding the effects of RPA on cognitive tasks in healthy subjects (Colent et al., 2000; Michel et al., 2003; Loftus et al., 2009; Bultitude et al., 2013; Reed and Dassonville, 2014; Schintu et al., 2014), extending these findings to a much longer time scale of 8 hours.

To the best of our knowledge, only two studies have reported modulations of line bisection performance following RPA in healthy subjects. In one study (Goedert et al., 2010), the visuospatial modulation was in the expected leftward direction, but limited to the sub-group of participants who, in a *manual line bisection* task, showed a rightward baseline bias instead of the comparatively more frequent pseudoneglect. These authors' suggestion that the asymmetrical efficacy of left and right PA in modulating visuospatial cognition may depend upon the bias shown by the participants at baseline is partially supported by the present study. We indeed found that the direction of the effect induced by LPA is modulated by the bias at baseline, while RPA never altered visuospatial cognition. In the only other study showing a visuospatial modulation after RPA, the effect was opposite to the expected direction (i.e., rightward) and was limited to far extrapersonal space (Berberovic and Mattingley, 2003), which is at odds with more recent work reporting similar effects of PA in both near and far extrapersonal space (Patané et al., 2016).

The absence of RPA-dependent visuospatial effects, now extended to a longer time-scale, cannot be attributed to the rate/level of adaptation, as these did not differ between LPA and RPA in the present study. An alternative explanation is that while RPA is supposed to act upon the left PPC, line bisection is thought to rely mostly on the right PPC (Fierro et al., 2000; Fink et al., 2000). Left-to-right interhemispheric action at the level of the PPC (Koch et al., 2011) may not be sufficient to allow RPA to induce a large enough imbalance between the hemispheres to produce overt perceptual changes in line bisection judgements. Importantly, a recent fMRI study reported significant changes in the BOLD signal in the inferior parietal cortices of both hemispheres of healthy participants immediately after adaptation to RPA that were not accompanied by significant changes at the behavioral level

on a visuospatial detection task (Crottaz-Herbette et al., 2014). Thus, the absence of behavioral changes does not imply the absence of neural changes.

Another possible explanation for why RPA does not alter visuospatial judgments even up to 8 hours after adaptation could lie in the presence of asymmetrical parieto-parietal interhemispheric communication, as parietal to parietal interhemispheric inhibition appears to be stronger from right-to-left than from left-to-right (Koch et al., 2011). Using a triple-pulse TMS approach, Koch and collaborators showed that a conditioning pulse over the right PPC induced a greater decrease in parieto-motor connectivity within the left hemisphere than vice versa. They proposed that these results reflect anatomical and physiological asymmetries of interhemispheric connections. One such candidate might be the fibers found in the posterior part of the corpus callosum (the splenium), which are important for interhemispheric communication between visual areas, including occipital and posterior parietal cortices (see Berlucchi, 2014 for a review), and appear to contain more right-to-left than left-to-right connections (Putnam et al., 2010). In addition to this anatomical asymmetry, there is also evidence for a general asymmetry in the speed of interhemispheric communication, with communication being faster from right-to-left (see van der Knaap and van der Ham, 2011 for a review).

The present findings concur with previous reports in suggesting that the right hemisphere may be more difficult to modulate from the left hemisphere than vice versa. This possibility is further supported by the results of a recent study from our group showing that changes in interhemispheric inhibition between the two primary motor cortices occurred after LPA only and were consistent with a right-to-left modulation of inter-parietal inhibition (Martín-Arévalo et al., 2016). Based on the anatomo-functional model of PA proposed by Pisella and colleagues (e.g. Pisella et al., 2006) LPA– by inhibiting the right PPC (and probably releasing the left PPC from right-to-left inhibition Martín-Arevalo et al., 2016) only affects visuospatial behavior in healthy because in patients the lesion to the right hemisphere may *prevent PA to act*. On the other hand, RPA by inhibiting the left PPC (probably without releasing efficiently the right PPC from left-to-right inhibition Martín-Arevalo et al., 2016), significantly modulates behavior solely in patients in which the right hemisphere lesion may *allow RPA to act* because it may have induced pathological left PPC hyperactivation (Koch et al. 2008). Hence, RPA effects might be visible at the behavioral level in patients and not in healthy subjects likely because of the changes in the strength of interhemispheric connections caused by the right hemisphere lesion.

Differential effect of LPA based on bias exhibited at baseline

The asymmetrical visuospatial shifts induced by LPA on the two sub-populations of baseline bias in the landmark task cannot be attributed to differences in the strength or direction of the sensorimotor adaptation, as the sensorimotor measure we used as a proxy for PA aftereffects clearly showed, as expected, sensorimotor effects in the same direction and of comparable size, independent of the baseline bias. Similarly, we can rule out the possible role of fatigue in the after effect induced by LPA on the landmark task as should fatigue have played a role we would have expected it to similarly affect the RPA+ and LPA+ groups, but this was not the case. In addition, the visuospatial modulation in both the LPA+ and LPA–

groups cannot be attributed to either ‘time on task’ (Benwell et al. 2013) or “regression to the mean” effects. Indeed, since the experimental design was identical for the left and right PA groups, if the visuospatial modulation were merely due to an effect of time or repeated administration of the landmark task, we would have observed similar modulation, independent of the direction of the prims or the bias at baseline.

For LPA to produce a leftward shift on the landmark task in right-biased individuals it could either i) inhibit the left hemisphere or ii) increase right hemisphere activation. The possibility that PA could inhibit the PPC ipsilateral to the optical deviation seems unlikely since an inhibitory effect of LPA on the left PPC would improve performance in neglect patients who are in fact improved solely by RPA. Similarly, an inhibitory effect of RPA on the right PPC would alter Landmark performance in healthy subjects, which is not supported by the present findings. The second possibility, that LPA increases RH activation, seems more likely. In light of the present results, it would thus appear that PA’s effect on the PPC contralateral to the optical deviation (at least in the case of LPA) might also depend on the state of interhemispheric equilibrium at baseline. Further investigations are necessary in order to clarify why LPA induced such a long-lasting leftward deviation on the Landmark task in a population with an initial rightward bias while in the pseudoneglect population it induced a rapid, short-lasting leftward bias. Recent neuroimaging evidence (Zago et al., 2017) suggests that the Landmark task is an appropriate tool for investigating spatial lateralization in healthy individuals and is sensitive in determining the factors underlying the variability of spatial cerebral lateralization. It is possible that differences in functional and structural connectivity (Thiebaut de Schotten et al., 2011, Chechlacz et al., 2015) are the neural underpinnings of the presence and strength of these directional biases. Hence, different brain organization and/or lateralization can be a major source of the high variability observed in the line bisection tasks (Jewell and McCourt, 2000), as well as in the responsiveness to PA. We acknowledge a possible limitation in the present study concerning the single baseline measurement in the Landmark task. Despite recent data showing that the line bisection judgement is a proper tool to investigate spatial cerebral lateralization (Zago et al., 2017), in the present work we did not provide multiple measure to categorize the visual spatial bias at baseline. While this study highlights the effects of PA relative to the immediately preceding visuospatial bias (i.e., the state bias), further research is needed to ascertain the stability of such a visuospatial bias (i.e., the trait bias).

In conclusion, this is the first report showing that LPA biases visuospatial cognition in healthy subjects in opposite directions and with different durations depending on initial visuospatial bias. These results indicate that the state of the visuospatial system needs to be taken into account when attempting to understand and modulate the effects induced by PA in healthy individuals and brain-damaged populations.

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References

- Berberovic N, Mattingley JB. Effects of prismatic adaptation on judgements of spatial extent in peripersonal and extrapersonal space. *Neuropsychologia*. 2003; 41:493–503. [PubMed: 12559165]
- Berlucchi G. Visual interhemispheric communication and callosal connections of the occipital lobes. *Cortex*. 2014; 56:1–13. [PubMed: 23489777]
- Brighina F, Bisiach E, Oliveri M, Piazza A, La Bua V, Daniele O, Fierro B. 1 Hz repetitive transcranial magnetic stimulation of the unaffected hemisphere ameliorates contralesional visuospatial neglect in humans. *Neuroscience Letters*. 2003; 336:131–133. [PubMed: 12499057]
- Bultitude JH, Van der Stigchel S, Nijboer TCW. Prism adaptation alters spatial remapping in healthy individuals: Evidence from double-step saccades. *Cortex*. 2013; 49:759–770. [PubMed: 22386659]
- Colent C, Pisella L, Bernieri C, Rode G, Rossetti Y. Cognitive bias induced by visuo-motor adaptation to prisms: a simulation of unilateral neglect in normal individuals? *Neuroreport*. 2000; 11:1899. [PubMed: 10884040]
- Corbetta M, Kincade MJ, Lewis C, Snyder AZ, Sapir A. Neural basis and recovery of spatial attention deficits in spatial neglect. *Nature Neuroscience*. 2005; 8:1603–1610. [PubMed: 16234807]
- Crottaz-Herbette S, Fornari E, Clarke S. Prismatic Adaptation Changes Visuospatial Representation in the Inferior Parietal Lobule. *The Journal of Neuroscience*. 2014; 34:11803–11811. [PubMed: 25164675]
- Farnè A, Rossetti Y, Toniolo S, Làdavas E. Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures. *Neuropsychologia*. 2002; 40:718–729. [PubMed: 11900724]
- Fierro B, Brighina F, Oliveri M, Piazza A, La Bua V, Buffa D, Bisiach E. Contralateral neglect induced by right posterior parietal rTMS in healthy subjects. *Neuroreport*. 2000; 11:1519–1521. [PubMed: 10841369]
- Fink GR, Marshall JC, Shah NJ, Weiss PH, Halligan PW, Grosse-Ruyken M, Ziemons K, Zilles K, Freund HJ. Line bisection judgments implicate right parietal cortex and cerebellum as assessed by fMRI. *Neurology*. 2000; 54:1324–1331. [PubMed: 10746605]
- Goedert KM, Leblanc A, Tsai S-W, Barrett AM. Asymmetrical Effects of Adaptation to Left- and Right-Shifting Prisms Depends on Pre-existing Attentional Biases. *Journal of the International Neuropsychological Society*. 2010; 16:795–804. [PubMed: 20598215]
- Hatada Y, Miall RC, Rossetti Y. Two waves of a long-lasting aftereffect of prism adaptation measured over 7 days. *Experimental Brain Research*. 2006; 169:417–426. [PubMed: 16328305]
- Jacquin-Courtois S, O’Shea J, Luauté J, Pisella L, Revol P, Mizuno K, Rode G, Rossetti Y. Rehabilitation of spatial neglect by prism adaptation: A peculiar expansion of sensorimotor after-effects to spatial cognition. *Neuroscience & Biobehavioral Reviews*. 2013; 37:594–609. [PubMed: 23428624]
- Jewell G, McCourt ME. Pseudoneglect: a review and meta-analysis of performance factors in line bisection tasks. *Neuropsychologia*. 2000; 38:93–110. [PubMed: 10617294]
- Kerkhoff G, Schenk T. Rehabilitation of neglect: An update. *Neuropsychologia*. 2012; 50:1072–1079. [PubMed: 22306520]
- Kinsbourne M. Hemi-neglect and hemisphere rivalry. *Advances in neurology*. 1977; 18:41. [PubMed: 920524]
- Koch G, Cercignani M, Bonni S, Giacobbe V, Bucchi G, Versace V, Caltagirone C, Bozzali M. Asymmetry of Parietal Interhemispheric Connections in Humans. *J Neurosci*. 2011; 31:8967–8975. [PubMed: 21677180]
- Koch G, Oliveri M, Cheeran B, Ruge D, Lo Gerfo E, Salerno S, Torriero S, Marconi B, Mori F, Driver J, Rothwell JC, Caltagirone C. Hyperexcitability of parietal-motor functional connections in the intact left-hemisphere of patients with neglect. *Brain*. 2008; 131:3147–3155. [PubMed: 18948300]
- Loftus AM, Vijayakumar N, Nicholls MER. Prism adaptation overcomes pseudoneglect for the greyscales task. *Cortex*. 2009; 45:537–543. [PubMed: 19231481]
- Luauté J, Halligan P, Rode G, Jacquin-Courtois S, Boisson D. Prism adaptation first among equals in alleviating left neglect: a review. *Restor Neurol Neurosci*. 2006; 24:409–418. [PubMed: 17119314]

- Martín-Arévalo E, Schintu S, Farnè A, Pisella L, Reilly KT. Adaptation to Leftward Shifting Prisms Alters Motor Interhemispheric Inhibition. *Cereb Cortex*. 2016
- Michel C, Pisella L, Halligan PW, Luauté J, Rode G, Boisson D, Rossetti Y. Simulating unilateral neglect in normals using prism adaptation: implications for theory. *Neuropsychologia*. 2003; 41:25–39. [PubMed: 12427563]
- Milner AD, Brechmann M, Pagliarini L. To halve and to halve not: an analysis of line bisection judgements in normal subjects. *Neuropsychologia*. 1992; 30:515–526. [PubMed: 1641116]
- Newport R, Schenk T. Prisms and neglect: What have we learned? *Neuropsychologia*. 2012; 50:1080–1091. [PubMed: 22306519]
- Nijboer TCW, Nys GMS, van der Smagt MJ, van der Stigchel S, Dijkerman HC. Repetitive long-term prism adaptation permanently improves the detection of contralesional visual stimuli in a patient with chronic neglect. *Cortex*. 2011; 47:734–740. [PubMed: 20691433]
- Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*. 1971; 9:97–113. [PubMed: 5146491]
- Oliveri M, Bisiach E, Brighina F, Piazza A, La Bua V, Buffa D, Fierro B. rTMS of the unaffected hemisphere transiently reduces contralesional visuospatial hemineglect. *Neurology*. 2001; 57:1338–1340. [PubMed: 11591865]
- Patané I, Farnè A, Frassinetti F. Prismatic Adaptation Induces Plastic Changes onto Spatial and Temporal Domains in Near and Far Space. *Neural Plast*. 2016; 2016:3495075. [PubMed: 26981286]
- Pisella L, Rode G, Farnè A, Tilikete C, Rossetti Y. Prism adaptation in the rehabilitation of patients with visuo-spatial cognitive disorders. *Curr Opin Neurol*. 2006; 19:534–542. [PubMed: 17102690]
- Pisella L, Rossetti Y, Michel C, Rode G, Boisson D, Pelisson D, Tilikete C. Ipsidirectional impairment of prism adaptation after unilateral lesion of anterior cerebellum. *Neurology*. 2005; 65:150–152. [PubMed: 16009906]
- Putnam MC, Steven MS, Doron KW, Riggall AC, Gazzaniga MS. Cortical projection topography of the human splenium: hemispheric asymmetry and individual differences. *Journal of Cognitive Neuroscience*. 2010; 22:1662–1669. [PubMed: 19583478]
- Reed SA, Dassonville P. Adaptation to leftward-shifting prisms enhances local processing in healthy individuals. *Neuropsychologia*. 2014; 56:418–427. [PubMed: 24560913]
- Rossetti Y, Rode G, Pisella L, Farnè A, Li L, Boisson D, Perenin MT. Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature*. 1998; 395:166–169. [PubMed: 9744273]
- Saj A, Cojan Y, Vocat R, Luauté J, Vuilleumier P. Prism adaptation enhances activity of intact fronto-parietal areas in both hemispheres in neglect patients. *Cortex*. 2013; 49:107–119. [PubMed: 22154751]
- Schintu S, Pisella L, Jacobs S, Salemm R, Reilly KT, Farnè A. Prism adaptation in the healthy brain: The shift in line bisection judgments is long lasting and fluctuates. *Neuropsychologia*. 2014; 53:165–170. [PubMed: 24291512]
- Schmitz R, Peigneux P. Age-related changes in visual pseudoneglect. *Brain Cogn*. 2011; 76:382–389. [PubMed: 21536360]
- Serino A, Barbiani M, Rinaldesi ML, Ladavas E. Effectiveness of Prism Adaptation in Neglect Rehabilitation: A Controlled Trial Study. *Stroke*. 2009; 40:1392–1398. [PubMed: 19246708]
- Sparing R, Thimm M, Hesse MD, Küst J, Karbe H, Fink GR. Bidirectional alterations of interhemispheric parietal balance by non-invasive cortical stimulation. *Brain*. 2009; 132:3011–3020. [PubMed: 19528092]
- Striemer CL, Danckert JA. Through a prism darkly: re-evaluating prisms and neglect. *Trends in Cognitive Sciences*. 2010; 14:308–316. [PubMed: 20444640]
- Szczepanski SM, Kastner S. Shifting Attentional Priorities: Control of Spatial Attention through Hemispheric Competition. *J Neurosci*. 2013; 33:5411–5421. [PubMed: 23516306]
- van der Knaap LJ, van der Ham IJM. How does the corpus callosum mediate interhemispheric transfer? A review. *Behavioural Brain Research*. 2011; 223:211–221. [PubMed: 21530590]
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013; 310:2191–2194. [PubMed: 24141714]

Zago L, Petit L, Jobard G, Hay J, Mazoyer B, Tzourio-Mazoyer N, Karnath H-O, Mellet E.
Pseudoneglect in line bisection judgement is associated with a modulation of right hemispheric spatial attention dominance in right-handers. *Neuropsychologia*. 2017; 94:75–83. [PubMed: 27916670]

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Highlights

- Sensorimotor aftereffects of LPA and RPA are symmetrical and last up to 8 hours.
- Timing and direction of LPA-induced visuospatial shift depends on baseline bias.
- The initial state of the system should be taken into account to modulate visuospatial cognition.
- RPA does not shift Landmark performance irrespective of healthy subjects' baseline.

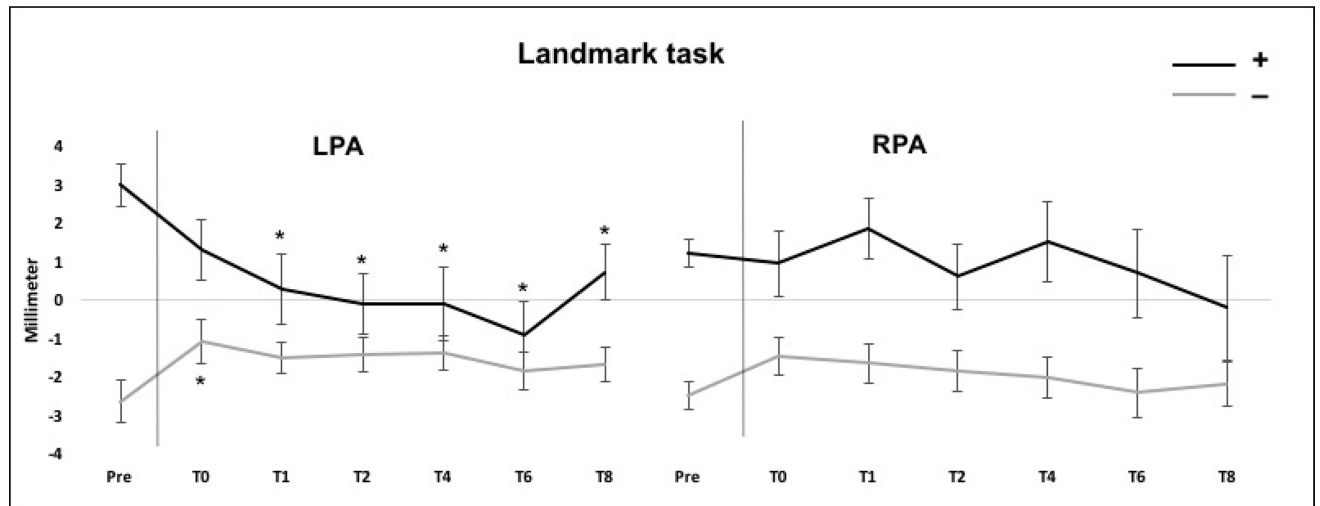


Figure 1.

Landmark: Average performance of all 80 subjects at baseline before (left of the dotted vertical line) and after adaptation to leftward (LPA) or rightward-deviating prisms (RPA) at each of the subsequent testing times (T0 = 2 minutes, T1 = 1 hours, T2 = 2 hours, T4 = 4 hours, T6 = 6 hours, and T8 = 8 hours after PA), as a function of the rightward (+) or leftward (-) Bias at Baseline. Negative and positive values represent leftward or rightward errors/deviation in PSE judgments. Error bars represent 1 SEM. * $p < .05$ (Bonferroni-corrected t-test against pre).

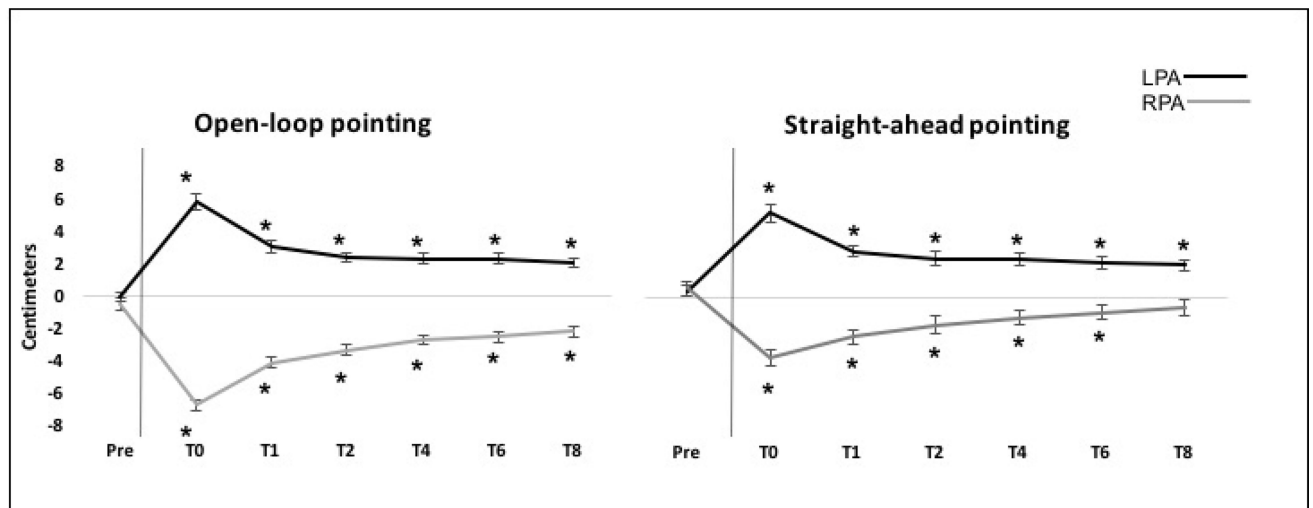


Figure 2.

A) Open-loop pointing; B) Straight-ahead pointing: Average performance of all 80 subjects on both tasks before (left of the dotted vertical line) and after adaptation to leftward (LPA) and rightward-deviating prisms (RPA). Negative and positive values represent leftward or rightward errors/deviation in both open loop and straight ahead pointing. Error bars represent 1 SEM. * $p < .05$ (Bonferroni-corrected t-test against pre).