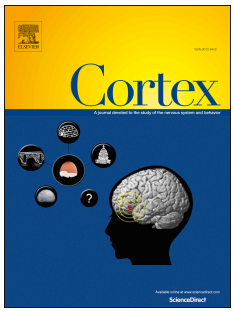
Accepted Manuscript



Exploring prism exposure after hemispheric damage: reduced aftereffects following left-sided lesions

Roberta Ronchi, Irene Rossi, Elena Calzolari, Nadia Bolognini, Giuseppe Vallar

PII: S0010-9452(18)30347-2

DOI: https://doi.org/10.1016/j.cortex.2018.10.014

Reference: CORTEX 2448

To appear in: *Cortex*

Received Date: 30 April 2018

Revised Date: 27 July 2018

Accepted Date: 23 October 2018

Please cite this article as: Ronchi R, Rossi I, Calzolari E, Bolognini N, Vallar G, Exploring prism exposure after hemispheric damage: reduced aftereffects following left-sided lesions, *CORTEX*, https://doi.org/10.1016/j.cortex.2018.10.014.

Exploring prism exposure after hemispheric damage: reduced aftereffects following left-sided lesions

Roberta Ronchi[1,2 *], Irene Rossi[1,3], Elena Calzolari[1,4], Nadia Bolognini[1,3], and Giuseppe Vallar[1,3 *]

[1] Neuropsychological Laboratory, S. Luca Hospital, IRCCS Istituto Auxologico Italiano, Via Mercalli 32, 20122 Milano, Italy;

[2] Département de Neurosciences Fondamentales, Faculté de Médecine, University of Geneva, Campus Biotech H8, Chemin des Mines 9, 1202 Geneva, Switzerland ;

[3] Department of Psychology, University of Milano-Bicocca, Piazza dell'Ateneo Nuovo 1, 20126 Milano, Italy ;

[4] Neuro-Otology Unit, Division of Brain Sciences, Imperial College London, London W6 8RP, UK.

* Corresponding Authors: Roberta Ronchi, roberta.ronchi@unige.ch and Giuseppe Vallar, giuseppe.vallar@unimib.it

Acknowledgements. Giuseppe Vallar and Nadia Bolognini were supported in part by Ricerca Corrente Grants from the IRCCS Istituto Auxologico Italiano, and Fondo di Ateneo per la Ricerca Grants from the University of Milano-Bicocca.

Abstract

Prism adaptation is a well-known method used to investigate brain plasticity, and a promising technique for the rehabilitation of unilateral spatial neglect (USN). Only little evidence about the mechanisms of prism adaptation (PA) in patients with left-brain damage is on record, and about putative differences of PA, and the aftereffects (AEs), between patients with left and right brain damage. In the present study, PA and the AEs were assessed in 30 brain-damaged patients, 20 with right-sided lesions (10 with and 10 without USN), and 10 with left-sided lesions without USN, as well as in a control group of 24 age-matched participants. All patients underwent adaptation to lenses shifting the field of vision towards the side of the lesion, followed by two measures for detecting AEs: the proprioceptive (P) and the visuo-proprioceptive (VP) straight-ahead tasks. To investigate the temporal course of AEs in the different groups, the two measures were recorded immediately and 10 minutes after PA. Before PA, and at the end of the 10-minute delayed evaluation, two tasks to assess USN (target cancellation and drawing) were also administered. All patients adapted to prisms. However, left-brain-damaged (LBD) patients presented with reduced AEs, as compared with right-brain-damaged (RBD) patients with USN. Moreover, while both controls and LBD patients adapting to left-shifting prisms had reduced VP AEs in the delayed condition, AEs were not different from zero (i.e., no AEs) in LBD patients. Finally, in the delayed condition USN patients showed an improvement in the drawing, but not in the cancellation, tasks. These results suggest that adaptation to leftward shifting lenses is associated with larger decay of VP AEs, and a role of the left hemisphere in maintaining these AEs after PA. These findings can be of relevance for the clinical application of this technique in neurological populations.

Keywords: prism adaptation; left- and right-brain-damaged patients; proprioceptive and visuo-proprioceptive aftereffects.

Highlights:

- Left- and right-brain-damaged patients both adapt to prism exposure.
- Aftereffects are reduced in left-brain-damaged patients.
- Results suggest a role of the left hemisphere in maintaining aftereffects after prism adaptation.

1. Introduction

When a person wears a pair of prismatic lenses that deviate the visual field, the first attempts to reach a target, such as an object (e.g., the tip of a pen), produce final errors in movements in the direction of the visual displacement, because the object is visually perceived in a position that is not the real one. After subsequent repeated reaching movements, adaptation to this new environmental condition occurs, with the person performing correct movements, and being able to reach the object accurately. After this adaptation phase, when the prismatic lenses are removed, aftereffects (AEs) occur, namely: a reaching error in the opposite direction with respect to the one induced by the deviation caused by the prismatic lenses, for example, AEs towards the left side of the space for adaptation to rightward shifting lenses (Redding & Wallace, 1996).

Beside the investigation of brain plasticity, prism adaptation (PA) has been shown to be a very promising and effective tool for the rehabilitation of unilateral spatial neglect (USN), a syndrome in which patients fail to perceive, explore and orient to stimuli in the part of space contralateral to the side of the lesion (contralesional), usually the left side of space after a right hemispheric lesion (Heilman, Watson, & Valenstein, 2003; Vallar & Bolognini, 2014; Vallar & Calzolari, 2018). The first elegant demonstration of the effectiveness of PA for temporarily reducing signs of USN was provided by Rossetti and colleagues (1998): they had six right-brain-damaged (RBD) patients to adapt to optical prisms bringing about a displacement of the visual field of 10° towards the right; after prisms' removal all patients showed an improvement of the clinical manifestations of USN, as assessed by psychometric tests, including copy of drawings, line bisection, and target cancellation. Following this pioneering study, many protocols have been developed to reduce the pathological symptoms of USN affecting different modalities and domains, such as visuo-motor, auditory and representational spatial biases (Farnè, Rossetti, Toniolo, & Làdavas, 2002; Goedert, Chen, Boston, Foundas, & Barrett, 2014; Jacquin-Courtois et al., 2010; Maravita et al., 2003; Rode, Rossetti, Li, & Boisson, 1998; Saevarsson, Kristjánsson, Hildebrandt, & Halsband, 2009; Watanabe & Amimoto, 2010). Rehabilitative protocols using repeated daily sessions of PA have also been developed. There is evidence that a 2-week training is effective in ameliorating several symptoms of USN, and that this improvement lasts in the long term, up to six months after the end of the training (Fortis et al., 2010;

Frassinetti, Angeli, Meneghello, Avanzi, & Ladavas, 2002; Serino, Bonifazi, Pierfederici, & Làdavas, 2007). Some studies in acute or recent stroke patients not showing a significant difference between PA and control-placebo treatments are however on record (Nys, de Haan, Kunneman, de Kort, & Dijkerman, 2008, a Randomized Controlled Trial, RCT, in 16 acute stroke patients, treated with PA for four days; Rousseaux, Bernati, Saj, & Kozlowski, 2006, 10 right-brain-damaged patients, with a single sesssion PA treatment; Ten Brink, Verwer, Biesbroek, Visser-Meily, & Nijboer, 2017, a RCT in 70 patients, treated with PA for two weeks).

Which is the brain network involved in PA? In healthy participants PA has been used to study sensorimotor plasticity in the brain, mainly the adaptation to left-shifting lenses associated with AEs in the cognitive domain, as demonstrated, for example, by the presence of a bias in line bisection tests (Michel, 2016). A distributed and complex network provides the neural underpinnings of PA, with a key role of the posterior parietal cortex (PPC), and of the cerebellum of both hemispheres. On the one hand, the inferior PPC, contralateral to the arm used during the PA procedure, is crucial for its first phase, namely *recalibration*, that consists in the early detection of the visuo-motor error, and in a quick strategic correction of it (Chapman et al., 2010; Clower et al., 1996; Luauté et al., 2009). On the other hand, the *realignment* process of PA (namely: the automatic remapping of the visuo-proprioceptive coordinates) involves the cerebellum with a key role (Luauté et al., 2009; Pisella et al., 2005); realignment contributes to the building up of the AEs (Redding, Rossetti, & Wallace, 2005; Redding & Wallace, 2006). Recent evidence points to a role of the right cerebellum in both the realignment and recalibration phases of PA, as demonstrated by a global interference in PA mechanisms when an inhibitory electrical brain stimulation is applied to this area (Panico, Sagliano, Grossi, & Trojano, 2016). Additionally, the primary motor cortex (M1) plays a role in visuo-motor learning: in healthy participants, using the right hand for the execution of the task, the excitatory modulation of the left M1, through transcranial direct current stimulation (tDCS), influences the retention of a learnt configuration when a visuo-motor distortion is induced (Galea, Vazquez, Pasricha, Orban de Xivry, & Celnik, 2011), and it re-activates the AEs 24 hours after the adaptation procedure (Panico et al., 2017). Finally, the subsequent cognitive effects of PA on higher-level spatial representations seem to require a later bilateral involvement of the superior temporal cortex (Luauté et al., 2009).

Studies in brain-damaged patients have been conducted, mainly in RBD participants exposed to right-shifting prisms, as used for left USN rehabilitation (Fortis et al., 2010; Frassinetti et al., 2002). Starting from data on healthy participants, Luautè and colleagues (Luauté et al., 2009, 2012; Luauté, Halligan, Rode, Jacquin-Courtois, & Boisson, 2006) have proposed a model for brain-damaged patients: as the left hemisphere seems involved in different phases of prism exposure (i.e., error detection, late cognitive effects), the clinical benefits of prism exposure on left USN would result from the modulation of a left hemispheric network, which, via a bottom-up signal produced by the cerebellum, would restore an interhemispheric equilibrium disrupted by right brain damage. This hypothesis is based on well-known attentional theories of USN, which postulate that the right hemispheric lesion brings about an imbalance between the two hemispheres (Kinsbourne, 1970). Saj et al. (Saj, Cojan, Vocat, Luauté, & Vuilleumier, 2013) performed an fMRI study testing seven RBD patients with left USN, and showed that both hemispheres have a key role: PA to rightward prisms in RBD patients induces changes in a bilateral fronto-parietal network, including the PPC and the superior-middle frontal cortex. A role of the posterior parietal cortices (particularly the Intraparietal Sulcus, and the Superior Parietal Lobule, IPS/SPL) is envisaged by the hypothesis that the modulation by the cerebellum on the left hemisphere also influences the right one, in turn modulating, through callosal connections, the activity of parietal areas responsible for a leftward orientation (Striemer & Danckert, 2010). To sum up, a complex network of brain regions is involved in PA, including several left hemispheric areas, such as the PPC, the medial temporal lobe and the mid-frontal cortex (Luauté et al., 2012, 2006; Saj et al., 2013).

As previously mentioned, so far the neuropsychological investigation of PA has mainly focused on the study of RBD patients. The majority of such studies aimed at unveiling the beneficial rehabilitative effects of right-shifting lenses in RBD patients with left USN (Newport & Schenk, 2012; Redding & Wallace, 2006), or, in general, at investigating the PA modulation of various visuo-spatial functions in RBD patients (Hugues et al., 2015). Instead, the evidence about if and how PA works in patients with a left hemispheric damage is still sparse (Bultitude & Rafal, 2010; Facchin, Beschin, & Daini, 2017; Magnani, Oliveri, Mancuso, Galante, & Frassinetti, 2011), and no study has systematically compared the development of AEs in RBD and left-brain-damaged (LBD) patients (with or without USN) over time. This is a topic of relevance, both to better

understand the involvement of each hemisphere in the neural mechanisms of PA, and to identify similarities and differences between modulations of spatial functions after unilateral hemispheric lesions.

To fill this gap, the present study aimed at investigating if and how LBD and RBD patients adapt to prismatic lenses shifting the field of vision towards the side of the lesion. The choice of having patients to adapt to an ipsilesional deviation of the visual field was based on clinical reasons: there is evidence that RBD patients with left USN do not adapt to left-shifting prisms, with a consequent null effect on signs of USN (Luauté et al., 2012; O'Shea et al., 2014; Rossetti et al., 1998). Moreover, as we wished to increase knowledge about how PA works as a rehabilitative technique, we decided to rely on the type of adaptation which is well-known to reduce the spatial bias of brain-damaged patients. In fact, based on the principles of PA (Redding & Wallace, 2006, 2010), during prism exposure a spatial discordance between vision and proprioception generates the need of a *spatial realignment* (visual and/or proprioceptive realignment), and, after prisms' removal, AEs, which are in the opposite direction of the visual field displacement. Considering that RBD patients with left USN have a defective attention towards the left side of space, we wanted to adapt them to prism inducing AEs towards this side of space. Therefore, we did not include adaptation to lenses displacing the field of vision contralateral to the side of the lesion. This manipulation is ineffective for the treatment of left USN (Luauté et al., 2012; O'Shea et al., 2014; Rossetti et al., 1998), and, altough in principle theoretically interesting, was outside the main goal of our study. This directional effect of the visual-field prism-induced deviation is the one that brings about AEs towards the contralesional side, and an amelioration of USN in RBD patients, as previously discussed, as well as in LBD with right USN, as assessed by a few recent studies (Bultitude & Rafal, 2010; Facchin et al., 2017).

Furthermore, we also wanted to verify how different types of AEs evolve over time. In order to measure the sensorimotor AEs, immediately after, and 10 minutes after PA, two measures were used: i) the *Proprioceptive task*, which is a measure of the proprioceptive realignment following visual PA, and an estimation of the subjective body midline, as assessed by asking participants, blind-folded, to point straight ahead in front of them; ii) the *Visuo-Proprioceptive task*, which assesses AEs following PA taking into consideration the eye-hand coordination. The latter is usually measured by asking participants to point directly at a visual target, or at the vertical projection of the visual target on the table, without seeing neither

the arm/finger's path nor the end of the movement (invisible pointing) (Redding & Wallace, 1997). The Proprioceptive and the Visuo-Proprioceptive tasks are standard indexes of the AEs after PA. Importantly, in the context of our study, these two tests have been shown to be sensitive to the presence and/or the recovery of USN, Firstly, there is wide evidence that RBD patients with left USN present with a bias in the proprioceptive estimation of their body midline[1] (Farnè, Ponti, & Làdavas, 1998; Karnath, 1994), which improves after PA (Rossetti et al., 1998). Secondly, while USN may affect the reaching of contralesional visual targets (Heilman et al., 2003; Vallar & Bolognini, 2014), USN patients typically do not exhibit a general impairment in pointing to visual targets (Angeli, Meneghello, Mattioli, & Ladavas, 2004; Calzolari et al., 2015; Coulthard, Parton, & Husain, 2006; Fortis et al., 2010; Frassinetti et al., 2002; Jackson, Newport, Husain, Harvey, & Hindle, 2000; Maravita et al., 2003), but the visuo-proprioceptive invisible AEs have been found to correlate with the extent of USN improvements after the PA therapy (Fortis et al., 2010).

Finally, we also verified whether the procedure modulates the presence of left USN in RBD patients; to this aim, at the end of each session, we administered two visuo-motor spatial tasks to RBD with USN: the Star Cancellation test (Wilson, Cockburn, & Halligan, 1987), and the copy of a five-element complex drawing (Gainotti, Messerli, & Tissot, 1972). The study aimed at assessing the extent and the duration of PA-induced AEs: accordingly, the clinical tests for USN were administered at the end of the experiment, and not immediately after the PA session, in order avoid possible interference with the measure of the AEs, namely with the primary aim of the study.

Based on the current literature on PA in RBD and LBD patients (Magnani et al., 2011), we expected adaptation and AEs to prismatic lenses displacing laterally the visual field in both RBD and LBD patients; for patients with USN we also expected a reduction of signs of USN after a single PA session (Rossetti et al., 1998). Our explorative study allows to assess whether adaptation and AEs, as well as the decay of AEs, are comparable or different in LBD and RBD patients, and with or without USN; we had no further more specified hypotheses about how the different groups of brain-damaged patients could behave.

[1] In the context of the interpretation of the USN syndrome in terms of a displacement of the egocentric reference towards the side of the hemispheric lesion (see Ventre, Flandrin, & Jeannerod, 1984) the results of Farnè, Ponti & Làdavas (1998) are more complex, and their discussion is outside the aims of this study.

2. Materials and Methods

2.1. Participants

One hundred brain-damaged patients were screened continuously during 1.5 year: 70 of them were excluded, because of general cognitive impairment (LBD= 10 patients; RBD= 16 patients), lack of compliance (LBD= 8 patients; RBD= 12 patients), and a severe comprehension deficit due to aphasia (LBD= 24 patients; RBD= 0 patients). Thirty right-handed patients (18 males; mean ± SD age: 64.7 ± 13 years, range: 32-89; mean education: 12 ± 4.4 years, range: 5-18) with unilateral hemispheric lesion were included in the study. Twenty patients presented with a lesion affecting the right hemisphere (P#1-20, RBD group: 13 males; mean age: 63.4 ± 12.6 years, range: 32-78; mean education: 11.9 ± 0.8 years, range: 5-18), and 10 with a damage of the left hemisphere (P#21-30, LBD group: 5 males; mean age: 67.4 ± 13.8 years, range: 44-89; mean education: 12.3 ± 3.8 years, range: 8-18). The three groups of patients were comparable with respect to age ($F_{2,27}$= 0.95, p=0.398). RBD patients were further divided into two subgroups, with (RBD/N+) and without (RBD/N-) USN (see section 2.2 below).

The aetiology of the lesion was vascular in 28 patients (20 ischemic, 8 haemorrhagic) and neoplastic in two. Lesion site was assessed by CT or MRI Scan. The extent and the location of the cerebrovascular lesions (see Figure 1) were drawn on a standard MRI template with a 1 mm slice distance using the MRIcro software (Rorden & Brett, 2000).

None of the participants had a clinical history or evidence of previous neurological (including cerebrovascular and neurodegenerative diseases, brain tumour, hydrocephaly), or psychiatric disorders. Motor, somato-sensory, and visual half-field defects contralateral to the side of the hemispheric lesion (contralesional) were assessed by a standardized exam (Bisiach & Faglioni, 1974). Anosognosia for motor and sensory neurological deficits was evaluated by a standard interview (Bisiach, Vallar, Perani, Papagno, & Berti, 1986). Table I summarizes demographic and neurological data of the 30 brain-damaged patients.

Twenty-four right-handed age-matched healthy participants, with no history of neurological and psychiatric disorders, entered the study as the control group (7 males; mean age: 68.3 ± 9.9 years, range: 46-82; mean education: 12.3 ± 4.8 years, range: 5-18).

All participants (brain-damaged and neurologically unimpaired participants) were selected from the inpatient population of the Neurorehabilitation and Orthopaedic units of the Istituto Auxologico Italiano in Milan (Italy). All participants had normal or corrected-to-normal vision, and they were naïve to the purpose of the study. The study was conducted in accordance with the principles of the Declaration of Helsinki, and was approved by the Ethics Committee of the hospital; all participants gave written informed consent for participating in the study.

-Table I and Figure 1 about here-

2.2. General cognitive and language assessment

In addition to the lack of history of cognitive impairment and previous neurological disorders, the presence of a general cognitive impairment was assessed and excluded for all brain-damaged participants using the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975). As the score of the Mini Mental State Examination was influenced by USN and/or language deficits in a few patients (i.e., resulting in a pathological score or preventing task's administration), the absence of a general cognitive impairment (see Table II) was also checked with reasoning tasks: a verbal reasoning task was used as a screening criterion for RBD patients (Spinnler & Tognoni, 1987), while a non-verbal reasoning task was used as a screening criterion for LBD patients (Basso, Capitani, & Laiacona, 2016).

Moreover, for all LBD patients a screening evaluation of language deficits was administered. With relevance for our study, Table III shows the scores of the individual patients in a non-contextual verbal comprehension test (Spinnler & Tognoni, 1987), and in a verbal comprehension test of words and sentences (from the E.N.P.A. battery, see Capasso & Miceli, 2001). Whenever present, aphasia was clinically classified accordingly to the parameter Fluent/Non-Fluent (Basso & Cubelli, 1999); patients were classified as having a pathological score based on the available standardized norms. A perusal of the single scores showed that most LBD patients had a diagnosis of aphasia, with some of them showing a defective score at the Token task (Cut-off: 26.5); word (Cut-off: 18.4) and/or sentence (Cut-off: 11.6) comprehension was in a normal range for all patients except for P28. All LBD patients showed a good contextual oral comprehension, both during the baseline psychometric assessment, and the experimental task (see 2.6 Procedure).

2.3. Neuropsychological assessment of USN

The presence of USN was assessed by the following neuropsychological standardized tests, administered to all RBD and LBD patients (Ronchi et al., 2014):

a) *Star cancellation task* (Wilson et al., 1987). Patients were asked to cross out all of the 56 black small stars printed on an A4 sheet (30 in the left-hand-side, 26 in the right-hand-side), together with distracters (large stars, letters, and words). The scores were the sum of crossed targets, and the left-right difference of omitted targets.

b) *Bell cancellation task* (Gauthier, Dehaut, & Joanette, 1989). The patient's task was to cross out the 35 bell targets (18 on the left-hand side and 17 on the right-hand side) printed on an A3 sheet, together with distracters (objects like trees, horses and keys). The scores were the sum of crossed targets, and the left-right difference of omitted targets.

c) *Line bisection task*. The patients' task was to mark with a pencil the mid-point of six horizontal black lines (two 10 cm, two 15 cm, and two 25 cm in length, all 2 mm in width), presented in a random fixed order. Each line was printed on an A4 sheet, with the centre of each line being aligned with the mid-sagittal plane of the subject's body. The score was the mean deviation of the participant's mark from the objective midpoint, measured to the nearest mm; positive scores denoted a rightward displacement of the subjective midpoint, negative scores a leftward displacement.

d) *Drawing task: five-element complex drawing by copy* (Gainotti et al., 1972). Patients were required to copy a complex five-element figure with two trees in the left-hand-side, two pine trees in the right-hand-side, and a house in the centre of an A4 sheet. Each element was scored: 2 (flawless copy), 1.5 (partial omission of one side of an element), 1 (complete omission of one side of an element), 0.5 (complete omission of one side, together with partial omission of the other side of the same element) or 0 (no drawing, or no recognizable element). The total omission score ranged from 0 to 10.

All patients performed the tasks using the hand ipsilateral to the side of the hemispheric lesion (ipsilesional), unaffected by motor deficits. Patients were classified as showing USN based on the available standardized norms for the Bell cancellation test (Vallar, Rusconi, Fontana, & Musicco, 1994), or on the performance of

the control group for the remaining tasks when no normative data were available. The following cut-off scores were applied: i) Star cancellation: a difference of omissions between the two sides of the sheet greater than 2; ii) Bell cancellation: a difference of omissions between the two sides of the sheet greater than 4; iii) Line bisection: a mean deviation score greater than +5.7 or smaller than -7.7, iv) Five-element complex drawing: a number of omissions greater than 0.5, lateralized on one (the right or left ipsilesional) side. Patients who obtained a defective score, indicative of an ipsilesional spatial bias, in one of the four tests assessing USN, were classified as affected by USN. According to this categorisation procedure, all LBD patients were classified as not affected by USN.

Worthmentioning, right USN after left brain lesion can recover over the first three months after stroke (Stone, Patel, Greenwood, & Halligan, 1992): most of our LBD stroke patients (6 out of 10) were assessed within three months from the onset of the cerebrovascular disease, but all of them showed no sign of USN, both at the hospital admission and at the time of testing. On the contrary, 10 of our RBD patients were classified as affected (P#11-20, RBD/N+) and 10 as not affected (P#1-10, RBD/N-) by USN (see Table II for the results of the neglect assessment of the three groups of patients).

-Tables II and III about here-

2.4. Prismatic Adaptation (PA)

Participants sat at a table and positioned their (right or left) upper limb inside a two-layer wooden box (32 cm high, 74 cm wide). The lower and upper surfaces of the box had a pentagonal shape, with the long side facing the participant. The pentagon's depth at the centre was 32 cm, 19 cm at the lateral sides (Fortis et al., 2010). Participants sat in front of the middle of the box, while wearing prism goggles. LBD patients were exposed to left-shifting lenses, and RBD patients (both N- and N+) to right-shifting lenses; neurologically unimpaired participants were sub-divided into two groups, with half of them adapting to left-shifting lenses (Group CL), and half to right-shifting lenses (Group CR). Participants were asked to point with their index finger (right index for participants exposed to rightward shifting prisms, left index for participants exposed to leftward-shifting prisms) at a target (a red pen), presented by the examiner at the distal side of the box. Participants were instructed to perform a quick out-and-back movement, starting from, and coming back to

their own stern bone. A black cloth occluded to participants the vision of the arm from the stern to the box, with only the final movement of the index finger emerging from the distal side of the box being visible to the participant.

Each participant performed 90 pointing movements. The target was presented in a pseudorandom fixed order, in one of the two positions, at 10° to the right or to the left of the participant's mid-sagittal plane. The distance between the target and the participant's finger was measured after each movement in degrees of visual angle, using a scale with angular gradations attached on the distal part of the box on the examiner's side. A positive score denoted a rightward displacement of the finger with respect to the position of the target, a negative score a leftward displacement. The pointing adaptation task lasted about 20 minutes.

2.5. Proprioceptive and Visuo-Proprioceptive straight-ahead

Participants sat at a table with their body aligned with the middle of the experimental panel used during the tasks; a chin-rest was used to maintain this position during the tasks. A transparent square panel (50 cm side), marked with a goniometer with lines radiating from -90° to +90°, was placed on the table, with 0° corresponding to the participant's mid-sagittal plane. The participant's hand used in the pointing task (the right one for participants exposed to rightward shifting lenses, the left one for participants exposed to leftward shifting lenses) was positioned on the panel, with the index finger on the starting position (marked with a little sponge) in correspondence of the 0°, near the body: this position served as a starting point for all movements required.

Participants were tested in a dark, quiet room. In the Proprioceptive (P) test, each participant was blind-folded, and instructed to indicate the subjectively estimated position of the body midline, laying the index finger on the panel's surface. Each participant made 10 straight-ahead pointing movements: after each trial the experimenter recorded the position of the finger on the panel, as the deviation (leftward or rightward) from the objective body midline, in degrees of visual angle. In the Visuo-proprioceptive (VP) task, a red LED was mounted on the top of a black wooden box (35 cm high), 70 cm distant from the participant's head. Each participant was required to perform 10 pointing movements on the panel surface to indicate the downward projected position of the LED. On each trial, participants were asked to close their eyes, to allow

the experimenter to place the LED in the appropriate position; the LED was in fact always placed in correspondence of the participants' body midline (at 0°), but they were unaware of its position. During the pointing movement, the arm was occluded from vision by a wooden box (30 cm high, 75 cm width, 50 cm depth). After each trial the experimenter recorded the position of the finger on the panel as the deviation from the veridical downward projection of the LED position (rightward or leftward deviation), in degrees of visual angle. In both the P and the VP tasks, participants were required to perform the pointing movements as fast and accurate as they could. The order of the two tasks (P and VP) was counterbalanced across participants.

2.6. Procedure

The experiment included three successive phases, and overall lasted about 60 minutes.

1. *Pre-exposure phase*, before adaptation to prisms. In this phase (PRE), two tests assessing the egocentric reference were administered, namely: the P and VP straight ahead tests, as described in detail above (Calzolari et al., 2015; Calzolari, Albini, Bolognini, & Vallar, 2017; Fortis, Ronchi, Calzolari, Gallucci, & Vallar, 2013).

2. *Exposure phase: PA*. Participants were exposed to prism, displacing laterally the visual field of 12.4°, leftward or rightward (Fortis, Goedert, & Barrett, 2011).

3. *Post-exposure phase*, after adaptation to prisms. The P and VP tests were administered immediately after prism adaptation (POST1), and at a 10-minute delay (POST2). Finally, at the end of the POST2 assessment, the effects of PA on left spatial neglect in RBD/N+ patients were assessed by two tests: Star Cancellation (Wilson et al., 1987), and copy of a five-element complex drawing (Gainotti et al., 1972).

During all phases of the procedure, the examiner carefully checked that each instruction was fully understood, and verified the comprehension of each task with a first trial, not considered in the final count and analysis: this procedure was followed to confirm that all patients, particularly the LBD patients with language impairments, could correctly perform the experiment.

2.7. Scoring and statistical analyses

With respect to the *pre- and post-exposure measures*, the average deviation scores of the 10 pointing movements were computed for the P and VP tasks. To evaluate the presence of AEs following the adaptation procedure, the differences between the post- and the pre-exposure mean deviation scores were computed, to express the relative shift for each task (P Shift, VP Shift); two P and VP shifts were computed for the POST1 and the POST2 assessments. For the tests assessing USN, administered after the second post-exposure phase (POST2), the omission scores in the target cancellation and drawing tasks were computed using the same procedure described for the baseline evaluation of USN (see section 2.2).

For the *exposure* phase, the mean deviation error of the pointing movements towards the target, brought about by the prism-induced displacement of the visual field, was computed for the first (1-4), and the last (87-90) four pointing trials, out of the 90 movements performed during the exposure condition. The initial (four) and the final (four) pointing trials included two pointing movements towards the left-sided target, and two movements towards the right-sided target.

Finally, in order to make comparable the directional error made by the various groups of brain-damaged and unimpaired participants, with respect to the side of the prism-induced visual shift (left- and right-shifting prisms), all scores were converted as follows: a positive value corresponded to a deviation ipsilateral to the prism-induced visual field shift, a negative value to a deviation contralateral to the prism-induced visual field shift. For example, the deviation of a pointing towards the right-side of space (or to the right of the target, during the exposure phase) performed by a participant adapted to rightward shifting prisms, corresponded to a positive score; the same movement performed by a participant adapted to left-shifting prism corresponded to a negative score. Thus, according to the current literature, we expected errors ipsilateral to the prism-induced visual field deviation for the first trials during the exposure adaptation (positive scores), followed by the subsequent reduction of such pointing error (i.e., values close to 0°) in the last trials. Instead, for the AEs scores we expected values indicating a shift contralateral to the prism-induced visual field deviation (negative scores). Table IV shows a schematic summary of the sign attributed to right and left movements' deviation, for each group.

Statistical analyses were performed using the softwares Statistica™ (version 7.0) and SPSS (Version 25). To evaluate if and to what extent participants adapted to prism exposure, correcting the lateral deviation induced by the prismatic displacement, repeated-measures analyses of variance (ANOVA) were performed, with Time (first/last four pointing trials) as the within-subjects, and Group as the between-subjects, main factors. Parametric analyses (t-tests, ANOVA) were applied to the mean P and VP scores, and to P and VP shifts, to assess the presence of AEs, and the differences across groups. The presence of a significant P and VP shifts was computed comparing the mean shift against zero, that is the intercept of the ANOVA, or with ad-hoc t-tests against zero. Post-hoc tests were computed using the Newman-Keuls correction for multiple comparisons. Non-parametric analyses (Siegel & Castellan, 1988) were computed in order to compare in RBD/N+ patients the neglect omission scores in the Star and Drawing tasks, before and after PA.

The alpha-level was set at 0.05. To quantify the magnitude of the effects we report, we provide partial eta squared (η_p^2) values for F-tests.

-Table IV about here-

3. Results

3.1. Prismatic adaption

Figure 2 shows the average pointing deviation errors of the first and of the last trials for controls (left panel), and for LBD and RBD patients (right panel). All participants reduced their pointing error from the first to the last trials, showing adaptation to the optical prisms. CR participants made an overall larger error than CL participants.

At first, ANOVAs were conducted, in order to assess whether participants adapted to the visual field displacement induced by prisms. With respect to the performance of controls, the ANOVA with Time (2 levels: first pointing deviation, last pointing deviation) as the within-subjects main factor, and Group (2 levels: CR and CL) as the between-subjects main factor, revealed a significant main effect of Time ($F_{1,22}$ = 256.68, $P< 0.001$, η_p^2 = 0.921), with control participants showing a reduction of the pointing error from the first trials (M = 7.48) to the last trials (M = 0.91). Also, the main effect of Group was significant ($F_{1,22}$ = 8.81,

P= 0.007, η_p^2 = 0.286), with CR showing a greater deviation error than CL, independently from the Time main factor. Finally, the interaction Time by Group showed a tendency towards significance ($F_{1,22}$ = 3.82, *P*= 0.063, η_p^2 = 0.148): a perusal of the data suggested that CR and CL tended to differ with respect to the deviation in the first trials (CR: M = 8.69; CL: M = 6.27), while this difference was not present for the last pointings of the adaptation phase (CR: M = 1.31; CL: M = 0.50).

With respect to the performance of brain-damaged patients, the ANOVA with the within-subjects main factor Time (2 levels: first pointing deviation, last pointing deviation), and the between-subjects main factor Group (3 levels: RBD/N-, RBD/N+, LBD), showed a significant main effect of Time ($F_{1,27}$ = 140.55, *P*< 0.001, η_p^2 = 0.839): all patients adapted to the prisms, exhibiting an error reduction from the first trials (M = 7.05) to the last trials (M = 0.92). No other significant main effects or interactions emerged [Group ($F_{1,27}$ = 0.53, *P*= 0.60, η_p^2 = 0.037); Time by Group ($F_{1,27}$ = 1.58, *P* = 0.22, η_p^2 = 0.105)].

A comparison between patients and controls, who underwent the same type of PA, was also conducted. Both the first ANOVA [main within-subjects factor Time (2 levels: first pointing deviation, last pointing deviation), main between-subjects factor Group (3 levels: RBD/N-, RBD/N+, RC)], and the second ANOVA [main within-subjects factor Time (2 levels: first pointing deviation, last pointing deviation), main between-subjects factor Group (2 levels: LBD, CL)], revealed a significant main effect of Time [for right prismatic adaptation: ($F_{1,29}$ = 163.12, *P*< 0.001, η_p^2 = 0.849); for left prismatic adaptation: ($F_{1,20}$ = 353.28, *P*< 0.001, η_p^2 = 0.946)], with a reduction of the deviation errors from the first trials to the last trials. No other significant difference was found [for right prismatic adaptation: Group ($F_{1,29}$ = 1.18, *P*= 0.32, η_p^2 = 0.075), Time by Group ($F_{1,29}$ = 0.62, *P*= 0.55, η_p^2 = 0.041); for left prismatic adaptation: Group ($F_{1,20}$ = 0.68, *P*= 0.42, η_p^2 = 0.033), Time by Group ($F_{1,20}$ = 1.57, *P*= 0.23, η_p^2 = 0.073)].

-Figure 2 about here-

3.2. Post-Pre differences: Proprioceptive and Visuo-proprioceptive AEs

Figure 3 shows the amount of AEs in the two tasks for controls and brain-damaged patients: the P shift decreases in CR participants, and the VP shift decreases in CL and LBD participants, with the LBD being to zero (i.e., no POST-PRE differences) in the VP Shift 2. The scores of the individual patients in the VP and P

Shift 1 and Shift 2 are reported in the Appendix. The presence of immediate and long-term AEs was assessed by the following analyses, comparing the extent of the shift over time (Shift 1: POST1-PRE; Shift 2: POST2-PRE) for controls and patients.

For control participants, an ANOVA with Time (2 levels: Shift 1 and Shift 2) and Task (2 levels: P and VP) as the within-subjects main factors, and Group (2 levels, CR and CL) as the between-subjects main factor, was conducted on the deviation scores. The intercept was significant ($F_{1,22} = 59.77$, $P < 0.001$, $\eta_p^2 = 0.731$), revealing the presence of AEs independently of the time and task considered. Also the Time by Task by Group interaction was significant ($F_{1,22} = 12.04$, $P = 0.002$, $\eta_p^2 = 0.354$). This significant interaction was first explored by Newman-Keuls post-hoc tests, that did not reveal any significant difference; then, Fisher post-hoc tests were used: the analyses showed that for CR there was a significant difference for the P shift between Shift1 and Shift 2 ($p < 0.01$), with a reduction of the P AEs in the delayed condition; for CL, a significant reduction of the VP shift between Shift 1 and Shift 2 ($p < 0.01$) was detected. No other main factor or interaction were significant [Group ($F_{1,22} = 1.16$, $P = 0.29$, $\eta_p^2 = 0.050$), Time ($F_{1,22} = 3.18$, $P = 0.09$, $\eta_p^2 = 0.126$), Task ($F_{1,22} = 0.43$, $P = 0.52$, $\eta_p^2 = 0.019$), Time by Group ($F_{1.22} = 0.05$, $P = 0.82$, $\eta_p^2 = 0.002$), Task by Group ($F_{1,22} = 0.41$, $P = 0.53$, $\eta_p^2 = 0.018$), Task by Time ($F_{1,22} = 0.13$, $P = 0.72$, $\eta_p^2 = 0.006$)]. To summarize, control participants showed a reduction of the P shift (CR), and of the VP shift (CL) in the delayed condition.

For patients, an ANOVA with Time (2 levels: Shift 1 and Shift 2), and Task (2 levels: P and VP) as the within-subjects main factors, and Group (3 levels, RBD/N-, RBD/N+, LBD) as the between-subjects main factor, showed the presence of AEs, independent from Time and Task (Intercept: $F_{1,27} = 54.26$, $P < 0.001$, $\eta_p^2 = 0.668$), and a significant effect of Group ($F_{2,27} = 4.20$, $P = 0.026$, $\eta_p^2 = 0.237$). The Group effect was due to a significant difference between LBD and RBD/N+ patients ($p < 0.05$), while the difference between LBD and RBD/N- patients was not significant, although with a trend in the same direction ($p = 0.068$). No other factor or interaction were significant [Time ($F_{1,27} = 2.08$, $P = 0.16$, $\eta_p^2 = 0.072$), Task ($F_{1,27} = 0.01$, $P = 0.92$, $\eta_p^2 = 0.000$), Time by Group ($F_{2,27} = 2.69$, $P = 0.09$, $\eta_p^2 = 0.166$), Task by Group ($F_{2,27} = 1.22$, $P = 0.31$, $\eta_p^2 =$

0.083), Task by Time ($F_{1,27}$ = 0.11, *P*= 0.74, η_p^2 = 0.004), Task by Time by Group ($F_{2,27}$ = 0.40, *P*= 0.68, η_p^2 = 0.029)].[2]

The comparison between brain-damaged patients and controls was performed by two analyses. A first Time by Task by Group ANOVA was run to compare RBD/N-, RBD/N+ patients and CR participants: the intercept was significant, to confirm the presence of AEs ($F_{1,29}$ = 96.64, *P*< 0.001, η_p^2 = 0.769), with no other significant main effects or interactions [Group ($F_{2,29}$ = 0.96, *P*= 0.40, η_p^2 = 0.062), Time ($F_{1,29}$ = 0.53, *P*= 0.47, η_p^2 = 0.018), Task ($F_{1,29}$= 1.44, *P*= 0.24, η_p^2 = 0.047), Time by Group ($F_{2,29}$= 1.07, *P*= 0.36, η_p^2 = 0.069), Task by Group ($F_{2,29}$= 0.03, *P*= 0.97, η_p^2 = 0.002), Task by Time ($F_{1,29}$= 1.47, *P*= 0.23, η_p^2 = 0.048), Task by Time by Group ($F_{2,29}$= 0.88, *P*= 0.43, η_p^2= 0.057)].

A second Time by Task by Group ANOVA was run to compare LBD patients and CL participants. The intercept was significant, to indicate the presence of significant AEs ($F_{1,20}$ = 19.57, *P*< 0.001, η_p^2 = 0.495). Moreover, the main factor Time was significant ($F_{1,20}$ = 7.23, *P*= 0.014, η_p^2 = 0.265), with a significant decrease of the AEs in the Shift 2. Also, the interaction Time by Task was significant ($F_{1,20}$ = 6.74, *P*= 0.017, η_p^2 = 0.252): post-hoc tests showed no differences between Shift 1 and Shift 2 for the P task, but a significant decrease of the VP AE between Shift 1 and Shift 2 (p< 0.01). No other main factor or interaction reached significance [Group ($F_{1,20}$ = 1.17, *P*= 0.29, η_p^2 = 0.055), Task ($F_{1,20}$= 1.69, *P*= 0.21, η_p^2 = 0.078), Time by Group ($F_{1.20}$= 0.19, *P*= 0.67, η_p^2 = 0.009), Task by Group ($F_{1.20}$= 1.72, *P*= 0.20, η_p^2 = 0.079), Task by Time by Group ($F_{1.20}$= 0.28, *P*= 0.60, η_p^2 = 0.014)]. Therefore, in both groups adapting to left deviating lenses, there was a reduction of VP AEs in the Shift 2.

In the two control groups, t-test *vs.* zero analyses were performed to assess whether the overall Shift (i.e., the VP and the P shifts, averaged over the two time-periods) was significantly different from zero (i.e., no POST-PRE differences), revealing the presence of AEs (CL : t_{11}= -4.37, *P*= 0.001; CR: t_{11}= -6.79, *P*< 0.001). Further analyses specifically explored the persistence of the two assessed AEs at the delayed assessment (Shift 2). In both control groups, Shift 2 was still significantly different from zero, indicating that the AEs were still present: CR (P Shift 2: t_{11}= -2.46, *P*= 0.032; VP Shift 2: t_{11}= -5.46, *P*< 0.001); CL (P Shift 2: t_{11}= -2.59, *P*= 0.025; VP Shift 2: t_{11}= -2.34, *P*= 0.039).

[2] The ANOVA showed similar results even if the RBD/N+ patient P14, who exhibited large AEs (see Appendix), is excluded from the analysis.

In brain-damaged patients, these analyses showed significant differences from zero for the overall Shift of RBD patients (RBD/N+ t_9= -4.72, *P*= 0.001; RBD/N- t_9= -7.06, *P*< 0.001), but not for the overall Shift of LBD patients, for whom only a trend was detected (t_9= -2.11, *P*= 0.065). Therefore, LDB patients presented with little, if any, AEs, which in fact did not differ from zero, indicating the absence of a POST-PRE difference. t-test *vs.* zero statistics further assessed specifically whether Shift 2 in the P and VP tasks differed significantly from zero, indicating in turn whether significant deviations (AEs) were still present at the delayed assessment: LBD patients (P Shift 2: t_9= -2.11, *P*= 0.064; VP Shift 2: t_9= 0.07, *P*= 0.945); RBD/N+ patients (P Shift 2: t_9= -4.95, *P*= 0.001; VP Shift 2: t_9= -3.20, *P*= 0.011); RBD/N- patients (P Shift 2: t_9= -4.71, *P*= 0.001; VP Shift 2: t_9= -4.01, *P*= 0.003). To summarize, RBD patients exhibited persistent P and VP AEs in the delayed assessment; conversely, LBD patients showed shifts not significantly different from zero at the delayed assessment, namely: no AEs.

-Figure 3 about here-

3.3. USN assessment

The Wilcoxon signed ranks test was used to compare the USN scores of RBD/N+ patients (n= 10) before and after the exposure to prisms. No significant differences were found for the omission scores in the Star cancellation task (z = 0.76, *P*= 0.445; omission errors pre-PA: mean ± SD: 23.11±19.74; omission errors post-PA: 20.9±20.79). A significant difference was found for the omission score at the copy of a Five-Element Complex Drawing (z = 2.25, *P*= 0.024; omission errors pre-PA: 5.4±3.81; omission errors post-PA: 3.95±3.23), with a reduction of the number of omissions after adaptation to prismatic lenses (before prisms = 5 omissions; after prisms = 3 omissions). These findings are overall in line with the evidence, reviewed in the introduction, that PA to prisms displacing the visual scene rightward improves signs of left USN.

3.4. Lesion analyses

Figure 1 shows the localisation and the maximum overlap of the lesions of the LBD, RBD/N- and RBD/N+ groups (P1, P14 and P15 scan images were not available for mapping; P2 was not mapped because the lesion had neoplastic origin). For the RBD/N- group the maximum overlap (n = 4 patients) was on a

small area in the white matter under the right temporal lobe and in the right insula. For the RBD/N+ group the maximum overlap (n = 8 patients) was in the mesial and superior right temporal lobe, including the right insula. For the LBD group the maximum overlap (n = 5 patients) was in the left putamen.

The size lesion of the three groups of patients was compared. An one-way ANOVA was conducted: the analysis showed a significant effect of Group ($F_{2,23}$= 8.23, *P*= 0.002, η_p^2= 0.417), with LBD patients having smaller lesion (mean ± SD: 14887 cc ± 17506, range: 1048-56570 cc) than RBD/N- (89115cc ± 89850, range: 4651-242457 cc) (p< 0.05) and RBD/N+ (148090 cc ± 86771, range: 70718-241024 cc) (p< 0.01) patients. Even if RBD/N- patients had smaller lesions with respect to RBD/N+, the difference between these two groups did not reach the significance level (p= 0.09).

The mean duration of disease of all stroke patients was 6.61 months (±10.61, range: 0.57-35.53; RBD/N-: 8.73 ± 14.5, range: 1.13-49.2; RBD/N+: 6.58 ± 10.9, range: 0.90-35.53; LBD: 4.53 ± 4.9, range: 0.57-15.97). No significant differences in time since stroke across the three groups were detected ($F_{2,27}$= 0.37, *P*=0.692).

4. Discussion

4.1. Adaptation and AEs after left and right brain damage

In this study, the immediate and delayed (i.e., after 10 minutes) effects of exposure to prisms in brain-damaged patients, taking into account the extent of PA after left- and right-sided hemispheric lesions, were examined. Both RBD and LBD patients adapt to prismatic exposure, with consequent P and VP AEs after prism removal, but, in LBD patients, the averaged AEs tend to be close to zero (t-test vs. zero: p=0.065) and appear globally reduced, as compared to those of RBD/N+ patients. In particular, when the left hemisphere is damaged, the VP AEs do not differ from zero by 10 minutes after prism exposure (see Figure 3). Also healthy controls adapting to left-shifting lenses show reduced VP AEs in the 10-minute delayed condition. Unlike the case of LBD patients, however, these AEs are still present, being significantly different from zero. In RBD patients the AEs were comparable in the P and in the VP tasks. In a previous study (Sarri et al., 2008), larger AEs in the P task were found in RBD patients with USN. However, while the present P task

was comparable to the one adopted in that study, this was not the case for the VP task, in which vision was available to participants. Indeed, in the study by Sarri et al. (2008), the task was a "target pointing" one, with participants being "asked to make repeated pointing movements to a single visible target placed at the actual centre of their mid-sagittal plane", although Sarri et al. (2008) write that "the correct response was identical to the objectively correct response for the Subjective Straight Ahead task". Instead, our VP task did not require a pointing to a visual target, with participants being required instead to perform pointing movements on the panel surface to indicate the downward projected position of a LED (corresponding to the straight ahead), but not to point to an actual visual target. Therefore, results from the study by Sarri et al. (2008), and from the present experiment, are not directly comparable with respect to their visual component. Furthermore, in stroke patients more variable patterns of PA effects on both P and VP tasks (more similar to the present one) have been reported by Facchin and colleagues (Facchin, Beschin, Toraldo, Cisari, & Daini, 2013), who analysed their data with a multiple single case approach (see Shallice, 2015).

Complementary to these data, the present study shows that, independently from the presence of USN, the two groups of patients adapted to the prismatic lenses. In particular, during the exposure to prisms, both RBD and LBD patients presented the well-known reduction of pointing errors from the first to the last movements (Fortis et al., 2010). After removal of the prisms, both patients' groups displayed P and VP shifts towards the contralesional side of space, with respect to the visual field deviation induced by the goggles. However, when the first and the delayed assessments were analysed together, the averaged AEs of LBD patients did not significantly differ from zero (t-test vs. zero, $p=0.065$). On average, the two P and VP AEs were also smaller and significantly different in LBD patients compared to RBD/N+ patients; the same pattern was present when LBD patients were compared to RBD/N- patients, although this comparison did not reach the statistical significance. Additionally, the VP (t-test vs. zero, $p=0.945$) and the P (t-test vs. zero, $p= 0.064$) shifts in the delayed condition were not different from zero in LBD patients. This finding can be of relevance for the use of prismatic goggles in LBD patients, as the visuo-motor integration seems to return to the pre-exposure situation in ten minutes. This could (at least in part) explain the findings of the previous case reports of patients with right USN after left brain damage, in whom the improvement in visuo-motor tasks returns (Facchin et al., 2017), or tends to return (Bultitude & Rafal, 2010), to the pre-PA levels in the long-

term assessment. Compared to such an evidence, it is noteworthy that our LBD patients did not show right USN; it follows that, potentially, different mechanisms may be recruited by PA if spatial functions are mainly lateralized in the right or in the left hemisphere, in turn influencing the PA outcomes.

With relevance for our data, a previous study (Magnani et al., 2011), which investigated if PA modulates time perception, assessed PA effects in RBD and LBD patients. Patients performed the adaptation with the ipsilesional hand, and were adapted to ipsilesional and contralesional lenses. LBD patients, although adapting to prisms as RBD patients did, presented with a reduced pointing deviation in the first trials of PA, but showed a pattern of quick error reduction during exposure to prisms. In our experiment, this latter effect was found only in healthy control participants, adapting to leftward shifting *vs.* rightward shifting lenses, but not in brain-damaged patients. Magnani et al. (2011) assessed the consequent AEs only with a VP task: interestingly, their LBD patients exhibited reduced leftward AEs compared to RBD patients, when both groups adapted to rightward shifting lenses; for adaptation to leftward shifting prisms, the AEs in the two groups of patients were comparable. At variance from our study, the amounts of contralesional AEs induced by lenses displacing the visual scene towards the ipsilesional side (i.e., rightward displacing prisms for RBD patients *vs.* leftward displacing prisms for LBD patients) were not directly compared by Magnani et. al. (2011), who also did not analyse the AEs' time-course. In sum, although a precise comparative discussion of the present findings and of those of Magnani and coworkes (2011) can not be performed, due to the inherent methodological differences, the suggestion can be made that PA in LBD patients can take place, but the subsequent AEs may be less pronounced and long lasting. This finding might be due to a reduction of the visuo-motor deviation in the first phase of prisms exposure, as demonstrated by Magnani et al. (2011). In our study, in LBD patients, but not in LC control participants, for the global AEs the difference between the assessments made before and after PA did not differ from zero, as well as the delayed shift, possibly indicating in LBD patients a reduced duration of AEs.

The reduction of VP AEs in the delayed assessment has been found also for healthy participants adapting to leftward shifting lenses (LC), but not for adaptation to rightward shifting lenses (where the delayed P AEs decreased). One possible interpretation is that the effect induced by leftward shifting prisms (and/or by the use of the left hand during prism exposure) is weaker than the one brought about by rightward

shifting prisms (and/or the use of the right hand during prism exposure) in maintaining the VP AEs, independently from the presence of the lesion. The reverse appears however to be the case for the association between decreasing of the P AEs with PA to rightward shifting lenses and the use of the right hand. The two groups of control participants (CR and CL) show then a complex pattern of interaction between the direction of the prismatic shift and the used hand, with the decay of specific AEs, that however remain different from zero at the assessed delay. Nevertheless, the present results in LBD patients cannot be completely explained by an effect of the direction of the visual-field displacement. In fact, although the direct comparison between patients and controls (LBD and LC) did not show statistically significant differences, the LC group's VP AEs remain significantly different from zero at the delayed 10-minute assessment, although reduced in size (see Figure 3); this is not the case for the AEs of LBD patients. As the VP task requires the coordination of visual and motor/proprioceptive information, an ability required in most activities of daily life, this result may have a relevant clinical impact. In fact, USN patients are usually impaired in ecological daily-life visuo-motor tasks, beyond the traditional standardized tests (Azouvi, 2016), and their undamaged left hemisphere may provide a relevant neural network for the PA-induced amelioration.

4.2. Effects of prism adaptation on left and right USN

As additional results, we also found that a single PA session brings about improvement of USN in the Five-Element Complex Drawing task, but not in the Star Cancellation tastk. This finding is broadly in line with previous evidence showing the immediate effectiveness of a single session of PA on a variety of manifestations of the USN syndrome, including defective drawing, target cancellation and line bisection (Rossetti et al., 1998), spatial dysgraphia (Rode et al., 2006), left auditory extinction (Jacquin-Courtois et al., 2010), wheel-chair navigation (Jacquin-Courtois, Rode, Pisella, Boisson, & Rossetti, 2008), bisection of body parts (Bolognini, Casanova, Maravita, & Vallar, 2012). One recent study (Facchin, Bultitude, Mornati, Peverelli, & Daini, 2018) found effects of PA on target cancellation, only when two counterbalanced sesssions of PA of concurrent and terminal exposure[3] were combined, with no effects of a single session of PA; interestingly, as in the present experiment, effects of PA on USN were the last to be assessed in the

[3] In the concurrent exposure paradigm the pointing arm is visible to participants; in the terminal exposure paradigm only the participants' finger, when close to the target, is visible to them (Redding et al., 2005).

experimental sequence. Other evidence of effects of PA on neglect signs only at a delayed (after 1 hour) assessment is on record (Rode, Pisella, Rossetti, Farnè, & Boisson, 2003, Figure 3b). Even if the beneficial effect of a single exposure to prisms can last up to a few hours after adaptation (Farnè et al., 2002; Luauté et al., 2006; Rode et al., 2003; Rossetti et al., 1998), our finding can be accounted for by the combination of a single session of prism exposure with a delayed psychometric assessment (i.e., after the POST2 evaluations of AEs) of USN, since the investigation of the effects of PA on USN was not the primary objective of the study.

The PA method has been successfully used in the rehabilitation of left USN after right brain damage (Fortis et al., 2018; Frassinetti et al., 2002; Làdavas, Bonifazi, Catena, & Serino, 2011; Mizuno et al., 2011; Serino, Barbiani, Rinaldesi, & Làdavas, 2009; Shiraishi et al., 2010; Shiraishi, Yamakawa, Itou, Muraki, & Asada, 2008; Vangkilde & Habekost, 2010). The long known hemispheric asymmetry in the occurrence of USN, contralateral to the side of the lesion, after right- *vs.* left-brain lesions, is reported in most studies in terms of a greater frequency of left USN after right brain damage (Beis et al., 2004; Bisiach, Cornacchia, Sterzi, & Vallar, 1984; Stone et al., 1992; Vallar, Rusconi, Geminiani, Berti, & Cappa, 1991), in line with findings from the present study. When frequency and severity were compared, USN was found to be more frequent, but not more severe, after right brain damage than after left damage (Suchan, Rorden, & Karnath, 2012), more severe, but not more frequent (Ogden, 1985a), and comparably frequent (Ogden, 1985b, 1987). Right USN seems also featured by a prevailing “allocentric” pattern, at least in the acute or sub-acute stage of illness in stroke patients (Chechlacz et al., 2012; Kleinman et al., 2007). So far, then, the vast majority of investigations have focused on the effect of PA to rightward shifting lenses in patients with left USN following right brain damage.

To our knowledge, only two studies have investigated the effects of leftward shifting prisms on the symptoms of right USN. Bultitude and Rafal (Bultitude & Rafal, 2010) examined a patient with a large left fronto-parietal haemorrhagic lesion and a mild right USN. After exposure to leftward shifting prisms, the patient’s performance significantly improved in a line bisection task, as compared to a sham stimulation with goggles not inducing any deviation of the visual field. In the follow-up assessment, administered 11 days after prism exposure, the patient’s performance in line bisection was still improved, but tended to return to

the pre-PA. In another recent case report (Facchin et al., 2017), an amelioration of right spatial and personal neglect after exposure to leftward shifting prisms, administered to a left-brain-damaged patient for 4 times, was found; however, in a 1-week follow-up USN scores returned to the baseline level. These data suggest that leftward shifting prisms can be effective in modulating right USN after left-sided brain lesions, and they may involve mechanisms similar to those effective in the left-sided deficit associated with right brain damage.

4.3. Neural underpinnings of prism adaptation

As detailed in the introduction, the procedure of PA and the induced AEs rely on a vast bilateral cerebral network. Our results support to a role of left hemispheric, cerebral (and cerebellar), activity. Complementary to our findings, there are two single-case neuropsychological studies showing that a left-sided hemispheric lesion, injuring the left cerebellum, may disrupt rightward [the patient wears prisms deviating the visual scene leftward (Pisella et al., 2005)], and leftward [the patient wears prisms deviating the visual scene rightward (Calzolari et al., 2015)] AEs. Accordingly, in right-brain damaged patients with left USN, the cathodal-inhibitory transcranial direct current stimulation (tDCS) of the left PPC reduces the clinical benefits of the PA rehabilitation (Làdavas et al., 2015), while the anodal-excitatory tDCS of the left (but not of the right) PPC is able to restore the proprioceptive AEs, disrupted by a left cerebellar and bilateral occipital damage (Calzolari et al., 2015). It is worth noting that in our LBD patients, the lesion size was smaller than that of RBD patients. This may imply that the overall integrity of the left hemispheric activity is relevant for obtaining reliable and long-lasting AEs, and that a comparatively smaller lesion may be effective in reducing AEs after left brain damage. Also, some more specific regions in the left hemisphere may be more relevant for PA to occur. The inspection of the lesion maps indicates that most LBD patients had subcortical lesions, mainly affecting the left putamen (5 out of 10 patients), although this finding should be treated with some caution, considering the size of the patients' sample. In healthy participants, an fMRI study (Seidler, Noll, & Chintalapati, 2006) reports activations in the basal ganglia, bilaterally, including the putamen, during the process of sensorimotor adaptation, using the right hand. Hence, subcortical regions seem to work in concert with cortical areas such as the primary sensorimotor, premotor, posterior parietal,

prefrontal and temporal cortices (Clower et al., 1996; Ghilardi et al., 2000; Inoue et al., 1997, 1998), as well as the cerebellum (Imamizu et al., 2000; Küper et al., 2014, using PA). For instance, in sensorimotor paradigms using PA, activations in healthy participants have been reported in the PPC contralateral to the adapting upper limb (Clower et al., 1996), and in the anterior cingulate, in the left PPC, and in the left primary motor cortex contralateral to the right adapting upper limb (Danckert, Ferber, & Goodale, 2008). A main role of the left hemisphere is further suggested by a study in brain-damaged patients, showing that damage to the left, but not to the right parietal, mainly posterior, cortex impairs visuo-motor adaptation to a 30º deviated visual feedback in a pointing task (Mutha, Sainburg, & Haaland, 2011). However, in the study by Mutha et al., at variance with our experiment, patients used their contralateral, affected, upper limb, namely: LBD patients the right arm, RBD patients the left arm. No left-right differences in the severity of hemiparesis, defined overall as "mild", were reported (Mutha et al., 2011); in this study, at variance from the present one, lesion site and size were comparable in both LBD and RBD patients. In sum, the available evidence, from both activation experiments in healthy participants and LBD patients, is compatible with the suggestion of a role of left-sided brain structures, including subcortical grey nuclei, in PA and AEs, as also suggested by the present study. The association of left-hemisphere damage along with a subcortical lesion may exert a greater impact on the prism-induced AEs, with a faster decay.

4.4. Limitations and Conclusions

This study did not address some issues, which may be considered for future research. Firstly, since the study aimed at analysing the effects of PA with a therapeutic perspective, we did not include in our experiment adaptation lenses deviating the field of vision contralesionally, namely leftward in RBD patients (rightward AEs), which in healthy participants can mimic left USN (Michel et al., 2003; Schintu et al., 2014, 2017), and alter motor interhemispheric inhibition (Martín-Arévalo, Schintu, Farnè, Pisella, & Reilly, 2018). Secondly, purely visual (Calzolari et al., 2017; Fortis et al., 2013) AEs measures of PA were not assessed. Thirdly, some of our LBD patients presented with linguistic deficits, differently from RBD patients; in our sample, such deficit did not prevent the correct comprehension and execution of the tasks in this group. Finally, since we required patients to perform the pointings during PA, as well as the the tasks assessing the

AEs, with the non-paretic upper limb, we should consider that the non-dominant left upper limb was used by LBD patients, and the dominant (Oldfield, 1971) right upper limb by RBD patients. The use of the dominant (in LBD patients) and of the non-dominant (in RBD patients) upper limbs features also the study by Mutha et al. (2011), although reversed with respect to the present experiment, since patients used the upper limb contralateral to the side of the lesion, and possibly affected by a primary motor deficit. Both investigations, however, concur to suggest a role of the left hemisphere in sensorimotor adaptation even if different paradigms (PA, in the present experiment, and the manipulation of the cursor visual feedback relative to the hand motion in Mutha at al., 2011) were used. Furthermore, in that study both RBD and LBD patients had lesions of comparable size, confined to the PPC; in the present study, the lesion size of LBD patients was smaller than that of RBD patients, with an overlap in the left putamen. Taken together, these findings further suggest a role of left hemispheric cortical and subcortical regions in sensorimotor adaptations, including AEs induced by PA.

In conclusion, the present study demonstrates that both LBD and RBD patients, with and without USN, show a similar quick pattern of adaptation to prismatic lenses during exposure, which is also similar in magnitude. However, the weaker AEs in LBD patients support the contribution of a left-sided hemispheric (intact in healthy participants, and not structurally damaged in RBD patients) network on the presence, and the persistence of AEs following prism exposure. This novel evidence may have an impact on the implementation of the PA procedure as a rehabilitative technique in brain-damaged patients.

APPENDIX

Immediate and delayed (after 10 minutes) P and VP shifts of the 30 brain-damaged patients

Patient	Group	Shift P1	Shift P2	Shift VP1	Shift VP2
P1	RBD/N-	-6,2	-5,25	-1,8	-4,35
P2	RBD/N-	-3,2	-6,5	-8,75	-7,45
P3	RBD/N-	-0,15	0,4	-1,9	-3,4
P4	RBD/N-	-1,5	-3,55	-1,9	-1,15
P5	RBD/N-	-4,1	-2,05	-5,2	1,4
P6	RBD/N-	-4,05	-2,3	-4,9	-5,5
P7	RBD/N-	-8,1	-1,1	-4,9	-10,45
P8	RBD/N-	-4,8	-4,7	-4,25	-3,45
P9	RBD/N-	-4,5	-2,15	-2,1	-2,1
P10	RBD/N-	-1,15	-3,35	-10,4	-5,9
P11	RBD/N+	-8,4	-9,9	-7,4	-7,4
P12	RBD/N+	-0,55	-0,85	-6,4	-3,6
P13	RBD/N+	-3,2	-6,9	-0,5	-1,9
P14	RBD/N+	-7,05	-5	-18,8	-20,5
P15	RBD/N+	-2,35	-4,6	-4,7	-6,1
P16	RBD/N+	-7,15	-5,6	-5,45	-5,55
P17	RBD/N+	-0,85	-4,75	-4,6	-2,5
P18	RBD/N+	-7,1	-5,6	-2,4	-5,8
P19	RBD/N+	-7,8	-6,5	4,5	-3
P20	RBD/N+	0,1	1,2	-5,6	-0,6
P21	LBD	-4,45	-1,45	-3,4	-1,2
P22	LBD	-2,35	1,45	1,9	7,45
P23	LBD	1,05	-1,1	-0,85	0,35
P24	LBD	-7,75	-8,85	-2,85	-3,8
P25	LBD	-1,1	0,6	-3,1	-1,5
P26	LBD	0,5	-2,2	-4,9	-0,6
P27	LBD	-3,6	1,3	3,6	4,6
P28	LBD	-3,4	-4,3	-1,2	-1,1
P29	LBD	-4,95	-4,8	-5,2	-5,3
P30	LBD	-1,85	-1,8	-2,95	1,95

RBD/N-: right-brain-damaged patients without left USN; RBD/N+: right-brain-damaged patients with left USN; LBD: left-brain-damaged patients. SHIFT: differences between the post- and the pre-exposure mean deviation scores. A positive value corresponds to a deviation ipsilateral to the prism-induced visual field shift, a negative value to a deviation contralateral to the prism-induced visual field shift (see section 2.7 for more details). P: Proprioceptive task, administered immediately after prism adaptation (P1), and after a 10-minute delay (P2). VP: Visuo-proprioceptive task, administered immediately after prism adaptation (VP1), and after a 10-minute delay (VP2).

Captions to Figures

Figure 1. Lesion localization of brain-damaged patients, with left (LBD), and right (RBD/N-, RBD/N+) hemispheric lesions, and overlay lesion plots (bottom row = frequencies of overlapping lesions, from dark violet, n=1, to red, n= maximum group patients' number). Lesions were drawn on standard MRI template with a 1-mm slice distance (voxels of 1 mm^3). Scan images were not available for mapping for patients P01, P14 and P15. Patient P02 was not mapped because the lesion had neoplastic origin. Montreal Neurological Institute (MNI) Z-coordinates of each transverse section are reported.

For RBD/N- group the maximum overlap (n = 4 patients) was on a small area in the white matter under the right temporal lobe and in the right insula. For RBD/N+ group the maximum overlap (n = 8 patients) was in the mesial and superior right temporal lobe, including the right insula. For LBD group the maximum overlap (n = 5 patients) was in the left putamen.

Figure 2. Adaptation to prismatic lenses. Left/right panels: controls'/patients' groups. Pointing deviation from the visual target (mean pointing errors in angle degrees in the first and last four trials, SEM) induced during prism exposure. Positive values indicate pointing deviations ipsilateral to the prism-induced visual field shift (see section 2.7 for more details).

Figure 3. Immediate and long-term AEs: proprioceptive (A) and visuo-proprioceptive (B) shifts immediately after prism exposure (POST1-PRE exposure) and after a 10-minute delay (POST2-PRE exposure), in mean angle degrees (SEM). Dashed lines show the immediate AEs values, full-colour lines show the long-term shift values. Control (on the left side) and brain-damaged (on the right side) participants are illustrated. Negative values indicate pointing deviations contralateral to the prism-induced visual field shift (see section 2.7 for more details).

References

Angeli, V., Meneghello, F., Mattioli, F., & Ladavas, E. (2004). Mechanisms underlying visuo-spatial amelioration of neglect after prism adaptation. *Cortex*, *40*(1), 155–156.

Azouvi, P. (2016). The ecological assessment of unilateral neglect. *Annals of Physical and Rehabilitation Medicine*, *60*(3), 186–190. https://doi.org/10.1016/j.rehab.2015.12.005

Basso, A., Capitani, E., & Laiacona, M. (2016). Raven ' s Coloured Progressive Matrices : Normative values on 305 adult normal controls. *Functional Neurology*, *2*(2), 189–194.

Basso, A., & Cubelli, R. (1999). Clinical aspects of aphasia. In G. Denes & L. Pizzamiglio (Eds.), *Handbook of Clinical and Experimental Neuropsychology* (pp. 181–193). Hove, East Sussex: Psychology Press.

Beis, J.-M., Keller, C., Morin, N., Bartolomeo, P., Bernati, T., Chokron, S., … Azouvi, P. (2004). Right spatial neglect after left hemisphere stroke: qualitative and quantitative study.French Collaborative Study Group on Assessment of Unilateral Neglect (GEREN/GRECO). *Neurology*, *63*(9), 1600–1605. https://doi.org/10.1212/01.WNL.0000142967.60579.32

Bisiach, E., Cornacchia, L., Sterzi, R., & Vallar, G. (1984). Disorders of perceived auditory lateralization after lesions of the right hemisphere. *Brain*, *107*(1), 37–52. https://doi.org/10.1093/brain/107.1.37

Bisiach, E., & Faglioni, P. (1974). Recognition of random shapes by patients with unilateral lesions as a function of complexity, association value and delay. *Cortex*, *10*(2), 101–110.

Bisiach, E., Vallar, G., Perani, D., Papagno, C., & Berti, A. M. (1986). Unawareness of disease following lesions of the right hemisphere: anosognosia for hemiplegia and anosognosia for hemianopia. *Neuropsychologia*, *24*(4), 471–482. https://doi.org/10.1016/0028-3932(86)90092-8

Bolognini, N., Casanova, D., Maravita, A., & Vallar, G. (2012). Bisecting real and fake body parts: effects of prism adaptation after right brain damage. *Frontiers in Human Neuroscience*, *6*(154), 1–15. https://doi.org/10.3389/fnhum.2012.00154

Bultitude, J. H., & Rafal, R. D. (2010). Amelioration of right spatial neglect after visuo-motor adaptation to leftward-shifting prisms. *Cortex*, *46*(3), 404–406. https://doi.org/10.1016/j.cortex.2009.06.002

Calzolari, E., Albini, F., Bolognini, N., & Vallar, G. (2017). Multisensory and Modality-Specific Influences on Adaptation to Optical Prisms. *Frontiers in Human Neuroscience*, *11*(568), 1–12.

https://doi.org/10.3389/fnhum.2017.00568

Calzolari, E., Bolognini, N., Casati, C., Bianchi Marzoli, S., Vallar, G., Marzoli, S. B., & Vallar, G. (2015). Restoring abnormal aftereffects of prismatic adaptation through neuromodulation. *Neuropsychologia*, *74*, 162–169. https://doi.org/10.1016/j.neuropsychologia.2015.04.022

Capasso, R., & Miceli, G. (2001). *Esame neuropsicologico per l'afasia (E.N.P.A.)*. Milano: Springer Verlag.

Chapman, H. L., Eramudugolla, R., Gavrilescu, M., Strudwick, M. W., Loftus, A., Cunnington, R., & Mattingley, J. B. (2010). Neural mechanisms underlying spatial realignment during adaptation to optical wedge prisms. *Neuropsychologia*, *48*(9), 2595–2601.

Chechlacz, M., Rotshtein, P., Roberts, K. L., Bickerton, W.-L., Lau, J. K. L., & Humphreys, G. W. (2012). The prognosis of allocentric and egocentric neglect: evidence from clinical scans. *PloS One*, *7*(11), e47821. https://doi.org/10.1371/journal.pone.0047821

Clower, D. M., Hoffman, J. M., Votaw, J. R., Faber, T. L., Woods, R. P., & Alexander, G. E. (1996). Role of posterior parietal cortex in the recalibration of visually guided reaching. *Nature*, *383*(6601), 618–621.

Coulthard, E., Parton, A., & Husain, M. (2006). Action control in visual neglect. *Neuropsychologia*, *44*(13), 2717–2733. https://doi.org/10.1016/j.neuropsychologia.2005.11.004

Danckert, J., Ferber, S., & Goodale, M. A. (2008). Direct effects of prismatic lenses on visuomotor control: An event-related functional MRI study. *European Journal of Neuroscience*, *28*(8), 1696–1704.

Facchin, A., Beschin, N., & Daini, R. (2017, June). Rehabilitation of right (personal) neglect by prism adaptation: A case report. *Annals of Physical and Rehabilitation Medicine*. https://doi.org/10.1016/j.rehab.2016.09.004

Facchin, A., Beschin, N., Toraldo, A., Cisari, C., & Daini, R. (2013). Aftereffect induced by prisms of different power in the rehabilitation of neglect: A multiple single case report. *NeuroRehabilitation*, *32*(4), 839–853. https://doi.org/10.3233/NRE-130908

Facchin, A., Bultitude, J. H., Mornati, G., Peverelli, M., & Daini, R. (2018). A comparison of prism adaptation with terminal versus concurrent exposure on sensorimotor changes and spatial neglect. *Neuropsychological Rehabilitation*, 1–28. https://doi.org/10.1080/09602011.2018.1484374

Farnè, A., Ponti, F., & Làdavas, E. (1998). In search of biased egocentric reference frames in neglect.

Neuropsychologia, *36*(7), 611–623. https://doi.org/10.1016/S0028-3932(97)00164-4

Farnè, A., Rossetti, Y., Toniolo, S., & Làdavas, E. (2002). Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures. *Neuropsychologia*, *40*(7), 718–729.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189–198.

Fortis, P., Goedert, K. M., & Barrett, A. M. (2011). Prism adaptation differently affects motor-intentional and perceptual-attentional biases in healthy individuals. *Neuropsychologia*, *49*(9), 2718–2727. https://doi.org/10.1016/j.neuropsychologia.2011.05.020

Fortis, P., Maravita, A., Gallucci, M., Ronchi, R., Grassi, E., Senna, I., … Vallar, G. (2010). Rehabilitating patients with left spatial neglect by prism exposure during a visuomotor activity. *Neuropsychology*, *24*(6), 681–697. https://doi.org/10.1037/a0019476

Fortis, P., Ronchi, R., Calzolari, E., Gallucci, M., & Vallar, G. (2013). Exploring the effects of ecological activities during exposure to optical prisms in healthy individuals. *Frontiers in Human Neuroscience*, *7*(1), 1–11. https://doi.org/10.3389/fnhum.2013.00029

Fortis, P., Ronchi, R., Velardo, V., Calzolari, E., Banco, E., Algeri, L., … Vallar, G. (2018). A home-based prism adaptation training for neglect patients. *Cortex*. https://doi.org/https://doi.org/10.1016/j.cortex.2018.09.001

Frassinetti, F., Angeli, V., Meneghello, F., Avanzi, S., & Ladavas, E. (2002). Long-lasting amelioration of visuospatial neglect by prism adaptation. *Brain*, *125*(3), 608–623. https://doi.org/10.1093/brain/awf056

Gainotti, G., Messerli, P., & Tissot, R. (1972). Qualitative analysis of unilateral spatial neglect in relation to laterality of cerebral lesions. *Journal of Neurology, Neurosurgery & Psychiatry*, *35*(4), 545–550. https://doi.org/10.1136/jnnp.35.4.545

Galea, J. M., Vazquez, A., Pasricha, N., Orban de Xivry, J.-J., & Celnik, P. (2011). Dissociating the Roles of the Cerebellum and Motor Cortex during Adaptive Learning: The Motor Cortex Retains What the Cerebellum Learns. *Cerebral Cortex*, *21*(8), 1761–1770. https://doi.org/10.1093/cercor/bhq246

Gauthier, L., Dehaut, F., & Joanette, Y. (1989). The Bells Test: A quantitative and qualitative test for visual

neglect. *International Journal of Clinical Neuropsychology*, *11*(2), 49–54.

Ghilardi, M.-F., Ghez, C., Dhawan, V., Moeller, J., Mentis, M., Nakamura, T., … Eidelberg, D. (2000). Patterns of regional brain activation associated with different forms of motor learning. *Brain Research*, *871*(1), 127–145. https://doi.org/10.1016/S0006-8993(00)02365-9

Goedert, K. M., Chen, P., Boston, R. C., Foundas, A. L., & Barrett, A. M. (2014). Presence of motor-Intentional aiming deficit predicts functional improvement of spatial neglect with prism adaptation. *Neurorehabilitation and Neural Repair*, *28*(5), 483–493. https://doi.org/10.1177/1545968313516872

Heilman, K. M., Watson, R. T., & Valenstein, E. (2003). Neglect and related disorders. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 296–346). New York: Oxford University Press.

Hugues, A., Di Marco, J., Lunven, M., Jacquin-Courtois, S., Rossetti, Y., Bonan, I., & Rode, G. (2015). Long-lasting reduction in postural asymmetry by prism adaptation after right brain lesion without neglect. *Cognitive Processing*, *16*, 371–375. https://doi.org/10.1007/s10339-015-0704-y

Imamizu, H., Miyauchi, S., Tamada, T., Sasaki, Y., Takino, R., Pütz, B., … Kawato, M. (2000). Human cerebellar activity reflecting an acquired internal model of a new tool. *Nature*, *403*(6766), 192–195. https://doi.org/10.1038/35003194

Inoue, K., Kawashima, R., Satoh, K., Kinomura, S., Goto, R., Koyama, M., … Fukuda, H. (1998). PET Study of Pointing With Visual Feedback of Moving Hands. *Journal of Neurophysiology*, *79*(1), 117–125. https://doi.org/10.1152/jn.1998.79.1.117

Inoue, K., Kawashima, R., Satoh, K., Kinomura, S., Goto, R., Sugiura, M., … Fukuda, H. (1997). Activity in the parietal area during visuomotor learning with optical rotation. *NeuroReport*, *8*(18), 3979–3983. https://doi.org/10.1097/00001756-199712220-00026

Jackson, S. R., Newport, R., Husain, M., Harvey, M., & Hindle, J. V. (2000). Reaching movements may reveal the distorted topography of spatial representations after neglect. *Neuropsychologia*, *38*(4), 500–507.

Jacquin-Courtois, S., Rode, G., Pavani, F., O'Shea, J., Giard, M. H., Boisson, D., & Rossetti, Y. (2010). Effect of prism adaptation on left dichotic listening deficit in neglect patients: glasses to hear better?

Brain, *133*(3), 895–908.

Jacquin-Courtois, S., Rode, G., Pisella, L., Boisson, D., & Rossetti, Y. (2008). Wheel-chair driving improvement following visuo-manual prism adaptation. *Cortex*, *44*(1), 90–96. https://doi.org/10.1016/j.cortex.2006.06.003

Karnath, H.-O. (1994). Subjective body orientation in neglect and the interactive contribution of neck muscle proprioception and vestibular stimulation. *Brain*, *117*(5), 1001–1012. https://doi.org/10.1093/brain/117.5.1001

Kinsbourne, M. (1970). A model for the mechanism of unilateral neglect of space. *Transactions of the American Neurological Association*, *95*, 143–146.

Kleinman, J. T., Newhart, M., Davis, C., Heidler-Gary, J., Gottesman, R. F., & Hillis, A. E. (2007). Right hemispatial neglect: frequency and characterization following acute left hemisphere stroke. *Brain and Cognition*, *64*(1), 50–59. https://doi.org/10.1016/j.bandc.2006.10.005

Küper, M., Wünnemann, M. J. S., Thürling, M., Stefanescu, R. M., Maderwald, S., Elles, H. G., … Timmann, D. (2014). Activation of the cerebellar cortex and the dentate nucleus in a prism adaptation fMRI study. *Human Brain Mapping*, *35*(4), 1574–1586. https://doi.org/10.1002/hbm.22274

Làdavas, E., Bonifazi, S., Catena, L., & Serino, A. (2011). Neglect rehabilitation by prism adaptation: different procedures have different impacts. *Neuropsychologia*, *49*(5), 1136–1145. https://doi.org/10.1016/j.neuropsychologia.2011.01.044

Làdavas, E., Giulietti, S., Avenanti, A., Bertini, C., Lorenzini, E., Quinquinio, C., & Serino, A. (2015). A-tDCS on the ipsilesional parietal cortex boosts the effects of prism adaptation treatment in neglect. *Restorative Neurology and Neuroscience*, *33*(5), 647–662. https://doi.org/10.3233/RNN-140464

Luauté, J., Halligan, P., Rode, G., Jacquin-Courtois, S., & Boisson, D. (2006). Prism adaptation first among equals in alleviating left neglect: a review. *Restorative Neurology & Neuroscience*, *24*(4–6), 409–418.

Luauté, J., Jacquin-Courtois, S., O'Shea, J., Christophe, L., Rode, G., Boisson, D., & Rossetti, Y. (2012). Left-deviating prism adaptation in left neglect patient: Reflexions on a negative result. *Neural Plasticity*, 1–10. https://doi.org/10.1155/2012/718604

Luauté, J., Schwartz, S., Rossetti, Y., Spiridon, M., Rode, G., Boisson, D., & Vuilleumier, P. P. (2009).

Dynamic changes in brain activity during prism adaptation. *Journal of Neuroscience*, *29*(1), 169–178. https://doi.org/10.1523/JNEUROSCI.3054-08.2009

Magnani, B., Oliveri, M., Mancuso, G., Galante, E., & Frassinetti, F. (2011). Time and spatial attention: Effects of prism adaptation on temporal deficits in brain damaged patients. *Neuropsychologia*, *49*(5), 1016–1023. https://doi.org/10.1016/j.neuropsychologia.2010.12.014

Maravita, A., McNeil, J., Malhotra, P., Greenwood, R., M., H., & Driver, J. (2003). Prism adaptation can improve contralesional tactile perception in neglect. *Neurology*, *60*(11), 1829–1831.

Martín-Arévalo, E., Schintu, S., Farnè, A., Pisella, L., & Reilly, K. T. (2018). Adaptation to Leftward Shifting Prisms Alters Motor Interhemispheric Inhibition. *Cerebral Cortex*, *28*(2), 528–537. https://doi.org/10.1093/cercor/bhw386

Michel, C. (2016). Beyond the sensorimotor plasticity: Cognitive Expansion of Prism Adaptation in Healthy Individuals. *Frontiers in Psychology*, *6*(1979), 1–7. https://doi.org/10.3389/fpsyg.2015.01979

Michel, C., Pisella, L., Halligan, P. W., Luaute, J., Rode, G., Boisson, D., … Rossetti, Y. (2003). Simulating unilateral neglect in normals using prism adaptation: implications for theory. *Neuropsychologia*, *41*(1), 25–39. https://doi.org/10.1016/S0028-3932(02)00135-5

Mizuno, K., Tsuji, T., Takebayashi, T., Fujiwara, T., Hase, K., & Liu, M. (2011). Prism adaptation therapy enhances rehabilitation of stroke patients with unilateral spatial neglect: A randomized, controlled trial. *Neurorehabilitation and Neural Repair*, *25*(8), 711–720. https://doi.org/10.1177/1545968311407516

Mutha, P. K., Sainburg, R. L., & Haaland, K. Y. (2011). Left Parietal Regions Are Critical for Adaptive Visuomotor Control. *Journal of Neuroscience*, *31*(19), 6972–6981. https://doi.org/10.1523/JNEUROSCI.6432-10.2011

Newport, R., & Schenk, T. (2012). Prisms and neglect: what have we learned? *Neuropsychologia*, *50*(6), 1080–1091. https://doi.org/10.1016/j.neuropsychologia.2012.01.023

Nys, G. M. S., de Haan, E. H. F., Kunneman, A., de Kort, P. L. M., & Dijkerman, H. C. (2008). Acute neglect rehabilitation using repetitive prism adaptation: a randomized placebo-controlled trial. *Restorative Neurology & Neuroscience*, *26*(1), 1–12.

O'Shea, J., Gaveau, V., Kandel, M., Koga, K., Susami, K., Prablanc, C., & Rossetti, Y. (2014). Kinematic

markers dissociate error correction from sensorimotor realignment during prism adaptation. *Neuropsychologia*, *55*, 15–24. https://doi.org/10.1016/j.neuropsychologia.2013.09.021

Ogden, J. A. (1985a). Anterior-posterior interhemispheric differences in the loci of lesions producing visual hemineglect. *Brain and Cognition*, *4*(1), 59–75.

Ogden, J. A. (1985b). Contralesional neglect of constructed visual images in right and left brain-damaged patients. *Brain and Cognition*, *4*(1), 273–277. https://doi.org/10.1016/0278-2626(85)90054-5

Ogden, J. A. (1987). The "neglected" left hemisphere and its contribution to visuospatial neglect. In M. Jeannerod (Ed.), *Neurophysiological and neuropsychological aspects of spatial neglect* (pp. 215–233). Amsterdam: Elsevier.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, *9*(1), 97–113.

Panico, F., Jacquin-Courtois, S., Di Marco, J., Perrin, C., Trojano, L., & Rossetti, Y. (2017). tDCS reactivation of dormant adaptation circuits. *Cortex*, *94*, 196–199. https://doi.org/10.1016/J.CORTEX.2017.02.003

Panico, F., Sagliano, L., Grossi, D., & Trojano, L. (2016). Cerebellar cathodal tDCS interferes with recalibration and spatial realignment during prism adaptation procedure in healthy subjects. *Brain and Cognition*, *105*, 1–8. https://doi.org/10.1016/j.bandc.2016.03.002

Pisella, L., Rossetti, Y., Michel, C., Rode, G., Boisson, D., Pélisson, D., & Tilikete, C. (2005). Ipsidirectional impairment of prism adaptation after unilateral lesion of anterior cerebellum. *Neurology*, *65*(1), 150–152. https://doi.org/10.1212/01.wnl.0000167945.34177.5e

Redding, G. M., Rossetti, Y., & Wallace, B. (2005). Applications of prism adaptation: A tutorial in theory and method. *Neuroscience and Biobehavioral Reviews*, *29*(3), 431–444. https://doi.org/10.1016/j.neubiorev.2004.12.004

Redding, G. M., & Wallace, B. (1996). Adaptive spatial alignment and strategic motor control. *Journal of Experimental Psychology: Human Perception and Performance*, *22*(2), 379–394.

Redding, G. M., & Wallace, B. (1997). Prism adaptation during target pointing from visible and nonvisible starting locations. *Journal of Motor Behavior*, *29*(2), 119–130.

https://doi.org/10.1080/00222899709600827

Redding, G. M., & Wallace, B. (2006). Prism adaptation and unilateral neglect: review and analysis. *Neuropsychologia*, *44*(1), 1–20. https://doi.org/10.1016/j.neuropsychologia.2005.04.009

Redding, G. M., & Wallace, B. (2010). Implications of prism adaptation asymmetry for unilateral visual neglect: Theoretical note. *Cortex*, *46*(3), 390–396. https://doi.org/10.1016/j.cortex.2009.05.009

Rode, G., Pisella, L., Marsal, L., Mercier, S., Rossetti, Y., & Boisson, D. (2006). Prism adaptation improves spatial dysgraphia following right brain damage. *Neuropsychologia*, *44*(12), 2487–2493. https://doi.org/10.1016/j.neuropsychologia.2006.04.002

Rode, G., Pisella, L., Rossetti, Y., Farnè, A., & Boisson, D. (2003). Bottom-up transfer of sensory-motor plasticity to recovery of spatial cognition: visuomotor adaptation and spatial neglect. *Progress in Brain Research*, *142*, 273–287.

Rode, G., Rossetti, Y., Li, L., & Boisson, D. (1998). Improvement of mental imagery after prism exposure in neglect: a case study. *Behavioural Neurology*, *11*(4), 251–258.

Ronchi, R., Bolognini, N., Gallucci, M., Chiapella, L., Algeri, L., Spada, M. S., & Vallar, G. (2014). (Un)awareness of unilateral spatial neglect: A quantitative evaluation of performance in visuo-spatial tasks. *Cortex*, *61*(12), 167–182. https://doi.org/https://doi.org/10.1016/j.cortex.2014.10.004

Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioural Neurology*, *12*(4), 191–200.

Rossetti, Y., Rode, G., Pisella, L., Farné, A., Li, L., Boisson, D., & Perenin, M. T. (1998). Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature*, *395*(6698), 166–169. https://doi.org/10.1038/25988

Rousseaux, M., Bernati, T., Saj, A., & Kozlowski, O. (2006). Ineffectiveness of prism adaptation on spatial neglect signs. *Stroke*, *37*(2), 542–543. https://doi.org/10.1161/01.STR.0000198877.09270.e8

Saevarsson, S., Kristjánsson, Á., Hildebrandt, H., & Halsband, U. (2009). Prism adaptation improves visual search in hemispatial neglect. *Neuropsychologia*, *47*(3), 717–725. https://doi.org/10.1016/j.neuropsychologia.2008.11.026

Saj, A., Cojan, Y., Vocat, R., Luauté, J., & Vuilleumier, P. (2013). Prism adaptation enhances activity of

intact fronto-parietal areas in both hemispheres in neglect patients. *Cortex*, *49*(1), 107–119. https://doi.org/10.1016/j.cortex.2011.10.009

Sarri, M., Greenwood, R., Kalra, L., Papps, B., Husain, M., & Driver, J. (2008). Prism adaptation aftereffects in stroke patients with spatial neglect: pathological effects on subjective straight ahead but not visual open-loop pointing. *Neuropsychologia*, *46*(4), 1069–1080. https://doi.org/10.1016/j.neuropsychologia.2007.11.005

Schintu, S., Patané, I., Caldano, M., Salemme, R., Reilly, K. T., Pisella, L., & Farnè, A. (2017). The asymmetrical effect of leftward and rightward prisms on intact visuospatial cognition. *Cortex*, *97*, 23–31. https://doi.org/10.1016/j.cortex.2017.09.015

Schintu, S., Pisella, L., Jacobs, S., Salemme, R., Reilly, K. T., & Farnè, A. (2014). Prism adaptation in the healthy brain: the shift in line bisection judgments is long lasting and fluctuates. *Neuropsychologia*, *53*, 165–170. https://doi.org/10.1016/j.neuropsychologia.2013.11.013

Seidler, R. D., Noll, D. C., & Chintalapati, P. (2006). Bilateral basal ganglia activation associated with sensorimotor adaptation. *Experimental Brain Research*, *175*(3), 544–555. https://doi.org/10.1007/s00221-006-0571-y

Serino, A., Barbiani, M., Rinaldesi, M. L., & Làdavas, E. (2009). Effectiveness of prism adaptation in neglect rehabilitation a controlled trial study. *Stroke*, *40*(4), 1392–1398. https://doi.org/10.1161/STROKEAHA.108.530485

Serino, A., Bonifazi, S., Pierfederici, L., & Làdavas, E. (2007). Neglect treatment by prism adaptation: what recovers and for how long. *Neuropsychological Rehabilitation*, *17*(6), 657–687. https://doi.org/10.1080/09602010601052006

Shallice, T. (2015). Cognitive neuropsychology and its vicissitudes: The fate of Caramazza's axioms. *Cognitive Neuropsychology*, *32*(7–8), 385–411. https://doi.org/10.1080/02643294.2015.1131677

Shiraishi, H., Muraki, T., Itou, A., Sampei, Y., Hirayama, K., Ayaka Itou, Y. S., & Hirayama, K. (2010). Prism intervention helped sustainability of effects and ADL performances in chronic hemispatial neglect: A follow-up study. *NeuroRehabilitation*, *27*(2), 165–172. https://doi.org/10.3233/NRE-2010-0593

Shiraishi, H., Yamakawa, Y., Itou, A., Muraki, T., & Asada, T. (2008). Long-term effects of prism adaptation on chronic neglect after stroke. *NeuroRehabilitation*, *23*(2), 137–151.

Siegel, S., & Castellan, N. J. (1988). *Nonparametric Statistics for the Behavioral Sciences.* New York: McGraw-Hill.

Spinnler, H., & Tognoni, G. (1987). Standardizzazione e taratura Italiana di Test Neuropsicologici. *The Italian Journal of Neurological Sciences*, *8*(S6), S1–S120.

Stone, S. P., Patel, P., Greenwood, R. J., & Halligan, P. W. (1992). Measuring visual neglect in acute stroke and predicting its recovery: the visual neglect recovery index. *Journal of Neurology, Neurosurgery, and Psychiatry*, *55*(6), 431–436.

Striemer, C. L., & Danckert, J. A. (2010). Through a prism darkly: re-evaluating prisms and neglect. *Trends in Cognitive Sciences*, *14*(7), 308–316. https://doi.org/10.1016/j.tics.2010.04.001

Suchan, J., Rorden, C., & Karnath, H. O. (2012). Neglect severity after left and right brain damage. *Neuropsychologia*, *50*(6), 1136–1141. https://doi.org/10.1016/j.neuropsychologia.2011.12.018

Ten Brink, A. F., Verwer, J. H., Biesbroek, J. M., Visser-Meily, J. M. A., & Nijboer, T. C. W. (2017). Differences between left- and right-sided neglect revisited: A large cohort study across multiple domains. *Journal of Clinical and Experimental Neuropsychology*, *39*(7), 707–723. https://doi.org/10.1080/13803395.2016.1262333

Vallar, G., & Bolognini, N. (2014). Unilateral spatial neglect. In A. C. Nobre & S. Kastner (Eds.), *Oxford Handbook of Attention* (pp. 972–1027). Oxford: Oxford University Press. https://doi.org/10.1093/oxfordhb/9780199675111.013.012

Vallar, G., & Calzolari, E. (2018). Unilateral spatial neglect after posterior parietal damage. In G. Vallar & H. B. Coslett (Eds.), *The Parietal Lobe. Handbook of Clinical Neurology* (Vol. 151, pp. 287–312). Amsterdam: Elsevier. https://doi.org/10.1016/B978-0-444-63622-5.00014-0

Vallar, G., Rusconi, M. L., Fontana, S., & Musicco, M. (1994). Tre test di esplorazione visuo-spaziale: taratura su 212 soggetti normali. *Archivio Di Psicologia, Neurologia, e Psichiatria*, *55*(4), 827–841.

Vallar, G., Rusconi, M. L., Geminiani, G., Berti, A., & Cappa, S. F. (1991). Visual and nonvisual neglect after unilateral brain lesions: Modulation by visual input. *International Journal of Neuroscience*, *61*(3–

4), 229–239. https://doi.org/10.3109/00207459108990740

Vangkilde, S., & Habekost, T. (2010). Finding Wally: prism adaptation improves visual search in chronic neglect. *Neuropsychologia*, *48*(7), 1994–2004. https://doi.org/10.1016/j.neuropsychologia.2010.03.020

Ventre, J., Flandrin, J. M., & Jeannerod, M. (1984). In search for the egocentric reference. A neurophysiological hypothesis. *Neuropsychologia*, *22*(6), 797–806.

Watanabe, S., & Amimoto, K. (2010). Generalization of prism adaptation for wheelchair driving task in patients with unilateral spatial neglect. *Archives of Physical Medicine and Rehabilitation*, *91*(3), 443–447. https://doi.org/10.1016/j.apmr.2009.09.027

Wilson, B., Cockburn, J., & Halligan, P. (1987). Development of a behavioral test of visuospatial neglect. *Archives of Physical Medicine & Rehabilitation*, *68*(2), 98–102.

Table II. Performance scores of 30 brain-damaged patients in neuropsychological tasks assessing USN and general cognitive impairment.

Patient	Group	Line Bisection	Target cancellation				Complex Drawing	MMSE	Colored Progressive Matrices	Verbal Judgments
			Bell		Star					
			Total	L-R	Total	L-R				
P1	RBD/N-	2.8	2	2	0	0	0	29	36	52.25
P2	RBD/N-	-0.5	4	2	0	0	0	29	n. a.	35.25
P3	RBD/N-	3.3	3	1	0	0	0	28	32.5	48.25
P4	RBD/N-	-0.5	6	2	0	0	0	30	32	48
P5	RBD/N-	4.2	0	0	1	1	1#	28	25.5	39.5
P6	RBD/N-	2.2	1	1	2	0	0	30	31	51.25
P7	RBD/N-	-0.8	1	1	0	0	0.5	25	19.5	38.5
P8	RBD/N-	0.2	0	0	0	0	0	29	19.5	45.75
P9	RBD/N-	0.5	0	0	0	0	0	29	36	50.25
P10	RBD/N-	3.5	1	1	3	1	0	29	22	43
P11	RBD/N+	19.8*	n.a.	n.a.	49	11*	10*	19*	n. a.	40
P12	RBD/N+	10.8*	3	3	1	1	0	29	32	43
P13	RBD/N+	-2.3	4	4	16	14*	1*	26	14.5*	38.25
P14	RBD/N+	74.3*	2	2	41	9*	8*	28	n. a.	27.75*
P15	RBD/N+	46.2*	2	0	48	12*	5.5*	25	n. a.	46.5
P16	RBD/N+	60.8*	2	2	13	1	5*	n.a.	n. a.	n. a.
P17	RBD/N+	-2	6	4	6	6*	1*	28	21.5	37
P18	RBD/N+	66*	33	3	40	10*	8.5*	28	n. a.	44.75
P19	RBD/N+	24*	1	1	1	1	0	28	18	52.5
P20	RBD/N+	34.2*	31	5*	34	18*	7*	27	n. a.	n. a.
P21	LBD	1.7	0	0	0	0	0	n.a.	33	n. a.
P22	LBD	-1.3	1	1	0	0	0	n.a.	30.5	n. a.
P23	LBD	-0.5	3	1	0	0	0	n.a.	30.5	n. a.
P24	LBD	-2.2	0	0	0	0	0	27	29	n. a.
P25	LBD	-2.0	4	2	0	0	0	n.a.	22.5	n. a.
P26	LBD	-2.3	0	0	0	0	0	n.a.	24	n. a.
P27	LBD	-0.7	1	0	0	0	n.a.	n.a.	20	n. a.
P28	LBD	-2.7	0	0	0	0	0	n.a.	36	n. a.
P29	LBD	-0.3	0	0	0	0	0	29	30.5	n. a.
P30	LBD	-0.8	0	0	0	0	0	26	28.5	44.5

RBD/N -/+: right-brain-damaged patients without/with left USN. LBD: left-brain-damaged patients.
Line bisection: percent deviation of the participants' mark from the objective midpoint. *Cancellation tasks:* omission errors (total), and difference between omissions on the two sides of the sheet (left - right). *Complex Drawing:* omission errors. *MMSE:* scores compared with tailored age- and education-adjusted cut-off. *Colored Progressive Matrices:* scores adjusted for age and education, cut-off= 18. *Verbal Judgments: scores* adjusted for age and education, cut-off= 33.
n. a.: not assessed. * Defective scores.
Omission errors bilateral or lateralized in the side of the element ipsilateral to the side of the lesion.

Table I. Demographic and neurological data of 30 brain-damaged patients.

	Group	Sex	Age	Education (years)	Time after lesion (days)	Aetiology/ Lesion site	Lesion Size (cc)	Neurological deficits M	SS	V	Associated deficits AN	PN	SP
P1	RBD/N-	F	71	18	34	I/P	n.a.	+	-	-	-	-	-
P2	RBD/N-	M	32	10	232	N/P s-cort	n.a.	+	-	-	-	-	-
P3	RBD/N-	M	57	13	101	I/FTIn	115469	+	+	-	-	-	-
P4	RBD/N-	F	50	18	164	I/FP	194345	+	+	-	-	-	-
P5	RBD/N-	M	57	13	292	I/sylvian areas	242457	+	+	+	-	-	-
P6	RBD/N-	M	77	13	63	H/F wm	22222	+	+	-	-	-	-
P7	RBD/N-	M	75	6	80	I/bg s-cort wm	4651	+	-	-	-	-	-
P8	RBD/N-	M	64	13	85	I/PO crb	28605	+	-	+	-	-	-
P9	RBD/N-	M	71	13	91	H/bg wm	12026	+	+	-	-	-	+
P10	RBD/N-	M	47	18	1476	H/Tin wm	93147	+	-	-	-	-	-
P11	RBD/N+	F	77	5	48	I/FTP bg	239970	+	+	-	+	+	-
P12	RBD/N+	M	78	5	34	I/wm bg	12120	-	+	-	-	-	-
P13	RBD/N+	M	60	13	36	I/sylvian areas	241024	+	+	+	+SS-V	+	-
P14	RBD/N+	M	70	13	29	N/T	n.a.	+	+	+	+V	+	-
P15	RBD/N+	F	76	8	1066	H/FT	n.a.	+	+	+	+SS-M	+	-
P16	RBD/N+	F	73	5	27	I/PO wm	70718	+	+	+	+SS-V	+	-
P17	RBD/N+	M	60	5	37	I/sylvian areas	78502	+	+	+	+V-M	+	-

P18	RBD/N+	F	60	18	234	I/sylvian areas wm bg	206067	+	+	+	+SS-V	+	-
P19	RBD/N+	F	67	13	396	H/TP s-cort	135435	+	+	+	+SS	-	-
P20	RBD/N+	M	45	18	66	I/FTOIn s-cort	200887	+	+	+	+SS-V	+	-
P21	LBD	F	44	14	38	H/TP	56570	-	+	-	-	-	-
P22	LBD	M	65	8	479	I/FTPO	32249	+	+	-	-	-	-
P23	LBD	M	65	13	127	I/sylvian areas	5007	+	+	-	-	-	-
P24	LBD	F	78	8	242	I/ic	3158	+	+	-	-	-	-
P25	LBD	M	70	18	246	I/F wm bg	17127	+	+	-	-	-	-
P26	LBD	M	69	13	17	I/bg wm	2649	+	+	-	-	-	-
P27	LBD	F	89	18	84	H/Th wm	1048	+	+	-	-	-	-
P28	LBD	F	70	10	41	I/sylvian areas wm bg	15470	+	+	-	-	-	-
P29	LBD	M	46	13	40	H/swm bg	12102	-	+	-	-	-	-
P30	LBD	F	78	8	45	I/ic	3490	+	+	-	-	-	-

RBD-N-/+: right brain-damaged patients without/with left USN. LBD: left brain-damaged patients.
Lesion aetiology: I/H/N (ischemic/hemorrhagic/neoplastic).
Lesion site. F: frontal; P: parietal; T: temporal; O: occipital; In: insula; ic: internal capsule; bg: basal ganglia; s-cort: sub-cortical; crb: cerebellum; wm: white matter, pnt: pontine.
Neurological and neuropsychological spatial deficits contralateral to the side of the lesion. M/SS/V: motor/somatosensory/visual half-field deficits; e: extinction to double simultaneous stimulation; AN: anosognosia for neurological deficits; PN: personal neglect; SP: somatoparaphrenia.
+/-: presence/absence of deficit. n.a.: not available.

Table III. Language assessment of LBD patients

	Diagnosis	Token test	Word Co.	Sentence Co.
P21	No aphasia	26.5	n. a.	n. a.
P22	Non-fluent aphasia	30.25	18.4	14
P23	Non-fluent aphasia	7.5*	18.4	13.1
P24	No aphasia	30.5	19.6	14
P25	Non-fluent aphasia	26.25*	20	12.8
P26	Fluent aphasia	25.75*	20	13.1
P27	Fluent aphasia	26.25*	17.6*	13
P28	Non-fluent aphasia	20.25*	19.4	10.1*
P29	No aphasia	31.75	20	14
P30	No aphasia	30.75	19.9	14

Scores represent the sum of corrected answers, adjusted for age and education (years).
Token test: scores adjusted for age and education, cut-off= 26.5. *Word Co.*: auditory comprehension of individual words, cut-off= 18.4. *Sentence Co.:* auditory comprehension of sentences, cut-off =11.6.
n. a.: not assessed. * Defective scores.

Table IV. Summary of the sign attributed to the measures recorded in the pre and post- exposure assessments, and during the adaptation phase, depending on the direction of the movement and on the visual-field displacement induced by prisms.

	Prism-induced visual field deviation				
	Rightward			Leftward	
	CR	RBD/N-	RBD/N+	CL	LBD
Movement deviation:					
Ipsilateral to prism-induced deviation	+	+	+	-	-
Contralateral to prism-induced deviation	-	-	-	+	+

C: healthy controls R/L: Rightward/Leftward; RBD/N-/+: right-brain-damaged patient without/with left USN; LBD: left-brain-damaged patients.
-/+: sign attributed to data.