Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures

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Abstract

Previous studies have shown that adaptation to rightward displacing prisms improves performance of neglect patients on visuo-manual (VM) tasks such as line cancellation, figure copying, and line bisection [Nature 395 (1998) 166]. The present study further evaluated the effect of prism adaptation (PA) on neglect symptoms by investigating: (a) the range of beneficial effects on common visuo-spatial deficits as well as less frequent phenomena like neglect dyslexia; (b) the duration of improvement following a single exposure to the right optical deviation; (c) the extent to which visuo-spatial performance can be comparatively ameliorated in VM tasks and visuo-verbal (VV) tasks (i.e. involving or not the adapted arm, respectively) and (d) the presence and duration of the manual visuo-motor bias induced by the prismatic adaptation (i.e. the after-effect). We investigated these issues in a group of neglect patients with right hemispheric damage who were also affected by neglect dyslexia. Following a single, brief prismatic adaptation the results showed that (a) several visuo-spatial abilities, including accuracy in reading single words and non-words, considerably improved, (b) the amelioration was long-lasting, continuing for at least 24 h, (c) the presence, amount, and duration of neglect amelioration was not limited to VM tasks, but extended to VV tasks and (d) the presence and duration of the after-effect induced by prismatic adaptation remarkably paralleled the presence and duration of the improvement of neglect symptoms. These findings clearly demonstrate that beneficial effects induced by a single PA are very long-lasting and spread over a wide range of visuo-spatial deficits, independent of the type of response required. In addition, our results strongly suggest that the process of adaptation, as revealed by the presence of a visuo-motor after-effect, might be essential for establishing amelioration. In light of its characteristics, the prismatic adaptation technique should be a priority tool for the rehabilitation of the multifaceted hemispatial neglect syndrome. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Hemispatial neglect is defined as the patient’s failure to report, respond to, or orient toward novel and/or meaningful stimuli presented to the side opposite the brain lesion [21]. This condition is frequently found in right brain damaged (RBD) patients, often in association with contralesional hemiplegia or hemiparesis [5,50]. In addition to inducing many functional debilitating effects on everyday life, left visuo-spatial neglect has been shown to be responsible for poor functional recovery and reduced ability to benefit from treatment of impaired motor functions [11,17,19,27,38].

For these reasons, many attempts have been made in the past 15 years to rehabilitate hemispatial neglect, which has lead to a variety of different approaches [29,33,40,47]. More recently, researchers have paid particular attention to physiological manoeuvres that induce a strong amelioration to many pathological aspects of the neglect syndrome (for review, see [56,65]). These manoeuvres consist of temporarily manipulating some spatial aspect of the sensory input to overcome the contralesional visuo-spatial deficit in neglect patients. Furthermore, neglect can be improved by several sensory manipulations, such as caloric vestibular stimulation [7,25,64], neck muscles [26] or plantar vibration, transcutaneous [66] or optokinetic stimulation [32,41], active/passive limb proprioceptive stimulation [14,18,28,49,52] or non-spatial manipulations such as arousal increase [51]. However, in all such cases, the effects of a single application of these sensory manipulations were usually very transient, lasting only a few minutes.
Another sensory manipulation that seems to be very promising in terms of inducing a durable amelioration of neglect symptoms has been recently reported by Rossetti et al. [57], and is constituted by the adaptation to a right prismatic shift of the visual field. In contrast to previous studies where the direct effects of physiological manipulations were tested, these authors investigated the adaptive after-effects of a short visuo-motor adaptation period. They showed that a single, short-lasting period of visuo-motor adaptation to the visual shift was efficacious in ameliorating visual neglect in a group of patients. Classical neuropsychological testing based upon visuo-spatial tasks (e.g. cancellation, copying, bisection) strongly improved immediately after the prismatic adaptation procedure. Strikingly, this improvement was maintained or even further developed over a period of 2 h after the prism adaptation (PA) when neglect patients performed the same neuropsychological testing again. More recently, single-case studies have demonstrated that visuo-spatial tasks performed over a different scale (e.g. wheel-chair driving) or involving a different sensory modality (e.g. haptic exploration) could also be improved by PA [34,58]. Other investigations have also shown that posture [63] and even mental imagery [53,54] can be improved after PA.

The present study was designed to further investigate the beneficial effects induced by a single, short-lasting session of PA in a group of neglect patients and to address several of the issues raised by this procedure as a technique to rehabilitate neglect.

First of all, we sought to replicate and extend the finding that prismatic adaptation induces amelioration of neglect symptoms. To this aim, a wide battery of neglect-sensitive tasks was used to investigate visuo-spatial abilities of RBD patients with neglect, before and after a single exposure to a PA procedure similar to that used in a previous experiment [57]. In addition to the most common visuo-spatial deficits, the group of neglect patients who participated in this study was selected on the basis of the presence of single-word neglect dysexia to directly verify whether this peculiar deficit can also be ameliorated by the prismatic adaptation technique. Due to the spatial nature of this “linguistic” deficit [3,24,30,31,48], we expected that a single exposure to the PA procedure should improve the reading abilities of neglect dyslexia patients.

Second, the issue of the duration of neglect improvement was evaluated in the same group of patients. This concern was particularly important since the long-term effects of prismatic adaptation, initially shown to last 2 h post-adaptation [57], have been documented to last longer (up to 4 days) in recent single-case observations [39,58]. No systematic study, however, has been conducted at a group level. Therefore, in the present study, we followed the patients over a longer period of time after a single PA procedure; in particular, the same battery of tests was used to elucidate whether (and to what extent) the amelioration found immediately after prismatic adaptation (immediate) was maintained after 1 day (late 1 day) and 1 week time intervals (late 1 week). In a follow-up study conducted on a subgroup of patients, we also investigated whether possible beneficial effects found after a long delay from adaptation might be due to the immediate execution of the same battery of tests; indeed, tests repetition could facilitate the learning of visuo-motor strategies for solving the tasks. In addition, this follow-up session allowed us to investigate whether repeating the adaptation procedure at a 1-week interval from the previous one can induce cumulative effects.

Third, we directly assessed a possible mechanism through which neglect might be ameliorated following PA. Indeed, a number of questions remain to be answered in this respect, especially since previous studies assessed neglect almost only by means of visuo-spatial tasks that required the use of the very same hand/arm employed during the adaptation procedure [39,57]. Thus, the possibility should be considered that the amelioration of high-order visuo-spatial functions depends upon a low-order factor, namely, the leftward sensory-motor bias of the ipsilesional arm induced by the adaptation to the right visual shift itself. Findings in healthy subjects demonstrated the initial disorganisation of visuo-motor behaviour following prismatic exposure is corrected during the process of visuo-motor adaptation. The major compensating consequence of this adaptation is a shift of visual and proprioceptive representations, which are reflected in a typical visuo-motor bias, the so-called “after-effect” [23]. Subjects systematically deviate in the direction opposite to the prismatic shift when manually pointing or reaching for visual objects with the adapted hand [44,45]. In the case of adaptation to a right prismatic deviation, the after-effect consists of a leftward visuo-motor bias exhibited by the exposed hand, which is present in normal subjects [55] as well as in patients with neglect [39,57].

For this reason, it is crucial to verify whether the leftward visuo-motor bias is a key element leading to the improved performances shown by neglect patients. Indeed, the presence of a leftward after-effect in the manual behaviour of neglect patients might act as a visual and/or a spatio/motor cue [18,52] in many “visuo-spatial” tasks, such as manual cancellation of lines, letters, or shapes. To assess the possible role played by the leftward visuo-motor bias, half of the visuo-spatial tests included in the present study required a right manual response (e.g. cancellation and bisection tests), whereas the remaining half only involved a verbal response (e.g. object naming and string reading tests). The fact that patients were affected by single-word neglect dyslexia, besides being affected by common visuo-spatial deficits, ensured a sensitive comparison between visuo-manual and visuo-verbal performances and their evolution in time. If the arm visuo-motor bias hypothesis were true, the amelioration of neglect symptoms should be only (or more strongly) evident in visuo-spatial tests involving the use of right hand (visuo-manual (VM) tasks), whereas it should be absent (or weaker) in visuo-spatial tests that do not require an ipsilesional manual response (visuo-verbal (VV) tasks).
The fourth and final purpose of the present study is to investigate the possible relationships intervening between neglect amelioration and the visuo-motor after-effect. To this aim, the presence and amount of the after-effect (i.e. the directional bias in patients’ visuo-motor behaviour), as well as its possible long-lasting duration, was evaluated in parallel with the evaluation of visuo-spatial abilities. To measure the after-effect, we adopted a classic paradigm with an open-loop pointing task, which required patients to manually indicate a visual target without the visual feedback of their own hand [42,43].

In particular, we asked whether the phenomenon of the after-effect was temporally linked to the improvement of neglect deficits and its maintenance over time. This question is very important because neglect amelioration has been proven to last much longer in patients after a single PA than the after-effect duration that has been reported in the literature on normal subjects [67]. Therefore, in principle, the phenomena of neglect improvement and visuo-motor after-effect could be completely independent. In the present study, we directly tested this issue to shed more light onto the possible mechanism through which PA can ameliorate visuo-spatial deficits of the neglect syndrome.

2. Methods

2.1. Subjects

A non-consecutive series of six neurological patients with left visual neglect following right unilateral vascular lesions gave informed consent to participate in this study. On clinical examination, all patients were alert and well-oriented in time and space. They were all right handed and affected by left hemiplegia or hemiparesis. Four out of six patients had visual field defects, as assessed by confrontation test (see Table 1). The side and the site of the lesion were assessed by computerised tomography (CT) or MRI scan. Age, sex, length of illness, as well as other clinical details are provided in Table 1. Patients were recruited in two different hospitals (I Fraticini Hospital, Firenze and San Giacomo, Ponte dell’Olio), where they had been selected on the basis of their defective performance in several visuo-spatial tasks including star cancellation, copy of a drawing and drawing from memory. Another criterion for the patients to be included in the study was the presence of single-word neglect dyslexia. Presenting them letter strings, forming a single word or non-word to be read aloud, assessed neglect dyslexia. A list of 20 letter strings was used to detect signs of neglect dyslexia, such as omissions or substitution errors on the left part of the letter string in the reading performance. Patients with neglect dyslexia were selected from a larger population of RBD patients with neglect from the inpatient population of both hospitals. Once the patient’s performance met both criteria, she/he completed a wider battery of tests to ascertain in greater detail the presence and severity of neglect symptoms that also constituted the first baseline evaluation of the experimental investigation.

2.2. Materials

To assess neglect severity, a battery of eight visuo-spatial tasks was administered to each patient. The battery consisted of a series of (a) VM tasks that required the use of the ipsilesional right hand and (b) VV tasks that did not require the use of the ipsilesional right hand. In particular, VM tasks included line and bell cancellation tests [1,16], and two sub-tests taken from the behavioural inattention test (BIT) battery [68], namely, letter cancellation and line bisection. The tests included in the series of VV tasks of the battery consisted of the following. A visual scanning test, also taken from the BIT, required a verbal description of the objects depicted on a coloured picture. The patients also completed an object-naming task in which 30 Snoddgrass pictures of familiar objects [61], depicted on an A4 sheet of paper and intermingled with geometric shapes as distractors, had to be named. In addition, two reading tasks (words and non-words) were included. A list of 50 words, 10 words each in five length classes (6–10 letters), was used to investigate single-word reading abilities. The list of

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (year)</th>
<th>Months post-stroke</th>
<th>Hemianopia</th>
<th>Lesion site</th>
</tr>
</thead>
<tbody>
<tr>
<td>EZ</td>
<td>F</td>
<td>85</td>
<td>10</td>
<td>+</td>
<td>T, O, Th, Wm</td>
</tr>
<tr>
<td>CZ</td>
<td>M</td>
<td>67</td>
<td>18</td>
<td>+</td>
<td>T, O, Th, Wm</td>
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<tr>
<td>MB (I)</td>
<td>F</td>
<td>75</td>
<td>3</td>
<td>+</td>
<td>T, P, O</td>
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<tr>
<td>SL (I)</td>
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<td>GB (D)</td>
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<td>13</td>
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<td>BG, Th, Wm</td>
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<tr>
<td>AS (D)</td>
<td>M</td>
<td>50</td>
<td>13</td>
<td>+</td>
<td>F, T, P</td>
</tr>
</tbody>
</table>

*Clinical and demographic details for neglect patients are reported. The table also shows the patients who participated to the follow-up investigation (see Section 2) in which, after a supplementary prism adaptation performed at 1 week of interval, visuo-spatial performances were assessed again, either immediately after the second PA (I), or after a longer delay (6 h) from the second PA (D).

The presence (+) or absence (−) of visual field defects is reported for each patient. The presence (+) or absence (−) of visual field defects involved by the lesion: F: frontal; T: temporal; P: parietal; O: occipital; Ic: internal capsule; Th: thalamus; BG: basal ganglia; Wm: white matter.
toward a visual target, a cardboard panel (71 cm × 59 cm × 0.5 cm) was employed to prevent them from receiving any visual feedback from their hand (open-loop visuo-motor task). The visual target was a red plastic cylinder (1 cm diameter and 14 cm high).

We also used a similar panel to adapt patients to the rightward optical shift of the visual field. The prismatic shift was obtained by Glacier Goggles (Cébé®) that were fitted with wide-field, point-to-point prismatic lenses, which created an optical shift of $10^\circ$ (Société Optique Peter, Lyon).

2.3. Procedure

Patients were seated at a table in front of the experimenter in the same quiet room in all of the four experimental sessions. After completing the first session (hereafter referred to as the “baseline” session), patients were submitted to a brief PA. Patients’ performance was then investigated in sessions that took place immediately after the prismatic adaptation (immediate), 1 day (late 1 day), and 1 week (late 1 week) after the prismatic adaptation.

In addition, a subgroup of four patients (see Table 1) was submitted to a second PA procedure after having completed the fourth session (late 1 week). Following the supplementary prismatic exposure, their performance was investigated in a fifth session (post-second adaptation) by using the same battery of tests. This session was run either immediately (patients MB, SL) or after a delay of 6 h from the second adaptation (patients GB, AS). This session allowed us to control whether possible beneficial effects found after a long delay from adaptation may result from a general “practice effect”, due to the execution of the same battery of tests immediately after PA. In addition, this follow-up session allowed us to investigate whether any cumulative effect could be found by repeating the adaptation procedure at a 1-week interval from the previous one.

Each session started with the neuropsychological assessment of patients’ visuo-spatial neglect and ended with a visuo-motor assessment of their pointing performance.

2.3.1. Assessment of visuo-spatial performances

The severity of visuo-spatial neglect was investigated by using the battery of tests described above. All tests were randomly presented in each testing session. While VM tasks were all performed by using the ipsilesional right hand, patients were instructed to remain from using that hand during the execution of VV tasks; also spontaneous pointing to objects to be named or letter strings to be read aloud was not allowed. In both word and non-word reading tasks, strings of different length were randomly presented one at a time.

2.3.2. Assessment of visuo-motor performances

A cardboard panel was held horizontally just below the patient’s chin by one of the experimenters who stood upright behind the patient. The proximal edge of the panel was gently kept in contact with patient’s chest in order to completely conceal from view the starting position as well as the entire movement of the right hand/arm while pointing.

A second experimenter manually presented the visual target at the distal edge of the panel, which was semicircular. It was randomly presented in one of three possible positions: a central position aligned with subject’s mid-sagittal plane ($0^\circ$), and a lateral position on the left and on the right of that axis ($-20^\circ$ and $+20^\circ$, respectively). Positions were marked on the vertical section of the panel, which also carried a graduated scale allowing the second experimenter to record patient’s pointing performance for each target position.

Subjects were asked to keep their right ipsilesional hand on their chest, at the level of the sternum (hand starting position) and to point with their index finger, at a fast but comfortable speed, towards the red cylinder as soon as it was presented. Due to the interposed panel, patients could not see their movement nor they could actually reach and touch the visual target. Once the second experimenter had recorded possible leftward or rightward deviation (in $^\circ$) of patients’ pointing performance with respect to the position of the cylinder, the patient was instructed to retrieve the arm and to prepare for the successive trial. Five pointing trials were recorded for each position.

Patients’ accuracy in the pointing task was investigated after they completed all the neuropsychological tests, both in the baseline and in the sessions following the prismatic adaptation, thus providing a direct measure of whether the sensory-motor after-effect induced by the prismatic adaptation was still present after the VM and VV tasks had been completed.

2.3.3. Prism adaptation

The apparatus used during the prismatic exposure was identical to that employed for the visuo-motor testing described above, except as noted. A variable portion of the proximal part of the horizontal panel (according to patient’s arm-length) was folded in order to shorten its length. This procedure allowed patients to see not only the visual target, but also the second half of their pointing trajectory and their terminal error. Visual targets were singularly presented at the same angular positions as the visuo-motor testing. The exposure period consisted of making 60 pointing movements to visual targets, 20 for each of the three positions (left, centre, right). Also for the prism exposure during which pointing deviations were not recorded, subjects were asked to point at a fast but comfortable speed. Depending on each patient’s rate, the exposure duration ranged from about 5–7 min. At variance with a previous study that directly investigated the
effect of shifting the left half of the visual field towards the right [60], our experiment evaluated the effect of prismatic adaptation, and all subjects were subsequently tested without prisms, as in the "baseline" session.

2.4. Statistical analysis

For each session, patients’ accuracy in the neuropsychological testing was calculated in percentage both for VM and VV tasks. Performance scores reflected the proportion of items that were verbally reported (VV tasks: picture and objects naming; word and non-word reading) or manually cancelled (VM tasks: lines, letters and bells). Only correct responses were considered in both types of tasks. On the VM line bisection task, accuracy was calculated as maximal (100% correct) if a patient crossed the real centre of the line, progressively decreasing as a function of rightward deviation. In the visuo-motor testing, the mean constant error of the final finger position was calculated for each target position. Patients’ pointing performance was quantified in terms of deviation with respect to the actual object location (in °) and carried a minus (−) or a plus (+) sign for leftward or rightward displacement, respectively.

With the aim of verifying whether patients actually adapted to the rightward deviation induced by prisms exposure, an analysis of variance (ANOVA) was performed on the pointing performance to reveal the presence, amount, and duration of PA after-effects. A second ANOVA was carried out on accuracy scores obtained by patients in the neuropsychological testing to evaluate the presence of an amelioration of neglect symptoms after PA, as well as to show the time course and duration of this improvement across sessions.

3. Results

All patients adapted quite easily to the optical displacement induced by the prismatic goggles, which they found well tolerable. A clear visuo-motor after-effect was present in their pointing performances immediately after, as well as 1 day after PA, which disappeared after 1 week. All patients also showed a clear improvement in all the visuo-spatial tests considered, which was completely maintained after a 1-day delay from the prismatic adaptation, but substantially decayed after a 1-week interval. This qualitative description of patients’ behaviour was fully supported by the results of the statistical analyses that will be described in the same order.

3.1. Prism adaptation after-effect

For each patient, the mean constant error of the final finger position was calculated for each target position and submitted to a two-way ANOVA with “position” (left, centre, right) and session (baseline, immediate, late 1 day, late 1 week) as within-subject factors. The main effect position was significant \[F(2, 10) = 5.82, P < 0.02\]. The Newman–Keuls post-hoc test showed that the amount of after-effect differed as a function of movement direction; that is, patients made larger leftward deviations in pointing towards both the centre (-1.6°) and right-sided (-1.6°) locations with respect to the left-sided location (-1.2°, \(P < 0.04\) for both comparisons).

The main effect “session” was also highly significant \[F(3, 15) = 225.5, P < 0.0001\]. The Newman–Keuls post-hoc test showed the presence of a significant leftward after-effect in both the immediate and late 1 day sessions (-3.2° and -2.9°, respectively) with respect to the pre-adaptation baseline session (-1.2°, \(P < 0.0002\) in both comparisons). As shown in Fig. 1, the leftward deviation of patients’ pointing was larger in the immediate session (-3.2°) than in the late 1 day session (-2.9°, \(P < 0.05\)). A substantial reduction of leftward deviation was found 1 week after PA (0.2°, \(P < 0.0002\) in both comparisons), when patients’ pointing performance was absolutely comparable to that obtained in the pre-adaptation baseline session (0.2°).

The interaction “position × session” was not significant.

3.2. Neglect amelioration

An analysis of variance was performed to verify the presence of an improvement of neglect symptoms after PA, as...
well as to illustrate the time course and duration of this amelioration. Since a different score represented the maximum level of accuracy in each test (e.g. different number of items to be cancelled or named), the mean correct performances of each patient were transformed in arc-sine values. Transformed scores were then submitted to a three-way ANOVA with type of test (VM, VV), test (four tests for each type), and session (baseline, immediate, late 1 day, late 1 week) as within-subject factors. The main factor session was highly significant \( F(3, 15) = 47.75, P < 0.0001 \).

The Newman–Keuls post-hoc test revealed that immediately after PA patients’ accuracy was strongly ameliorated with respect to the baseline condition (58.7% versus 34.4% accuracy, respectively, \( P < 0.0002 \)). Similarly, when tested 24 h after PA, patients’ accuracy was also significantly improved with respect to the baseline condition (55.9% versus 34.4%, respectively, \( P < 0.0002 \)). As displayed in Figs. 2 and 3, patients’ accuracy did not significantly differ whether it was evaluated immediately after (58.7%) or 1 day after PA (55.9%).

In contrast, patients’ performance assessed 1 week from the single adaptation (33.9%) showed a substantial reduction in accuracy with respect to both the post-adaptation immediate and late 1 day sessions (58.7 and 55.9%, respectively, \( P < 0.0002 \) in both comparisons). Indeed, performances obtained by patients in the “baseline” condition and in the late 1 week condition were comparable (34.4 and 33.9%, respectively). No other significant source of variance was found; in particular, the main factor type of task (i.e. VM and VV) was neither significant nor involved in any significant interaction, but showed a similar improvement in both types of test (see Fig. 4).

In order to verify the consistency of these results across different tests, a series of one-way ANOVA was additionally performed on the accuracy score of each test included in the neuropsychological evaluation, with the same within-subject factor session as in the previous ANOVA. The same pattern of results found in the previous analysis was also present in these supplementary ANOVAs. Thus, for sake of brevity, statistical details reported in Figs. 2 and 3 clearly demonstrate that the effect of a single prismatic adaptation was extremely consistent across the different tests considered. As shown in Fig. 5, the improvement obtained after PA, as well as its temporal evolution, was also extremely consistent when individual performances of neglect patients were considered.

Finally, a further ANOVA was performed on a subgroup of patients (see Section 2) with the two-fold aim of verifying (a) whether the long-lasting amelioration of neglect might result as a sort of “practice effect”, due to the execution of the same battery of tests in the immediate session and (b) whether a second prismatic adaptation, after 1 week from the first one, could induce cumulative beneficial effects. To this aim, arc-sine values of mean correct performances were submitted to a four-way ANOVA with group (second adaptation: immediate, delayed) as a between-subject factor

![Fig. 2.](image-url)
and type of test (VM, VV), test (four tests for each type) and session (baseline, immediate, late 1 day, late 1 week, post-second adaptation) as within-subject factors.

The main factor session was highly significant \( F(4, 8) = 27.98, P < 0.0001 \), showing a strong improvement of neglect after the second prismatic adaptation session (63% accuracy) with respect to both the pre-adaptation baseline and the late 1 week sessions (40 and 36%, respectively, \( P < 0.001 \) for both comparisons). This improved performance (63%) was comparable to that manifested in both the immediate and late 1 day session (62 and 59%, respectively). No source of variance involving the factor “group” was significant, showing that the amelioration found after 6 h was not inferior to that found immediately after the second prismatic adaptation (see Fig. 6).

The results of the first prism exposure analysis exactly replicated those obtained in the previous ones (Fig. 6). In particular, patients’ accuracy in both the immediate and late 1 day sessions (62 and 59%, respectively) was significantly ameliorated with respect to the pre-adaptation baseline session (40%, \( P < 0.001 \) in both comparisons). No significant difference was found between the immediate and late 1 day sessions. Patients’ accuracy in these two latter sessions was largely better with respect to that obtained in the late 1 week session (36%, \( P < 0.0006 \)), which was comparable to that obtained in the baseline session (40%). Finally, the benefi-
showing that all the patients manifested a remarkable amelioration following a single, short-lasting period of adaptation to a rightward shift of the visual field (Fig. 5). The improvement found immediately after PA was highly consistent across a wide variety of visuo-spatial tasks; indeed, it manifested in each of the tests considered, which assessed different visuo-spatial abilities such as those required to bisect a line or to perform simple as well as complex cancellation and naming tasks. Furthermore, the amount of amelioration, with respect to the baseline performance, was comparable across all the tasks considered.

Most interestingly, we found here for the first time that symptoms of left neglect dyslexia can also be strongly ameliorated following right prismatic exposure (see Fig. 3C and D). The ability of reading aloud letter strings forming single words and non-words was markedly improved in the RBD patients investigated, which were all affected by neglect dyslexia. The rate of omissions of the left portion of a letter string, which constituted almost the only type of error produced by patients prior to intervention, was significantly reduced immediately after the PA, thus resulting in a substantial increase in the reading accuracy. The amount of amelioration shown by patients in reading single words and non-words was comparable. Even if the recovery of neglect dyslexia can occur independently from visuo-spatial neglect [6], the improvement of reading abilities following PA was comparable to that obtained in the other tasks, which involved quite diverse aspects of visuo-spatial analysis.

These findings clearly confirm and considerably extend the notion that the prismatic adaptation technique is strongly efficacious in ameliorating neglect deficits. Indeed, a single, very short-lasting exposure to a right optical deviation of the visual field seemed to be sufficient to reduce the severity of the neglect symptoms exhibited in the neuropsychological testing by 25%, on average.

Moreover, the beneficial effects that follow the PA procedure appear to spread over a disparate congeries of tasks, each of which require different solving strategies, but whose common feature can be identified in the basic visuo-spatial nature. Still, this common spatial feature is rather abstract, since very different visuo-spatial analyses are necessary to bisect a line, to identify and cross out or name a two-dimensional silhouette intermingled with several distractors and, finally, to read aloud a word or non-word formed by a string of letters. Thus, it is possible to conceive that the cognitive effects induced by the PA technique can directly influence a relatively higher-order level of visuo-spatial representations.

Another important finding of this study was the very rapid establishment of the visuo-spatial improvement. While in a previous investigation, the stress was mainly laid upon the long duration of neglect amelioration [57], here we wanted to emphasise (also) the very short time needed for this amelioration to take place. The very same visuo-spatial problems faced by patients while performing the tests appeared to be almost insurmountable before PA, but were much more successfully solved by all neglect patients immediately...
A PA-based treatment (B) that, even if interrupted (A version of an ABA design. In other words, the pathological specificity of the effects induced by PA by adopting a modified non-treated group, and to internally control for the specificity about 7 days. This evolutionary pattern turned out to be pilot study, patients’ performance substantially decayed after 1 week; at this much longer interval, the severity of neglect contrast, no transfer of beneficial effects was found after 1 are well consolidated over a period of (at least) 24 h. By quantitative but also qualitative aspects of the amelioration and for each individual patient, clearly showing that not only results of the present study converge in showing that manipulations spatial aspects of the sensory inputs for a short time is a more viable way to quickly ameliorate neglect than using strategic, top-down approaches that usually need a much longer training period. However, it seems that the beneficial effect of a single prismatic adaptation can further develop, increasing more progressively than the abrupt but ephemeral improvement produced by caloric stimulation.

When considering the second aim of the present study, i.e. the duration of PA-induced beneficial effects, the results clearly showed that neglect amelioration was fully maintained over 1 day after a single PA procedure (Figs. 2 and 3). This result thus extends the beneficial duration found in a previous group study with a limited 2 h follow-up of the patients [57]. Most interestingly, this 1-day-long maintenance was manifest in each of the visuo-spatial tasks considered and for each individual patient, clearly showing that not only quantitative but also qualitative aspects of the amelioration are well consolidated over a period of (at least) 24 h. By contrast, no transfer of beneficial effects was found after 1 week, at this much longer interval, the severity of neglect symptoms in the tests considered here had regained the level preceding the PA session. The weekly interval was chosen because, on the basis of a pilot study, patients’ performance substantially decayed after about 7 days. This evolutionary pattern turned out to be exploitable to treat all the subjects instead of distinguishing a single prismatic adaptation can further develop, increasing more progressively than the abrupt but ephemeral improvement produced by caloric stimulation.

The results of the present study unequivocally showed that this was not the case. As mentioned above, the PA procedure produced a widespread beneficial effect on neglect deficits. In particular, VM tasks that involved the use of the right adapted arm, as well as VV tasks, that did not involve its use to be executed, were both ameliorated. Most importantly, the degree of this amelioration was highly comparable between the two kinds of tasks (Fig. 4). Since patients exhibited a defective performance in both types of tasks, the design of the present study was particularly appropriate to investigate the possible role played by the adapted arm for the recovery of neglect, which could be otherwise underestimated in patients without a clear “perceptual” component of neglect. Therefore, our findings do not support the idea that the amelioration might depend upon a low-order factor, namely, the leftward visuo-motor bias of the right arm. As we reasoned in Section 1, this possibility had to be investigated in the first place in order to verify whether the improvement was merely a peripheral by-product of the shifted visuo-motor correspondences. If this were true, the potential impact of PA as a valuable technique to rehabilitate neglect would have been considerably weakened. In contrast, the findings of the present study strongly support the idea that the effects induced by the PA procedure affect higher-level spatial representations [34,54,56,59]. As another illustration, recent experiments have shown that normal subjects can be biased, in a neglect-like way, while performing line bisection judgements after adaptation to a leftward prismatic shift of the visual field [9].

However, before a firm conclusion can be drawn on this issue, an alternative account based on a different low-order visuo-motor factor needs to be considered. This factor could
be constituted by a leftward error in the direction of gaze resulting in a sustained ocular posture, that is a sort of after-effect related to the position of the eye in the orbit and/or to eye-muscle potentiation [13]. Adaptation to image displacement brought about by looking through wedge prisms has been shown to produce a change in registered eye position in normal subjects [10,35,36]. However, it has been suggested that very lengthy prism exposures (days rather than minutes) only lead to a small adaptation of the registered eye position [20,22], unless extremely slow movements are performed in terminal feed-back exposure conditions [45]. The possibility should nevertheless be considered that such a gaze-deviation effect might be potentiated following a cerebral lesion. Indeed, we already demonstrated that the duration of post-adaptation after-effects, usually ephemeral in healthy subjects [8,67], was remarkably protracted in RBD patients with neglect. In addition, Rode et al. [53,54] have shown that a purely cognitive representation of space such as mental imagery (a map-of-France version of the Piazza del Duomo study by Biasiach and Luzzatti [4]) can also be improved following a short PA session, but the possible implication of covert or overt eye movements in this task cannot be rejected. Indeed, the possibility should be considered that the execution of leftward eye movements or a sustained leftward eyeball orientation, might contribute to improving patients’ performance, as reported in other imagery tasks [37].

The role played by oculo-motor adaptation in the PA treatment of neglect seems to be supported by recent evidence [2]. With the prismatic condition adopted in the present study, however, the proprioceptive shift is usually much greater than the visual after-effect. In addition, Rossetti et al. [57] have shown that the proprioceptive component of the PA in neglect patients was about 80% of the prismatic displacement, which implies that the potential amount of visual component in the after-effect should be very limited (see also [12]).

As a final aim, we sought to unravel the temporal relationship between the amelioration of the visuo-spatial deficits and the presence of visuo-motor after-effect, as measured by the open-loop pointing task. First of all, it should be emphasised that the present group of neglect patients adapted to right-deviating prisms despite a right brain lesion. Interestingly, both the presence and the duration of neglect amelioration were extremely well paralleled by the presence of a leftward after-effect in patients’ pointing performances. Neglect improvements as well as leftward after-effect were both rapid in taking place, being evident immediately after PA procedure, with respect to the first baseline assessment. In addition, they both continued to significantly manifest after a 1-day delay from PA. At variance with the very short after-effect duration usually reported in healthy subjects (in the order of minutes), neglect patients were still showing a significant “negative after-effect” in their pointing performance after 24 h from PA (see Fig. 1). Finally, the achieved amount of amelioration of neglect symptoms almost completely disappeared after a 1-week delay from PA, as did the leftward visuo-motor after-effect.

This important finding, reported here for the first time, seems to suggest that a key element of the rehabilitation effect following PA might be found in the process of adaptation and in its prolonged duration manifested in RBD patients. Indeed, it would be tempting to speculate that the cumulative nature of the temporal relationship we found in the present study has a potential causative role. However, dissociated behaviour between adaptation and after-effect has been reported in normal subjects as, for example, a high degree of adaptation with no sign of after-effect [62]. In order to verify the potential causal relationship between PA and neglect amelioration, an on-line measure of the adaptation process [55] should be added to the measure of the after-effect in future studies [15].

Altogether, the results of this study considerably extend our knowledge about the amelioration of neglect symptoms that follows adaptation to a right prismatic shift of patients’ visual field. Quite diverse aspects of the defective spatial cognition of brain damaged patients can be restructured by acting on transformed sensorimotor input [15,34,39,59]. We confirmed that the duration of the effects following a single application of the PA procedure was much longer than that described for other sensory stimulations [56,65], and extended this duration to at least 24 h. The present results obtained on a group of patients are, therefore, compatible with the single case studies, which reported effects lasting beyond 1 day [34,39,58]. This finding could be particularly important when considering the potential impact the PA procedure might have on neglect symptoms in more “naturalistic” settings, e.g. at home. This possibility is supported by several anecdotal reports given by the patient’s family and friends. In particular, we can mention the case of a patient living in an assisted residence who, after receiving a single intervention, is now able to orient herself independently in the house, and capable of finding her way to and from her room (see also [34]).

In addition, here we concluded that the use of the adapted arm does not play any crucial role as a possible mechanism responsible for the rehabilitating effects. In this respect, it should be noted that while a reduction in the ipsilesional bias of the subjective body-midline was observed following PA [57], recent experiments have shown that the improvement of neglect cannot simply result from a shift in the manual straight-ahead demonstration produced by PA [39]. These findings suggest that the effect of PA may be conceived as triggering or improving active processes involved in brain plasticity related to multisensory integration and space representation. These active processes seem to produce long-lasting effects than the passive processes stimulated by several other sensory manipulations.

When considering passive processes, we refer to the activity of mechanisms underlying the classic sensory stimulation techniques that are known to ameliorate neglect rapidly, but temporarily; i.e. the duration of their beneficial effects is
temporally confined to the approximate duration of the sensory modification and the improvement in neglect tends to disappear as soon as the manipulation is interrupted. These processes are "passive" in that they emerge without requiring any additional process to counteract the bias artificially induced by the sensory information. For example, this would be equivalent to a situation in which the patient wears displacing prisms without physically interacting with the environment or without receiving any feedback from the visual discrepancy. In contrast to PA, this situation is known to produce a weak amelioration of neglect symptoms [60].

Unlike these manipulations, which could be described as corrective, the effect of PA is observed after the removal of the goggles, i.e. it consists of a subsequent effect rather than a direct effect. The processes at work during PA act "active" in that they require an additional process, namely, the adaptation, to cope with the discrepancy introduced between the agent and its environment. Adaptation is obtained through the performance of voluntary goal-directed actions without altering the body or the environment, but rather the relationship between them.

While sensory alterations of both passive and active processes act upon low-order factors and proceed in a bottom-up direction, in our conception, an active process would reinforce and stabilise a new relationship between the patient and the environment could be affected. This, in turn, might influence the manifestations of neglect as well as the various factors participating in or exacerbating neglect (e.g. eye movement patterns). On the other hand, top-down approaches to the rehabilitation of neglect can affect high-order factors at one specific level of the interaction between the patient and the environment (e.g. improving scanning strategies or orienting of attention), whereas adaptation to prisms seems to affect different levels of this interaction, by inducing a homogeneous re-mapping at many levels of visual-motor interactions.

In light of the magnitude, duration, and widespread effects of PA on hemispatial neglect, we suggest that this method may become a priority tool for the rehabilitation of this debilitating syndrome.

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References


