Neglect and prism adaptation: A new therapeutic tool for spatial cognition disorders

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Abstract. Purpose: A large proportion of right-hemisphere stroke patients show unilateral neglect, a neurological deficit of perception, attention, representation, and/or performing actions within their left-sided space, inducing many functional debilitating effects on everyday life, and responsible for poor functional recovery and ability to benefit from treatment. This spatial cognition disorder affects the orientation of behaviour with a shift of proprioceptive representations toward the lesion side.

Methods: This shift can be reduced after a prism adaptation period to a right lateral displacement of visual field (induced by a simple target-pointing task with base-left wedge prisms). The modification of visuo-motor or sensory-motor correspondences induced by prism adaptation involves improvement of different symptoms of neglect.

Results: Classical visuo-motor tests could be improved for at least 2h after adaptation, but also non-motor and non-visual tasks. In addition, cross-modal effects have been described (tactile extinction and dichotic listening), mental imagery tasks (geographic map, number bisection) and even visuo-constructive disorders. These cognitive effects are shown to result from indirect bottom-up effects of the deeper, adaptive realignment component of the reaction to prisms. Lesion studies and functional imaging data evoke a cerebello-cortical network in which each structure plays a specific role and not all structures are crucial for adaptation ability.

Conclusions: These cognitive effects of prism adaptation suggest that prism adaptation does not act specifically on the ipsilesional bias characteristic of unilateral neglect but rehabilitates more generally the visuo-spatial functions attributed to the right cortical hemisphere. These results reinforce the idea that the process of prism adaptation may activate brain functions related to multisensory integration and higher spatial representations and show a generalization at a functional level. Prism adaptation therefore appears as a new powerful therapeutic tool for spatial cognition disorders.

Keywords: Neglect, prism adaptation, rehabilitation, after-effect, right hemisphere

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1. Neglect, a behavioural ipsilesional bias

Hemispatial neglect is classically 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 [1]. This condition is frequently found in right-brain damaged patients, often in association with contralesional hemiplegia or hemiparesis. Neglect thus constitutes a space-oriented behaviour disorder with an ipsilesional bias toward the right side. This disorder may be illustrated by the clinical observation of the patient suffering from neglect. Spontaneously the patient displays an ocular and cephalic deviation toward the side right. When asking to orient his gaze toward the contralesional space, the pursuit movements are reduced and sometimes are unable to cross the central region. Moreover an asymmetry of ocular saccades may also be observed. This behavioural bias will be evidenced in a bisection task or in asking to the patient to point in a straight-ahead position in darkness. In this situation, a shift of pointing movements is demonstrated reflecting a shift of the proprioceptive egocentric reference towards the lesion side.

The strong core of neglect is that this behavioural ipsilesional bias is associated to an unawareness of the contralesional space with reduction of perception, action and attentional and/or representational processes performed within it [2,3]. The unilateral neglect patient is thus unable to compensate his illness by a voluntary orientation of attention unlike the patient with a hemianopia who could orient his gaze toward the blind hemi-field. These both factors explained that neglect induces many functional debilitating effects on everyday life and has been shown to be responsible for poor functional recovery and reduced ability to benefit from treatment of impaired motor functions [4,6].

2. Reduction of behavioural bias after rehabilitation

Numerous attempts to improve neglect have been made over the last forty years. The main question which remains debated is how one could reduce the behavioural bias of neglect and corollary improve the consciousness of the left peripersonal and personal space (see review [7]). Two theoretical tracks may be thus distinguished in rehabilitation of neglect: a "top-down" and a "bottom-up" approach. The first is a pragmatic clinical approach which is aimed at improving the perceptual and behavioural biases by acting on the patient’s awareness of the deficit, i.e. at the highest cognitive levels, including visual scanning training, cueing or sustained attention training [8,9]. The second physiological approach is aimed at modifying the sensorimotor level by passive sensory manipulations, or visuo-motor adaptation which allow to bypass the central awareness deficit and directly influence the highest cognitive levels of space and action representation (see reviews [10,11]).

These two levels of representation, sensori-motor and cognitive are supported by the posterior parietal cortex particularly the inferior parietal lobule (BA thirty-nine and forty). The inferior parietal lobule is a sensori-motor interface between space representation and action. The damage of these areas involves a severe and persistent contralesional neglect [12,13]. Damage of other areas, as BA areas 6, 8 and forty-four and superior temporal sulcus could also produce neglect [14, 16]. Such an interaction between space representation and action may be experimentally provoked by prismatic adaptation procedure. The aim of this paper is thus to review the different studies showing that a prismatic adaptation (PA) may reduce the behavioural bias of neglect and awareness deficit according a bottom-up track.

3. Experimental behavioural bias after prism exposure in normals

In normal subjects a transient behavioural bias may be experimentally induced by a prism adaptation procedure [17,18]. This optical manipulation may produce a shift of proprioceptive representations, evidenced by the displacement of manual straight-ahead pointing in the dark in the direction opposite to the visual shift produced by the prisms. The exposure to an optical alteration of the visual field involved initially a disorganization of visuo-motor behaviour which could be corrected through visuo-motor adaptation. The shift of proprioceptive representations constitutes one major compensatory effect of short-term wedge-prism exposure. Negative after-effects also include a measure of the total after-effect by open loop pointing and of the visual after-effect by requiring subjects to set a visual target to their straight-ahead. After-effects reflect the plasticity of coordinate transformations involved in multisensory and sensorimotor integration. They are used to assess and quantify the presence of true adaptation [18, 19]. In addition, subjects exhibit error reduction curves.
The patient wore a pair of goggles fitted with wide-field point-to-point prismatic lenses creating a rightward optical shift of 10°. Prism exposure consisted of 50 fast pointing movements made to visual targets presented either 10° to the left or 10° to the right of the body midline, given in pseudorandom order. A shelf was placed under the patient’s chin to prevent viewing of the hand at its starting position, but allowing an unobstructed view of the targets and terminal pointing errors. This adaptation procedure took between 6–10 min. 

**Perception of visual error-signal:** At the start of the process, the subject will misreach to the right of the target, an error referred to as the direct effect. **Adaptation:** The error will swiftly diminish and disappear entirely as the participant adapts to the visual shift. **After-effect:** After removal of the prism, the subject will misreach in the opposite direction to the visual shift, an error referred to as the after-effect.

During the prism exposure period, which also reflects the ability to strategically compensate for the optical shift [18,19]. These adaptive realignment and strategic contribution to the compensation of the optical shift have been ascribed to distinct neuroanatomical substrates [18,20]: the strategic component mainly relies on the parietal cortex [21,23] whereas the adaptive realignment component relies on the cerebellum [19,24]. The relevant point for unilateral neglect rehabilitation is that after an optical deviation of the visual field to the right, subjects show a systematic leftward deviation of visuo-motor responses with the adapted limb. The hypothesis proposed by Rossetti et al. [25,26] was to use this after-effect as method to help the neglect patient to orient his behaviour toward the neglected side. An interesting and additional question was to specify whether a lower-order visuo-motor action may influence higher-level spatial representation.

4. **After-effect and improvement of neglect after PA**

In the first study, Rossetti et al. [25] have clearly demonstrated that a short period of pointing toward targets viewed through prisms that displaced the visual field 10 degrees in the rightward direction (50 pointing movements for an exposure period of two to five minutes) involved a shift in manual straight-ahead pointing toward the left side in the dark (see Fig. 1).

Prior to prism exposure six patients pointed, on average, about 9 degrees to the right (ipsilesional side), but after exposure the same test showed an average pointing of 2 deg rightward: an after-effect of about 8 deg or 70 percent compensation for the 10 deg optical displacement. This after-effect is much larger than the 30 percent shown by normal control participants, showing that neglect patients, in spite of brain damage were more affected by the adaptation than the controls were. Surprisingly neglect symptoms were ameliorated for six patients exposed to prism adaptation. Improvement was evidenced in visuo-manual tasks as line bisection [27], copy drawing [28], line cancellation [29], daisy drawing and text reading. Aspects of object-based neglect and space-based neglect were equally improved by the adaptation procedure.

From this previous paper, 18 different studies were published about the effects of prism adaptation on symptoms of neglect and possible underlying mechanisms. Eighty-three right brain damaged patients entirely benefit from this treatment with different results on after-effects, clinical effects and duration of improvement (See Table 1).

The table clearly shows that the amount of the after-effect varies from 2.7° [30] to 14° [31,32] with a mean value of 7.1°. It appears that the quantitative relationship between the amplitude of after-effect and neglect amelioration is not obvious. As shown by numerous studies, the main interest of PA is that the effects produced by a single 5-min session of adaptation last for much longer than any other rehabilitation method. Two group studies showed fully sustained effects after at least 2 h [25] and 1 day [33], respectively. Case studies reported even more prolonged improvements, lasting for about 4 days [34,35]. It is possible that some patients are improved for a longer period than others [36].
But the best prospect for rehabilitation purposes is to repeat adaptation sessions. Recently a treatment with prismatic lenses in twice-daily sessions over a period of 2 weeks was applied in a group of seven neglect patients compared with a control group. The results showed an improvement in the experimental patient’s performance after PA, which was maintained during a 5-week period after treatment. This long-term improvement of neglect symptoms was found in standard as well as in behavioural tests and in all spatial domains [30].

Recently ineffectiveness of PA was reported in ten right brain damaged patients with neglect assessed by visuomotor and visuo verbal tasks [37]. In this study the partial improvement which was observed with repetition of tests could be related to a learning effect or an increase of vigilance or sustained attention. This factor was taken into account in the only randomised controlled clinical trial in a sample of 10 right-brain damaged patients with neglect [38,39]. The authors extended the study of Rossetti et al. [25] using identical procedures: Post tests were measured at 2 and 5 hours post adaptation and further testing was employed. Patients were sampled from different stages of rehabilitation, showing neglect for more than 3 months. The experimental group was compared to a control group of patients treated by goggles made of window glasses. The results showed a clear difference between experimental and control groups, in favour of a selective effect of PA on unilateral neglect (see Fig. 2).

5. What are the neural mechanisms involved by PA?

This point was recently assessed by Serino et al. [40] in a group of 16 neglect patients submitted to a PA treatment for 10 daily sessions compared to a control group. Effects of PA were assessed by the recovery of neglect (measured by the B.I.T. Conventional and Behavioural scales, a reading task but also an eye movement analy-
Fig. 3. Effect of prism adaptation on neglect and constructional apraxia in two right brain-damaged patients assessed by the Taylor’s figure (patient A) and the Rey’s figure (patient B) before adaptation (pre-test), immediately upon the 10\(^\circ\) prism removal (post-test) and 2–4 hours later (late-test). Before adaptation, the figures displayed a neglect of the left part and graphic errors in the entire of drawing consistent with an associated constructional apraxia. After PA, improvement of the drawing was observed both for left neglect and visuo-constructive disorders.

Moreover PA visuo-motor effects (the error reduction and the after-effect) were also measured. Serino et al. [40] showed that no correlation between recovery of neglect and after-effect. The after-effect has to be considered as the demonstration that the patient was able to adapt to a prismatic deviation of his visual environment but this should not be considered as a predictive factor of neglect recovery after PA. In this study on the other hand, a significant correlation between leftward oculo-motor deviations produced by PA and recovery of neglect was evidenced and even patients with greater leftward deviation of the first saccade displayed the greater improvement of visuo-spatial tasks. For these authors it is therefore possible to speculate that the increase in the amplitude of the first leftward saccade obtained after PA produces also a shifting of visual attention towards the left side of the visual field. However Ferber et al. [31] reported in a neglect patient exposed to a prismatic deviation, a shift of the exploratory eye movement toward the left but a persistent deficit in awareness of the left side assessed by the ability of the patient to judge the happiness of vertically arranged pairs of chimeric faces composed of half-smiling and half-neutral faces.

The effects of PA from a low-order visuo-motor to a high-order level rely also probably on other mechanisms.

6. Prism adaptation, a bottom-up track

The first findings which can not be explained by a modification of exploratory eye movements concern the effects of PA on sensory neglect, particularly in the tactile and auditory domains where no visuo-manual response could be involved. MacIntosh et al. [36] in a single case study of a chronic patient showed that PA involves improvement not only of visual components of neglect, but also non-visual haptic neglect assessed by tactile exploration of a circle. Maravita et al. [41] reported in four neglect patients an improvement of contralesional visual and tactile extinction. Same results are reported in the auditory domain. Indeed following a right-brain-damage, unilateral omissions of auditory
Table 1

<table>
<thead>
<tr>
<th>Studies</th>
<th>Cases</th>
<th>After-effect (degrees)</th>
<th>Clinical effects</th>
<th>Duration of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossetti et al., 1998 (25)</td>
<td>6</td>
<td>8°</td>
<td>visuo-motor tasks (bisection, cancellation, drawing, reading)</td>
<td>&gt; or = 2 h</td>
</tr>
<tr>
<td>Rode et al., 2001 (44)</td>
<td>2</td>
<td>9°</td>
<td>visuo-motor tasks (drawing) mental imagery task</td>
<td>immediate</td>
</tr>
<tr>
<td>Tilikete et al., 2001 (51)</td>
<td>5</td>
<td>no assessed</td>
<td>postural imbalance</td>
<td>immediate</td>
</tr>
<tr>
<td>Pisella et al., 2002 (35)</td>
<td>2</td>
<td>9°</td>
<td>visuo-motor tasks (bisection, cancellation, straight-ahead pointing)</td>
<td>96 h</td>
</tr>
<tr>
<td>Farnè et al., 2002 (33)</td>
<td>6</td>
<td>3°</td>
<td>visuo-motor tasks (bisection, cancellation)</td>
<td>24 h</td>
</tr>
<tr>
<td>Frassinetti et al., 2002 (30)</td>
<td>6</td>
<td>2.7°</td>
<td>visuo-motor tasks (bisection, cancellation, drawing) behavioral measures</td>
<td>5 weeks</td>
</tr>
<tr>
<td>MacIntosh et al., 2002 (36)</td>
<td>1</td>
<td>no given</td>
<td>visuo-motor tasks (bisection, cancellation, drawing) neglect dyslexia tactile spatial task</td>
<td>three repeated sessions</td>
</tr>
<tr>
<td>Ferber et al., 2003 (31)</td>
<td>4</td>
<td>14.3°</td>
<td>eye movement pattern</td>
<td>immediate</td>
</tr>
<tr>
<td>Maravita et al., 2003 (41)</td>
<td>4</td>
<td>8°</td>
<td>visuo-motor tasks (bisection, cancellation)</td>
<td>immediate</td>
</tr>
<tr>
<td>Dijkerman et al., 2003 (57)</td>
<td>3</td>
<td>no given</td>
<td>tactile extinction</td>
<td>immediate</td>
</tr>
<tr>
<td>Klos et al., 2004 (39)</td>
<td>10</td>
<td>no assessed</td>
<td>visuo-motor tasks (bisection, cancellation, drawing)</td>
<td>5 h</td>
</tr>
<tr>
<td>Angel et al., 2004 (58)</td>
<td>4</td>
<td>4.33°</td>
<td>attentional task judgement of temporal order</td>
<td>immediate</td>
</tr>
<tr>
<td>Rossetti et al., 2004 (46)</td>
<td>2</td>
<td>4.8° and 9.4°</td>
<td>mental number bisection task</td>
<td>immediate</td>
</tr>
<tr>
<td>Dijkerman et al., 2004 (60)</td>
<td>1</td>
<td>no given</td>
<td>visuo-motor tasks (bisection, cancellation)</td>
<td>immediate</td>
</tr>
<tr>
<td>Morris et al., 2004 (61)</td>
<td>4</td>
<td>7°</td>
<td>visuo-motor tasks (bisection)</td>
<td>immediate</td>
</tr>
<tr>
<td>Serrino et al., 2005 (40)</td>
<td>16</td>
<td>3.6°</td>
<td>visuo-motor tasks (B.I.T.) reading task eye movement pattern</td>
<td>3 months</td>
</tr>
<tr>
<td>Rousseaux et al., 2006 (37)</td>
<td>10</td>
<td>4.8°</td>
<td>visuo-motor tasks (bisection, cancellation, drawing)</td>
<td>no effect</td>
</tr>
<tr>
<td>Jacquin-Courtois et al., 2006 (34)</td>
<td>1</td>
<td>6.72°</td>
<td>visuo-motor tasks (bisection, cancellation, drawing)</td>
<td>96 h</td>
</tr>
<tr>
<td>Rode et al., 2006 (32)</td>
<td>1</td>
<td>14.8°</td>
<td>visuo-motor tasks (bisection, cancellation)</td>
<td>72 h</td>
</tr>
</tbody>
</table>

Mean: 7.1°

Targets occur frequently in the situation where two auditory stimuli are presented simultaneously from the right and from the left, while no omission is observed when presenting one single stimulus. Jacquin-Courtois et al. [42] have thus studied effects of PA on left auditory extinction in two groups of right-brain damaged patients with neglect: the first receiving a classical prism treatment, the second performing the same pointing procedure, but wearing neutral glasses creating no optical shift. Effects of PA were assessed on conventional visuomotor tasks and a dichotic listening test immediately upon prism removal and 2 hours later. Results displayed a long-lasting improvement of both visuomotor tasks and auditory extinction, only in patients exposed to PA.

These results show that the beneficial effects of PA are not restricted merely to visuomotor tasks but can also affect perception in non visual modalities. These results suggest that the calibration of sensory-motor transformations induced by PA, which directly affects visual space representation and action, may also alter the orientation of attention in other sensory modalities. In all these experiments, the patients were blindfolded and it is difficult to explain that this orientation is consecutive to a leftward exploratory eye movements.

The second findings concern the effect of PA on manifestations of imaginal neglect. Rode et al. [43,44] explored the effect of prism adaptation on visual imagery in two neglect patients asked to evoke mentally the map of France. Before adaptation, both patients are unable to evoke town names on the left part of map; named towns were located to the right half of the map consistent with a left representational neglect. After adaptation, a clear-cut improvement is demonstrated, reflecting an ability of both patients to generate or explore a symmetrical inner representation of the map. This imagery task is explicitly spatial in nature. More recently, similar effects were obtained in a non explic-
ity mental task, a mental number-bisection task in two neglect patients. This task was recently described by Zorzi et al. [45] who reported that the mental bisection between two numbers was systematically shifted to the right (i.e., toward bigger numbers) in neglect patients, parcelling their bias when asked to mark the center of a physical line. The two neglect patients displayed a stable number-bisection bias during the first two sessions; after PA, the two patient’s reliable bias was greatly improved, suggesting an effect of PA on highly cognitive task [46].

Both findings suggest that PA may influence the high level multimodal representations associated with spatial attention. The effects of PA may be considered as stimulating processes involved in brain plasticity related to multisensory integration and space representation. A supplementary question is to know whether PA favors the spontaneous recovery of neglect or facilitates the occurrence of selective compensation mechanisms. This question refers either to the cerebral plasticity naturally involved after the cerebral damage or to the cerebral plasticity specifically activated by the visuo-motor adaptation task. In normal subjects, neural structures considered to be involved in PA have long been restricted to the cerebellum [26,46], as shown by the inability of adaptation of patients with focal olivocerebellar lesion [19,47]. The posterior parietal cortex contralateral to the acting hand might be activated during adaptation to a prism-induced shift of the visual field [21]. The reciprocal connections between the deep cerebellar structures and the posterior parietal cortex provide an anatomical substrate that may support the cerebellar participation also in high-order processing [48,49].

In order to answer this question, Luaut et al. [23] performed a functional imaging PET study in five neglect patients after a prism exposure period. This study confirms a strong implication of the cerebellum which may be implied in the realignment of visuo-motor coordinates but also significant activations in different cortical and sub-cortical structures as the left thalamus, the left temporo-occipital cortex, the left medial temporal cortex and the right posterior parietal cortex. These activation patterns suggest that the low level sensorimotor adaptation may activate a distributed network between cerebellum, thalamus and cortical areas. This network may underline the cognitive effects of PA independently from modification of exploratory eye movements. Supplementary studies will be useful to precisely the respective cerebral structures involved in the two components of PA (strategic and adaptive).
7. From neglect to spatial cognition

Two main lines of arguments can be used to argue that PA may produce effects that may be more specific to spatial cognition than to unilateral neglect per se. First, effects of PA have been demonstrated in normal subjects [50] Second, the effects found in the right brain damaged patients appear to be found on non-neglect symptoms and on non-neglect patients. The best example comes from a study where patients with right hemisphere lesion and no unilateral neglect were tested [51]. As patients with right hemisphere lesion, whether or not they present with neglect, tend to exhibit a postural balance biased to the right [51,52] attempted to improve postural balance in a group of patients with no or resolved neglect and found significant therapeutic effects of PA. This result has been interpreted as an indirect effect of PA on the central level of space representation. At a more directly high-level, the common characteristic of PA cognitive effects (especially the cross-modal and mental imagery effects) is the enlargement or the shift of space represented parallel to the reduction of the attentional bias. This disturbance refers to the general visuo-spatial functions attributed to the right cortical hemisphere. We could thus postulate that PA may improve more generally spatial cognition. The better symmetry (object-based neglect) and spatial organisation of drawing following prism adaptation in individuals e.g. in the Gainotti test (Rode et al. [11] Fig. 6 [25, p. 284]) suggest for example a possible effect of PA on visuo-constructive disorders (see Fig. 3).

This point was recently assessed in a neglect patient also showing a spatial dysgraphia following right brain damage. Spatial dysgraphia has been defined as “a disturbance of graphic expression due to an impairment of visuospatial perception resulting from a lesion in the nonlanguage-dominant hemisphere” [53,54]. According to these authors, four main features define spatial dysgraphia: (i) ‘right-page’ preference: writing is crowded onto the right side of the page leaving an excessively wide “margin” on the left side; (ii) sloping lines (inclination): patients fail to write horizontally and produce oblique or wavy lines; (iii) broken lines: patients leave abnormally large space between words, thus leading to the fragmentation of the line into small segments and (iv) graphic errors: production of an uncorrect number of strokes for a given letter or of letters for a given word. The first feature reflects the left-sided neglect although the second and third reflect visuoconstructive disorders. After a PA procedure, an improvement of neglect was evidenced (with a reduction of the right page preference) as well as a long lasting reduction of sloping and broken lines (see Fig. 4).

The ability to place and orient correctly the words in the page and relatively to each others was durably improved; The positive effect of PA on visuo-constructive disorders suggests that PA does not act specifically on the ipsilesional bias characteristic of unilateral neglect but rehabilitates more generally the visuo-spatial functions attributed to the right cortical hemisphere [32]. Prism adaptation may thus enlarge or shift the part of space represented in the spared cortical hemisphere [55]. This different distribution of the representation of space between hemispheres could explain the improvement of both the right-oriented behavioural disorders and the visuo-constructive disorders.

8. Conclusions

These different cognitive effects (mental imagery, sensory cross-modal effect, visuo-constructive disorders) of PA suggest that PA does not act specifically on the ipsilesional bias characteristic of unilateral neglect but rehabilitates more generally the visuo-spatial functions attributed to the right cortical hemisphere. These reinforce the idea that the process of PA may activate brain functions related to multisensory integration and higher spatial representations and show a generalization at a functional level. Prism adaptation therefore appears as a therapeutic tool for spatial cognition disorders and a useful tool in the theoretical attempt to identify the underlying ‘core’ mechanisms of the neglect syndrome.

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