Prism adaptation first among equals in alleviating left neglect: A review

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Abstract. Purpose: The current paper was designed to provide a critical overview on the different methods proposed for the rehabilitation of left spatial neglect.

Methods: On the basis of a previous systematic review of the literature, we analyzed all articles available aiming at reducing left spatial neglect which included a long term functional assessment.

Results: The aim of most early rehabilitation approaches, such as visuo-scanning training, was to re-orient visual scanning toward the neglected side. This review confirmed the utility of this method for rehabilitation purposes. More recent – theory driven – procedures, also based on a training approach, include limb activation, mental imagery training and video-feedback training. Although there is ground for optimism, the functional effectiveness of these methods still relies on few single-case studies. Newer methods have tried to stimulate automatic orientation of gaze or attention towards neglected space in a bottom-up fashion. Sensory stimulations can remove most of the classical signs of left neglect but their effects are short-lived. Such stimulations are not functionally relevant for rehabilitation except for trunk rotation or repeated neck muscle vibrations if they are associated with an extensive training program. A more promising intervention is prism adaptation given the growing evidence of relatively long-term functional gains from comparatively short term usage.

Conclusion: Overall, there is now evidence for several clinically relevant long-term benefits in the case of visual scanning training, mental imagery training, video feedback training, neck muscle vibration and trunk rotation if associated with visual scanning training and prism adaptation. However, the amount of evidence is still limited to a small number of relevant published articles and it is mandatory to continue the research in this field. In this review, the possible routes for new rehabilitation procedures are discussed on the basis of the actual knowledge regarding the neuro-cognitive mechanisms underlying the therapeutic effect of prism adaptation.

Keywords: Left neglect, stroke, rehabilitation, prism adaptation, review

1. Introduction

Patients with right cerebral hemisphere lesions often show a reduced tendency to respond to stimuli and to search actively for them in the left part of space [1].
This condition, described as left neglect, is frequently associated with contralesional motor or somato-sensory deficit. In addition, left neglect provides for poor motor and functional recovery [2–4]. Spatial neglect occurs in about 25–30% of all stroke patients [5] and for a high proportion of them, the disorder can be chronic [6]. For these reasons, left neglect represents a challenging problem for rehabilitation. It is not surprising that over the past 60 years, many different attempts to alleviate this impairment have been developed; but the question remains as to how effective these treatments are, given the heterogeneity of the population and spontaneous recovery. Furthermore, in a rehabilitation perspective, it is mandatory to take into account functional outcomes and the chronicity of the effect.

The purpose of this study was to analyze the current literature in order to provide a critical review of the methods available for the rehabilitation of left neglect. Twenty one articles [7–27] were selected on the base of a systematic search (for more details concerning the methodology see [28]). In the following section, the current evidence of the different methods analyzed in these articles is reported with regard to their clinical effectiveness. A summary of these data is provided in the Table 1. These results also give the opportunity to discuss the mechanisms by which such interventions may foster recovery with special emphasis on the putative neural mechanism by which prism adaptation modulate left spatial neglect.

1.1. Visual scanning training

In the early 1970’s Diller and Co-workers investigated the use of various strategies to compensate for the right side deviation of the gaze [29]. The idea was to favour a re-orientation of visual scanning toward the neglected side by means of a top-down training program based on explicit instruction. From a practical point of view, the training programme was progressive, based on the principles of “anchoring, pacing, density and feedback”. Anchors to the left were frequently ensured by visual cues such as a red line located in the left part of the page that the patient was asked to look at before beginning the exercise (e.g. [23]). In order to enhance visual exploration to the left, a scanning board was some times used (e.g. [27]).

Two randomized control trials showed (on the base of partial data) a long lasting improvement, over 6 months after the end of the procedure, on functional skills such as reading and writing [23,27]. In a single-case study with multiple baseline and follow-up assessments, Pizamiglio et al. (1992) [12] showed evidence for the generalization of visuo-scanning training to other activities of daily living (utilizing commonly used object; description of figures, environment; serving tea; card sorting). Improvement of wheelchair navigation was shown by Webster et al. (1984) [22]. However, other authors claimed that a generalization to functional skills was not systematic unless the duration of the training program lasted more than a month and that the training material was very similar to the test material [30–32]. According to the studies analyzed in the current review, it seems that the beneficial effect was maintained after the rehabilitation terminated. However, only partial data were reported in these studies and it is also possible that training influenced the rate of learning compensatory strategies but not the final level of performances.

Collectively, there is now good evidence for the functional utility of this classical rehabilitation method, currently still used by many in occupational therapy.

1.2. Limb activation

In keeping with the results of Halligan et al. [33] and the need to make use of existing perceptual cues present on the left, Robertson and North [34] used the patient’s own left arm as a cue to improve left neglect. Using single-case reports, latter studies showed that active left limb movements in the left hemi-space significantly reduced neglect, compared with no movement, movements performed with the right hand and movements of the left hand performed in the right hemi-space [35]. These results subsequently inspired the development of the limb activation rehabilitation technique. In clinical practice, the patient is required to initiate movements with his/her left paretic limb in the left part of the space. Robertson et al. [14] developed a specific apparatus to elicit limb activation: the Neglect Alert Device (NAD). This device emits a loud buzzing noise and a red light if the switch is not pressed within a predetermined time interval. The device is placed in the left part of the space and the patient is required to press the switch with his impaired left arm to turn off the buzzer during a variety of situations.

In our review two randomized control trials [11, 15] and four single-case studies with appropriate design [14,17,25,26] were analyzed. All the single-case studies showed that limb activation produced significant long term gains in several ADL areas such as reading, walking strategy, dressing, cleaning, feeding and meal preparation.
Results of the two RCT are less clear-cut in the sense that Robertson et al. (2002) [15], showed a significant improvement of motor functions in the group treated by limb activation but failed to show significant generalization on functional skills as assessed by 3 scales (Barthel index, Bergego’s scale and the behavioural BIT). Kalra et al. (1997) [11] reported a significant reduction in median length of hospital stay (42 versus 66 days) in the group of patients receiving spatio-motor cueing and a trend toward Barthel Index improvement.

Altogether, single-case studies showed interesting results; however the functional effectiveness of limb activation still remains to be demonstrated in randomized controlled trials. It is possible that limb activation may be effective in some conditions but this could depends on the duration of the procedure and also depend on the version of limb activation employed (visuo-motor cueing, spatio-motor cueing or neglect alert device). It is also likely that limb activation is more conductive for some patients than others. Moreover, an important constraint that limits the use of this intervention for many stroke patients is the requirement that patients must have recovered minimal contralateral limb movement.

1.3. Mental imagery training

These techniques, currently used in sport competition, are directly inspired by the representational theory of left spatial neglect [36]. The purpose is to restore space representation by enhancing or training mental imagery through a top-down mechanism. In one single-case study, Smania et al. [19] used visual and movement imagery exercises to enhance left space representation [19]. In this study, improvement of the Zoccoli’s semi-structured scale was reported in two patients. The effect persisted over 6 months after the end of the training.

The observation that the use of an elongated stick could produce a virtual extension of “body space” (presumably the result of remapping of far space as near space [37]) led to the development of a more specific technique: space remapping training. The principle here was to generalize the effect into and toward the neglected left space. Castiello et al. (2004) [38] used this method in a clinical trial in which patients with left neglect were instructed to reach and grasp a real object in right space while simultaneously observing the grasping of a virtual object by a virtual hand in the left space. Results of this study revealed significant improvement in grasping accuracy for the left side of the space following specific training. More studies are however needed to confirm these promising results.

1.4. Feedback training

Since left visuo-spatial neglect is often associated with anosognosia (lack of appropriate awareness for a neurological/neuropsychological deficit and also a recognized contributor of poor outcome), some researchers have suggested the need to alleviate anosognosia before an effective training procedure can be implemented [39]. In keeping with this hypothesis, specific feedback training procedures were developed involving a bottom-up mechanism to produce the feedback (i.e. aiming to restore self awareness) and a top-down mechanism to compensate for neglect behaviour.

Soderback et al. [20] video-recorded their 4 patients in order to provide a feedback of their neglect behaviour, in a cooking task, before employing a learning strategy in order to help patients to improve their performance [20]. In this single case-study, a long term beneficial effect was reported for the four patients. Tham et al. [21], administered a guided interview during which the patient’s neglect behaviour was pointed out to him/her in order to increase self-awareness [21]. After the training period, the four patients included in this study, improved their skills on a cooking task and on the motor and process skills (AMPS) scale. Like mental imagery training, these results need to be confirmed by larger series and if possible randomized controlled trials.

However, as argued by Harvey et al. (2003) [40], all these approaches require the patients to voluntary initiate and maintain attention to the left side, a demanding task in its own right and one that many patients find difficult to apply in everyday life.

1.5. Sensory stimulations

Other approaches to neglect rehabilitation involved the idea of enhancing automatic orientation toward the left space, without the requirement of language mediated attentive learning. Vestibular stimulation, optokinetic stimulation (OKP), neck muscle vibration (NMV), trunk rotation (TR) proved to alleviate most of the classic symptoms of left neglect (for a review see [41,42]). These effects provide clear evidence of how simple bottom-up mechanisms can overcome high level cognitive deficits. Hence it seems likely that these stimulations work by affecting the activity of cortical networks responsible for calibrating spatial coordinate’s frames. Functional imaging studies in healthy subjects showing contralateral cortical activation after vestibular stimulation support this hypothesis [43].
### Table 1
Studies designed to alleviate left neglect with long term functional outcome assessment

<table>
<thead>
<tr>
<th>Articles’ Ref.</th>
<th>Interventions</th>
<th>Design</th>
<th>Patients (n=)</th>
<th>Duration</th>
<th>Outcome</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weinberg et al., 1977 [23]</td>
<td>VST</td>
<td>RCT</td>
<td>25</td>
<td>4 w</td>
<td>Reading; Copying</td>
<td>Improv &gt; 1 yr*</td>
</tr>
<tr>
<td>Young et al., 1983 [27]</td>
<td>VST</td>
<td>RCT</td>
<td>18</td>
<td>4 w</td>
<td>Reading; Copying</td>
<td>Improv &gt; 6 mth*</td>
</tr>
<tr>
<td>Pizzamiglio et al., 1992 [12]</td>
<td>VST Single case MB</td>
<td>13</td>
<td>8 w</td>
<td>Reading; Zoccolotti</td>
<td>Improv &gt; 5 mth*</td>
<td></td>
</tr>
<tr>
<td>Webster et al., 1984 [22]</td>
<td>VST Single case MB</td>
<td>3</td>
<td>4 w</td>
<td>WC navig.</td>
<td>Improv &gt; 1 yr</td>
<td></td>
</tr>
<tr>
<td>Worthington, 1996 [26]</td>
<td>LA Single case MB</td>
<td>1</td>
<td>10 w</td>
<td>Reading</td>
<td>Improv &gt; 18 mth</td>
<td></td>
</tr>
<tr>
<td>Robertson et al., 1998 [14]</td>
<td>LA (NAD) Single case MB</td>
<td>1</td>
<td>18 d</td>
<td>Combing; Navig.; BTT</td>
<td>Improv &gt; 9 d</td>
<td></td>
</tr>
<tr>
<td>Samuel et al., 2000 [17]</td>
<td>LA (SMc) Single case MB</td>
<td>2</td>
<td>8 w</td>
<td>Bergego</td>
<td>Improv &gt; 1 mth</td>
<td></td>
</tr>
<tr>
<td>Robertson et al., 2002 [15]</td>
<td>LA</td>
<td>RCT</td>
<td>17</td>
<td>12 w</td>
<td>BI; Bergego; B-BIT</td>
<td>Improv of motor function &gt; 2 yr</td>
</tr>
<tr>
<td>Brunila et al., 2002 [7]</td>
<td>LA + VST Single case MB</td>
<td>4</td>
<td>3 w</td>
<td>Reading</td>
<td>Improv &gt; 3 w</td>
<td></td>
</tr>
<tr>
<td>Smania et al., 1997 [19]</td>
<td>Mental imagery</td>
<td>Single case MB</td>
<td>2</td>
<td>8 w</td>
<td>Zoccolotti</td>
<td>Improv &gt; 6 mth</td>
</tr>
<tr>
<td>Tham et al., 2001 [21]</td>
<td>Feedback</td>
<td>Single case MB</td>
<td>4</td>
<td>4 w</td>
<td>AMPS (reading, writing, cooking, garden); BTT</td>
<td>Improv &gt; 9 w</td>
</tr>
<tr>
<td>Wiart et al., 1997 [24]</td>
<td>TR + VST</td>
<td>RCT</td>
<td>11</td>
<td>4 w</td>
<td>FIM</td>
<td>Improv &gt; 1 mth*</td>
</tr>
<tr>
<td>Schindler et al., 2002 [18]</td>
<td>NMV + VST Cross-over</td>
<td>10</td>
<td>3 w</td>
<td>Reading; personal care spatial orientation</td>
<td>Improv &gt; 2 mth</td>
<td></td>
</tr>
<tr>
<td>Frassinetti et al., 2002 [9]</td>
<td>Prism adaptation</td>
<td>CT</td>
<td>7</td>
<td>2 w (10 sess)</td>
<td>Reading; B-BIT</td>
<td>Improv &gt; 5 w</td>
</tr>
<tr>
<td>Farne et al., 2002 [8]</td>
<td>Prism adaptation</td>
<td>Single case MB</td>
<td>6</td>
<td>1 sess</td>
<td>Reading</td>
<td>Improv &gt; 1 d</td>
</tr>
<tr>
<td>Jacquet-Courtois et al., In press [10]</td>
<td>Prism adaptation</td>
<td>Single case MB</td>
<td>1</td>
<td>1 sess</td>
<td>WC navig.</td>
<td>Improv &gt; 96 h</td>
</tr>
</tbody>
</table>

Footnotes and abbreviations:
**Interventions:** VST: Visual scanning training; LA: Limb activation; SMc: Spatio-motor cueing; NAD: Neglect alert device; TR: Trunk rotation; NMV: Neck muscle vibration; OPK: Optokinetic stimulation.
Design: RCT: Randomized control trial; MB: multiple baseline; CT: control trial.

Patient: n = number of patients in the experimental group.

Duration refers to the duration of the procedure: w : week(s); d : day(s); sess: session.

Outcome: B-BIT: Behavioural BIT [85]; Zoccolotti: Zoccolotti’ semi structure scale [86]; WC navig.: Wheelchair navigation; BI: Barthel index [87]; Bergego: Bergego’s functional scale [88]; FIM: functional independence measure [89]; BTT: Baking tray task; AMPS: Assessment of motor and process skills [90].

Results: Improv: Improvement; yr: year; mth: month(s); w : week(s); d : day(s); h : hour(s). #: partial data.

Circulatory diagrams with two types of segmentations: vertical segmentation for the different functional topics (Roman numbers) and horizontal segmentation for the levels of evidence (Arabic numbers):

### Functional topics:

<table>
<thead>
<tr>
<th>N°</th>
<th>Functional outcomes</th>
<th>N°</th>
<th>Functional outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Spatial orientation</td>
<td>XIV</td>
<td>Problem solving</td>
</tr>
<tr>
<td>II</td>
<td>Feeding</td>
<td>XV</td>
<td>Memory</td>
</tr>
<tr>
<td>III</td>
<td>Dressing</td>
<td>XVI</td>
<td>Utilising commonly used object</td>
</tr>
<tr>
<td>IV</td>
<td>Grooming</td>
<td>XVII</td>
<td>Description of figures, environment</td>
</tr>
<tr>
<td>V</td>
<td>Cleaning</td>
<td>XVIII</td>
<td>Serving tea</td>
</tr>
<tr>
<td>VI</td>
<td>Transfers</td>
<td>XIX</td>
<td>Card sorting</td>
</tr>
<tr>
<td>VII</td>
<td>Posture</td>
<td>XX</td>
<td>Map navigation</td>
</tr>
<tr>
<td>VIII</td>
<td>Walking strategy</td>
<td>XI</td>
<td>Picture scanning</td>
</tr>
<tr>
<td>IX</td>
<td>Stairs climbing</td>
<td>XXII</td>
<td>Sentence copying</td>
</tr>
<tr>
<td>X</td>
<td>Wheelchair navigation</td>
<td>XXIII</td>
<td>Reading and setting time</td>
</tr>
<tr>
<td>XI</td>
<td>Reading</td>
<td>XXIV</td>
<td>Telephone dialling</td>
</tr>
<tr>
<td>XII</td>
<td>Writing</td>
<td>XXV</td>
<td>Handling money</td>
</tr>
<tr>
<td>XIII</td>
<td>Social interaction</td>
<td>XXVI</td>
<td>Cooking</td>
</tr>
</tbody>
</table>

I–V: Bergego’s functional scale.  
II–IX: Barthel index.  
XVI–XIX: Zoccolotti semi-structured scale  
XX–XXV: Behavioural BIT

### Improvement

Arabian numbers: levels of evidence adapted from Ball et al. (2001) [91]:
1: level 1 (randomized control trial).  
2–3: level 2 (cohort studies) and level 3 (case-control, cross-over and single-case studies with multiple base line assessment).
4: level 4 (other types of studies).

However, the remediation is usually short-lived and thus is not functionally relevant for rehabilitation. A sustained functional gain was only found in two studies: (i) Wiart et al. (1997) [24], found (on the base of partial data issued from a randomized control trial) a long term (> 1 month) functional improvement on the functional independence measure (FIM) after a training programme combining trunk rotation and visual scanning solicitation (ii) Schindler et al. (2002) [18] reported, in a cross-over trial, a long-lasting improvement of reading, personal care and spatial orientation using a combined treatment – repeated neck muscle vibration stimulations and visual exploration training – compared with the standard treatment (only visual exploration training). The association of a standard visual scanning training and OPK stimulation was also followed by a beneficial effect [13]; however, the group comparison showed that OPK did not provide additional effect. Altogether, the combination of trunk rotation with visual scanning training or repeated NMV with visual scanning training appears to facilitate the recovery of patients with left neglect.

### 1.6. Prism adaptation

Recently, a promising intervention – prism adaptation – was described by Rossetti et al. (1998) [44]. This took advantage of the effect of the well known phenomenon of visuo-motor adaptation. Prism adaptation has been widely used since the end of the nineteenth century as a paradigm to demonstrate visuo-motor short-term plasticity [45]. Exposure to prisms produces a lateral shift of the visual field so that the visual target appears at a displaced position. Adaptation to such an optical induced shift critically requires a set of successive perceptual-motor pointing movements. While the initial movements tend to approximate to the virtual position of the target, subsequent pointing movements ensure that the pointing error rapidly decreases so that subjects can readily point towards the real target position [46]. This initial error reduction comprises a “strategic component” of the reaction to prisms and does not necessarily produce adaptation at this stage [47]. To obtain robust compensatory after-effects, following removal of prisms, further pointing
movements are required. These reinforce the sensory motor adaptation and are considered characteristic of the “real or true” adaptive component of the adaptation [48]. The after-effects result from a compensatory shift in manual straight-ahead pointing in a direction opposite to the original visual shift produced by prisms. Rossetti et al. [44] proposed that right prism adaptation with leftward negative after-effects (using the intact right hand) improved left neglect symptoms. A significant reduction of left neglect was demonstrated across a variety of different standard tests following a brief period (3–5 minutes) of prism adaptation [44].

There are now several articles that showed a long-lasting generalization of the effect across different measures including wheelchair navigation [10], reading [8] and spatial dysgraphia [16] after a single prism adaptation session. Furthermore, a long-lasting amelioration using the behavioural measures of the BIT was reported following a twice-daily adaptation program during a period of two weeks [9].

Hence, although relatively new, prism adaptation is an exciting method which has shown relatively long-term functional gains from comparatively short-term usage. To clearly establish the functional benefits of prism adaptation, a large-scale RCT is currently in progress.

2. Discussion and conclusion

Overall, there is now growing evidence for several clinically relevant long term benefits (4–6 weeks) for a number of treatment methods currently available. These include visual scanning training (VST), limb activation, mental imagery training, feedback training, neck muscle vibration (NMV) and Trunk rotation – if associated with VST – and prism adaptation.

From a theoretical point of view, these results give the opportunity to discuss rehabilitation-induced plastic reorganization of lesioned brain system. As previously argued, conventional methods, such as VST and feedback training, are essentially based on a top-down approach involving attentional and language processes spared by the lesion. Mental imagery training also involves the training of high level functions but in this case, the idea is to restore the impaired cognitive function. Hence, according to the model proposed by Code (2001) [49], VST and feedback training would be considered as involving a behavioural and cognitive compensatory mechanism whereas mental imagery training would be considered as involving a cognitive restorative mechanism.

The rationale underlying Limb activation is based on activating a poorly attended body schema by making voluntary initiated contra-lesional limb movements in the left side of the space which in turn activates corresponding areas of extra-personal space [50]. More generally, it can be hypothesized that rehabilitation techniques which stimulate neural circuits non-impaired but functionally connected with the lesion might favour recovery. Indeed, neuro-plasticity following brain damage could share common mechanisms with normal Hebbian learning mechanisms [51]. In this Hebbian learning connectionist model, it is argued that strengthening of synaptic connections occurs when pre and post-synaptic neurons are coactive: “cells that fire together, wire together”. Limb activation also seems to take advantage of an inter-hemispheric inhibitory process given that Robertson and North (1994) [52] showed that the beneficial effects of single left limb activation in left hemi-space could be eliminated if the right limb was simultaneously moved.

Sensory stimulations can temporarily remediate hemi-spatial neglect, including the most cognitive aspects of this condition, which provide clear evidence for a bottom-up mechanism. These interventions are also characterized by their specific directional effect both in terms of the side of the stimulation and also in terms of the side of the brain affected by the stimulation. Hence, sensory stimulations probably modulate lateralized spatial cognition processes via a bottom-up mechanism [41]. However, a functional gain was reported only when lateralized neck muscle vibration and lateralized trunk rotation were associated with classical VST [18,24]. These results tend to confirm the hypothesis proposed by Husain and Rorden [53] that it might be noteworthy to combine an intervention based on non-lateralized attentional processes and a lateralized stimulation.

Concerning prism adaptation, the specificity of the effect on left spatial neglect has been investigated in two experiments (unpublished work) [54]. In the first one, five stroke patients with left neglect were exposed to left prisms in order to assess the lateral specificity of prism adaptation. A battery of five neuropsychological tests (line bisection, line cancellation, figure copying, drawing a daisy from memory and a reading task) were performed before, immediately after adaptation and 2 hours later. Analysis of variance (ANOVA) was performed to compare the mean score of the 5 patients, on each neuropsychological test, across sessions. Con-
trary to right prism adaptation, no significant effect was observed after a single session of left prism adaptation. Hence this experiment favours a specific effect of prism adaptation on left spatial neglect in terms of the direction of prisms: only right prisms can improve neglect. Interestingly, the cognitive effects of prism, in non-brain damaged subjects, are also supported by an asymmetrical pattern of performance on line bisection judgment tasks, depending on the direction of prisms [55, 56]. Contrary to right brain damaged patients with left neglect, only adaptation to left-deviating prisms induced a rightward bias in normals. These asymmetric results may reflect the inherent asymmetry of the brain’s structural organisation related to space cognition. On the bases of these latter studies and considering that the right parietal cortex seems to be specifically involved in line bisection judgment tasks [57,58], it could be hypothesized that the right parietal lobe would be critically sensitive to prism adaptation at least for those tasks involving explicit linear judgements [56].

In the second experiment, we searched if the therapeutic effect of this technique could rely on the error signal generated by the first pointing movements performed through prisms. Five different patients with left neglect following stroke performed a series of 50 pointing movements toward visual targets whose locations was shifted to the right (10°) immediately after the onset of movement, thus reproducing the error signal produced by prismatic goggles that produce a 10° rightward shift of the visual wide-field (cf. [44]). Experimental paradigm, neuropsychological tests and statistical analysis were comparable to the first experiment. Results showed no significant difference between sessions, which argues against a role of error signal and support the hypothesis that only adaptation to rightward prisms – i.e. visuo-motor realignment – can ameliorate left spatial neglect.

Improvement of numerous neglect-related manifestations such as visual exploration toward the left hemispace [59], postural balance [60], contralesional somato-sensory perception [61–63], temporal order judgment [64], visuo-verbal tasks [8], mental representation [65–67] as well as the generalization to functional tasks [8–10,16], suggest that this low-level sensory-motor intervention modulates cortical areas in a bottom-up fashion [68].

The neural substrate underlying the therapeutic effect of this method remains to be fully elucidated. One possibility is that prism adaptation reduces left spatial neglect by facilitating the recruitment of intact brain areas responsible for controlling normal visuo-spatial output by way of short-term sensori-motor plasticity. Such an account would predict the implication of at least three brain structures: (i) the cerebellum which is known to be implicated in visually directed movements [69] and eye-hand coordination [70]. The involvement of the cerebellum is also supported by lesion-studies in both monkey [71] and man [48,72,73]. (ii) The posterior parietal cortex (PPC) is also clearly implicated in sensori-motor and multi-sensory integration [74]. Moreover, the only functional imaging study using prism adaptation in normal subjects showed that the PPC, contralateral to the hand used for adaptation was clearly activated [75]. It should be noted that in this latter study, the optical deviation was reversed (left to right) every five trials to maintain the subject in a state of on-going adaptation. This suggests that the PPC probably participates in the “strategic corrections” after visuo-motor transformation induced by prisms but not necessarily in sensori-motor realignment. Pisella et al., (2004) [76] recently confirmed this hypothesis by showing that a patient with a bilateral parietal region was fully able to adapt to an optical deviation. (iii) Finally, the ventral pre-motor cortex (PMv) seems also to be involved in short-term sensori-motor plasticity. It has been shown in monkeys that this region plays an important role in visually guided movements [77] and in spatial visual information processing [78]. Furthermore, Kurata and Hoshi (1999) [79] showed that the monkeys loose their ability to adapt to wedge prisms after muscimol injection into the PMv.

However, as indicated by Danckert and Ferber [80], the gap might be important between what we know about sensori-motor plasticity in normal subjects and what happens in brain damaged neglect patients. In a recent functional imaging study, we investigated the anatomical substrates underlying the beneficial effect of prism adaptation in five patients with left spatial neglect following right stroke [81]. We used a co-variation analysis to examine linear changes over sessions as a function of neglect improvement. The network of significant brain regions associated with improvement of left neglect performance produced by prism adaptation included the right cerebellum, left thalamus, left temporal cortex, right frontal cortex and right parietal cortex. These results suggest that prism adaptation actively modulates cerebral areas implicated in visuo-motor plasticity albeit now relying on intact cerebello-cerebral connections. This study also highlighted a potential role for the temporal cortex in neglect improvement after prism adaptation. This was not expected but the recent implication of this region in
spatial cognition could explain this activation. Indeed, it has been recently shown that the right temporal lobe is damaged significantly more often in patients with left neglect than in patients with right brain damage without neglect [82]. Moreover, recovery of spatial deficit attention seems to depend on the reactivation of this region [83].

These results also illustrate the complexity to investigate how a given intervention can modulate brain plasticity in the domain of neurological rehabilitation. From the perspective of functional imaging techniques, plasticity can be defined as the reorganization of distributed brain activity that accompanies an intervention. Hence, the first step is to know the neural network associated with this intervention in normal subjects. Then, in these intervention studies, the post effect session is by definition the second session. Therefore an order effect cannot be ruled out in a classical factorial design comparing brain activity before and after the intervention. To get around this irrelevant order effect, a covariation analysis has to be performed to search for specific brain areas associated with the beneficial effect of the intervention. Finally, spontaneous recovery must be taken into account by appropriate designs using for instance multiple baseline assessment of the condition.

The combined knowledge of brain lesion location and the network of brain areas activated by an intervention could serve to choose more appropriately rehabilitation techniques for a given patient. Moreover, these informations could serve to enhance the recovery of spatial neglect by “theory-driven” combination of several interventions. Following this idea, the combination of a classical VST program and prism adaptation could represent a good example given that the first one is a top down intervention involving language and memory processes whereas the other is a bottom-up intervention involving sensory-motor plasticity. Alternatively, it is possible that combining two methods which share a common network of activation enhances the beneficial effect. The association of prism adaptation and limb activation is in line with this hypothesis. Indeed, both methods depend on active motor procedures and highlight the role of action in neglect rehabilitation [84].

References


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