Prism adaptation in the rehabilitation of patients with visuo-spatial cognitive disorders

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Purpose of review

The traditional focus of neurorehabilitaion has been on the patients' attention on their deficit, such that they should become aware of their problems and gain intentional control of compensatory strategies (descending approach). We review prism adaptation as one of the approaches that emphasize ascending rather than descending strategies to the rehabilitation of visuo-spatial disorders. The clinical outcome of prism adaptation highlights the need for a theoretical reconsideration of some previous stances to neurological rehabilitation.

Recent findings

Recent years have given rise to a growing body of experimental studies showing that the descending strategy is not always optimal, especially when higher-level cognition is affected by the patients' condition. Ascending approaches have, for example, used visuo-manual adaptation for the rehabilitation of visuo-spatial deficits. A simple task of pointing to visual targets while wearing prismatic goggles can produce remarkable improvements of various aspects of unilateral neglect.

Summary

The neural mechanisms underpinning visuo-manual plasticity can be viewed as a powerful rehabilitation tool that produces straightforward effects not only on visual and motor parameters, but on visuo-spatial, attentional and higher cognitive neurological functions. The use of prism adaptation therapy in neglect and other visuo-spatial disorders has just started to reveal its potential, both at a practical and theoretical level.

Keywords

neglect, prism adaptation, rehabilitation, visuo-spatial

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Abbreviation

PPC posterior parietal cortex

1350-7540

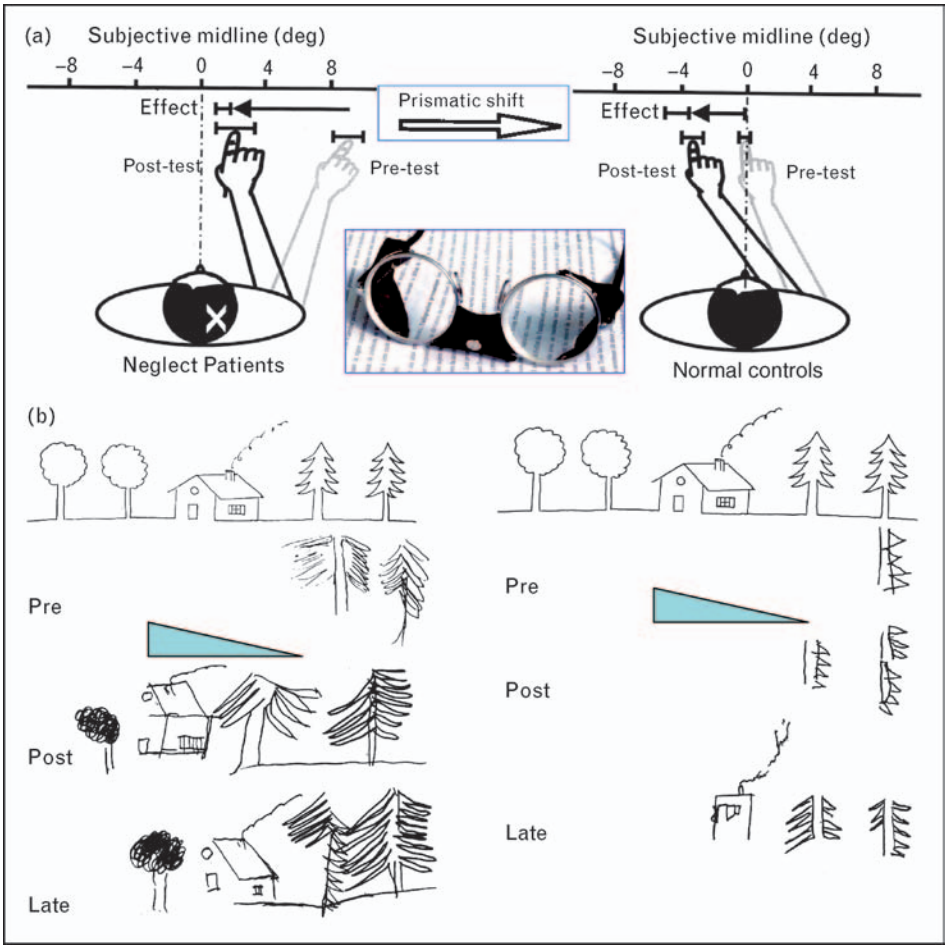
Introduction

A large proportion of right-hemisphere stroke patients show unilateral neglect. This is a multifaceted neurological deficit potentially affecting perception, attention, representation and/or motor control within their left-sided space [1–3,4•], as well as the right-sided hemispace [5•,6,7], inducing many functionally debilitating effects on everyday life, and is responsible for poor functional recovery and ability to benefit from treatment [8–10].

The various manifestations of unilateral neglect share one major feature – patients remain unaware of the deficits they exhibit or at least fail to fully consciously attend to these deficits. This lack of awareness is dramatically expressed in anosognosia and hemiasomatognosia [1]. It is therefore astonishing that the first methods proposed for neglect rehabilitation were mainly based on leftward voluntary orienting of attention. This paradox was already underlined by Diller and Weinberg ([11], p. 67): 'The first step in the treatment of hemi-inattention is to make the patient aware of the problem. This is particularly difficult in hemi-inattention since this failure in awareness appears to be at the heart of the patient's difficulty'. It may indeed appear paradoxical to base a rehabilitation procedure on awareness and intention in patients with a deficit in consciousness. Accordingly, these techniques have produced significant results, but are clearly exposed to several limitations, i.e. the voluntary monitoring of attention is restricted to a specific context and does not apply as soon as more automatic control is required.

To act on higher-level cognition in such a way as to bypass the impaired conscious awareness and intention one should, at least in principle, find another entry route to space representation systems. Rubens [12] pioneered such an ascending alternative, both theoretically and experimentally, by providing preliminary support to the prediction made by Jeannerod and Biguer [13]: a unilateral lesion would produce an illusory displacement

Figure 1 Prism adaptation in neglect



(a) Neglect patients adapt more than normals. In the pre-adaptive test, neglect patients exhibit a manual straight-ahead demonstration shifted to the right with respect to normals. In the post-test, they reveal larger after-effects (redrawn from [15]). (b) Two examples of pre, immediate post and late (+2 h) performance of copy drawing.

of the egocentric reference, somewhat as if the subject felt being constantly rotated toward the lesion side. Rubens reported that vestibular stimulation, obtained by pouring cold water into the neglect patient's left ear, instantly produced a dramatic, although transient improvement of neglect.

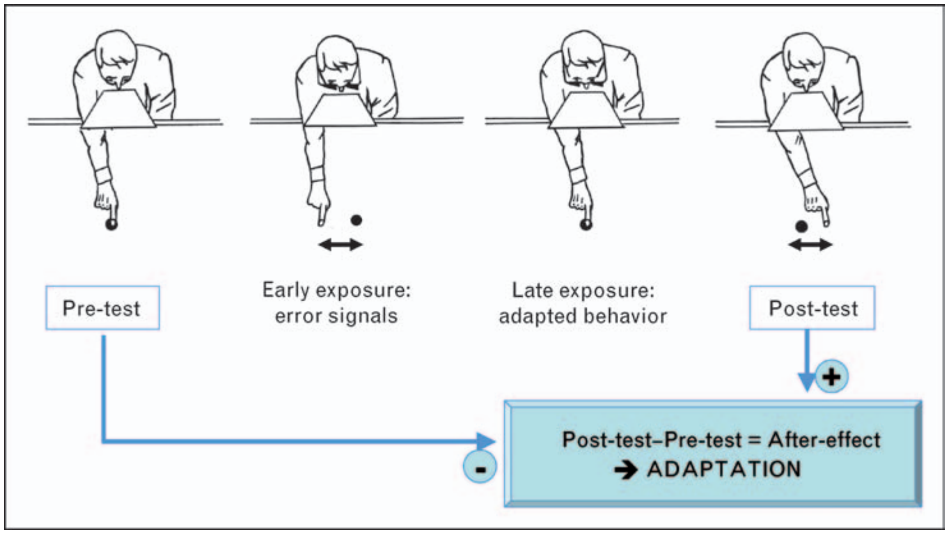
Cognitive effects of prism adaptation

Both approaches to neglect rehabilitation have, however, important limitations either in terms of absence of generalization (descending approach) or in terms of very limited duration (ascending approach) of the beneficial effects. It was therefore a challenge to develop a strategy to combine the advantages of the two approaches and to propose a technique that, bypassing the awareness level, could also promote long-lasting effects. Adaptation to wedge prisms is a simple way of producing low-level, automatic modifications of visuo-motor correspondences, demonstrated by the presence of measurable after-effects after the prism-exposure phase (Fig. 1a). In contrast to more complex visual reorganization requiring extended exposure [14], adaptation to wedge prisms has long been known to quickly develop over the course of a 5-min simple pointing session. Despite over 100 years of studies, only visuo-motor after-effects had been described until the discovery that prism adaptation can improve higher cognitive deficits such as unilateral neglect [15] (Fig. 1b).

The principles of prism adaptation

When someone first looks through wedge prisms that optically displace the visual field, e.g. 10° in the rightward direction, he/she may have little feeling that anything is out of the ordinary, until he/she experiences extraordinary difficulty in perceptual-motor tasks (i.e. direct effects of prism exposure). For example, pointing toward a visual target produces an error to the right of the target position. First, a relatively abrupt reduction of the lateral

Figure 2 Prism adaptation procedure



A proper prism adaptation session should include three periods: pre-tests, prism exposure and post-tests. During the early phase of the exposure, error reduction (mainly accounted for by the strategic component) does not imply that prism adaptation is already effective. The post and pre-tests, optimally performed with nonexposed targets, are used to compute the amount of after-effect, i.e. proper adaptation.

error can be observed due to a strategic component of adaptation. Then, a more gradual reduction of the terminal error is observed, returning to pre-exposure levels as the person makes repeated attempts at target pointing. Whereas the strategic component is at work only over a short period of time [16], the true adaptation to the prismatic displacement (or realignment) develops more gradually and is more purely expressed during the subsequent slow phase of error reduction. When the prisms are removed the person experiences unforeseen errors in the opposite direction, to the left of the target! This negative after-effect of prism exposure demonstrates persistence of the adaptation acquired during exposure. In most of our studies sham goggles were (and should be) used to control for the spurious effects due to directional visuo-motor activity. They were made of two pairs of 5° prisms producing opposite shifts, i.e. a total shift of 0° (same weight and same opacity as the 10° prisms). The real and sham prisms were fitted into glacier goggles (Cébé) in order to prevent any access to unshifted vision (Optique Peter, Lyon, France; www.optiquepeter.com). Vision of the starting hand position is usually occluded to ensure the optimal development of the adaptation [17]. A pointing task without visual feedback (open loop) is performed before and after the adaptation procedure to evaluate the development of a visuo-manual adaptation to the visual shift.

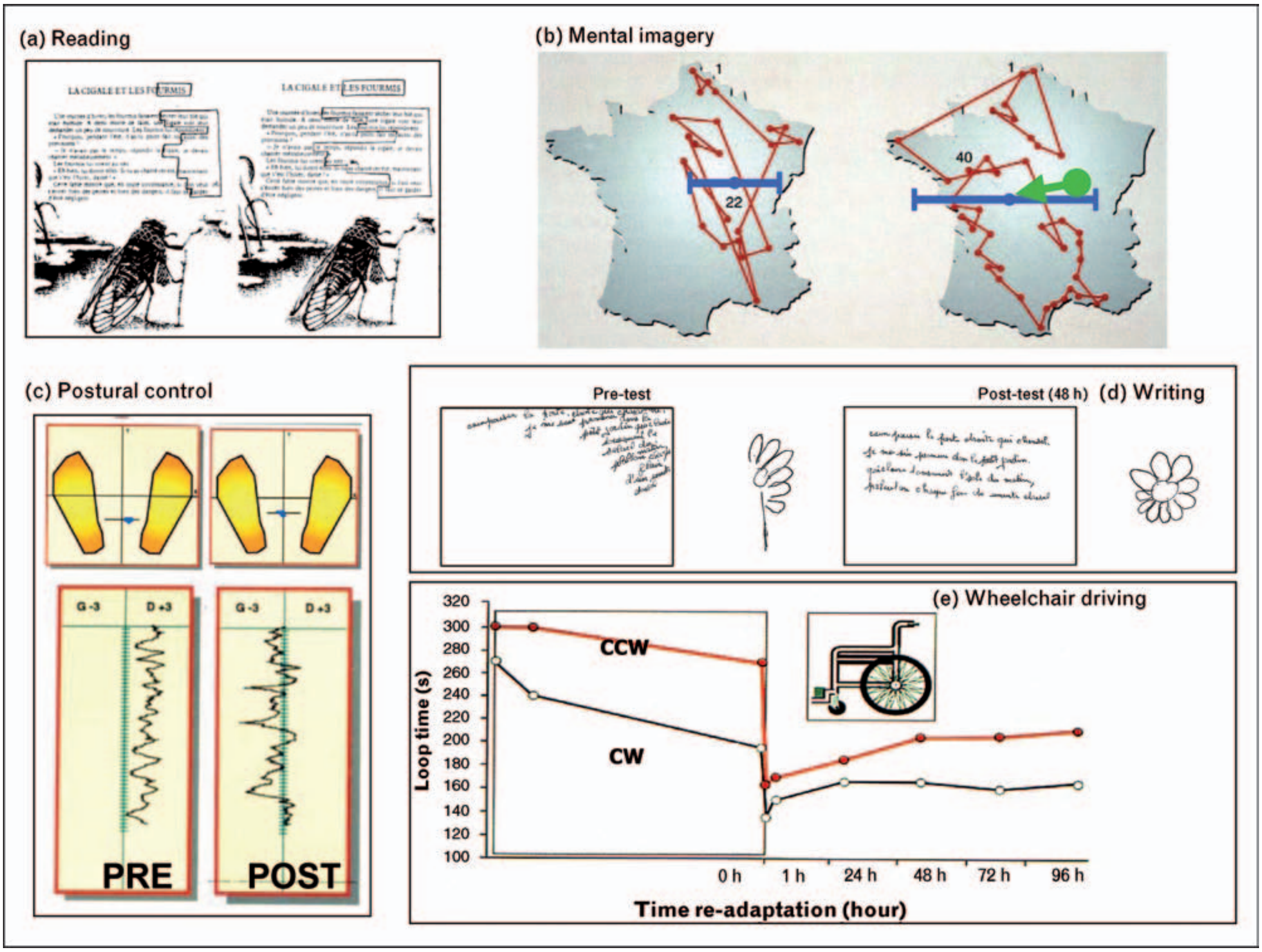
Thus, the basic prism adaptation procedure simply involves (1) pre-exposure baseline measurement of pointing performance, (2) active exposure to prismatic displacement to produce adaptation and (3) post-exposure after-effect measurement of adaptation persistence (Fig. 2). Is this all there is to prism adaptation? Prism adaptation may misleadingly appear simple when compared to the profound effects it can exert on spatial cognition.

Generalization

Logically, the effects of prism adaptation should be restricted to, or at least be best for, visuo-motor tasks, because they share more common features with the visuo-manual adaptation procedure. In our original study, we observed the best improvement for the Schenkenberg line bisection test (6/6 patients markedly improved), whereas the weakest improvement was obtained for text reading (2/6 patients markedly improved) [15]. Many of the therapeutic effects described since actually involved a visual or a manual component, which may be directly affected by the visuo-manual adaptation procedure [18]. It was therefore of prime interest to investigate the possibility that prism adaptation could also improve symptoms of unilateral neglect that may not be directly affected by the adaptation (Fig. 3) and numerous other neglect symptoms were therefore investigated (reviewed in [19–21]).

The level of space representation assessed by mental imagery tasks, for example, clearly differs from the sensory-motor level that is directly involved in the prism adaptation procedure. Rode *et al.* [22,23] explored the effect of prism adaptation on visual imagery and found clear-cut improvements in neglect patients who initially could not evoke city names on the western half of an

Figure 3 A variety of therapeutic effects



(a) Reading performance before and after prism adaptation. The delineated area depicts the area that was correctly read by the patient. (b) Mental imagery task performed before and after prism adaptation. The patient was asked to imagine the map of France and then to name as many cities he could see on this internal map. The mental path followed the lines from 1 to the total number of cities. The dot and whiskers indicate the average location and horizontal extent of this internal scanning (redrawn from [22]). (c) Postural control before and after prism adaptation. The sagittal position of the centre of mass was recorded for 50 s (redrawn from [32]). (d) Writing under dictation before and after prism adaptation. The patient performance is shown together with his daisy drawing from memory (from [71•]). (e) Wheelchair driving before and after prism adaptation. Clockwise and, more markedly, counter-clockwise directions of driving were improved by prism adaptation (from [31•]).

internally generated map of France. This result strongly suggests that the after-effects of visuo-manual adaptation are not restricted to visual and motor parameters. In the same vein, Farnè *et al.* [24] compared the effects of prism adaptation in six neglect patients on both (1) visuo-motor tasks, such as line and bell cancellation, and two subtests taken from the Behavioral Inattention Test (letter cancellation and line bisection) battery, and (2) visuo-verbal tasks (the visual scanning test, also taken from the Behavioral Inattention Test, requiring a verbal description of the objects depicted on a colored picture, an object-naming task with 30 Snodgrass pictures of familiar objects intermingled with geometric shapes as distractors, word and nonword reading). They observed that both types of tasks followed a parallel improvement, which lasted for at least 24 h.

The fact that different tasks based upon other sensory modalities can be improved (haptic circle centering [25–27]) and that several nonmanual tasks (postural control, wheelchair driving, imagery, verbal reports) were also improved, demonstrates that the effects of prism adaptation on visuo-spatial defective abilities go well beyond the visuo-manual parameters usually affected in normal subjects. Recently, Berberovic *et al.* [28] have shown that even a nonspatial and nonmanual aspect of neglect could be improved, i.e. temporal order judgment.

Furthermore, we recently described beneficial effects of prism adaptation on a new feature of unilateral neglect reported by Zorzi *et al.* [29]. They introduced a mental number bisection test, whereby patients have to verbally indicate the middle between two numbers (e.g. between

11 and 19) and found a bias towards larger numbers in neglect patients, as if their 'mental number line' was distorted (similar to what classically occurs in line bisection). Even for this abstract task, we found that prism adaptation strongly improved the bisecting bias [30]. Overall, these results make clear that adaptation to wedge prisms affects a core component of unilateral neglect's complex spatial deficits.

Although generalization beyond purely visuo-motor tasks is crucial for any putative rehabilitation technique, the plasticity triggered by prism adaptation also produces effects on nontrained tasks in the motor domain, such as wheelchair driving [31•] and postural control [32]. Such effects are presumably mediated via spatial cognition levels. In addition, the intentional component of neglect deficits can also be improved by prism adaptation [18,33]. In this case, patients were asked to reach and grasp a centrally located ball, and then to throw it into a left or right-sided basket. The kinematics of the centrally directed reach-to-grasp movements showed that neglect patients are overall slower when the secondary movement is directed to the left [33]. After a short prism adaptation session, this asymmetry was modified for several movement parameters (reaction time, movement time, peak velocity, time to peak velocity). The pattern of result observed immediately after prism adaptation even showed the reverse pattern – reach movements were slower when the ball had to be thrown to the right. Therefore, the intentional control of action can be modified as well by prism adaptation.

Still at a motor level, there are several qualitative observations that prism adaptation can improve the motor behavior of patients in everyday life [25]. One of the crucial questions raised by the observation of a strong and sustained improvement of unilateral neglect by a single short adaptation session is whether this plastic effect is restricted to the acute phase of the deficit. In our original study patients were tested between 3 weeks and 14 months poststroke [15]. We have now collected data on a group of patients who were exposed to the adaptation procedure between 5 and 28 years poststroke, and amazingly found comparable amounts of improvement [20,21].

Duration

Retention over time is another crucial feature of any rehabilitation method. The effects of a single prism adaptation session (for repeated sessions, see below) last much longer (at least 2 h) than for any other sensory stimulations (about 15 min) reported to date. A group of patients showed a sustained improvement 24 h after the training session [24], but individual cases may exhibit even longer-lasting amelioration of neglect, now demonstrated to last up to about 1 week (e.g. [25,34]). An interesting feature of prism adaptation is that its cognitive beneficial effects, although often present immediately after adaptation, seem to develop over short periods of time thereafter, thus lagging somewhat behind the lower-level after-effects. Indeed, delayed cognitive effects (i.e. 2–4 h after prism adaptation) tend to be stronger then immediate ones (measured just after prism adaptation) even in chronic patients [15,35•]. Although prism adaptation has long been thought to give rise to short-lasting after-effects in healthy subjects, recent investigations showed that the unaware mode of prism exposure can give rise to astonishingly stronger after-effects [36•,37]. As suggested below, a strong clinical interest of prism adaptation may be found in the repetition of adaptation sessions.

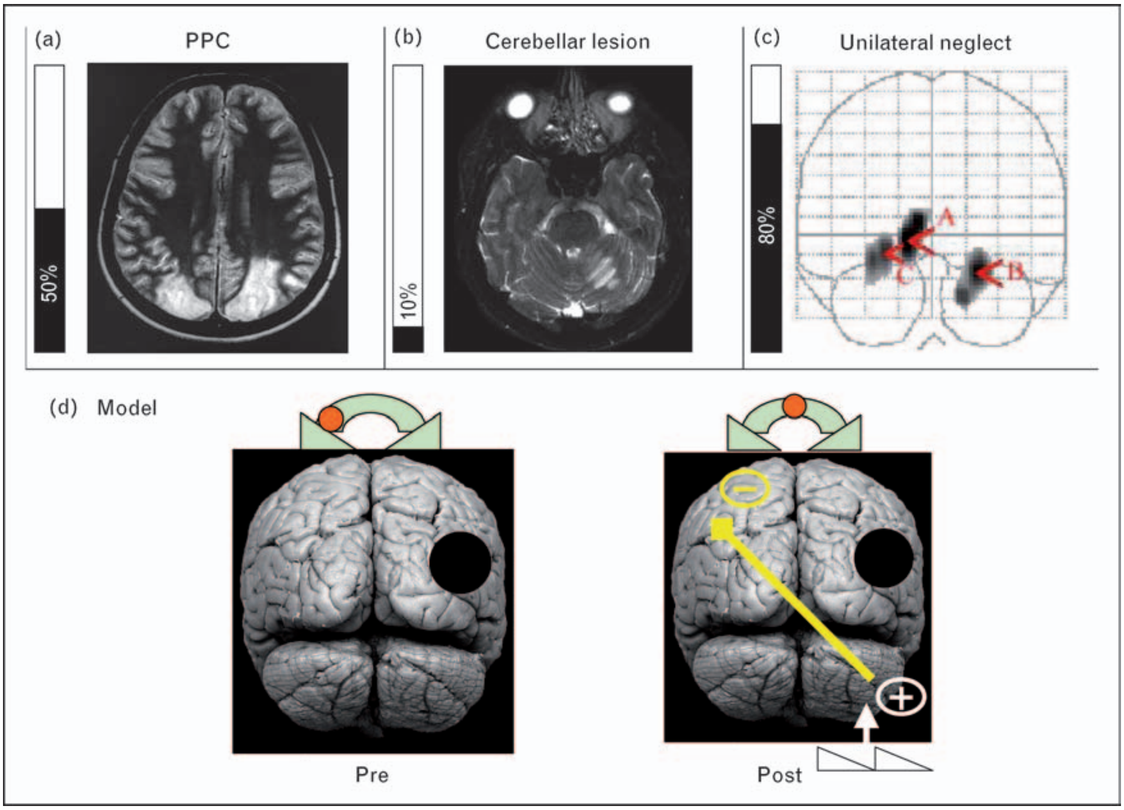
Anatomo-functional hypothesis

The literature is somewhat controversial about the neural structures involved in prism adaptation. On the one hand, neuropsychological evidence historically suggested that only cerebellar patients are impaired in prism adaptation (e.g. [38], reviewed in [39]). On the other hand, recent imaging data [40] have suggested that the human posterior parietal cortex (PPC) contralateral to the adapted arm is the only area activated during prism exposure.

More recently, we established that the superior parietal lobule, which when damaged leads to impairment of visuo-manual guidance (optic ataxia), is not crucially involved in visuo-manual prism adaptation [41]. The clinical effect of prism adaptation on visual neglect also precludes that the inferior parietal lobule, at least in the right hemisphere, could be crucial for adaptation to right-ward prisms. Rather, neglect patients exhibit 'hyper-adaptation', characterized by more robust and durable after-effects [15,24,25,32,34,42]. A bilateral optic ataxia patient also demonstrated a larger inter-manual transfer, highlighting the cerebellum as the most likely neural substrate of true adaptation, although the PPC may also contribute to the strategic component. We therefore proposed a simple model [41] in which the cerebellum and the PPC are, respectively, specialized for the adaptive and strategic components of prism adaptation (Fig. 4): if the lesion of the PPC reduces the strategic component, adaptation would consequently be mostly achieved by realignment processes (true adaptive component); hence, it would more likely be stronger, longer-lasting and having more potential to generalize. Accordingly, neglect patients do not notice the alteration resulting from the optical deviation and normal subjects exhibit larger adaptive after-effects when the prismatic deviation is not noticeable [36•,43].

In a patient with a cerebellar lesion (including the superior part of the dentate nucleus and mostly the anterior lobe of the left cerebellar hemisphere) we

Figure 4 An anatomo-functional model



(a) A patient with a bilateral posterior parietal cortex (PPC) lesion has been shown to produce normal after-effects [41]. (b) Lesion of the right cerebellum impairs adaptation to right-shifting prisms, independent of the arm used [44•]. (c) Positron emission tomography showed that both right cerebellum and left hemisphere structures exhibited a blood flow increase correlated with neglect score improvement [48•]. In (a–c) the amount of adaptation found in these patients is indicated in black on the vertical bar and should be compared with a normal after-effect ranging from about 30–50%. (d) According to the interhemispheric balance framework, neglect patients exhibit a bias to the left side ('Pre'). We speculate that prism adaptation acts at the cerebellar level and indirectly interferes with the left hemisphere, such that the balance is improved or restored ('Post').

found adaptation to be limited to a rightward (not leftward) prism deviation, independent of the hand used during exposure [44•]. This observation led us to confirm the crucial involvement of the cerebellum in prism adaptation, and to propose a lateralized model for prism adaptation and its beneficial effect on spatial cognition. The pattern of impairment of this patient suggested a visual lateralization within the cerebellum with the involvement of the cerebellar hemisphere ipsilateral to the prismatic deviation in the processing of visual errors, in addition to the well-known motor lateralization that involves mainly the cerebellar hemisphere contralateral to the hand for the modification of the visuo-motor correspondences [45]. To our knowledge, only one other anatomo-functional study has compared, in monkeys, adaptation to right and left prismatic deviations [46]. In this study, deficit in adaptation was observed after inactivation of the ventral premotor cortical area only when vision was shifted contralaterally to the inactivated ventral premotor cortical area. Since connections between the cerebellum and the cerebral cortex are crossed [47], this makes a consistent cerebro-cerebellar lateralized network for the computation and integration of directional visual error in prism adaptation. The implication of such a lateralized cerebello-cerebral network in the functional anatomy of the therapeutic effects of prism adaptation on neglect has been recently confirmed by functional neuroimaging in neglect patients [48•] showing that the right cerebellar hemisphere and the right dentate nucleus were both significantly activated in the positive covariation analysis between the prism adaptation-induced changes in regional cerebral blood flow and in neuropsychological performance (assessed by the Behavioral Inattention Test). The activation of the left temporal cortex also appeared to covariate positively with the left spatial neglect improvement [48•].

Altogether, anatomical and behavioral data suggest that the clinical effect of prism adaptation on neglect relies on a network of brain areas where the visual error-signal generated by right prisms is initially processed in the left occipital cortex. The information is then transferred to the right cerebellum where the visuo-motor realignment (i.e. 'true adaptation') takes place in congruence with the rightward deviation of prisms. The clinical effect could be mediated through the modulation of cerebral areas in the left hemisphere via a bottom-up signal generated by the cerebellum [20,44•,49]. Notably, the temporal cortex, the frontal cortex and the PPC have been shown to be targets of output from the cerebellum via a neuronal loop also implicating the dentate nucleus and subcortical structures, such as the thalamus and the globus pallidus [50–52]. The clinical effect might therefore be mediated by the recruitment of pathways in the left hemisphere that are functionally homologous to those involved in spatial cognition in the damaged hemisphere.

Reciprocally, the cognitive effects of prism adaptation found in healthy subjects [53–55], demonstrated by an asymmetrical pattern of performance on several spatial tasks, are strictly dependent upon the direction of the prismatic shift [49]. On the basis of the latter studies and considering that the right parietal cortex seems to be specifically involved in line bisection judgment tasks [56–57], we hypothesized that the function of the right parietal lobe would be inhibited by inputs from the left cerebellar cortex, coherent with the use of the leftward prismatic deviation, and create 'neglect-like' symptoms [58•].

In principle, the proposed model is compatible with the involvement of the prism adaptation-induced realignment of the oculomotor system that, by reducing the rightward scanning bias, may facilitate exploration of the left neglected side of space [59,60,61•]. Several dissociations have, however, been documented between oculomotor change and the amelioration of visuo-spatial behavioral performances [62,63]. Another proposal is that adaptation acts through plastic modification of the integration of proprioceptive and visual information, which would be particularly beneficial in neglect patients whose symptoms result in part from an impaired visual-motor mapping of space (see [64]). One could speculate that prism adaptation permits an enlargement of this visual-motor mapping of space not only on the left side, but also on the right side, as suggested by the improvement of constructional apraxia [21] and spatial dysgraphia following prism adaptation. Recent findings mainly point to the need for appropriately applying prism exposure conditions and quantification [18], for evaluating the role played by the type of prism adaptation (strategic vs. realignment; [59,60]), as well as the sufficient amount of adaptation (as measured in terms of after-effect) required to produce consistent neglect improvement [65]. There is still the need to build up a coherent framework integrating one century of prism adaptation investigations with the recent body of patient literature [66]. An interesting issue also remains to identify domain-specific aspects of neglect, such as chimeric face perception, which seem even intractable by prism adaptation [35•,63,67].

Conclusion

Adaptation to prismatic displacement is particularly suited for clinical application [38] because its incremental nature permits examination over relatively short time periods, in contrast to prismatic distortions like left–right or up–down reversal of the visual field that require extended exposure for adaptation to occur [68]. The efficacy of single-session prism adaptation has proven to generalize the improvement to several neglect symptoms. Several non-motor as well as motor aspects of the neglect syndrome, such as motor neglect and/or extinction, might actually benefit from prism adaptation as well. It can be considered the most-promising rehabilitation method for unilateral neglect to date [4•,69], especially in light of the fact that spontaneous recovery from neglect is very limited [70]. We wish to put forward that prism adaptation might improve spatial-cognition deficits in neglect as well as in other pathologies. Constructional deficits, dysgraphia [71•], as well as spatial attention distortions contributing not only to neglect [22,72,42], but also to other pathological manifestations affecting spatial and bodily representations [73] (e.g. Complex Regional Pain Syndrome [74,75]), are on the list of candidates for this bottom-up rehabilitation track. In spite of these possibilities, it is now clear that not all neglect patients can benefit from prism adaptation and not to the same extent. Unfortunately, to our knowledge, only one randomized controlled trial has been performed to date [21]. In addition, several important questions still await definitive answers: why is adaptation quantitatively more important and lasts longer in patients vs. healthy controls, why it affects higher-order cognitive domains, why it is direction-specific and what are the predictors of prism adaptation clinical efficacy? Beyond prism adaptation in and of itself, it is also promising to consider that other original bottom-up approaches may prove to be more effective on cognitive disorders than the traditional top-down stance.

The practical clinical potential of repetitive-session prism adaptation procedures has just begun to be explored. Frassinetti *et al.* [76] reported that a group of patients who benefited from two prism adaptation sessions daily over 2 weeks (a total of 10 sessions) exhibited an improvement that lasted over 5 weeks after the end of the treatment. A daily prism adaptation session has been reported to improve neglect up to 3 months after treatment [60]. Long-standing chronic neglect (11 years) has also been demonstrated to improve with repetitive prism adaptation sessions [35•]. Using the neck vibration technique and visual-scanning training in a rigorous cross-over design, Schindler *et al.* [77] also explored the effects of repetitive sessions, and found a sustained improvement following an intensive daily programme. Obviously, such rigorous studies should be systematically undertaken to determine the optimal training frequency and duration, as well as the optimal combination of techniques that can be used routinely for rehabilitation [78].

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•• of outstanding interest
Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 619–620).

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