Through a Prism Darkly: Re-evaluating Prisms and Neglect

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Through a prism darkly: re-evaluating prisms and neglect.

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Abstract:

Many studies have demonstrated that prism adaptation can reduce several symptoms of visual neglect, a disorder in which patients fail to respond to information in contralesional space. The dominant framework to explain these effects suggests that prisms influence higher order visuospatial processes by acting on brain circuits controlling spatial attention and perception. However, studies that have directly examined the influence of prisms on perceptual biases inherent to neglect have revealed very few beneficial effects. We propose an alternative explanation whereby many of the beneficial effects of prisms arise via the influence of adaptation on circuits in the dorsal visual stream controlling attention and visuomotor behaviours and suggest that prisms have little influence on the pervasive perceptual biases that characterize neglect.

Prism adaptation and visual neglect.

Lesions to the right temporo-parietal cortex typically result in neglect, a disorder in which patients fail to respond to information in contralesional (left) space [1, 2]. In severe cases, neglect patients act as if the left half of their world has simply ceased to exist. It is now widely accepted that neglect is a complex, heterogeneous disorder which includes both spatially lateralized ([i.e., attentional and exploratory motor biases 3, 4]) and non-lateralized ([e.g.., sustained temporal attention, spatial working memory, and temporal perception 5, 6-8]) deficits. Thus, the clinical presentation of neglect varies greatly with respect to both the presence and severity of symptoms [9].

One technique that has recently become widely used to treat neglect patients is prism adaptation. When neurologically healthy participants wear prisms that shift their vision in one direction (e.g., 10° to the right) they will initially mis-reach in the direction of the prismatic shift (e.g., to the right) when they attempt to pick up or point to an object. However, after a few attempts, participants quickly learn to reach in the opposite direction (i.e., to the left) to compensate for the shift in vision. If this training continues over a number of trials, then, when the prisms are removed, participants will mis-reach in the direction opposite the prismatic shift (i.e., the after-effect). This reflects the fact that the motor system has recalibrated the reference frames for the eye and hand in order to bring them back into alignment [10]. A decade ago Rossetti and colleagues [11] published a remarkable study in which they demonstrated that adaptation to rightward shifting prisms produced dramatic, and in some cases, long-lasting remediation of many neglect symptoms (Box 1). Specifically, following adaptation, patients' performance on traditional tests of neglect (i.e., line bisection, cancellation, figure copying) significantly improved.

Since this original study there have been numerous demonstrations of similar beneficial effects on a multitude of different tasks (Table 1). Specifically, studies have demonstrated that prisms influence postural balance [12], visual imagery [13], tactile extinction [14], neglect dyslexia [15], oculomotor biases [16-19], visuospatial attention [20-23], and even wheelchair navigation [24]. In addition, further studies revealed that leftward prisms (i.e., the direction opposite that used for patients) induce ‘neglect-like’ behaviour in healthy individuals [25-29]. Taken together, these results have been used to argue in favour of the idea that, rather than simply producing a basic visuomotor realignment, prisms influence higher order visual cognition [for reviews see 10, 30].

--Insert Box 1 here—

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Here we argue that this evidence needs to be critically re-assessed in light of recent randomized control trials which indicate that prisms have no long-term beneficial effects in neglect [31, 32]. In addition, although several studies have shown that prisms improve attention and other tasks tied to motor behaviours, very few studies have been able to demonstrate robust effects on perceptual aspects of neglect. We put forward an alternative explanation which suggests that prisms influence attention and motor related circuits in the dorsal posterior parietal cortex (PPC), but have relatively little influence on perceptual aspects of neglect which are likely mediated by higher order perceptual areas in ventral-temporal cortex. Ultimately, this hypothesis suggests that prisms will primarily influence processes inherently linked to attentional and visuomotor circuits in the dorsal visual stream (e.g., clinical tests of neglect, simple target detection), but will have much less influence on tasks which require more explicit perceptual judgments and thus rely heavily on the ventral stream (e.g., perceptual biases, spatial working memory, time perception, etc).

Are prisms really a cure for neglect?

Given the multitude of studies demonstrating a wide variety of changes to behaviour in neglect patients post-adaptation (Table 1), it seems reasonable to conclude that prisms dramatically reduce neglect symptoms. However, some recent randomized control trials (the industry standard for determining the clinical efficacy of treatments) have failed to find any clear long-term beneficial effects of prisms [31, 32]. These null results raise important questions regarding the generalizability of the effects of prisms in neglect found with single case or small group studies, and may well reflect the heterogeneity of functions tested in these studies. That is, if, as we are suggesting, prisms influence dorsal streams functions (e.g., attention, visuomotor control) more so than ventral stream functions (e.g., perceptual biases) then the measures included in a study of prism adaptation are of vital importance.

There are two important aspects that are often overlooked when interpreting studies of prism adaptation in neglect. First, in many instances, studies (including some of our own) involve only single cases or small groups of patients. This is not to say that single cases have no value (we would strongly argue to the contrary), but that, just as the neglect syndrome is heterogeneous and highly variable in presentation, the influence of prisms on neglect may also be heterogeneous and variable across patients. Thus, while prisms might have a dramatic effect in one patient, they may have little or no effect in others. This could, in fact, explain why larger controlled trials fail to observe clear effects at the group level.

Another important point, often overlooked in these studies, is that in many cases the patient is asked to respond with the very same hand they used to adapt to prisms. In a sense then, it is perhaps not surprising that prism adaptation can influence line bisection, cancellation, or figure copying, when the adapted hand is being used. Specifically, if the hand adapts leftward to compensate for the rightward shift in vision induced by prisms, then the performance of tasks carried out with the adapted hand (i.e., traditional tests of neglect) will also shift leftward following adaptation (Box 1).

Some authors have argued that the absence of any correlation between the shift in proprioceptive straight-ahead judgments following adaptation and the beneficial effects of prisms on performance implies that the observed after-effects must occur by influencing higher level spatial cognition, and not simply as a direct consequence of adaptation [15]. However, one recent study which examined a larger group of patients [33] observed a strong correlation between subjective straight-ahead judgments following adaptation (the most commonly used procedure to measure adaptation; Box 1) and improvements in performance on clinical tests of neglect. That is, neglect patients who demonstrated a larger leftward shift in subjective straight-ahead judgments also demonstrated significantly greater improvements on traditional tests of neglect. Thus, improvements in performance on the traditional tests of neglect can (and do) arise as a direct consequence of the adaptation procedure used. Unfortunately, many studies which have evaluated the effects of prisms on neglect have largely (or exclusively) used these traditional paper-and-pencil measures of neglect (most notably the Behavioural Inattention Test).

When 'seeing' is not believing: The influence of prisms on attention and perception in neglect.

In order to overcome the limitations of using traditional tests to measure the effects of prisms on neglect, some studies have examined the influence of prisms on well known cognitive paradigms that measure attention and perception more directly. For example, a series of recent studies have examined the influence of prisms on attention in neglect with two important implications. First, it seems clear that prisms can influence covert shifts of visual attention (i.e., shifting attention without moving the eyes) [20-23] and extinction (i.e., failing to report contralesional stimuli or events when they are presented simultaneously with ipsilesional stimuli)[14]. In addition, a recent study by Bultitide and colleagues [35] found that prisms could even reverse the local processing bias in patients with right brain damage such that they were better able to "disengage" attention from local elements and "engage" attention on global elements in the display. Presumably this resulted from increased activity in undamaged regions of the right hemisphere that normally attend to global elements [36] following adaptation. However, previous work has failed to observe any significant effect of prisms on serial visual search tasks which measure attention in what could be considered a more "real-world" scenario [37].

In addition to the conflicting data regarding the effects of prisms on covert attention and visual search, several studies have demonstrated a dissociation between the influence of prisms on motor behaviours (e.g., eye or arm movements) and perceptual abilities [16, 19, 38]. Exploratory eye movements made by neglect patients are typically restricted to the right (non-neglected) side of stimuli with perceptual judgments also heavily biased by information presented on the right. Remarkably, however, two studies have shown that even though patients who had undergone adaptation now directed many more eye movements to the left (previously neglected) side of stimuli, they continued to show a strong right-sided bias in perceptual judgments [16, 19]. That is, it was as if the patients were looking at, but not 'seeing' information in their neglected field (Box 2; [for other work demonstrating an influence of prisms on oculomotor biases see 17, 18]).

In a recent study [38], we examined the relationship between the influence of prisms on motor and perceptual abilities more directly by asking neglect patients (and healthy controls) to manually bisect lines in their centre (using a pen held with the adapted hand), or to make perceptual judgments about pre-bisected lines ([i.e., "is the bisection mark closer to the left or right end of the line" 39]), prior to and following prism adaptation (Box 2). The results indicated, as predicted, that prisms had a dramatic influence on manual bisection (using the adapted hand) such that it effectively eliminated the bisection error in these patients. In contrast, prisms had no effect whatsoever on perceptual judgments when patients were asked to judge whether the pre-bisection mark was closer to the right or left end of the line. That is, patients continued to insist that the pre-bisection mark was closer to the left end of the line indicating that they perceived the left end of the line to be shorter than the right.

In summary, several studies have highlighted the fact that there appears to be a striking dissociation between the influence of prisms on tasks which influence motor behaviors that share many of the neural networks also involved in adaptation, and those that require a purely perceptual judgment.

--Insert Box 2 here--

Potential inconsistencies.

Although there is a good deal of evidence to suggest that prisms influence primarily attention and motor behaviours in patients with neglect, there are a few studies which appear, at first glance, to be inconsistent with our central hypothesis. Specifically, in contrast to the absence of any effects of prisms on visual search performance reported by Morris and colleagues, [37] a recent study by Saevarsson and colleagues [40] suggests that visual search performance may improve following adaptation. However, this study used an unspeeded colour 'pop-out' search which measures pre-attentive mechanisms and not search per se [41]. In addition, patients detected 85% of left sided stimuli prior to adaptation suggesting that they had only mild impairments to begin with. While these effects are certainly interesting, they may simply indicate that if patients have enough time and the task is easy enough, they may eventually show some limited benefits from prisms.

In addition, one could argue that perceptual bias tasks may simply not be sensitive enough to detect changes post prism adaptation. However, several studies in healthy individuals using the very same tasks have shown that these tasks are, in fact, sensitive enough to index changes in behaviour post adaptation [25, 38, 42]. Given that the after-effects in neglect patients are typically much larger than those in controls (Box 1), it is all the more surprising that no effects of prisms have been observed in these tasks.

Furthermore, in contrast with the dissociation we observed between performance on the landmark and manual bisection tasks (Box 2), a study by Sarri and colleagues [43] observed that prisms reduced neglect for the left sides of chimeric objects (i.e., one object comprised of halves of two different objects) but not chimeric faces (similar to those used by Ferber and colleagues [19]). However, in this study the chimeric objects task was much easier than the chimeric faces task. For example, one of the chimeric objects was comprised of the front half of a zebra and the rear half of an ant. In contrast, the chimeric faces task required patients to make decisions regarding the emotional expression depicted on two halves of the same face. In short, detecting that an object was made of two completely different animals was much easier than detecting that two halves of the same face were depicting different emotions. Again, it may be the case that for relatively simple tasks, with unlimited time, it is possible to demonstrate limited benefits of prisms on perception (Box 2).

Finally, our central hypothesis that prisms have limited effects on perception in neglect patients may seem to be contradicted by studies which have demonstrated improvements in mental imagery post prisms [13, 44]. However, it is important to note that patients with severe damage to object recognition areas in the ventral-temporal cortex also continue to make use of mental imagery effectively [45]. Thus, "perceptual" areas are not necessarily required for imagery. Another reason these data are not convincing is that both studies used images that patients were highly familiar with prior to the onset of neglect (i.e., a map of France, a mental number line), making it very likely that they "mentally scanned" these previously learned images. Thus, any benefits of prisms in these instances may simply reflect changes in eye movements evoked by adaptation. [46]. That is, prisms led to a shift in oculomotor behaviours that in turn proved critical for the effects of prisms on mental imagery tasks.

Prism adaptation and the dorsal and ventral streams: A new look forward.

The key question raised by the dissociations presented above is how one can reconcile the beneficial effects of prisms on tasks which measure covert attention or overt motor responses on the one hand, with the failure of prisms to influence many perceptual biases on the other. One way to answer this important question is to examine the brain regions involved in adapting to prisms and how these same regions might be important for creating beneficial after-effects. Unfortunately, relatively little work has directly examined the neural correlates of adapting to prismatic shifts. Nevertheless, this work has shown prominent involvement of the right cerebellum and left PPC [PPC; 47, 48]. In addition, a recent study in non-human primates shows direct pathways from regions of the cerebellum to the anterior intraparietal sulcus [49], a region of the PPC that is active during prism adaptation [48, 50]. Although even less has been done to explore the neural correlates of the after-effects of prisms [51], it seems reasonable to assume that many of the regions involved in adaptation may also be involved in the beneficial after-effects.

We suggest that the influence of prisms in neglect can best be understood in terms of its effects on the dorsal and ventral streams of visual processing, which mediate ‘vision for action’ and ‘vision for perception’ respectively [52]. We propose that prisms influence patients with neglect by acting on circuits in the superior parietal lobe (SPL) and intraparietal sulcus (IPS) in the dorsal stream which are known to control visually guided motor behaviours (eye and arm movements) and visual attention [for reviews see 52, 53]. Importantly, these regions are undamaged in many neglect patients [54], as the critical lesion site for neglect tends to involve the inferior parietal lobe and superior temporal gyrus of the right hemisphere [55, 56]. This notion is supported by imaging [51, 57] and patient studies [33, 58] which have implicated the SPL/IPS in the beneficial after-effects induced by prisms. That is, imaging studies have linked activity in the SPL/IPS with the beneficial effects of prisms in patients with neglect, and patients with lesions in these regions do not show the normal benefits from prisms. The critical role of the SPL/IPS in recovery from neglect following prism adaptation is further supported by an elegant fMRI study [59] which linked changes in BOLD activity in the SPL/IPS with the spontaneous recovery from neglect.

Thus, we believe that prism adaptation influences neglect symptoms by directly influencing circuits in the dorsal stream that are known to be related to normal neglect recovery. Interestingly, it is not yet clear whether the left SPL/IPS or the right SPL/IPS is critical for generating the beneficial after-effects of prisms. We suggest that the beneficial effects of prisms are likely to rely on the SPL/IPS in both the left and right hemispheres (Figure 1). Specifically, during rightward prism adaptation, leftward realignment signals are generated in the right cerebellum [60, 61]. These leftward realignment signals are then transferred to the dorsal stream in the contralateral (left) hemisphere via connections with the dentate nucleus in the cerebellum [62] – a link that has recently been demonstrated in healthy individuals using fMRI [48]. A recent review of mainly functional neuroimaging data suggests that the SPL in each hemisphere is largely responsible for contralateral orienting behaviours, either overtly (e.g., eye and hand) or covertly ([e.g., shifts of attention; 53]). Homotopic callosal connections between each hemisphere's SPL would enable the leftward realignment signals processed in the left SPL to be transmitted to the right SPL which is normally responsible for orienting leftwards. This final connection would enable patients to orient attention towards previously neglected space via the influence of prisms on eye and arm movements, without any significant influence on perception.

In other words, if the after-effects of prisms are largely dependent on the SPL in either hemisphere, then any beneficial effects would likely be limited to those behaviours normally carried out by the dorsal visual pathway (e.g., attention and visuomotor behaviours). In contrast, the failure of prisms to have any clear influence on perception in neglect may result from the fact that the critical lesion site in neglect (i.e., the inferior parietal lobe and superior temporal gyrus) represents a multimodal association area thought to be important for linking visual information in the ventral stream with motor outputs in the dorsal stream [52, 63]. Without this link it is unlikely that there will be any major changes to the pervasive perceptual biases evident in neglect following prism adaptation.

--insert Figure 1 about here--

Concluding remarks and future directions

We have argued that the reduction in some neglect symptoms following prism adaptation stems from the influence of adaptation on circuits in the dorsal stream that normally control attention, as well as visually guided eye and arm movements. However, a lesion in the inferior parietal lobe and/or superior temporal gyrus – the critical lesion site for neglect and a region essential for integrating information between the dorsal and ventral streams – effectively prevents any major influence of prisms on perceptual abilities. Such influence would depend upon effective communication between the dorsal stream – where we postulate the beneficial after-effects are generated – and the ventral stream, which is specialized for perceptual processing. It is this disconnection which, we argue, is at the heart of the dissociation between the beneficial effects of prisms on attention and visuomotor abilities on the one hand, and the much more limited influence of prisms on perceptual biases on the other.

It is important to note that we are not suggesting that prisms have no beneficial effects in patients with neglect, nor are we suggesting that prisms never have an influence on perception. Our contention is that the beneficial effects of prisms may be largely limited to circuits in the dorsal visual stream that control spatial attention and motor behaviours. While the work examining the effects of prisms on perception versus motor behaviours is still in its infancy, we feel that it provides a novel (and useful) framework to characterize the effects of prisms in patients with neglect, and generates a number of interesting hypotheses for future research examining the link between visuomotor adaptation, attention, and visual awareness.

Specifically, further research is needed to determine the extent to which prism adaptation influences attention and action, but not perception in neglect. For example, visual search (i.e., serial but not 'pop-out' search) performance measured in conjunction with eye movements pre- and post-adaptation will presumably indicate instances in which the eyes fixate a target but no response is made. Although we suggest that prisms will typically fail to improve this dissociation between perception and action, any circumstances under which it is reduced by prisms will highlight conditions necessary for improving perception.

Furthermore, contrasting performance for attentional orienting tasks which require detection vs. discrimination may also highlight the limits of prism adaptation. To date, all studies examining the effect of prisms on attention in neglect have examined only detection [20, 22, 23]. Our hypothesis suggests that patients should benefit most when they are asked to detect a target, but should demonstrate relatively little improvement when they are asked to make a speeded discrimination between different targets or distinct perceptual characteristics within a target.

Although a great deal of research has examined the influence of prisms on spatial biases in neglect, almost no research has addressed the extent to which prisms might influence other non-spatially lateralized components of neglect such spatial working memory (which has been shown to be impaired for vertically aligned targets in central and right space; [6, 7]), sustained temporal attention [8], or time perception [5]. If prisms primarily influence spatial attention and exploratory motor biases then they should have little influence on these deficits that are not inherently linked to spatial attention or motor effectors.

We suggest that the dorsal stream is critical for generating the beneficial after-effects of prisms. This does not preclude, however, that other areas may also be involved in generating beneficial after-effects. For example, it is well known that the PPC is highly interconnected with the frontal eye fields (FEF), an area known to be involved in overt and covert shifts of attention [53]. Perhaps the after-effects of prisms also influence processing in other areas that are connected with the dorsal stream.

There are a number of different methods one can use to adapt people to prisms. Two commonly used methods are concurrent exposure (i.e., with view of the target and the reaching limb) and terminal exposure (i.e., only the fingertip and the target are visible at the end of the reach). Although beneficial effects of prisms (and null effects) have been reported using both procedures, it will be important for future research to identify potentially more powerful and immersive methods of adaptation that may result in even greater effects of prisms in neglect.

Finally, given that changes in performance on traditional assessments of neglect can arise as a direct consequence of adaptation [33], future randomized control trials aimed at assessing the influence of prisms on neglect should also include measures that assess alterations in perception that do not rely on responding with the adapted hand. This will aid in our understanding of how neglect symptoms change following adaptation over and above any influence on the motor effectors used during adaptation.

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The authors have no conflicts of interest to declare.

Boxes

Box 1: Prism adaptation and neglect.

In their original study, Rossetti and colleagues [11] blindfolded neglect patients and asked them to point straight-ahead of their body midline. Many of the patients pointed to the right of true centre, presumably because their egocentric reference frame had been shifted rightward (Box 1 Figure A). During adaptation patients wore goggles that shifted vision 10° to the right (i.e., further into the non-neglected field). While wearing the prisms they were asked to point to targets located to the left and right of their body midline. Initial pointing movements were biased rightwards due to the visual shift induced by the prisms (i.e., the direct effects of prisms). However, after a few trials, patients adjusted their pointing movements leftwards to accurately acquire the targets. After approximately 5 minutes of pointing, the prisms were removed and the patients were blindfolded again and asked to point straight-ahead. Amazingly, following prism adaptation their subjective straight-ahead judgments had shifted significantly leftward, closer to true centre (i.e., the after-effect of prisms; Box 1 Figure A). Presumably, because patients had to learn to point leftward to compensate for the rightward shift in vision, their judgments of straight-ahead also shifted significantly leftward. Even more surprising were the effects that prism adaptation had on clinical tests of neglect. Specifically, prism adaptation improved performance on manual line bisection (Box 1 Figure B), cancellation (Box 1 Figure C), and figure copying. These data provided the impetus for a great number of subsequent studies that have examined the effects of prism adaptation on neglect symptoms.

Another remarkable aspect of prism adaptation in neglect patients is the abnormally larger after-effects that typically arise. Part of the reason that the after-effects are so much larger in neglect patients may stem from the fact that many of these patients are unaware of the mis-alignment caused by the prismatic shift. If patients are unaware of the mis-alignment then presumably realignment is achieved using mainly adaptive, but not strategic (e.g., “point further leftward on the next trial”) aspects of adaptation [10]. Previous work has shown that abnormally large after-effects can occur in the absence of “strategic” control [64]. Thus, the primary deficit in neglect – a loss of visual awareness – may in fact be the reason why prism adaptation has such remarkable effects in these patients.

--Insert Box 1 Figure here—

Box 2: Prism adaptation and perceptual biases in neglect.
Neglect is considered a disorder of spatial attention with low-level perception left unscathed [65]. It is possible to demonstrate, however, that neglect patients have strong perceptual biases such that the right half of stimuli are preferentially responded to. When presented with chimeric faces – faces smiling on one half and neutral on the other – neglect patients report that faces smiling on the right appear to be ‘happier’ [66], in stark contrast to healthy individuals who choose the left-smiling face as appearing happier. Similarly, when presented with two dark-light gradients (i.e., the ‘greyscales’ task; [66]) and asked which is ‘darker’, neglect patients report that the gradient that is dark in right space appears darkest – again, in contrast to healthy individuals. It is clear from this work that neglect patients demonstrate strong perceptual biases favouring right-sided stimuli (Box 2 Figure A).

We examined the influence of prisms on chimeric faces in one patient [19] and showed that while eye movements explored the left side of faces post prisms, the rightward bias for happiness judgments was unaltered. Although this work was criticized on the grounds that faces are special (i.e., Sarri and colleagues [43] showed improved responding to chimeric objects but not faces), others have shown similar dissociations for non-face stimuli [16]. Using a size distortion task in which patients judge which of two rectangles is wider (Box 2 Figure A), they showed that post prisms, eye movements shifted towards left space despite no change in the perceptual bias for (erroneously) reporting that the right stimulus was wider than the left [16]. In addition, although Sarri and colleagues [67] recently demonstrated that 3/6 neglect patients improved at detecting whether or not a face was chimeric following adaptation; these patients were explicitly ‘coached’ in the sense that they were told that the faces could be chimeric, and what details to look for.

Finally, we compared performance on the line bisection and landmark tasks in three neglect patients after prisms [38]. The landmark task requires patients to report which end of a line is closest to a prebisection mark (Box 2 Figure B) [39]. Responding ‘left’ most often indicates the patient perceives the left end to be shorter than the right. Again, prisms improved line bisection performance but failed to alter biases on the landmark task (Box 2 Figure B). Similarly, Sarri and colleagues [67] found that the rightward bias on the greyscales task was unaltered by prisms. It seems clear to us that strong rightward perceptual biases in neglect are not altered by prisms even when motor behaviours show a dramatic leftward shift.

Table 1: A summary of the effects of prisms in neglect.

Outcome measures:	Number of patients:	Main result:	Reference:
Line bisection (LB), cancellation (C), figure copying (FC), drawing from memory (DM)	6 (prisms) 6 (sham)	Beneficial effects on all measures.	[11]
DM, mental imagery	2	Improved drawing, improved recall of towns on left of imagined map of France.	[13]
LB	2	Dissociation between successful adaptation and no change in LB in one patient and vice versa in the other.	[68]
Behavioural Inattention Test (BIT), fluff test, reading, room description	7 (prisms) 6 (no prisms)	Patients adapted twice a day, five days/week for two weeks. Beneficial effect on BIT, reading and room description lasting up to 5 weeks post final exposure	[69]
C, LB, visual scanning, object naming, reading	6	Improved performance on all tasks up to 24 hours after adaptation.	[15]
C, LB, FC, haptic exploration, reading	1	Three adaptation sessions over three weeks. Improved LB and C and reduction in rightward errors for haptic exploration.	[70]
C, chimeric faces, eye movements	1	Eye movements shifted leftward post prisms but perceptual bias unchanged (see Box 3).	[19]
Size estimation	3	Eye movements shifted towards left of objects, but perceptual judgments unchanged (see Box 3).	[16]
Temporal order judgment.	5	50% reduction in rightward TOJ bias (i.e., left stimulus precedes right by ~400ms pre-prisms before being detected as coming first and by ~200 ms post prisms).	[21]
Mental number line	2	Reduced mental number line bias (i.e., bias to choose a number to the right of the midpoint of an interval (i.e., 5 as the midpoint between 1-7).	[44]
Reading, eye movements	8 (prisms) 5 (sham)	Neglect dyslexia reduced.	[17]

Outcome measures:	Number of patients:	Main result:	Reference:
Touch pressure sensitivity, passive finger position sense	1	Increased pressure sensitivity and finger position sense for contralesional (left) limb.	[71]
Visual search	4	No influence on visual search.	[37]
BIT, reading, eye movements, lesion analysis	16 (prisms) 8 (no prisms)	Patients underwent 10 adaptation sessions over 2 weeks. Improved neglect dyslexia and BIT scores. The reduction in oculomotor bias correlated with improvements on BIT scores. Patients with occipital lesions did not benefit.	[18]
LB, C, FC, reading	10 (prisms, sham)	No effects of prisms on any measures.	[72]
LB, Drawing from memory, handwriting	Single case	Improvements in drawing accuracy, LB. Patient's handwriting was no longer restricted to the right side of the page.	[73]
Chimeric faces and objects	3 (prisms)	Improvements for chimeric objects but not chimeric faces (Box 2).	[43]
BIT, landmark task, positron emission tomography (PET)	5 (prisms)	Improvements in C but not LB, FC, or landmark task. Improvements in C related to increased activity in left temporo-occipital cortex and decreased activity in right SPL.	[51]
Line cancellation	9 (prisms)	Improvements in cancellation, decrease in perseverative errors	[74]
C, LB, obstacle avoidance	4 (prisms)	Improvements in all measures.	[75]
C, LB, reading, chimeric faces, grasping	Single case	Long-term improvements on C, LB, grasping, no effects on reading or chimeric faces.	[76]
Reflexive covert attention	4 (prisms)	Faster leftward reorienting, reduction in rightward attentional bias.	[23]

Outcome measures:	Number of patients:	Main result:	Reference:
BIT, C, reading, room description, eye movements, fluff test, tactile extinction, proprioception, motricity index	21 (prisms)	10 adaptation sessions over 2 weeks. Improvements in all measures except proprioception and motricity. Improvements apparent for 6 months post adaptation.	[77]
Subjective straight-ahead (SSA) and visual straight ahead (VSA) pointing, C	13 (prisms)	Larger effect on SSA compared to VSA. Beneficial effects on C correlated with SSA. Patients with right IPS showed no benefit.	[33]
Reflexive covert attention	Single case	Patient with bilateral SPL/IPS lesions adapted to prisms, but had no beneficial effects on reflexive covert attention.	[58]
Voluntary and reflexive covert attention	2 (prisms, sham)	Influence on voluntary but not reflexive orienting (Box 2).	[22]
C, LB, Wheel chair driving	Single case	Improvements in all measures.	[24]
C, LB, FC	10 (prisms) 6 (sham)	Randomized placebo control design. No long-term improvement on any measures relative to sham prisms group.	[31]
Eye movements, center of mass, SPECT imaging	7 (prisms)	Adaptation (four 50-min sessions/week for 8weeks) involved ball throwing, ring-toss, peg-board. Improvements in leftward eye movements and leftward shift in center of mass. SPECT revealed activation in left SPL following prisms.	[57]
Within vs. between object covert attention	20 (10 neglect, prisms, sham)	Faster leftward reorienting for between-object shifts of attention.	[20]

Outcome measures:	Number of patients:	Main result:	Reference:
C	Single case	Reduced left sided omissions but perseverative responses merely shifted from the right to the left side.	[78]
LB, C, FC, ‘pop-out’ visual search, BIT	4 (prisms) Exp. 1 4 (prisms) Exp. 2	Improvement in LB, C, FC, increase in accuracy for left sided targets in pop out search.	[40]
BIT	10 (prisms) 10 (sham)	10 adaptation sessions over 2 weeks. Significant effects on BIT scores in both prisms and sham groups. Larger improvement in prisms group.	[79]
Global/local interference	5 (prisms)	Prisms reversed the local processing bias.	[35]
BIT, self care	16 (prisms) 18 (sham)	Randomized control trial. Adapted each day for two weeks. No effects on BIT or self care (note: used 6° rather than 10° right prisms).	[32]
Greyscales, chimeric faces	11 (prisms)	Prism adaptation increased chimeric face detection in 3/6 patients, but had no effect on perceptual biases for chimeric emotional faces or greyscales.	[67]

F**igure captions (main text):**

Figure 1: A neuro-anatomical model of the beneficial effects of prisms in neglect. This figure depicts a hypothetical lesion to the right temporo-parietal cortex leading to left visual neglect and rightward spatial (i.e., attentional and exploratory motor) biases. 1. During rightward prism adaptation (top panel) leftward realignment signals (dotted red arrows) are generated in the right cerebellum and are transferred (2. solid red arrow) to the left superior parietal lobe (SPL) and intraparietal sulcus (IPS). 3. The beneficial after-effects of prisms (lower panel) are thought to emerge when the leftward realignment signals from the left SPL/IPS are transferred through homotopic callosal connections (red arrow) to undamaged regions of the right SPL/IPS that are important for attending, and directing actions, towards left space. This then leads to a leftward shift in spatial biases (yellow arrow).

Box Figure Captions:

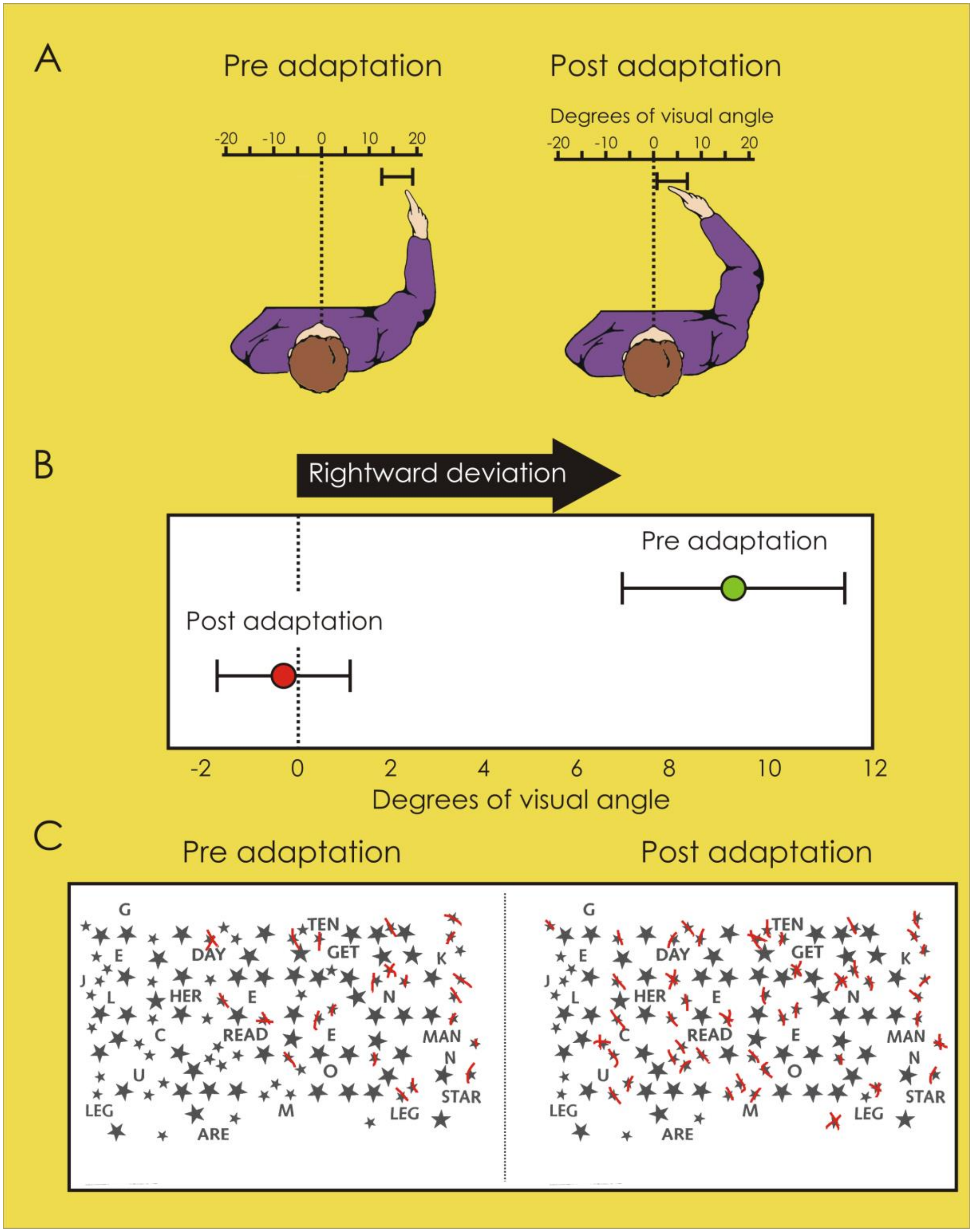
Box 1: The effects of prism adaptation on neglect symptoms.

A) The after-effect of the prism adaptation procedure. Prior to adaptation neglect patients' subjective judgments of straight-ahead (without vision) are typically biased rightward (left panel). Immediately following rightward prism adaptation their judgments of straight ahead are shifted significantly leftward, closer to true midline (right panel). **B)** Prior to adaptation patients bisect lines far to the right of their true centre. Following adaptation the patients' bisection mark is shifted leftward, closer to true centre. **C)** Prior to adaptation patients fail to cancel out many targets on the left side of cancellation tasks. Again, following adaptation, patients now begin to cancel out many more targets on the left side.

Box 2: The influence of prisms on perceptual biases.

Panel A depicts examples of tasks used to demonstrate perceptual biases in neglect patients. Left is a representation of the chimeric faces task in which two vertically aligned chimerics are presented, one smiling on the left, the other on the right. Patients indicate which appears happier with healthy controls showing a strong bias (~70% of trials) for the face shown smiling on the left, whereas patients prefer the face shown smiling on the right. In the middle is a depiction of the greyscales task in which two horizontal light-dark gradients are presented one above the other with patients asked to indicate which one appears to be darker (typically they choose the gradient that is darkest in right space; the upper gradient in the example given). The right schematic shows the size-distortion task in which two horizontally aligned rectangles are presented and patients are asked to indicate which one appears to be wider, typically choosing the right one even when the two rectangles are of the same size (as in the current example). Panel B shows data from our recent study [38] comparing line bisection and landmark performance pre and post adaptation (schematics for the tasks are presented above the data) in three neglect patients. On the left, prisms clearly improve line bisection performance which was to the right of true centre prior to prisms and veridical (i.e., not different from true centre) after prisms. In contrast (to the right), performance on the landmark task was unaltered with patients indicating that the left end of the line was closest to the prebisection mark on around 97% of trials before and after prisms.

Box 1 Figure.


A
Pre adaptation
Post adaptation
Degrees of visual angle
-20 -10 0 10 20
-20 -10 0 10 20
B
Rightward deviation
Pre adaptation
Post adaptation
-2 0 2 4 6 8 10 12
Degrees of visual angle
C
Pre adaptation
Post adaptation

Box 2 Figure.

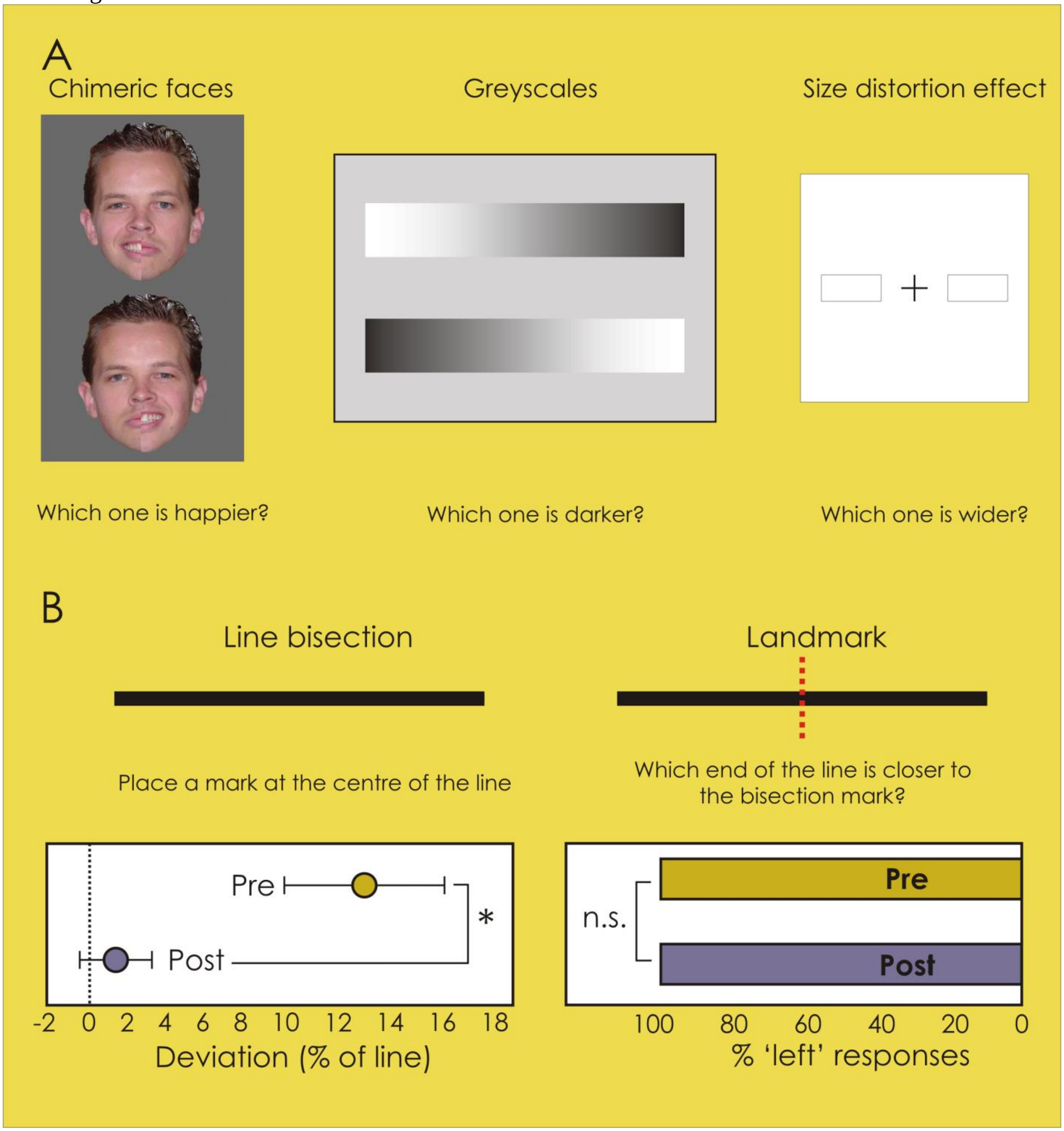
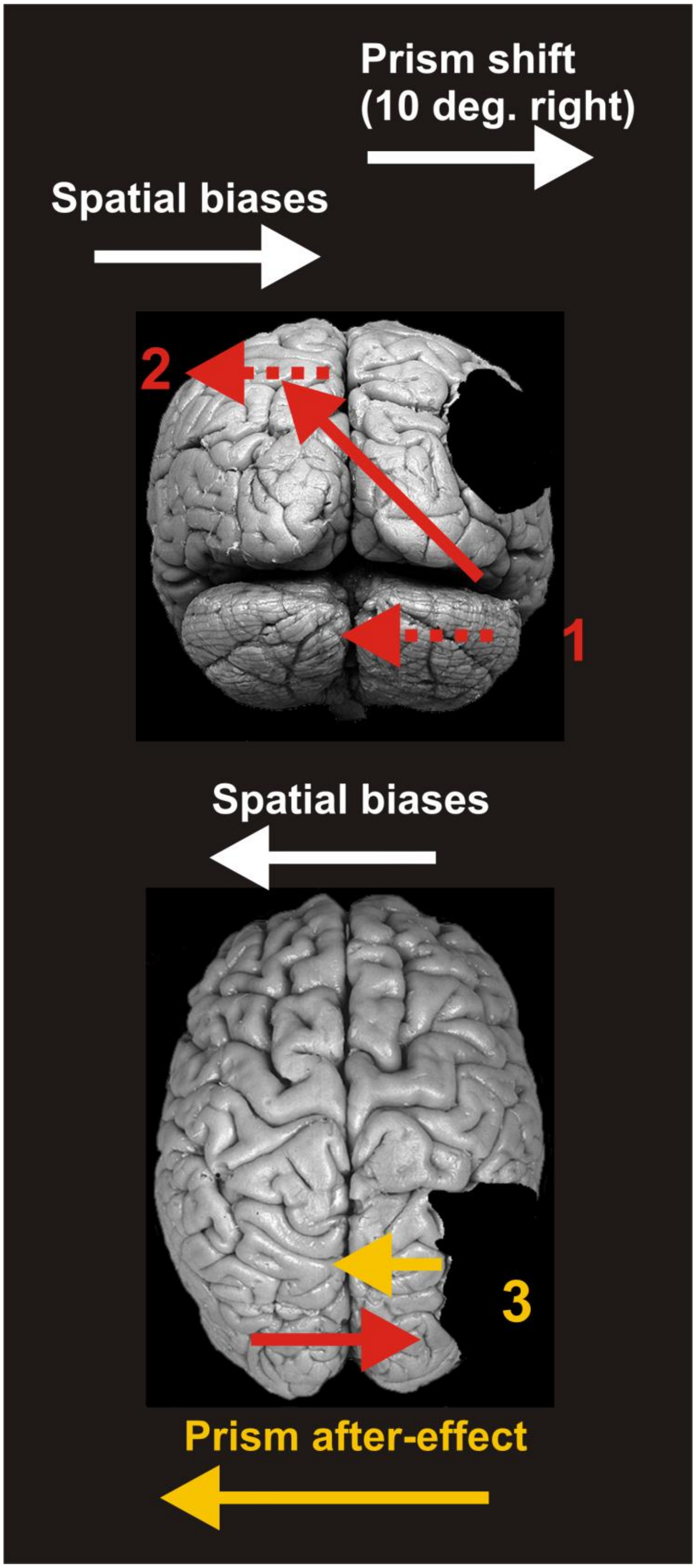

A
Chimeric faces
Greyscales
Size distortion effect
Which one is happier?
Which one is darker?
Which one is wider?
B
Line bisection
Landmark
Place a mark at the centre of the line
Which end of the line is closer to the bisection mark?
Pre
Post
*
-2 0 2 4 6 8 10 12 14 16 18
Deviation (% of line)
n.s.
Pre
Post
100 80 60 40 20 0
% 'left' responses

Figure 1.


Prism shift
(10 deg. right)
Spatial biases
2
1
Spatial biases
3
Prism after-effect

References

1 Husain, M., and Rorden, C. (2003) Non-spatially lateralized mechanisms in hemispatial neglect. *Nat Rev Neurosci* 4, 26-36
2 Danckert, J., and Ferber, S. (2006) Revisiting unilateral neglect. *Neuropsychologia* 44, 987-1006
3 Bartolomeo, P., and Chokron, S. (2002) Orienting of attention in left unilateral neglect. *Neurosci Biobehav Rev* 26, 217-234
4 Karnath, H.O., *et al.* (1998) Space exploration in neglect. *Brain* 121 (Pt 12), 2357-2367
5 Danckert, J., *et al.* (2007) Neglected time: impaired temporal perception of multisecond intervals in unilateral neglect. *J Cogn Neurosci* 19, 1706-1720
6 Ferber, S., and Danckert, J. (2006) Lost in space--the fate of memory representations for non-neglected stimuli. *Neuropsychologia* 44, 320-325
7 Husain, M., *et al.* (2001) Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. *Brain* 124, 941-952
8 Husain, M., *et al.* (1997) Abnormal temporal dynamics of visual attention in spatial neglect patients. *Nature* 385, 154-156
9 Robertson, I.H., and Halligan, P.W. (1999) *Spatial neglect: A clinical handbook for diagnosis and treatment*. Psychology Press Ltd.
10 Redding, G.M., and Wallace, B. (2006) Prism adaptation and unilateral neglect: review and analysis. *Neuropsychologia* 44, 1-20
11 Rossetti, Y., *et al.* (1998) Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature* 395, 166-169
12 Tilikete, C., *et al.* (2001) Prism adaptation to rightward optical deviation improves postural imbalance in left-hemiparetic patients. *Curr Biol* 11, 524-528
13 Rode, G., *et al.* (2001) Prism adaptation improves representational neglect. *Neuropsychologia* 39, 1250-1254
14 Maravita, A., *et al.* (2003) Prism adaptation can improve contralesional tactile perception in neglect. *Neurology* 60, 1829-1831
15 Farné, A., *et al.* (2002) Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures. *Neuropsychologia* 40, 718-729
16 Dijkerman, H.C., *et al.* (2003) Ocular scanning and perceptual size distortion in hemispatial neglect: effects of prism adaptation and sequential stimulus presentation. *Exp Brain Res* 153, 220-230
17 Angeli, V., *et al.* (2004) Recovery of oculo-motor bias in neglect patients after prism adaptation. *Neuropsychologia* 42, 1223-1234
18 Serino, A., *et al.* (2006) Mechanisms underlying neglect recovery after prism adaptation. *Neuropsychologia* 44, 1068-1078
19 Ferber, S., *et al.* (2003) Eye movements tell only half the story. *Neurology* 60, 1826-1829
20 Schindler, I., *et al.* (2009) The disengage deficit in hemispatial neglect is restricted to between-object shifts and is abolished by prism adaptation. *Exp Brain Res* 192, 499-510

21 Berberovic, N., *et al.* (2004) Prismatic adaptation reduces biased temporal order judgements in spatial neglect. *Neuroreport* 15, 1199-1204
22 Nijboer, T.C., *et al.* (2008) Prism adaptation improves voluntary but not automatic orienting in neglect. *Neuroreport* 19, 293-298
23 Striemer, C., and Danckert, J. (2007) Prism adaptation reduces the disengage deficit in right brain damage patients. *Neuroreport* 18, 99-103
24 Jacquin-Courtois, S., *et al.* (2008) Wheel-chair driving improvement following visuo-manual prism adaptation. *Cortex* 44, 90-96
25 Colent, C., *et al.* (2000) Cognitive bias induced by visuo-motor adaptation to prisms: a simulation of unilateral neglect in normal individuals? *Neuroreport* 11, 1899-1902
26 Girardi, M., *et al.* (2004) Sensorimotor effects on central space representation: prism adaptation influences haptic and visual representations in normal subjects. *Neuropsychologia* 42, 1477-1487
27 Michel, C. (2006) Simulating unilateral neglect in normals: Myth or reality? *Restorative Neurology and Neuroscience* 24, 419-430
28 Michel, C., *et al.* (2003) Simulating unilateral neglect in normals using prism adaptation: implications for theory. *Neuropsychologia* 41, 25-39
29 Michel, C., *et al.* (2003) After-effects of visuo-manual adaptation to prisms on body posture in normal subjects. *Exp Brain Res* 148, 219-226
30 Pisella, L., *et al.* (2006) Prism adaptation in the rehabilitation of patients with visuo-spatial cognitive disorders. *Curr Opin Neurol* 19, 534-542
31 Nys, G.M., *et al.* (2008) Acute neglect rehabilitation using repetitive prism adaptation: a randomized placebo-controlled trial. *Restor Neurol Neurosci* 26, 1-12
32 Turton, A.J., *et al.* (2009) A single blinded randomised controlled pilot trial of prism adaptation for improving self-care in stroke patients with neglect. *Neuropsychol Rehabil*, 1-17
33 Sarri, M., *et al.* (2008) Prism adaptation aftereffects in stroke patients with spatial neglect: Pathological effects on subjective straight ahead but not visual open-loop pointing. *Neuropsychologia* 46, 1069-1080
34 Striemer, C., *et al.* (2007) Deficits in peripheral visual attention in patients with optic ataxia. *Neuroreport* 18, 1171-1175
35 Bultitude, J.H., *et al.* (2009) Prism adaptation reverses the local processing bias in patients with right temporo-parietal junction lesions. *Brain* 132, 1669-1677
36 Robertson, L.C., *et al.* (1988) Effects of lesions of temporal-parietal junction on perceptual and attentional processing in humans. *J Neurosci* 8, 3757-3769
37 Morris, A.P., *et al.* (2004) Prism adaptation and spatial attention: a study of visual search in normals and patients with unilateral neglect. *Cortex* 40, 703-721
38 Striemer, C.L., and Danckert, J. (in press) Dissociating perceptual and motor effects of prism adaptation in spatial neglect. *Neuroreport*
39 Milner, A.D., *et al.* (1993) Line bisection errors in visual neglect: misguided action or size distortion? *Neuropsychologia* 31, 39-49
40 Saevarsson, S., *et al.* (2009) Prism adaptation improves visual search in hemispatial neglect. *Neuropsychologia* 47, 717-725
41 Wolfe, J.M., and Horowitz, T.S. (2004) What attributes guide the deployment of visual attention and how do they do it? *Nat Rev Neurosci* 5, 495-501
42 Loftus, A.M., *et al.* (2009) Prism adaptation overcomes pseudoneglect for the greyscales task. *Cortex* 45, 537-543

43 Sarri, M., *et al.* (2006) Prism adaptation changes perceptual awareness for chimeric visual objects but not for chimeric faces in spatial neglect after right-hemisphere stroke. *Neurocase* 12, 127-135
44 Rossetti, Y., *et al.* (2004) Does Action Make the Link Between Number and Space Representation? *Psychol Sci* 15, 426-430
45 Servos, P., and Goodale, M.A. (1995) Preserved visual imagery in visual form agnosia. *Neuropsychologia* 33, 1383-1394
46 Laeng, B. (2002) Eye scanpaths during visual imagery reenact those of perception of the same visual scene. *Cogn Sci* 26, 207-231
47 Clower, D.M., *et al.* (1996) Role of posterior parietal cortex in the recalibration of visually guided reaching. *Nature* 383, 618-621
48 Danckert, J., *et al.* (2008) Direct effects of prismatic lenses on visuomotor control: an event-related functional MRI study. *Eur J Neurosci* 28, 1696-1704
49 Clower, D.M., *et al.* (2005) Basal ganglia and cerebellar inputs to 'AIP'. *Cereb Cortex* 15, 913-920
50 Luaute, J., *et al.* (2009) Dynamic changes in brain activity during prism adaptation. *J Neurosci* 29, 169-178
51 Luaute, J., *et al.* (2006) Functional anatomy of the therapeutic effects of prism adaptation on left neglect. *Neurology* 66, 1859-1867
52 Milner, A.D., and Goodale, M.A. (2006) *The visual brain in action*. Oxford University Press
53 Corbetta, M., and Shulman, G.L. (2002) Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 3, 201-215
54 Coulthard, E., *et al.* (2006) Action control in visual neglect. *Neuropsychologia* 44, 2717-2733
55 Karnath, H.O., *et al.* (2001) Spatial awareness is a function of the temporal not the posterior parietal lobe. *Nature* 411, 950-953
56 Mort, D.J., *et al.* (2003) The anatomy of visual neglect. *Brain* 126, 1986-1997
57 Shiraishi, H., *et al.* (2008) Long-term effects of prism adaptation on chronic neglect after stroke. *NeuroRehabilitation* 23, 137-151
58 Striemer, C., *et al.* (2008) Bilateral parietal lesions disrupt the beneficial effects of prism adaptation: evidence from a patient with optic ataxia. *Exp Brain Res*
59 Corbetta, M., *et al.* (2005) Neural basis and recovery of spatial attention deficits in spatial neglect. *Nat Neurosci* 8, 1603-1610
60 Baizer, J.S., *et al.* (1999) Cerebellar lesions and prism adaptation in macaque monkeys. *J Neurophysiol* 81, 1960-1965
61 Pisella, L., *et al.* (2005) Ipsidirectional impairment of prism adaptation after unilateral lesion of anterior cerebellum. *Neurology* 65, 150-152
62 Dum, R.P., and Strick, P.L. (2003) An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. *J Neurophysiol* 89, 634-639
63 Husain, M., and Nachev, P. (2007) Space and the parietal cortex. *Trends Cogn Sci* 11, 30-36
64 Newport, R., and Jackson, S.R. (2006) Posterior parietal cortex and the dissociable components of prism adaptation. *Neuropsychologia* 44, 2757-2765
65 Driver, J., and Mattingley, J.B. (1998) Parietal neglect and visual awareness. *Nat Neurosci* 1, 17-22

66 Mattingley, J.B., *et al.* (1994) Can task specific perceptual bias be distinguished from unilateral neglect? *Neuropsychologia* 32, 805-817
67 Sarri, M., *et al.* (in press) Prism adaptation does not change the rightward spatial preference bias found with ambiguous stimuli in unilateral neglect. *Cortex*
68 Pisella, L., *et al.* (2002) Dissociated long lasting improvements of straight-ahead pointing and line bisection tasks in two hemineglect patients. *Neuropsychologia* 40, 327-334
69 Frassinetti, F., *et al.* (2002) Long-lasting amelioration of visuospatial neglect by prism adaptation. *Brain* 125, 608-623
70 McIntosh, R.D., *et al.* (2002) Prism adaptation improves chronic visual and haptic neglect: a single case study. *Cortex* 38, 309-320
71 Dijkerman, H.C., *et al.* (2004) A long-lasting improvement of somatosensory function after prism adaptation, a case study. *Neuropsychologia* 42, 1697-1702
72 Rousseaux, M., *et al.* (2006) Ineffectiveness of prism adaptation on spatial neglect signs. *Stroke* 37, 542-543
73 Rode, G., *et al.* (2006) Prism adaptation improves spatial dysgraphia following right brain damage. *Neuropsychologia* 44, 2487-2493
74 Vallar, G., *et al.* (2006) Productive and defective impairments in the neglect syndrome: graphic perseveration, drawing productions and optic prism exposure. *Cortex* 42, 911-920
75 Keane, S., *et al.* (2006) Use of fresnel prism glasses to treat stroke patients with hemispatial neglect. *Arch Phys Med Rehabil* 87, 1668-1672
76 Humphreys, G.W., *et al.* (2006) Long-term effects of prism adaptation in chronic visual neglect: A single case study. *Cogn Neuropsychol* 23, 463-478
77 Serino, A., *et al.* (2007) Neglect treatment by prism adaptation: What recovers and for how long. *Neuropsychol Rehabil* 6, 657-687
78 Nys, G.M., *et al.* (2008) Prism adaptation moves neglect-related perseveration to contralesional space. *Cogn Behav Neurol* 21, 249-253
79 Serino, A., *et al.* (2009) Effectiveness of prism adaptation in neglect rehabilitation: a controlled trial study. *Stroke* 40, 1392-1398