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Prism adaptation improves visual search in hemispatial neglect

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ABSTRACT

Visuomotor prism adaptation has been found to induce a lateral bias of spatial attention in chronic hemispatial neglect patients. Here, two experiments were conducted to explore the effects of 10° prism adaptation on visual search tasks and standard visual inattention tests. Baselines and intervention effects were measured on separate days for all patients. The first experiment explored whether prism adaptation affects performance on a time restricted visual search task (maximum 3500 ms presentation followed by visual and auditory feedback). No positive effects of prism adaptation were found on accuracy in visual search nor on traditional neglect tests. These results accord well with previous studies showing that increased cognitive load can lead to prism de-adaptation or unchanged performance following prism adaptation. Response times in visual search became faster following intervention but this was not the case for the standard neglect tests. In the second experiment, the same single-featured search task was used, but the participants had unlimited search time and received no feedback on their response. This time, the patients showed accuracy improvements in visual search and all four on regular neglect tests. Therapeutic effects lasted for at least 90–120 min. Response times on all tasks became faster after prism adaptation. The results are consistent with studies showing effects of prism adaptation on neuropsychological neglect tests and other attentional tasks that are not speeded or time restricted, where feedback is not provided, or are performed following non-feedback-based tasks. The current findings show that prism adaptation improves visual search in neglect and that these beneficial effects can disappear with feedback.

1. Introduction

Hemispatial neglect, an attentional deficit towards stimuli contralateral to a brain lesion, usually follows a right-sided brain lesion, normally generated by a stroke in the *a. cerebri media* (Heilman, Bowers, Valenstein, & Watson, 1987; Vallar, 1993). Lesions in superior temporal cortex (Brodmann's areas (BAs) 22 and 37; Karnath, Berger, Küker, & Rorden, 2004; Karnath, Ferber, & Himmelbach, 2001) or in the inferior parietal cortex (BAs 7 and 40) and the medial temporo-parietal junction (BAs 39 and 40; e.g. Mort et al., 2003; Vallar & Perani, 1987) have been shown to produce neglect symptoms. In addition, lesions in the frontal lobes (BAs 4, 6, 44 and 45; Husain & Kennard, 1996), insular cortex (BAs 13 and 14; Manes, Paradiso, Springer, Lamberty, & Robinson, 1999) and basal ganglia (Karnath, Himmelbach, & Rorden, 2002) have also been found to cause neglect symptoms (Halligan, Fink, Marshall, & Vallar, 2003; Smania et al., 1998). Zoccolotti et al. (1989) reported that 27–52% of right hemisphere stroke patients show neglect symptoms for more than 2 months following their haemorrhage. Neglect has an enormous impact on the health services of the modern Western world and lays a heavy burden on patients' families (Kerkhoff & Rossetti, 2006; Milner & McIntosh, 2005). Effective treatments for neglect are, therefore, of great value.

1.1. Rehabilitation of neglect and visual search

Many different interventions have been developed to treat neglect, but most have shown limited or no clinical effects. Luauté, Halligan, Rode, Rossetti, and Boisson (2006) concluded, in a comprehensive review of the literature, that there are only a handful of interventions that have reliably been shown to result in benefits for neglect patients. These include visual scanning training, repeated neck muscle vibration associated with an extensive training program, mental imagery training, video feedback training and prism adaptation (PA). However, studies where patients are randomly assigned to treatments groups are still lacking (Bowen & Lincoln, 2006).

Prism adaptation is a relatively new treatment for neglect (Rossetti et al., 1998) although such adaptation effects have fascinated scientists since the nineteenth century (Helmholtz, 1962); Ivo

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Kohler was the first to explore PA systematically (see e.g. Spillmann & Wooten, 1984). Since PA has been found to affect many important neglect symptoms such as target detection in the neglected hemifield, many authors have concluded that spatial attention mechanisms in neglect may be beneficially affected by PA (e.g. Rode, Klos, Courtois-Jacquin, Rossetti, & Pisella, 2006). Studies of healthy populations have, however, failed to provide a clear understanding of PA effects (e.g. Redding & Wallace, 2006). In line with behavioural results of PA, physiological effects have also been shown to occur in neglect patients and healthy subjects. For instance, Luauté, Michel, et al. (2006) found that low level visuomotor adaptation modulates neural activity in posterior parietal cortex, an area that has been found to be important in spatial cognition and visual search (e.g. Clower et al., 1996; Geng et al., 2006; Himmelbach, Erb, & Karnath, 2006; Müller et al., 2003; Ruff, Kristjánsson, & Driver, 2007).

Impaired visual search is a common symptom in neglect (e.g. Behrmann, Ebert, & Black, 2004; Husain et al., 2001). Visual search tasks are useful tests for neglect since they mimic in many ways the attentional requirements of many daily circumstances. Typically, patients miss a great number of the targets that are presented on the left side of a search array (e.g. Husain et al., 2001; Kristjánsson, Vuilleumier, Malhotra, Husain, & Driver, 2005; Saevarsson, Jóelsdóttir, Hjaltason, & Kristjánsson, 2008).

Only a few treatments have been shown to affect visuospatial cognition problems specifically. For instance, exploration training has been reported to improve visual search in neglect in contrast to visuospatial training (Kerkhoff, 1998). Few studies have explored the effects of PA on visual search in neglect. Rossetti et al. (1998), Rode, Klos, et al. (2006) and Rode, Pisella, et al. (2006) showed that PA improves neglect symptoms on search tasks such as Albert's test, letter cancellation, and other standard tests of neglect. This is in apparent contrast to the findings of Morris et al. (2004), who used computerized single feature, *pop-out* and *conjunctive* search tasks where search time was limited. Patients received visual feedback on whether their key press responses were correct or incorrect. They found therapeutic effects of PA on *non*-time restricted standard paper and pencil tests but not on visual search that was performed after the standard tests. Morris et al. (2004) concluded that PA does not affect the allocation of spatial attention in visual search. They argued that speeded search tasks are a better measure of visuospatial attention than non-time restricted tests, since patients can use other strategies to complete the non-time restricted tasks. They concluded that "...prism adaptation may not improve core aspects of neglect" (Morris et al., 2004, p. 720) and that "...the perceptual after-effects in normals and amelioration of unilateral neglect following prism adaptation are not mediated by an adaptive redistribution of spatial attention" (Morris et al., 2004, p.703). In other words, one might imagine that PA would simply shift the patients' perceived midline, without having any beneficial effects upon the orienting of spatial attention. This conclusion is, however, in seeming contradiction to the results of several PA studies that were both unspeeded (e.g. Rossetti et al., 1998) and speed based (e.g. Berberovic, Pisella, Morris, & Mattingley, 2004; Maravita et al., 2003).

Some aspects of the Morris et al. (2004) study can be criticized, however. For example, the mean response times of the patients were much faster than the 8000 ms search displays that were presented, so it is doubtful that the time restrictions, which are critical to their argument, had much of an effect on the patients' performance, and consequently that time restraints can explain the absence of an effect of PA on visual search. Also, their study may have had insufficient experimental power because of too few search trials despite pooling of different set sizes. Pooling different set sizes could, in fact, lead to null effects when the same search times for the largest (48 search items) and the smallest (12 search items) set sizes are combined. This may undermine their claim that PA is impaired by time restrictions. Furthermore, their choice of prism lenses (with 15° deviation to the right) can be questioned since a large majority of PA studies are based on lenses, with 10° not 15° displacement. The study may therefore not be directly comparable with other studies. Ten degree visual displacement has been found to be the optimal gaze shift for PA and visual comfort (Rossetti & Rode, 2002). Furthermore, Morris et al. (2004) performed all baseline and intervention measures on the same day which may explain their null findings for visual search since it is well known that prolonged testing and fatigue can amplify neglect symptoms (Fleet & Heilmann, 1986; Hjaltason & Saevarsson, 2007). It is therefore preferable to test patients on separate days. Lastly, Morris et al. (2004) did not take into account that the order of non-feedback and feedback-based tasks may potentially influence the performance of prism-adapted neglect patients. For these reasons, it is still unclear whether visuospatial attention or visual search performance of neglect patients can be improved or modulated with PA.

1.2. Current questions

The purpose of the current experiments was to assess any beneficial effects of PA on single feature visual search in neglect. This was explored for two groups of patients who performed two different visual search tasks: time restricted and feedback based in experiment one, and with neither feedback nor time restrictions in experiment two. Contrasting tasks with and without feedback may prove important, since cognitive load, strategic thinking and feedback have been found to lead to recalibration of PA (Lee & Lee, 2006; Redding, Rader, & Lucas, 1992; Redding, Rossetti, & Wallace, 2005). This might explain the null results of Morris et al. (2004), who used feedback and time restrictions; and why the study of Rossetti et al. (1998) resulted in benefits of PA on performance on tasks without time restrictions or feedback.

In light of this evidence the aim was to investigate whether PA would lead to improvements on non-feedback versus feedback-based visual search tasks, in an attempt to elucidate some important aspects of PA in neglect and inconsistencies in the results of previous studies.

2. Methods

2.1. Participants

Eight right-handed chronic hemispatial neglect patients participated, four in experiment one (N1, N2, N3 and N4) and four in experiment two (N5, N6, N7 and N8). Patients with *chronic neglect* are defined here as those with symptoms persisting for at least 2 months following the occurrence of a brain trauma resulting from stroke.

Table 1 shows basic information on the patients. The patients were randomly assigned to one of the two experiments. The main inclusion criteria for participation were right hemisphere brain lesions, intact cerebelli, stable affective conditions, impaired performance on at least three neglect tests and no clear evidence of hemianopia. The patients were tested at a similar time every day of the study. Table 2 shows a summary of the lesioned brain regions for all participants of both experiments.

Fig. 1A and B shows how the lesions of the patients overlap with each other, separately for the two experiments. To trace the lesions of three patients, we used T2-weighted MRI for two subjects and additional diffusion weighted MRI scan for one of the three participants (Roberts & Rowley, 2000) depending on the time the MRI was performed. For the remaining five patients CTs from the acute phase of the infarct were available. The brain scans of all patients were inspected and manually transferred onto a standard brain using MRIcro (Version 1.4; Rorden & Brett, 2000). Following the thickness of CT scan slices, we used ten slices with a thickness of 10 mm. The first slice showed the anterior part the inferior temporal gyri at the temporal pole and for the posterior part the cerebellum (see slice 1 of Fig. 1A and B for a transversal and Fig. 1C for a coronal and saggital slice scout). The last slice was located at the most rostral part of the brain. None of the patients had lesions outside this series of slices, most likely due to the restricted brain regions supplied by the middle brain artery (Bogousslavsky & Caplan, 2000).

The subtraction procedure of MRIcro was used to calculate the percentage of overlap for the lesions in both experimental groups (by comparing them with a phantom patient with a lesion in the brain stem; see Fig. 1A and B). Yellow in the

Table 1
Summary of patient data for all subjects in both experiments.

Experiment	Patient	Sex	Age (years)	Onset of illness (months) time between stroke and PA	Ocular deviation	Cephalic deviation	Left hemiplegia	Days between base-line and experimental days
One	N1	Male	57	26	+	+	+	2
One	N2	Male	69	18	–	–	+	4
One	N3	Female	62	42	–	+	+	7
One	N4	Male	41	20	–	–	+	20
Two	N5	Male	67	61	+	+	+	3
Two	N6	Female	73	7	–	–	–	7
Two	N7	Female	45	9	+	+	+	18
Two	N8	Male	60	3	–	–	+	12

Table 2
Lesioned brain areas of the patients that participated in the study.

Lesion localization	Patients of experiment one				Patients of experiment two			
	N1	N2	N3	N4	N5	N6	N7	N8
Frontal	+	–	+	+	+	–	+	–
Insular	+	–	+	–	+	+	+	–
Temporal	+	+	+	+	+	+	–	+
Parietal	–	+	+	+	–	+	–	+
Occipital	–	–	–	–	–	–	–	–
Thalamus	–	–	–	–	–	–	–	–
Basal ganglia	+	+	+	–	+	+	+	+

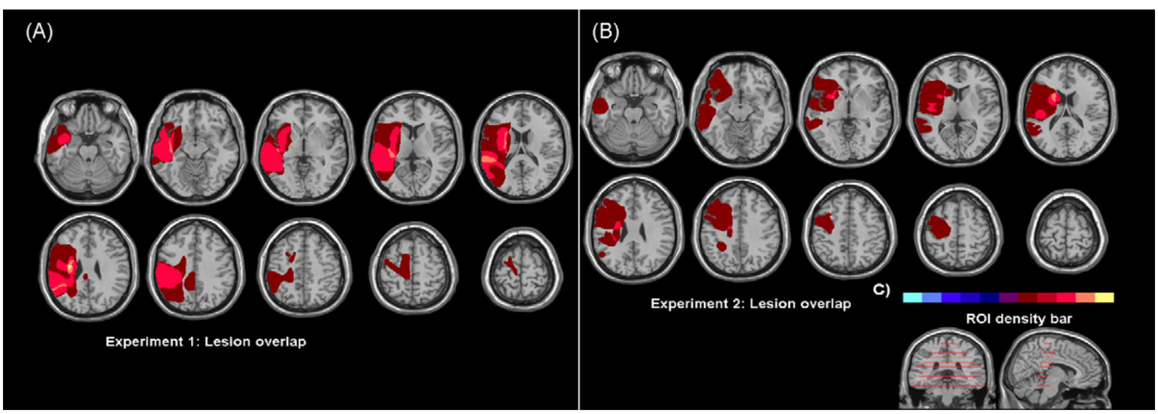

Fig. 1. Panel A and B show MRI's and PET's images of lesion overlap for patients in experiment one and two. Panel C shows the density bar and the location of the slices.

ROI (region of interest) density bar means that all four patients had a lesion in this area, orange means that three of four patients had lesions in these areas, light red two patients and dark red one patient. As can be seen from Fig. 1A and B the groups did not differ by much in lesion size, but the second group tended to have more anteriorly located lesions (slices 2, 7, and 8). In general, both patient groups showed the highest amount of overlap in the head of the caudate nucleus (see slices 5 of Fig. 1A and B) and periventricularly, or in the body of, the caudate nucleus (see slices 6 of Fig. 1A and B).

2.2. Stimuli

All patients in the study were tested with six standard paper and pencil visual inattention tests after they completed the computerized visual search task, before and after PA. The following tests were used: Albert's test (Albert, 1973), line-bisection (Wilson, Cockburn, & Halligan, 1987), number cancellation, copy drawing (Greek cross) and free hand drawing (a clock and a flower; Halsband, Gruhn, & Ettlinger, 1985).

Two different types of computer-based visual search *pop-out* tasks were used in the experiments. Both visual search tasks were based on the same single feature search displays, but the two tasks differed in whether search time was limited or not, and whether feedback was provided on whether the response was correct or incorrect. In the first experiment the search display was visible for a maximum of 3500 ms and was followed by strong visual and auditory feedback (visual: "Richtig" was presented for correct and "Falsch" for wrong; auditory: high frequency tone for wrong responses and low frequency tone for correct responses). In the second experiment the search display was present on the screen until the patient responded and no feedback was provided. The dependent measures were response time (RT) and accuracy in both tasks.

Participants searched for a green target circle among blue distractor circles and responded by key press whether the target was present or not (see Fig. 2). The diam-

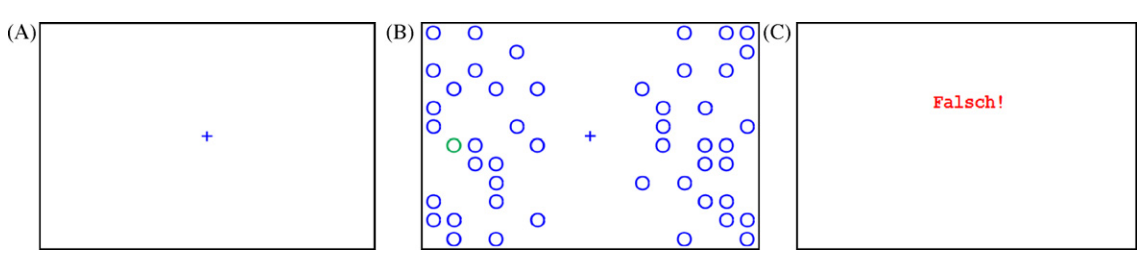

Fig. 2. The three main displays in the search task in experiment one. Panel A shows the fixation cross. Panel B shows an example of a search display (with a target present). Panel C shows the visual feedback for a wrong key press.

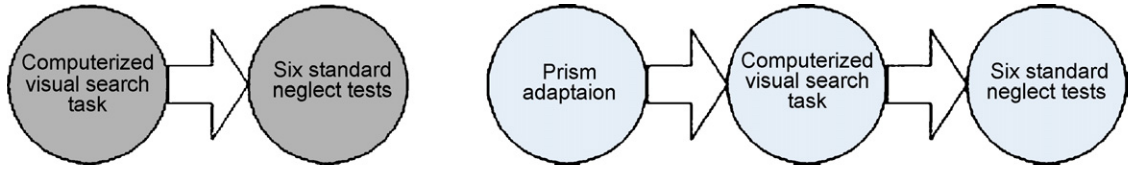

Fig. 3. The figure shows the chronological order of the experimental procedure; dark shaded rings indicate baseline and light shaded the day of intervention.

eter of all the circles was 0.6 arc degree and the viewing distance was kept as close to 67 cm as possible from the monitor display. The dimensions of the search display on the monitor were 13.7 arc degree (vertically) by 19.5 arc degree (horizontally). The target was present on the screen on half of the trials of the search task (25% in the left and 25% in the right visual field). Forty-eight stimuli were presented on each trial, a target and 47 distractors (a target-present trial); or 48 distractors (a target-absent trial). Targets on the left and right were separated by a vertical 5.2 arc degree gap at the middle of the screen, to increase the distinction between the hemifields (as shown in Fig. 2; see e.g. Saevarsson, Kristjánsson, & Halsband, 2008; Saevarsson, Jóelsdóttir, et al., 2008).

Whether a target was present or not on a particular trial was determined randomly. The intertrial interval was at minimum 7000 ms in both experiments, and at maximum 10,500 ms in experiment one or until the participant pressed a key in experiment two. Fig. 2 gives an example of a target present display in experiment one.

2.3. Apparatus

Ten degree rightward-displacing prism lenses were used (on both eyes) for the visuomotor adaptation. A similar adaptation box to the one described by Rossetti et al. (1998) was used. Pointing movements were recorded with a video-camera while patients performed an open loop task before and after PA. Pads were used to adjust the height contrast between the box and the patients. An IBM Thinkpad T41 laptop computer with a 15 in. LCD screen was used to display the visual search tasks in both experiments. Subjects pressed one of the two buttons on a computer mouse, depending on whether the target was present or not. E-prime 1.1 was used for the presentation of the stimuli, which were prepared with Photoshop 7.0 pro.

2.4. Procedure

All subjects were tested in their homes except patient N7 who was tested at a medical institution. On the day of baseline measurements, participants performed the visual search task, followed by the standard neglect tests. On the day of intervention, patients performed the same tests, the open loop task (pre- and post-adaptation) two times, before and after PA, followed by the visual search tasks, and finally the standard neglect tests (Fig. 3). Testing on each day lasted 1.5–2 h. The time interval between baseline and intervention measure was from at least 2–20 days. While the participants performed the experimental tasks, the experimenter was seated to the right of the participants to ensure their alertness and to aid their understanding of the task.

2.4.1. Visual search

Participants were instructed to press a green colored mouse button as quickly as they could if they found a green target, and a blue colored mouse button if no target was present on the screen. Participants were instructed to fixate on a cross at the centre of the display, at the beginning of each search trial.

2.4.2. Standard paper and pencil neglect tests

The participants were informed that they should indicate when they were ready to start the tests and when they had completed them. Participants were told to perform all tests as quickly and accurately as possible. The order of each of the standard tests for individual observers was determined randomly to prevent any confounding influences of learning.

2.4.3. Open loop task (pre- and postadaptation)

Participants were asked to perform ten non-visible pointing movements with their index finger (using their right hand; without the prism lenses and blindfolded with sleeping glasses) straight forward from their midline. Patients were also asked to hold their finger still for a moment to allow the experimenter to record the pointing direction at the time of testing (see e.g. Hauer & Quirbach, 2007). Following each pointing movement, subjects were asked to return their hand to the starting position in front of their body. Accuracy was assessed by subsequent inspection of the video recordings.

2.4.4. Prism adaptation

Patients were asked to perform sixty fast pointing movements randomly to two dots that were displayed in front of them while wearing 10° right shift prism lenses. Patients could only see their pointing visually for the last 1–2 cm before they reached the dot to prevent visual feedback. Because of the prism lenses, the patients' visual space was distorted and initially they tended to make finger pointing errors to their right side. With repeated pointing, the errors gradually decreased until the pointing was aligned with the target location. Patients were encouraged to keep their body posture as straight as possible during the adaptation process and testing (Rossetti et al., 1998).

2.4.5. Ethical issues

The ethics committee of the University of Freiburg approved the study in line with the Declaration of Helsinki of 1964.

2.5. Data analysis

Standard paper and pencil tests were scored by dividing the total number of errors by the total number of points for each test. Albert's test, number cancellation and drawing tests were only scored on the left side because of ceiling effects on the right side. Tests that patients performed without errors were included in calculations for mean scores. The results on the open loop test and on the standard neglect test were analysed with paired *t*-tests. For the visual search tasks, log-linear analyses were used to compare accuracy scores for the different experimental conditions for all participants while Wilcoxon matched-pairs signed-rank tests (see e.g. Howell, 2002) were used to assess differences in response times, since their distribution deviated significantly from normal. Statistical comparisons were made between three major conditions for the search task, for right-hemifield targets, left-hemifield targets and target-absent trials, before and after intervention. The critical α-level (p) was set at 0.05.

3. Results

3.1. Experiment one

3.1.1. Open-loop tests

Open-loop tests before and after PA revealed significant visuomotor adaptation effects ($p < 0.05$) for all patients. Patients N1, N3 and N4 showed 10.4°, 1.7° and 11.7°, respectively, shift after-effects to the left side. The only anomaly was that patient N2 showed a 15.8° PA after-effect to the right side (see Sarri et al., 2008).

3.1.2. Paper and pencil tasks

The average percent correct on the seven paper and pencil tests for all four patients was 88.1% before PA and 87.9% following PA. This difference was not significant ($t(23) = 0.091$, n.s.). Similarly, no difference ($t(23) = -0.709$, n.s.) was found for patients' RT on the standard neglect testing (baseline: $M = 44.3$ s and after PA: $M = 47.6$ s) (Fig. 4).

3.1.3. Visual search tasks

The aim of the first experiment was to explore the effects of PA on visual search with limited search time and strong visual and auditory feedback. All four patients finished 640 search trials each (4 × 160 trials) both before and after PA. Fig. 5 shows average percent correct for all four patients in experiment one where participants received visual and auditory feedback on each trial following their key press.

Group statistics revealed no difference (χ^2 (1) = 1.433, n.s.) for participants between the three visual search conditions before and after intervention (average percent correct).

Fig. 6 shows the RT's for all participants. Differences in RT between the experimental conditions before and after PA were found for targets on the right ($z = -13.869$, $p < 0.001$), on the left ($z = -16.663$, $p < 0.001$) and for target absent trials ($z = -8.384$, $p < 0.001$). In short, responses for the left and right target search

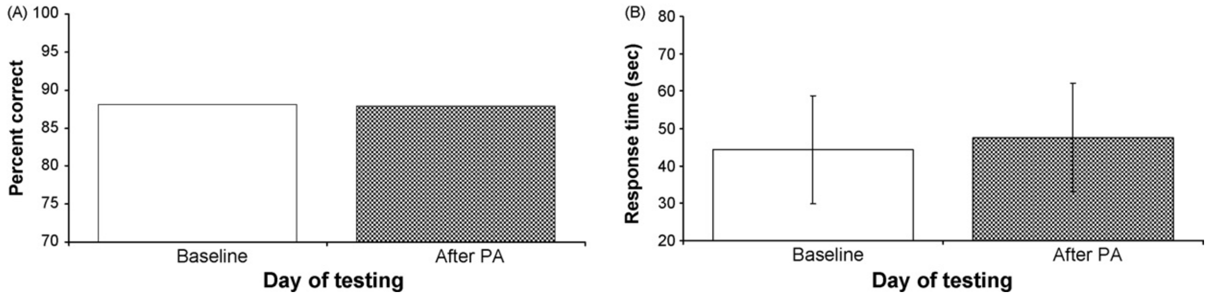

Fig. 4. Panel A shows mean percent correct and panel B shows the average response times (s) for all six standard neglect tests used in experiment one. The error bars present the standard deviations for both experimental conditions.

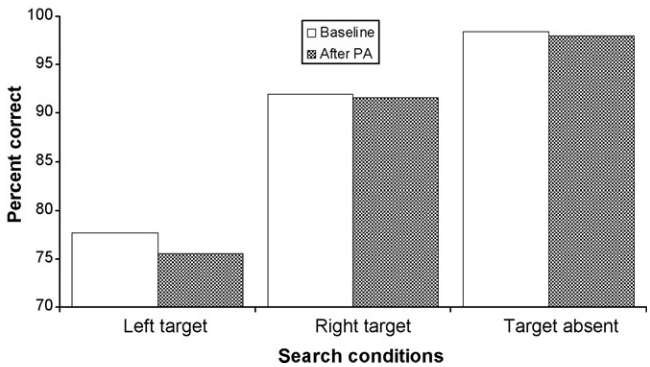

Fig. 5. The mean percent correct scores for the three conditions in the visual search, before and after PA, for all patients in experiment one.

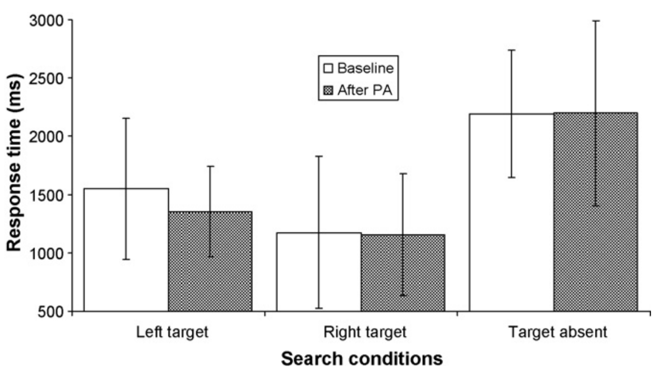

Fig. 6. Average RTs from experiment 1 for the three visual search conditions, before and after PA treatment. The error bars show the standard deviations for each search condition.

conditions got faster while search on target-absent trials became slower.

In sum, the results of experiment one were that PA does not improve accuracy in the visual search task nor on the paper and pencil tests. However, patients showed slightly faster RTs on the target present trials in the visual search task after PA which was not the case for the paper and pencil tests. These results are similar to those reported by Morris et al. (2004).

3.2. Experiment two

3.2.1. Open-loop tests

Open-loop tests before and after PA showed significant visuomotor adaptation shifts to the left side for patients N5, N6, N7 and N8 (14.5°, 10.7°, 7.4° and 1.9°, respectively; $p < 0.05$).

3.2.2. Paper and pencil tasks

The average percent correct on the seven paper and pencil tests was 84.2% for the baseline and 94.8% following PA. Results for the right side of the neglect tests are not reported because of ceiling effects. On the left side, statistical analysis revealed differences between the baseline and intervention ($t(23) = -2.549$, $p = 0.018$). Differences were found for RT ($t(23) = -3.183$, $p = 0.004$), between the baseline ($M = 55.8$) and intervention ($M = 44.0$) (Fig. 7).

3.2.3. Visual search tasks

The aim of the second experiment was to explore the effects of PA on visual search with unlimited search time and no feedback. Each patient finished 640 search trials (4 × 160 trials) before and after PA. Fig. 8 shows the average percent correct for the four patients.

Patients detected more targets on both the left (χ^2 (1) = 25.887, $p < 0.001$) and right (χ^2 (1) = 7.008, $p = 0.008$) sides after PA. On the other hand, there was only a non-significant hint of a beneficial PA effect on accuracy in the target-absent condition (χ^2 (1) = 2.703, $p = 0.1$).

Fig. 9 shows RT on visual search for all participants. A significant reduction in response times was found following PA for all three conditions (target on the right: $z = -21.584$, $p < 0.001$; on the left: 1, $z = -20.011$, $p < 0.001$; target-absent: $z = -19.585$, $p < 0.001$), when compared with the baseline.

In sum, experiment two indicates that the average percent correct in visual search improved for the patients both for right and

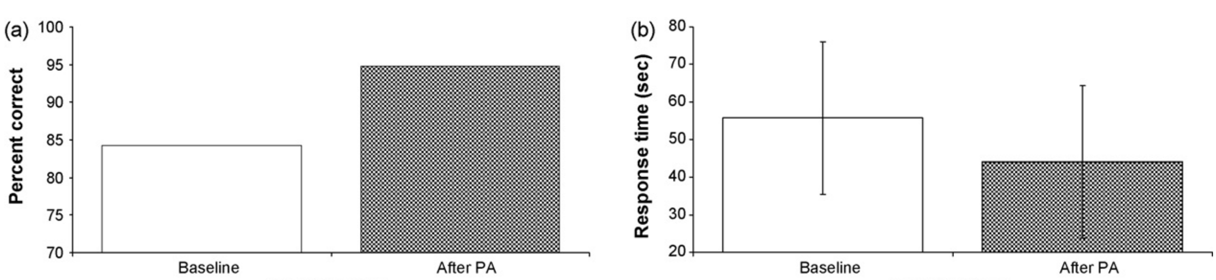

Fig. 7. Panel A shows average percent correct and panel B presents average RT (s) on the six standard neglect tests in experiment two. The error bars in panel B show the standard deviations from the mean.

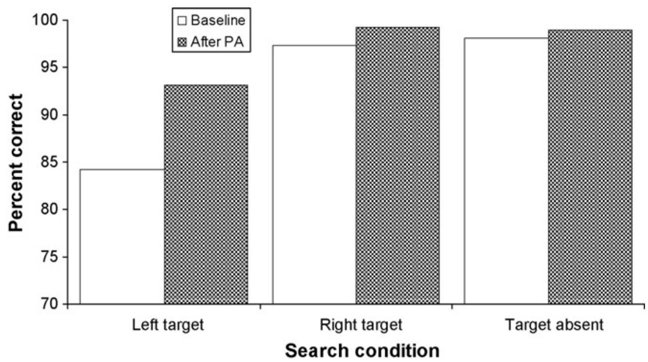

Fig. 8. Average percent correct for the three visual search conditions in experiment two.

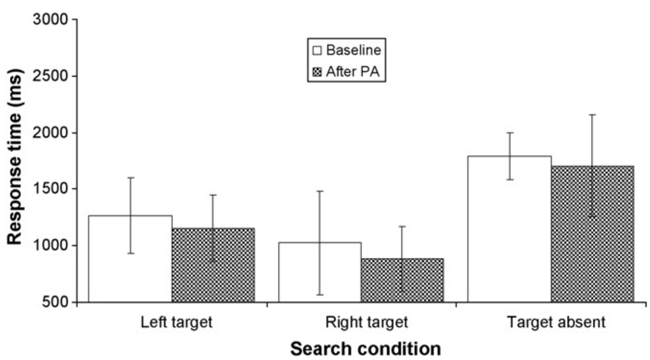

Fig. 9. The columns show the average RTs from experiment two. The error bars presents the standard deviations from the mean.

left targets after PA. Also, response times became faster in the visual search task following PA. Furthermore, the patients showed improvements on standard neglect tests in terms of percent correct and RT.

4. Discussion

We have investigated the effects of PA on visual search and other hemispatial neglect symptoms. Our findings show how feedback in visual search tasks can disrupt positive after-effects of PA in neglect. In experiment one accuracy remained unchanged in feedback-based visual search following PA in line with the study of Morris et al. (2004), while in experiment two we found that PA has positive effects on visual search performance when the search is not followed by feedback. These results indicate that PA affects spatial attention in neglect, consistent with previous results (e.g. Maravita et al., 2003; Rossetti et al., 1998). Paper and pencil tests revealed comparable effects of PA on accuracy as was found for the visual search task in experiment 2. These tests were non-feedback-based and not time-restricted. We speculate that these results for the paper tests may be explained by the order in which the experimental tasks were performed.

Our results are consistent with the studies of Rossetti et al. (1998), Rode, Klos, et al. (2006), Rode, Pisella, et al. (2006) and Morris et al. (2004), once the role of feedback in visual search has been delineated and we have clarified under which conditions PA lead to benefits in neglect, and what sort of tasks may abolish such effects.

4.1. Theoretical accounts of PA

Redding and Wallace (2006) suggested in their comprehensive review that neglect patients have a dysfunctional and reduced "task-work space", and have difficulties shifting its locus from the right to the left or from the left to the right. They claim that visuomotor recalibration ameliorates such pathological spatial reference frames and visual calibration, but not the affected task work space nor the higher order visuo-spatial representation. Many studies have, however, shown that PA may lead to improvements of several forms of disrupted higher level cognitive functioning such as imagery of geographic maps, mental number bisection, spatial dysgraphia, disrupted spatial and body representations and regional pain syndrome (e.g. Rode, Pisella, et al., 2006; Rode, Rossetti, & Boisson, 2001; Rossetti et al., 2004; Serino, Angeli, Frassinetti, & Ladavas, 2006; Sumitani et al., 2007). Our results suggest that PA may lead to temporary amelioration of disrupted spatial working memory and exogenous attention (see e.g. Husain et al., 2001; Malhotra et al., 2005; Natale, Posteraro, Prior, & Marzi, 2005; Wojciulik, Husain, Clarke, & Driver, 2001, for examples). To account for the contradiction between studies that assume improved higher cognition and the theory of Redding and Wallace (2006), it has been suggested that PA may not change patient's awareness as such but rather some essential antecedents of consciousness (Danckert & Ferber, 2006).

The physiological effects of PA have been investigated with functional brain imaging. Using PET, Luauté, Michel, et al. (2006) found low level visuomotor adaptation to modulate activity in the right cerebellum, the right posterior parietal cortex, the left thalamus, the left temporo-occipital cortex, and the left medial temporal cortex (see also Clower et al., 1996; Shiraishi, Yamakawa, Itou, Muraki, & Asada, 2008; Wischusen, Schütze, & Fahle, 2007). This activation pattern shows partial overlap with activations found during visual search in healthy subjects, which have been found in the intraparietal sulcus and the superior parietal lobule (e.g. Geng et al., 2006; Himmelbach et al., 2006; Müller et al., 2003; Ruff et al., 2007). The overlap between the physiological effects of PA and visual search strengthens the conclusion that PA leads to improvements of disrupted search processes in neglect. Results of some other studies on patients with parietal lesions have, on the other hand, argued against the importance of parietal cortex in PA (e.g. Pisella et al., 2004; Rossetti et al., 1998; Striemer et al., 2008).

It is, however, interesting that these regions show overlap with regions connected with beneficial effects on search found for repetition priming of visual search (Geng et al., 2006; Kristjánsson, Vuilleumier, Schwartz, Macaluso, & Driver, 2007). Such priming is important with regard to neglect as shown by Kristjánsson et al. (2005), who found that target color repetition speeds visual search performance in neglect, even when the patients did not notice the targets in their neglected hemifield.

4.2. Disruption of PA benefits

Our results suggest that feedback in visual search can lead to de-adaptation effects for neglect patients. This might reflect that feedback results in strategic thinking and may increase the cognitive load for the patients. This fits well with results of studies on healthy subjects showing that increased cognitive load (Redding et al., 1992) age related declines in working memory (Anguera, Reuter-Lorenz, Noll, Willingham, & Seidler (2007)), and strategic thinking (Lee & Lee, 2006) can lead to such de-adaptation. Husain et al. (2001) (see also Malhotra et al., 2005) have argued that neglect patients suffer from impairments in spatial working memory which might explain why increased cognitive load eliminates PA. Indeed, Habekost and Rostrup (2007) have shown that white-matter connectivity has significant effects upon visual short-term memory and speed of ipsilesional processing in a group of patients with large anterior hemisphere brain damages. Note however, that feedback-based visual learning intervention has been found to improve visual search in neglect (Kerkhoff, 1998). In addition, Rossetti et al. (1998)

found escalated improvements following PA in neglect when the therapeutic effects were measured 2 h after intervention as compared with measurements immediately following the removal of PA glasses. This may imply that feedback quickly following PA, abolishes some brain plasticity processes or late onset corrections of egocentric reference frames (Hatada, Miall, & Rossetti, 2006) that could explain why patients in experiment one did not show improvement following PA. Interestingly, recent studies show how unaware prism exposure procedure creates stronger after-effects than regular single step exposure mode in healthy participants (see Pisella, Rode, Farnè, Tilikete, & Rossetti, 2006). Furthermore, one might speculate that factors such as feedback and time course after PA might explain null findings in studies that have reported null findings of PA on neglect (e.g. Rousseaux, Bernati, Saj, & Kozlowski, 2005).

4.3. The effects of time

In contrast to Morris et al. (2004), some studies have concluded that time limited displays do not seem to impair the therapeutic effects of PA. Behrmann et al. (2004) used a speed-based (1296 ms max) spatial temporal-order-judgement task resulting in beneficial effects of PA on spatial attention in neglect. Maravita et al. (2003) found that PA improves speeded (100 ms) tactile perception in a group of patients with unilateral neglect. Similarly, Nijboer, McIntosh, Nys, Dijkermann, and Milner (2007) used a speed based cueing task (300–700 ms) to show how PA improves voluntary orienting of attention. This does not, however, exclude the possibility that shorter display times, compared to the average responses might impair therapeutic effects of PA on spatial attention in neglect. This remains an open question.

In general, the RTs in both experiments became faster for the visual search but not for standard neglect testing. Only the patients in experiment two showed faster RTs on the standard tests. Both experimental groups showed similar RTs for visual search. However, time restriction does not seem to play an important role in the current study since the average RTs in the first experiment were shorter than the maximum display time (3500 ms) for each search set. Therefore, the display time of the search set seems to be sufficient for the patients in experiment one. Note that the RTs are similar to those in the Morris et al. (2004) study. Saevarsson, Kristjánsson, et al. (2008) and Saevarsson, Jóelsdóttir, et al. (2008) have also reported comparable RTís for neglect patients in similar visual search tasks.

4.4. Some unresolved issues

The patients in our study showed relatively homogenous performance on the visual search task and the classical neglect tests in both experiments. However, patient N8 did not show statistically significant effects of PA on visual search accuracy unlike the other participants in experiment two. Moreover, the open-loop data for patient N2 may indicate that this patient showed no after-effects because of the prism adaptation. But this does not explain the null findings in experiment one because the other three patients showed the same null results [not reported]. Also, the patients in experiment one showed faster RT's in visual search, but not on the standard neglect tests. The reason for this is unclear at present. Studies based on more homogeneous patient samples might reveal more consistent results. This falls in line with other studies showing that PA does not help to reduce neglect symptoms in all patients (e.g. Vuilleumier, 2007).

4.5. Conclusions and future directions

The current findings call for further studies: It would be of interest to find out how neglect patients would perform on the visual search task without feedback after placebo PA intervention, like the one used by Rossetti et al. (1998). Investigating whether the effects of feedback on different time course of testing are specific to the beneficial effects of PA would be of great interest. Combining PA with, for instance, neck vibration (Johannsen, Ackermann, & Karnath, 2003) may improve the therapeutic effects (see Saevarsson, Kristjánsson, et al., 2008 for some preliminary evidence for this). Also, it would be interesting to further explore how the order of non-feedback and feedback-based tasks can affect PA intervention in neglect. Furthermore, the use of a relatively pure measure of attentional effects, such as cueing studies (Kristjánsson, Mackeben, & Nakayama, 2001; Kristjánsson & Nakayama, 2003; Nakayama & Mackeben, 1989; Nijboer et al., 2007; Posner & Cohen, 1984; see e.g. Kristjánsson, 2006, for review) might shed further light on the issue of whether PA can have beneficial effects on spatial orienting, and such studies are already under way in our laboratories.

In conclusion, the current results shed new light on the nature of the positive after-effects of PA on visual search in neglect showing that feedback upon performance can abolish the beneficial effects of PA. The findings may have uncovered some important limitation to the beneficial effects of PA in neglect. The data are in accord with other studies suggesting that cognitive load and strategic thinking can play a critical role in the efficacy of PA. Overall, the results add to increasing evidence that PA improves spatial cognition in neglect and may help to elucidate under which conditions this happens. But the results may suggest that this benefit might be short-lived or easily abolished; repeated or combined treatment could be necessary for longer lasting effects.

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