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Finding Wally: Prism adaptation improves visual search in chronic neglect

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ABSTRACT

Several studies have found that visuo-motor adaptation to rightward deviating prismatic goggles (prism adaptation) can alleviate symptoms of neglect after brain damage, but the long-term effect and clinical relevance of this rehabilitation approach have been questioned. In particular, the effect on visual search performance is controversial. In the present study 6 patients with chronic spatial neglect due to rightsided focal brain damage were given 20 sessions of prism adaptation over a period of two weeks. These patients, as well as a matched control group of neglect patients ($n = 5$), were tested using a variety of effect measures with special emphasis on visual search at baseline, shortly after training, and five weeks later. A positive and very consistent long-term effect of prism adaptation was found across clinical tests of neglect, lateral bias of eye movements, and measures of everyday function, including subjective reports. The results show that prism adaptation can provide durable and clinically significant alleviation of neglect symptoms, even in the stable phase of recovery.

1. Introduction

Hemispatial neglect denotes a complex of symptoms commonly seen after right-sided brain damage. It is characterized by a failure to report, respond, or even orient to stimuli presented in the contralesional side of space, despite intact motor and sensory processes (Heilman, 1977/1993). Neglect is not limited to the visual domain and may also occur for auditive, olfactory, tactile, and somatosensory stimuli (Bellas, Novelly, Eskenazi, & Wasserstein, 1988; Maravita et al., 2003; Pavani, Husain, Làdavas, & Driver, 2004; Vallar, Rusconi, Bignamini, Germiniani, & Perani, 1994). Neglect can even affect the contralesional side of mental representations where no sensory input is required (cf. Bisiach & Luzzatti, 1978). Neglect symptoms are seen in at least 50% of all acute patients with right hemisphere injuries (Buxbaum et al., 2004; Pedersen, Jørgensen, Nakayama, Raaschou, & Olsen, 1997; Stone, Halligan, & Greenwood, 1993), and though most patients recover spontaneously (Ferro, Mariano, & Madureira, 1999), chronic neglect is severely debilitating and notoriously difficult to rehabilitate (Robertson, 1999). It has also been questioned whether the recovered patients in fact show full functional restoration or if remaining (subclinical) symptoms go unnoticed when using standard clinical tests (Appelros, Nydevik, Karlsson, Thorwalls, & Seiger, 2003; Habekost & Rostrup, 2006). An effective treatment for chronic neglect is therefore much needed.

Many rehabilitation approaches for neglect have been investigated over the last decades. In general, these procedures have focused on either cognitive, top-down based strategies (e.g., Antonucci et al., 1995; Barrett et al., 2006; Pizzamiglio et al., 1992) or bottom-up based sensory or motor stimulation (e.g., Karnath, Christ, & Hartje, 1993; Pierce & Buxbaum, 2002; Rossetti & Rode, 2002; Vallar, Guariglia, Nico, & Pizzamiglio, 1997). The reported effects have either been small, inconsistent, or very short lasting (Bowen & Lincoln, 2007a; Luauté, Halligan, Rode, Rossetti, & Boisson, 2006). Rossetti et al. (1998) generated new enthusiasm in the field after reporting that a single, brief period of simple visuo-motor adaptation to a lateral shift of the visual field (prism adaptation) ameliorated visual neglect symptoms for two hours. Pisella, Rode, Farnè, Boisson, and Rossetti (2002) subsequently found that the symptom reduction could persist for several days, and later studies have shown an effect of 20 sessions of prism adaptation lasting for five to twelve weeks after training (Frassinetti, Angeli, Meneghello, Avanzi, & Làdavas, 2002; Serino, Angeli, Frassinetti, & Làdavas, 2006; Serino, Barbiani, Rinaldesi, & Làdavas, 2009).

In standard prism adaptation therapy, patients are trained on a pointing task while wearing wedge prisms that distort visual input by displacing it 10 degrees rightward. This change in sensory input produces a misalignment between perceptual and motor representations of external space inducing visuo-motor responses that are misdirected to the right. During continued prism exposure and with feedback on erroneous responses, visuo-motor representations are gradually brought back into alignment through an adaptation process (the *error reduction effect*). However, when the prisms are removed patients overcompensate by pointing too far

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to the left (the *aftereffect*). Apart from improvements in traditional paper-and-pencil neglect measures, beneficial effects of this procedure have been reported in non-motoric visuo-verbal tasks, where patients were required to describe objects or scenes (Farnè, Rossetti, Toniolo, & Làdavas, 2002). Other studies have shown effects on motor exploration and spatial perception (McIntosh, Rossetti, & Milner, 2002), improved awareness of tactile stimulations (Maravita et al., 2003), and better postural balance and contralesional somatosensory functions (Dijkerman, Webeling, ter Wala, Groet, & van Zan, 2004; Tilikete et al., 2001).

Despite these positive findings there is no general agreement on what sort of changes (neural or cognitive) that underlie the observed positive effects of prism adaptation (Redding & Wallace, 2006a, 2006b). One influential hypothesis emphasizes the importance of changes in eye movements (Serino et al., 2006; Shiraishi, Yamakawa, Itou, Muraki, & Asada, 2008). The spontaneous eye movements of neglect patients are typically displaced towards the right both during passive waiting and active search of visual scenes, and fixations in the left visual field are fewer and shorter (Behrmann, Watt, Black, & Barton, 1997; Fruhmann-Berger & Karnath, 2005; Karnath, Niemeyer, & Dichgans, 1998). Recalibration of the oculo-motor system plays a decisive role in the model put forth by Serino et al., but the functional significance of the altered eye movements is debated. Ferber, Danckert, Joanisse, Goltz, and Goodale (2003) found that exploratory eye movements clearly deviated to the left after prism adaptation, but this change in motor behaviour did not lead to greater awareness of left-side stimuli. Other studies have found that a more equal distribution of fixations in the visual field does improve neglect symptoms (Angeli, Benassi, & Làdavas, 2004; Angeli, Meneghello, Mattiolo, & Làdavas, 2004).

The discussion about changes in eye movements is closely related to the issue of visual search performance. Visual search has long been a central paradigm for theories of attention in healthy subjects (Neisser, 1964; Treisman & Gelade, 1980; Wolfe, 1994). Search tasks are of particular interest in understanding attentional deficits after brain damage, as they simulate the complexity of the everyday environment more closely than most other perceptual tasks (Eglin, Robertson, & Knight, 1989). The effect of prism adaptation on visual search performance has only been targeted directly in two studies. Morris et al. (2004) studied the effect of one prism adaptation session on visual search in neglect patients and healthy controls, using both an (easy) unique-feature search task and a (hard) feature-absent search. Both normal subjects and patients failed to show changes in reaction time patterns in the two search tasks, and the authors concluded that the amelioration of neglect symptoms seen after prism adaptation is not mediated by an adaptive redistribution of spatial attention. This finding was partly challenged in a recent study by Saevarsson, Kristjánsson, Hildebrandt, and Halsband (2009) who in one experiment found beneficial effects of one prism adaptation session on standard paper and pencil neglect tests as well as a visual feature search task. However, a similar experiment in the same study indicated that providing feedback on search performance and restricting search time eliminated the positive effects of prism adaptation. This latter finding questions the stability of the attentional improvements seen after prism adaptation.

Several unresolved issues in the prism adaptation literature call for further investigations. First, both the immediate and long-term efficacy of this rehabilitation method has been questioned (Beversdorf & Heilman, 2003). Rousseaux, Bernati, Saj, and Kozlowski (2006) failed to find positive effects of prism adaptation either immediately after training or after an interval of three days, despite using almost the same rehabilitation procedure that had previously yielded significant effects (Rossetti et al., 1998). The efficacy of prism adaptation is also questioned by the fact that studies investigating long-term effects of the treatment have typically included patients that are either acute (Nys, de Haan, Kunneman, de Kort, & Dijkerman, 2008) or who could still be expected to show some spontaneous recovery (<six months postinjury, cf. Ferro et al., 1999). A related problem is that many studies do not include control groups, which makes it difficult to separate possible benefits of prism adaptation from simple practice and placebo effects (see however Serino et al., 2009). Second, most studies examining eye movements and visual search before and after prism adaptation have used simple, stylized objects or letter strings as stimuli. Neither solitary objects, (random) letter strings, nor simple idealised search displays mirror the visual demands that neglect patients face in the real world. A few studies have used tasks that more directly assess everyday behaviour such as searching for objects in a room (Frassinetti et al., 2002) or driving a wheel-chair (Jacquin-Courtois, Rode, Pisella, Boisson, & Rosetti, 2008), but these are exceptions. In general, more clinically relevant measures seem to be needed (Bowen & Lincoln, 2007a, 2007b; Cicerone, 2005). Third, the two mentioned studies on search performance after prism adaptation only investigated the outcome of a single training session, although many repeated sessions are the standard procedure in rehabilitation settings. The clinical relevance of prism adaptation treatment for visual search ability therefore remains unclear.

The main aim of the present study was to investigate the efficacy of prism adaptation training for visual search ability in chronic neglect patients. The general hypothesis was that training would lead to positive and stable changes in the lateral bias that is characteristic of search processes in neglect patients. The study was designed to address the methodological concerns presented above. To control for spontaneous recovery processes as well as placebo and nonspecific training effects, we investigated only patients in the stable phase of recovery and included a closely matched patient control group. Visual search ability was assessed on multiple functional levels. Besides using standard clinical tests we measured search in complex pictorial scenes, including a detailed analysis of eye movement patterns, as well as in a real-life situation. The assessment also included subjective measures of real-life improvements from patients and their relatives. To further ensure the clinical relevance of our findings we used a full-scale prism adaptation programme (20 sessions) and measured both the immediate and long-term effects of the treatment.

2. Methods

2.1. Subjects

11 patients (four females) with neglect after damage to the right side of the brain participated in the study, which was approved by the local ethical committee (KF, 01 283696). The mean age was 57 years (range 35–71). Informed consent according to the Helsinki Declaration was obtained from each person before participation. The patients were selected according to the following inclusion criteria: (1) significant neglect behaviour (defined as two or more clinical neglect tests where the patient scored below cut-off level, see below), (2) focal damage confined to the right side of the brain (confirmed by CT or MR scans), (3) stable phase of recovery (at least six months post injury), (4) age between 18 and 75 years, and (5) a spouse or other relative who was willing to evaluate the patient's daily function. Exclusion criteria were: (a) dementia (defined as a Mini Mental State Examination score < 24), (b) other severe neuropsychiatric disturbances (e.g., psychosis or major depression; assessed from medical records) or (c) poor visual acuity (Snellen score > 9/6).

A large number of medical records from four clinical institutions in the greater Copenhagen area were retrospectively screened for patients who had focal right hemisphere damage and clinically significant neglect (typically observed in the acute stage of recovery). This resulted in 28 potential participants, each of whom was invited to a screening session to check if the neglect symptoms had persisted into the stable phase of recovery. In this session seven tests for neglect were given: (1) Line bisection (cut-off: BIT score ≤ 7; Wilson, Cockburn, & Halligan, 1987), (2) Confrontation test for visual extinction (cut-off: $\geq$30% left-side omissions under bilateral stimulation and $\leq$80% correct reports under unilateral left-side stimulation; Vallar et al., 1994), (3) Mesulam Star Cancellation (max. 150 s allowed for each stimulus array; cut-off: $\geq$4 more omissions on the left side than on the right; Weintraub & Mesulam, 1985), (4) Mesulam Letter Cancellation (same as 3), (5) Text reading (Dan-

Table 1
Clinical and lesion characteristics.

Subject	Age/sex	Aetiology	Location (right hemisphere)	Postinjury	Hemianopia	Paralysis	<Cut-off
Experimental group							
E1	49/M	Infarct	Capsula interna	23	+	–	5
E2	63/F	Infarct	Occipito-parietal	18	–	–	5
E3	71/M	Infarct	Frontal	138	–	+	2
E4	61/M	Glioblast	Fronto-parietal + thalamus	6	–	+	3
E5	55/M	Haemo	Frontal (subarach.)	42	+	++	5
E6	51/F	Haemo	Temporal (subarach.)	12	+	–	5
Control group							
C1	60/F	Haemo	Frontal (subarach.)	22	–	–	3
C2	35/F	Infarct	Fronto-parietal	22	+	++	4
C3	52/M	Haemo	Temporo-parietal + thalamus	10	+	+	4
C4	63/M	Infarct	Fronto-parietal	11	+	+	5
C5	60/M	Haemo	Fronto-temporal	11	–	–	5

Aetiology: infarct, haemorrhage, or glioblastoma; Location: place of injury reported from MR or CT scan; Postinjury: months between injury and test A; Hemianopia: presence of left-sided hemianopia in confrontation test; Paralysis: "–" no motor difficulties, "+" left arm and hand slightly affected, "++" left-sided hemiplegia; <Cut-off: number of tests below cut-off of seven screening tests.

ish version of the BIT Article reading task; cut-off: ≥3% of the left-side words were omitted or misread), (6) Baking Tray task (cut-off: ≤6 elements placed in the left half of the tray; Tham & Tegnér, 1996), and (7) Complex figure copying (Rey-Osterrieth Figure; cut-off: ≥1 omission to the left; Hubley & Tremblay, 2002). 12 patients scored below cut-off levels in two or more of these tests and were thus characterized as having significant neglect. One of these patients was excluded due to an epileptic seizure during the training period, leaving 11 participants in the study. Visual field cuts were assessed by the confrontation method. See Table 1 for an overview of the patient data.

Patients were pseudo-randomly assigned to either an experimental group or a control group. The experimental group received two weeks of prism adaptation training (adding up to five hours of training in total; see details in Section 2.2). During the same period, the participants in the control group on average received eight hours of general cognitive rehabilitation. Two control patients took part in out-patient cognitive courses at a rehabilitation centre involving supervised, group-based sustained attention training and reading and writing exercises. One patient was in a full-time rehabilitation programme involving both individual and group-based attention and working memory training as well as supervised work-related tasks. The last two control patients spent 30–45 min per day on a computer-based rehabilitation programme at home. Furthermore, three out of the five control participants received at least two hours of physiotherapy and circulatory system exercise each week. The randomization procedure was designed to yield an approximately equal number of patients in each group and worked as follows: The first two participants drew from a set of two available slots in each group. For each additional participant, one more potential slot was added to each group if the distribution of patients was so far equal. If the distribution was unequal two slots were added to the smallest group. This pseudorandomisation resulted in five patients being allocated to the control group and six to the experimental group. At baseline there were no significant differences between the two patient groups in terms of age, gender, education, time since injury, prevalence of hemianopia, scores on any of the above mentioned neglect tests, or in the number of screening scores below cut-off.

2.2. Treatment procedure

The prism adaptation training followed the procedure laid out by Frassinetti et al. (2002). The whole training programme lasted two weeks (10 individual days). Patients were trained two times daily (separated by a break for 90 min) with each session lasting approximately 15 min. The task was to point to a visual target with the right index finger while wearing prismatic goggles that shifted the visual field 10 degrees rightward. The goggles had a large viewing area and a thick black frame minimizing the part of the visual field not distorted by the prisms or covered by the frame. The visual targets were presented randomly at one of three positions, either directly in front of the patient or 21 degrees to the left or the right. Each of the three positions was located 60 cm away from the patient's midline. Patients pointed through a box that shielded the movement visually from their perspective. The box could be calibrated either to hide the movement completely or to reveal the index finger at the very end of the pointing trajectory. The distal edge of the box was graduated (in degrees) allowing the experimenter to note deviations in the patients' pointing accuracy.

Each training session comprised three different conditions. In the *pre-exposure* condition pointing was performed without goggles. Pointing was first done with no visual feedback of performance to obtain a measure of the baseline level of pointing accuracy (30 trials; only performed in the first training session since this measure could hypothetically be influenced by training in later sessions), then with feedback serving as baseline comparison for the exposure condition (30 trials). In the *exposure* condition the patient wore prismatic goggles and performed 90 pointing movements while receiving visual feedback on the landing position of the finger. The feedback enabled the patient to progressively correct the pointing errors induced by the prism goggles. In the *post-exposure* condition, immediately after the goggles had been taken off, the task was to point 30 times without visual feedback. The goggles used for training were constructed from a pair of standard glasses with a large viewing area covered with Fresnel prisms of 15 dioptre from 3 M, that shifted the visual field approximately 10 degrees to the right.

2.3. Effect measures: assessment of neglect behaviour

To monitor the effect of the training procedure, all patients were tested three times: At baseline (time A), within a day or two after training (time B), and five weeks later (time C). The effect measures covered three general domains: clinical testing, distribution of eye movements during a visual search task (the Where's Wally test), and everyday functioning measured by a naturalistic search task (the Cupboard test) as well as a questionnaire for behavioural observations in daily life. The two search tasks and the questionnaire were specifically designed for the present study. The clinical tests were employed in the order described in the screening procedure (see Section 2.1). They were followed by the Cupboard test and the Where's Wally test. The same test sequence was used in all three sessions to avoid confounding test performance with possible decreasing alertness over the course of a test session.

2.3.1. Clinical neglect testing

Some of the tests used to screen for neglect were also used as effect measures: Line bisection, Mesulam Star Cancellation, Mesulam Letter Cancellation, the Baking Tray task, and the copying of complex figures (to avoid retest effects, Rey's complex figure was replaced by Taylor's complex figures I and II at testing times B and C, respectively).

2.3.2. Measurement of eye movements during search

To measure possible changes in eye movements when searching for a target in complex visual scenes the Where's Wally test was devised. "Where's Wally" is a series of children's books (Handford, 1997, 2001, 2004) consisting of large illustrations of hundreds of tiny people doing various things in extremely crowded settings where the task is to find a certain character called Wally (see Fig. 3). Thus, the test served as an experimentally controllable version of the everyday attentional problem of finding a face or a person in a large crowd. Using excerpts (in dimensions 3:4) of the full-page illustrations and in some cases mirroring these, 30 different scenes were made. All scenes were resized to 1024 by 756 pixels and converted to gray scale colours in order to avoid a colour pop-out effect caused by Wally's characteristic red and white clothes. The scenes were rated for search difficulty on a subjective scale from 1 to 5 (1 being the easiest and 5 the most difficult) by four healthy, young subjects and divided into three groups with equal total difficulty to be used at the three consecutive sessions. During the ten scenes of a session Wally would appear five times on the left side and five times on the right side of the picture (specifically, three times in both upper quadrants and two times in both lower quadrants of the scenes).

Eye movements were recorded using the Eyelink II system (SR Research Ltd., Canada), which consists of three miniature cameras mounted on a padded headband; Two eye cameras allow binocular eye tracking by measuring pupil position at 250 Hz and an optical head-tracking camera integrated into the headband is used to correct for any head movements. Accurate information on the duration and position of fixations as well as the amplitude and direction of saccades are directly available after an initial calibration procedure.

Subjects were tested in a dimly lit room and positioned about 60 cm from a 19″ CRT screen. For the calibration procedure a 9-point grid was used, and to avoid movement confounds drift correction was performed before each new scene. Every trial began with a drift correction after which a primer showing Wally against a

Fig. 1. Example of the Cupboard test setup. In each session 40 everyday objects, 10 targets and 30 distractors, were distributed evenly on three shelves as shown in the photograph.

white background came on to remind the subject of what to look for. When the subject indicated that he/she was ready a fixation cross came on for 3 s at the centre of the screen before the actual scene was shown. The scene was terminated once the subject had found Wally or after 120 s if the subject had not found Wally within that time. The subjects were instructed to find Wally as quickly as possible and retain fixation once they had found him. Before the test started it was stressed that Wally would appear only once in each scene and equally often to the right and left sides. Finally, subjects were reminded to search the entire scene. In addition to recording the number of fixations and fixation duration during search, the subjects' reaction times and the number of missed targets as a function of target side were also measured.

2.3.3. Measures of everyday functioning

A very common complaint of neglect patients is difficulty finding ordinary household objects in cupboards or closets; 8 out of our 11 participants spontaneously mentioned this at the baseline examination. We designed the Cupboard test to assess performance in this naturalistic situation under standardized conditions. In the Cupboard test 30 everyday objects (e.g., keys, brush, shaver, beer can) are arranged in a fixed setup on three shelves in a cupboard (see Fig. 1). Ten of the objects are search targets, whereas the remaining twenty serve as distractors. Five of the targets are located in the left side of the cupboard, five to the right side. With the patient standing directly in front of the cupboard, the names of twenty objects (half of them present, half of them absent; in random order) are read out, one by one. The task is to report as quickly as possible whether a given object is present in the cupboard. When retesting at times B and C, 10 new targets (as well as 10 new absent items on the list) were introduced, while the 20 distractor objects were rearranged. Reaction times (measured by stopwatch) and errors as a function of target side were registered.

We also wanted to assess a more broad range of the patients' everyday functions by means of self-report. To this end, we developed a set of questions in consultation with a group of experienced clinical neuropsychologists from the Danish Center for Brain Injury Rehabilitation. The questionnaire contained 24 questions on the patient's subjective experiences within seven different functional domains: (A) deficit awareness, (B) ADL-function (ADL, Activities of Daily Living), (C) motor function, (D) spatial orienting, (E) reading/writing, (F) transportation, and (G) social interaction. Examples are: "do you experience problems brushing your teeth?" (category B), "do you find it difficult to find your way around your local area?" (category D), and "do you sometimes bump into people on your left?" (category G). The questionnaire was given to the patient at baseline (time A) and five weeks after training (time C). Patients were instructed to answer the questions based on experiences from the last two weeks. To support memory, the patient filled out a short observation form every evening for two weeks before answering the questionnaire. The task was to write down specific experiences from the same day within each of the functional areas. The reports in the questionnaire were made on a 5-point Likert scale (never, rarely, occasionally, often, always; plus "irrelevant"). The questionnaire was also given to the patient's relative (with questions phrased in the third instead of the first person) at both baseline and five weeks following training.

3. Results

3.1. Prism adaptation

For all pointing conditions the mean deviation in visual angle between the finger and the visual target was calculated (positive values for rightward deviance, negative for leftward deviance). To assess the patients' ability to adapt to the optical displacement induced by the goggles the *error reduction* (mean pointing deviance in the exposure condition) and the *after effect* (mean pointing deviance in the post-exposure condition) were examined for each individual subject. The hypotheses were that (1) if patients were able to effectively compensate for the prismatic displacement, little or no difference should be observed between the exposure condition and the pre-exposure condition with visual pointing (error reduction), and (2) if the adaptation procedure was efficient, a systematic deviation of pointing towards the left should be observed in post-exposure condition compared to the pre-exposure condition with invisible pointing (after effect). The average pointing performance in the three training conditions is shown in Fig. 2A. Paired samples t-tests comparing error reduction and after effect to pre-exposure performance supported the two hypotheses; error reduction (mean = 0.17°) was not significantly different from the mean pointing deviation in the pre-exposure condition with visible pointing (mean = −0.06°) ($t(5) = -2.12$, $p = .088$). In contrast, the after effect (mean = −1.96°) showed a significant leftward deviance compared to the pre-exposure condition with invisible pointing (mean = 0.29°) ($t(5) = 8.46$, $p < .001$). However, the first comparison approached statistical significance, which might be due to a continuous online correction throughout the 90 trials in the exposure condition. An initially large deviation followed by a gradual adaptation could lead to an inflation of the difference between the error reduction and the pre-exposure condition. To test this explanation, the exposure condition was divided into three parts with 30 trials in each (Exp1, mean = 0.39°; Exp2, mean = 0.12°; Exp3, mean = −0.01°). The mean values clearly show that pointing displacement was largest during the first 30 trials after which the deviation was gradually reduced and approached 0° in the last 30 trials (see Fig. 2B). A repeated measures ANOVA with one within-subjects factor, "Level of exposure", and three levels (Exp1, Exp2, and Exp3) confirmed that there was a significant effect of the level of exposure ($F(2, 10) = 15.65$, $p = .001$). That a full adaptation had occurred during the exposure condition was also evident from the fact that no difference between the last 30 trials of the exposure condition and the pre-exposure condition with visible pointing was found ($t(5) = -.61$, $p = .57$).

3.2. Main effect measures

All effect measures except the questionnaire were analysed using two-way mixed ANOVAs with session (A, B, and C) as within-subjects factor and group (experimental and control) as between-subjects factor. Unless specifically stated all effect measures showed no difference between the two groups at baseline. An alpha level of .05 was used for all statistical tests. Effect sizes for the

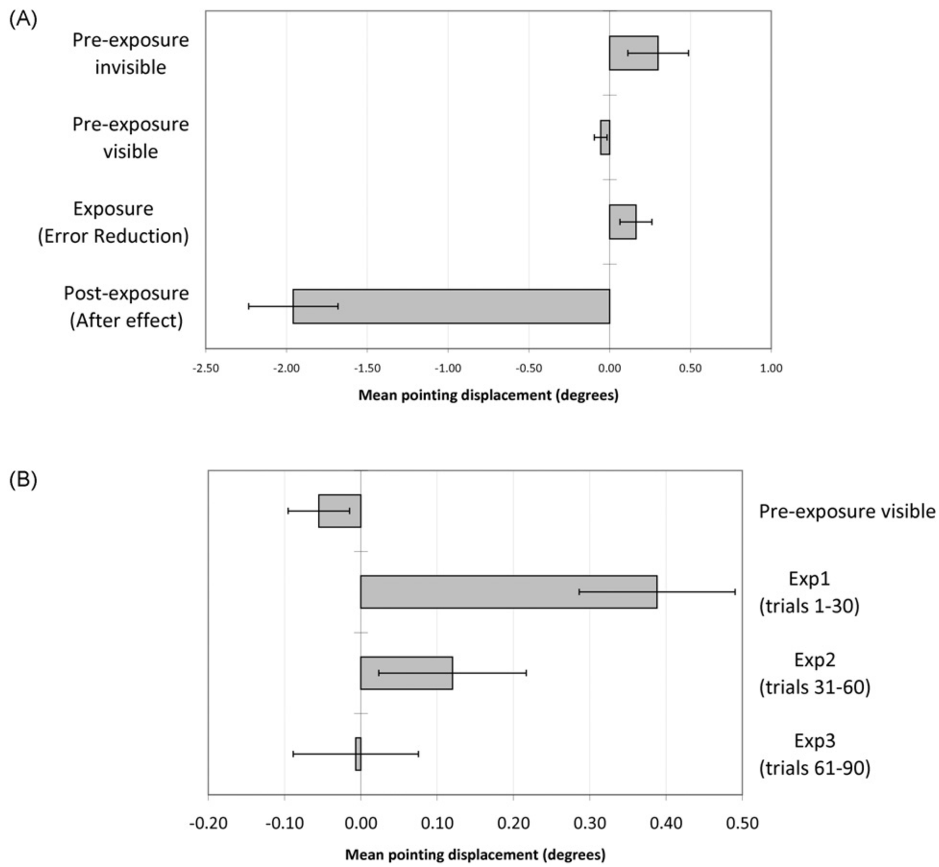

Fig. 2. Panel A shows the mean pointing displacement for all patients in the experimental group in different conditions of the prism adaptation procedure. Panel B shows the mean pointing displacements during three different parts (Exp 1–3) of the exposure condition compared with visible part of the pre-exposure condition.

interaction effects are stated as partial η^2-values (for a discussion on the use of partial η^2 as a measure of effect size see Pierce, Block, & Aguines, 2004). Effect sizes for independent samples *t*-tests are stated as Cohen's *d*-values.

3.2.1. *Clinical neglect testing*

The scores on the Mesulam Star Cancellation test were calculated as the difference between the number of omissions in the left vs. right side. Neither the main effects of session nor group were significant, $F(2, 18) = 2.78$, $p = .09$; $F(1, 9) = 0.002$, $p = .96$. However the ANOVA showed a highly significant interaction effect between group and session, $F(2, 18) = 11.30$, $p = .001$, $\eta_p^2 = .56$. The patients in the experimental group strongly improved from the baseline level (mean = 9.8 errors) to session B (mean = 3.2 errors) and maintained this level at session C (mean = 2.8 errors), whereas the scores of the patients in the control group actually declined over time (mean = 3.6 errors at baseline vs. mean = 5.8 errors and mean = 6.0 errors at sessions B and C, respectively; the trend was not significant). The results were very similar for the Letter Cancellation version of the Mesulam search task: Again the main effect of group was not significant ($F(1, 9) = 0.74$, $p = .41$), but there was a main effect of session: $F(2, 18) = 4.19$, $p = .032$. More importantly, the ANOVA showed a significant interaction between group and session ($F(2, 18) = 8.17$, $p = .003$, $\eta_p^2 = .48$). Scores in the patient group strongly improved from baseline (mean = 8.3 errors) to session B (mean = 3.0 errors) and session C (mean = 2.5 errors). In contrast, the control patients performed similarly over time (mean = 7.2 errors at baseline vs. mean = 8.6 errors at session B and mean = 7.8 errors at session C).

The effect measure in the Baking Tray task was the average deviation (in cm) from the midline of the 16 elements (left: positive, right: negative). Testing showed no main effects of session ($F(2, 18) = 1.48$, $p = .25$) nor group ($F(1, 9) = 0.47$, $p = .51$), but a significant interaction between the two main factors, $F(2,18) = 5.73$, $p = .012$, $\eta_p^2 = .39$. The leftward deviation in the experimental group went from an average of 5.5 cm at baseline to 1.3 cm in session B and 2.4 cm in session C. There was a reverse (non-significant) trend in the control group towards poorer performance over time: From a mean deviation at baseline of 2.7–4.1 cm in session B and 6.1 cm in session C. No significant results, either in main effects or interactions, were found for the two other effect variables in the clinical test category: Line Bisection and Figure Copying.

3.2.2. *Eye movements during visual search*

To test whether prism adaptation had induced a leftward bias in the Where's Wally search task, differences in the number of fixations and the total fixation time during search in the left vs. right sides of the scenes were analysed. For each session comprising 10 trials, two lateralization indices were calculated by dividing the number of fixations in the left hemifield with the total number of fixations (and similarly for the fixation duration). This resulted in an index between 0 and 1, with .5 indicating a perfectly equal spatial distribution between left and right and 0 indicating no fixations (or no fixation duration) in the left hemifield. See Fig. 3 for an example. The hypothesis was that the neglect symptoms of the participants would be reflected in below 0.5 values in both indices before prism adaptation, but that they would increase significantly after prism adaptation for the experimental group whereas the control group would show similar values regardless of the time of testing.

At baseline the patient group as a whole clearly exhibited neglect behaviour: The fixation count index was significantly lower than 0.5 ($t(10) = -2.68$, $p = .02$, $d = 1.69$), which was also the case

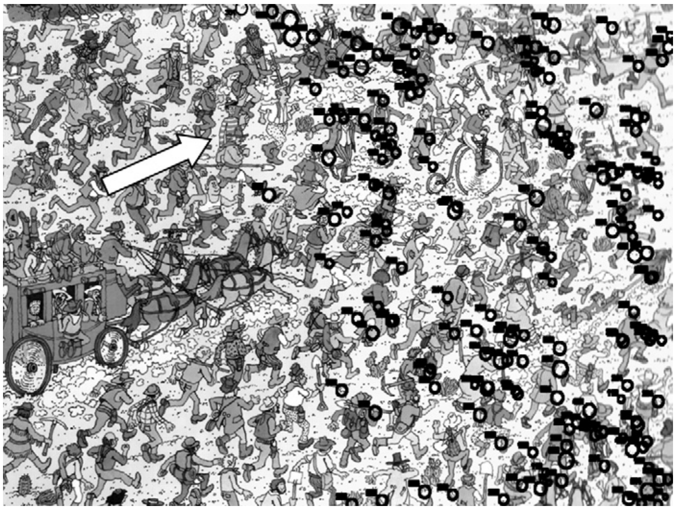

Fig. 3. Severe rightward eye movement bias in the Where's Wally test at the baseline testing of experimental patient E3. Each circle represents a fixation and the circle size reflects the duration of the fixation. "Wally" dressed in striped sweater and glasses was located in the upper left quadrant of the picture (shown by the white arrow) and the laterality index of this scene was 0.09 for fixation durations and 0.07 for the number of fixations. At baseline the average indices for this patient were both 0.18, after the intervention they had risen to 0.32 (fixation duration) and 0.33 (number of fixations). This indicates that the extreme rightward bias had been markedly reduced, corresponding to a two-fold increase in the total duration and number of fixations spent on the left side.

for the fixation duration index ($t(10) = -2.66$, $p = .02$, $d = 1.68$). See Table 2 for an overview of the main results. A 2-way mixed ANOVA on the fixation count index showed no significant main effects (session: $F(2, 18) = 2.44$, $p = .12$; group: $F(1, 9) = 0.03$, $p = .87$). The interaction between group and session was however significant, $F(2, 18) = 4.59$, $p = .024$, $\eta_p^2 = .34$. Similarly, for the fixation duration index there were no main effects of session nor group (session: $F(2, 18) = 2.59$, $p = .10$; group: $F(1, 9) = 0.03$, $p = .86$), but a significant interaction between the two main factors, $F(2,18) = 5.74$, $p = .012$, $\eta_p^2 = .39$. Thus, the hypothesis was supported for both main measures.

Search accuracy in the Where's Wally test was scored similarly to the Mesulam search task, as the difference between the number of missed targets in the left and right side during the session (10 trials). At baseline the patient group as a whole overlooked significantly more targets to the left ($t(10) = -3.07$, $p = .01$, $d = 1.94$). There was no main effect of group ($F(1, 9) = 0.35$, $p = .57$), but both groups improved over time resulting in a main effect of session, $F(2, 18) = 8.15$, $p = .003$. However the improvement in the experimental group was larger than in the control group, giving rise to a significant interaction effect, $F(2, 18) = 3.66$, $p = .047$, $\eta_p^2 = .29$.

Another measure of search efficiency is the reaction time, specifically the difference between the time taken to find Wally in the left and right side. To reduce the distorting effect of reaction time outliers, the analysis was conducted using the median reaction time of each participant. At baseline, the patient group as a whole was significantly slower to detect left-side targets ($t(10) = 3.09$, $p = .01$, $d = 1.95$). There was no main effect of neither session ($F(2, 18) = 2.3$, $p = .13$) nor group ($F(1, 9) = 0.40$, $p = .54$). The interaction between session and group was significant: $F(2, 18) = 4.18$, $p = .03$, $\eta_p^2 = .32$. As can be seen from Table 2 the interaction effect was caused by a nearly stable reaction time pattern over sessions in the control group, whereas the reaction time asymmetry in the experimental group was essentially normalised by session C.

3.2.3. *Everyday function*

In the Cupboard test, one effect variable was the difference in the number of omissions between leftsided and rightsided targets. At baseline the whole group of patients had a clear tendency to overlook more items in the left side ($t(10) = 3.35$, $p = .007$, $d = 2.12$). Testing showed no differences between the experimental and control group (main effect of group, $F(1, 9) = 0.05$, $p = .83$) but a significant effect of the time of testing (main effect of session, $F(2, 18) = 5.59$, $p = .013$). The performance of the control group was nearly constant over time whereas the performance of the experimental group was nearly normalised by the follow-up testing (see Fig. 4A). This difference resulted in a significant interaction effect, $F(2, 18) = 4.14$, $p = .033$, $\eta_p^2 = .32$.

The other effect variable in the Cupboard test was the difference in search time between targets located in the left and right side of the shelves. Again, in the patient group as a whole, there was a strong tendency at baseline to respond slower to left-side targets ($t(10) = 4.27$, $p = .02$, $d = 2.66$). There were significant main effects of both session ($F(2,18) = 6.7$, $p = .007$) and of group ($F(1, 9) = 8.07$, $p = .019$). Further a significant group by session interaction was found, $F(2, 18) = 10.25$, $p = .001$, $\eta_p^2 = .52$. The patients in the experimental group went from a mean difference in reaction times of 2.3 s at baseline to a difference of 0.8 s in session B and −0.9 s (i.e., faster in the left side) in session C. In comparison, the patients in the control group had a mean difference in reaction times between the two sides of 3.7 s at baseline, 4.1 s in session B, and 4.1 s in session C (see Fig. 4B).

The second measure of everyday function was the questionnaire, which aimed at highlighting the participants' subjective experience of functional improvements. The results of the patients and their relatives were treated separately to check for discrepancies in their answers. To examine the agreement between the

Table 2
Results from the Where's Wally test.

Time	Number of fixations (laterality index)		Fixation duration (laterality index)		Target accuracy (Left–right targets)		Target reaction time (Left–right RT)	
	M	SD	*M*	SD	*M*	SD	*M*	SD
Experimental								
A	0.33	0.07	0.32	0.07	−2.00	0.52	28.60	12.93
B	0.37	0.07	0.37	0.07	−1.33	0.42	11.41	11.46
C	0.44	0.07	0.43	0.07	0.17	0.48	−3.21	9.89
Control								
A	0.42	0.06	0.42	0.07	−0.80	0.80	17.12	6.86
B	0.37	0.04	0.37	0.04	−0.80	0.58	22.23	9.59
C	0.39	0.05	0.39	0.04	−0.40	0.40	21.73	8.33

Number of fixations and Fixation duration: all results are based on a laterality index where .5 indicates perfect balance between left and right side of the scenes, and 0 an exclusive rightward bias; Target accuracy: difference in the mean number of targets found on the left side vs. targets found on the right side of the scenes (negative values indicate that more right sided targets were detected); Target reaction time: difference in the mean reaction time (seconds) taken to detect a left sided versus a right sided target (negative values indicate that left sided targets were detected faster).

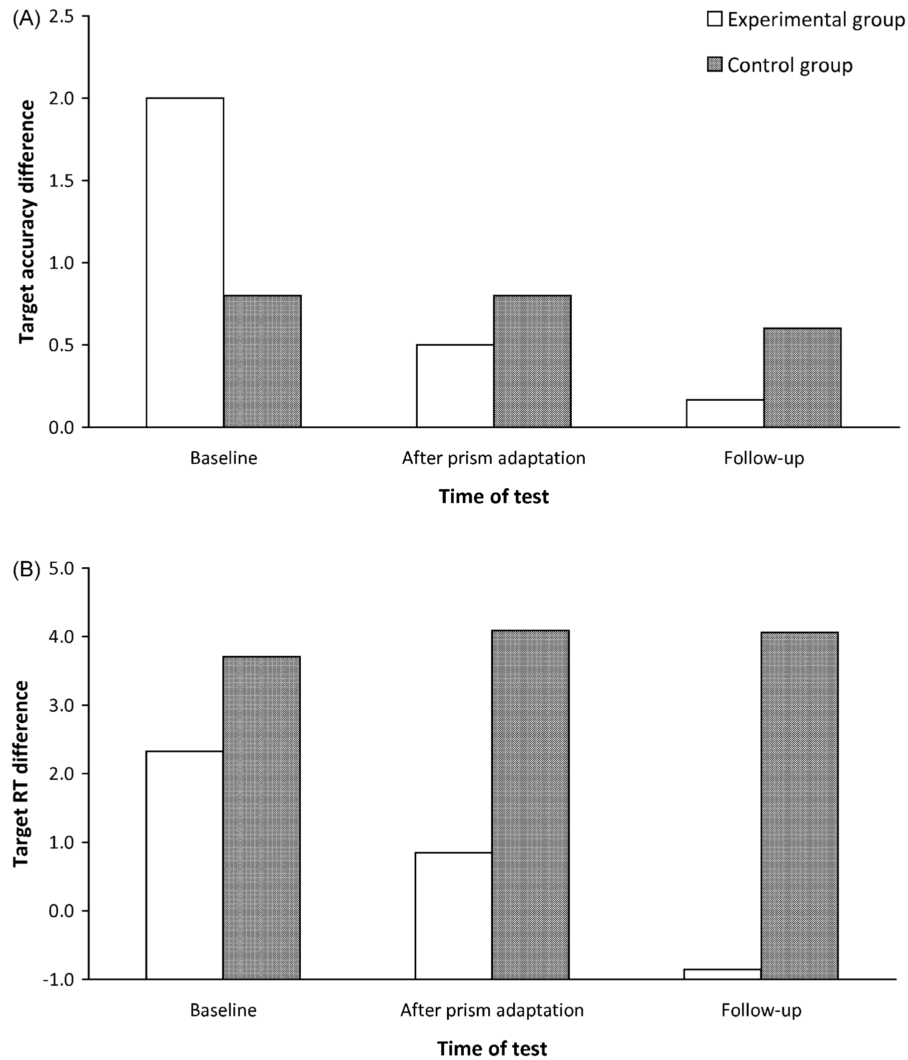

Fig. 4. Performance on the Cupboard test for the experimental group (white) and the control group (grey) at different test times. Panel A shows the target accuracy score given by the difference between omitted targets on the left side and the right side of the cupboard. Panel B shows the difference in seconds between the average reaction time of a leftsided target versus a rightsided target. For both variables a score of "0" implies no difference between left and right, whereas positive values reflect a rightward bias in performance.

reports of these two groups the sum of the reported answers at baseline and follow-up was compared between pairs of patients and relatives. The lowest possible sum score of 24 could only be obtained if the participant answered "never" to all the questions and the highest possible sum score of 120 could only occur if the participant consistently answered "always". At both baseline (mean sum score patients: 54.55 and relatives: 49.55) and the follow-up session (mean sum score patients: 46.55 and relatives: 43.45) the sum scores of the patients and their relatives were strongly correlated, baseline: $r(9) = .80$, $p = .003$ and follow-up: $r(9) = .85$, $p = .001$. These results indicate a high level of agreement between patients and relatives, which was further supported by paired samples t-tests showing that the patients and relatives did not differ significantly from one another neither at baseline: $t(10) = 1.79$, $p = .10$, nor at follow-up: $t(10) = 1.58$, $p = .15$. Therefore only results from the patients will be presented in the following.

The average change in every variable was calculated separately for the experimental group and control group. In one of the 24 variables the number of reports was not sufficient and it had to be excluded, leaving 23 variables for the rest of the analysis. The experimental group showed a larger positive change than the control group in 18 out of the 23 variables, while four of the variables showed no difference in effect between the groups. Only in one case (for the variable "When drawing I use mainly the right side of the paper") did the control group experience a larger positive effect than the experimental group. This result was highly significant ($T = 23.5$, $p = .001$, $r = .7$).

To examine in which areas of daily life the changes were most pronounced, we grouped the variables into their predefined categories (see Fig. 5). Several conclusions can be drawn from this analysis. The experimental group experienced larger positive changes than the control group in all main categories. Further, the average positive change in the experimental group was 0.55, whereas for the control group it was almost non-existent at 0.09, a very large effect that was highly significant when comparing the two groups within the seven categories in a t-test, $t(6) = 7.21$, $p < .001$, $d = 5.89$. The retest reliability of the questionnaire was assessed by comparing the sum of the reported answers at baseline and at follow-up in the control group, where no change between the two sessions should be expected. These sum scores (baseline: mean = 51.4 and follow-up: mean = 49.4) showed a significant and very strong correlation, $r(3) = .94$, $p = .02$, signifying virtually no change in responses from the first to the second questionnaire session.

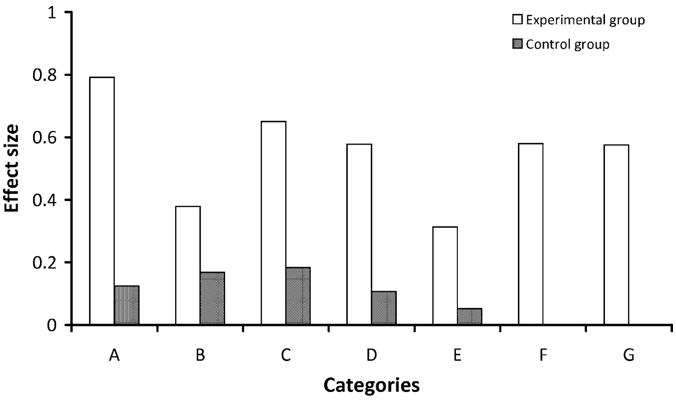

Fig. 5. Average effect of experimental (white) and control patients (grey) for each category in the questionnaire: (A) Deficit insight, (B) ADL-function, (C) Motor function, (D) Spatial orientation, (E) Reading/writing, (F) Transportation, and (G) Social interaction. A change of 1 corresponds to a positive change from for example "often" to "sometimes" on the five point Likert scale used.

In summary, in addition to improvement in the experimental group's self rating of function, nine of the eleven effect variables in the study showed a significant interaction effect between group and time of testing, all in the predicted direction (see Table 3). The treatment effects were quite pure (i.e., limited to interactions): only in one case, the Cupboard test reaction time measure, was there a significant general difference between the experimental group and the control group. The majority of variables showed no significant effects of the time of testing, which supports that the positive findings in the experimental group were not due to general training effects. The limited sample size of this study makes it particularly important to consider if the experimental design used provides sufficient statistical power to detect relevant treatment effects. Using the programme G*power (Faul, Erdfelder, Lang, & Buchner, 2007) to assess the design employed here ($n = 11$, two groups, three repeated measures, an alpha-level of .05 and – following Cohen, 1994 – a desired power of .80) we found that any treatment effects should be close to medium (.30) to be detected. In other words, with only eleven patients we might not detect small but relevant treatment effects. However, this also shows that the treatment effects reported in this study are of a considerable size

3.3. Effects of hemianopia

It has been suggested that hemianopia aggravates the symptoms of neglect patients (Gainotti, De Luca, Figliozzi, & Dorrichi, 2009) and that large occipital lesions (causing visual field cuts) might impair patients' responsiveness to prism adaptation (Serino et al., 2006). To explore the effects of hemianopia, the performance at baseline of patients with hemianopia ($n = 6$) was compared to performance of patients with a full visual field ($n = 5$). One-way ANOVA tests showed no significant differences between the two groups in any of the neglect measures presented in Table 3 (all p-values > .14). Further, we found no differences in the sizes of the treatment effects shown by the experimental group depending on the presence of hemianopia: In a two-way mixed ANOVA with session (A, B, and C) as within-subjects factor and hemianopia (present or absent) as between-subjects factor, all interaction effects were non-significant (all p-values > .40).

4. Discussion

This is the first study to investigate the efficacy of a full-scale prism adaptation programme on multiple levels of visual search performance in chronic neglect patients. The results clearly support the value of prism therapy: On nine out of eleven effect measures, patients in the experimental group showed significant amelioration of their neglect symptoms after the training programme. The positive changes were evident both a few days following training and at a follow-up investigation five weeks later. In standard clinical tests of neglect, the measures that improved the most were two cancellation tasks that involve search for simple objects. To investigate search of more complex visual scenes, we devised the Where's Wally test, which mimics the demanding situation of finding objects or people in crowded settings. The task allowed for a detailed quantification of search performance through changes in eye movements, reaction times, and accuracy. Prism adaptation resulted in an attenuation of the rightward bias in eye movements and a marked improvement in both reaction time and search accuracy. To evaluate visual search performance in a more naturalistic setting, the Cupboard test was designed. The test assesses one of the most common everyday complaints of neglect patients: Inability to find objects in cupboards, closets, and the like. Again, patients in the experimental group were significantly better and

Table 3
Results from analyses of variance for the effect measures.

	Group (G)			Session (S)			G × S		
	df	*F*	*p*	*df*	*F*	*p*	*df*	*F*	*p*
Clinical measures									
Line bisection	1	0.02	n.s.	2	1.25	n.s.	2	0.22	n.s.
Star cancellation	1	0.00	n.s.	2	2.77	n.s.	2	11.3	***
Letter cancellation	1	0.74	n.s.	2	4.19	n.s.	2	8.17	**
Baking Tray task	1	0.47	n.s.	2	1.48	n.s.	2	5.73	*
Figure copying	1	0.34	n.s.	2	3.65	n.s.	2	1.52	n.s.
Where's Wally test									
Laterality fixations	1	0.03	n.s.	2	2.44	n.s.	2	4.59	*
Laterality duration	1	0.03	n.s.	2	2.59	n.s.	2	5.74	*
Target difference	1	0.35	n.s.	2	8.15	n.s.	2	3.66	*
RT difference	1	0.40	n.s.	2	2.3	n.s.	2	4.18	*
Cupboard test									
Target RT	1	8.07	*	2	6.7	*	2	10.25	*
Target ACC	1	0.05	n.s.	2	5.59	*	2	4.14	*

n.s. = not significant.
Group: Main effect of Group (Experimental and Control); Session: Main effect of Session (A, B and C); G × S: Interaction effect of Group and Session.
* $p < .05$.
** $p < .01$.
*** $p < .001$.

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faster at finding left-sided objects after prism adaptation. Finally, in the questionnaire that was used as the second everyday measure, the experimental group reported substantial positive changes after prism adaptation in a large majority of the function variables. There was a high degree of consistency between the replies of the patients and their relatives, which indicates that the participants did not lack awareness of their symptoms and disabilities. The positive changes that could be observed in the experimental group were not mirrored by similar changes in a matched control group of neglect patients. On the contrary, the control group showed no systematic variation in their performance over the three test sessions.

Our results contrast with a number of studies that have found no or negligible effects of prism adaptation. Rousseaux et al. (2006) could not replicate immediate effects nor sustained benefits (three days) after adaptation. Ferber et al. (2003) found no functional relevance of changes in eye movements after prism adaptation, which supports the claim that prism adaptation does not improve the core, attentional aspects of the neglect syndrome (Morris et al., 2004). Furthermore, studies focusing specifically on changes in visual search performance have either not found any beneficial effect (Morris et al., 2004) or a transitory effect disappearing after feedback (Saevarsson et al., 2009). These results challenge the general usefulness of prism adaptation as a rehabilitation tool. However, the null findings in these studies may be explained by the specific methods and procedures employed. A common feature is that the effect was measured after just one session of prism adaptation. Though amelioration of neglect symptoms after one session has been reported (e.g., Rossetti et al., 1998), several authors claim that any symptom reduction after a single session is short lived and that a full prism adaptation programme is required stabilise the effects for the majority of patients (Serino et al., 2009; Redding & Wallace, 2006b). Morris et al. (2004) and Saevarsson et al. (2009) however suggested alternative explanations for their negative results: the use of time limited tests and feedback on performance. Morris et al. claim that speeded effect measures are more sensitive in detecting residual neglect symptoms (not affected by prism adaptation) that the patients can compensate for in unspeeded tests. Saevarsson et al. propose that feedback promotes strategic thinking, which adds to the cognitive load of the task and interferes with the adaptation effect. Our findings contradict these hypotheses. We observed positive effects on both time restricted (e.g., the Where's Wally search task and the cancellation tasks) and unrestricted measures (e.g., the Cupboard test and the Baking Tray task). Furthermore, the Where's Wally test included feedback after every trial, which may have added to the strategic thinking of the patients, but in any case did not disrupt the positive effects of prism adaptation in this task. Indeed, if feedback disrupts the effects of prism adaptation, the continuous everyday feedback that patients receive from their surroundings should have abolished all positive effects during the five week period before the follow-up test. We found no sign of such decay, but a very stable effect over time. In fact, test performance was typically slightly better at follow-up compared to immediately after training. Overall, our results support the claim that an extended prism training programme is necessary for stable improvements.

The positive effects that we observed are in agreement with several other studies (Frassinetti et al., 2002; Keane, Turner, Sherrington, & Beard, 2006; Nys et al., 2008; Sarri et al., 2008; Serino, Bonifazi, Pierfederici, & Làdavas, 2007; Shiraishi et al., 2008), but extend these investigations in various ways. As explained in the introduction several methodological concerns may be raised in relation to most studies that have investigated prism adaptation as a rehabilitation tool. For the sake of comparison only studies that employed a full adaptation procedure (at least several days of training) will be taken into consideration. First of all, control groups have not been regularly used in these studies (e.g., Keane et al., 2006; Serino et al., 2007; Shiraishi et al., 2008), which makes it difficult to conclude if prism adaptation is the determining factor in the positive changes observed after training. To address this concern we included a patient control group that was randomly selected and matched on several important parameters (age, gender, education, neglect severity, presence of hemianopia, and post-injury time). The importance of a control group becomes particularly pronounced if one cannot be certain that the patients are in the stable phase of recovery. In a large study of spontaneous recovery in neglect patients Farnè et al. (2004) concluded that spatial attention deficits improved partially during the acute phase (<6 weeks after stroke), but that improvements of neglect symptoms were still taking place at least three months after their injury. This time line is supported by a review study where it was found that the majority of neglect patients who present with symptoms in the acute phase recover within three to six months after their injury (Ferro et al., 1999). Apart form a study by Shiraishi et al. (2008) that did not include a control group, our study is the only one that has exclusively used patients who are at least half a year post-stroke. The mean post-injury interval in our patients was in fact as long as 29 months (range 6–138 months). In all other comparable investigations over half of the neglect patients in the intervention groups were less than six months post-stroke (Frassinetti et al., 2002; Keane et al., 2006; Nys et al., 2008; Sarri et al., 2008; Serino et al., 2006, 2007) and in one case several patients had less than three months to recover before testing (Serino et al., 2009). This variable use of the term "chronic patient" makes it difficult to evaluate the possibility of spontaneous recovery versus the effect of prism adaptation. Further, establishing the chronicity of the patients is crucial when investigating the long-term benefits of prism adaptation. No studies using a prolonged (several days) adaptation programme have failed to find immediate effects of prism adaptation, but only a handful of studies have investigated the long-term amelioration of neglect symptoms (Frassinetti et al., 2002; Nys et al., 2008; Serino et al., 2006, 2007, 2009). Though these studies generally found lasting improvements at the follow-up test(s), none of them included both a control group and patients that were at least six months post-injury as in the present study.

Although we did include a matched control group, one should still consider whether the improvements in the experimental group could have arisen due to placebo or other non-specific mechanisms (e.g., test–retest effects). We find this unlikely for several reasons. First, there is nothing in the prism adaptation procedure per se that gives preference to the left hemispace: The training involves an equal number of pointing motions towards the left, right, and straight ahead. Second, the patients in the control group also received an extensive amount of other training during the study period, which should have induced similar deficit awareness and placebo effects. Third, the timing and content of the test battery was identical for the two patients groups, which should rule out changes due to test–retest effects. Overall, the fact that only the experimental group improved over time seems directly related to the prism training.

Another critical issue is the functional measures chosen to elucidate the effects of prism training. Recalibration of the oculo-motor system is often suggested as the main mechanism underlying the beneficial effects of prism adaptation (Serino et al., 2006, 2007; Shiraishi, 2008). This hypothesis strongly points towards measurements of eye movements and visual search performance. Deficits in these functional areas are also central features of the neglect syndrome, as mentioned in the introduction. Prior investigations of eye movements and visual search after prism adaptation have almost exclusively used letter strings (e.g., Angeli, Benassi et al., 2004; Angeli, Meneghello et al., 2004; Serino et al., 2009), a type of stimuli that comes with important limitations. Letter strings often trigger highly overlearned responses of reading behaviour (i.e., scanning from left to right), which set them apart from most other search situations and may obscure the changes in spontaneous orienting bias that are induced by prism adaptation. Further, letters and words are only negligibly similar to the complex visual impressions of everyday life. While reading is one important functional area for patients, many other aspects of visual search and orienting do not seem to be well characterized by such tasks. In our investigation we therefore employed a variety of different stimulus types: letters, simple objects, faces, and real 3D objects. We also targeted visual search ability in multiple settings, ranging from stylized paper-and-pencil tasks to search of complex visual scenes and naturalistic situations. All of these tasks were challenging enough to elicit neglect-like performance, and our measures may therefore be said to represent more levels of relevant search behaviour than previous studies in the prism adaptation literature.

A related question is whether the performance changes measured in our study are in fact functionally important to the patients. Ferber et al. (2003) found that prism adaptation resulted in more leftward exploratory eye movements, but did not lead to increased awareness of the objects now actively explored. However, in our Where's Wally test the changes in eye movements did lead to increased awareness of leftsided targets (as measured by reaction time and accuracy) and were thus functionally useful. Presenting a more general critique, a recent Cochrane review by Bowen and Lincoln (2007b) concluded that rehabilitation for spatial neglect often improves test performance, but not the everyday disabilities of the patients. To ensure the general validity of our findings we included several measures that directly target everyday functioning. The Cupboard test was designed to assess visual search performance under naturalistic conditions while keeping experimental control. Support for the validity of this new measure comes from the fact that at baseline, patients had a strong tendency to search slower and make more errors with items in the left side of the cupboard; a clear indicator of neglect behaviour. Our other naturalistic measure, the questionnaire, was designed to capture a broad range of everyday difficulties for neglect patients. The individual items of the questionnaire were chosen in consultation with highly experienced clinical neuropsychologists. Further support for the validity of these measurements comes from the fact that the subjective reports of the patients closely matched those of their relatives. Importantly, the results from both the Cupboard test and the questionnaire were very similar to our other experimental data. This supports the claim that prism adaptation not only ameliorates performance in laboratory based tests, but also leads to significant long-term improvements of the patients' everyday disabilities and in the number of perceived problems arising from the disabilities.

Our findings of clear, stable effects of prism training may not apply to all neglect patients. Neglect patients are an anatomically heterogeneous group (Husain & Rorden, 2003), which was also true for the patients in this study. Their lesion sites were obtained from the results of sub-acute MR or CT scans reported in the medical records, but as the actual scans were not available, no systematic lesion mapping could be done. This restricts the possibility of linking neuroanatomy and symptom reduction after prism adaptation. Specifically, we cannot evaluate the claim that prism therapy is ineffective when certain parts of the brain are damaged (e.g., with cerebellar or occipital lesions; Luauté et al., 2006a, 2006; Serino et al., 2006). Besides lesion location, another potentially relevant factor is the presence of hemianopia. There is an ongoing controversy as to whether hemianopia exacerbates the symptoms of neglect patients (Behrmann, Ebert, & Black, 2004; Rousseaux et al., 2006) or decreases the responsiveness to prism adaptation (Serino et al., 2006). Our subject group comprised both patients with and without hemianopia, who were divided approximately equally between the experimental group and the control group. We found no evidence that patients with hemianopia performed worse at baseline, had more serious symptoms, or responded differently to prism adaption. On the contrary, the three patients with hemianopia in the experimental group all benefitted substantially from the prism adaptation procedure. The positive treatment effects in these patients may have been mediated by similar mechanisms as in the neglect patients without hemianopia: For both groups, an increase in the number of exploratory eye movements towards the left side of space should improve visual search performance. Indeed, hemianopic patients without neglect often spontaneously develop such changes in the exploratory bias to compensate for their visual deficit (Ishiai, Furukawa, & Tsukagoshi, 1987). Finally, even though all patients in the present study had clinically significant neglect symptoms, none were severe cases with minimal awareness of the left side of their own body, their symptoms, or the left space around them. Even though we cannot say whether patients with more aggravating symptoms would benefit equally from the training procedure, our subjects do match the typical profile of a chronic neglect patient undergoing post-acute rehabilitation. As such, our study strongly supports the use of prism adaptation in the clinic to ameliorate chronic neglect symptoms.

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