



Does prism adaptation affect visual search in spatial neglect patients: A systematic review

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Prism adaptation (PA) is a widely used intervention for (visuo-)spatial neglect. PA-induced improvements can be assessed by visual search tasks. It remains unclear which outcome measures are the most sensitive for the effects of PA in neglect. In this review, we aimed to evaluate PA effects on visual search measures. A systematic literature search was completed regarding PA intervention studies focusing on patients with neglect using visual search tasks. Information about study content and effectiveness was extracted. Out of 403 identified studies, 30 met the inclusion criteria. The quality of the studies was evaluated: Rankings were moderate-to-high for 7, and low for 23 studies. As feature search was only performed by five studies, low-to-moderate ranking, we were limited in drawing firm conclusions about the PA effect on feature search. All moderate-to-high-ranking studies investigated cancellation by measuring only omissions or hits. These studies found an overall improvement after PA. Measuring perseverations and total task duration provides more specific information about visual search. The two (low ranking) studies that measured this found an improvement after PA on perseverations and duration (while accuracy improved for one study and remained the same for the other). This review suggests there is an overall effect of PA on visual search, although complex visual search tasks and specific visual search measures are lacking. Suggestions for search measures that give insight in subcomponents of visual search are provided for future studies, such as perseverations, search path intersections, search consistency and using a speed–accuracy trade-off.

Unilateral visuo-spatial neglect ('neglect') is a common disorder after a stroke (Nijboer, van de Port, Schepers, Post, & Visser-Meily, 2013). It is defined as an attentional failure to report, respond to, or orient to stimuli presented in the contralesional hemisphere, not caused by motor or sensory deficits (Heilman & Watson, 1977). Neglect is a complex, multicomponent disorder, including not only the abovementioned spatially lateralized, but also non-lateralized (e.g., spatial working memory) deficits (Husain & Rorden, 2003). It is associated with a lower functional (i.e., activities in daily living) recovery from stroke

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(Nijboer, van de Port, *et al.*, 2013). In 40% of patients, neglect becomes chronic and is still present 1 year post-stroke onset (Nijboer, Kollen, & Kwakkel, 2013).

A promising method for the rehabilitation of neglect is prism adaptation (PA), first applied by Rossetti *et al.* (1998) and widely used ever since. Reduction of neglect symptoms can last for a short period of time after a single PA session (e.g., 2 hr; Rossetti *et al.*, 1998) and for a long period of time after multiple sessions (up to 24 months after 3 months of daily sessions; Nijboer, Nys, van der Smagt, Van der Stigchel, & Dijkerman, 2011). Although symptom reductions have been reported in various domains, not all symptoms improve. The underlying (neural) mechanisms of the interaction between PA and specific aspects of neglect remain unclear (Newport & Schenk, 2012).

Most studies looked into the effects of PA on tasks using visual stimuli. These tasks typically involve actively scanning a visual environment for targets among distractors, in which often visuo-motor responses are assessed. Patients with neglect generally have problems with visual search and achieving proper visual overview (Ten Brink, Van der Stigchel, Visser-Meily, & Nijboer, 2015) which can result in a disorganized search pattern during cancellation tasks. Spatial working memory also plays a crucial role in visual search and is considered to be an important component of the neglect syndrome (Husain *et al.*, 2001; Malhotra, Mannan, Driver, & Husain, 2004). Eye tracking research has indicated that patients with neglect tend to refixate and re-examine previously examined targets more than healthy controls, showing an inability to keep track of previously examined targets (Husain *et al.*, 2001; Malhotra *et al.*, 2004) as would be seen in spatial working memory deficits.

The effects of PA on visual search might depend on the procedure (Jacquin-Courtois *et al.*, 2013). Two main procedures can be distinguished: Either the second half and final part (including the pointing error) of the pointing movement are visible (i.e., concurrent feedback) or only the final part (i.e., terminal feedback). Làdavas, Bonifazi, Catena, and Serino (2011) compared these procedures and found greater effects after terminal feedback, which they explained in terms of a correction of visuo-motor eye–hand coordinates when using terminal feedback, whereas the concurrent feedback procedure causes a correction of proprioceptive coordinates.

It is unknown which subprocesses of visual search are affected by PA in patients with neglect. There is debate in the literature about whether PA affects the dysfunction in the attentional and visuo-motor circuits in the dorsal visual stream (e.g., Fortis, Chen, Goedert, & Barrett, 2011; Striener & Danckert, 2010) and/or in the explicit perceptual judgement circuits in the ventral stream (e.g., Serino, Bonifazi, Pierfederici, & Làdavas, 2007). However, there is evidence that the orienting of attention (e.g., Ferber, Danckert, Joanisse, Goltz, & Goodale, 2003) and exploratory motor behaviours (e.g., Dijkerman *et al.*, 2003; Striener & Danckert, 2007) are influenced after PA, whereas perceptual judgements (e.g., estimating shape size and judging chimeric faces) are unaffected (Dijkerman *et al.*, 2003; Striener & Danckert, 2007).

Improvements of rehabilitation techniques for neglect are commonly evaluated using cancellation and other visual search tasks. It remains unclear which visual search outcome measures are the most sensitive for the beneficial effects of PA. We aim to evaluate effects of PA on various visual search measures. This can help us understand which measures, and which aspects of visual search, are ameliorated by PA.

Methods

Search method and article selection

A literature search was performed using PubMed and Scopus for studies published up until January 2015. Three searches were performed. First, we searched for 'neglect' combined with 'PA'. Second, we searched for 'stroke or cerebrovascular disease' combined with 'PA'. Last, in order to be more specific, we searched for 'visual search or search accuracy or search efficiency or search strategy or cancellation or BIT or behavioral inattention test' combined with 'PA'. The majority of studies were found after the first two searches. Studies were selected if they met the following inclusion criteria: (1) stroke patients with neglect; (2) ≥ 18 years of age; (3) measures of visual search (cancellation tasks or other types of visual search tasks); (4) a PA intervention; and (5) at least two visual search measurements (pre-PA and post-PA). Non-English studies, review papers, and book chapters were excluded. Subsequently, duplicates were excluded. Two authors (LDW and ATB) screened the titles and abstracts. From screen-positive titles and abstracts or in case of ambiguity, full-text articles were collected and evaluated with the aforesaid criteria.

Data extraction

LDW and ATB extracted the following characteristics from the articles: aim, design, number of patients, mean age, side of neglect, time post-stroke onset, duration and intensity of treatment sessions, procedure, deviation of prism goggles, alternative intervention, timing of measurements, type of visual search tasks, outcome measures, and results (i.e., differences between pre- and post-measurements or between treatment and control group).

Quality assessment

LDW and ATB independently appraised the characteristics and the quality of the studies. The methodological quality was evaluated based on elements from Tijssen and Assendelft (2003): (1) comparison of an experimental group and a control group; (2) randomization of conditions; (3) comparability of groups at the start of the study; (4) equal treatment of groups (excluding intervention); (5) blinding of effect evaluators; and (6) reporting completeness of follow-up (follow-up measurements were defined as ≥ 3 months post-treatment). Two criteria were added: (7) reporting time post-stroke, as this might affect the efficacy of PA; and (8) reporting effect size, as this is informative about the magnitude of the intervention effect.

The criteria 'blinding of the practitioner' and 'blinding of participants' of Tijssen and Assendelft (2003) were not applied, as the prism goggles provide information about the experimental condition. In case a criterion was not applicable, 0 points were assigned. This checklist yielded a total score ranging between 0 and 8. Studies were labelled as high (total scores ≥ 6), moderate (4 and 5), or low (≤ 3) ranking.

Results

In the initial search, 402 articles were identified, of which 30 were included (Figure 1). The selected articles yielded an inter-rater reliability of 98.1%, with an agreement of 100% after discussion. The specifics of the selected studies are presented in Table 1.

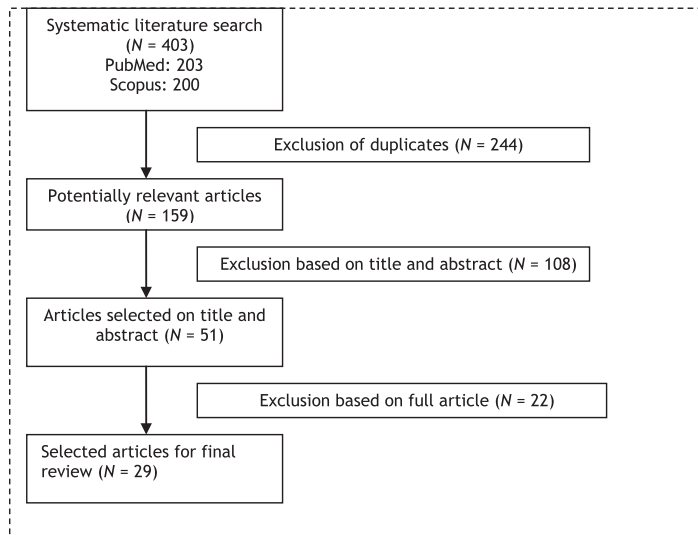


Figure 1. Flow chart of article selection.

Quality assessment

The quality assessment yielded an inter-rater reliability of 96.3%, with an agreement of 100% after discussion with TN. The studies of Serino, Barbiani, Rinaldesi, and Ladavas (2009) and Priftis, Passarini, Pilosio, Meneghello, and Pitteri (2013) were ranked as high (Table 2). The studies of Mancuso *et al.* (2012), Nys, de Haan, Kunneman, de Kort, and Dijkerman (2008), Rossetti *et al.* (1998), Vangkilde and Habekost (2010), and Saevarsson, Kristjansson, and Halsband (2010) were ranked as moderate. All other studies ($N = 23$) were ranked as low (Table 2).

Study, intervention, and patient characteristics

Study characteristics

There were eight randomized controlled trials, four studies with a crossover design, and 18 studies with a pre–post design (12 studies testing a group of participants, five case studies, and one pilot study without reporting statistical analyses).

Intervention characteristics

There is no standard protocol for PA treatment. Most studies used 10° prism goggles, with the exception of Mancuso *et al.* (2012; 5°), Morris *et al.* (2004; 15°), Shiraishi, Muraki, Ayaka Itou, and Hirayama (2010; 15°), and Saj, Cojan, Vocat, Luauté, and Vuilleumier (2013; 20°). Visual targets were located at 10° to 25° from the midline, with or without a central target. Keller, Lefin-Rank, Lösch, and Kerkhoff (2009) only used one central target. In one study, targets were pointed at with a digital stylus (Smit *et al.*, 2013). In all other studies, participants used their finger. The number of pointing movements ranged from 8

Table 1. The extracted information from the discussed studies

Study	N patients				Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure						
Serino et al. (2009)	RCT	10 + 10	1–60 m	10 (2) Terminal	SA	Pre, PA/SA, post (2 and 4 wk)	Bell-Star+ Letter ^a	%Hits left side	Session: $p < .0003$, $\eta^2 = .77$ Post-hoc: PA in comparison with other treatments: $p < .008$	High
Piffis et al. (2013)	RCT	11 + 10 + 10	31–223 d	20 (2) Terminal	Visual scanning, training, limb activation treatment	Pre (2 ×), PA, post (direct, 2 wk)	Picture scanning Room description	Hits	Session: $p < .001$, $\eta^2 = .209$ (pre2–post [direct]: $p < .05$) Intervention type*session: NS Session: NS (pre2–post [direct]: NS) Intervention type*session: NS	High
Rossetti et al. (1998)	RCT	6 + 6	3 wk to 14 m	1 Concurrent	SA	Pre, PA/SA, post (direct, 2 h)	Line	Omissions per half	Group*session: $p < .05$ Pre–post [direct]: $p < .01$ Pre–post [2 h]: $p < .01$ Post [direct]–post [late]: $p > .95$ Session: NS; group*session: $p = .045$ Session: $p < .001$ Pre–post [1 m]: NS	Moderate
Nys, de Haan, et al. (2008)	RCT	10 + 6	2–23 d	4 (1) Concurrent	SA	For every session: pre, PA/SA, post (direct, 1 m)	Letter Star	Hits Hits	Session: NS; group*session: $p = .045$ Session: $p < .001$ Pre–post [1 m]: NS	Moderate

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Vangkilde and Habelkost (2010)	RCT	6 + 5	6–138 m	20 (2) Terminal	General cognitive rehabilitation	Pre, PA, post (1–2 d, 5 wk)	Cupboard test Mesulam star Mesulam letter Where is Wally	Omdiff Time Omdiff Omdiff Omdiff RT	$p = .033$, $\eta_p^2 = .32$ $p = .001$, $\eta_p^2 = .52$ $p = .001$, $\eta_p^2 = .56$ $p = .003$, $\eta_p^2 = .48$ $p = .047$, $\eta_p^2 = .29$ $p = .003$, $\eta_p^2 = .32$ N.B. All of these results are group*session interaction effects Session: $p = .009$; group*session: $p = .508$ Session: $p = .148$; group*session: $p = .011$ Session: $p = .015$; group*session: $p = .824$ Session: $p = .724$; group*session: $p = .035$ Session: $p = .164$; group*session: $p = .732$ Treatment*session: $p > .4$ (NS) Treatment*session: $p > .2$ (NS) Treatment*session: $p = .018^b$ Treatment*session:	Moderate
Mancuso et al. (2012)	RCT	13 + 9	20–1,140 d	5 (1) Terminal	SA	Pre, PA/SA, post	Bell Object	%Hits left side %Hits right side %Hits left side %Hits centre %Hits right side	Interaction effects Session: $p = .009$; group*session: $p = .508$ Session: $p = .148$; group*session: $p = .011$ Session: $p = .015$; group*session: $p = .824$ Session: $p = .724$; group*session: $p = .035$ Session: $p = .164$; group*session: $p = .732$ Treatment*session: $p > .4$ (NS) Treatment*session: $p > .2$ (NS) Treatment*session: $p = .018^b$ Treatment*session:	Moderate
Saevarsson et al. (2010)	RCT	6 NV/PA + 6 NV	3–57 m	1 Terminal	NV without PA	Pre, PA, post (1 d)	Pop-out task Albert's+Digit+ Star+Letter ^a Pop-out task Albert's+Digit+ Star+Letter ^a	Between groups: RT %Hits RT %Hits Within PA	Treatment*session: $p > .4$ (NS) Treatment*session: $p > .2$ (NS) Treatment*session: $p = .018^b$ Treatment*session:	Moderate

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Frassinetti et al. (2002)	RCT	7 + 6	3–27 m	20 (2) Terminal	None	Pre, PA, post (2 d, 1 and 5 wk)	Line+Letter+ Star+Bell ^a	group: Target absent pop-out RT Target present pop-out RT Target absent pop-out %Hits Target present pop-out %Hits RT%Hits	p = .037 p < .001 p < .001 NS p < .001 NS p = .089 (NS)	Low
								%Hits transformed into arcsine values	Side*session: p < .0007 Session: p < .00001 (pre-post [2 d]: p < .0007; pre-post [1 wk]: p < .0002; pre-post [5 wk]: p < .0002) Control group, session: NS N.B. Only the scores of the total search array are reported. The same analyses were done for the left side (significant) and the right side (NS) Session*group: p = .40 Session*group: p < .05 Session*group: p = .11 Follow-up (average of	
Fortis et al. (2010)	Crossover	10 Follow-up: 4/10	3.4 m	10 (1) CPA Terminal +10 (1) EPA	CPA	Pre (3×), CPA/EPA, post (direct, 0.5 and	Letter Bell Star	%Hits %Hits %Hits		Low

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Eramudugolla et al. (2010)	One group pre and post	12	1–15 m	2 (1–2) Terminal	NA	Pre (2×), PA1, post (direct), PA2, post (direct)	Balloons	Hits left vs. right side task A Hits left vs. right side task B	$p = .0002$ Pre–post [3 m]: $p = .0002$ Pre–post [5 m]: $p = .0002$ All measures: session: $p > .10$ Target location*session: $p > .10$ All measures: session: $p < .05$, $\eta_p^2 = .27$ Target location*session: $p = .05$, $\eta_p^2 = .23$ $p < .05$ $p = .104$ (NS)	Low
Shiraishi et al. (2010)	One group pre and post	5 Follow-up: 5/7	14–84 m	±24 (8) Procedure unclear	NA	Follow-up (of study 2–3.5 y earlier) Pre, PA, post (3 m after start), follow-up (3, 6 and 24 m after final PA session)	Letter Star	Omissions left side Omissions left side	Session: $p = .008$ Session: $p = .001$ Session: $p < .001$	Low
Nilboer et al. (2011)	Case study	1	70 m	Daily for 3 months Concurrent	NA		Star	Omissions Perseverations Duration		Low
Rusconi and Carelli (2012)	One group pre and post	7 Follow-up: 7/7	2–6 m	20 (2) Terminal	NA	Pre, PA, post (2 wk), follow-up (8–30 m)	Line Letter Star	BIT scores BIT scores BIT scores	Pre–post [2 wk]: NS Pre–follow-up: NS Pre–post [2 wk]: NS Pre–follow-up: NS Pre–post [2 wk]: significant, p -value unclear Pre–follow-up: $p < .05$	Low

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Farnè et al. (2002)	One group pre and post	6	2-8 m	I Concurrent	NA	Pre, PA, post (direct, 1 d, 1 wk), PA2, post (direct)	Line Bell Letter	%Hits %Hits %Hits N.B. The percentages of hits were transformed into arcsine values	For all tests: Pre-post [direct]: $p < .05$ Pre-post [1 d]: $p < .05$ Pre-post [1 wk]: NS	Low
McIntosh et al. (2002)	Case study	I	9 m	3 (3) Terminal	NA	Pre (2×), PA, post (direct), pre, PA2, post (2 h), pre, PA3, post (direct) SA, pre, PA, post (direct)	Star	Omissions per half	Pre-post: $p < .001$ (all pre and post data were pooled) Week: $p < .001$ (all data were pooled per week)	Low
Morris et al. (2004)	One group pre and post	First task: 4 Second task: 3	1-6 m	I Concurrent	NA	Unique feature search Absent feature search	RT RT	RT RT	Pre-post: For 2/4 patients: $p < .01$ For 2/4 patients: NS Interaction horizontal target location-adaptation: For 3/4 patients: $p > .10$ For 1/4 patients: $p = .066$ Pre-post: For 3/3 patients: $p > .05$ (NS) Interaction horizontal target ^c location-adaptation: For 1/3 patients: $p < .05$ For 2/3 patients: $p > .10$	Low
Humphreys et al. (2006)	Case study	I	11 y	10 (5) + 8 (4) Procedure unclear	NA	Pre (2×), PA1, post (direct 2×, 1 m), PA2,	Star Letter	Omissions Omissions	Pre-post after PA1: $p < .05$ Pre-post after PA2: $p < .01$ Pre-post after PA1: $p < .01$ Pre-post after PA2: $p < .01$	Low

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Rousseaux et al. (2006)	Crossover	10	17–102 d	I Concurrent	SA	post (1 and 5 wk) Pre (2×), PA/SA, post (direct, 3 h, 1 and 3 d); after 1 wk break alternative treatment (same times of measurements (counterbalanced)) Pre, PA, post (direct, 60 min)	Bell	Ondiff	NS	Low
Vallar et al. (2006)	One group pre and post	9	2–36 d	I Procedure unclear	NA		Line	Omissions Perseveration errors	Session: $p < .05$ (pre-post [direct]: $p < .05$; pre-post [60 min]: $p < .05$) Session: $p < .05$ (pre-post [direct]: $p < .05$; pre-post [60 min]: $p < .05$) $p < .01$ NS $p < .01$ $p < .01$	Low
Nys, Seurinck, et al. (2008)	Case study	1	11 m	4 (I) Concurrent	NA	For every session: pre, PA, post (direct)	Star	%Hits left %Hits right %Perseverations left %Perseverations right		Low
Sarri et al. (2008)	One group pre and post	12 ^c	1–174 m	I Concurrent	NA	Pre, PA, post (direct)	Mesulam shape	%Hits	For 7/12 patients significant: $p < .001$, $p < .001$, $p < .05$, $p < .05$, $p < .001$, $p < .001$, $p < .05$	Low

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Keller et al. (2009)	Crossover	10	2–4.5 m	1 Procedure unclear	OKSP; visual scanning; OKSP + arm movements; OKSP + PA	For every treatment: pre, treatment, post (direct), 1 wk break; subsequently alternative treatments (same times of measurements) (counterbalanced)	Cancellation (not further specified)	Omissions	For 5/12 patients: NS p = .045	Low
Saevarsson et al. (2009)	One group pre and post	Exp. 1: 4 Exp. 2: 4	3–61 m	1 Terminal	NA	Pre (20 d before PA), PA, post (direct)	Pop-out search task ^d	Exp. 1: RT left Exp. 1: RT right Exp. 1: RT target absent Exp. 1: %Hits Exp. 2: RT left Exp. 2: RT right Exp. 2: RT target absent Exp. 2: %Hits left Exp. 2: %Hits right Exp. 2: %Hits target absent	p < .001 p < .001 p < .001 (significantly slower!) NS p < .001 p < .001 p < .001 p < .001 p < .001 NS	Low
Luauté et al. (2012)	One group pre and post	5	1–2.5 m	1 Concurrent	NA	Pre, PA, post (direct, 2 h)	Line Balloon pop-out Balloon search Apples	Hits Hits Hits	p = .32 (NS) p = .46 (NS) p = .98 (NS)	Low
		16	36 d		NA		Hits	Hits		Low

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Gossmann <i>et al.</i> (2013)	One group pre and post			4 (1) Concurrent		Pre (2 ×), PA, post (5–6 and 10–12 d)			Pre-post [5–6 d]: p = .041 Pre-post [10–12 d]: p = .006 NS	
Saj <i>et al.</i> (2013)	One group pre and post	7	10–32 d	1 Procedure unclear	NA	Pre (2 ×), PA, post (direct)	Visual search of single-odd item	RT %Hits %Hits	NS Pre1–post [direct]: p = .005 Pre2–post [direct]: p = .008 NS	Low
Smit <i>et al.</i> (2013)	One group pre and post	33	63.73 d	1 Procedure unclear	NA	Pre, PA, post (direct)	Object Letter	Omissions Time Search time ipsilateral Search time contralateral Centre of cancellation Omissions Time Search time ipsilateral Search time contralateral Centre of cancellation Omissions	NS p = .003 p = .0001 p = .004 NS NS p = .025 NS p = .027 NS	Low
Keane <i>et al.</i> (2006)	Pilot	4	<60 d	5 (12–17 d) Concurrent	NA	Albert's line: for every session pre, PA, post Letter: pre, PA (entire	Line Letter	Errors Errors N.B. Errors most likely equals omissions,	No statistical analyses were done. The non-statistical results are not discussed in the text	Low

Continued

Table 1. (Continued)

Study	Design	N patients (exp. + control group)	Time post-stroke	N sessions (wk) and PA procedure	Alternative intervention	Times of measurement	Visual search task	Visual search outcome measures	p-values and effect sizes	Ranking
Jacquin-Courtois et al. (2008)	Case study	1	3 or 5 m	1 Concurrent	NA	treatment), post Pre (3 ×), PA, post (direct, 1, 24, 48, 72, 96 h)	Line	but this is not explicit Omissions	Pre-overall post: $p < .05$ Pre-early post [direct, 1 and 24 h]: $p < .05$ Pre-late post [48, 72, 96]: NS	Low

Note. y = years; m = months; wk = weeks; d = days; h = hours; min = minutes; s = seconds; NS = not statistically significant; pre = baseline measurement; post = post-prism adaptation measurement; follow-up = measurement at least 3 months after last session of prism adaptation; NA = not applicable; PA = prism adaptation; SA = sham adaptation; CPA = classic prism adaptation; EPA = ecological prism adaptation; OKSP = optokinetic stimulation; %Hits = percentage of hits; %Omissions = percentage of omissions; %Perseverations = percentage of perseverations; Omdiff = omission difference score between contralateral and ipsilesional side of the search array; RT = reaction time; BIT = behavioral inattention test; RCT = randomized controlled trial.

Table is sorted by quality (from high to low), and subsequently by year (from oldest to most recent).

^aResults for all cancellation tasks together.

^bInconsistency with the article regarding the p-value. After consulting the authors, this p-value was adapted.

^cOne patient was excluded as her cancellation performance was close to a ceiling at baseline; hence, analyses regarding cancellation were carried out on 12 of 13 patients.

^dCancellation tasks were also reported. However, of those no separate scores were reported (only total scores of 6 standard cancellation tasks).

Table 2. Scores of the quality assessment of the discussed studies, based on 8 elements

Study	1. Comparison of groups	2. Randomization	3. Comparable groups	4. Equal treatment	5. Blinding	6. Reporting completeness follow-up	7. Reporting time post-stroke	8. Reporting effect size	Total
Serino <i>et al.</i> (2009)	1	1	1	1	0	0	1	1	6
Priftis <i>et al.</i> (2013)	1	1	1	1	0	0	1	1	6
Rossetti <i>et al.</i> (1998)	1	1	1	1	0	0	1	0	5
Nys, de Haan, <i>et al.</i> (2008)	1	1	1	1	0	0	1	0	5
Vangkilde and Habekost (2010)	1	1	1	0	0	0	1	1	5
Mancuso <i>et al.</i> (2012)	1	1	1	1	0	0	1	0	5
Saevarsson <i>et al.</i> (2010)	1	1	0	1	0	0	1	0	4
Frassinetti <i>et al.</i> (2002)	1	0	1	0	0	0	1	0	3
Fortis <i>et al.</i> (2010)	0	0	0	0	0	1	1	1	3
Serino <i>et al.</i> (2007)	0	0	0	0	0	1	1	0	2
Eramudugolla <i>et al.</i> (2010)	0	0	0	0	0	0	1	1	2
Shiraishi <i>et al.</i> (2010)	0	0	0	0	0	1	1	0	2
Nijboer <i>et al.</i> (2011)	0	0	0	0	0	1	1	0	2
Rusconi and Carelli (2012)	0	0	0	0	0	1	1	0	2
Farnè <i>et al.</i> (2002)	0	0	0	0	0	0	1	0	1
McIntosh <i>et al.</i> (2002)	0	0	0	0	0	0	1	0	1
Morris <i>et al.</i> (2004)	0	0	0	0	0	0	1	0	1
Humphreys <i>et al.</i> (2006)	0	0	0	0	0	0	1	0	1
Rousseaux <i>et al.</i> (2006)	0	0	0	0	0	0	1	0	1
Vallar <i>et al.</i> (2006)	0	0	0	0	0	0	1	0	1
Nys, Seurinck, <i>et al.</i> (2008)	0	0	0	0	0	0	1	0	1
Sarri <i>et al.</i> (2008)	0	0	0	0	0	0	1	0	1
Keller <i>et al.</i> (2009)	0	0	0	0	0	0	1	0	1
Saevarsson <i>et al.</i> (2009)	0	0	0	0	0	0	1	0	1
Luaute <i>et al.</i> (2012)	0	0	0	0	0	0	1	0	1

Continued

Table 2. (Continued)

Study	1. Comparison of groups	2. Randomization	3. Comparable groups	4. Equal treatment	5. Blinding	6. Reporting completeness follow-up	7. Reporting time post-stroke	8. Reporting effect size	Total
Gossmann et al. (2013)	0	0	0	0	0	0	1	0	1
Saj et al. (2013)	0	0	0	0	0	0	1	0	1
Smit et al. (2013)	0	0	0	0	0	0	1	0	1
Keane et al. (2006)	0	0	0	0	0	0	0	0	0
Jacquin-Courtois et al. (2008)	0	0	0	0	0	0	0	0	0

Note. 0, negative; 1, positive.

Elements: 1, Comparison of an experimental group and a control group; 2, Randomization of different conditions; 3, Comparable groups; 4, Equal treatment of groups (excluding intervention); 5, Blinding of effect evaluators; 6, Reporting completeness of follow-up; 7, Reporting time post-stroke; 8, Reporting effect size.

Table is sorted by quality (from high to low), and subsequently by year (from oldest to most recent). High was considered total scores ≥ 6 , moderate 4 and 5, and low ≤ 3 .

to 20 (Keller *et al.*, 2009) up to 200 (Morris *et al.*, 2004) per session. Moreover, Fortis *et al.* (2010) compared the classic pointing procedure (Rossetti *et al.*, 1998) with a new method in which prismatic goggles had to be worn while performing ecologically valid activities.

The view of the pointing movement was obstructed in most studies, by either holding a board above the patients arm or using an adaptation box. The terminal feedback procedure was used in 12 studies (Eramudugolla, Boyce, Irvine, & Mattingley, 2010; Fortis *et al.*, 2010; Frassinetti, Angeli, Meneghello, Avanzi, & Làdavas, 2002; Mancuso *et al.*, 2012; McIntosh, Rossetti, & Milner, 2002; Priftis *et al.*, 2013; Rusconi & Carelli, 2012; Saevarsson, Kristjánsson, Hildebrandt, & Halsband, 2009; Saevarsson *et al.*, 2010; Serino *et al.*, 2007, 2009; Vangkilde & Habekost, 2010). Eleven of these found (some) significant effects of PA. Twelve studies used the concurrent feedback procedure (Farnè, Rossetti, Toniolo, & Làdavas, 2002; Gossman, Kastrup, Kerkhoff, López-Herrero, & Hildebrandt, 2013; Jacquin-Courtois, Rode, Pisella, Boisson, & Rossetti, 2008; Keane, Turner, Sherrington, & Beard, 2006; Luauté *et al.*, 2012; Morris *et al.*, 2004; Nijboer *et al.*, 2011; Nys, Seurinck, & Dijkerman, 2008; Nys, de Haan, *et al.*, 2008; Rossetti *et al.*, 1998; Rousseaux, Bernati, Saj, & Kozłowski, 2006; Sarri *et al.*, 2008), of which nine found (some) significant effects of PA. In several studies the obstruction procedure was not clearly described (Humphreys, Watelet, & Riddoch, 2006; Keller *et al.*, 2009; Saj *et al.*, 2013; Shiraishi *et al.*, 2010; Smit *et al.*, 2013; Vallar, Zilli, Gandola, & Bottini, 2006). None of the studies explicitly described blinding of the effect evaluators.

The number of PA sessions ranged from one up to daily sessions for a period of 3 months (Nijboer *et al.*, 2011). Fourteen studies only conducted post-measurements within 24 hr after the treatment. The other 15 studies had at least one post-measurement between 24 hr and 2.5–3 years (Shiraishi *et al.*, 2010) after the treatment. All studies with more than one session conducted sessions at least once per week with a maximum time span of 5 weeks, with the exception of the study by Humphreys *et al.* (2006), in which patients had two sessions per week, for 5 weeks, followed by a month break and then two sessions per week for another 4 weeks.

Patient characteristics

All studies included patients with left-sided neglect after right brain damage due to stroke. The mean time post-stroke varied from 8 days (Nys, de Haan, *et al.*, 2008) to 11 years (Humphreys *et al.*, 2006). In 11 studies only patients in the chronic phase, and in six studies only patients in the subacute phase were included.

Visual search results

Feature search tasks

Five studies used feature search tasks. In these tasks, participants have to find a target among distractors as quickly as possible and indicate its presence or location by pressing a button. Four studies used simple feature search tasks in which stimuli consisted of letters (i.e., 'Q' and 'O'; Morris *et al.*, 2004), coloured circles (i.e., blue and green; Saevarsson *et al.*, 2010, 2009), or shapes (i.e., squares and diamonds; Saj *et al.*, 2013). The tasks of Vangkilde and Habekost (2010) were more ecologically valid, but can be seen as feature search. In the 'Where is Wally' task, a character had to be found between many people. In the 'cupboard' task, patients had to locate everyday objects (e.g., keys, brush) among

distractors (Vangkilde & Habekost, 2010). In all feature search tasks, both accuracy and reaction time (RT) were evaluated, with the exception of the study of Morris *et al.* (2004) which only measured RT.

Accuracy. Vangkilde and Habekost (2010; moderate ranking) reported more improvement after PA than after a different type of treatment. Saevarsson *et al.* (2010; moderate ranking) found similar results in accuracy after a combination of PA and neck vibration therapy and vibration therapy only. Of the low-ranking studies, an improvement was found by Saj *et al.* (2013). Saevarsson *et al.* (2009) found no improvement in accuracy in the target absent condition or when both feedback and a time limit were given. Accuracy did improve in the target present condition without feedback and time limit.

Reaction time. Vangkilde and Habekost (2010; moderate ranking) found that RTs decreased more after PA than after general cognitive rehabilitation. Saevarsson *et al.* (2010; moderate ranking) found comparable RTs and accuracy scores after neck vibration therapy compared to both neck vibration and PA. Within group, there was a significant improvement in RTs after the combination of neck vibration and PA therapy, while no changes were found in accuracy. No improvements were found on RT in the cancellation task. Of the low-ranking studies, no improvement in RT was found by Saj *et al.* (2013). Morris *et al.* (2004) only found an improvement for some of the patients but did not report accuracy as a measure. Saevarsson *et al.* (2009) found that RT decreased following PA in both experiments, with the exception of a target absent condition in one of the two experiments, while accuracy measures improved or remained the same.

Cancellation tasks

Most studies used simple pen-and-paper cancellation tasks in which letters, stars, bells, lines, balloons, or other objects had to be cancelled. These tasks were all visuo-manual: Targets had to be cancelled by reaching to them. Priftis *et al.* (2013) used a task in which objects in a room or a picture had to be verbally reported. This task is comparable to cancellation tasks in the sense that the amounts of hits, misses, and RT were scored; however, no manual response was requested.

Omissions or hits. The number or percentage of omissions or hits was commonly used as an outcome measure. The analyses were either performed on the total search array, separately for the contralesional (and in some studies also the ipsilesional) side of the search array, or on the difference score (i.e., the difference in omissions or hits between sides).

Total number of omissions or hits. Both high-ranking studies (Priftis *et al.*, 2013; Serino *et al.*, 2009) found more improvement in number of hits after PA. Whereas Serino *et al.* (2009) found more improvement after PA than after sham adaptation, Priftis *et al.* (2013) compared PA treatment with visual scanning training and limb activation and found an equal improvement for all treatments.

All five moderate-ranked studies reported that patients improved more on cancellation in the PA condition than in other or no-treatment conditions on at least one task (Fortis *et al.*, 2010; Mancuso *et al.*, 2012; Nys, de Haan, *et al.*, 2008; Rossetti *et al.*, 1998; Saevarsson *et al.*, 2010; Vangkilde & Habekost, 2010). There were 19 low-ranked studies that conducted cancellation tasks and used omissions or hits as an outcome measure. One of these did not report statistical analyses (Keane *et al.*, 2006). Of the remaining studies, 11 found an improvement after PA (Farnè *et al.*, 2002; Frassinetti *et al.*, 2002; Gossmann *et al.*, 2013; Humphreys *et al.*, 2006; Jacquin-Courtois *et al.*, 2008; Keller *et al.*, 2009; McIntosh *et al.*, 2002; Nijboer *et al.*, 2011; Nys, Seurinck, *et al.*, 2008; Serino *et al.*, 2007; Vallar *et al.*, 2006). Effects were less consistent in four studies. More specifically, Sarri *et al.* (2008) found improvement after PA for only some of the patients. Eramudugolla *et al.* (2010), Shiraishi *et al.* (2010), and Fortis *et al.* (2010) found an improvement on only one of the used tasks. Luauté *et al.* (2012), Smit *et al.* (2013), and Rousseaux *et al.* (2006) found no improvement on cancellation.

Omissions split for side. Nys, Seurinck, *et al.* (2008; low ranking) and Serino *et al.* (2007; low ranking) evaluated the number of omissions for both sides of the search array separately. They reported an improvement for the contralesional side. Serino *et al.* (2007) also observed a significant improvement regarding omissions at the ipsilesional side, whereas in the study of Nys, Seurinck, *et al.* (2008) patients only had very few ipsilesional omissions, so no improvement after PA was found.

Centre of cancellation. Smit *et al.* (2013; low ranking) used the centre of cancellation (CoC) (Rorden & Karnath, 2010), which is informative about both the number of omissions and the location of cancelled targets. No significant improvement after PA was found.

Perseverations. Nijboer *et al.* (2011), Nys, Seurinck, *et al.* (2008), and Vallar *et al.* (2006; all low ranking) consistently showed that the amount of perseverations was lower after PA compared to baseline.

Duration. Nijboer *et al.* (2011) and Smit *et al.* (2013) investigated the total duration for completion of the cancellation task. Besides an improvement in accuracy, Nijboer *et al.* (2011) found that patients with neglect became faster after PA. Smit *et al.* (2013) did not find an improvement in accuracy but did confirm faster search. Both studies did not use a control group to counteract learning and/or motivational effects.

GENERAL DISCUSSION AND CONCLUSION

The aim of this review was to evaluate the effect of PA on visual search in patients with neglect. Other reviews have looked into PA as a rehabilitation method for neglect in general (Fasotti & van Kessel, 2013; Newport & Schenk, 2012), PA in comparison with other rehabilitation methods (Yang, Zhou, Chung, Li-Tsang, & Fong, 2013), or to a limited extent on effects in oculo-motor exploration (Jacquin-Courtois *et al.*, 2013), but none

have specifically addressed the effect of PA on visual search. Thirty studies were included in the current review, of which seven were rated as moderate-to-high-quality studies and 23 were rated as low-quality studies.

Visual search

Only five studies had the specific aim to investigate the influence of PA on visual search tasks (thus no cancellation tasks). All of these studies used features search tasks, in which participants have to find a target among distractors as quickly as possible. The remaining 25 studies used cancellation tasks, in which multiple targets have to be found. Perseverations can be informative about working memory deficits in visual search behaviour (Husain *et al.*, 2001): To prevent revisits and omissions, patients have to keep track of targets that are already cancelled and simultaneously scan the remaining area. Although omissions or duration does not differentiate between subprocesses of visual search, these measures are dependent on subprocesses of visual search (e.g., search organization (Ten Brink *et al.*, 2015) or spatial working memory (Husain *et al.*, 2001)). Hence, omissions and search duration might be more of a 'compound' measure of these subprocesses. Although we recommend more specific visual search measures for future studies, like intersections between consecutive cancelled targets or search consistency (Ten Brink *et al.*, 2015), we will discuss what has been found with these widely used 'compound' measures. The evaluation of visual search outcome measures for both feature search tasks and cancellation tasks is described below.

Feature search outcome measures

Vangkilde and Habekost (2010; moderate ranking) found improvements regarding both RT and accuracy after PA compared to general cognitive rehabilitation. Saevarsson *et al.* (2010) found improvements between the pre- and post-measurements in the PA combined with neck vibration group, but no additional beneficial effects compared with neck vibration only. The low-ranked studies found improvements on either both RT and accuracy (Saevarsson *et al.*, 2009), only accuracy (Saj *et al.*, 2013), or on RT for a subgroup of patients (Morris *et al.*, 2004). Hence, there seems to be a beneficial effect of PA on feature search. However, as only five studies of low-to-moderate quality looked into feature search after PA, we cannot draw any strong conclusions. Monitoring the speed-accuracy trade-off provides additional information regarding visual search efficiency.

Cancellation outcome measures

Investigating the number of omissions, all high- and moderate-ranked studies found that there was more improvement in the PA group than in the control group, with the exception of Priftis *et al.* (2013). Regarding omissions at the ipsilesional side, Serino *et al.* (2007) observed a significant decrease after PA, whereas Nys, Seurinck, *et al.* (2008) did not. This can be explained by a *ceiling effect*, as the patient might have already cancelled all ipsilesional targets at baseline. As some patients omitted less ipsilesional targets after PA, the ratio between the contralesional and ipsilesional side might be a less sensitive measure and is not recommended. This ceiling effect could also lessen the measured outcome when analyses are carried out on the total search array, or when the CoC measure is used.

The question remains to what extent omissions and hits are informative about visual search. As the targets do not disappear after cancellation, patients who search slowly and/or disorganized could eventually find all targets. Even though it is more likely that targets are omitted when no structured search pattern is adopted, search efficiency cannot be evaluated when only omissions are scored. Only two (low ranking) studies evaluated total duration of cancellation. Both showed that patients became faster after PA (with improved or equal accuracy). Although learning effects need to be taken into consideration, total task duration might be a useful measure in addition to number of omissions. Again, having a speed–accuracy trade-off can be informative regarding visual search efficiency. Another advantage is that no ceiling effect is expected for both duration and RT. This possibly makes these measures more sensitive, enabling them to uncover milder search impairments.

Three studies reported a decrease of perseverations after PA (Nijboer *et al.*, 2011; Nys, Seurinck, *et al.*, 2008; Vallar *et al.*, 2006). This is a promising measure for the evaluation of visual search. Revisiting previously cancelled targets could indicate that their locations were not remembered, which could be related to spatial working memory or spatial remapping deficits that are commonly found in neglect (Pisella *et al.*, 2011). However, these studies were ranked low. More studies are needed to confirm the effects.

PA: The current state of the literature

The current state of the literature on PA mainly consists of studies that do not explicitly describe blinding of the effect evaluators and do not use specific visual search measures. A standard protocol for PA treatment is lacking. The inconsistency in (PA) procedures, the possibly biased effect evaluation, and the variety of tests for assessing neglect and/or visual search prevents us from being able to draw direct conclusions about the PA effect on visual search in neglect and provide recommendations about the use of PA in patients with neglect. To facilitate the replication of studies and the comparison of PA protocols, we recommend providing a clear and detailed description of PA procedure for future experimental studies. This should eventually lead to a consensus about the most beneficial protocol for PA therapy. A consensus should also be reached about a standard set of neuropsychological and experimental tests and outcome measures. Additionally, as neglect is a relatively heterogeneous disorder, a set of standard criteria regarding the inclusion of patients is needed. These criteria should also specify when to use restrictive inclusion criteria and when to aim for a broader sample.

Limitations of the current review

A limitation of the current review is that only patient studies were included. Additionally, investigating the behavioural and neuronal effects of PA-induced neglect on visual search behaviour and search efficiency in healthy participants could be informative about the mechanisms of PA on visual search. No studies were included using eye movements as an outcome measure. Eye movements could provide insight in the specific mechanisms underlying visual search deficits, such as spatial memory deficits (when locations are repeatedly fixated) or poor uptake of (contralesional) information (when targets are omitted after fixating them).

PA and visual search organization: Suggestions for future research

The current paper reviews all outcome measures that are used to investigate the effect of PA on visual search. Although most studies did not use specific visual search tasks or measures, hence no conclusions can be drawn about the PA effect on subprocesses of visual search, directions for future studies can be made.

Cancellation tasks with outcome measures such as omissions are to some extent informative about visual search but do not provide information about the subcomponents of visuo-spatial processing or the organization of search (e.g., visual overview, search efficiency, and search strategies). More high-quality studies looking into the effect of visual search by doing feature search or other types of visual search tasks are needed. Moreover, when cancellation tasks are conducted, we recommend to include more informative measures of search organization such as perseverations, duration of task completion, and saccadic eye movements. When measured digitally, the organization of visual search can be objectified by computing the amount of intersections with paths between previous cancelled targets, as this measure is thought to be the best to depict organization of search in a stroke population (Ten Brink *et al.*, 2016).

Acknowledgement

This work was supported by a 'Revalidatiefonds' Grant (R2012134).

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Received 29 June 2015; revised version received 12 January 2016