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A gaze-contingent saccadic re-referencing training with simulated central vision loss

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Patients with central vision loss (CVL) adopt an eccentric retinal location for fixation, a preferred retinal location (PRL), to compensate for vision loss at the fovea. Although most patients with CVL are able to rapidly use a PRL instead of the fovea, saccadic re-referencing to a PRL develops slowly. Without re-referencing, saccades land the saccade target in the scotoma. This results in corrective saccades and leads to inefficient visual exploration. Here, we tested a new method to train saccadic re-referencing. Healthy participants performed gaze-contingent visual search tasks with simulated central scotoma in which participants had to fixate targets with an experimenter-defined forced retinal location (FRL). In experiment 1, we compared single-target search and foraging search tasks in the course of five training sessions. Results showed that both tasks improved the efficiency of gaze sequences and led to saccadic re-referencing to the FRL. In experiment 2, we trained participants extensively for 25 sessions, both with and without a gaze-contingent FRL-marker visible during training. After extensive training, observers' performance approached that of foveal vision. Thus, gaze-contingent FRL-fixation may become an efficient tool for saccadic re-referencing training in patients with central vision loss.

Introduction

A central problem of eye movement control following central vision loss (CVL) is that saccades lead to the foveation of peripheral saccade targets. Although this is normally adaptive, bringing peripheral points of interest in full view, it is obviously maladaptive after CVL, requiring corrective saccades to bring the point of interest into view at a preferred retinal location (PRL), typically bordering the area of vision loss. What would be more adaptive in this case is to re-reference the saccade target location to an extrafoveal PRL. It is important to note that PRL-use is different from saccadic re-referencing to the PRL. In fact, PRL use typically develops rapidly, saccadic re-referencing to the PRL has been found to develop only slowly - over months - in clinical populations suffering from foveal vision loss (Von Noorden & Mackensen, 1962; White & Bedell, 1990; Whittaker, Cummings, & Swieson, 1991; Crossland, Culham, Kabanarou, & Rubin, 2005).

The persistent use of the fovea as the saccadic reference after foveal vision loss is not a trivial problem. Patients as well as normal-sighted participants with gaze contingent central scotoma simulation exhibit inefficient search with reduced number of fixations and longer attentional dwell times (suggesting larger attentional foci; Geringswald, Herbik, Hoffmann,

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& Pollmann, 2013; Geringswald & Pollmann, 2015; Geringswald, Porracin, & Pollmann, 2016). Therefore, training patients with foveal vision loss to use an intact perifoveal part of their retina as the saccadic reference point might enable them to return to the effortless, automatic exploration of the environment that they used to have before the onset of vision loss.

Recent experiments with central scotoma simulation in normal-sighted participants (Kwon, Nandy, & Tjan, 2013; Walsh & Liu, 2014; Rose & Bex, 2017; Maniglia, Visscher, & Seitz, 2020; Maniglia, Jogin, Visscher, & Seitz, 2020; Song, Ouchene, & Khan, 2021) have demonstrated feasible approaches to induce a PRL and saccadic re-referencing to an induced PRL over hours rather than months in the absence of training, as has been reported in patient studies (von Noorden & Mackensen, 1962; White & Bedell, 1990; Whittaker, Cummings, & Swieson, 1991; Crossland, Culham, Kabanarou, & Rubin, 2005). For example, in one of the proposed paradigms, it took between 15 and 25 hours of training for target fixations with the PRL in the presence of central scotoma simulation to become comparably accurate as foveal fixation in normal viewing (Kwon et al., 2013). In another study, Walsh and Liu (2014) trained their subjects over roughly 4 to 6 hours spread over 3 to 6 weeks. They observed that last fixations before target detection moved from the foveal region before training, to the individual PRL after training. However, the consistency of the last PRL fixations was not as high as the foveal fixations before training, suggesting that further training may have led to additional improvement of saccadic re-referencing to the PRL. Overall, a reduction of training hours with improved training techniques would be a considerable progress, making future training programs for patients more feasible.

Available training protocols used a variety of paradigms. For instance, Kwon et al. (2013) used a visual search task with cluttered realistic scenes. Although such a realistic scene search may have high ecological validity, it is difficult to describe and manipulate in terms of attentional demands posed by the search. In contrast, Walsh and Liu (2014) used a conjunction search task, where an O-shaped target had to be found among C-shaped distractors. This task is known to lead to inefficient, attention-dependent search in normal-sighted individuals, typically requiring overt eye movements to find the target (Treisman & Gelade, 1980). In both studies, participants had to search in the presence of a gaze-contingent central scotoma simulation that forced them to use an extrafoveal PRL for the search.

Here, we propose a new paradigm to train saccadic re-referencing. We first introduce the basic features of the method and then show its application with normal-sighted participants with simulated vision loss. A predetermined eccentric location was chosen to be trained and healthy participants underwent a “pop-out” search task in the presence of a gaze-contingent scotoma for an hour for 5 days in Experiment 1 and 25 days in Experiment 2.

In contrast to Walsh and Liu (2014), we used an efficient (“pop-out”) search task, in which a salient target in the periphery is automatically detected and may lead to reflexive eye movements toward the target. We think that pop-out search is an ideal paradigm to train saccadic re-referencing because the aim of a saccadic re-referencing training should be to enable effortless, not attention-dependent, fixation of peripheral points of interest with the PRL instead of the fovea.

Walsh and Liu (2014) needed to use an inefficient search task because they used a manual target-present response that in a pop-out task could have been executed without fixating the salient target. Instead, we used the actual eye movement that locates the target within a predetermined parafoveal location as a response, enabling us to use a pop-out search task for saccadic re-referencing training. Specifically, participants were instructed to fixate salient targets in a visual search display as fast as possible by locating them with eye movements into a predetermined (“forced”) extrafoveal retinal location (FRL; Lingnau, Schwarzbach, & Vorberg, 2008) adjacent to a gaze-contingent central scotoma. “Fixating” a target with the FRL ended the search and started the next trial.

A gaze-contingent FRL-fixation response has several advantages over a manual target detection response. (1) FRL fixation is immediately followed by feedback – for example, display disappearance - and (2) the speed of display presentation is directly linked to FRL-fixation. This contiguity should be optimal for learning. (3) Importantly, the use of the FRL can be tested at any time during the experiment without the need to implement an FRL marker (Kwon et al., 2013) or a blur mask that covers the visual field outside the FRL (e.g. Lingnau et al., 2008; Lingnau, Schwarzbach, & Vorberg, 2010; Lingnau, Albrecht, Schwarzbach, & Vorberg, 2014; Liu & Kwon, 2016).

Together with the classical single-target search task described so far, we also tested a multiple-target - “foraging” - search task. In the latter, multiple X-shaped targets were presented in a display with O-shaped distractors (Figure 1). The multiple-targets had to be “foraged” with eye movements by bringing the targets sequentially into the FRL. This multiple-target foraging paradigm allows additional analyses about the strategies used to prioritize potential targets in a scene (Kristjánsson, Jóhannesson, & Thornton, 2014). However, it also requires a decision process that is absent in single-target pop-out search. Although identical stimuli (the Xs and Os) were used for the single-target search, participants needed

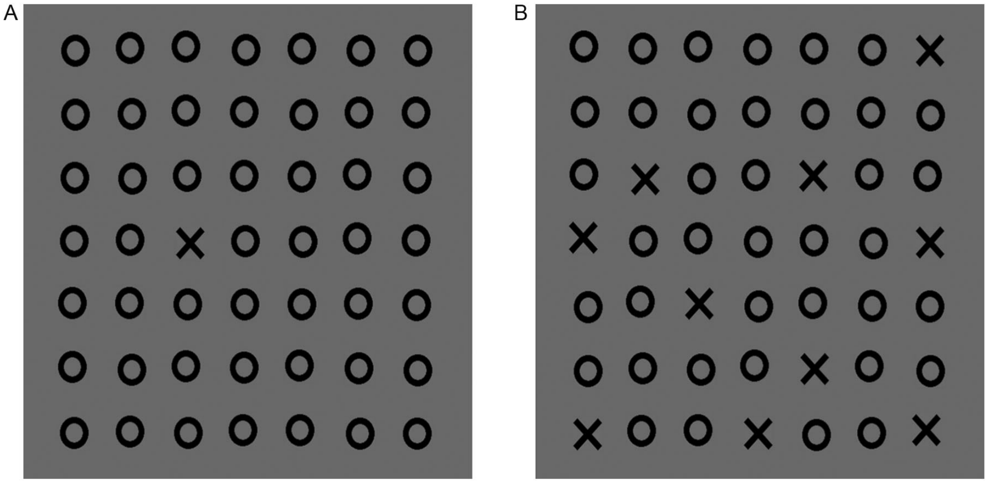

Figure 1. Examples of displays used in the experiment: single-target search (A) and multiple-target (foraging) search (B).

to decide (implicitly or explicitly) which target to look at next. Thus, the search may rely more on endogenous control than in the single-target search task, determining in which sequence the targets will be fixated.

Experiment 1: Single-target versus multiple-target search task

In Experiment 1, participants completed a single or multiple-target search task, in the presence or absence of a gaze-contingent scotoma. We tested whether saccadic re-referencing to the FRL developed in the course of training and evaluated which of the two target search tasks produced larger benefits for saccadic re-referencing training.

Methods

Participants

Twenty-four healthy participants (8 men and 16 women, Range = 19-33 years, mostly students of the Otto-von Guericke University, Magdeburg) participated in the experiment. All participants reported normal or corrected-to-normal visual acuity. Participants' visual acuity was tested using a Landolt C chart before the experiment. The experiment was approved by the ethics committee of the Medical Faculty of the Otto-von Guericke University Magdeburg. Informed written consent was obtained before the experiment. Participants were compensated with course credits or received compensation of 8 EUR/hour.

Apparatus

Stimuli were presented on a 24-inch Iyama Prolite GB2488HSU LED monitor set at a resolution of 1920 × 1080 pixels and a vertical refresh rate of 144 Hz. Participants viewed the display from 60 cm. The screen dimensions were 508 × 286 mm (48.58 degrees × 27.32 degrees). That is, each pixel was 0.025 degrees or 1.51 arcminute of visual angle. Eye movements were recorded using an Eyelink 1000 Desktop Mount (SR Research Ltd., Mississauga, Ontario, Canada) with 1000 Hz, using corneal reflection and pupil tracking. The experiment was implemented in MATLAB (R2012b) on a PC running Debian 8. Stimulus presentation and behavioral and eye-tracking data collection were done using Psychtoolbox (Brainard, 1997; Pelli, 1997) and the Eyelink toolbox (Cornelissen, Peters, & Palmer, 2002).

We simulated central visual field loss with a gaze-contingent scotoma. The real-time gaze position was sent to the display computer through a high-speed Ethernet link. Continuous gaze information was used to draw a scotoma on the display screen. The delay between the eye position update and the stimulus update in the display was 16.6 ms. This was measured using a setup that included a photodiode and an artificial eye driven by a stepper motor (Felsberg & Strazdas, 2022). Saccades were generated, and based on the artificial eye movement, a gaze-contingent white scotoma of 8 degrees was rendered on a black background. The delay was measured from the time the eye moved and the time the stimulus was drawn on the screen after the movement. The photodiode was placed at one end of the eye's landing position. The fluctuations in the voltage channels from the photodiode and from the eye movement were connected to a digital oscilloscope. The delay time or the time difference between the eye

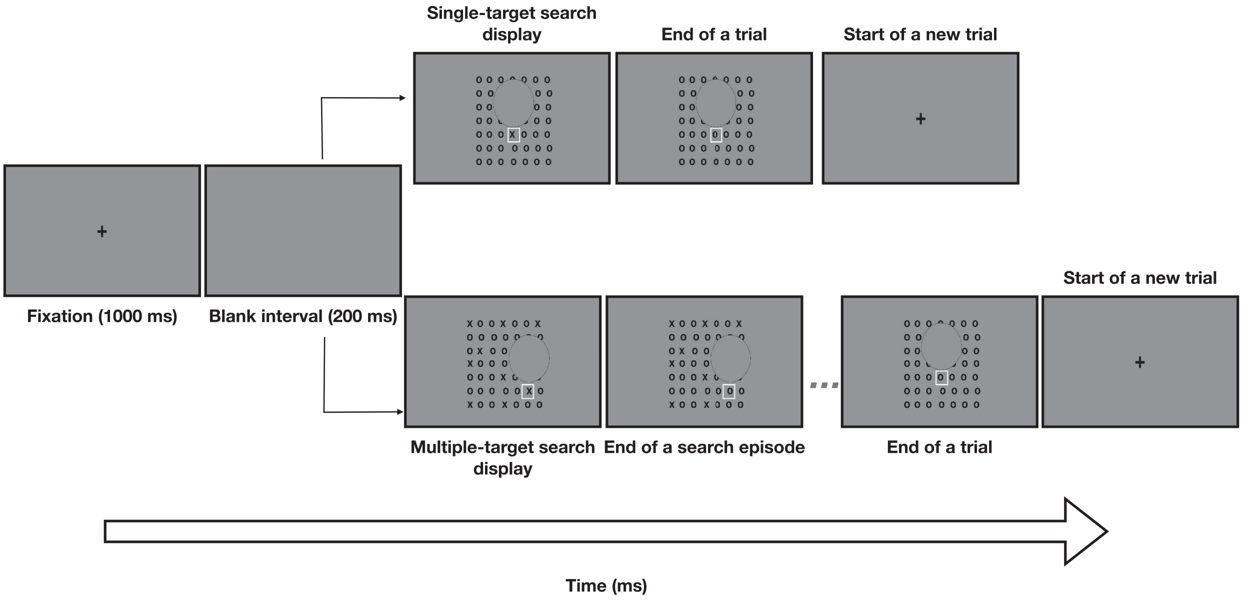

Figure 2. Time course of a trial in the scotoma condition (stimuli not drawn to scale; see text for details). Participants searched for a single X-target (single-target search task; *top*). Fixating the target with the FRL (indicated by a *white square* in the first two sessions) ended the display presentation. In the multiple-target search task (*bottom*), fixating the target with the FRL changed the X-shaped target into an O-shaped distractor (end of a search episode). A multiple-target search trial ended when the last remaining target had been fixated with the FRL zone.

movement and the stimulus update was calculated by measuring the time between the artificial eye motor signaling the correct position and the 85% rise time of the luminance change in the photodiode. The gaze data retrieved for the gaze-contingent simulation was filtered by the heuristic 1-sample filter (Cornelissen et al., 2002; Stampe, 1993) implemented in the Eyelink software, removing single-sample noise artifacts. A chin- and forehead rest was used to minimize participants' head movements. Participants were tested individually in a dimly lit sound-attenuated chamber under binocular viewing conditions.

Participants had fully developed binocular coordination of eye movements. Prior to the experiment, all participants successfully passed the Broad-H test showing no deviation in their ocular motility and no indication of pathological deviation of conjugate eye movements for both distance and near. Thus, only the participant's left eye was tracked.

Stimuli

Stimuli consisted of X-targets and O-distractors arranged on a 7 × 7 square grid spanning an area of 20.2 degrees × 20.2 degrees. In the single-target search task, each search display consisted of one X-target and 48 O-distractors (Figure 1A). In the multiple-target search task, each search display consisted of 10 X-targets and 39 O-distractors (Figure 1B). In both search tasks, the positions of the X-target were pseudo-randomly distributed with the only restriction that in multiple-target displays each X-target was separated by two O-distractors in both the horizontal and vertical directions. Distractors and target(s) were presented in black (0.65 cd/m^2) on a gray (74.84 cd/m^2) background at the grid nodes with a random offset of 0.2 degrees to prevent collinearity. The height and the width of the distractors and targets subtended a visual angle of 1 degree. The width of a stroke was 0.2 degrees.

Procedure

The task was to search for a single-target or 10 targets in a distractor-filled display either in the presence or absence of a gaze-contingent scotoma (scotoma and control groups, see Design). In the scotoma group, foveal vision was obstructed by a sharp-edged central scotoma (radius = 4 degrees). The scotoma was completely opaque within the scotoma diameter and 100% transparent beyond its diameter. The scotoma area color matched the display background (Figure 2). A white (238.41 cd/m^2) gaze-contingent reference frame, twice the target size (i.e. 2 degrees × 2 degrees with the width of frame subtending 0.1 degrees) constantly indicated the area of the FRL zone throughout the trial. In a pilot study, we observed a drastic drop in the search time from day 1 to day 2 suggestive of steep general learning of the task during the initial days of training. Therefore, the reference frame was provided for all participants for the first 2 days of training both in the scotoma and the control group and was removed for all participants in the subsequent sessions.

Each trial began with a central fixation cross (0.53 degrees [length of the stroke] × 0.08 degrees [width of the stroke]) presented for 1000 ms followed by a blank interval for 200 ms. Following the blank interval, the search display was shown. Scotoma simulation began with the presentation of the search display. The FRL was positioned outside of the scotoma and was defined as an area of 1 degree × 1 degree centered 5 degrees below the foveal fixation. Participants were instructed to "place the target within the square." In the single-target search task, when the X-target was "fixated" with the FRL for a total duration of 800 ms, the whole display disappeared and the central fixation cross appeared, indicating the start of the next trial. In the multiple-target search task, when an X-target was fixated with the FRL for a total duration of 800 ms, it changed into an O-shaped distractor. Once the target changed into a distractor, participants searched for another X-target (see Figure 2). When the last target was fixated, the display presentation ended, and the next trial began. In the control group, no scotoma was shown; participants performed the same tasks but with foveal vision.

Participants were instructed to minimize blinking and head and body movements during the trial. They could take breaks in between the trials and were given compulsory breaks of 5 to 10 minutes between blocks.

Trials were divided into blocks. A block consisted of 100 single-target search trials or 10 multiple (10) target search trials, leading to 100 target fixations in both tasks. At the beginning of each block, the eye-tracker was calibrated with a 9-point gaze calibration protocol and the spatial accuracy of the gaze data was validated. If the average offset errors exceeded 1 degree visual angle, the eye-tracker was recalibrated. A drift check was performed after each calibration and validation procedure, and before each trial. The eye-tracker was re-calibrated and re-validated in the middle of a block and whenever participants took their chin from the chinrest.

Design

Participants were assigned to one of four groups (with 6 participants in each group): foveal single-target search, foveal foraging/multiple-target search, single-target search in the presence of scotoma, and foraging/multiple-target search task in the presence of scotoma. The inclusion of participants in each group was based on their order of appointment on the first day of the experiment.

The experiment consisted of a training phase and three follow-up sessions. During the training phase, each participant completed a 1-hour training session per day for 5 consecutive days. On each training session, participants completed about 400 trials per day (average number of trials across all groups/day = 413; range = 386–448) depending on the participants' performance. Participants were given compulsory breaks between blocks. The 1-hour training session consisted of training time, break time for participants, and time taken for calibration.

The retention of the FRL after training was assessed on the 12th, 19th, and 36th day from the last day of the training session (day 5) without the presence of the reference frame. For each of the three follow-up sessions, participants completed one block without the presence of the reference frame (100 single-target trials or 10 trials with multiple-targets displays).

Data preprocessing

Raw gaze data were filtered with the Savitzky–Golay FIR smoothing filter (Savitzky & Golay, 1964) algorithm with second-order polynomials and a filter length of 21 ms. Invalid samples due to blinks or losses during the signal recording were removed and velocity thresholds were estimated. We identified saccade events by using a saccade detection algorithm (Engbert & Kliegl, 2003). Fixations were identified as the inter-saccadic events with a stable gaze for at least 50 ms (SD not exceeding 0.5 degrees in any direction; see also Kwon et al., 2013 for a detailed description of the method). A trial in the single-target search consisted of one search episode, whereas a trial in the multiple-target search consisted of 10 search episodes.

During data preparation, each search episode was separated and processed individually.

Behavioral and eye movement measures

Data exclusion and missing data: There were no dropouts during the training session. Twenty-three, 22, and 21 of 24 participants took part in the first, second, and final follow-up sessions, respectively.

Trial-based exclusion of behavioral, as well as gaze data, was based on reaction times (RTs). Trials with RTs greater than 2.5 times the standard deviation or less than 80 ms were excluded. The average number of trials discarded (RT exclusion, and blink or missing data) across subjects for each condition (including the follow-up) are as follows: single-target control: 11.4% (SD = 10.4%); single-target scotoma: 9.4% (4.6%); multiple-target control: 15.5% (8.1%); and multiple-target scotoma: 13.6% (5.9%).

We calculated the following behavioral and eye movement measures: RTs, average fixation duration, number of fixations, scan pattern ratio (SPR), bivariate contour ellipse area (BCEA) on first saccade landing location, and fixational stability (see Supplementary information for fixational stability methods and its results).

RTs were defined as the time taken to successfully detect the target. A target was considered to be detected when the FRL zone intersected with the target coordinates, before the start of the 800 ms duration in the FRL. In multiple-target search display, RTs were calculated as the time taken between the appearance of the distractor after the end of the 800 ms fixation of the previously detected target and the fixation of the new target. Average fixation duration (ms) was computed as the mean duration of all fixations that were detected from the onset of the search display (or the end of the previously detected target in the multiple search task) until the (next) target detection.

The number of fixations were computed as the number of fixations required to find the target stimulus from the onset of the search display (or the end of the previously detected target in the multiple search task) until the target detection. This is inclusive of fixational saccades less than 1-degree amplitude. However, to calculate the first saccade landing position, saccades that were less than 1-degree amplitude were excluded.

To calculate the scan pattern ratio, we divided the sum of saccade amplitudes during the search episode (for the multiple-target search) or search trial (for single-target search) by the distance between the first (central) fixation and the target location (Brockmole & Henderson, 2006). The scan pattern ratio reflects how circuitous the search was: the lower the SPR, the more direct the scan path.

Data analysis: To analyze the progression of the training over 5 days, the derived measures (RTs, scan pattern ratio, number of fixations, and average fixation duration) were entered into a mixed-design ANOVA with Session (days 1–5) as within-subject factor and Vision (control and scotoma) and Search Type (single and multiple targets) as between-subjects' factors. To analyze the performance during the retention period, the derived measures were entered into a mixed-design ANOVA with Session (days 5, 12, 19, and 36) as within-subject factor and Vision (control and scotoma) and Search Type (single and multiple targets) as between-subjects factors. For all ANOVA analyses, Greenhouse–Geisser corrections (noted as F_{GG}) were used when the sphericity assumption was violated. Post hoc two-tailed *t*-tests were adjusted according to Bonferroni's correction.

Moreover, to investigate if the training performance in the form of search times, SPR, fixation duration, and number of fixations was retained on the last post-test (day 36) when compared with the last day of training (day 5), Bayesian *t*-tests were calculated, separately for single-target search and multiple-target search. We calculated Bayes factor, BF0-, which indicates the relative probability under the null hypothesis that values (e.g. the mean RT) on day 5 were greater than or equal to values on day 36, relative to the alternative hypothesis that values on day 5 were lower than on day 36. Following convention, a BF0- between 1 and 3 would be seen as anecdotal evidence for the null hypothesis and a BF0- >3 as moderate evidence (Wagenmakers, Love, Marsman, Jamil, Ly, Verhagen, Selker, Gronau, Dropmann, Boutin, Meerhoff, Knight, Raj, van Kesteren, van Doorn, Smira, Epskamp, Etz, Matzke, de Jong, van den Bergh, Sarafoglou, Steingroever, Derks, Rouder, & Morey, 2018).

First saccade landing location: We analyzed the first saccade landing location for each trial to test whether saccadic re-referencing training was effective. It was estimated from the BCEA encompassing 68% of the fixation points collected from the eye movement data. The BCEA values were calculated using a custom-written program in MATLAB using the formula:

$$\mathrm{BCEA} = \chi^2\pi * \sigma_H * \sigma_v * \left(1 - \rho^2\right)^{1/2}$$

where χ^2 is the chi-square value (2 degrees of freedom) corresponding to a probability value of 0.682 (+1 SD); where σ_H and σ_V is the standard deviation of the fixation position in the horizontal and the vertical meridian, respectively, and ρ is the product-moment correlation of these components (Steinman, 1965; Crossland, Sims, Galbraith, & Rubin, 2004; Crossland, Culham, Kabanarou, & Rubin, 2005; Timberlake, Sharma, Grose, Gobert, Gauch, & Maino, 2005). The FRL position was estimated from the kernel density estimation from the end point of the first saccade landing locations and was defined to be the peak of the density (Kwon et al., 2013). BCEA on the first saccade landing location was calculated and the FRL position was estimated.

To analyze the first saccade landing location BCEA, after natural log transformation of BCEA values, we conducted a mixed-design ANOVA with Session (days 1–5) as within-subject factor and Vision (control and scotoma) and Search Type (single and multiple targets) as between-subjects factors. To analyze the performance during the retention period, log-transformed BCEA measures were entered into a mixed-design ANOVA with Session (days 5, 12, 19, and 36) as within-subject factor and Vision (control and scotoma) and Search Type (single and multiple targets) as between-subjects factors.

In addition to the above analysis, we calculated the Euclidean distance from the center of the trained FRL zone to the calculated PRL position from the first saccade landing positions for the scotoma group. We conducted ANOVA analysis with Session (day 1 and day 5) as within-subject factor and Search Type (single and multiple targets) as between-subjects' factor.

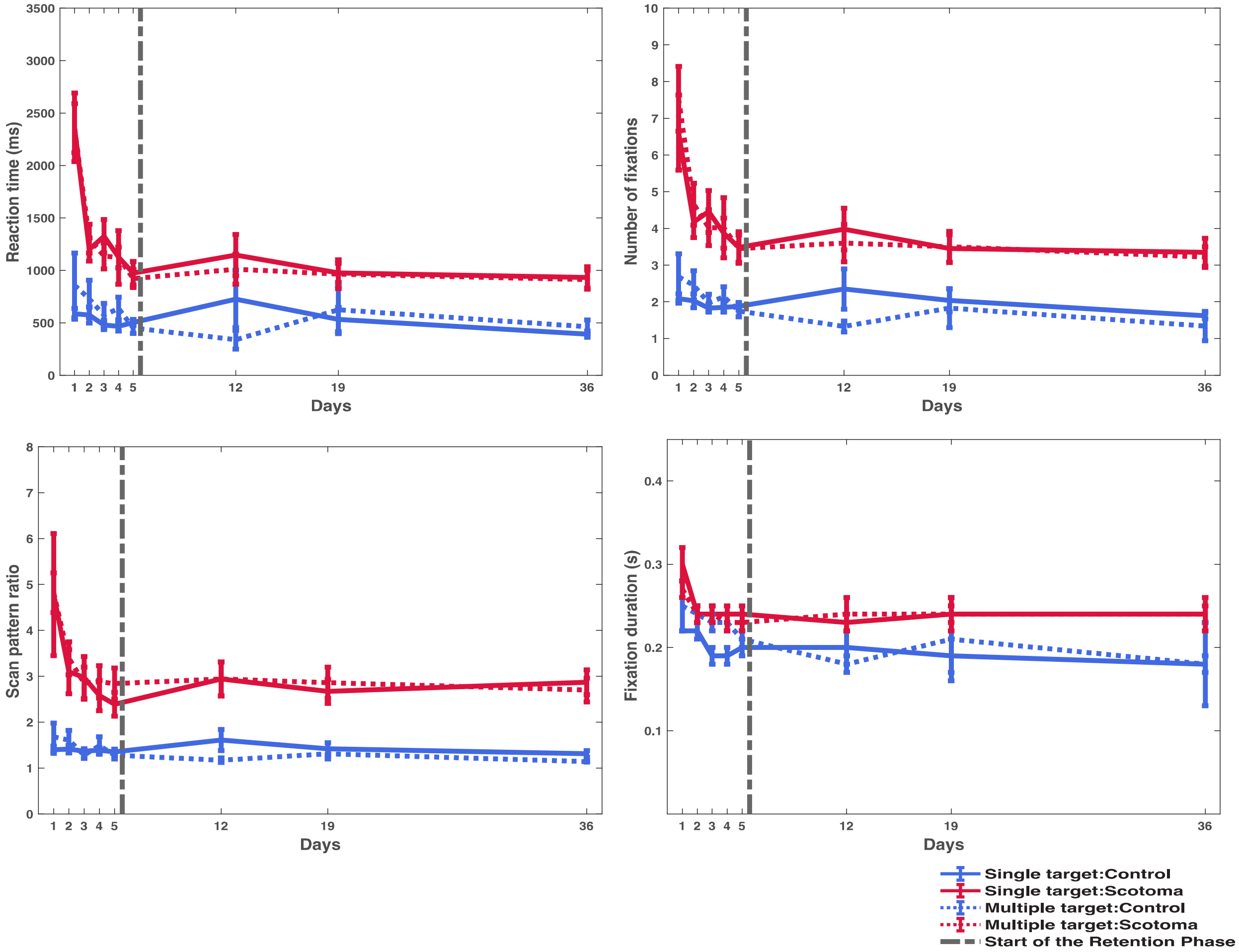

Figure 3. Average reaction time (*top left*), scan pattern ratio (*bottom left*), number of fixations (*top right*), and fixation durations (*bottom right*) as a function of days of training (days 1–5) and follow up (days 12, 19, and 36). The average data for all the variables are plotted for four groups: Control – Single and multiple targets, Scotoma – Single and multiple targets. Error bar indicates ±SEM.

We also analyzed the fixational stability data, which was measured before the training, after the training, and during the follow-up (for details on the methods and its results, see Supplementary information).

Data cleaning and analysis were performed using custom-made MATLAB scripts, Microsoft Excel software (2019), and JASP (JASP Team, 2020). JASP was used for Bayes factor analysis (Rouder, Speckman, Sun, Morey, & Iverson, 2009; Wetzels, Matzke, Lee, Rouder, Iverson, & Wagenmakers, 2011; Wagenmakers et al., 2018).

Results

The average number of trials per participant a day including the follow-up across participants were 268 and 267 for single-target and multiple-target search tasks, respectively.

Training results

The analysis of the training phase yielded a significant main effect of Session for reaction times, number of fixations, fixation duration, and scan pattern ratio, reflecting an improvement on all these measures over sessions (see Figure 3, Tables 1, 2 for the results of statistical comparisons).

The analysis also yielded a significant main effect of Vision for reaction times, number of fixations, fixation duration, and scan pattern ratio (see Table 2). These effects indicated overall higher RTs (mean $RT_{scotoma} = 1382.61$ ms vs. mean $RT_{control} = 585.44$ ms), longer fixation durations (mean fixation $durations_{scotoma} = 0.25$ seconds vs. mean fixation $durations_{control} = 0.22$ seconds), higher number of fixations (mean number of $fixations_{scotoma} = 4.63$ vs. mean number of $fixations_{control} = 2.07$) and longer scan paths (mean $SPR_{scotoma} = 3.23$ vs. mean $SPR_{control} = 1.43$) in the scotoma groups compared to the control groups.

		Single-target			Multiple-target		
Condition	Measures	Day 1	Day 5	Day 36	Day 1	Day 5	Day 36
Scotoma	RT (ms)	2364.23 (327.17)	973.06 (111.92)	991.33 (101.69)	2354.94 (233.62)	921.54 (85.50)	912.61 (91.77)
	Number of fixations	6.61 (1.02)	3.48 (0.43)	3.35 (0.38)	7.53 (0.88)	3.45 (0.37)	3.22 (0.28)
	Scan pattern ratio	4.78 (1.33)	2.40 (0.26)	2.87 (0.27)	4.82 (0.43)	2.84 (0.34)	2.70 (0.26)
	Fixation duration (s)	0.30 (0.02)	0.24 (0.01)	0.24 (0.01)	0.27 (0.01)	0.23 (0.01)	0.24 (0.02)
Control	RT (ms)	585.18 (50.77)	504.06 (28.85)	392.50 (29.61)	857.60 (307.47)	451.07 (53.16)	462.74 (64.03)
	Number of fixations	2.09 (0.13)	1.88 (0.10)	1.62 (0.08)	2.68 (0.63)	1.75 (0.16)	1.34 (0.40)
	Scan pattern ratio	1.41 (0.08)	1.35 (0.06)	1.31 (0.07)	1.68 (0.30)	1.28 (0.08)	1.14 (0.01)
	Fixation duration (s)	0.22 (0.004)	0.20 (0.01)	0.18 (0.01)	0.25 (0.03)	0.21 (0.01)	0.18 (0.05)

Table 1. Summary of mean data for all the conditions on day 1, day 5, and day 36. *Note:* SEM in parentheses.

	RT			SPR			Number of fixations			Fixation duration			First saccade landing BCEA		
Effect	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2
Session	31.01	<0.001***	0.61	14.49	<0.001***	0.42	28.94	<0.001***	0.59	16.25	<0.001***	0.45	11.69	<0.001***	0.37
Vision	45.52	<0.001***	0.70	28.61	<0.001***	0.59	38.62	<0.001***	0.66	7.47	0.01**	0.27	14.62	0.001***	0.42
Search Type	0.17	0.68	0.01	0.27	0.61	0.01	0.35	0.56	0.02	0.89	0.36	0.04	10.72	0.004**	0.35
Session x Search Type	0.63	0.53	0.03	0.46	0.57	0.02	1.57	0.22	0.07	0.83	0.45	0.04	0.75	0.47	0.04
Session x Vision	16.96	<0.001***	0.46	10.42	0.001***	0.34	16.28	<0.001***	0.45	1.98	0.15	0.09	1.81	0.18	0.08
Search Type x Vision	0.44	0.51	0.02	0.07	0.79	0.004	0.003	0.96	<0.0001	3.96	0.06*	0.17	13.48	0.002**	0.40
Session x Vision x Search Type	0.32	0.71	0.02	0.44	0.59	0.02	0.33	0.70	0.02	1.68	0.2	0.08	0.44	0.64	0.02

Table 2: Statistical results of the group comparison for search time, number of fixations, fixation duration, scan pattern ratio, and first saccade landing BCEA for the training phase. Notes: ***$p <= 0.001$, **$p <= 0.05$, and *$p <= 0.1$. Session: day 1–5, Vision: control/scotoma, and search type: single/multiple.

There was no significant main effect of Search Type for any of the extracted variables. This indicates that the presence of single target or multiple target search types do not influence reaction times, number of fixations, fixation duration, and scan pattern ratio over sessions.

The interaction between Session and Vision was significant for all the extracted variables except fixation duration (see Table 2). These interactions reflected a greater improvement in these variables over sessions in the scotoma groups (mean difference day 1 vs. day 5 for RTs = 1412.28 ms, $t(20) = 12.18$, $p < 0.0001$, number of fixations = 3.61, $t(20) = 11.97$, $p < 0.0001$, and scan pattern ratio = 2.18, $t(20) = 8.35$, $p < 0.0001$) versus the control group (mean difference day 1 vs. day 5 for RTs = 243.82 ms, $t(20) = 2.10$, $p = 1.00$, number of fixations = 0.57, $t(20) = 1.90$, $p < 0.86$, and scan pattern ratio = 0.23, $t(20) = 0.87$, $p = 1.00$; see Table 1). The performance improved for all the extracted variables except fixation duration in the scotoma group than the control group over sessions.

Finally, the interaction between Search Type and Vision showed a trend toward significance for the fixation duration, reflecting higher fixation duration of the scotoma group relative to the control group in single-target search. No other interactions were significant for neither variable (reaction times, all $F <= 0.63$, $p >= 0.53$; scan pattern ratio, all $F <= 0.46$, $p >= 0.57$; number of fixations, all $F <= 1.57$, $p >= 0.22$; fixation durations, all $F <= 1.68$, $p >= 0.20$). The presence or absence of the scotoma and the target types influenced only the fixation duration.

Retention results

The analysis of the retention period with Session (days 5, 12, 19, and 36) as within-subjects factor, showed no relevant main effects or interactions for any extracted variables, suggesting a stable performance across days (see Figure 3, Table 3 for the results of statistical comparisons). Only the main effect of Vision was significant across RTs, number of fixations, and scan pattern ratio, indicating worse performance in the scotoma group. The performance was stable for all the extracted variables during the retention phase. The differences in the extracted variables during the retention was primarily due to the presence or the absence of the scotoma.

To further test whether RTs remained constant or were even reduced post training, we calculated Bayesian *t*-tests comparing day 5 (last day of training) and day 36 (last post-test) for the scotoma groups, separately for single and multiple-target searches.

	RT			SPR			Number of fixations			Fixation duration			First saccade landing BCEA		
Effect	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2
Session	1.44	0.24	0.08	0.78	0.51	0.05	1.49	0.24	0.09	0.66	0.58	0.04	1.35	0.27	0.08
Vision	23.95	<0.001***	0.60	34.03	<0.001***	0.68	29.41	<0.001***	0.65	2.84	0.24	0.08	7.80	0.01**	0.33
Search Type	0.56	0.47	0.03	0.40	0.54	0.03	0.62	0.44	0.04	1.57	0.23	0.09	5.13	0.04**	0.24
Session x Search Type	1.04	0.36	0.06	0.95	0.43	0.06	0.64	0.53	0.04	1.18	0.33	0.07	1.91	0.14	0.11
Session x Vision	0.21	0.80	0.01	0.52	0.67	0.03	0.16	0.84	0.01	1.25	0.30	0.07	0.11	0.96	0.007
Search Type x Vision	0.05	0.83	0.003	0.05	0.82	0.003	0.007	0.94	<0.0001	1.44	0.25	0.08	7.03	0.02**	0.31
Session x Vision x Search Type	0.54	0.58	0.03	0.82	0.47	0.05	0.35	0.70	0.02	0.99	0.40	0.06	1.48	0.23	0.09

Table 3. Statistical results of the group comparison for search time, number of fixations, fixation duration, scan pattern ratio, and first saccade landing BCEA for the retention phase. Notes: ***$p <= 0.001$, **$p <= 0.05$, and *$p <= 0.1$. Session: days 5, 12, 19, and 36, Vision: control/scotoma, and search type: single/multiple.

For RTs, these analyses yielded BF0- = 3.86 for the single-target search and BF0- = 2.83 for the multiple-target search. Thus, for single-target search, the null hypothesis (“RT [day 5] >= RT [day 36]”) was 3.86 times more likely than the alternative hypothesis (“RT [day 5] < RT [day 36]”), and the null hypothesis was 2.83 times more likely than the alternative hypothesis for multiple-target search. For the number of fixations, we observed a BF0- = 4.13 for the single-target search and a BF0- = 4.18 for the multiple-target search, obtaining therefore moderate evidence in favor of the null hypothesis. In the case of the fixation duration, comparisons yielded BF0- = 2.10 for the single-target search and BF0- = 0.96 for the multiple-target search thus indicating anecdotal evidence in support of the null hypothesis for single-target search and for the alternative hypothesis for multiple-target search. Finally, for scan pattern ratio, these analyses yielded a BF0- = 0.15 for the single-target search and BF0- = 4.10 for the multiple-target search. Thus, for the single-target search, the BF0- factor yields moderate evidence for the alternative hypothesis of increased SPR at the end of the retention period. In contrast, for the multiple-target search, there was moderate evidence for the null hypothesis.

To summarize, the search performance improved with training across the four variables. As expected, this improvement was predominantly seen in the scotoma group, irrespective of the search type. In addition, the improvement observed was retained in the retention period regardless of the trained task.

First saccade landing location results

The reduced reaction times, fixation numbers, and scan pattern ratios after training are only indirect hints that saccadic re-referencing might have occurred. To yield more direct evidence for saccadic re-referencing, we investigated the location of the first saccade landing after display onset (in single-target search) and target conversion to distractor in the multiple-target search. Because the X-among-O search is highly efficient - the X-targets pop out from the distractor background, we expected that targets would be foveated with the first saccade in the control condition. In the scotoma condition, we also expected target foveation at day 1. However, if saccadic re-referencing occurred, the first saccade landing position should be shifted to the upper border of the scotoma after training and remain there during the retention period, so that the target would fall into the FRL below the scotoma.

The ANOVA analyses for training on the saccade landing location revealed a significant main effect of Session (F (1,10) = 19.39, $p = 0.001$, $\eta_p^2 = 0.66$), reflecting decreasing distance between the landing location and the center of the trained FRL. We also observed a significant main effect of Search Type (F (1,10) = 8.09, $p = 0.02$, $\eta_p^2 = 0.45$). Participants showed significant improvement in the landing location from day 1 to day 5 especially in the multiple-target search task (mean difference-single-target: day 1 vs. day 5 = 1.31 degrees, t(10) = 2.51, $p = 0.18$; mean difference-multiple-target: day 1 vs. day 5 = 1.93 degrees, t(10) = 3.71, $p = 0.02$). There was no significant interaction between Session and Search Type (F (1,10) = 0.72, $p = 0.42$).

In other words, the saccade landing positions were closer to the center of the trained FRL over sessions. In addition, participants who were trained with multiple target search display were able to land their saccades closer to the trained FRL than the single target group.

We further investigated if the first saccade would directly land the target in the FRL after saccadic re-referencing training. The FRL zone was defined as an area of 1 degree × 1 degree in diameter. Therefore, the maximum Euclidean distance to classify the saccadic re-referencing training as “successful” was defined as the diagonal of 1 degree × 1 degree which is 0.71 degrees radius from the FRL center. If the training is successful or when saccades are redirected to the trained FRL, we would expect data points to fall within the dashed red line (Figure 4). Some participants

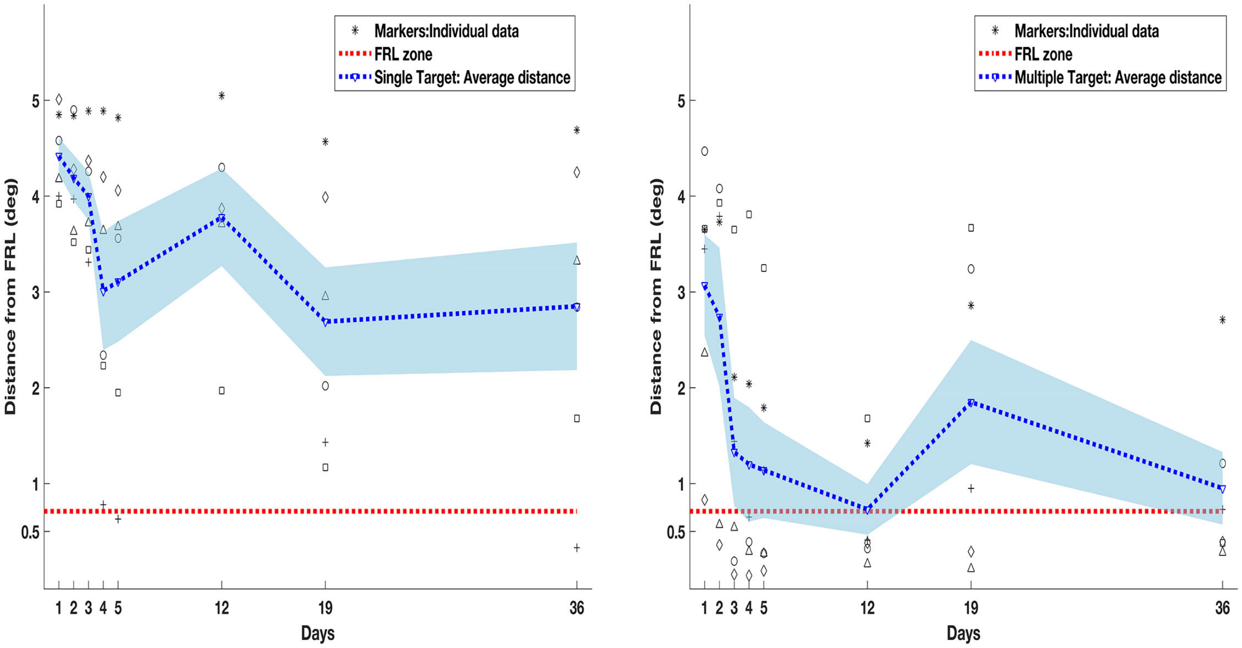

Figure 4. Euclidean distance between the estimated PRL from the first saccade landing positions and the center of the trained FRL as a function of training days (days 1–5) and follow-up (days 12, 19, and 36) for both single-target (*left*) and multiple-target (*right*) search tasks. On the x-axis is the days and on the y-axis is the distance from the FRL in degrees. The average distance in *blue*, different markers in *black* indicate individual subject data, and the *red dotted line* indicates the FRL zone. The shaded region indicates ±SEM.

had their first saccade landing with a distance of almost a radius of the simulated scotoma from the center of trained FRL even after training. In other words, the participants first saccade landing location was beyond the FRL location and participants did make corrective saccades to do the task even after the training. Based on this cutoff limit, in single-target search, a shift of the first saccade landing location into the FRL was on average observed in only one of the six participants during the training and the retention phases (Figures 4, 5). In contrast, in the multiple-target search, the shift was observed in four of six participants during the training and the retention phases (Figures 4, 6).

The analysis of the BCEA for the first saccade landing position during the training phase yielded a significant main effect of Session, reflecting improvement in the saccade landing to the trained FRL over sessions and a significant main effect of Vision, due to better saccadic re-referencing in the foveal group, driven by the multiple-target search task, when compared to the scotoma group (see Figure 7, Table 2). There was also a significant main effect of Search Type. The mean log unit difference between the multiple and the single-target search type was -0.60 log deg^2 ($p = 0.004$), suggesting better performance in the multiple-target search type. The interaction between Search Type and Vision was significant as well due to an advantage of foveal viewing over peripheral viewing. The remaining interactions between Session and Search Type or between Session and Vision or between Session, Vision, and Search Type were not significant (all $F <= 1.81$, $p >= 0.18$).

The analysis of the retention phase indicated that there was no significant main effect of Session. There were significant main effects of Search Type, and Vision, and a significant interaction between the Search Type and Vision, suggesting better performance in the multiple-target display under foveal viewing. None of the other interactions were significant (all $F <= 1.91$, $p >= 0.14$; see Figure 7, Table 3).

From the above analyses, both the FRL location and BCEA on the first saccade landing site for the scotoma groups improves as a function of training. This indicates that the scotoma group "adapts" to the scotoma and the foveal location is replaced by the trained peripheral retinal location. In the case of controls, the BCEA of the saccade landing position improves for the multiple-target search as a function of training.

Discussion

Training to "fixate" a search target among distractors at an FRL adjacent to a simulated central scotoma led to a more efficient search as indexed by reaction time, number and duration of fixations, and scan

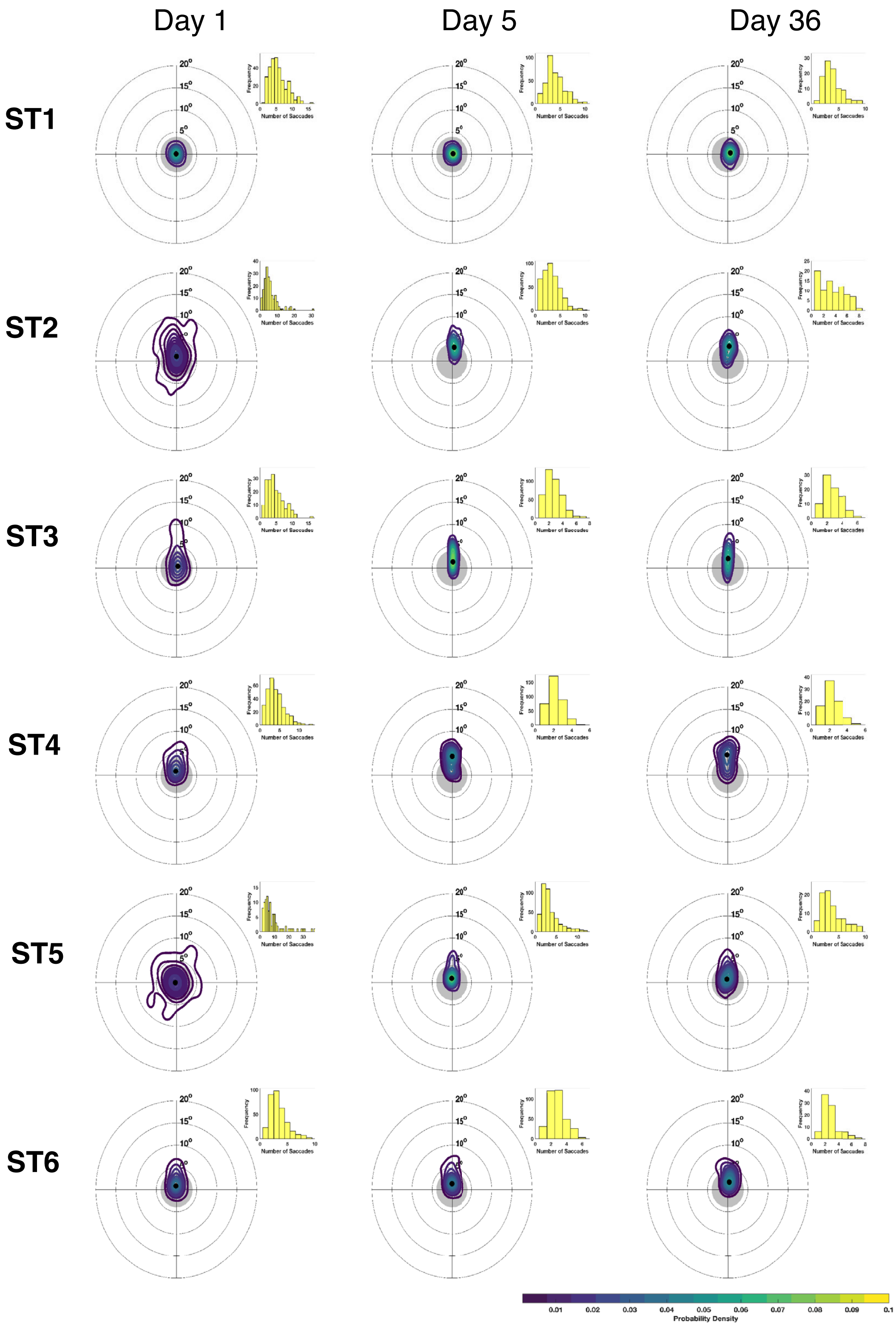

Figure 5. Probability density maps of first saccade landing positions for single-target search task for day 1, day 5, and day 36 for the scotoma group. Each row represents one participant. The inset figure represents the frequency distribution of the number of saccades. The black dot is the calculated PRL position.

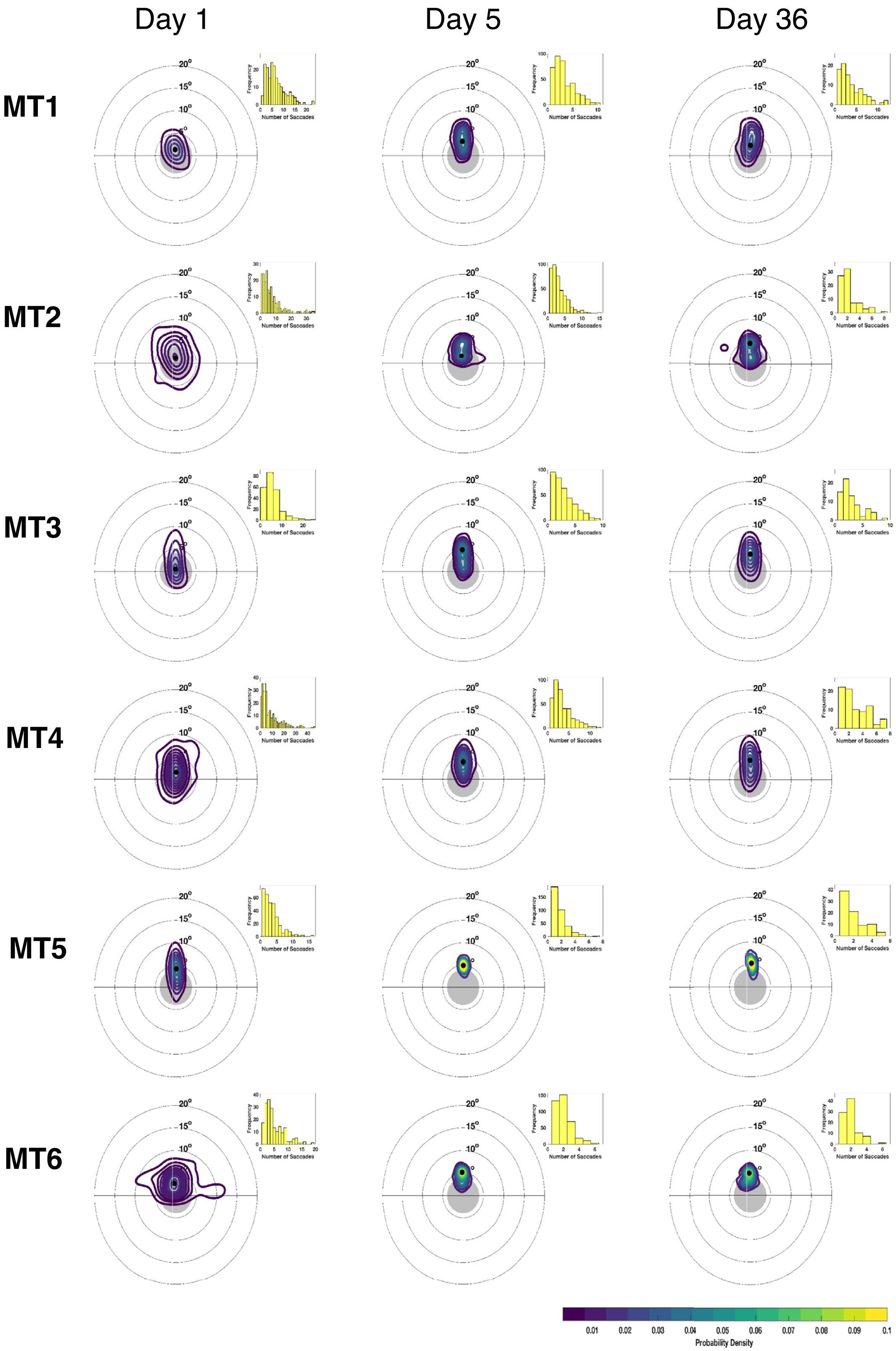

Figure 6. Probability density maps of first saccade landing positions for the multiple-target search task for day 1, day 5, and day 36 for the scotoma group. Each row represents one participant. The inset figure represents the frequency distribution of the number of saccades. The *black dot* is the calculated PRL position.

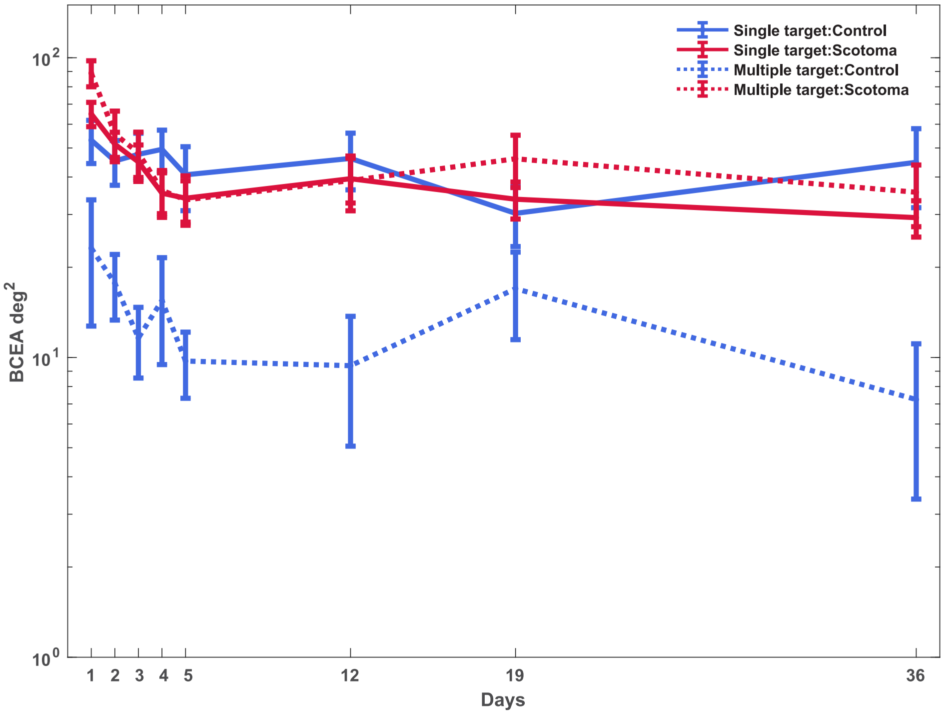

Figure 7. Average BCEA for the first saccade landing positions as a function of days of training (days 1-5) and follow-up (days 12, 19, and 36). On the x-axis is the days and on the y-axis is the BCEA in deg^2. The average BCEA is plotted for all the groups: Control – Single and multiple targets, Scotoma – Single and multiple targets. Error bar indicates ±SEM.

pattern ratio. This was observed for the single and multiple-target search tasks alike. The training gains were mostly retained during the 1-month follow-up period. There was solid evidence for retention of gains in RT and fixation number. More efficient scan pattern ratios were particularly preserved over the retention period in the multiple-target search.

As a more direct indicator of saccadic re-referencing, the landing location of the first saccade was shifted toward the upper border of the scotoma after training in multiple-target search, as expected if saccadic re-referencing to an FRL below the scotoma was learned. This shift was retained in the 1-month follow-up. In single-target search, this shift of the first saccade landing location was observed in only one of the six participants. In addition, there was an overall improvement in the fixational stability when comparing pre and post BCEA measures.

The reason for larger BCEA for the single target control group was that a few participants made, on average, two saccades to perform each trial. This was similar to the performance of the single target scotoma group. In addition, the distance between the first saccade location and the target was greater by a factor of two in the single target control group when compared with the multiple target control group. This suggests that the BCEA variability seen especially in the single target control group was due to the increased number of saccades made by a few participants during the search task (Figures 8, 9).

The difference between comparable training gains for the single and multiple-target searches in terms of RT, fixation numbers, and SPR but less efficient FRL fixation in the single-target search was puzzling. A potential explanation may be that the pop-out single-target search required less attentional focusing than the selection of one of the multiple targets in the multiple-target search. Thus, although the target needed to be "fixated" with the FRL eventually, there might have been less pressure for an exact first fixation bringing the target into the FRL in the pop-out single-target search.

Experiment 2: Extensive training of saccadic re-referencing

The results of Experiment 1 showed that the proposed method is efficient in terms of training FRL use in search with a simulated scotoma. The performance metrics used (search RT, number of fixations, fixation durations, and SPR) were successfully retained even beyond 4 weeks of follow-up. In addition, the training performance was observed for both the single and multiple-target searches, with somewhat better performance in the latter.

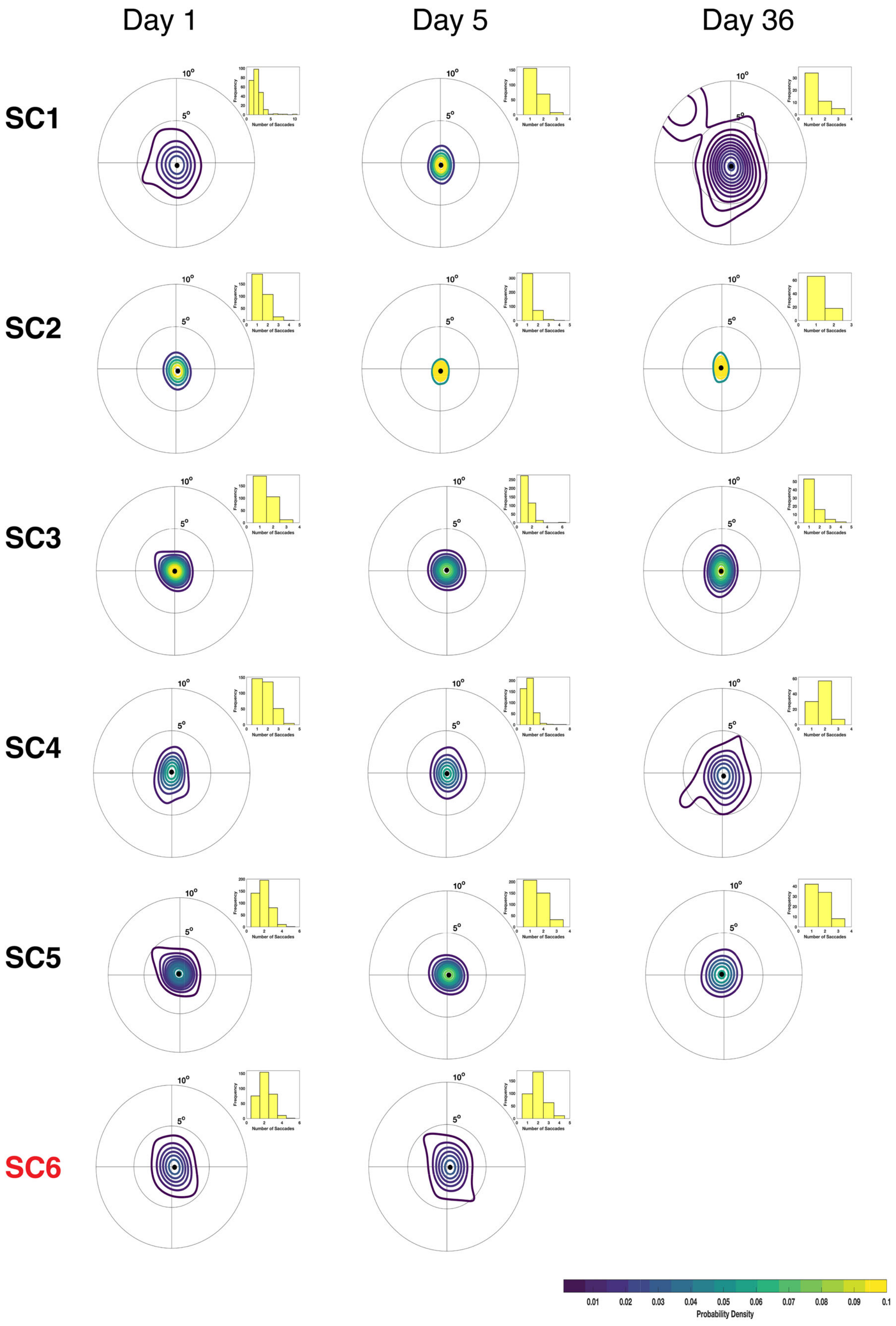

Figure 8. Probability density maps of first saccade landing positions for single-target search task for day 1, day 5, and day 36 for the control group. Each row represents one participant. The inset figure represents the frequency distribution of the number of saccades. The *black dot* is the calculated PRL position. Participant SC6 (*red*) did not participate for the third follow-up.

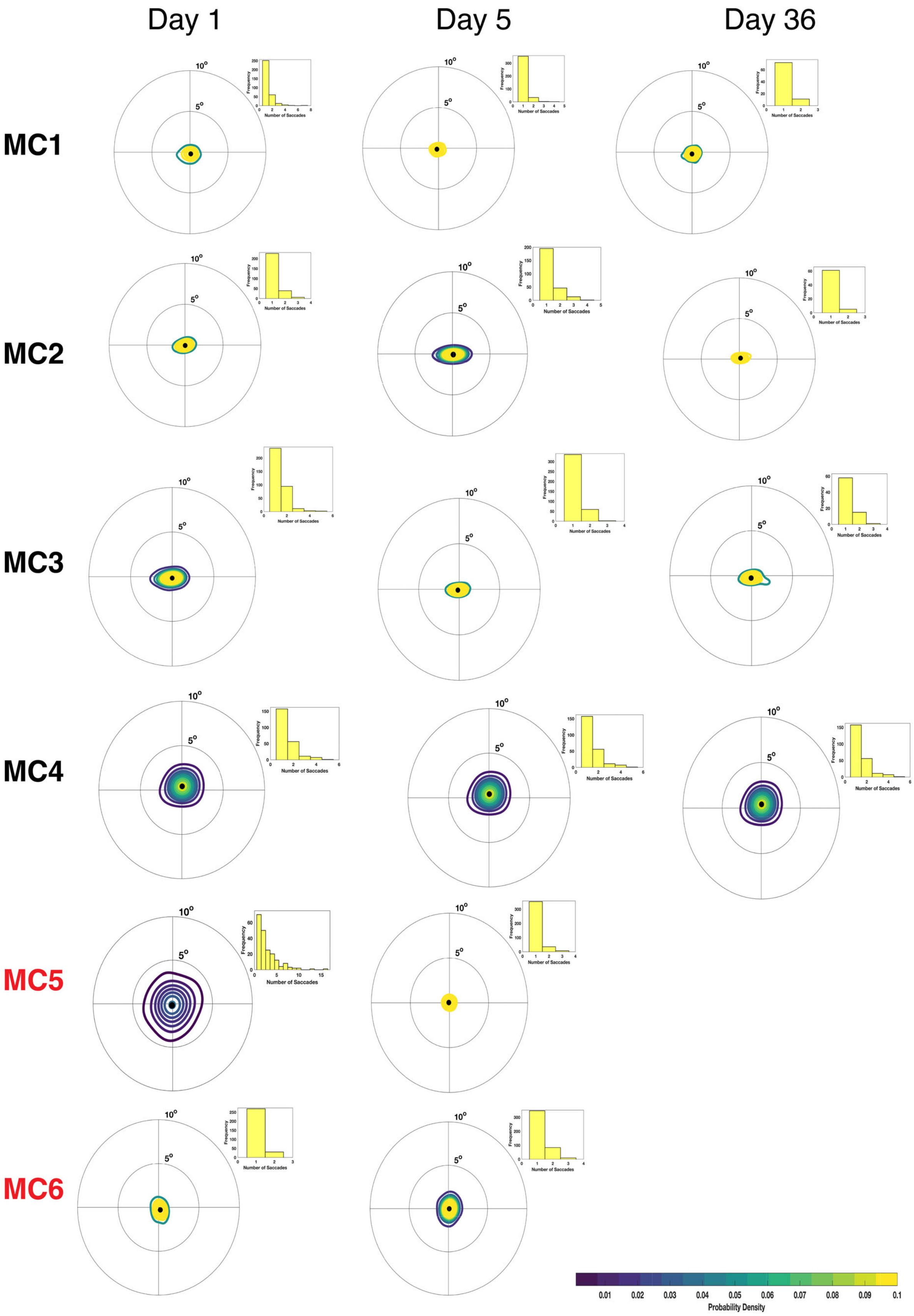

Figure 9. Probability density maps of first saccade landing positions for the multiple-target search task for day 1, day 5, and day 36 for the control group. Each row represents one participant. The inset figure represents the frequency distribution of the number of saccades. The *black dot* is the calculated PRL position. Participants MC5 and MC6 did not participate for the third follow-up (in *red*).

Nevertheless, search after saccadic re-referencing training was still less efficient than the normal search without scotoma simulation. Therefore, in Experiment 2, we investigated if additional saccadic re-referencing training would lead to search improvement comparable to search with an intact fovea. In addition, we investigated the contribution of the FRL-reference frame which was either absent or remained present during training. Only the multiple-target search task was used based on the results of Experiment 1.

Methods

Participants

Six healthy participants (3 men and 3 women, range = 19–34 years), including the first author, participated in the experiment. All participants reported normal or corrected to normal visual acuity. The experiment was approved by the ethics committee of the Medical Faculty of the Otto-von Guericke University Magdeburg. Informed written consent was obtained before the experiment. Participants were compensated with course credits or received compensation of 8 EUR/hour.

Procedure

The stimuli and procedure in Experiment 2 were the same as in Experiment 1 except for the following changes. Only the multiple search task was used. All participants performed training with simulated scotoma vision. They completed 1 hour of training for 25 consecutive days excluding weekends. Fixation stability was measured before and after each session. All participants completed 20 practice trials with the FRL reference frame before commencing the training on day 1. This was done to familiarize participants with the location of the FRL. Subjects were divided into two groups. One group ("Reference group," $N = 3$) completed the task with the FRL reference frame, while the other group ("No-reference group," $N = 3$) performed the task without the reference frame. On day 25, all participants completed saccadic re-referencing training without the reference frame as a common test of training efficiency. On the 25th day, after the regular fixational stability measure in the presence of scotoma, the foveal BCEA was measured in the absence of scotoma for all participants. Foveal BCEA was measured to investigate if there was an after-effect of the saccadic re-referencing training that might transfer to non-scotomatous vision.

Data analysis

Data pre-processing, exclusion, and analysis procedures were the same as in Experiment 1. Repeated-measures ANOVAs with Session (day 1 to day 24) as within-subject factor and Frame (present and absent) as a between-subject factor were calculated. We further investigated the time course of learning by running separate analyses for day 1 - day 12 and day 13 - day 24. Independent sample *t*-test analysis was performed on data from the 25th day of training between the no-reference group and the group that switched from reference to no-reference.

Results

Training results

The ANOVA of the extensive training phase yielded a significant main effect of Session for reaction times, number of fixations, fixation durations, and scan pattern ratio. This reflected an improvement on all these measures except scan pattern ratio over sessions (see Figure 10, Table 4).

The analyses yielded no significant main effect of Frame for reaction times, number of fixations, fixation duration, and scan pattern ratio. This suggests that the improvement in performance did not depend upon the presence or absence of the reference frame.

The interaction between Session and Frame was significant for scan path ratio, due to the more variable development of the SPR over time in the no-reference group. However, no significant interaction between Session and Frame was found for the remaining variables.

Time course of the training results

The session effect was further analyzed for all the variables for days 1 to day 12 and for day 13 to day 24. The learning effects due to training was seen for all extracted variables for both the first (day 1 to day 12) and second half of the training (day 13 to day 24) except for fixation durations and scan pattern ratio which was neither significant for days 1 to 12 or days 13 to 24 (see Table 4).

Finally, the analysis of the last session (on which the reference frame was removed for the reference group) showed no significant differences for any of the extracted variables (reaction time: $t(4) = -0.94$, $p = 0.40$; scan pattern ratio: $t(4) = 1.06$, $p = 0.35$; number of fixations: $t(4) = -0.94$, $p = 0.40$; and fixation durations: $t(4) = 0.12$, $p = 0.91$).

To summarize, the search performance improved with training across the three variables (reaction times, number of fixations, and fixation durations) and consistent learning of the training occurred during the initial half or later half of the training for all the extracted variables excluding scan pattern ratio.

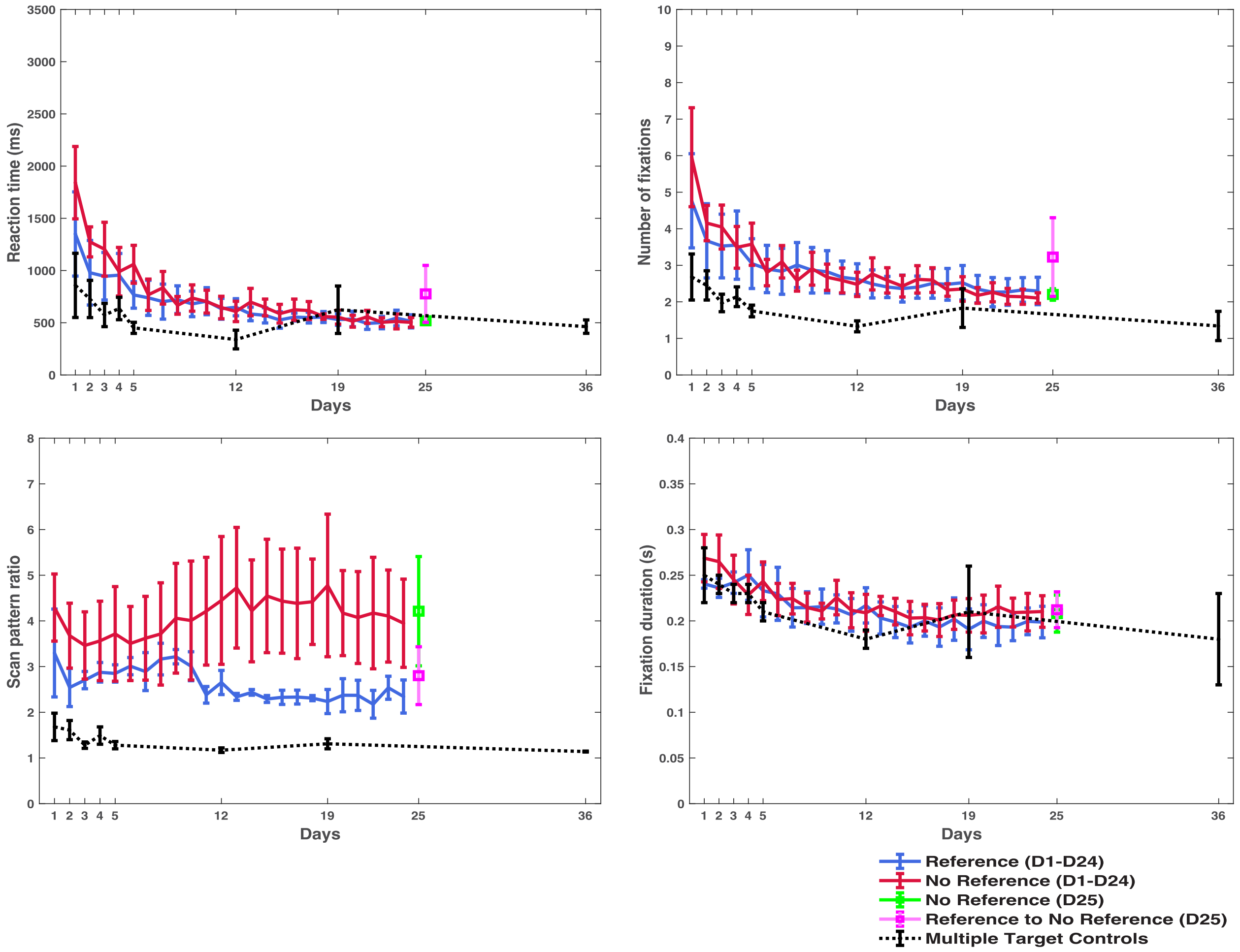

Figure 10. Mean reaction times (*top left*), scan pattern ratio (*bottom left*), number of fixations (*top right*), and fixation durations (*bottom right*) as a function of days of training. Control data of multiple-target search from Experiment 1 (*black dotted line*) are added. On the 25th day, the participants from the reference group switched to the no-reference condition (magenta data point), whereas the no-reference group remained as a no-reference group (*green* data point). Error bar indicates ±SEM.

Overall, this shows that the training was effective regardless of the presence or absence of the reference frame.

First saccade landing location

For first saccade landing BCEA, the ANOVA yielded a significant main effect of Session. There

	RT			SPR			Number of fixations			Fixation duration			First saccade landing BCEA		
Effect	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2	F	*p* value	η_p^2
Session	15.23	<0.001***	0.79	0.67	0.86	0.14	11.69	<0.001***	0.75	6.42	<0.001***	0.62	6.10	<0.001***	0.60
Frame	0.25	0.64	0.06	2.10	0.22	0.34	0.01	0.92	0.003	0.13	0.74	0.03	0.08	0.79	0.02
Session x Frame	0.99	0.49	0.20	2.01	0.01**	0.34	0.66	0.87	0.14	0.56	0.94	0.12	0.51	0.97	0.11
†Session	13.64	<0.001***	0.77	0.68	0.75	0.15	10.02	<0.001***	0.72	5.94	<0.001***	0.60	6.29	<0.001***	0.62
Frame	0.30	0.62	0.07	1.07	0.36	0.21	0.04	0.86	0.01	0.05	0.84	0.01	0.26	0.64	0.03
Session x Frame	1.27	0.28	0.24	0.66	0.77	0.14	0.79	0.65	0.97	0.48	0.20	0.08	0.44	0.93	0.10
§Session	4.02	<0.001***	0.50	0.88	0.57	0.18	3.57	0.001***	0.47	0.62	0.80	0.13	0.88	0.57	0.18
Frame	0.15	0.72	0.04	3.21	0.15	0.45	0.002	0.97	<0.001	0.22	0.67	0.05	<0.001	0.98	<0.001
Session x Frame	1.19	0.32	0.23	1.24	0.29	0.24	1.18	0.33	0.23	0.34	0.97	0.08	0.42	0.94	0.09

Table 4. Statistical results of the group comparison for search time, number of fixations, fixation duration, scan pattern ratio, and first saccade landing BCEA for the extensive training phase. Notes: ***$p <= 0.001$, **$p <= 0.05$, and *$p <= 0.1$. Session: days 1–24, †days 1–12, and § days 13–24. Frame: present/absent.

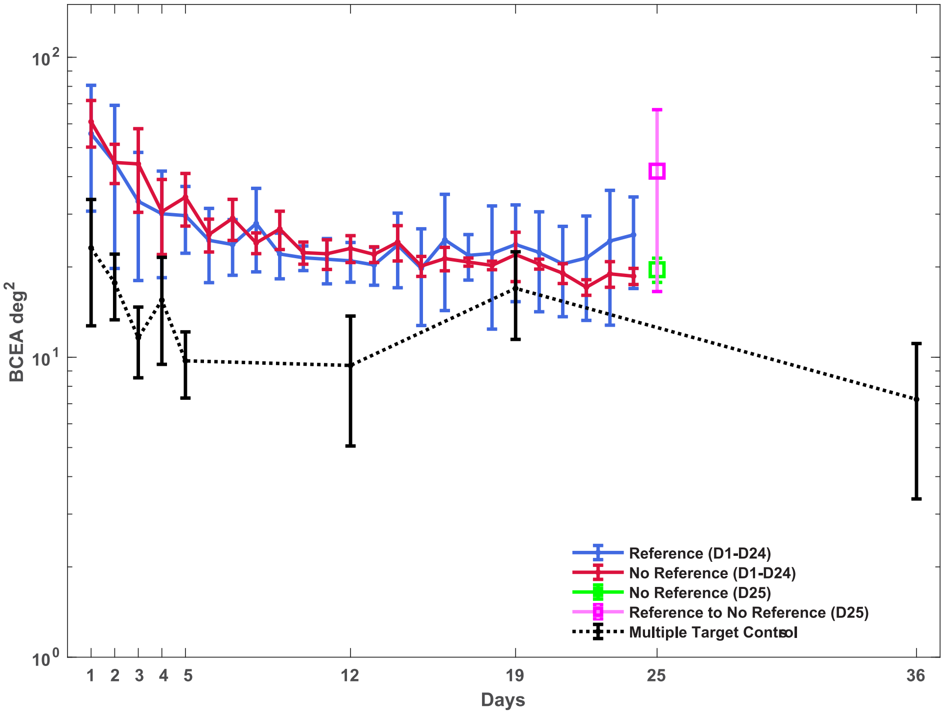

Figure 11. BCEA on first saccade landing position as a function of days of training. On the x-axis is the days and on the y-axis is the BCEA in deg^2. The average BCEA is plotted for the groups: reference and no-reference condition, and control data of the multiple-target search from Experiment 1 (*black dashed line*). On the 25th day, the participants from the reference group switched to the no-reference condition (*magenta* data point), whereas the no-reference group remained as a no-reference group (*green* data point). Error bar indicates ±SEM.

was no significant main effect of Frame and no significant interaction (Figures 11, 12, Table 4). In other words, over the course of the training, participants were able to more consistently land the first saccade on the FRL region. This was independent of the presence or absence of the reference frame.

The ANOVA for day 1 to day 12 showed a significant main effect of Session, but there was no significant main effect of Session in the ANOVA for day 13 to day 24 (see Figures 11, 12, Table 4).

In summary, similar to Experiment 1, the FRL location and the BCEA on the first saccade landing site improved with training. Four out of six participants showed FRL landing site within the trained FRL zone during training (Figure 13).

Discussion

Experiment 2 replicated the training-induced improvement of search efficiency observed in Experiment 1. In addition, we found that the more extensive training led to further improvement of search efficiency. While the use of a gaze-contingent frame demarcating the FRL borders appeared to lead to less variable first saccade landing locations (see Figure 12), this effect was not significant. Likewise, the presence of the FRL frame did not significantly affect search efficiency. There was an overall improvement in the fixation stability due to training. The improvement in the fixational stability did not rely on the presence or the absence of the frame. Three out of six participants had their estimated PRL closer to the trained location (see Supplementary information for fixational stability results). Thus, overall, the improvement did not rely on the presence of the frame.

General discussion

CVL interferes with normal effortless exploration of the environment with eye movements. In typical vision, saccades lead to the foveation of peripheral locations of interest. After CVL, corrective saccades are needed to bring the location into a non-foveal PRL followed by its development which usually takes months (Timberlake, Mainster, Peli, Augliere, Essock, & Arend, 1986; Whittaker, Budd, & Cummings, 1988; Fletcher, Schuchard, & Watson, 1999; Schuchard, 2005; von Noorden & Mackensen, 1962;

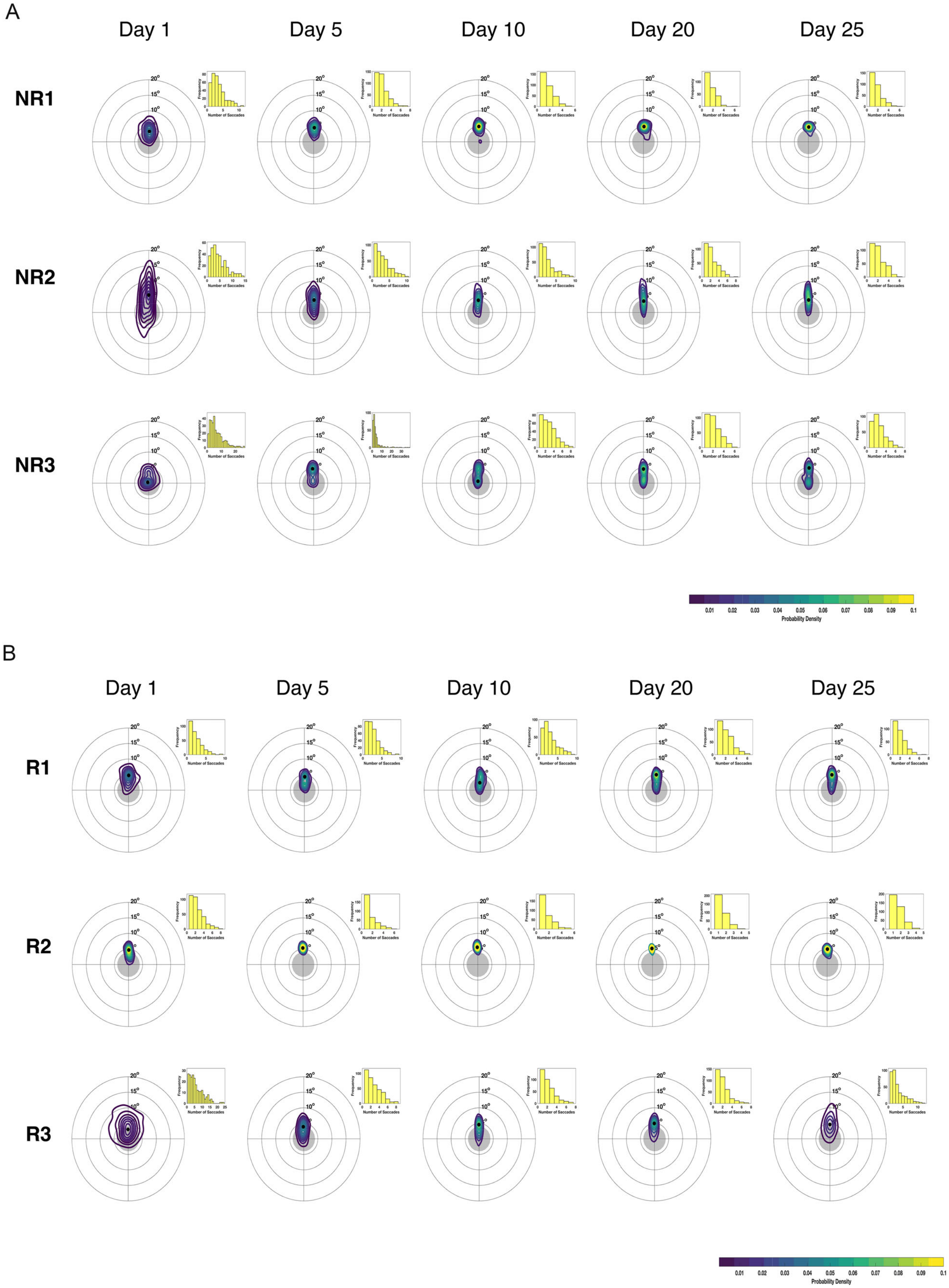

Figure 12. Probability density maps of the first saccade landing positions for the multiple-target search task without the reference frame (NR) (A) and with the reference frame (R) (B) for day 1, day 5, day 10, day 20, and day 25. Each row in both the figures represents one participant. The inset figure represents the frequency distribution of the number of saccades. The black dot is the calculated PRL position.

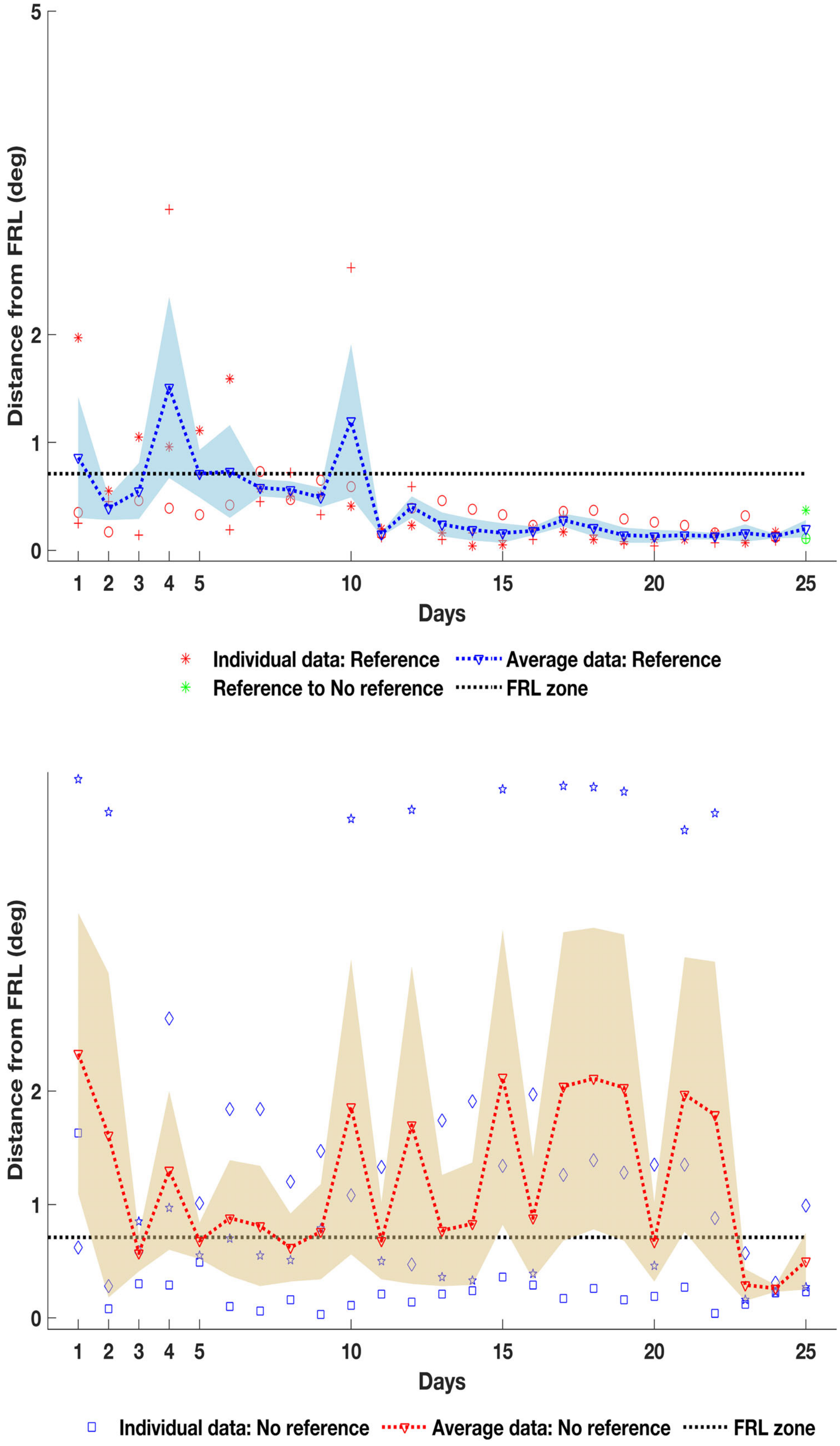

Figure 13. Euclidean distance between the estimated PRL from the first saccade landing location and the center of the trained FRL as a function of training days (days 1–25) for multiple-target search (*top*: with reference frame; *bottom*: without reference frame). Days of training are given on the x-axis whereas the distance from the FRL is indicated on the y-axis. The average distance in *blue* (*top*), *red* (*bottom*), different markers in *red* (*top*), *blue* (*bottom*), *green* (*top*, reference to no reference) indicates individual subject data for each day, and the *black dotted line* (both plots) indicates the border of the FRL zone. The shaded region indicates ±SEM.

White & Bedell, 1990; Whittaker, Cummings, & Swieson, 1991; Heinen & Skavenski, 1992). Therefore, it would be adaptive if the saccade would bring the location of interest not into the fovea, but directly into the PRL. Here, we propose a new method that uses the PRL as the saccade target (instead of the fovea). We devised two gaze-contingent visual search tasks where participants had to fixate target items with a predetermined FRL below the fovea, adjacent to the scotoma border. Fixating a target in this way ended a trial or search episode and led to the continuation of the experiment. In the course of training, response times and various eye movement parameters improved, indicating a more efficient search. These effects were stable over 4 weeks after training, indicating that our training had lasting effects.

Our training paradigm differs from previous saccadic re-referencing training methods in several ways. Some previous training methods used visual search paradigms, just as we did. In a few studies, visual search in naturalistic scenes was used (Kwon et al., 2013; Liu & Kwon, 2016; Chen, Shin, Millin, Song, Kwon, & Tjan, 2019) whereas another study used a classical visual search paradigm, search for an O-shaped target among C-shaped distractors (Walsh & Liu, 2014), known to create an inefficient search. In contrast to the latter, our search paradigm allowed for efficient – "pop-out" – search. Taken together, these studies show that saccadic re-referencing training can be successful using a range of search tasks, from search among abstract letter-like shapes to search in naturalistic scenes and from efficient to inefficient search. Particularly the latter comparison is theoretically important, in that efficient search is based primarily on stimulus-driven gaze sequences whereas inefficient search requires more endogenously controlled eye movements. Further studies may directly compare the efficiency of saccadic re-referencing training using these two kinds of search and particularly the transfer of saccadic re-referencing from efficient to inefficient search and vice versa.

The use of an efficient search paradigm in our study was made possible by the requirement to fixate the target with the FRL. Had we used manual target detection or discrimination responses, as customarily used in visual search tasks, participants would not have needed to make eye movements toward the target, because as a pop-out target it was, by definition, visible without any foveating eye-movements. Thus, the use of a gaze-contingent fixation response broadens the scope of visual search tasks that can be used for saccadic re-referencing training.

Another advantage of gaze-contingent fixation training may be that the intended behavior - fixation with the FRL - itself is the response, enabling immediate feedback. Given the well-known importance of contiguity for learning, this may be an advantage for learning. Indeed, we observed the largest training gains from the first to the second training session and we found significant training gains after five training sessions that were stable in the post-test a month later (Experiment 1). Nevertheless, we still found search improvements after extensive training in Experiment 2, showing that the continued training after the first five training sessions was effective as well.

Many studies have reported successful saccadic re-referencing to the trained location with a variety of methodologies and training durations (Pidcoe & Wetzel, 2006; Kwon et al., 2013; Walsh & Liu, 2014; Liu & Kwon, 2016; Janssen & Verghese, 2016; Rose & Bex, 2017; Chen et al., 2019; Costela, Reeves, & Woods, 2020; Maniglia, Jogin, Visscher, & Seitz, 2020; Maniglia, Visscher, & Seitz, 2020). For theoretical and practical purposes, it might be worthwhile to compare the available saccadic re-referencing training methods. However, this is made difficult by the differences in paradigms, measures (e.g. manual vs. gaze responses), and participants, asking for future studies that directly compare training methods in a standardized setting.

We compared two visual search methods, single-target and multiple-target searches for highly salient "X"-shapes among "O"-type distractors. Although increased efficiency in terms of lower reaction times, fewer fixations, and reduced scan path ratios were observed in both tasks, the tasks differed in terms of the first saccade landing location after training. In the multiple-target search, the first saccade of a search episode moved from foveating the target before training to centering the target in the FRL after training. This shift, indicative of saccadic re-referencing to the FRL, was much less observed in single-target search. Thus, the training led to more efficient placement of the target into the FRL in both search tasks, but it appeared to lead to direct placement of the target into the FRL primarily in multiple-target search. A possible reason for this discrepancy may be that the highly salient single-targets may have been less conducive to precise initial target localization in the FRL because target identification was possible in a large focus of attention. Multiple targets in a display, in contrast, may have led to a narrower focus of attention because of the necessity to focus on the selected target and exclude the other remaining targets. Because of the close relationship between covert attention and saccade planning, a narrow focus of attention would lead to a more precise localization of the target into the FRL. The analysis of the BCEA on the first saccade landing site also revealed reduced dispersion due to training.

Search for a single target may have been delayed when the target was obscured by the scotoma at display onset. However, search times on day 1 differed by only 10 ms, thus this potential issue appeared to have no major impact on the results. Conversely, multiple target search afforded selection processes – for example, which target should I fixate next - that were absent in single target search. Observers might have been able to see at least half of the target positions at once before the initiation of the first saccade and plan the sequence of their saccades (Caspi, Beutter, & Eckstein, 2004). Due to this, the search times for multiple targets might be shorter when compared to single target search times. But, the similarity of reaction times on day 1 showed that these selection processes did not delay search in a major way, presumably because the targets were very distinct from the distractors, enabling efficient search.

Experiment 2 showed that training gains were still achieved even after extensive training. Thus, whereas the target gains were achieved in the first few sessions, continuing the training was worthwhile. The consistent presence of a gaze-contingent frame indicating the FRL borders did not significantly improve training gains. Training without a reference frame may lead to a smoother transition to unassisted viewing after the training in patients with foveal vision loss. This is at least suggested by the more variable BCEA when our participants had to switch from searching with the re-reference frame to search without (see Figure 11, day 25).

Another important aspect is the location of the FRL. Here, we have chosen an FRL below the fovea which has been found to be beneficial for tasks like reading (Guez, Le Gargasson, Rigaudiere, & O'Regan, 1993; Whittaker & Lovie-Kitchin, 1993; Petre, Hazel, Fine, & Rubin, 2000; Déruaz, Whatham, Mermoud, & Safran, 2002; Chung, Legge, & Cheung, 2004; Frennesson & Nilsson, 2007). However, other FRLs may be better for other tasks. We did not vary FRL location because our primary interest was saccadic re-referencing to the FRL. However, it should be noted that techniques exist to guide the selection of a particular FRL which might be optimal for a specific task (Lingnau, Schwarzbach, & Vorberg, 2008; Barraza-Bernal, Ivanov, Nill, Rifai, Trauzettel-Klosinski, & Wahl., 2017; Barraza-Bernal, Rifai, & Wahl, 2017a, Barraza-Bernal, Rifai, & Wahl, 2017b, Barraza-Bernal, Rifai, & Wahl, 2018; Prahalad & Coates, 2020; Maniglia, Jogin, Visscher, & Seitz, 2020).

One potential concern of saccadic re-referencing training may be that a permanent re-referencing might be achieved, which would be maladaptive in everyday life for our normal-sighted participants. This, however, was not the case. Our participants immediately returned to a foveal fixation pattern when the simulated scotoma was removed (see Agaoglu, Fung, & Chung, 2019, for similar results).

Another possible limitation would be tracking and training the non-dominant eye under binocular viewing. The function of eye dominance is not fully understood. Previous studies suggested that eye dominance plays only a minor role when the stimulus is viewed binocularly (e.g. Warren & Clark 1938; and Mapp, Ono, & Barbeito, 2003), as in our setup. On the other hand, other authors (e.g. Walls, 1951 & Money 1972) discussed the relation of eye dominance to eye movements. In particular, Walls (1951) suggested that the dominant eye has the function of initiating muscular adjustment when fixating, and the non-dominant eye's role is to maintain binocular vision through small reflexive motions. We agree that, in principle, a fraction of right eye dominant participants could have directed their gaze differently in some trials. However, we argue that even if there were deviations in the eye movements due to eye dominance, the differences would be subject-specific (resulting in added noise to the data). In addition, the deviations, when observed, were typically reported to be of the magnitude of several characters (e.g. Paterson, Jordan, & Kurtev, 2009). Because we used a relatively big scotoma (of 8 degrees diameter), small discrepancy in the eye positions would not influence the results.

In addition, we tested only young and healthy subjects whose binocular coordination of eye movements was already developed and who passed the Broad-H test that indicated no deviation in their ocular motility. There was also no indication of pathological deviation of conjugate eye movements for both distance and near. None of the participants complained of double vision, which means it was well within the Panum's fusional range. In addition, participants were given adequate breaks between sessions to ensure they did not have any asthenopia, a common symptom of any binocular vision problem, due to training. Thus, it is not probable that the not-tracked eye's line of sight could have substantially deviated from that of the tracked eye. In any case, we would like to stress that our task was not about identification of the target (the X-shapes could be discriminated well from the O-shaped distractors with peripheral vision), but about using eye movements to place the target in the FRL. Therefore, if anything, deviations between the eyes might have been disadvantageous.

Beyond their theoretical importance, saccadic re-referencing training studies with simulated scotomata should aim at making patient training possible. Simulated studies use symmetric scotomata but in patients with CVL always present with asymmetric progressive scotomata. Future research should investigate saccadic re-referencing training on elderly populations with asymmetric or progressive scotomata. Given the high prevalence of age-related macular degeneration in older population, a large number of patients with CVL might benefit from saccadic re-referencing training. To our knowledge, no patient saccadic re-referencing training study and its transfer to natural environments has yet been published, but this should undeniably be one of the next steps in this field.

Keywords: preferred retinal locus (PRL), central vision loss (CVL), oculomotor learning, saccades

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