VISION
RESEARCH

Check for
updates

A new perceptual training strategy to improve vision impaired by central vision loss

Xin-Yu Xie[a], Lei Liu[b,*], Cong Yu[a,*]

[a] School of Psychology, IDG/McGovern Institute of Brain Research, and Peking-Tsinghua Center for Life Sciences, Peking University, Beijing, China
[b] School of Optometry, University of Alabama at Birmingham, Birmingham, AL, United States

A B S T R A C T

Patients with central vision loss depend on peripheral vision for everyday functions. A preferred retinal locus (PRL) on the intact retina is commonly trained as a new "fovea" to help. However, reprogramming the fovea-centered oculomotor control is difficult, so saccades often bring the defunct fovea to block the target. Aligning PRL with distant targets also requires multiple saccades and sometimes head movements. To overcome these problems, we attempted to train normal-sighted observers to form a preferred retinal annulus (PRA) around a simulated scotoma, so that they could rely on the same fovea-centered oculomotor system and make short saccades to align PRA with the target. Observers with an invisible simulated central scotoma (5° radius) practiced making saccades to see a tumbling-E target at 10° eccentricity. The otherwise blurred E target became clear when saccades brought a scotoma-abutting clear window (2° radius) to it. The location of the clear window was either fixed for PRL training, or changing among 12 locations for PRA training. Various cues aided the saccades through training. Practice quickly established a PRL or PRA. Comparing to PRL-trained observers whose first saccade persistently blocked the target with scotoma, PRA-trained observers produced more accurate first saccade. The benefits of more accurate PRA-based saccades also outweighed the costs of slower latency. PRA training may provide an efficient strategy to cope with central vision loss, especially for aging patients who have major difficulties adapting to a PRL.

1. Introduction

Patients who lost central vision to diseases such as aged-related macular degeneration (AMD) may regain good functional vision by learning to use a preferred retinal locus (PRL) on the intact retina for fixation and vision related activities (Crossland, Culham, Kabanarou, & Rubin, 2005; Fletcher & Schuchard, 1997; Von Noorden & Mackensen, 1962; Whittaker, Budd, & Cummings, 1988). Such a PRL can be developed spontaneously in some patients (Crossland et al., 2005; Fletcher & Schuchard, 1997) or through training (Kwon, Nandy, & Tjan, 2013). However, reprograming the adamant fovea-centered oculomotor system to a PRL-centered one is difficult and may take several years to complete (White & Bedell, 1990; Whittaker, Cummings, & Swieson, 1991). Patients with newly acquired central scotoma often direct their defunct fovea to the target of interest in the first saccade, rendering the target invisible (White & Bedell, 1990; Whittaker et al., 1991). In addition, many AMD patients have large central scotomas. For example, the median width and height of scotomas in patients with 0 to 22.8 years of macular disease were 21.8° and 17.6°, respectively

(Schuchard, Naseer, & de Castro, 1999). Because the amplitudes of most naturally occurring saccades are 15° or less (Bahill, Adler, & Stark, 1975), aligning the PRL with a target on the opposite side of a large scotoma would require multiple saccades, or combined head and eye movements, which takes longer time and may further affect accuracy.

To overcome these problems, we propose a new sensory-oculomotor training scheme for functional compensation of central vision loss. Instead of training observers to develop a brand new PRL-centered oculomotor control, we train them to modify the amplitude of the existing fovea-centered control to achieve the goal of placing a target in a relatively intact retinal location outside the central scotoma. Specifically, we train observers to use retinal locations on an annulus around the central scotoma, or a preferred retinal annulus (PRA). A PRA location on a given retinal meridian is responsible for targets around that meridian. Fig. 1a shows saccades that direct a healthy fovea, a PRL abutting the central scotoma, or a PRA around the central scotoma, to E targets in different directions. It is apparent that PRL-centered saccades (Fig. 1a, middle) differ from the normal foveating saccades (Fig. 1a. upper) in direction and/or amplitude, depending on

---
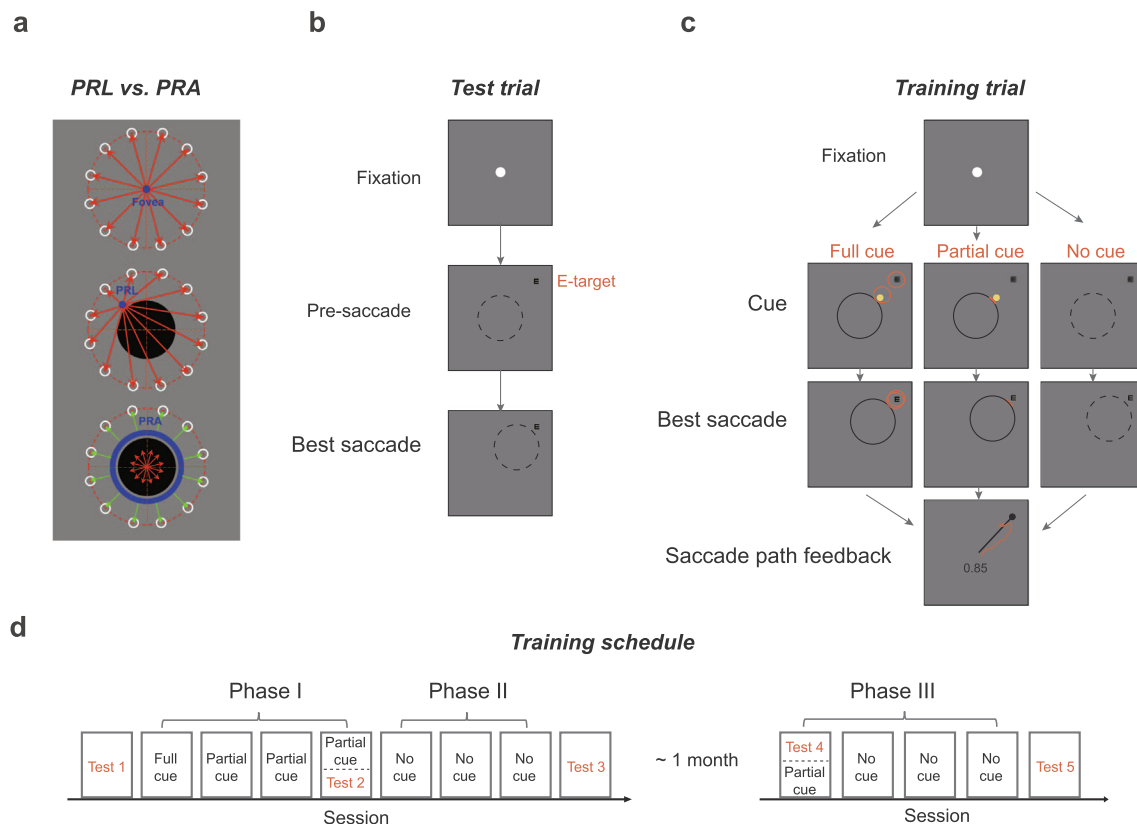
Fig. 1. Ideal eye movement patterns, test and training trials, and the training schedule. a. Perfect saccades (solid red arrows) move the preferred viewing retinal location, including the fovea (blue circle in upper drawing), a preferred retinal locus (PRL, blue circle in middle drawing), or a preferred retinal annulus (PRA, blue ring in lower drawing), to target locations in different directions (white circles). Green arrows in lower drawing indicate the movements of the PRA caused by the corresponding saccades. Black disks in middle and lower drawings represent a central scotoma. b. A test trial. After fixation, a clear tumbling E target was randomly presented at 1 of 12 evenly distributed locations at 10° eccentricity. An observer with an invisible, gaze-contingent, simulated central scotoma (5° radius, indicated by the dashed circle) was asked to move the eyes to identify the orientation of the E and report with a key press, which also ended the trial. c. A training trial. The target was blurred and would become clear only when it fell into the clear window. The full-cue (outlines of the scotoma, a clear window abutting the scotoma, a circle indicating the target location, and a yellow dot suggesting the optimal saccade landing position), partial-cue (outlines of the scotoma, a yellow dot, and a small red arc indicating the abutting position of the scotoma and the clear window), and no-cue conditions were successively used to help observers learn to move the clear window to the target with saccades. Several types of feedbacks were provided, including the real eye movement path (red curve), the optimal eye movement path (black line), the proportion of the target that fell in the clear window at the time of response (digits in the center), and the correctness of the response. d. Training schedule. There were three training phases, each consisting of training sessions with different training cues and test sessions at the beginning and end of the phase. The training consisted of 12 training sessions and 5 test sessions in total. Each training session contained 480 trials.

the target location. In comparison, the PRA saccades (Fig. 1a, lower) are much simpler. For targets in all directions, PRA saccades have the same directions as the corresponding foveating saccades but with reduced amplitudes. This modification of normal, fovea-centered oculomotor control should be easier to accomplish than building a new PRL-centered control from scratch. We hypothesized that human observers should be able to learn from brief sensory-oculomotor training to move the PRA to a target in any direction in their first saccades without risking obscuring the target in the scotoma.

2. Methods

2.1. Observers

Twenty naïve and unexperienced observers (age = 20.2 ± 2.7 yrs) with normal or corrected-to-normal vision were recruited. Informed written consent, which was approved by Peking University Institutional Review Board, was obtained before data collection from each observer. This work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Apparatus

The stimuli were generated with Psychtoolbox-3 (Pelli, 1997) and presented on a 27-inch Acer XB271HU monitor (2560 × 1440 pixels, 165 Hz frame rate, and 37.62 cd/m² mean luminance). Viewing was binocular at a distance of 60 cm, and a chin-and-head rest stabilized the head. Experiments were run in a dimly lit room.

Eye movements were monitored through an EyeLink 1000 eye-tracker (SR Research, Kanata, Ontario, Canada) with a nominal sampling frequency of 1000 Hz and a maximum spatial resolution of 0.01° in theory. A five-point calibration and validation sequence was performed at the beginning of each session, and eye drift was corrected at the beginning of each block of 48 trials. Calibration and validation were repeated until the validation error was < 1° on average. A trial was aborted and restarted when an eye blink was detected.

2.3. Stimuli

The continuous gaze information was used to draw a scotoma on the display. The simulated scotoma was a 10° diameter gray (the background color) circular disc centered at the fovea (Fig. 1b). The invisible scotoma resembled real scotomas in a way that the patient was not aware of its location and shape, and could infer its existence only by

seeing the E target disappearing into it. A tumbling E target of 15×15 pixels in four orientations was first generated with slight Gaussian blur ($\sigma = 1.5$ pixels), and then resized to 12×12 pixels (0.26°) to match the pre-determined target identification threshold at 5° eccentricity (0.268°) with normal vision. In training sessions, this E target was further Gaussian-blurred ($\sigma = 5$ pixels) so that it would be un-recognizable at the edge of the central scotoma (5° eccentricity). This blur was removed when the target fell into a 2° radius circular clear window (the red circle abutting the central scotoma, Fig. 1c). The localized sharpening of the target forced the observers to use the desired retinal location to see.

The temporal layouts of the test and training trials were the same. A trial started with a small central fixation (500 ms). It would restart if the eye positions deviated from the fixation point more than 2°. Then the fixation point disappeared and the E target appeared at one of 12 locations at 10° eccentricity. At the same time, the gaze-contingent simulated central scotoma was activated. The task of the observer was to identify the orientation of the tumbling E and report it with a key press, which also ended the trial.

2.4. Procedures

The training procedures for PRA and PRL observers were the same except for the location of the clear window. For PRA training, the clear window that was always in the direction of the target was activated. For PRL training, only one clear window at a fixed direction was activated for targets of all directions. The fixed clear window location was pre-assigned for each PRL observer, seven in the lower visual field and three in the upper visual field. Fewer locations in the upper visual field were assigned because some observers had difficulties using an upper clear window. This bias might have led to overestimates of overall PRL training outcomes.

To facilitate learning, different cueing conditions were progressively used to guide observers to direct the clear window to the target during training (Fig. 1c). Under the full-cue condition, the area of the simulated scotoma was demarcated by a black circle. The target area and the boundary of the clear window were each highlighted by a 2°-radius red circle. A yellow dot indicated the designated location to which the observer should saccade to view the target optimally. To discourage foveating saccades, an auditory warning would be given if the scotoma covered the target anytime during the first 300 ms after the target onset. The target location varied in a clockwise order trial by trial to reduce spatial uncertainty and aid learning (Kuai, Zhang, Klein, Levi, & Yu, 2005). An observer made saccades to align the two red circles, and then the yellow dot disappeared and the target became clear. Under the partial-cue condition, red circles were no longer used, but the black scotoma circle and the yellow dot remained, and a small red arc at the edge of the scotoma was added to indicate the location of the clear window. The target location also varied in a clockwise order. An observer would try to place the red arc next to the target. Finally, under the no-cue condition, none of the assisting cues were provided, and the target location started to vary randomly from trial to trial. After each training trial, the actual and optimal eye movement paths were shown as feedback. The proportion of target (from 0.00 to 1.00) that fell into the clear window at the time of key press was also shown on the center of the screen. Auditory feedback was given on incorrect responses (Fig. 1c).

The training consisted of three phases (Fig. 1d): Phase I consisted of four sessions (10 blocks each, 48 trials per block). Full cues were provided in the first session and partial cues in the other sessions. Phase II consisted of three sessions (10 blocks each) with no cue. Phase III was conducted one month after Phase II, including four sessions. Partial cues were provided in the first session (6 blocks) and no cues were provided in other sessions (10 blocks each). Five tests, including Test 1 before Phase I, Tests 2 and 3 after Phases I and II, respectively, and Tests 4 and 5 before and after Phase III, respectively, were conducted to assess the training effects (Fig. 1d). Each test consisted of four blocks, each with 48 trials. In a testing trial, the cues and the clear window were not presented and the E target was not blurred. The observers were free to choose any retina location to see the target.

2.5. Data analysis

2.5.1. Gaze analysis

EyeLink parsing algorithms were used to analyze the gaze data. To distinguish saccades from fixations, the saccadic velocity threshold was set at 30°/s, the saccadic acceleration threshold at 9500°/s², and the saccadic motion threshold at 0.1°. To eliminate the effects of micro-saccades, we also merged a fixation into the previous one when the distance between the two fixations was < 0.5° and/or the second fixation duration was < 80 ms. The number of fixations was reduced by 2.9% after the merge.

2.5.2. Target probability density map and TSD

To analyze fixation patterns during tests, we plotted target probability density maps at each test session. The maps represented the probabilities of post-saccade retinal positions of the target relative to the fixation via kernel density estimation with a bivariate Gaussian kernel (Kwon et al., 2013). The quality of saccades was measured by target-scotoma distance (TSD), which was the distance between the target center and the scotoma center minus the sum of the scotoma and target radii. Negative, zero, and positive TSDs indicated that the target was at least partially inside the scotoma, abutting the scotoma on the outside, and completely outside the scotoma, respectively.

2.5.3. Distance and direction accurate trials

The proportions of distance and direction accurate trials were computed. After the first saccade, a trial would be distance accurate when the first saccade TSD was within 0-2°. After two (or three) saccades, a trial would be distance accurate when the first or second (or the first or second or third) saccade TSD was within 0–2°. A direction accurate trial was defined as the target falling into a $2° \times 2°$ area around the designated PRL/PRA location. This $2° \times 2°$ criterion was slightly more stringent than the area of fixation stability found in patients with central scotoma (2.5-3°) (Fletcher & Schuchard, 1997; Whittaker et al., 1988). We only analyzed eye movement patterns up to the third saccade because only 37.6% of trials had four or more saccades after training.

2.5.4. PRL-near and PRL-far

Because the target locations in PRA training were isotropic, PRA training outcomes could be averaged over all target locations. However, PRL training differed depending on whether the target and the designated PRL were on the same side from the scotoma or on opposite sides. We thus divided PRL training data into two sets: PRL-near were data from the five target locations that were on the PRL side relative to the scotoma, and PRL-far were data from the five target locations on the opposite side of PRL. Data for the two remaining target locations belonging to neither the near nor the far types were excluded from data analysis.

2.6. Bootstrapping

A bootstrapping method estimated the average time to achieve 34.9% distance accurate trials, which was the proportion of distance accurate first saccade after PRA training (Fig. 5b). We created 5000 resamples by sampling with replacement from the original PRA, PRL-near, and PRL-far trial sets, respectively (see Results). Each resample was the same size as the original trial set. Then we randomly grouped trials in a resample of one-saccade, two-saccade, and three-saccade trials, each for a certain percentage, and calculated the durations from target onset to the end of the first saccade for one-saccade trials, of the
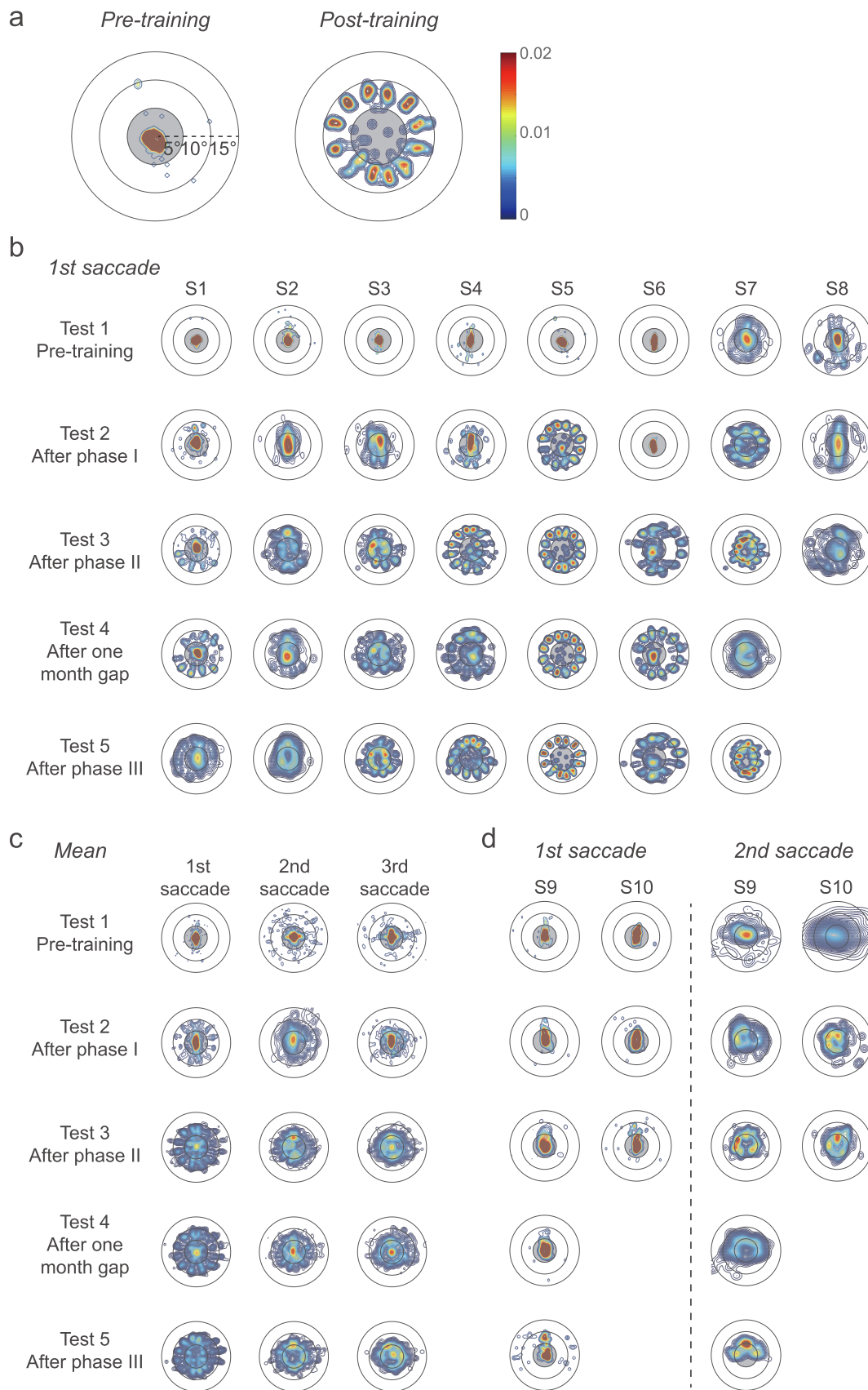
Fig. 2. Training of preferred retinal annulus (PRA). a. A nearly perfect probability density map after training from observer S5. The left is the pre-training map, and the right is the post-training map. The gray area in the maps indicates the simulated central scotoma (r = 5°). b. Individual probability density maps of target locations in the visual field after the first saccade through PRA training (from top to bottom). Each column represents the density maps from one observer (S1-S8). c. Mean probability density maps of target locations after the first, second, and third saccades over all observers except S9 and S10. d. Probability density maps of target locations of observers S9 and S10. For S9 and S10, targets were mostly placed within the scotoma after the first saccade, which was improved after the second
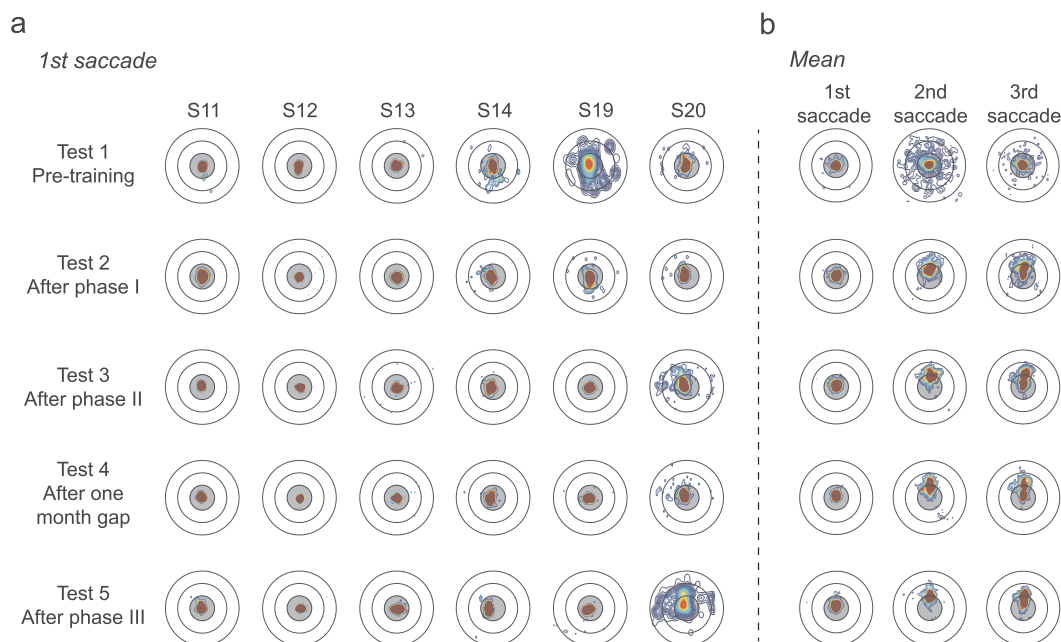
Fig. 3. Training of preferred retinal locus (PRL). a. Individual probability density maps of target locations in the visual field after the first saccade throughout PRL training (from top to bottom). Each column represents the probability density maps from one observer (S15-18, which were very similar to S11-S14, were not shown). The gray area indicates the simulated central scotoma (r = 5°). b. Mean probability density maps of target locations after the first, second, and third saccades over all observers (S11-S20). Because observers were trained to use different PRLs, individual maps were rotated to make the PRL always at the top before averaging.

second saccade for two-saccade trials, and of the third saccade for three-saccade trials. For PRA group, all trials were grouped as one-saccade trials. For PRL-near, the percentages of one-saccade trials (p_1) and two-saccade trials ($1-p_1$) were determined so that the sum of distance accurate rates of one-saccade (acc_1) and two-saccade (acc_2) trials $acc_1 \cdot p_1 + acc_2 \cdot (1-p_1) = 34.9\%$. For PRL-far, the second saccade accuracy was still < 34.9%, so we assumed that it took one more saccade to achieve 34.9% distance accuracy. Accordingly, only the percentages of two-saccade trial (p_2) and three-saccade trial ($1-p_2$) were determined, so that the sum of distance accuracy rates of two-saccade (acc_2) and three-saccade (acc_3) trials $acc_2 \cdot p_2 + acc_3 \cdot (1-p_2) = 34.9\%$. The distribution of the 5000 resample means was the bootstrap distribution of each group.

3. Results

The progressions of PRA and PRL training were indicated by the target probability density maps at different training stages (Figs. 2 & 3). These maps represented the probabilities of post-saccade retinal positions of the target relative to the fixation. As shown in Fig. 1a, when a scotoma is present, ideal saccades would move preferred non-foveal retinal location(s) to the target. Therefore, a nearly perfect target probability density map would be like the one by observer S5 of the PRA group after training (Fig. 2a). In this map, post-saccade locations of 12 targets were mostly abutting the scotoma for best viewing, with some unwanted locations within the scotoma that prevented target viewing.

Before training, the target was mostly centered in the scotoma after the foveating first saccade in all PRA and PRL observers (red central dots in Figs. 2b & 3a, first rows) and was invisible. Target viewing was not improved after the second and third saccades that were also predominantly foveating (Figs. 2c & 3b, first rows). As training progressed, the target became more likely placed in the designated retinal locations after the first saccade for most PRA observers (S1-S8), which was manifested as the flower petal-like probability density maps around the central scotoma (Figs. 2b, last row). Among these PRA observers, S1 was a slower learner, with a large percentage of foveating first saccade

until Test 5, while S5's probability density map was nearly perfect at Test 5. PRA observers S9 and S10 were two exceptions (Fig. 2d). For S9 and S10, a majority of target locations were still inside the scotoma after training as their first saccade were mostly foveating (Fig. 2d, left). However, the target was more likely placed on the edge of the scotoma after the second saccade (Fig. 2d, right), suggesting that S9 and S10 were forming PRAs but had not overcome the foveating habit. Their data were not included in subsequent analysis.

In contrast, for most PRL observers (S11-S18), the target was almost always placed near the center of the scotoma after the first saccade throughout training (Fig. 3a, only data of S11-S14 are shown, to which data of S15-S18 were very similar). S19 placed the target outside the scotoma after first saccade in some trials before training, but mostly within the scotoma after training, as the first saccade became predominantly foveating. In contrast, S20 started to more frequently use the retinal locations outside the scotoma to see the target with the first saccade after training. In general, PRL training could not help most observers reprogram the first saccade, so that the scotoma blocked target viewing in most trials. It was only after the second saccade that the target started to be placed in the designated PRL (Fig. 3b. Individual density maps were rotated to align all maps with the clear window at the 12 o'clock location). It is evident that it took at least two saccades for PRL observers to move the target out of the scotoma (Fig. 3b, columns of 2nd saccade and 3rd saccade).

To quantify exactly how observers learned to use designated peripheral retinal locations for viewing, we analyzed the target-scotoma distance (TSD) between the target edge and the scotoma edge in the radial direction. A target inside, abutting, or outside the scotoma would have a negative, zero, or positive TSD, respectively. Before training, the target was placed within the scotoma after the first saccade of all observers (Test 1, $TSD_{PRA} = -2.60 \pm 0.59°$, and $TSD_{PRL} = -3.06 \pm 0.39°$; Errors are SEs here and elsewhere) (Fig. 4a). As PRA training progressed, the first-saccade amplitude became shorter and the TSD_{PRA} became positive in Test 3 ($0.71 \pm 0.38°$), and remained so at least one month without training in Test 4 ($0.77 \pm 0.37°$). Further training did not change the post-first saccade TSD_{PRA} much (Test 5, $0.69 \pm 0.32°$). In comparison, PRL training did
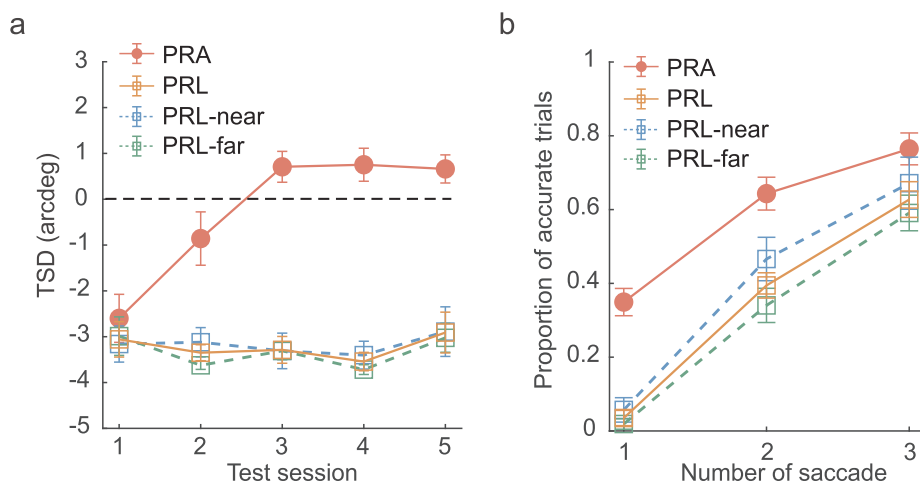
Fig. 4. Saccade accuracies with PRA and PRL training. a. Edge-to-edge target-scotoma distance (TSD) after the first saccade through five test sessions. For PRL training, the five target locations on the same side of the PRL were defined as PRL-near conditions, and the five target locations on the opposite side of the PRL were defined as PRL-far conditions. b. Proportion of accurate trials with $0° \leq TSD \leq 2°$ after one to three saccades in Test 5. Error bars indicate 1 standard error of the mean.

not change the post-first saccade TSD_{PRL}, which was $-2.97 \pm 0.42°$ in Test 5, indicating that the target was still deep inside the scotoma after the first saccade. A mixed-design ANOVA of TSD with test session (Test 1 to Test 5) as a within-subjects variable and training method (PRA vs. PRL) as a between-subjects variable showed significant main effects of test session ($F_{4, 64} = 9.47$, $p < 0.001$) and training group ($F_{1, 16} = 66.74$, $p < 0.001$), as well as a significant interaction of two variables ($F_{4, 64} = 11.58$, $p < 0.001$). Post-hoc analysis showed no difference between TSD_{PRA} and TSD_{PRL} before training (Test 1, $p = 0.508$), but TSD_{PRA} was significantly more positive than TSD_{PRL} after training (Test 5, $p < 0.001$).

We further compared PRL-near data from the five target locations on the same side of PRL relative to the scotoma, and PRL-far data from the five target locations on the opposite side of the PRL. We predicted that the first saccades would be less accurate with PRL-far locations than with PRL-near locations because the first saccades with PRL-near were more like those in the PRA condition. However, a repeated measures ANOVA of TSD among PRL-trained observers did not show significant main effects of PRL type (PRL-near vs. PRL-far: $F_{1, 9} = 0.28$, $p = 0.611$) and test session ($F_{4, 36} = 1.10$, $p = 0.373$) (Fig. 4a), suggesting that PRL observers were unaware of the better saccade strategy used by PRA observers.

Distance accurate trials were those that had positive TSDs and landed the target within 2° from the scotoma edge in Test 5 (Fig. 4b). After PRA training, 34.9% of the trials had distance accurate first saccades. In comparison, after PRL training, only 3.5% of the trials had distance accurate first saccades. As 93.8% of these distance accurate saccades were also "direction accurate", meaning that they placed the target into a $2° \times 2°$ area around the designated PRL/PRA location,

from now on we only used the saccade distance to define "accurate trials".

The cumulated proportions of accurate trials after the 1st, 2nd, and 3rd saccades were $34.9 \pm 4.1\%$, $64.3 \pm 5.0\%$, and $76.5 \pm 4.8\%$ after PRA training, and $3.5 \pm 2.1\%$, $39.4 \pm 3.4\%$, and $62.7 \pm 4.8\%$ after PRL training, respectively (Fig. 4b). A mixed-design ANOVA with the saccade number as a within-subjects variable and the training group as a between-subjects variable indicated significant main effects of saccade number ($F_{2, 32} = 213.31$, $p < 0.001$) and training group ($F_{1, 16} = 21.29$, $p < 0.001$), as well as their interaction ($F_{2, 32} = 6.53$, $p = 0.004$). Post-hoc analysis indicated that only after three saccades that the proportions of accurate trials became statistically insignificant between PRA and PRL groups ($p = 0.065$). In addition, slightly more PRL-near trials landed the target near the scotoma edge than PRL-far trials, but the difference was not significant ($F_{1, 9} = 2.53$, $p = 0.146$).

One striking finding of this study is the relatively quick adjustment of the amplitude of the first saccade with PRA training, so that the desired PRA locations on the edge of the scotoma can be directly moved to the targets of all directions. Such an adjustment, however, may incur a cost, as the oculomotor system may need more time to plan reduced amplitude saccades for PRA observers compared to the foveating saccades for PRL observers. This possibility was confirmed by a mixed-design ANOVA that compared the first saccade latencies between PRA and PRL groups (Fig. 5a). Here the first saccade latency was defined as the duration from the target onset to the onset of the first saccade. The results revealed significant main effects of test session ($F_{4, 64} = 7.82$, $p < 0.001$) and training group ($F_{1, 16} = 14.02$, $p = 0.002$), as well as a significant interaction ($F_{4, 64} = 2.86$, $p = 0.030$). Post-hoc analysis showed similar latencies before training (PRA: 309.20 ± 31.70 ms;
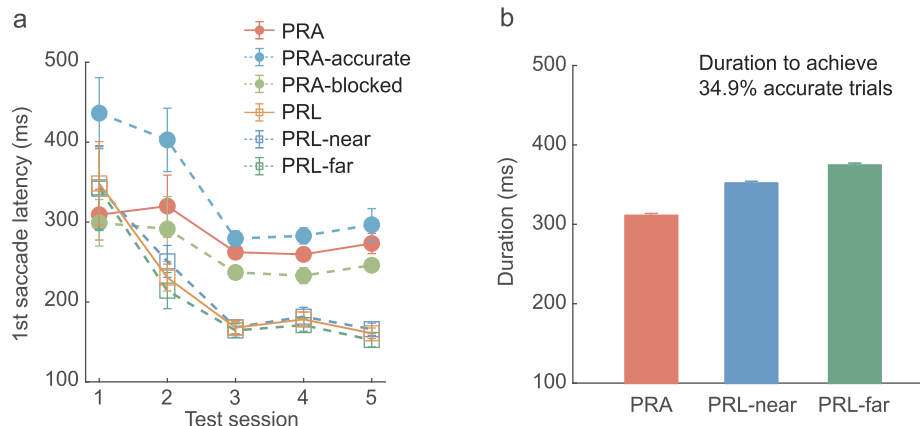
Fig. 5. a. The first saccade latencies of PRA and PRL training in five test sessions. The saccade latency was the duration from target onset to the onset of the first saccade. Error bars indicate 1 standard error of the mean. b. The estimated durations to achieve 34.9% accurate saccades in PRA, PRL-near and PRL-far conditions. Error bars of the estimated durations indicate bootstrap standard error.

PRL: 348.35 ± 52.40 ms; p = 0.566), but the post-training latencies in Test 5 were significantly longer for the PRA group than the PRL group (PRA: 273.25 ± 12.67 ms; PRL: 160.84 ± 6.61 ms; p < 0.001). Further analysis showed that for PRA observers, the latencies of the first saccades blocking the target (245.96 ± 7.88 ms) were shorter than the latencies of those moving to the scotoma edge properly (296.66 ± 22.59 ms; $t_7 = 2.67$, p = 0.032) in Test 5, but were still longer than the first-saccade latencies of PRL observers ($t_{16} = 8.34$, p < 0.001) (Fig. 5a).

However, the above latency differences might be irrelevant because almost all PRL observers' first saccades, although faster, rendered the target invisible. A more informative performance measure is to estimate how long it took for PRL observers to catch up the proportion of accurate trials with PRA observers' first saccades (34.9%). Using a bootstrap method (see Methods), we estimated the mean durations for 34.9% of the trials to land the target within 2° from the scotoma edge under the PRA, PRL-near, and PRL-far conditions in Test 5, which were 309.02 ± 2.46 ms, 349.11 ± 2.26 ms, and 371.57 ± 2.46 ms, respectively (Fig. 5b). It took PRL-trained observers longer to reach the same level of performance than PRA-trained observers, especially with PRL-far targets. Therefore, PRA-trained observers did see the target faster than PRL-trained observers, even if the first saccades started slower.

4. Discussion

The idea of PRA training came from a recent study of ours (Xie & Yu, 2020), in which we found that it takes the same number of trials to improve visual performance over multiple retinal locations equally well as at a single location. Indeed with PRA training, normal observers with a simulated central scotoma can quickly learn to make fovea-centered saccades with reduced amplitudes (i.e., hypometric saccades, HoS), so that a ring of retinal locations just outside a simulated central scotoma can be used consistently to view targets in all directions.

There are also other ways to induce HoS. Hallett (1978) showed that an observer was able to follow a verbal instruction to make HoS that landed half way between the fixation and the target. The observer could complete the task in the first or second attempt, and improve the landing precision in the first 50 trials. The key difference between this HoS task and PRA is that Hallett's observer was given an explicit metric on where to land the HoS, and the observer did not require retinal feedback to refine the performance. In comparison, PRA observers were given a visual task in peripheral vision, recognizing a letter. They had to rely on retinal feedback, such as the target falling into the scotoma, to discover, practice, and refine the eye movements. Because they were able to make PRA-appropriate HoS consistently after training, they must have an internal guidance or metrics. However, this metrics was learnt, not given. This might explain why PRA observers took much longer time (nearly 1000 trials, Fig. 4a) than Hallett's observer to develop the ability to make appropriate HoS. Another well-known form of induced HoS is the fast saccadic adaptation, in which the visual target that induces a saccade shifts its location during the saccade by an intrasaccadic step (ISS), resulting in a retinal error (McLaughlin, 1967). The observers learned to adjust the saccade amplitude to reduce the retinal errors quickly, within 100 saccades. Unlike PRA, this fast adaptation does not persist. When ISS stops, the saccade amplitude starts to recover, returning to the pre-adaptation level within a few hundreds of saccades (Hopp & Fuchs, 2004). Therefore, PRA training appears to be a lengthy learning process to develop persistent hypometric saccades. These saccades are appropriate for moving retinal locations on an annulus around the scotoma to the target of interest.

PRA-based peripheral viewing may have functional advantages over PRL-based peripheral viewing. First, there is no single PRL around a central scotoma that can avoid the scotoma interfering with visual tasks in all directions. For example, a PRL above or below the scotoma allows reading of horizontal text and pursuing a horizontally moving target

without interruption. But the same PRL may have difficulty dealing with vertical text or vertically moving targets that fall into the scotoma. PRA offers the flexibility of using a PRA location that is the most appropriate for the task at hand. Now that we know PRA can be trained, the next step is to study if PRA-trained observers can select and use appropriate PRA locations for different tasks, and to compare their performance with PRL-trained observers. Second, as shown in Fig. 1a middle drawing, a patient has to make large saccades to move the PRL to targets on the opposite side of the scotoma. As most naturally occurring saccades are 15° or less (Bahill et al., 1975), when the scotoma is as large as 20° or more as found in many AMD patients (Schuchard et al., 1999), combining head and eye movements or making a sequence of saccades is necessary to put the PRL on the target across the scotoma. Both of these processes are cumbersome and relatively slow, and could land the scotoma on the target. In comparison, the saccades moving the PRA to the target are smaller than the target eccentricity (Fig. 1a, lower), and there is no need to hurl the scotoma over the target. We will compare performances of fully trained PRA and PRL observers on time-limited tasks, such as recognizing letters presented for 100, 200, 300 and 400 ms in different directions relative to the fovea.

Complete adaptation to a central scotoma is hypothesized to take two steps: eccentric viewing and eccentric fixation (Von Noorden & Mackensen, 1962). Patients with recent onset of central vision loss can spontaneously learn to use one or a few PRLs to view targets (eccentric viewing) (Crossland et al., 2005; Von Noorden & Mackensen, 1962). However, they often make eye movements that move the defunct fovea, not the PRL, to targets (foveating saccades) (White & Bedell, 1990; Whittaker et al., 1991). Some patients do eventually learn to direct the PRL to the target in the first saccade (eccentric fixation) (Von Noorden & Mackensen, 1962), but this complete adaptation to the central scotoma may take 7–11 years (White & Bedell, 1990; Whittaker et al., 1991). Our findings suggest that PRA-trained observers' adaptation to the central scotoma is more similar to eccentric fixation, while PRL-trained observers still remain in eccentric viewing after the same amount of training. Considering that a majority of patients suffering from central vision loss are in old age, rapid acquisition of PRA skills through perceptual training may be an appropriate visual rehabilitation strategy.

A recent study (Liu & Kwon, 2016) showed that PRL-trained observers can direct the PRL to the target in first saccades (their Fig. 5). The results come from the "explicit training" phase where the simulated scotoma is clearly visible as a gray patch over colored pictures. The observers only need to find the PRL location relative to the visible scotoma with the assistance of a clear window in the first trial. Hypothetically, they could use this visual configuration to guide eye movements in subsequent trials. In contrast, in the current training, the simulated scotoma was invisible until it concealed the target. When visual guidance was not available, PRL-trained observers apparently resorted to the default oculomotor control: foveating. However, it remains mysterious why PRL observers kept making foveating saccades after thousands of trials. Maybe the presence of full and partial cues, which essentially encouraged observers to make foveally-guided saccades to the location of the yellow dot on each training trial, discouraged or interfered with the development of a non-foveal PRL. This possibility could be examined in future experiments using no cues during PRL training. Lastly, because most patients with real scotoma are not even aware of their central scotoma (Fletcher, Schuchard, & Renninger, 2012), providing visual guidance such as a visible scotoma slightly larger than the real one may facilitate eccentric fixation. It is thus worth testing in our future experiments whether PRA training outdoes PRL training in terms of training speed and saccade accuracy when a visible scotoma is presented.

We realize that some additional limitations of this study may be addressed in future experiments. First, the PRA first saccade accuracy is currently about 35% after training. Perhaps longer training may further improve the accuracy. Second, we only trained and tested the observers

with the target presented at one eccentricity at 12 directions. It would be worth examining whether training can transfer to untrained eccentricities and directions. Third, it is also worth testing whether PRA observers would outperform PRL observers in other visual tasks, such as reading and visual search.

CRediT authorship contribution statement

Xin-Yu Xie: Investigation, Formal Analysis, Writing - original draft. **Lei Liu:** Conceptualization, Formal Analysis, Writing -review & editing. **Cong Yu:** Conceptualization, Formal Analysis, Writing -review & editing.

Acknowledgements

References

Bahill, A. T., Adler, D., & Stark, L. (1975). Most naturally occurring human saccades have magnitudes of 15 degrees or less. *Investigative Ophthalmology & Visual Science, 14*, 468–469.

Crossland, M. D., Culham, L. E., Kabanarou, S. A., & Rubin, G. S. (2005). Preferred retinal locus development in patients with macular disease. *Ophthalmology, 112*, 1579–1585.

Fletcher, D. C., & Schuchard, R. A. (1997). Preferred retinal loci relationship to macular scotomas in a low-vision population. *Ophthalmology, 104*, 632–638.

Fletcher, D. C., Schuchard, R. A., & Renninger, L. W. (2012). Patient awareness of binocular central scotoma in age-related macular degeneration. *Optometry and Vision Science, 89*, 1395–1398.

Hallett, P. E. (1978). Primary and secondary saccades to goals defined by instructions. *Vision Research, 18*, 1279–1296.

Hopp, J. J., & Fuchs, A. F. (2004). The characteristics and neuronal substrate of saccadic eye movement plasticity. *Progress in Neurobiology, 72*, 27–53.

Kuai, S. G., Zhang, J. Y., Klein, S. A., Levi, D. M., & Yu, C. (2005). The essential role of stimulus temporal patterning in enabling perceptual learning. *Nature Neuroscience, 8*, 1497–1499.

Kwon, M., Nandy, A. S., & Tjan, B. S. (2013). Rapid and persistent adaptability of human oculomotor control in response to simulated central vision loss. *Current Biology, 23*, 1663–1669.

Liu, R., & Kwon, M. (2016). Integrating oculomotor and perceptual training to induce a pseudofovea: A model system for studying central vision loss. *Journal of Vision, 16*, 10.

McLaughlin, S. (1967). Parametric adjustment in saccadic eye movements. *Perception and Psychophysic, 2*, 359–362.

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. *Spatial Vision, 10*, 437–442.

Schuchard, R. A., Naseer, S., & de Castro, K. (1999). Characteristics of AMD patients with low vision receiving visual rehabilitation. *Journal of Rehabilitation Research and Development, 36*, 294–302.

Von Noorden, G. K., & Mackensen, G. (1962). Phenomenology of eccentric fixation. *American Journal of Ophthalmology, 53*, 642–660.

White, J. M., & Bedell, H. E. (1990). The oculomotor reference in humans with bilateral macular disease. *Investigative Ophthalmology & Visual Science, 31*, 1149–1161.

Whittaker, S. G., Budd, J., & Cummings, R. W. (1988). Eccentric fixation with macular scotoma. *Investigative Ophthalmology & Visual Science, 29*, 268–278.

Whittaker, S. G., Cummings, R. W., & Swieson, L. R. (1991). Saccade control without a fovea. *Vision Research, 31*, 2209–2218.

Xie, X. Y., & Yu, C. (2020). A new format of perceptual learning based on evidence abstraction from multiple stimuli. *Journal of Vision, 20*, 5.