Integrating oculomotor and perceptual training to induce a pseudofovea: A model system for studying central vision loss

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People with a central scotoma often adopt an eccentric retinal location (Preferred Retinal Locus, PRL) for fixation. Here, we proposed a novel training paradigm as a model system to study the nature of the PRL formation and its impacts on visual function. The training paradigm was designed to effectively induce a PRL at any intended retinal location by integrating oculomotor control and pattern recognition. Using a gaze-contingent display, a simulated central scotoma was induced in eight normally sighted subjects. A subject's entire peripheral visual field was blurred, except for a small circular aperture with location randomly assigned to each subject (to the left, right, above, or below the scotoma). Under this viewing condition, subjects performed a demanding oculomotor and visual recognition task. Various visual functions were tested before and after training at both PRL and nonPRL locations. After 6–10 hr of the training, all subjects formed their PRL within the clear window. Both oculomotor control and visual recognition performance significantly improved. Moreover, there was considerable improvement at PRL location in high-level function, such as trigram letter-recognition, reading, and spatial attention, but not in low-level function, such as acuity and contrast sensitivity. Our results demonstrated that within a relatively short time, a PRL could be induced at any intended retinal location in normally-sighted subjects with a simulated scotoma. Our training paradigm might not only hold promise as a model system to study the dynamic nature of the PRL formation, but also serve as a rehabilitation regimen for individuals with central vision loss.

Introduction

The fovea, which corresponds to about 1° of visual field, is responsible for high acuity vision. For this reason, when we view the world around us, we continuously bring points of interest onto the fovea with saccadic eye movements. As a result, the fovea is used as the locus for fixations and as the oculomotor reference for saccades. Hence, it is not surprising that disorders affecting the central retina, such as age-related macular degeneration (AMD) or Stargardt's disease, have a devastating impact on daily visual activities, such as reading and face recognition. Macular degeneration (MD) is the leading cause of blindness in the developed world (World Health Organization, 2015). In the United States, about 1.75 million individuals are affected, with that number expected to grow to almost 3 million by 2020 (The Eye Diseases Prevalence Research, 2004).

One clinically important and scientifically interesting phenomenon emerging from these patients is that they learn to compensate for the loss of central vision by adopting an eccentric retinal location outside the affected macular region for fixations (i.e., pseudofovea or preferred retinal locus, PRL) (Cummings, Whittaker, Watson, & Budd, 1985; Fuchs, 1938; Timberlake et al., 1986). A PRL, or pseudofovea, is often defined as a retinal area used for fixation and/or saccade reference for a task (Crossland, Engel, & Legge, 2011). Studies have shown that stable and effective use of a PRL leads to better visual performance, such as in reading (Crossland, Culham, & Rubin, 2004; Tarita-Nistor, Gonzalez, Markowitz, & Steinbach, 2008) and visual search (Kwon, Nandy, & Tjan, 2013; Van der Stigchel et al., 2013; Walsh & Liu, 2014), highlighting the

importance of the development of a PRL for form perception in peripheral vision. Despite its functional significance, the emergence of a PRL in human patients seems to be a rather slow process, taking approximately 6 months (Crossland, Culham, Kabanarou, & Rubin, 2005).

While considerable progress has been made over the past few decades in our understanding of the PRL (Cheung & Legge, 2005; Fletcher & Schuchard, 1997; Pijnacker, Verstraten, Van Damme, Vandermeulen, & Steenbergen, 2011; Timberlake et al., 1986; White & Bedell, 1990), some important aspects regarding the emergence of a PRL still remain to be answered. For example, we still do not have a good understanding of what determines the selection of a PRL, what accounts for a slow development of a PRL, whether there are any perceptual changes at the site of a PRL after the extensive use of previously underutilized retinal region, or whether there is any way to improve visibility at the PRL. Whereas these questions are important in addressing perceptual issues in individuals with central vision loss and developing effective rehabilitative regimens, there are obvious challenges and limitations in examining these questions on patient populations. These include the difficulty of having elderly patients for long experimental testing; the possible confounding effects of comorbid disorders; individual differences related to pathology; the nature of retinal changes with the progression in the disease; and the relatively slow development of a PRL in patients. Moreover, the unpredictable nature of the location of an emerging PRL makes pre/post comparison of perceptual changes at the PRL site almost impossible.

One alternative method could be to use gaze-contingent simulation as a model system. The use of model systems is a common and effective tool to study a complex system, because it enables us to examine the relationship between key variables while controlling for extraneous variables. Thus, it allows us to easily derive a set of testable hypotheses that can be tested and validated on patient populations. Over the past several decades, artificial scotoma (Aguilar & Castet, 2011), using a gaze-contingent display, has been a useful tool to simulate visual field loss in individuals with normal vision to study the impacts of visual field loss on various visual tasks (Bernard, Scherlen, & Castet, 2007; Janssen & Verghese, 2015; Kwon et al., 2013; Rubin, 2001; Varsori, Perez-Fornos, Safran, & Whatham, 2004; Walsh & Liu, 2014). For example, studies have also shown that a PRL can be spontaneously developed in response to an artificial scotoma over a relatively short time period (Kwon et al., 2013; Walsh & Liu, 2014). Once established, a PRL can be retained over an extended period of time (Kwon et al., 2013). Furthermore, both clinical and simulated-scotoma studies have shown that subjects could be

trained to use an eccentric retinal location instead of their innate PRL for carrying out a particular task, such as reading (Lingnau, Schwarzbach, & Vorberg, 2008; Nilsson, Frennesson, & Nilsson, 2003; Tarita-Nistor, Gonzalez, Markowitz, & Steinbach, 2009), suggesting the possibility of inducing a PRL at any intended location with proper training. Taken together, artificial scotoma appears to serve as a reliable (with relatively low cost) model system to study the mechanisms that underlie the formation of a PRL and possible compensatory changes in oculomotor and perceptual systems. (Also see potential pitfalls and caveats in using gaze-contingent simulation in Aguilar & Castet, 2011.)

The current study was thus undertaken to propose a model system that can effectively induce a PRL at any intended retinal location. This was achieved by integrating two key ingredients necessary for form perception: oculomotor control and pattern recognition.

Although these two components are seemingly indispensable for the foveal vision (that is the visual system continuously brings the target of interest into the fovea via eye movements to acquire detailed pattern information), integrating these two components has been largely ignored in previous peripheral vision training studies that focused on either perceptual training (Chung, Legge, & Cheung, 2004; Lee, Kwon, Legge, & Gefroh, 2010; Nguyen, Stockum, Hahn, & Trauzettel-klosinski, 2011; Seiple, Grant, & Szlyk, 2011; Yu, Cheung, Legge, & Chung, 2010; Yu, Legge, Park, Gage, & Chung, 2010), eccentric viewing (Frennesson, Jakobsson, & Nilsson, 1995; Nilsson et al., 2003; Nilsson, Frennesson, & Nilsson, 1998; Palmer, Logan, Nabili, & Dutton, 2010; Seiple et al., 2011), or oculomotor training (Nguyen et al., 2011; Seiple et al., 2011; Seiple, Szlyk, McMahon, Pulido, & Fishman, 2005; Tarita-Nistor et al., 2008; Vingolo, Cavarretta, Domanico, Parisi, & Malagola, 2007).

Herein, we induced a simulated central scotoma using a gaze-contingent display in eight normally sighted subjects. The entire peripheral visual field was blurred except for a small circular aperture (i.e., a clear window) displayed near the scotoma. One of four locations of the clear window (to the right, left, above, or below of the scotoma) was randomly assigned to each subject. In other word, subjects' central visions (12° in diameter) were completely occluded by the scotoma while their peripheral visual fields were severely blurred but for the small clear region (~5° in diameter). Under this viewing condition, subjects performed a highly demanding oculomotor and visual recognition task (i.e., word, face, and object recognition) in which a target item randomly jumped across the visual field six times while its identity concurrently changed (e.g., from a word to a nonword; or from a
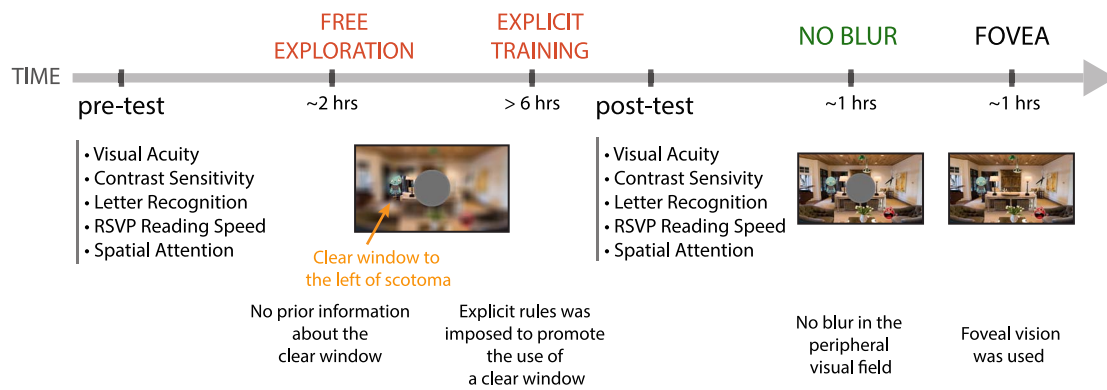
Figure 1. Schematic diagram of study design. The sequence of experimental conditions, duration of each session and a brief description of each session are provided.

female face to a male face). A subject's task was to report the target identity by pressing a key button. Subjects were encouraged to maintain their best performances as we provided both auditory and visual feedbacks on their oculomotor and pattern recognition performance. Subjects' gaze positions were recorded continuously, and gaze position data combined with target locations were used to estimate subjects' PRLs.

Using this model system, we asked the following questions: (a) We asked whether visibility in peripheral vision guides the selection of a PRL. We addressed this question by randomly assigning the location of the clear window to each subject to see if subjects spontaneously use this clear window for fixations and saccades, which may or may not be their innate PRL. No explicit instructions on the location of the clear window and how to use his/her peripheral vision were given. (b) We asked whether explicit training can help develop the formation of a PRL even it may not be their innate PRL location. (c) We asked whether the trained PRL persists even when the initial visibility advantage (i.e., a clear window embedded in blurred scenes) disappears. We addressed this question by assessing subjects' oculomotor behaviors after removing blur in the peripheral visual field. (d) We asked whether there are any perceptual changes at the site of PRL after prolonged use of a retinal location. To this end, we assessed various low- and high-level visual functions including visual acuity, contrast sensitivity, letter recognition, RSVP (Rapid Serial Visual Presentation) reading speed, and spatial attention before and after the training (Figure 1). Changes between pre- and posttests were compared for each task at both trained (the clear window) and untrained locations (on the opposite side with equal eccentricity).

Addressing these questions is expected to help us assess the validity of the model system while answering some of important questions about the development of PRLs in individuals with central vision loss.

Methods

Participants

A total of eight participants (age 27.25 ± 2.19 years, mean ± SD; four males, four females) recruited from the campus of the University of Alabama at Birmingham participated in this study. They all had normal vision with or without correction and they had no known cognitive or neurological impairments. Their mean acuity (ETDRS Visual Acuity Chart) was −0.15 ± 0.02 logMAR, and their mean contrast sensitivity (Pelli-Robson Contrast Sensitivity Chart) was 2.03 ± 0.04 log units. Their dominant eye was assessed by the Porta test. Subjects received monetary compensation for their participation. The experimental protocols were approved by the Internal Review Board (IRB) of the University of Alabama at Birmingham and written informed consents were obtained from all subjects prior to the experiment.

Stimuli and apparatus

High contrast 24-bit RGB color images of indoor scenes, objects, monsters, faces, words, and nonwords were chosen as stimuli. Images of 29 indoor scenes (1920 × 1080 pixels) were selected from an image database (Luo, Satgunam, & Peli, 2012). Images of 140 objects were selected from a commercially available set of photographs of real objects at www.photos.com (now at www.thinkstockphotos.com). Images of 96 monsters and one paper texture background (1920 × 1080 pixels) were selected from the Google image database (public domain). The length of all the objects and monsters was set to 50 pixels (1.6°). Images of 30 female and 54 male synthetic faces without hair were selected from the Max Planck Institute for Biological Cybernetics face database (http://faces.kyb.tuebingen.

mpg.de). Faces were cropped using an oval-shaped mask. The height of cropped faces was set to 138 pixels (4.3°). Both words ($n = 36$) and nonwords ($n = 40$) consisted of three or four lowercase Courier font letters. Words were chosen from the names of the objects, and nonwords were created manually. The letters were black (2.2 cd/m^2). Letter size defined as x-height was at least 1.2 times greater than that of each subject's acuity threshold obtained from the pretest. The stimuli were presented at a viewing distance of 57 cm.

The stimuli were generated and controlled using MATLAB (version 8.4) and Psychophysics and Eyelink Toolbox extensions (Brainard, 1997; Cornelissen, Peters, & Palmer, 2002; Pelli, 1997) for Windows 7, running on a PC desktop computer (model: Dell Precision Tower 5810). The display was a 27″ liquid crystal display monitor (model: Asus VG278H-E; refresh rate: 144 Hz; resolution: 1920 × 1080, subtending 60° × 34° visual angle) with the mean luminance of the monitor at 68 cd/m^2. The display monitor was linearized with photometric readings from a MINOLTA LS-110 Luminance Meter (Konica Minolta Inc., Japan).

Eye movement recording and simulated scotoma

Subjects' eye movements were monitored (monocular tracking) using an infrared video-based eye-tracker sampled at 500 Hz (EyeLink 1000 Plus/Desktop Mount, SR Research Ltd., Ontario, Canada) with a maximum spatial resolution of 0.01°. A nine-point calibration/validation sequence was performed at the beginning of every experimental session that relied on the eye-tracker. Calibration and/or validation were repeated until the validation error was smaller than 1° on average. The gaze position error, i.e., the difference between the target position and the computed gaze position, was estimated during the nine-point validation process. The average gaze position error was 0.25°. Chin and forehead rests were used throughout the experiment to minimize head movements and trial-to-trial variability in the estimation of gaze position. A real-time gaze position was sent to the display computer through a high speed Ethernet link. The continuous gaze information was used to draw a scotoma on the display screen at a refresh and update rate of 144 Hz where the gaze position corresponded to the center of the scotoma.

As illustrated in Figure 2a, the scotoma was a circular disc, subtended about 12° of visual angle in diameter, and was rendered as a uniform gray patch (luminance 68 cd/m^2) on the screen. The rest of the visual field was blurred except a small circular aperture (radius = 2.5°) externally tangent to the scotoma (hereafter called as "clear window"). The visual field was blurred by applying a Gaussian filter ($\sigma = 10$ pixels, corresponding to 0.31°) to the original images. Although its blur level was severe enough to eliminate detailed visual information, subjects were able to detect motion and color information easily. The gaze-continent clear window was displayed either to the left, right, above, or below of the scotoma at an eccentricity of 8.5° in visual space (Figure 2a).

The average delay between actual gaze and scotoma updates, measured by the photocell method (Bernard et al., 2007), was 16 ± 6 ms, which is comparable to that of previous studies (Aguilar & Castet, 2011; Bernard et al., 2007; Kwon et al., 2013). As none of our subjects reported any noticeable lag in their gaze-contingent view, the delay of 16 ms in our system appeared to be inconspicuous. As reported in the Aguilar and Castet (2011) study, a transient mismatch between gaze and scotoma locations may occur when a subject either blinks or squints. The current study minimized this transient mismatch by turning the entire display screen blank (solid gray) as soon as a blink was detected or pupil size was decreased down to a threshold value. However, even if a noticeable mismatch due to the delay or a squint had occurred, it was still difficult for our subjects to view the target using the fovea (i.e., "cheating") due to the severe blur presented to the entire background image and the large central scotoma (~12° in diameter). Furthermore, the fact that our subjects established their PRLs in the intended training location further confirmed that our gaze-contingent scotoma was effective in blocking subjects' foveal vision.

Procedure

In this study, we developed a novel training protocol that promotes the use of an eccentric retinal location through concurrent oculomotor and perceptual training (OPT). The training paradigm was like a video game interface. The current study consisted of four experimental conditions (*free exploration*, *explicit training*, *no blur*, and *fovea*) in which subjects performed the identical OPT task (Figure 1), but either viewing condition or the rules of the game differed across the experimental conditions. In addition, before *free exploration* and after *explicit training,* various untrained tasks such as visual acuity, contrast sensitivity, letter recognition, RSVP reading speed, and spatial attention were tested to evaluate the impacts of the OPT on low and high level visual processing. The sequence of the study was illustrated in Figure 1. All the subjects but one (s6) completed all the experimental conditions: *free exploration, explicit training, no blur,*
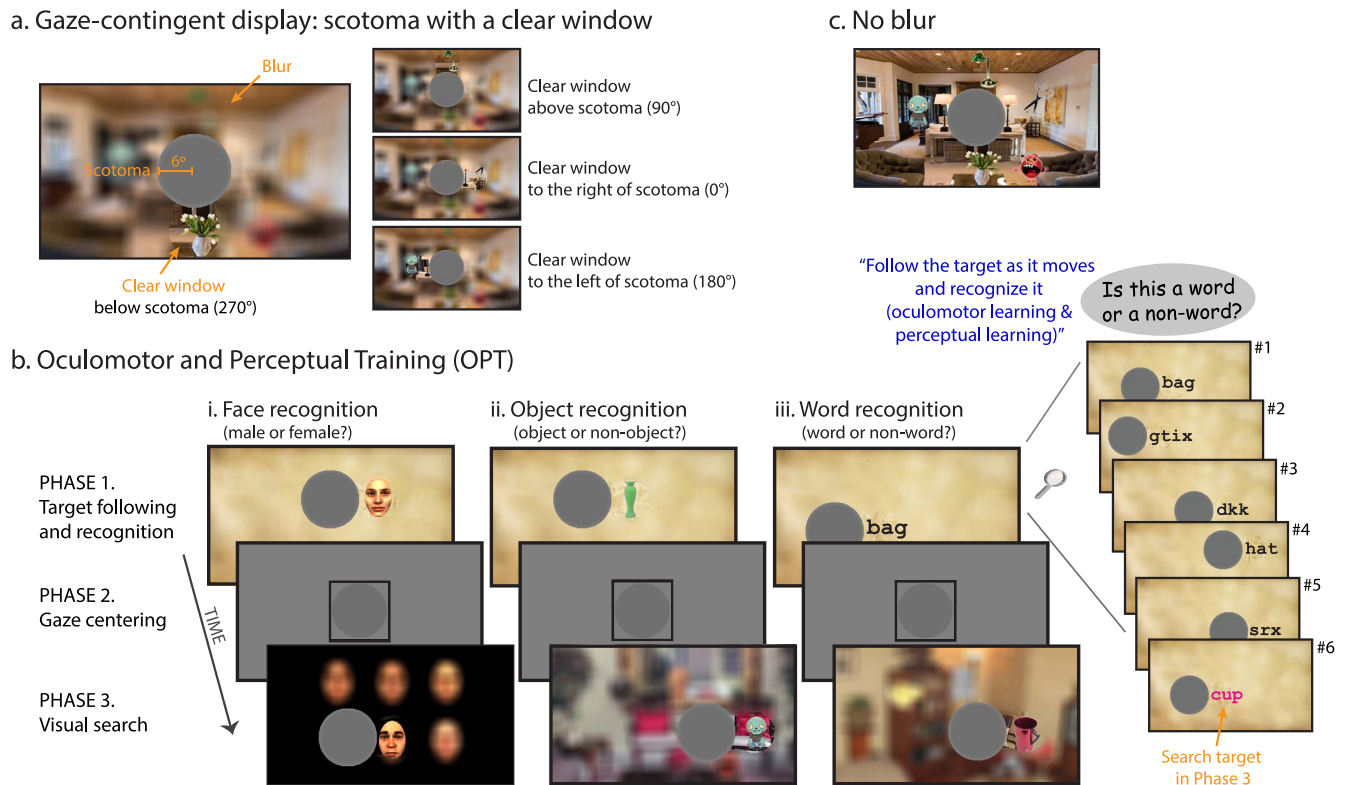
Figure 2. Illustration of the gaze-contingent display and task procedure. (a) The circular shaped scotoma (12° of visual angle in diameter) was rendered as a uniform gray patch while the rest of the visual field except a small circular window (5° diameter) was blurred. This clear window appeared at one of the four predetermined locations tangent to the scotoma (i.e., to the right 0°, to the left 180°, above 90°, and below 270° of the scotoma). The location of the clear window was randomly assigned to each subject. (b) Task sequence of the oculomotor and perceptual training (OPT). The OPT consisted of three kinds of visual recognition tasks: (i) face recognition, (ii) object recognition and (iii) word recognition. Each task was tested in a subblock comprised of 30 trials. One block contained three subblocks (one subblock for each task) and took approximately 45 min to 1 hr to complete. Each task followed the same sequence. This sequence shown here is an example of one trial. Each trial was comprised of three phases: Phase 1, target following and recognition, recognizing target as it changes its identity and position (a total of six changes per trial); Phase 2, gaze centering; Phase 3, visual search, searching for the last target object presented in the Phase 1. Subjects were instructed to report whether the target is present or absent amidst either a black solid background (face recognition task) or clutter background (object or word recognition task) with an array of nontarget distracters. (c) Illustration of the *no blur* experiment. The task procedure was identical to that of the *free exploration* experiment except that no blur was presented in the periphery. For ease of visibility in the figure, target objects and the clear window are rendered at two times their sizes used in the experiment, relative to the rest of the displayed elements.

fovea, and *pre/posttest*. The subject s6 only completed *free exploration*, *explicit training*, and *pre/posttest*.

Oculomotor and perceptual training (OPT)

The OPT consisted of three task phases (Figure 2b). *Phase 1: Target following and recognition*: In this phase, a target item was randomly repositioned six times against a paper texture background. Whenever the target moved to a new location, its identity also changed (e.g., male or female face; word or nonword; daily object or nonobject). A subject's task was to follow, recognize, and report the target via a key-press as quickly and as accurately as possible. Auditory feedback was provided for recognition response. Target moved only when subjects completed the recognition task (with a valid key-press) or when the onscreen positions of the subjects' scotomas did not occlude the target item for at least 2.5 s. This was done to promote eccentric viewing. The sixth target in this phase (i.e., the last target in Phase 1) served as the search target for the subsequent visual-search phase (Phase 3), and subjects were always reminded of this search target by an auditory cue.

Phase 2: Centering of gaze: Subjects centered their gaze in the middle of the screen so that their scotomas were placed inside a black rectangular box for 1.5 s. This was done right before the onset of visual search to minimize any positional bias.

Phase 3: Visual search: Subjects searched for the target item (the last target in Phase 1) amidst either a solid or cluttered background with an array of non-target distracters. Subjects were given an unlimited amount of time to perform the search, after which they indicated the presence or absence of the search target by a key-press ("p" for presence, "a" for absence). The probability of the target being present was 0.5. Subjects were instructed to perform the search task as quickly and as accurately as possible. Auditory feedback was provided for search response.

At the end of each subblock (30 trials), a summary of performance, including mean performance accuracy and task-completion time, was displayed on the screen along with either a cheering or booing sound depending on subjects' performances. This was done to encourage subjects to achieve their best possible performance. The recognition accuracy in Phase 1 and search accuracy in Phase 3 accounted for five-sixths and one-sixth of the overall performance accuracy respectively.

The OPT utilized three different kinds of visual tasks relevant to daily visual activities: reading and face and object recognition (Figure 2b). This was done on the following grounds: (a) word, face, and object are considered to be the most common types of object categories closely related to everyday visual activities; (b) patients with a central scotoma frequently report difficulties with reading or recognizing objects or faces and cite reading problems as one of their main anxieties (Bullimore, Bailey, & Wacker, 1991; Elliott et al., 1997; Kleen & Levoy, 1981); and (c) many studies on perceptual learning have shown that training with different visual stimuli makes learning more generalizable (Deveau, Lovcik, & Seitz, 2014; Deveau, Ozer, & Seitz, 2014; Xiao et al., 2008; Zhang et al., 2010). In short, by allowing exposure to different types of stimuli, we hoped to maximize training effect.

Each task followed the same three-phase procedure described above:

Word recognition: During Phase 1 (target following and recognition), subjects were told to report whether a given target item is a word (e.g., cup) or a nonword (e.g., tkc) via a key-press whenever the target item changes its identity, which occurred as the target moved to a new location (total six times). The sixth target was always a word referring to common objects (e.g., hat, bike, etc.) and served as the search target for the subsequent visual-search phase (Phase 3). Subjects were always reminded of the search target by a distinctive auditory cue so that subjects knew that they were supposed to recognize this word (e.g., cup) in order to perform the search task. In Phase 3 (visual search), subjects searched for the target object among nine distracters embedded in a cluttered scene and reported its presence or absence via a key-press. Both target and nontarget distracters were superimposed on

the scene rather than part of the scene. This was done in order to minimize any contextual effects on search performance (Figure 2b-iii).

Object recognition: The task procedure was the same as the word recognition, but here subjects were told to judge whether a given target item is an ordinary object or nonobject (cartoonish monster images were used as nonobjects). Similar to the word recognition task, the sixth target item served as the search target and was always an object. During Phase 3, subjects reported the presence or absence of the search object among nine distractors (four nontarget objects and five nonobjects) (Figure 2b-ii).

Face recognition: The task procedure was identical to that of the other two tasks, except that a subject's task was to tell whether a given target face was female or male during Phase 1. The sixth target face in Phase 1 was always female and served as the search target in the following visual search phase. In Phase 3, subjects were told to report whether the target face is present or absent among six faces (three males and three females) arranged in a 2 × 3 rectangular array against a solid black background (Figure 2b-i).

All three tasks were tested in a block made up of three subblocks, containing one task each. The test sequence of the three tasks within a block was counterbalanced between subjects. One subblock was composed of 30 trials and took about 15 to 20 min to complete without interruption. Thus, each block took 45 min to 1 hr to complete. On average, subjects took 18 hr to complete the entire study (including pre/posttests). This was spread into several sessions spanning several weeks. Subjects performed the task in a dimly lit room, seated in a comfortable position with chin and forehead supports. Subjects were given a few practice trials before training to make sure they fully understood the task and procedure. Each subblock started with the calibration/validation sequence described earlier (~3 min). The trial started with an auditory beep immediately after drift correction.

All subjects completed two blocks of the OPT task during *free exploration* in which subjects were not informed of the location of a clear window in the peripheral visual field nor given explicit instructions on how to use their gaze. Subjects were told that their goal is to attain the highest performance accuracy possible.

Subjects then received *explicit training* (at least six blocks and up to nine blocks) in which the subjects performed the same OPT task as in the *free exploration* experiment, but this time subjects were told to use the clear window (i.e., training location) as the point of gaze as much as they could. To facilitate the use of the clear window, we also imposed a new rule. During Phase 1, a subject's response (via a key-press) for the recognition task was valid only if the target fell inside the clear window and remained there for more than 1.25 s. Upon

completion of *explicit training* and posttests, subjects performed one block of the OPT task for the *no blur* experiment. During *no blur*, subjects performed the same OPT task as in the *free exploration* experiment, but this time blur was not presented in the peripheral visual field (Figure 2c). Last, subjects performed one block of the OPT task for the *foveal* experiment identical to the *free exploration* experiment, but subjects used their foveal vision to perform the task in the absence of a simulated scotoma and peripheral blur.

Some parts of the task phase and procedure are similar to those used in Kwon et al.'s (2013) study, but they are also different in several distinctive ways (see the Discussion for detailed information).

Pre- and posttests

To examine the effect of the OPT on low or high level visual functions, various visual tasks, including visual acuity, contrast sensitivity (contrast discrimination threshold), letter recognition, RSVP reading speed, and spatial attention, were assessed at the trained retinal location before *free exploration* and immediately after *explicit training* (Figure 1). For a control condition, we also tested untrained locations which were opposite from each subject's trained location with equal eccentricity. The order of two testing locations was counterbalanced within subjects, while the order of five tests was fixed. Each testing location was either above, below, to the left, or to the right of the scotoma at an eccentricity of 8.5°. In order to ensure our measurements were made at the intended retinal location, all the testing stimuli were displayed on the screen in a gaze-contingent manner using the eye-tracker. Subjects were given a series of practice trials before the pretest. Subjects performed the task in a dimly lit room while they were seated in a comfortable position with chin and forehead supports.

Measuring visual acuity: Visual acuity was measured using the psychophysical method of constant stimuli to determine the ability to resolve a gap in the Landolt C (Figure 3a). The Landolt C was rotated either 0°, 90°, 180°, or 270°, and the direction of rotation was determined at random in each trial. The stimulus letter was black against a uniform white background (134 cd/m^2) with a contrast of 98%. In a trial, the stimulus letter was presented for 150 ms followed by a brief interval (500 ms). A subjects' task was to report the orientation of the Landolt C gap by pressing one of four keys. Recognition accuracy was obtained for five different letter sizes, spanning a range of 0.9 log units. Trials with five different letter sizes were randomly interleaved. Each letter size was presented 10 times, so there were a total of 50 trials for each measure. The threshold acuity was estimated from the resulting psychometric function, a plot of percent correct recognition as a

function of letter size. Best fitting (least squares) cumulative Gaussian functions (Wichmann & Hill, 2001) were fit to the data, and threshold acuity was defined as the letter size yielding 80% correct responses. The final acuity was based on an average of two thresholds obtained from repeated measures.

Measuring contrast sensitivity (contrast discrimination thresholds): The test stimulus was a vertical sinusoidal grating (1.8° in diameter; 20% pedestal contrast) with 2 cycles/° displayed in a uniform gray field (68 cd/m^2) (Figure 3b). The stimulus contrast was defined as Michelson contrast. Contrast discrimination thresholds were measured with a temporal, two-alternative, forced-choice (2AFC) staircase procedure. The subject's task was to judge which stimulus interval contained the higher contrast by pressing one of two keys. Auditory feedback was given for incorrect responses. In a discrimination trial, the stimuli C and C + ΔC were each presented for 150 ms, accompanied by an auditory tone, and separated by 500 ms. A three-down, one-up staircase rule was adopted, yielding a threshold criterion of 79.4% correct (Wetherill & Levitt, 1965), and the step size of the staircase was 2 dB. The geometric mean of seven staircase reversals was taken as the contrast threshold for each staircase run. The final contrast threshold was based on an average of two thresholds obtained from repeated measures.

Measuring letter recognition: Letter recognition was measured with the trigrams method described in detailed by Kwon and Legge (2012). Figure 3c illustrates the procedure for a single trial of the trigram task. Trigrams (random strings of three letters) were presented for 200 ms at each subject's trained (or untrained) region. All stimulus letters were black on a gray background (68 cd/m^2) with a contrast of 97%. The letter size was at least 1.2 times larger than each subject's acuity threshold at a given testing location (at the eccentricity of 8.5°). Trigrams were centered at five letter positions, and each of the five trigram positions was tested 10 times in a random order. Subjects were instructed to fixate on the fixation cross on the computer screen during trials. The experimenter initiated each trial by pressing a key. Subjects were asked to read the letters from left to right as accurately as possible without a time limit. A letter was scored as being identified correctly only if its order within the trigram was also correct. Feedback was not provided to the subjects about whether or not their responses were correct. Proportion correct recognition was measured at each of the letter slots and combined across the trigram trials. The letter recognition was quantified by summing across the proportion correct in each slot (similar to computing the area under the curve) for a given testing location. The final accuracy (proportion correct) in each slot was based on an average of two accuracies obtained from repeated measures.
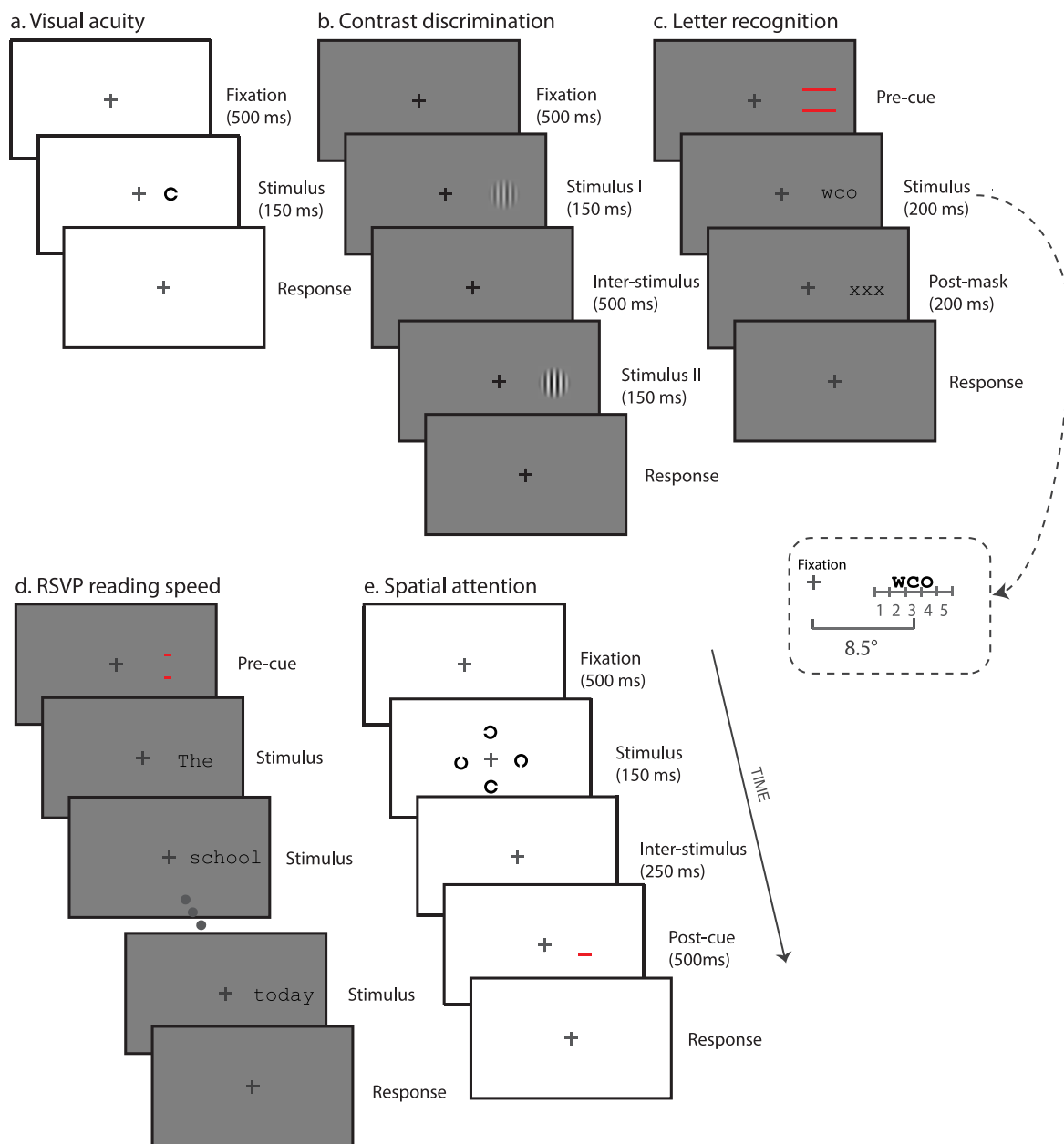
Figure 3. Illustrations of the task procedure for pre- and posttests. Changes between pre- and posttests were compared for each task at both trained (the clear window) and untrained locations (on the opposite side with equal eccentricity, 8.5°). In order to ensure our measurements were made at the intended retinal location, all the testing stimuli were displayed on the screen in a gaze-contingent manner using the eye-tracker. (a) Measuring visual acuity. Visual acuity was measured using the psychophysical method of constant stimuli to determine the ability to resolve a gap in the Landolt C.A subjects' task to report the orientation of the Landolt C gap by pressing one of four keys. (b) Measuring contrast discrimination threshold. Contrast discrimination thresholds were measured with a temporal, two-alternative, forced-choice (2AFC) staircase procedure. The two stimulus intervals only differed in stimulus contrast; otherwise they were identical. The subject's task was to judge which stimulus interval contained the higher contrast by pressing one of two keys. (c) Measuring letter recognition. Letter recognition was measured with the trigrams method described in detailed by Kwon and Legge (2012). Trigrams (random strings of three letters) were presented at five letter positions for 200 ms. Subjects were asked to read the letters from left to right as accurately as possible without a time limit. (d) Measuring RSVP reading speed. Oral reading speed was measured with Rapid Serial Visual Presentation (RSVP). The sentences were presented sequentially one word at a time at the same screen location for a given stimulus duration. Subjects were instructed to read the sentences aloud as accurately as possible. (e) Spatial attention task. The effect of spatial attention was measured as the ability to deploy attention to a particular location under an uncued condition. The Landolt Cs were simultaneously presented in each of the four locations 0°, 90°, 180°, and 270° at an eccentricity of 8.5° for 150 ms. For a given location, the direction of rotation (up, down, left, or right) was determined at random in each trial. The Landolt Cs were followed by a postcue interval during which a target location (a red line) was given. Subject's task was to judge the orientation of the Landolt C gap in the target location by pressing one of four keys.

Measuring RSVP reading speed: Oral reading speed was measured with Rapid Serial Visual Presentation (RSVP) (Figure 3d). We used the same procedures and sentences for measuring reading speed as Kwon et al. (2007), and Kwon and Legge (2012). The size and contrast of the stimulus letters were the same as those in the letter recognition test. The sentences were presented sequentially one word at a time at the same screen location (i.e., the center of each word occurred at the same screen location). There was no blank frame (interstimulus interval) between words. Subjects were instructed to read the sentences aloud as accurately as possible. Subjects were allowed to complete their verbalization after the sentence disappeared from the display. Words reported out of order were counted as correct, such as a correction made at the end of the sentence. During the testing session, five different exposure durations, spanning a range of ~1 log unit, were used. The range of exposure durations for each subject was chosen in order to make sure that at least 90% correct response (percent of words read correctly in a sentence) was obtained at the longest exposure time. The order of five durations was randomly interleaved within a block. Psychometric functions, percent correct versus RSVP exposure duration, were created by fitting these data with cumulative Gaussian functions (Wichmann & Hill, 2001). The threshold exposure duration, for words of a given length, was based on the 80% correct point on the psychometric function. For example, if an exposure time of 200 ms per word yielded 80% correct, the reading rate was 5 words per second, equal to 300 words per minute (wpm). The final reading speed was an average of two reading speeds obtained from repeated measures.

Measuring spatial attention: The effect of spatial attention was measured as the ability to deploy attention to a particular location under an uncued condition. In other words, we assessed whether there is any difference in the level of attention (defined as recognition accuracy) between trained and untrained regions while a subject's attention was distributed across the visual field. Figure 3e illustrates the procedure for measuring deployment of attention to four different peripheral locations (0°, 90°, 180°, and 270° in radial orientation at an eccentricity of 8.5°). The stimulus letters (0.65° in height) were black on a white background (134 cd/m^2) with a 98% contrast. In each trial, subjects fixated on a central cross. The Landolt C was simultaneously presented in each of the four locations for 150 ms. The Landolt C was rotated either 0°, 90°, 180°, or 270°. For a given location, the direction of rotation was determined at random in each trial. The Landolt Cs were separated by 250 ms, followed by a postcue interval for 500 ms during which the target indicator (a red line) appeared in one of the four locations. The subject's task was to judge the orientation of the Landolt C gap in the target location by pressing one of four keys. Within a block, the target was distributed equally across the four locations (i.e., each location was the target location for 35 trials in a block). The assignment of a target location was randomized so that it was not possible to predict the target location of the next trial. The final recognition accuracy was an average of two accuracies obtained from repeated measures.

Note that our attention paradigm is different from the classical Posner cueing paradigm. While the Posner cueing paradigm is designed to measure the effects of covert orienting of attention on visual processing (e.g., reaction time), our main interest was on whether there were any changes in attentional hotspot following peripheral vision training. This condition is more similar to what patients with central vision loss would experience in real life, where it is rare to receive any explicit cue (as in the precue paradigm) in a particular retinal location.

It has been reported that attentional resolution differs across the visual field, e.g., higher in the lower visual field (VF) than the upper VF, higher in the right VF than the left VF (S. He, Cavanagh, & Intriligator, 1996; Intriligator & Cavanagh, 2001; Lee et al., 2010). It has been suggested that this attentional hotspot might be related to visual experience in our daily lives (e.g., reading from the left to right; relevant signals, such as hazards, occur more often in the lower VF than the upper VF). Unlike the precue paradigm, our postcue paradigm allowed us to measure any intrinsic difference in static spatial attention between the trained and untrained location.

Data analysis

Gaze data were analyzed using the EyeLink parsing algorithm, which robustly classified fixations and saccades, excluding blinks. The saccadic velocity threshold of 30°/s, saccadic acceleration threshold of 8000°/s^2, and saccadic motion threshold of 0.1° were used to define saccades from fixations (Bethlehem et al., 2014; Lingnau et al., 2008; Smith, Glen, Monter, & Crabb, 2014; Van der Stigchel et al., 2013). Note that previous studies (Aguilar & Castet, 2011; Bernard et al., 2007) reported the unwanted triggering of slow eye movements (smooth pursuits) in the absence of a target for tracking (as if the scotoma becomes an actual moving target). Given the fact that the velocity of smooth pursuits is typically below 25°/s under a simulated scotoma condition (Aguilar & Castet, 2011), our saccade data are not likely to include smooth pursuit eye movements as the saccade velocity threshold of 30°/s was adopted in the current study. Furthermore, the average latency of saccades observed in our study was 216 ms (ranging from 159 ms to 321 ms), which is a typical latency for saccade, differing from a typical latency of smooth pursuits (~100 ms) (Orban de Xivry & Lefevre, 2007).

Fixation density maps were derived from the retinal positions of the target objects during periods of fixation via density estimation with a bivariate Gaussian kernel (Botev, Grotowski, & Kroese, 2010). We used the same analysis method used in Kwon et al. (2013). Briefly, the PRL was defined as the peak of the density. The variance of fixation was defined as the Bivariate Contour Ellipse Area (BCEA) (Steinman, 1965) that encompassed 68% of fixations around the mean (Castet & Crossland, 2012) and was used as an indicator of fixational stability. BCEAs were calculated from the density maps. The density maps for the first saccade-landing site were obtained in a similar manner from the retinal positions of the target objects at the end-point of the first saccade after object movement.

To examine the effects of the OPT on oculomotor control, or visual recognition and search performance, data were analyzed using the pairwise *t* test. We also performed the one-sample *t* test to evaluate the effect of the OPT on visual performance of the untrained tasks (pre- and posttests). We confirmed that the data were normally distributed with a Quantile-Quantile plot. The change in performance from pre- to posttests was quantified as the percent change (%) in posttest with respect to pretest. Thus, a value of zero indicates no change between pre- and posttests, whereas a value greater than zero (positive sign) means improvement in posttest.

Results

Effect of visibility on the selection of a PRL

In order to see if visibility alone plays a role in the selection of a PRL, we examined whether subjects spontaneously used the clear region for guiding their eye movements. To this end, we instructed subjects to perform the OPT task as best as they could without providing any information about the location of the clear window and how to use their peripheral vision to perform the task (*free exploration*). Subjects completed two blocks of the free exploration experiment. Figure 4a-i shows the data acquired from the second block (i.e., the last block) of the free exploration period. We found that the majority of subjects spontaneously used the clear region to perform the task, and four of them formed their fixational PRL (defined as the peak of the density map) within the clear window. Furthermore, for some of subjects, their first saccade after each target movement placed the target near the clear window (Figure 5a-i), suggesting a shift in oculomotor reference from the fovea toward the clear window.

Whereas these results suggest the potential role of visibility in the selection of a PRL, the fact that a majority of subjects still exhibited foveating behavior to some degree after the initial 2-hr exposure to the simulated scotoma called for the need for explicit training to facilitate the establishment of a PRL.

Development of a PRL during explicit training

We asked if explicit training designed to promote the use of the clear window (i.e., training location) would facilitate the development of a PRL. To promote the use of the clear window, we imposed a new rule: During Phase 1, subjects' responses for the recognition task were valid only if the target fell inside the clear window and remained there for more than 1.25 s. Otherwise, subjects performed the identical task as in the *free exploration* period. With 6 to 10 hr of such explicit training, all eight subjects used the clear window for fixations and saccade reference, forming a PRL within their clear window (Figures 4a-ii and 5a-ii). The mean variances of the fixational PRL and first saccade-landing site measured at the end of the explicit training were significantly smaller than at the beginning of the training ($t(7) = 4.13$, $p = 0.004$ for fixational PRL; $t(7) = 3.73$, $p = 0.007$) for first saccade-landing site. See Figures 4b and 5b.

We, however, observed that the variance of first saccade-landing site was much larger than that of fixational PRL ($t(7) = 3.88$, $p = 0.006$, comparing the fixational PRL and first saccade-landing site for the last block of the explicit training), which is consistent with previous studies showing that the refinement of saccadic rereferencing was slower than the refinement of fixational PRL (Heinen & Skavenski, 1992; Kwon et al., 2013). See the Discussion for our detailed discussion on the differences in the variance of PRLs between the current study and Kwon et al. (2013) study.

To further assess the robustness of the training, we also conducted the *no blur* experiment in which subjects performed the same OPT task as before, but this time the entire visual field appeared clear, except for the central scotoma. Therefore, there was no apparent advantage of using the clear window to perform the task. However, all subjects retained the same PRLs, even in this no blur condition (Figures 4a-iii and 5a-iii). Consistent with the findings in Kwon et al. (2013), the results of the no blur experiment assured that our training effect could persist at least one week after the training, as the no blur experiment was conducted about a week after the training.

Improvement of visual performance during PRL development

With the development of PRL, we observed corresponding improvements in visual recognition and search performance. Figure 6 shows recognition
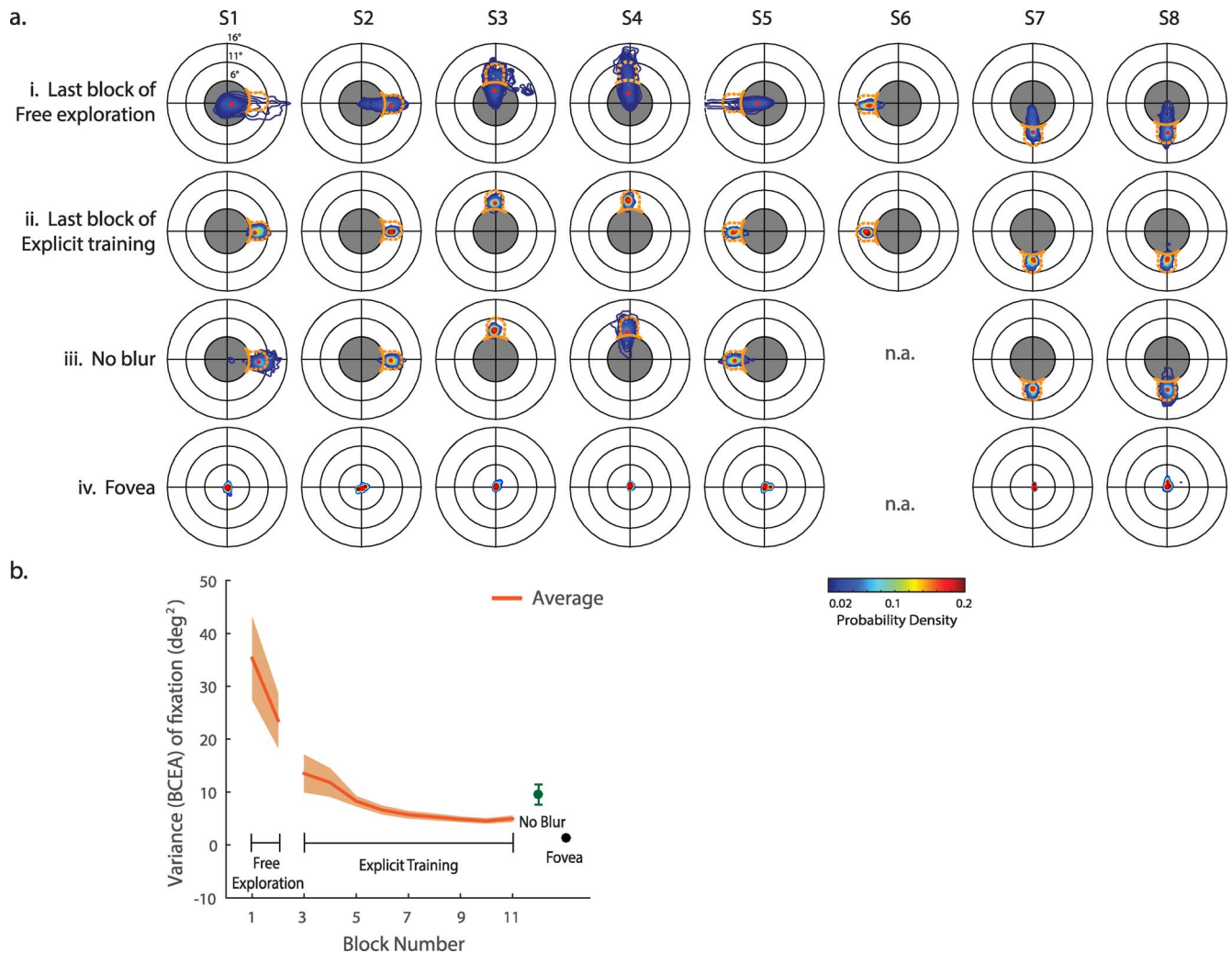
Figure 4. Preferred retinal locus (PRL) for fixation. (a) Probability density maps of the retinal positions of a target object at fixation are shown for all eight subjects (S1–S8). Rows, from left to right: the orientations of the clear window chosen for each two subjects are 0°, 90°, 180°, and 270° in the radial direction. Columns, from top to bottom: a density map estimated from the last (second) block of the free-exploration period, the last block of the explicit-training period, the no blur condition, and the fovea condition. Each block took approximately 1 hr to complete. Each polar plot represents the visual field. The gray patch depicts the central scotoma (12° in diameter). The orange dashed circle represents the region corresponding to the clear window. The red dot marks the location of peak density, which we took as the estimated location of the fixational PRL. The color bar shows the colors corresponding to different probability density values. (b) The mean variance of the fixational PRL as a function of block number. Variance was defined as the bivariate contour ellipse area (BCEA) that encompassed 68% of fixations around the mean. The solid orange lines indicate the average variance value across subjects. Error bounds are ±1 *SEM*.

accuracy, search accuracy, and search time as a function of block number. The recognition accuracy obtained from Phase 1 of the task significantly increased from 73% at the beginning of the explicit training to 87% at the end of the training (a 19% increase, $t(7) = 5.87$, $p < 0.001$) (Figure 6a). Similarly, there was a significant improvement in search accuracy at the end of the training compared to the beginning of the free exploration, a 22% increase ($t(7) = 5.10$, $p = 0.001$) (Figure 6b). At the same time, the search time at the end of the training was significantly shorter than it

was at the beginning of the free exploration (6.7 s versus 10.4 s, $t(7) = 3.33$, $p = 0.01$) (Figure 6c).

Perceptual changes at the PRL following the training

To see if there are any perceptual changes at the site of a PRL after the prolonged training, we assessed both low- and high-level visual functions before and after the training. In order to rule out any influence of a potential confounder (that is, an improvement in
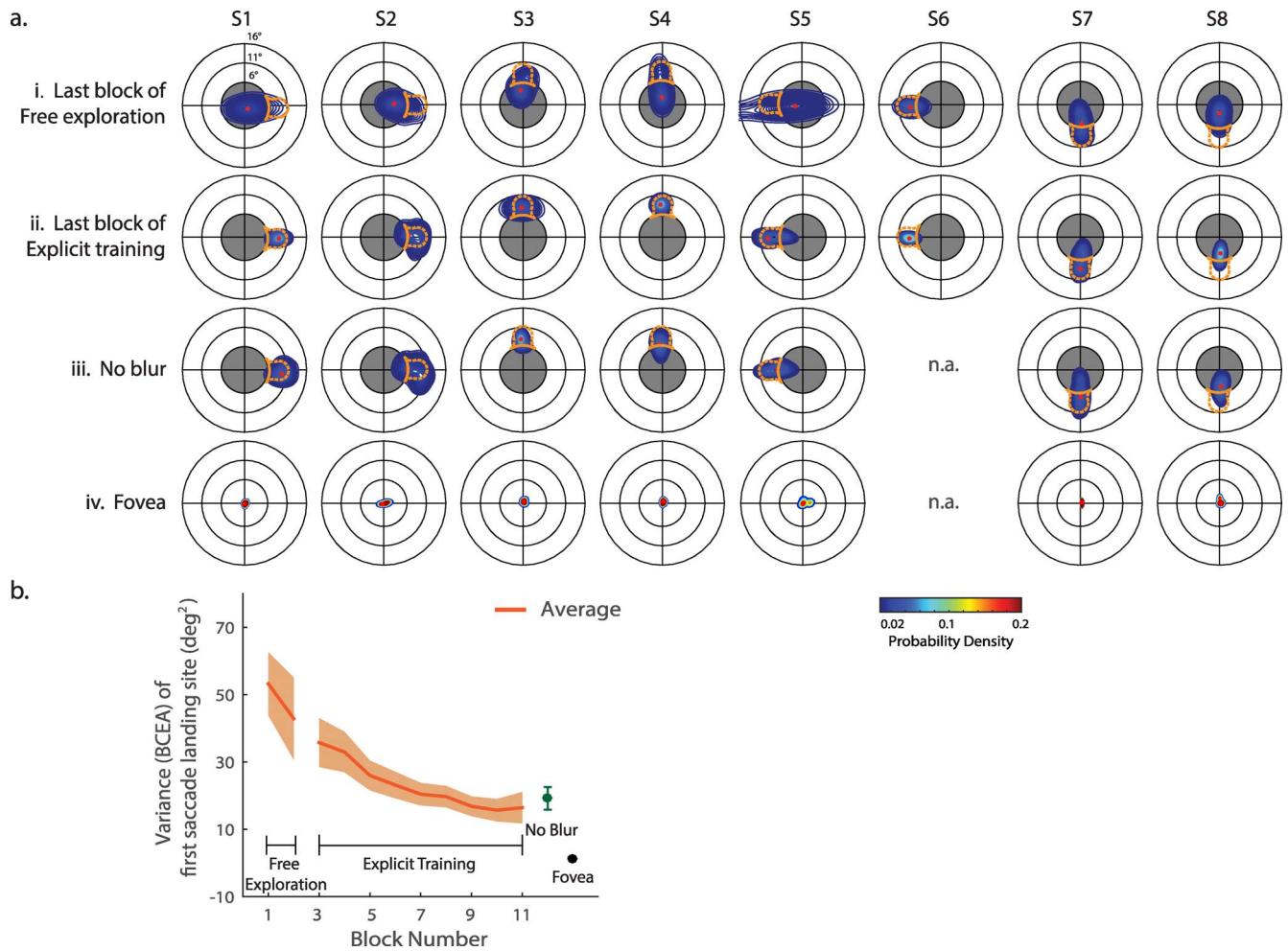
Figure 5. First saccade-landing site after each target move. (a) Probability density maps of the retinal position of a target at the completion of the first saccade following target movement (the same format as in Figure 4a). (b) The mean variance (BCEA) of the first saccade-landing site as a function of block number. The solid orange lines indicate the average variance value across subjects. Error bounds are ± 1 *SEM*.
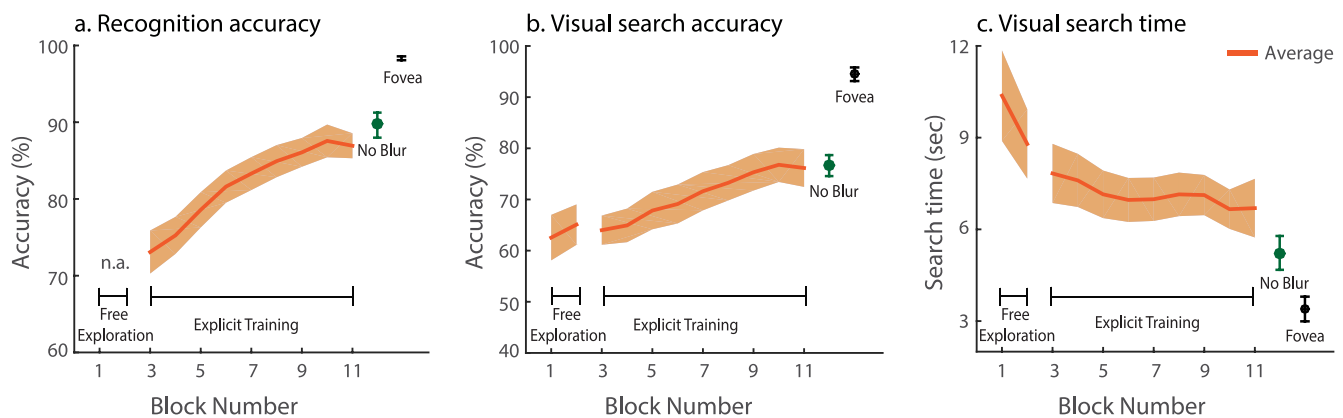

Figure 6. Improvements in recognition and visual search performance. (a) Recognition accuracy (% correct) in the target following and recognition phase (Phase 1) as a function of block number. (b) Visual search accuracy (% correct) in the visual search phase (Phase 3) as a function of block number. (c) Time taken to complete a search trial (only a trial with correct response) as a function of block number. The solid orange lines indicate the average value across subjects. Error bounds are ± 1 *SEM*.
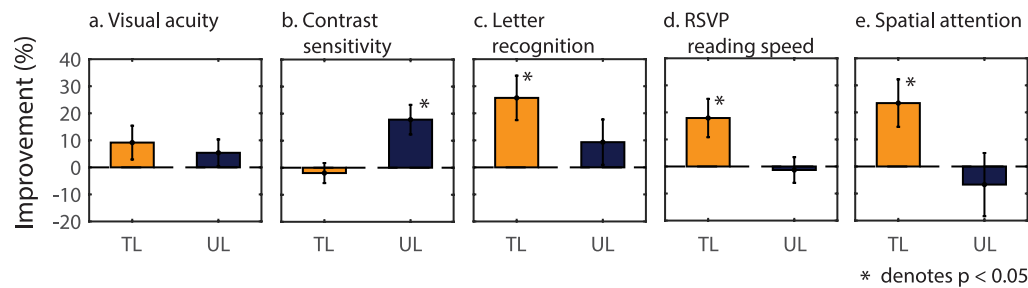
Figure 7. Changes in visual function between pre- and posttests. Improvements in posttests with respect to pretests are shown on the y axis. A value greater than 0 (positive sign) means improvements in performance. On the x axis, "TL" means trained locations (region corresponding to a clear window) while "UL" indicates untrained locations (the opposite from the trained locations). Error bounds are ± 1 SEM.

performance simply due to familiarity with the task procedure), we also obtained data from an untrained location as a control condition.

The change in performance from pre- to posttests was quantified as the percent change (%) in posttest with respect to pretest. A value of zero thus indicates no change between pre- and posttests while a value greater than zero (positive sign) means improvement in posttest. In order to present an improvement in performance with a positive sign on the ordinal axis of Figure 7, we computed either the ratio of pretest to posttest or the ratio of posttest to pretest depending on the task (e.g., the former for visual acuity). Figure 7 shows percent improvements for both trained and untrained locations for the five different visual functions: visual acuity, contrast sensitivity (contrast discrimination threshold at the spatial frequency of 2 c/°), letter recognition, RSVP reading speed, and spatial attention.

Whereas there were no significant changes in visual acuity and contrast sensitivity ($ps > 0.05$), we observed significant improvement in letter recognition (a 26% increase, $t(7) = 3.13$, $p = 0.02$) and RSVP reading speed (an 18% improvement, $t(7) = 2.53$, $p = 0.04$). However, we did not find any significant changes in the untrained location ($ps > 0.05$) except for contrast sensitivity. It is noteworthy that contrast sensitivity improved significantly at untrained locations ($t(7) = 3.25$, $p = 0.01$) while no changes were observed in the trained location. We believe this was due to blur adaptation in which contrast sensitivity improved following an exposure to blur. This phenomenon is common and well-documented in previous literature (George & Rosenfield, 2004; Rajeev & Metha, 2010; Rosenfield, Hong, & George, 2004; Webster, Georgeson, & Webster, 2002). Because, in our study, the untrained locations were blurred during the training, an improvement in contrast sensitivity for the posttest was expected.

Another noteworthy point is that there was a considerable improvement in spatial attention at the trained location (an average increase of 23%, $t(6) =$

2.67, $p = 0.04$) while a noticeable decrease was observed at the untrained location. Note that one outlier data point was excluded from this analysis (Figure 7e). These results suggested that through the training, a majority of subjects might have learned to allocate more attention to their trained location compared to the less relevant, untrained location. Whether patients tend to allocate more attention to the PRL location in the absence of any physical cue or stimuli is highly relevant to the effectiveness of processing visual information at the PRL location and guiding eye movements, as it helps prepare subjects for any upcoming events. Our attention task took place at least an hour after the training or sometimes even a day after the training. So, what we observed in our attention task is likely to be neither a result of iconic memory nor short-term memory from the training stimuli. Thus, the mechanism underlying enhanced attention at the trained location calls for further examination.

Discussion

Here, we demonstrated that using a novel oculomotor and perceptual training (OPT) protocol, a PRL could be effectively induced at any intended location in normally sighted individuals with a simulated central scotoma. Integrating oculomotor and perceptual training promoted the use of an eccentric location for guiding eye movements and for performing visual recognition by mimicking two fundamental functions of the foveal vision. With 6 to 10 hr of explicit training, all eight subjects were able to form a PRL in the training location (a clear window). Once a PRL developed, subjects continued to use the trained retinal location for guiding eye movements even after the peripheral blur was removed from the background (Figures 4a-iii and 5a-iii), suggesting persistence of oculomotor learning. The development of a PRL also

paralleled with significant improvements in visual recognition and search performance ($\geq$ 19%). Furthermore, at the trained PRL location, considerable improvements in high-level visual function, such as letter recognition (in trigrams), RSVP reading, and spatial attention, were observed, suggesting transfer of the learning to some untrained tasks. However, no improvement was observed in low-level visual function, such as single letter acuity and contrast sensitivity. Our results demonstrated that our training paradigm (i.e., the OPT task equipped with the gaze-contingent display) could be used to induce a PRL at any intended retinal location within a relatively short time.

It is noteworthy to mention how the current training method is similar and dissimilar to the method used in Kwon et al.'s (2013) study that investigated the development of a subject's innate PRL (as opposed to a trained PRL in the current study) in response to a simulated central scotoma. The two methods share certain essential features. For example, both training methods promoted the use of peripheral vision using three task phases: target following, gaze centering, and visual search. They both employed naturalistic (cluttered) scene images for the visual search task, which is likely to resemble visual search in the real world.

But these two methods differ in many ways. Whereas the Kwon et al.'s (2013) method largely focused on oculomotor training, the current method combined oculomotor and perceptual learning paradigms. This was achieved by incorporating, into the target following phase, one of three explicit pattern recognition tasks (word, face, and object recognition) in a video-game-like interface. The combination of perceptual leaning and oculomotor training may mutually facilitate and reinforce the training effect of each other (Achtman, Green, & Bavelier, 2008; Ostry & Gribble, 2016). Besides we believed that this integrative learning approach (including engagement of attention, reinforcement, multiple stimulus dimensions, and multisensory inputs: continuous background music, auditory feedback using synthetic voices or pure tones, and auditory cue for a target item) helps promote generalizability to other tasks as demonstrated in previous perceptual learning studies (Deveau, Lovcik et al., 2014; Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014; Li, Polat, Makous, & Bavelier, 2009; Xiao et al., 2008; Zhang et al., 2010). This integrative approach also distinguishes our method from ones used in previous peripheral vision training studies (Chung et al., 2004; Frennesson et al., 1995; Lee et al., 2010; Nilsson et al., 2003; Seiple et al., 2005; Seiple et al., 2011; Tarita-Nistor et al., 2009; Yu, Legge, et al., 2010).

Another distinctive feature of the current method is blurring the entire peripheral visual field except a training window. Under this viewing condition, subjects would naturally use the clear spot to perform the demanding pattern recognition task because using other areas would penalize their recognition performance. A similar blurring paradigm was introduced by Lingnau et al. (2008). They showed that normally sighted subjects learn to use a clear spot in the periphery for reading when the rest of the visual field is severely blurred, demonstrating the efficacy of this blurring paradigm in promoting the use of a particular retinal location. On the other hand, Kwon et al. (2013) used a gaze marker (a white cross) at a subject's emerged PRL as a reference point. Although the training with the gaze marker might be effective for training oculomotor control (e.g., they found that after 15 to 20 hr of training, the precision of PRL was refined to the level that is comparable to the control group who used their fovea), having a notable marker at the center of gaze might not be natural for pattern vision.

We thus believe that our OPT method might be more natural and effective in training peripheral vision. Therefore, the method appears to hold promise as a model system to study the mechanisms that underlie the formation of a PRL and possible compensatory changes in oculomotor and perceptual systems.

Effect of high visibility on the selection of a PRL

AMD patients do not always choose an effective retinal location for their PRL (Cheung & Legge, 2005). For instance, it has been shown that the PRL occurs in the inferior or in the left part of the visual field in a large proportion of patients (Fletcher & Schuchard, 1997; Sunness, Applegate, Haselwood, & Rubin, 1996; Tarita-Nistor et al., 2008; Trauzettel-klosinski & Tornow, 1996; White & Bedell, 1990) but this location may not be optimal for visual tasks such as reading (Cheung & Legge, 2005; Lingnau et al., 2008). Considering that the location of a patient's PRL is often evaluated by a static fixation task (during microperimetry), it is still open to discussion whether this patient uses the same PRL for everyday reading or not. Nevertheless, studies involving training of eccentric viewing in patients with a central scotoma demonstrated that various aspects of visual function, including fixational stability and reading speed, were significantly improved once a new trained retinal locus was established in an optimal area for reading (Nilsson et al., 1998, 2003; Tarita-Nistor et al., 2009). Furthermore, the effective use of a PRL has been also shown to improve visual performance in normally sighted subjects with a simulated scotoma (Varsori et al., 2004; Walsh & Liu, 2014). Whereas evidence suggests a potential benefit of establishing an optimal PRL, the exact mechanism that underlies the selection of a PRL is still elusive. As proposed in previous literature (Cheung & Legge, 2005; Lingnau et al., 2008), the

selection of a PRL might be related to the inherent visual field asymmetry in retinal anatomy, attentional resolution, or functional relevance. It might also be due to some inherent advantage associated with oculomotor control. In the current study, we found that normally sighted individuals with a simulated scotoma spontaneously use the region with the highest visibility (i.e., the clear window) for guiding eye movements during the free exploration experiment, although they still exhibited foveating behavior. A similar finding was reported in Lingnau et al.'s study (2008). However, whereas in their study, subjects were explicitly instructed at the beginning to use the clear spot for the task, the subjects in the current study were not given information about the clear spot (e.g., where it is located in the periphery or how to use it) during the *free exploration*. Thus, our results suggest a possible role of perceptual visibility in selecting a PRL. Our finding is also consistent with the notion that the human visual system utilizes the information about the intrinsic difference in sensitivity across the visual field to optimize its eye movement for visual search (Michel & Geisler, 2009; Najemnik & Geisler, 2005, 2008).

We, however, acknowledge that more work is needed to fully understand the role of perceptual visibility in selecting a PRL, given obvious limitations in our study. First, it seems unlikely that the natural variation of perceptual visibility in the periphery of a MD patient is as big as the difference between the blurred and clear regions used in the current study. Second, we manipulated perceptual visibility comprehensively in a way that it affects many stimulus dimensions simultaneously such as luminance contrast, color contrast, spatial resolution, and the amount of crowding.

Rapid and persistent oculomotor adaptability for the trained eccentric location

Despite slow development of a PRL in patients (Crossland et al., 2005), recent studies using a simulated central scotoma showed that normally sighted subjects could spontaneously develop a PRL over a relatively short period of time (3–4 hr) and retain it over an extended period of time, suggesting rapid and persistent adaptability in human oculomotor control (Kwon et al., 2013; Walsh & Liu, 2014). It remained, however, unclear whether this remarkable oculomotor adaptability is only pertinent to a spontaneously emerging retinal location, an innate PRL as opposed to a trained or forced PRL (Lingnau et al., 2008; Nilsson et al., 1998), or whether the observed oculomotor adaptability reflects the intrinsically adaptable nature of oculomotor system, and is thereby generalizable to any eccentric retinal location with proper training. We tested this idea by randomly assigning the locations of

the clear window (i.e., training location) to each subject to see if they could establish their PRL near or at the training location, which may or may not be their innate PRL.

We found that with 6 to 10 hr of explicit training, all eight subjects were able to fully establish their PRL in the training location (within the clear window) for fixations and saccades. Once developed, subjects continued to use their trained location for guiding eye movements even after the blur in the peripheral visual field was removed (the *no blur* experiment), suggesting robustness and persistence of oculomotor learning. These findings are consistent with previous work (Kwon et al., 2013; Walsh & Liu, 2014) demonstrating rapid and persistent oculomotor adaptability in response to a simulated central scotoma for a subject's innate PRL. In contrast, our study showed similar oculomotor plasticity even at the trained retinal location.

Then, how long did the learning effect persist? Although we did not conduct a separate retention test in the current study, we can speculate that our training effect could persist at least for a week in the absence of training, consistent with Kwon et al.'s (2013) findings. This is because our "no blur" condition was performed about one week after the explicit training. In other words, in the current study, the "no blur" condition was used as a surrogate for a retention test.

On the other hand, compared to the variance of PRLs observed in Kwon et al. (2013), we observed much larger variance of PRLs. Several factors might have contributed to larger variance in PRLs in the current study compared to the Kwon et al. (2013) study. First of all, it is possible that a longer training duration (15–25 hr) together with a patient's naturally occurring PRL (as opposed to the forced or trained PRL) in the Kwon et al. (2013) study might have resulted in much smaller variance of the PRL. We, however, think that a major contributor to the difference in variance lies in the difference in the size of target and training region between the two studies. The size of the training region (clear window) used in the current study is considerably larger than that of the Kwon et al. (2013) study. In Kwon et al. (2013), subjects were trained to align a small cross (~0.7° in height) with the target object during the object following phase. On the other hand, the current study allowed subjects to use a much larger circular region (~5° in diameter) to identify the target item. In addition, the target size of the current study (1.6°–4.3°) was much larger than that of the Kwon et al. (2013) study (2°–2.7°).

Because both fixational PRLs and saccade landing site were defined as a gaze position with respect to the center of the target, using a larger target size and training region is likely to result in an overestimation of the variance of PRLs. Consider face recognition, for

example. Subjects do not need to align the center of the face image with the center of the clear window for recognition. They can recognize the target image from just looking at part of it, which may or may not be at the center of the target image. Therefore, we would expect the variance of a PRL to significantly decrease as we decrease the size of the target and the clear window. It is noteworthy that whereas the focus of the explicit training in the Kwon et al. (2013) study was to test oculomotor adaptability by explicitly asking subjects to align the target with the small gaze marker, the primary goal of the current training was to induce a pseudofovea by encouraging subjects to use the clear region for object recognition. We believe the training paradigm adopted in the current study resembles what AMD patients would experience with their PRL in real life. Our view is further supported by the fact that whereas the variance of PRLs increased after cue was removed in both studies, the amount of increase was much smaller in the current study (~92% in the current study vs. ~225% in the Kwon et al., 2013 study).

Our results are also aligned with earlier findings showing that a new retinal location can be trained for a reading task in either patients (Nilsson et al., 1998, 2003; Tarita-Nistor et al., 2009) or normally sighted subjects with a simulated scotoma (Lingnau et al., 2008). Previous studies have shown that fixational stability is positively correlated with reading speed (Amore et al., 2013; Amore et al., 2014; Crossland et al., 2004; Crossland, Dunbar, & Rubin, 2009), face perception (Seiple, Rosen, & Garcia, 2013), and visual search (Kwon et al., 2013; Walsh & Liu, 2014). Consistent with these findings, we found that the development of a PRL led to better performance in visual recognition (19% improvement) and search performance (22% improvement), confirming the key role of a stable PRL for pattern recognition in peripheral vision.

Perceptual changes at the PRL following the training

From both clinical and neuroscience perspectives, it is important to know whether perceptual or neural changes occur at the PRL site after extensive use of a previously underused retinal region. However, little is known about the adaptive changes at the PRL site. A recent study done by Chung (2013) reported that visual crowding, a major perceptual bottleneck in peripheral object recognition (Bouma, 1970; Levi, 2008; Pelli et al., 2007; Whitney & Levi, 2011), was noticeably reduced at PRL locations compared to nonPRL locations with equal eccentricity. This suggests possible perceptual changes at PRL sites.

However, it is also possible that the retinal region was chosen as a PRL because of the observed

perceptual advantage (i.e., less crowding). Since it is difficult to predict PRL location, conducting a before- and after-comparison study can be quite challenging. For this reason, we utilized our model system to examine the changes at the PRL site. In the current study, before and after the training, we assessed low- and high-level visual functions: visual acuity, contrast sensitivity, trigram letter recognition, RSVP reading speed, and spatial attention. The measurements were made at both the trained (the clear window) and untrained locations (on the opposite side with equal eccentricity). Changes between pre- and posttests were compared for each task. Whereas we did not observe any significant changes in low-level functions, such as acuity and contrast sensitivity, we found considerable improvement in high-level functions, such as trigram letter recognition (26%) and RSVP reading speed (18%), at the trained location. The lack of significant change at the untrained location showed that the improvements in letter recognition and RSVP reading speed were unlikely to be due to familiarity with the task procedure.

Our pre- and posttests were conducted under eccentric viewing. Subjects fixated on a central cross while the test stimuli were presented at the intended retinal location using a gaze-contingent display. This was done to assess pure perceptual changes at the trained location, excluding oculomotor influence. (For this very reason, we also used RSVP reading, not ordinary eye-mediated reading.) Then, what could account for this improvement in letter recognition and RSVP reading performance?

It has been proposed that letter recognition measured by trigrams, i.e., the visual span, the number of letters that can be recognized at a glance (Legge, Ahn, Klitz, & Luebker, 1997), can be decomposed into three elements: letter acuity, mislocation (i.e., errors in the sequence of letters), and crowding (Y. He, Legge, & Yu, 2013; Legge, 2007). The visual span is known to correlate with RSVP reading speed (Chung et al., 2004; Kwon, Legge, & Dubbels, 2007; Legge et al., 2007); the smaller the visual span, the slower RSVP reading speed. It has been shown that the improvements in the visual span and RSVP reading speed from peripheral vision training were largely accounted for by a reduction in crowding (Y. He et al., 2013). To see if crowding played a significant role in the observed improvement in trigram letter recognition and RSVP reading speed, we analyzed our letter recognition data using the method adopted by Y. He et al. (2013). We found that a reduction in mislocation error accounted for only 6% of the improvement in letter recognition, whereas no change was observed in visual acuity after the training. These results suggest that the observed improvement in letter recognition and RSVP reading speed in the current study might be related to a considerable

reduction in crowding. Taken together, although speculative, our OPT training might have reduced crowding at the trained eccentric retinal region, consistent with Chung's (2013) empirical finding in AMD patients and Nandy and Tjan's (2012) crowding model which predicts a shrinkage of crowding in a PRL compared to nonPRL locations with equal eccentricity.

Whereas our training was shown to improve RSVP reading, in which oculomotor influence was considerably minimized (again this was done to assess perceptual changes at the trained location following the training), it is still important to know whether our OPT training would benefit patients' ordinary text reading (eye-mediated reading). As briefly mentioned in the Introduction, plenty of evidence shows that fixational stability plays a critical role in eye-mediated reading (Amore et al., 2013; Amore et al., 2014; Crossland et al., 2004; Crossland et al., 2009; Tarita-Nistor et al., 2009). Training oculomotor control in AMD patients improves eye-mediated reading (Nguyen et al., 2011; Seiple et al., 2011; Seiple et al., 2005; Tarita-Nistor et al., 2009; Vingolo et al., 2007; also see a review by Pijnacker et al., 2011). Given that the fact that our training significantly improved oculomotor control (Figures 4 and 5), we speculate that eye-mediated reading performance is likely to benefit from our OPT training.

On the other hand, unlike RSVP reading, the role of visual crowding in ordinary text reading (eye-mediated reading) is still unclear, as studies have reported little effect of reduced crowding on ordinary reading speed (Bernard et al., 2007; Calabrese et al., 2010; Chung, Jarvis, Woo, Hanson, & Jose, 2008). As reading is a complex cognitive process involving various perceptual and cognitive components (e.g., sensory and perceptual encoding of text, oculomotor control, and linguistic influences), the outcome is likely to be changed depending on its interaction with other components. Thus, the question of whether reduced crowding and improved oculomotor control observed in the current study is readily generalizable to ordinary eye-mediated reading remains to be addressed in a future study.

Thus, our results the pre- and posttests may highlight a few important points. There was a significant improvement in letter recognition measured with trigrams (crowded target recognition) and RSVP reading, but none for single letters. These improvements in trigram letter recognition and RSVP reading were observed in the trained location, but not in the untrained location. This pattern suggests several points. First, through our OPT, subjects learned to recognize objects in clutter. The training effect of crowded-letter recognition cannot simply be explained by extensive use of a particular peripheral region. Second, whatever was learned in our OPT training appears to transfer to some of untrained tasks and stimuli. Finally, whereas

learning transfers across tasks and stimuli, it does not appear to transfer across different retinal locations.

However, we recognize that it remains unclear whether the training of face and object recognition played any critical role in improving trigram letter recognition and RSVP reading. It is possible that transfer of learning might have occurred only in letter-like stimuli and tasks, such as trigram letter recognition and RSVP reading as our subjects were trained with word/nonword discrimination during the OPT. Whereas a detailed characterization of the transfer effect can be addressed in a future study, the observed differential effects of the training on various aspects of visual function provides helpful insights in our understanding of PRL formation and maintenance.

Given the perceptual and oculomotor benefits provided by the OPT, we believe that our training might be a useful rehabilitative tool to facilitate the establishment of a reliable PRL in AMD patients when their naturally emerging PRLs are detected.

In conclusion, a pseudofovea can be developed at the trained retinal location with a few hours of the oculomotor and perceptual training (OPT) and persists even without any training cue. The prolonged use of an eccentric retinal location appears to bring about adaptive changes in the corresponding retinal location, so that it becomes favorable for carrying out high-level visual functions, such as RSVP reading. Our results support the idea that the human oculomotor system is remarkably adaptable in response to nonfunctioning central vision. Our findings further suggest that the paradigm of integrating oculomotor and perceptual training might serve as an effective model system to induce a pseudofovea and can also be used for training peripheral vision for individuals with central vision loss.

Keywords: preferred retina locus, peripheral vision, central vision loss, oculomotor control

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