Novel strategies to enhance the visual performance of the visually impaired

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1. INTRODUCTION

1.1. MOTIVATION

Visual impairments affected almost two hundred million people by the year 2010 (Murray, et al., 2012; Stevens, et al., 2013). Age related macular degeneration (AMD), which often leads to central vision loss, is responsible for 8.7% of the visual impairments that lead to blindness worldwide. The countries that are mainly affected by AMD are countries of Asia Pacific, Western Europe, North America and Australia (Bourne et al., 2014). Furthermore, a series of population based studies published before the year 2013 determined the prevalence of any age-related macular degeneration to be 8.01% and predicted that 288 million people will suffer from AMD by the year 2040 (Wong et al., 2014).

Clinicians and the relatives of patients with AMD are not well aware of the impact that the disease has on the quality of life of patients (Stein et al., 2003). Studies showed how visual impairments limit social interactions and the independence of patients (Ivers et al., 1998; Klein et al., 1998). Impairments related to AMD are often accompanied by depression, and the psychological distress showed by the patients is comparable to that of individuals with other kind of serious chronic diseases (Rovner et al., 2002; Williams et al., 1998). The more severe the loss of vision is, the higher is the impact of the disease on all areas of daily life, which indicates a lack of adaptation to the disease (Hassell et al., 2006). Besides this lack of adaptation, service for low vision rehabilitation have been found to be delayed after vision loss occurs (Hassell et al., 2006). The combination of lack of adaptation and a delayed service of rehabilitation can aggravate the consequences on patient's life quality. Thus, rehabilitation of vision and implementation of visual aids must be applied as early as possible and should be tailored to the needs of the patient (Slakter & Stur, 2005).

Given the large and increasing prevalence of AMD and the high impact of the disease on the life quality of patients, treatments that help to enhance the visual performance should be applied. The research presented in this work is inspired on finding effective and accessible training strategies that can afterwards be applied for an enhancement of the visual performance and as a consequence, the quality of life of the visually impaired.

1.2. THE VISUAL SYSTEM IN THE PRESENCE OF FIELD LOSS

Individuals with a healthy visual system use a combination of saccadic and fixational eye movements to carry out daily visual tasks. The role of these eye movements is to direct and keep the fovea onto the region of interest. Saccadic eye movements are fast and ballistic movements which generally show a similar pattern and might reach speeds of 900 °/s (Fuchs, 1967). Fixations occur between saccadic eye movements and are events in which the eyes are partially stationary and the visual system acquires the visual input. Fig **1** shows an example of such eye movements. The blue line corresponds to a saccadic eye movement that occurred between two fixations A and B. The gray ovals encompassed the fixations and the respective fixational eye movements.

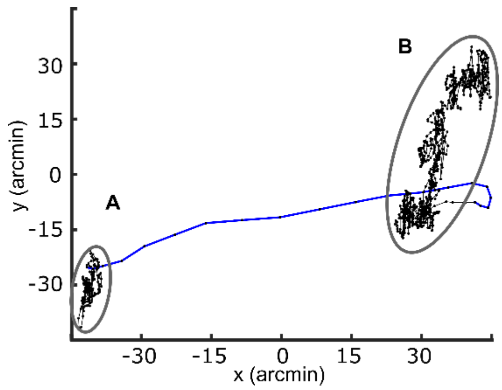

Fig 1: Eye traces during fixational (A, B) and saccadic (blue) eye movements.

The interaction between saccades and fixation is a strong evidence of sensory-motor coupling (Kowler, 2011; Krauzlis, 2017). Hence, when the sensory system suffers from impairments, this interactions may change. An example that may lead to this changes is when the retina is damaged. This kind of damage may lead to vision loss, and as a consequence, alternative strategies must be developed for the fulfillment of the daily visual tasks.

The retina is the light-sensitive layer of the eye that initiates cascade-like events that send transduced light signals to the brain (Tomita, 1970; Hubbell & Bownds, 1979). It consist of a number of cellular layers that fulfill different tasks. The three main layers are the ganglion cells layer, the bipolar cells layer and the photoreceptors layer (Hasland, 2012). The photoreceptor layer consist mainly of two kind of cells, the cones and rods (Schultze, 1866; Weale, 1961). These cells differ in function, size, geometric and topographic distribution (Osterberg, 1935). Given the differences found in the photoreceptors cells across the retina, the visual acuity, contrast sensitivity and color vision may vary at different retinal loci. The most common example on variations found across the retina, are the variations between the fovea and the peripheral retina. It is known that the visual acuity and contrast sensitivity decrease as a function of eccentricity to the fovea (Anderson et al., 1990; Virsu & Rovamo 1979). Moreover, in terms of color vision, the distribution of L, M and S cells are not equal across the retina (Wooten, & Wald, 1973). Nonetheless, the combination of foveal and peripheral vision mediated by eye movements plays an important role on the performance of visual tasks and everyday life interactions. For instance while navigating, the eyes are directed to the object of interest by means of a saccadic eye movement, in such a way that the object is imaged at the fovea. However, for a successful navigation, it is also important that the eyes can receive cues from peripheral locations of the visual field. These cues allow the visual system to anticipate upcoming objects and to redirect the fovea to the new object of interest. Thus, when peripheral or central vision is impaired, daily activities like navigation can also be impaired and social interactions can be affected (Decarlo et al., 2003; Brown et al., 2002; Rovner & Casten, 2002).

In the case of central vision loss, the visual information and the performance of the visual task will depend on peripheral vision. This is referred to as eccentric vision. Typically, patients with central vision loss use the remaining eccentric vision together with visual aids to compensate the lack of vision.

1.3. AIDS FOR CENTRAL VISION LOSS

The aim of the visual aids provided to central vision loss patients, is to help them to use the remaining vision in the most efficient way possible. Normally, the treatments offered are field enhancement devices which are adjusted to the visual distance of the tasks that the patient needs to fulfill. For example, for near vision, magnifiers are used as aids, whereas for far vision, spectacle mounted telescopes, hand monoculars and binoculars can be prescribed (Benjamin, 2006). In addition, when large magnifications are necessary and as a consequence the field of view is restricted, video-magnifiers are also recommended (Benjamin, 2006). However, due to the individual differences, the effectiveness and impact in life quality of such treatments are hard to quantify and the properties of vision loss are hard to assess. Alternative techniques that can help on such assessment were developed. An example is the use of eye tracking and the gaze-contingency paradigm.

1.4. EYE TRACKING AND THE GAZE-CONTINGENCY PARADIGM

Eye tracking is a technique used in the study of eye movements. The development of eye tracking techniques allowed important progress in the fields of vision science, psychology, marketing and others. One example of an eye tracking technique is the gaze-contingency paradigm. This paradigm corresponds to a dynamic presentation of stimuli whose appearance is in a closed loop with the subject's gaze position. Different types of gaze-contingency techniques can be found. The main difference among the techniques is determined by the application. An example of a gaze-contingency technique is the moving window paradigm, which was widely used to study the perceptual span in reading (McConkie, G.W., & Rayner, K., 1975, 1976; Rayner K., & Bertera J.H., 1979; Häikiö et al., 2009). In this particular paradigm, a small portion of the displayed stimulus is clear and the remaining portion is either blanked, blurred, changed or distorted. As a consequence, only the region of interest is perceived by the participant and the other regions are suppressed. In general, this paradigm is used to block peripheral information and as a consequence, investigate the mechanisms of central vision. Another example of gaze-contingent paradigm relies on the presentation of peripheral cues and the suppression of central vision. (Rayner K., & Bertera J.H., 1979). This paradigm allows the study of peripheral vision and the general changes in vision when the system is confronted with this kind of suppression. The paradigm was also widely used to simulate central suppressive scotomas and to study some of the basic mechanisms playing an important role in peripheral vision. The advantage of this method is that the technology used allows the presentation of scotomas with low spatial and temporal delays. Furthermore, in contrast to studies with patients, this method provides complete control on variables like the shape and the size of the scotoma. Hence, eccentric vision can be addressed in a reliable and controlled fashion.

The combination of eye tracking technology and gaze-contingency methods opened the possibility to simulate a central scotoma in rapid and accurate ways. As a consequence, researchers were able to study the nature of eccentric vision. For instance, studies showed that simulations of low vision decreased the search time and increased the fixation time of a target, and suggested that the central scotoma paradigm may be useful to study adaptation to visual field loss (Bertera, 1988). Other studies used the paradigm to investigate the identification accuracy of targets and showed that, although the identification was good, the eye movement behavior can be disrupted (Henderson, et al., 1997). The paradigm was also used to address reading behavior. Some authors showed that the reading performance was slower when the letters or words were presented in the left visual filed of the scotoma (Fine & Rubin, 1999). Furthermore, the simulations were also used to address the minimum requirements for useful peripheral reading. The results showed that when the stimulus was presented at eccentricities beyond 10° of visual angle or when the number of pixels of the stimulus was below a certain threshold, the reading performance dropped abruptly (Sommerhalder et al., 2003). Moreover, the effect of magnification and contrast on reading performance in different types of simulated scotoma were addressed. The results showed that in all different types of scotoma, the reading speed improved when magnification and contrast were increased (Christen, 2017). Besides, oculomotor adaptations during visual search were also investigated using the central scotoma paradigm. Whereas some authors found adaptation of fixation duration to task difficulty (Cornelissen et al., 2005; Walsh & Liu, 2014), others found impairments in visual search of natural scenes in the presence of central scotomas (McIlreavy et al., 2012). More recent work also used the paradigm to investigate oculomotor adaptations during eccentric view and found that accuracy and stability increased with training (Rose & Bex, 2017). Moreover, the paradigm was also used to investigate the effects of central vision loss on the performance of optimal saccades that maximize the acquisition of information. Subjects had to perform a face identification task under central scotoma simulation. The results showed that adaptations on the eye movements for simpler tasks such as object following and search tasks do not generalize to make complex tasks such a face identification (Tsank et al., 2017). Besides visual behavior, the paradigm was also used to assess the effectiveness of methods to measure scotoma sizes. For example, central scotomas were simulated to investigate whether population receptive field mapping enables size estimation of the visual scotomas. The results showed that estimations can be reliably done for small scotomas (4.7° diameter) in single subjects (Hummer, 2017).

The examples pointed out above, correspond only to a small part of the research performed using gaze-contingency methods. Another important applications of this method remains to be the study of the preferred retinal locus of fixation (PRL).

1.5. THE PREFERRED RETINAL LOCUS OF FIXATION

At the absence of central vision, the visual system compensates the lack of central information with the help of peripheral information. The system reorganizes the normal foveating mechanisms to accomplish daily visual tasks like navigation, reading or face recognition. Commonly, the system uses peripheral and healthy retinal locations for the performance of the visual tasks. These retinal locations are referred to as preferred retinal locus of fixation and were defined to be “one or more circumscribed regions of functioning retina, repeatedly aligned with a visual target for a specified task that may also be used for attentional deployment and as the oculomotor reference” (Crossland, et al., 2011). The PRL was studied in terms of fixation stability, location, and plasticity of fixation. Fixation stability has been shown to increase when the scotoma size decreases (Whittaker et al., 1988). Cheung (2005) compared the fixation stability obtained in studies with normally sighted subjects (Crossland & Rubin, 2002) and with patients that suffered from different forms of low vision (Fletcher & Schuchard, 1997) and found that the fixation stability of patients with central scotoma was substantially less than normally sighted subjects. Furthermore, the PRL location was shown to be determined by the visual task, the type of macular disease and even by the luminance level (Sunness et al., 1996; Lei & Schuchard, 1997). Also, in cases of long lasting disease, more than one PRL can be formed (Lei & Schuchard, 1997; Deruaz et al., 2002; Crossland et al., 2004). Moreover, patients with age-related macular degeneration showed a plasticity to develop PRLs at new locations and in addition, patients used the new PRL consistently while different targets were presented (Tarita-Nistor et al., 2009).

Although PRLs were studied in different terms, the mechanisms underlying their selection are not fully understood.

1.6. Neural and functional mechanism underlying the selection of the preferred retinal locus of fixation

A neural mechanism and two functional mechanisms were hypothesized for the development of the preferred retinal locus of fixation (Cheung & Legge, 2005).

The neural mechanism corresponds to a retinotopic driven explanation of the PRL. In the scheme of the visual pathways shown on the left side of Fig **2**, the axons from the retinal ganglion cells that come from the temporal and nasal part of the retina, form the optic nerve that hemidecussates at the optic chiasm and converge in the lateral geniculate nucleus (LGN). Visual signals are afterwards relayed to the primary visual cortex (V1). The right side of Fig **2** shows the representation of the area V1 on the visual cortex of the occipital lobe.

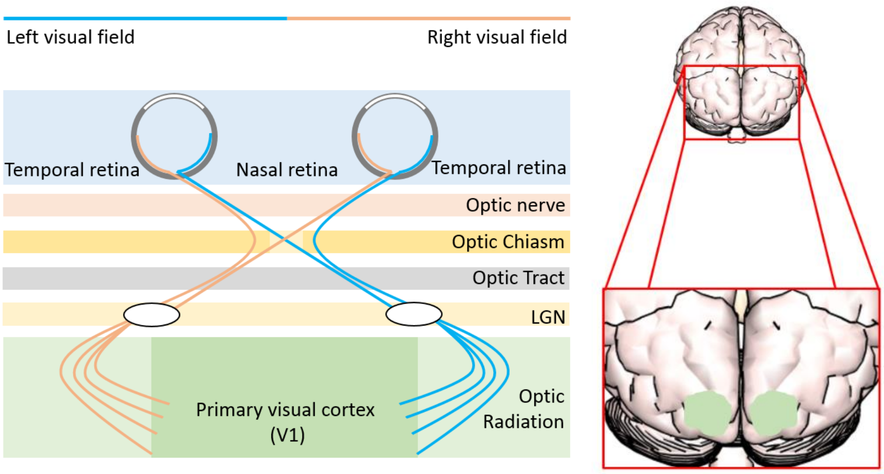

Fig 2: the figure on the left shows the scheme of the visual pathway from the visual field to the primary visual cortex (V1). The figure on the right shows a representation of the primary visual area V1 in the visual cortex.

The retinotopic driven explanation for the development of the PRL postulates that the selection might be a result of reorganizations from neurons of the primary visual cortex (V1) that would remap to the inputs from the healthy retinal cells located at the edge of the scotoma. The first attempts to address whether such reorganizations occur were performed in cats and monkeys. The studies showed that when lesions were induced on the retinal region responsible for central vision in cats or on the parafoveal regions of cats and monkeys, deafferented neurons became responsive to the retinal areas next to the lesions (Gilbert & Wiesel, 1992; Kaas et al., 1990). Other studies in patients with macular degeneration showed that they elicited responses on the parts of the visual cortex that would normally be excited by stimuli presented foveally (Baker et al., 2005, 2008; Masuda et al., 2008). In these studies, the excitations were performed at the current PRL of the patients. However, later studies addressed whether these kind of activations also occurred when the excitation was performed at other retinal locations of similar eccentricities. The results showed activations of formerly foveal cortex to stimuli presented at the PRL and at isoeccentric non-PRL locations (Dilks et al., 2009). This finding supported reorganizations that are driven by a passive and not use-dependent mechanism. Furthermore, plasticity in the human extrastriate cortex was observed on subjects that underwent a simulation of artificial scotoma (Gannon, 2017). All previously mentioned studies with humans used functional magnetic resonance imaging (fMRI) or electroencephalograms (EEG) to collect the responses. On the other hand, psychophysical methods were used on patients with macular lesions to address whether the properties of visual crowding were also reflected on their PRL. Results showed that at their PRLs, patients exhibit a loss of radial-tangential anisotropy (Chung, 2013). This anisotropy is typical for normal peripheral vision and refers to the difference on the distinguished critical spacing of stimuli, between the radial and the tangential direction toward the fovea (Bouma, 1970). These results were discussed as a distinct kind of cortical reorganization that modifies the representation of visual information in early sensory areas of the brain (Chung, 2013).

Alternatively, another hypothesis postulated that the neural mechanism underlying the PRL selection may be found in other brain areas related to the control of eye movements. Although different brain areas were linked to the control of eye movements, the superior colliculus was shown to be responsible for the computation of distance between gaze position and saccade landing position (Bergeron et al., 2003). Furthermore, studies in monkeys also showed retinotopic organization in the superior colliculus (Goldberg & Wurtz, 1972, a,b; Wurtz & Goldberg, 1972, a,b) and evidence for retinotopy in the human superior colliculus (Schneider et al., 2004). However, whether the superior colliculus shows reorganizations when central scotomas are present is still unknown.

The following two hypotheses for the selection of the PRL are function based and they may not exclude each other, thus, either one or both may play a role on the selection of the PRL (Cheung & Legge, 2005). The first corresponds to the function driven explanation of the PRL. This explanation attributes the PRL selection to the efficiency of the retinal location relative to the visual tasks that needs to be performed. For instance, it was shown that PRLs in the lower visual field are suitable in a range of important everyday tasks. For example, for left-to-right reading, the PRL is preferred to be above or below the central scotoma, given that the reader can better estimate the amplitude of the eye movement towards the next word or towards the next line. Also, during the performance of a locomotion task, most of the visual cues that allow an effective displacement are located in the lower part of the visual field. Thus, PRLs located at the lower visual field may be more beneficial (Turano et al., 2004). Although it is intuitive to think that PRLs may be developed at retinal locations beneficial for the visual task, several studies have shown some discrepancies to this hypothesis. Following the example of reading and locomotion, one could assume that patients may show a large incidence of PRLs developed on the lower part of the scotoma in the visual field. However, studies showed that there is a large prevalence on patients to locate their PRL on the left side of the visual field (Cummings & Rubin, 1992; Fletcher et.al., 1994; Sunness et al., 1996; Fletcher & Schuchard, 1997).

The second functional hypothesis corresponds to the performance driven explanation, which suggests that the PRL will be developed according to the optimum visual performance achievable at a determined retinal location. Thus, regions of good visual acuity or alternatively, with good visual attention may be the best candidates for the selection of PRL location. In terms of visual acuity, previous studies demonstrated the differences of visual acuity over different meridians and eccentricities of the retina (Wertheim, 1980; Carrasco et al., 2001). From these findings one can postulate that the PRLs may be located at the retinal region with the highest visual acuity. Nonetheless, as previously mentioned, the large prevalence to locate the PRL on the left side of the scotoma in the visual field does not agree with this hypothesis. In terms of visual attention, studies showed that the sustained component of visual attention enhances the visual performance and established a link between the attentional mechanism and the development of the PRL (MacKeben, 1999, Altpeter et al., 2000), however, the study compared the attentional performance of a centrally fixating eye with an eccentrically fixating fellow eye. Hence, it remains unclear whether the effect can be found on the same eye.

The contribution of each mechanism on the determination of the PRL is not known, but perhaps, each contribution plays a different role. The impact that this information may have on the visual rehabilitation field may be significant. Ideally, future training techniques should be tailored according to the contributions of each mechanism.

2. OBJECTIVES

The main objective of this work was to investigate the basic mechanisms underlying the development and selection of the preferred retinal locus of fixation.

The first study was conducted to address questions on the potential influences that can be applied on the development of the PRL. A gaze-contingency paradigm was used to target whether systematic stimulus relocations can influence the location of the PRL when a central scotoma is simulated. The PRLs were induced on the left and right hemifield in separate groups of five subjects. The relocations of the stimulus were applied every time that an eye movement located the stimulus on the hemifield opposite to the induced hemifield. Thus, a potential PRL development on the induced hemifield was expected.

In the second study, the transfer of the previously induced PRL to alternative visual tasks was investigated. The alternative visual tasks were selected to mimic everyday visual tasks that may challenge patients with central vision loss. The first visual task was a pursuit task which simulated an object following task. The second visual task was a reading task which simulated the reading of signage. Finally, the third visual task was a text reading task which simulated the reading of newspapers or magazines.

The third study was conducted to address question on the mechanisms underlying the selection of the preferred retinal locus of fixation. In this third study, one of the hypotheses that explains the selection of the PRL on the basis of visual attention was investigated. The sustained visual attention was measured in a new cohort of subjects and a simulation of central scotoma was performed until subjects developed a PRL. Afterwards, the location of the developed PRL was compared with the subject's individual attentional performance.

3. A PREFERRED RETINAL LOCATION OF FIXATION CAN BE INDUCED WHEN SYSTEMATIC STIMULUS RELOCATIONS ARE APPLIED

Barraza-Bernal M.J., Rifai K., & Wahl S., (2017). Journal of vision, 17(2):11, 1-13.

3.1. ABSTRACT

Patients with central vision loss obtain visual information by fixating on an object eccentrically with a preferred retinal locus of fixation (PRL). Patients do not always choose the most efficient PRL position and as a consequence, visual performance is not always fully exploited.

This study investigates whether PRLs can be induced by applying systematic stimulus relocations.

The PRL was trained using a central scotoma simulation in fifteen healthy subjects. They performed different visual tasks during four sessions, after which their reading performance was evaluated.

In five subjects the stimulus was relocated to the left hemifield whenever a saccade would place the stimulus on the opposite hemifield. In five different subjects the relocation was inversed, the stimulus was located in the right hemifield. The relocation was 7.5 degrees of visual angle and it was applied horizontally. Five additional subjects naturally chose the PRL location. They were used as the control group to evaluate the development of a PRL. After training, subjects performed visual search tasks on static stimuli.

Evaluation after training showed that systematic stimulus relocations can be used to influence the development of the PRL. These results might be significant for the development of training strategies for the visually impaired.

Key words: preferred retinal locus; central vision loss; oculomotor learning

3.2. INTRODUCTION

When performing daily tasks like reading, walking, or face recognition, healthy humans bring a target of interest onto the fovea with a saccade. Patients with central field loss have to develop strategies to compensate for the lack of foveal input. Since the field of view is restricted to non-foveal vision, they use a non-foveal retinal location to refer their saccades and fixations to. This non-foveal location acts as a pseudo-fovea and allows patients to acquire the relevant visual information (Nagel, 1911; Fuchs, 1922; Von Noorden, & Mackensen, 1962; Mainster, Timberlake, Webb, & Hughes, 1982; White, & Bedell, 1990; Guez, Le Gargasson, Rigaudiere, & O'Regan, 1993; Fletcher, & Schuchard, 1997; Schuchard, 2005; Cummings, Whittaker, Watson, & Budd, 1985). The location is referred to as preferred retinal locus (PRL) and defined to be "one or more circumscribed regions of functioning retina, repeatedly aligned with a visual target for a specified task that may also be used for attentional deployment and as the oculomotor reference" (Crossland, Engel, & Legge, 2011).

The mechanism underlying the selection of the PRL location is not fully understood. Cheung and Legge (2005) hypothesized three selection categories; function driven selection, performance driven selection and retinotopy driven selection. The function driven selection suggests that PRL locations may be determined by the nature of the visual task, for example, a PRL located on the lower visual field is preferable for English reading. On the other hand, the performance driven selection suggests that the PRL will be either located at the undamaged retinal location with the highest visual acuity or, on the basis of visual attention, the selection will be made in regions with high attentional performance due to the enhancement of visual performance in those regions. Finally, the retinotopy driven selection suggests that PRL selection might be a consequence of retinotopic reorganizations, where deafferented V1 neurons spontaneously remap to the inputs from retinal locations near the scotoma. Independently of the governing mechanism, the location in which the PRL develops may not always be the most efficient one. In a reading task, studies have demonstrated theoretical and experimental advantages of locating the PRL at the lower region of the visual field among other areas (Whittaker & Lovie-Kitchin, 1993; Guez, Le Gargasson, Rigaudiere, & O'Regan, 1993; Petre, Hazel, Fine, & Rubin, 2000; Deruaz, Whatham, Mermoud, & Safran, 2002; Chung, Legge, & Cheung, 2004; Frennesson & Nilsson, 2007). However, there is a comparable or higher prevalence to locate the PRL on the left field rather than on the lower field in patients with central scotoma (Fletcher, Schuchard, Livingstone, Crane, & Hu, 1994; Fletcher & Schuchard, 1997; Sunness, Applegate, Haselwood, & Rubin, 1996; Cummings & Rubin, 1992). As a consequence, the visual performance can be affected.

A central vision loss can be simulated in healthy subjects, and the nature of eccentric viewing can be studied (Bertera, 1988; Henderson, McClure, Pierce, & Schrock, 1997; Fine & Rubin 1999; Sommerhalder, Oueghlani, Bagnoud, Leonards, Safran, & Pelizzone, 2003; Cornelissen, Bruin, & Kooijman, 2005; Scherlen, Bernard, Calabrese, & Castet, 2008; Aguilar & Castet 2011; McIlreavy, Fiser, & Bex, 2012; Kwon, Nandy, & Tjan, 2013; Walsh & Liu, 2014). Healthy subjects under central vision loss simulation develop a PRL and suppress normal refoveating saccadic behavior in favor of this location. Furthermore, the development of a PRL is spontaneous and rapid (Pidcoe & Wetzel, 2006; Kwon, Nandy, & Tjan, 2013). Previous studies have also demonstrated that with different training procedures, a new or more favorable PRL can be used by patients with central vision loss (Nilsson, Frennesson, & Nilsson, 2003) or by normally sighted subjects (Lingnau, Schwarzbach & Vorberg 2008). The present study differs from these studies due to the fact that the inducement is neither confined to a narrow retinal area nor to a single visual task (reading task). In addition, the induced PRL is guided since the early stages of its development and is based on systematic stimulus relocations.

3.3. METHODS

3.3.1. Apparatus

Data acquisition was carried out using a gaze contingent setup based on MATLAB, the Psychtoolbox (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007), the Eyelink toolbox (Cornelissen, Peters, & Palmer, 2002), the Eyelink 1000 Plus eye tracker (SR Research, Ltd., Ontario, Canada) and a ViewPixx/3D display with a vertical refresh rate of 100 Hz and a spatial resolution of 1920 x 1080 pixels.

Vertical and horizontal positions of the right eye were recorded at 1 kHz while the left eye was patched. To simulate the central scotoma, a gaze contingent mask was presented at the momentary eye position. The mask was round, with a radius of 3 degrees of visual angle. It was presented in front of a light gray background. The presentation of the scotoma at the momentary eye position was temporally delayed by less than 20 ms after the detection of the eye's position.

A chin rest was used to prevent head movements and to locate the eyes at a fixed position 62 cm from the display.

3.3.2. Participants

The study was performed in accordance with the declaration of Helsinki. Fifteen participants took part in the study, five males and ten females aged between 24 and 33 years (mean 26.6 years). Thirteen subjects were naïve to the purpose of the study and the other two were authors who participated in the control group.

Subjects were eye-healthy and had normal or corrected to normal visual acuity.

3.3.3. Study design

The experiment consisted of four training sessions in which subjects had to solve a visual task and subsequently perform a reading task. The main task during the training procedure was to discriminate compound stimuli presented at varying positions on the screen.

Each subject was randomly assigned to either the left induced PRL or right induced PRL or control group. In the induced groups, the training was performed under central vision loss simulation. In addition, a stimulus relocation function was applied to discourage one of the two hemifields. The relocation depended on the momentary gaze and stimulus position. If a saccade located the center of mass of the stimulus on the opposite side of the inducement (between the edge of the scotoma and a distance of 2.5 degrees of visual angle from the edge of the scotoma), the stimulus was relocated on the intended induced hemifield. Consequently, the stimulus was drawn in its new position in the next frame. Fig **3** A describes the inducing mechanism for the subjects from the left induced group. If the subjects intended to locate the stimulus on the right hemifield, the relocation function shifted it to the left hemifield. On the contrary, Fig **3** B shows the same procedure for subjects from the right induced group. The relocation was always applied horizontally into the opposite hemifield and had a constant displacement value of 7.5 degrees of visual angle relative to the stimulus's center of mass. Using this procedure most relocations would let the stimulus reappear in the opposite hemifield, but in some situations the stimulus would actually disappear because it would be shifted to a location within the scotoma. Both situations prevent the usage of the discouraged hemifield. In the control group shown in Fig **3** C, the training was performed under central vision loss simulation and no changes were applied to the stimulus position. Thus while performing the task, control subjects were able to locate the stimulus at any desired position outside the scotoma for eccentric fixation. This group was used as a reference to compare the development of new oculomotor strategies to the induced groups and analyze potential effects of the inducing procedure on the development of the PRL.

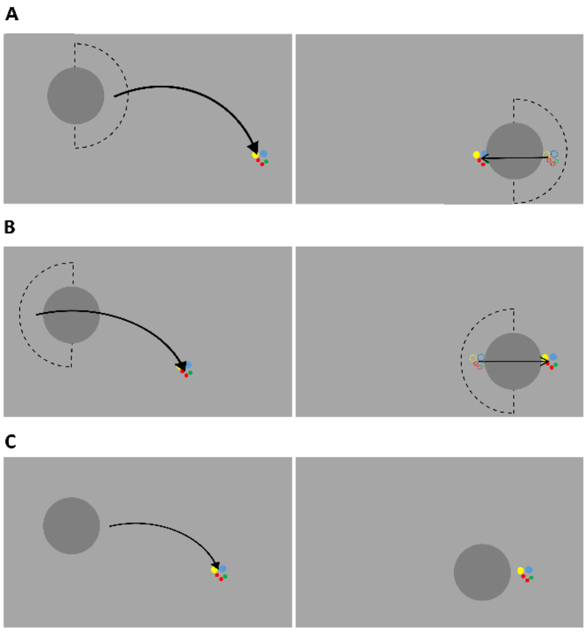

Fig 3: (A) The left induced group. Subjects performing a saccade might locate the target in the discouraged semi-circular area circumscribed by the dotted line (dotted only for demonstration). In this situation, the stimulus is shifted to the left half of the visual field. Within all other regions, subjects can freely locate the stimulus in the left half of the visual field. (B) The right induced group. In this situation, the stimulus is shifted to the right half of the visual field when a saccade locates the stimulus in the discouraged semi-circular area circumscribed by the dotted line. (C) In the control group, subjects perform a saccade to choose the location in which the stimulus is located.

3.3.4. Stimuli

Every phase of the experiment was conducted in complete darkness. The stimulus consisted of a foveally presented scotoma and a static discrimination target. The simulated scotoma was in a circular shape with ± 3 degrees of visual angle and was colored in dark grey. The discrimination targets were designed to cause a long fixation time, thus increasing the oculomotor learning.

The background of the screen was light gray in color with a luminance of 64 cd/m^2. To avoid fixations outside the screen, the location of the stimulus changed randomly within a window of 42 x 21 degrees of visual angle centered on the screen (the screen size being 48 x 27 degrees of visual angle). The overall size of the composed stimulus was 1.7 x 1.7 degrees of visual angle.

Given that the discrimination targets were big enough to be identified at distances of three degrees of visual angle relative to the fovea, the procedure might have become monotonous and unchallenging after two long sub-sessions. Therefore, and since crowding decreases the performance during eccentric viewing of a stimulus (Wallace, Chiu, Nandy & Tjan, 2013), the complexity of the task was increased by adding more components to the composed stimulus, which kept the subjects alert and challenged.

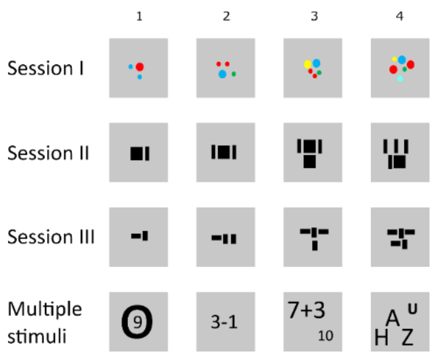

Fig 4: Examples of stimuli presented in each sub session. In Session I colored dots were presented in a random spatial arrangement and subjects had to judge whether there were more red than blue dots. In Session II, a set of vertical lines and squares were presented and subjects had to distinguish between the different shapes. In Session III, horizontal and vertical lines are presented and subjects had to distinguish between the different orientations. In the multiple stimuli session, numbers and letters were presented. For simplification, only one example of each stimulus is presented, however, an example of the complete screen can be found in Fig 9.

Fig **4** shows an example of the composed stimuli presented in each session and sub session during the performance of the visual task. In sessions I, II, and III, the position of the stimulus changed at every trial.

In session I, colored dots were randomly distributed around a pre-determined center of mass. In each sub session a new dot and color were added. Subjects had to differentiate between red and blue dots by reporting whether there were more red or blue dots using the up and down arrow keys accordingly.

In session II, a stimulus composed of squares and lines was presented. In every sub session, a new component was added. The components were randomly assigned to be either squares or lines. The task was different in every sub session. For example, in sub session 1, subjects had to report whether the components of the stimulus were the same or different and in sub session 4, subjects had to report whether there were more or fewer squares than lines. In addition, during session II and subsequent sessions, subjects had to press the space key causing an internal function to randomly select one or more components of the stimulus and mark this selection red (this action is repeated until required component/s were marked red). For example, in sub session 1, if the components of the stimulus were identical, then subjects had to mark both components red and if not, subjects had to mark only the square red. From sub session 2 to 4, subjects had to mark all squares red.

In session III, vertical lines were presented instead of squares and the task was the same as in session II.

In the multiple stimuli training, a set of targets were presented simultaneously (numbers or letters). In sub session 1, two random digits (from 1 to 9) were presented inside a ring. For simplification, only one stimulus is shown in Fig **4**. The horizontal positions of the stimuli were -12 and +12 degrees of visual angle relative to the center of the screen, while their vertical position varied randomly between -6.7, 0 and +6.7 degrees of visual angle relative to the center of the screen. The stimulus size was approximately 1 degree of visual angle. Again, the subjects had to press the space key causing an internal function to randomly select one or more components of the stimulus and marked this selection red (this action is repeated until required component/s were marked red). The task was to mark the digit with the highest value. In sub session 2, two simple arithmetic operations (addition or subtraction) were presented. The position of the two operations and the size of each digit were the same as in sub session 1. Again for simplification, only one arithmetic operation is shown in Fig **4**. Subjects had to solve the operation and use the space key to mark the operation with the highest solution as red. In sub session 3, the arithmetic operation was presented in the center of the screen. The size of the digits was 1.5 degrees of visual angle. Additionally, four numbers representing a solution were shown. Their positions (pos_n (x,y)) relative to the center of the screen were pos_1 = (12, 6.7) degrees of visual angle, pos_2 = (12, - 6.7) degrees of visual angle, pos_3 = (-12, 6.7) degrees of visual angle and pos_4 = (- 12, -6.7) degrees of visual angle. Their sizes were one degree of visual angle. Fig **4** shows an example of the arithmetic operation at the center of the screen and one of the possible solutions. The task was to calculate the solution of the arithmetic operation and find it among the four numbers. Subjects had to press the space key until the correct answer was marked red. Finally, in sub session 4, a group of three letters were shown at the center of the display. The letters were 1.5 degrees of visual angle in height. Additionally, four letters were presented at the same position as the numbers in sub session 3. Three of the four letters were identical to the ones in the center and one was different. Fig **4** shows an example of three letters shown at the center of the screen and one of the four letters shown at the corners of the screen. The task was to press the space key until the different letter was marked red. Fig **9** shows an example of the whole set of stimuli presented in each session and sub session.

3.3.5. Procedure

Training and reading performance assessment

A 13-point calibration was used at the beginning of the experiment to collect fixation samples from 13 known target points in order to map raw eye data to gaze position at known target positions. Subsequently, a validation with 13 points was performed, which provided information about calibration accuracy.

Fig **5** shows the events occurring during the experiment. The visual task block includes the central vision loss simulation and the presentation of the compound stimulus. Thereafter, the subject gave a response, and a drift correction was performed, ensuring that the accuracy of the calibration parameters was maintained, and a new trial began. A count-down timer with a starting time of 10 minutes was turned on during the performance of the visual task. After the time was completed, the experiment then continued with the reading performance. During the reading performance, subjects had to read a string of three words under central scotoma simulation without any inducement. The string of words covered 1.5 x 16 degrees of visual angle and were composed of similar letters in order to enhance the demand of the task, (e.g., WANT WENT WELL). Subjects were asked to read the three words with the central scotoma and press the space key to report successful reading. In this part of the experiment, the stimulus was not relocated, thus also the subjects from the induced groups were able to locate their PRL freely. Subsequently, without central scotoma, subjects were asked to find the string of three words shown previously among two alternatives and press the up or down key to report the answer (Fig **5**, answer block). After the subject gave an answer, a drift correction was performed and a new trial started. The measurement of reading performance continued for 2 minutes. During answer and drift corrections, the timer was paused.

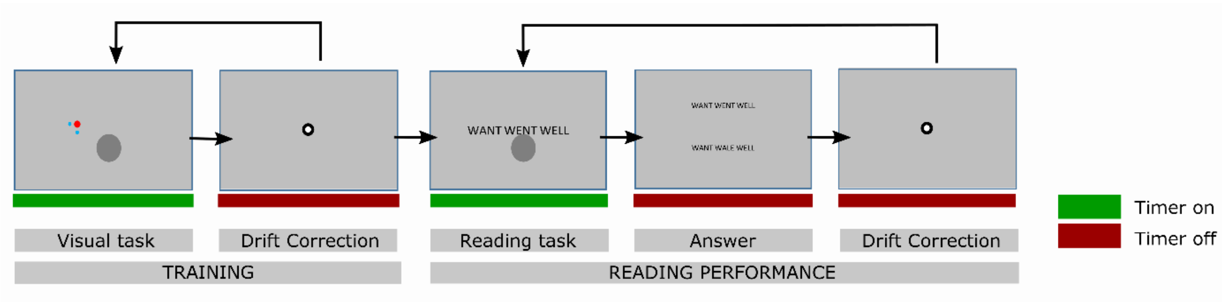

Fig 5: Events occurring during a sub session. Subjects had to perform a visual task under central scotoma simulation where a drift correction occurred after every trial. The experiment proceeded in a loop for 10 minutes. Subsequently the reading performance started, where the subjects had to read with central scotoma simulation to find the correct string of words and answer. Drift corrections were performed after every trial and the reading performance continued in a loop for 2 minutes.

Final performance assessment (FPA)

The final performance assessment is a measurement of the developed PRL position after the training and without the inducement procedure. The assessment was taken in a separate appointment at the end of the experiment (at least one day after the last training session). The analysis was performed to evaluate if the PRL was induced as intended. The visual tasks were identical to the training tasks, except that the function which changed the location of the stimulus was turned off. Thus, subjects from every group were free to choose the PRL during final performance assessment.

During final performance assessment subjects performed the fourth sub session of each session for 1.5 minutes. Firstly, colored dots were shown where the subject had to identify the red dots among blue dots in a five color stimulus. Secondly, lines and squares were shown and subject had to report whether there were more or fewer squares than lines in a five component stimulus. Thirdly, horizontal and vertical lines were shown and subjects had to report whether there were more or fewer horizontal than vertical lines in a five component stimulus. Fourthly, three letters at the center of the screen were shown and four in each corner of the screen. Subjects had to find, at one of the four screen corners, the letter that was not shown at the center.

3.3.6. *Data analysis*

Fixational behavior was evaluated from all gaze data collected during visual task performance. The beginning and end of fixations and blinks were obtained by applying the internal eye tracker criteria. According to these, fixations corresponded to events in which the saccade velocity was below the threshold of 30 deg/sec and blinks corresponded to periods of data where the pupil was undetected. Blinks and saccades were then eliminated from the data.

To quantify the position and the development of the PRL, the data (horizontal and vertical position components of the eye on the display) was translated to the origin of a Cartesian coordinate system located on the two dimensional image space. The stimulus position, saved after each trial, was recalculated relative to this origin and was also translated to this Cartesian system. The result obtained depicted the distribution of the stimulus position relative to the gaze (or center of simulated scotoma). It will be referred to as stimulus distribution map SDM (Fig **6**).

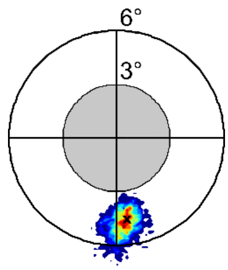

Fig 6: The stimulus distribution map SDM shows an example of the distribution of the stimulus location relative to the center of simulated scotoma after the performance of a training sub session (Subject 2, Session II, sub session 3).

Position of the PRL

The position of the PRL is defined as the spatial location in which the highest density of the stimulus distribution map is found (Kwon, Nandy, & Tjan, 2013). The density was obtained using a bivariate Gaussian kernel estimator (Botev, Grotowski, & Kroese, 2010). In Fig **6**, the small black cross on the red region of the SDM shows the position of the PRL for that case.

PRL value

A PRL value was introduced to track and quantify the PRL development in detail using the stimulus distribution maps. Thus, PRL value allows an assessment whether the presented paradigm affected the development of the new oculomotor strategies and a detailed comparison of PRL development in all three groups.

This value is a combined indicator of the three most important PRL features: PRL concentration, sphericity, and location. Thus, it depended on three criteria: the concentration of the distribution (CI), the index of symmetry of the distribution (SI) and the ratio quantifying the fraction of fixations placing the target out of the scotoma relative to the total fixations (R). To each of the three criteria, a value between 0 and 1 was assigned and the PRL value was calculated for each sub session using equation 1. Within the PRL value, the fraction of fixations out of the scotoma R integrated the effectiveness of an eccentric fixation together with the shape of the PRL, (SI + CI)/ 2. The PRL value ranged between 0 and 1, where values close to 1 represent a very narrow and rounded distributions, located out of the scotoma.

$$\mathbf{PRL\ value} = \mathbf{R} * \frac{\mathbf{SI} + \mathbf{CI}}{\mathbf{2}} \tag{1}$$

To calculate the index of symmetry (SI), a principal component analysis was used to obtain the coefficients of the longest and shortest components of the distribution map and to calculate their lengths. The length of the components was calculated by taking the 15th and 85th percentile and the index of symmetry was obtained by dividing the shortest dimension over the longest dimension (Cherici, Kuang, Poletti, & Rucci 2012). With this approach, index of symmetry values ranged from 0 to 1, where an index of symmetry of 1 represents a circular distribution.

The index of concentration (CI) was used to quantify the concentration of the data around its positional mean (horizontal and vertical). In other words, it is a measure of the concentration of data around its center of mass. To calculate it, the 60th percentile of the distance between every point of the stimulus distribution map and their mean in x and y was calculated (C). This quantity, in visual angle, was normalized and transformed to index values (between 0 and 1) by means of a linear equation (equation 2). The normalization factor beta ß was selected to be the highest value that C took among all subjects and sessions could take. With this approach, one assigns values close to 1 for high concentrated stimulus distribution maps and values close to 0 for low concentrated stimulus distributions maps.

$$\mathbf{CI} = \mathbf{1} - \left(\frac{\mathbf{C}}{\text{ß}}\right) \tag{2}$$

The ratio (R) quantifies how many fixations placed the target outside the scotoma. It was calculated by dividing the number of times that the stimulus was located out of the scotoma n_{out} over the total number of times that the stimulus was fixated n_{total}. Additionally, the lowest limit of the ratio factor (zero) was assigned to be the point in which 50% of the fixations are out of the scotoma and 50% inside the scotoma (equation 3). With this approach, values close to 1 represented efficient oculomotor behavior which localized the stimulus out of the scotoma, values close to 0 represented oculomotor behavior that by chance located the stimulus inside or outside of the scotoma and values below 0 represented fixations that located stimulus mainly in the scotoma region. In that case, R was assigned to be zero instead of the negative value. As a consequence, the PRL value was also zero.

$$\mathbf{R} = 2 * \left(\frac{\mathbf{n_{out}}}{\mathbf{n_{total}}} - \mathbf{0.5}\right) \tag{3}$$

Fig **7** shows three examples of different fixational behavior with their respective indexes and PRL values. On the left a subject that tried to foveate the stimulus. The symmetry and concentration indexes are relatively high, but the low R ratio leads to a low PRL value. The figure in the center shows an example case of a subject, who started to fixate eccentrically. In this case the index of concentration and index of symmetry decreased due to the elongation of the fixational pattern, however, the ratio that quantifies the eccentric fixations increased. This leads to a higher PRL value. Finally, on the right a subject with a trained PRL is shown. In this case, the stimulus is repeatedly fixated out of the scotoma on a location that was consistently selected, leading to a high PRL value.

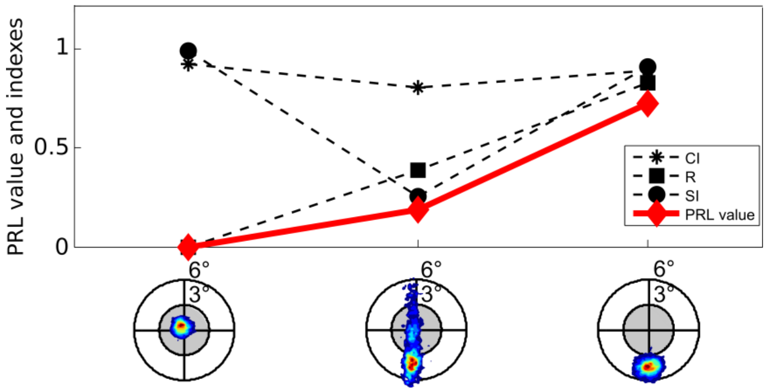

Fig 7: Example of PRL index and their influence on the PRL value.

3.4. Results

3.4.1. *Position* of the PRL

PRL position after the final performance assessment

In the final performance assessment the stimulus relocation function was turned off and subjects performed four visual tasks with static stimuli. The stimulus distribution map obtained after the performance of the four visual task was obtained for each subject. To calculate the position of the PRL, the point of peak density of the stimulus distribution maps was calculated and the results for every subject are presented in Fig **8**.

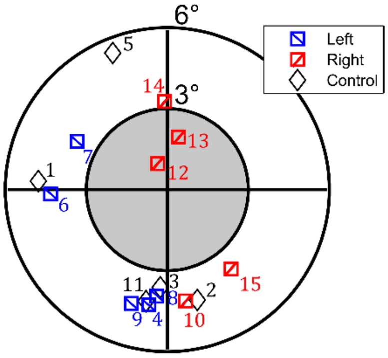

Fig 8: PRL positions of subjects after the final performance measurement. The two sample t-test applied to subjects from the left induced PRL versus right induced PRL results in significant differences (t (8) = -2.88, p = 0.02).

The horizontal component of the PRL from the left and the right induced group differ significantly in a two sample t-test (t (8) = -2.88, p = 0.02). The mean horizontal PRL position of subjects from the left induced group was -2.3 ± 1.2 degrees of visual angle and for the subjects from the right induced group was 0.3 ± 0.8 degrees of visual angle. Subjects from the control group showed a mean horizontal PRL position of -1.4 ± 2.2 degrees of visual angle.

Furthermore, all subjects but two showed a PRL located outside of the scotoma, but still in proximity to the scotoma, with a distance between the PRL location and the edge of the scotoma below 3 degrees of visual angle. The two subjects that presented the PRL inside the scotoma (subject 12 and 13) alternate a PRL position between two locations (outside and inside the scotoma, Fig S1).

Monitoring the PRL position after each training session

The PRL position was evaluated after 40 minutes of recording, equivalent to the time taken to record four sub sessions. This enabled a detailed analysis of the PRL development throughout the training. To obtain the position of the PRL, the point of peak density of the stimulus distribution maps was calculated and the results for every single subject are presented in Fig **9**.

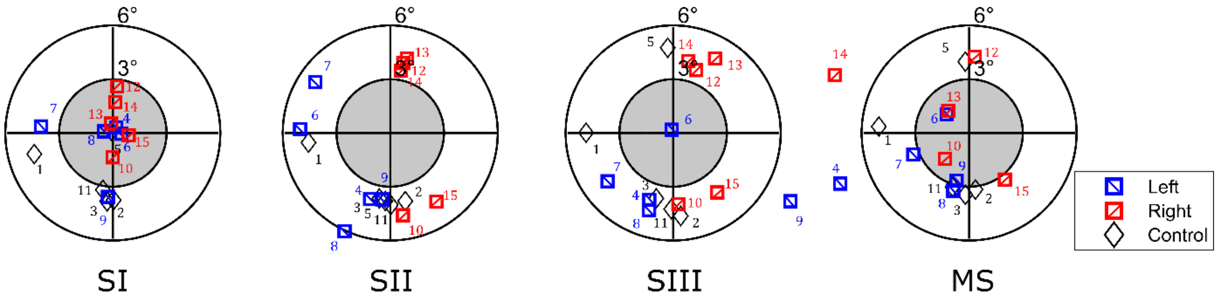

Fig 9: Position of the PRL after each training session. Each number represents a subject and the groups are separated by colors and shapes. Squares represent the subjects under the inducing procedure, blue squares for left and red squares for right and the black diamonds for the control group. The gray central region of ± 3 degrees of visual angle corresponds to the area covered by the scotoma.

In session I, nine subjects located the PRL in the center of the scotoma showing that, at the beginning of the training, subjects tried to gaze with the fovea repeatedly. But by session II, subjects already fixated eccentrically.

Notice that some PRLs seem to be located inside the scotoma, this is actually an artefact of two PRLs or distributed SDMs in this specific session. Nonetheless, clear PRLs outside of the scotoma are available for every subject in a late phase of training and can be found in Fig S2.

3.4.2. *PRL* value

Fig **10** shows the stimulus distribution maps of a sample subject for the complete training procedure with the corresponding performed tasks and PRL index values. Notice that during session I the subject brought the stimulus from the region of the scotoma to the region outside and during session II the stimulus was located mainly out of the scotoma. Note that, in session II the subject located the stimulus at two positions, but in session III, only one PRL remained. In the last training session, where multiple stimuli were presented, the stimulus distribution maps are broader.

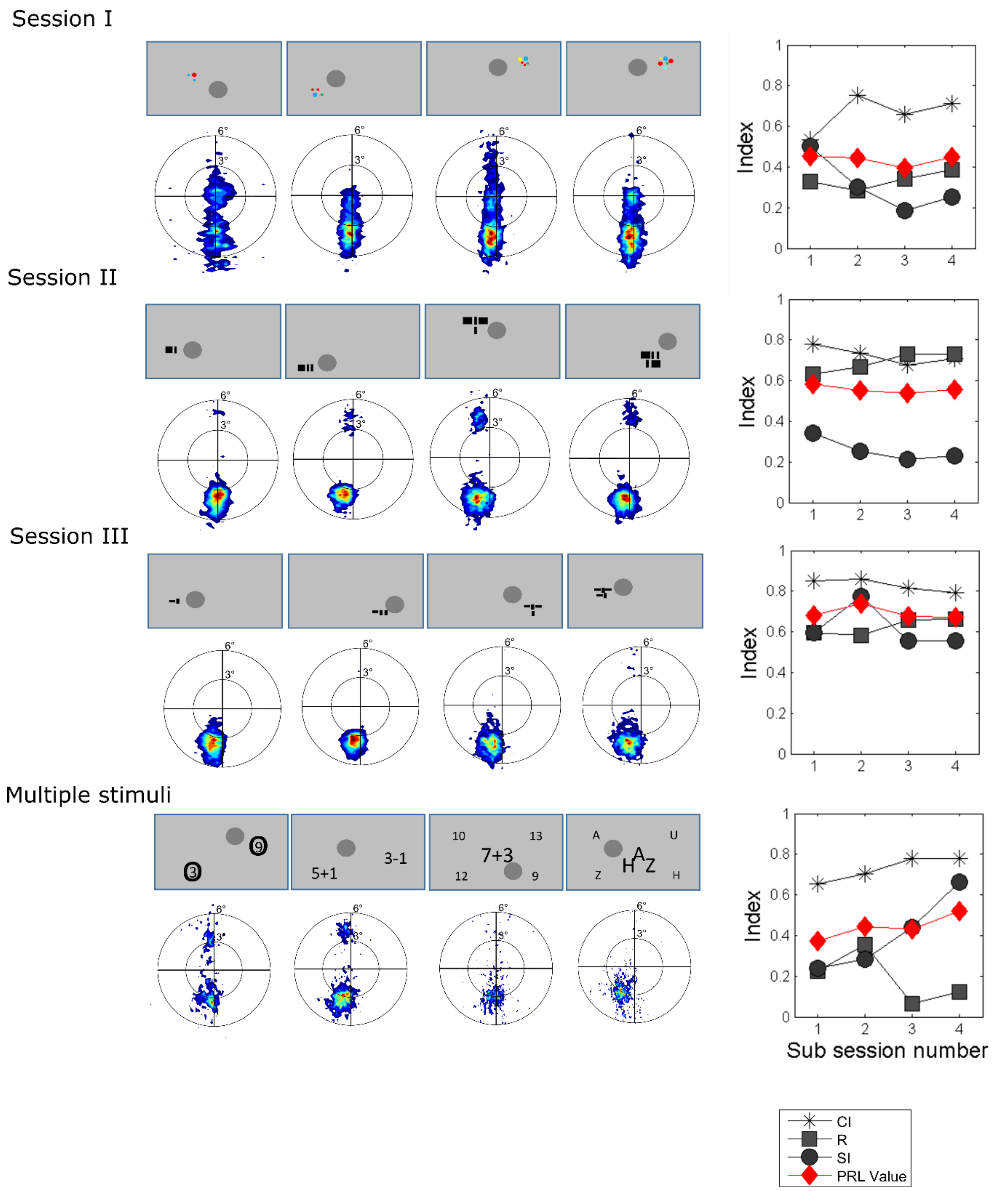

Fig 10: Stimulus distribution maps for sample subject number 3 (control group). Each stimulus distribution map plotted with its corresponding sub session is the result of 10 minutes of recording (while the timer was running). In addition, the indices used to calculate the PRL values are shown with their respective PRL value for every session. Note that the PRL value increased from session to session during the presentation of a single stimulus.

To analyze whether the training improves the oculomotor behavior and whether the paradigm affects the development of new oculomotor strategies, the PRL value was analyzed.

Fig **11** shows the mean PRL values for every subject of each group as a function of the sub session number. The blue shaded area corresponds to the mean PRL and standard deviations of the left induced group, the red shaded area to the right induced group and the gray shaded area to the control group. 'Single stimulus' corresponds to the PRL values collected during the performance of the first twelve sub-sessions (or first three sessions). 'Multiple stimuli' corresponds to the four sub sessions performed in the multiple stimuli session. During the performance of the single stimulus task, the PRL value appears to increase with training in every group. To test whether the improvement is significant, a paired t-test was performed between the first sub session (sub session 1) and last sub session (sub session 12) for every group independently. PRL values increased significantly in the right induced group ($t(4) = -2.55$, $p = 0.004$) and control group ($t(4) = -14.39$, $p = 0.0007$), showing a successful training. In the left induced group the PRL value did not increase significantly ($t(4) = -2.55$, $p = 0.062$). This might be due to the fact that the variance in final PRL values was high in this group. During the multiple stimuli training, the PRL values dropped.

Additionally, to see whether the paradigm affects the development of new oculomotor strategies, two sample t-tests were performed between the groups. The results showed significant differences between the induced groups ($t(22) = 2.64$, $p = 0.01$) and between right induced and control group ($t(22) = 2.65$, $p = 0.01$), but no significant differences between left induced and control group ($t(22) = -0.80$, $p = 0.42$). These results indicate that inducing the PRL on the right hemifield might require longer training time. On the other hand, significant differences were found between the beginning and end of the training in this group, indicating that the training is improving the general performance.

Regarding the multiple stimuli session, no statistically significant differences were found between the groups (induced groups $t(6) = -0.19$, $p = 8.85$; right induced versus control group $t(6) = -0.96$, $p = 0.37$; left induced versus control $t(6) = 0.58$, $p = 0.58$).

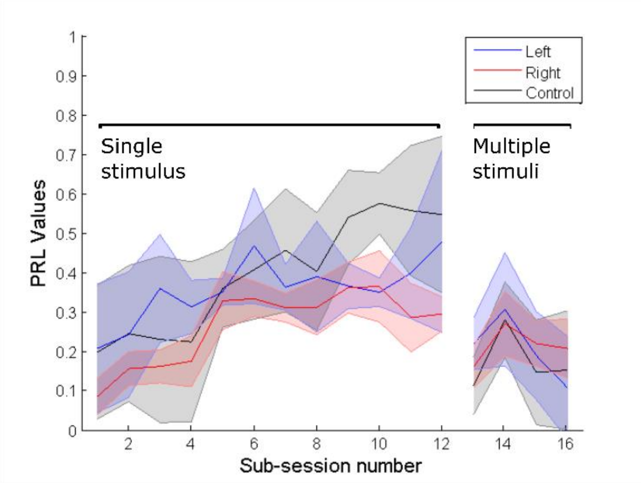

Fig 11: PRL values as a function of the training sub sessions. The PRL value increases along the performance of the single stimulus training and drops during the performance of the multiple stimuli session.

3.4.3. Reading performance assessment during training

During the experiment, the reading performance under central scotoma simulation was assessed with a reading task at the end of each training sub session. A group of three words composed of four letters was presented and the time spent to read the group of words was evaluated. In Fig **12** the mean elapsed time per trial with its respective standard error is shown as a function of the training session for the three groups.

The mean elapsed time at the beginning and the end of the training were tested separately in every group and on the reciprocal for equal variances. Results show significant improvements between beginning and end reading time for the left induced group ($t(4) = -5.69$, $p = 0.004$), the right induced group ($t(4) = -3.93$, $p = 0.01$) and the control group ($t(4) = -8.40$, $p = 0.001$).

Initially, subjects in the left induced group read a mean of 34.4 ± 9.8 wpm (words per minute), subjects of the right induced group a mean of 15.7 ± 7.7 wpm and subjects in the control group read a mean of 30.0 ± 12.5 wpm. After training, subjects of the left induced group increased their reading speed to 101.5 ± 24.3 wpm, of the right induced group to 74.0 ± 11.9 wpm and subjects of the control group to 106.4 ± 15.7 wpm.

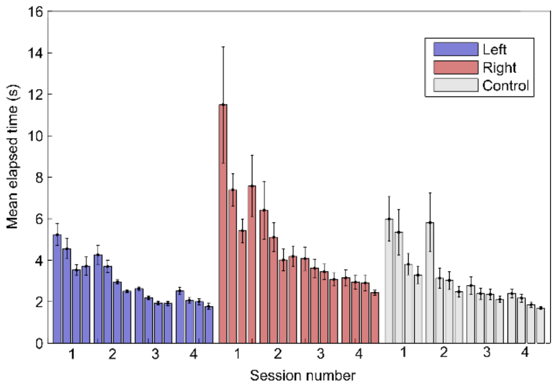

Fig 12: Mean elapsed time per trial as a function of the session number obtained during reading performance measurement. Each session number is divided into four values, corresponding to each sub session. Values at the beginning and end of training were significantly different for the left induced group ($t(4) = -5.69$, $p = 0.004$) right induced group ($t(4) = -3.93$, $p = 0.01$) and control group ($t(4) = -8.40$, $p = 0.001$).

3.5. Discussion

The PRL position

To answer the question of whether the location of the PRL can be induced at early stages of its development using systematic stimulus relocation, the location of the developed PRL was evaluated. After the inducement, once the stimulus was no longer relocated, all subjects from the left induced group placed the stimulus consistently on the left half of their visual field and three subjects from the right induced group placed the stimulus on the right half of their visual field. Two subjects from the right induced group had difficulties to develop a PRL on the right hemifield. Maybe the higher prevalence to locate the PRL on the left hemifield played a role on this difficulty (Fletcher, Schuchard, Livingstone, Crane, & Hu, 1994; Sunness, Applegate, Haselwood, & Rubin, 1996; Cummings & Rubin, 1992).

Previous studies have demonstrated that the PRL can be trained on normally sighted subjects (Lingnau, Schwarzbach & Vorberg 2008). The presented study demonstrates that the PRL can also be induced to be at a specific hemifield based on systematic stimulus relocation.

Additionally, our findings show that eight subjects located the PRL below the scotoma, four subjects above and three subjects to the left of scotoma. The fact that the majority located the PRL below the scotoma agrees with studies showing a higher tendency to locate the PRL on the lower side of the scotoma (Fletcher & Schuchard, 1997). As a PRL located on the lower visual field is better for English reading (Nilsson, Frennesson, & Nilsson 1998; Nilsson, Frennesson, & Nilsson, 2003), these results support the function driven selection hypothesis for the development of a PRL, which predict that PRL positions depend on the visual task. Moreover, most of the subject developed PRL positions close to the edge of the scotoma (distance less than 3 degrees of visual angle). These results agree with the study from Fletcher and Schuchard (1997), which showed that in 883 eyes with different forms of maculopathy, 88.7% of the PRLs were within 2.5 deg from the border of the scotoma. Additionally, Sunness, Applegate, Haselwood, and Rubin, (1996) found that among 27 eyes with dry age related macular degeneration and eccentric PRLs, the PRLs were always within 2 degrees from the scotoma border. These findings support the retinotopy driven selection mechanism for the development of a PRL, which predicts the PRL at the border of the central scotoma (Cheung & Legge, 2005).

The systematic stimulus relocation presented in this study can be tailored to the intended PRL location and thus be used to encourage other regions of the visual field. For example, confined regions of the visual field can be selected to induce PRLs. Potential encouraged regions could be narrower, such as regions at the left and right visual field quarters, or circular regions at any part of the visual field.

PRL development

In correspondence with the previous findings, healthy subjects learned to fixate a target eccentrically within two training hours and their behavior under simulated central vision loss showed a spontaneous and fast plasticity that can be attributed to oculomotor learning (Kwon, Nandy, & Tjan, 2013; Pidcoe & Wetzel, 2006). This is in contrast to the *c*linical observations that imply lengthy adjustment periods in patients with central vision loss (Crossland, Culham, Kabanarou, & Rubin, 2005; White & Bedell, 1990). However, a previous study demonstrated that older adults were slower and used excessive eye movement during a search task and during a central vision loss simulation (Kwon, 2012). Thus, future training procedures might have to be adjusted for the patient's age.

The PRL values during the first three training sessions increased gradually, suggesting that training improves the oculomotor behavior under scotoma simulation when single stimuli are presented. However, differences on PRL values between the right induced group and the other two groups were observed, two subjects from the right induced group showed central fixations and a slower development of PRL at the final performance assessment. These differences might be explained by the large incidence to locate the PRL on the left side of the scotoma in patients with central vision loss (Fletcher, Schuchard, Livingstone, Crane, & Hu, 1994; Fletcher & Schuchard, 1997; Sunness, Applegate, Haselwood, & Rubin, 1996; Cummings & Rubin, 1992) and suggest that the inducement in regions with low incidence might require an extra effort in the development of a PRL. Moreover, Liu (2016) used a gaze-contingent simulated scotoma to induce a reliable PRL on the left, right, above and below the scotoma. However, the training time used in their study was between 6 to 7 hours. In our study, subjects were a maximum of 2.6 hours under the training procedure. These results suggest that the duration of the training might play an important role on the development of reliable PRLs.

The difference in PRL values obtained during the multiple stimuli session might be paradigm induced. The subjects had to perform two different perceptual tasks which might have required different oculomotor behavior (the first task was to find the correct answer and the second task was to mark the correct answer red). Firstly, to find the correct answer, subjects needed to approach the stimulus and look at each of them eccentrically. Secondly, since parafoveal color vision does not differ in essential characteristics from foveal color vision under high retinal illumination (Gilbert, 1950), subjects were able to place the scotoma in a central position on the display and still see changes in the color on the stimuli when the space key was pressed. This might have altered the fixational behavior significantly. Consequently, the data used to calculate each index of the PRL value, which was always obtained by the transformation of stimulus position relative to center of scotoma's position, might have been reduced because of the time that the subject spent locating the scotoma at the central position of the screen. Therefore, further studies should consider the use of multiple and colored stimuli in their paradigm. Alternatively, the change from a single stimulus paradigm to a novel multiple stimuli paradigm might have impeded the transfer of the oculomotor behavior which might have led to the decay of the PRL values.

Reading performance during training

Subjects improved their reading speed in a similar way in all groups. The left induced group showed a mean improvement of 67.1 wpm, the right induced group of 58.3 wpm and the control group of 76.4 wpm. A comparable improvement was demonstrated by patients with PRL location initially located on the left field of view, which was then moved above or below the central scotoma. Reading speed for those patients showed an improvement from 9 ± 5.8 wpm to 68.3 ± 19.4 wpm (Nilsson, Frennesson, & Nilsson 1998).

3.6. CONCLUSIONS

This study demonstrates that the location of the PRL can be induced at an early stage of its development using systematic stimulus relocation and that this new paradigm does not impair the PRL development. In addition, the procedure confirmed that normally sighted people can develop the PRL in a fast and spontaneous way. This serves as a starting point for guiding the PRL formation in individuals suffering from visual impairments.

3.7. Supplementary material

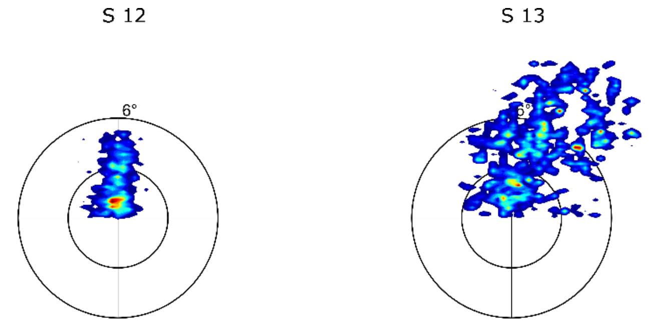

Fig S1: PRL after the final performance assessment of subject 12 and 13. Subjects performed eccentric as well as centric fixations showing a tendency to a slower adaptation.

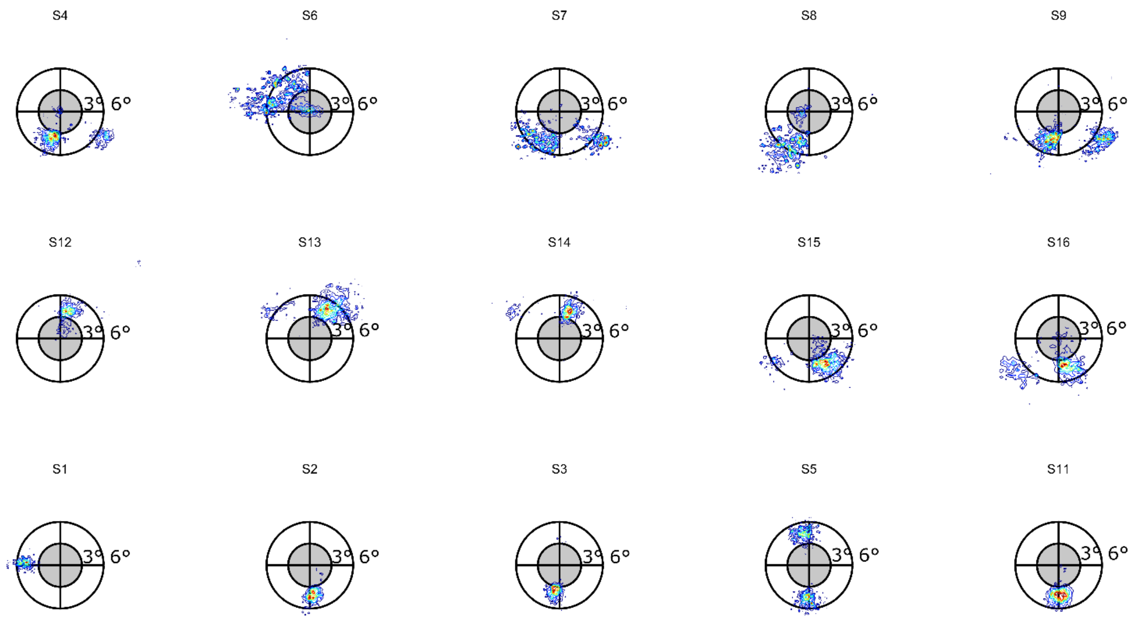

Fig S2: SDM for each subject, taken from session III, sub session 3. Each subject shows at least one confined area of fixation towards the end of the training.

4. TRANSFER OF THE INDUCED PREFERRED RETINAL LOCUS OF FIXATION

Barraza-Bernal M.J., Rifai K., & Wahl S., (2017). Journal of Vision, 17(14):2, 1-16.

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4.1. ABSTRACT

Subjects develop a preferred retinal locus of fixation (PRL) under simulation of central scotoma. If systematic relocations are applied to the stimulus position, PRLs manifest at a location in favor of the stimulus relocation.

The present study investigates whether the induced PRL is transferred to important visual tasks in daily life, namely pursuit eye movements, signage reading and text reading. Fifteen normally sighted subjects participated in the study. To develop a PRL, all subjects underwent a scotoma simulation in a prior study, where five subjects were trained to develop the PRL in the left hemifield, five different subjects on the right hemifield and the remaining five subjects could naturally chose the PRL location. The position of this PRL was used as baseline.

Under central scotoma simulation, subjects performed a pursuit task, a signage reading task and a reading-text task. In addition, retention of the behavior was also studied.

Results showed, that the PRL position was transferred to the pursuit task and that the vertical location of the PRL was maintained on the text reading task. However, when reading signage, a function driven change in PRL location was observed. In addition, retention of the PRL position was observed over weeks and months.

These results indicate, that PRL positions can be induced and may further transferred to everyday life visual tasks, without hindering function driven changes in PRL position.

Key Words: induced preferred retinal locus, oculomotor learning.

4.2. INTRODUCTION

Patients with damaged maculae have compromised the part of their visual field with the highest accuracy and sensitivity. Bereft of their main source of information, patients select an alternative and healthy retinal location which then acts as a pseudo-fovea and compensates the lack of foveal input. This retinal location is referred to as preferred retinal locus (PRL) for fixation (Nagel, 1911; Fuchs, 1922; Von Noorden et al., 1962; Mainster et al., 1982; White et al., 1990; Guez et al., 1993; Fletcher et al., 1997; Schuchard, 2005; Cummings et al., 1985).

In a previous study, we showed that the PRL location can be induced at a specific hemifield when systematic stimulus relocation is applied to a stimulus that evokes saccadic eye movements (Barraza-Bernal et al., 2017). Patients with central scotoma present a strong tendency to develop a PRL in the left side of the visual field (Fletcher et al., 1994, 1997; Sunness et al., 1996; Cummings et al., 1992), however, in contrast to this observation, other PRL positions were proven to be beneficial for the performance of some visual tasks (Whittaker et al., 1993; Guez et al., 1993; Petre et al., 2000; Deruaz et al., 2002; Chung et al., 2004; Frennesson et al., 2007). For example, a PRL for left-to-right reading will preferentially be below the central scotoma, since only then can the reader estimate the amplitude of the eye movement towards the next word or towards the next line. In this case, a PRL on the left side of the macular scotoma is not convenient and a relocation of the PRL might positively influence the performance of the reading task.

In our previous study, a PRL was induced to be either on the right or on the left hemifield. A stimulus that evoked a saccadic eye movement was always relocated to the induced hemifield when the saccadic eye movement located the stimulus on the opposite hemifield. For example, if the PRL was induced on the left hemifield, and a saccade located the stimulus on the right hemifield, the stimulus was relocated on the left hemifield and vice versa. The relocation was always applied horizontally and had a magnitude of 7.5° of visual angle. The inducement was studied in normally sighted subjects and was performed at early stages of its development. The study showed that systematic stimulus relocations may influence the location in which the PRL developed. Moreover, the training was more effective when the stimulus relocations were in favor of the left hemifield than the right hemifield. However, in everyday life, reactive saccades to appearing targets render only a fraction of occurring eye movements. But, visual impairments affect eye movements in tasks like reading, during locomotion and orientation, and social interaction as well (Trauzettel-Klosinski, 2011). Hence, in reality central vision loss patients are challenged to perform a diversity of visual tasks in their natural environment. Taking this into account, the present study addressed the question whether the PRLs induced in Barraza-Bernal et al. (2017) can be transferred to other important visual tasks. The transfer of the left-induced group, right-induced group, and the group without inducement procedure was analyzed separately using means and standard deviations of the distance between trained and transferred PRL. This analysis allowed the determination of potential impact of the inducing procedure on the transfer behavior.

All subjects underwent the PRL training and in 10 of them the PRL location was induced by systematic stimulus relocations. The induced PRL was taken as a baseline and was compared with the PRL used in the new visual tasks. Since PRLs can be trained to enhance the visual performance (Seiple et al., 2005; Tarita-Nistor et al., 2009; Chung, 2011) and, since explicit training can improve the variance of the PRL (Kwon et al., 2013), the only comparison parameter that we used was the PRL location.

The everyday life tasks consisted of a pursuit task, a signage reading task and a text reading task. These tasks were selected to mimic important daily tasks. The pursuit task mimicked object following tasks like cars or any other objects moving in the environment. The signage reading task mimicked the reading of instructional texts, like traffic signs. The text reading task mimicked tasks like reading newspaper or magazines.

The results showed an overall maintenance of PRL location when a pursuit task is evoked. Also for a text reading task, the results showed that the vertical location of the PRL was maintained. However, in the signage reading task, changes in the PRL locations were observed in favor of a functionally driven location selection of PRL.

4.3. METHODS

4.3.1. Apparatus

The performance of the experiment and of the data acquisition were carried out using a gaze contingent setup based on MATLAB, the Psychtoolbox (Brainard, 1997; Kleiner et al., 2007), the Eyelink toolbox (Cornelissen et al., 2002), the Eyelink 1000 Plus eye tracker (SR Research, Ltd., Ontario, Canada) and a ViewPixx/3D display with a vertical refresh rate of 100 Hz and a spatial resolution of 1920 x 1080 pixels.

To simulate the central scotoma, a gaze contingent round mask was presented at the momentary eye position. Scotoma presentation was temporally delayed by less than 20 ms after eyes position detection. Vertical and horizontal positions of the right eye were recorded at a spatial resolution of 0.01° and 1 kHz while the left eye was patched.

A chin rest was used to stabilize the head and to locate the eyes at a distance of 62 cm from the display.

4.3.2. Participants

Fifteen participants took part in the study, five males and ten females aged between 24 and 33 years (mean 26.6 years). Every participant had a developed PRL, acquired under simulation of central scotoma after four training sessions (Barraza-Bernal et al., 2017). Five participants had a PRL induced in the left hemifield, five different subjects had a PRL induced in the right hemifield. The remaining five subjects had a PRL developed without any inducement procedure.

The study was performed in accordance with the declaration of Helsinki. Subjects signed an Informed Consent before their participation. All subjects were eye-healthy and had normal or corrected to normal visual acuity.

4.3.3. Study design

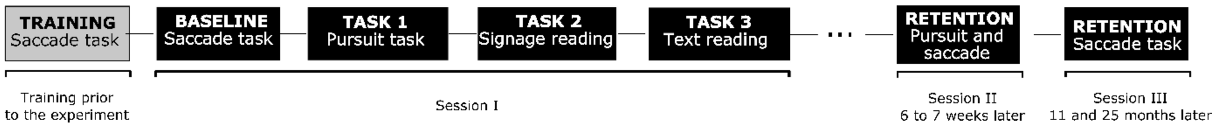

Fig 13: Sequence of experiments performed in the study. From left to right, the gray box represents the training procedure that the subjects fulfilled prior the performance of this study. In this training procedure, subjects were trained using a stimulus that evoked a saccadic eye movement to develop a PRL. All boxes marked black represent the steps followed in the present study. In the first session, the transfer of PRL was investigated. A baseline task was performed to determine the PRL location after the training. The task was performed using a stimulus that evoked a saccadic eye movement. Afterward the three tasks were performed (the pursuit task, signage reading task and text reading task). In a separate session six to seven weeks later, the retention of the pursuit and saccade task was studied. Finally, long-term retention was measured eleven and twenty five month after the performance of Session I in five subjects.

Fig **13** shows the sequence of experiments performed on the study. The gray box represents the training that subjects performed prior to the performance of this experiment (Barraza-Bernal et al. 2017). To develop a PRL, subjects underwent a visual task in which a single saccade target was presented at a time.

The black boxes represent the experimental blocks performed in this study. In Session I, the transfer of PRL was studied. The experiment started with a baseline measurement of the PRL location developed after training. These data were identical to the Final Performance Assessment data presented in Barraza-Bernal et al., 2017. The PRL location obtained in this measurement was used as a baseline for comparison with the PRL used in the performance of the three everyday life visual tasks. The baseline PRL position was acquired using a single appearing stimulus that evoked a saccade. Consecutively, subjects performed the three visual tasks under simulation of central scotoma: a pursuit task, a signage reading task and a text reading task. These measurement were performed right after the end of the training. Thereafter, the retention of the developed PRL location was determined in two separate sessions. Two sessions at different points in time after the performance of Session I were recorded. The first retention was acquired between six and seven weeks after the performance of Session I. Every subject participated in this session. The second retention was a long term retention measurement, taken 11 and 25 months after the performance of Session I. Five subject were available for the performance of this sessions.

4.3.4. Stimuli and procedure

All experiments were performed in a dark room. The simulation of the central scotoma consisted of a foveally presented circular scotoma spanning ± 3 degrees of visual angle. The color of the scotoma was dark gray whereas the background color was light gray. The luminance of the light gray screen was 64 cd/m^2.

At the beginning of any phase of the experiment a 13 point calibration was performed. This calibration collected fixation samples from 13 known target points in order to map raw eye data to gaze position. Subsequently, a validation with 13 points was performed, which provided information about the calibration's accuracy. The experiments continued only if the eye tracker qualified the validation to be good.

Baseline

In Session I, all subjects had to perform a visual task previous to the first task to determine their baseline PRL location.

The baseline PRL location was determined with stimuli identical to the PRL training. Saccade stimuli were presented at random locations on the screen and subjects had to perform a visual task in a set of four blocks. Fig **14** shows examples of the stimuli presented in each block. In the first block, a group of colored discs were shown and subjects had to identify red among blue discs in a 5 color stimulus. In the second block, a group of lines and squares were shown and subjects had to report whether there were more or less squares than lines in a five component stimulus. In the third block, horizontal and vertical lines were shown and subjects had to report whether there were more or less horizontal than vertical lines in a five component stimulus. Finally in the fourth block, three letters at the center of the screen and four letters at each corner of the screen were shown. In a comparison task, subjects had to find in one of the four corners the letter that was not presented in the center. The overall stimulus size was 1.7x1.7 degrees of visual angle. In every block the eye movement data were acquired for 1.5 minutes, however, the total duration of the experiment was different for every subject because drift corrections were performed between the trials.

The PRL location obtained after the performance of this task was later used to compare the PRL location used under the performance of the everyday life visual tasks.

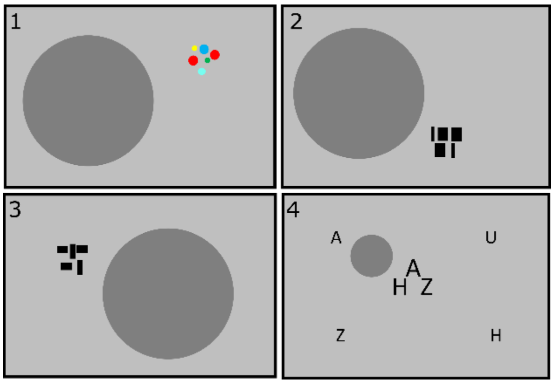

Fig 14: Example of stimuli presented on the baseline measurement. In the first part (1), five colored discs were presented and subjects had to report whether there were more red or blue discs. In the second part (2), squares and lines were presented and subjects had to report whether there were more squares or lines. In the third part (3), horizontal and vertical lines were presented and subjects had to report whether there were more horizontal or vertical lines. Finally, in the fourth part (4) a set of three letters were presented on the center of the display and subjects had to find in the corners of the display the letter that was not presented on the center.

Task 1: Performance of pursuit eye movements

Fig **15** shows an example of the task. Under simulation of central scotoma, subjects had to pursue a group of discs moving with a random trajectory over the screen at a speed that varied between 15°/s and 25°/s. The discs had always the same distance relative to each other, only the mean position changed over the screen. All the discs had different diameters. Overall the stimulus spanned 1.7x1.7 degrees of visual angle. At the beginning of a trial, every disc was black, but while the group of discs was moving on the screen, the discs changed their color at randomly selected times and locations. The colors varied between yellow, blue, magenta, cyan, green and red. The task was to press the space key when the disc located at the center turned red. Afterward, the discs turned black again and a new trial started. Eye movement data were acquired for 3 minutes.

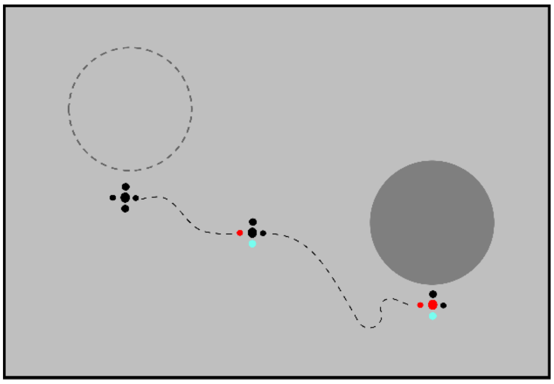

Fig 15: Example of the pursuit task. The group of discs moved following a random trajectory (dotted path) and subjects had to follow the discs until the center disc turned red. As a consequence, subjects had to report the change in color by pressing the space key. Notice that other discs also turned red along the trajectory.

Task 2: Performance of signage reading task

Fig **16** shows examples of the signage reading task. Subjects had to read three words. The group of words covered 1.5 x 16 degrees of visual angle and were composed of similar letters (e.g., WANT WENT WELL). The words were presented until the subject reported successful reading, thus, subjects were free to read for the time that they estimated necessary. Subjects were asked to read the words with the central scotoma and press the space key to report successful reading. Subsequently, without central scotoma simulation, two sets of three words were presented, and subjects were asked to find the string of words shown previously among these two alternatives and press the up or down key to report the answer.

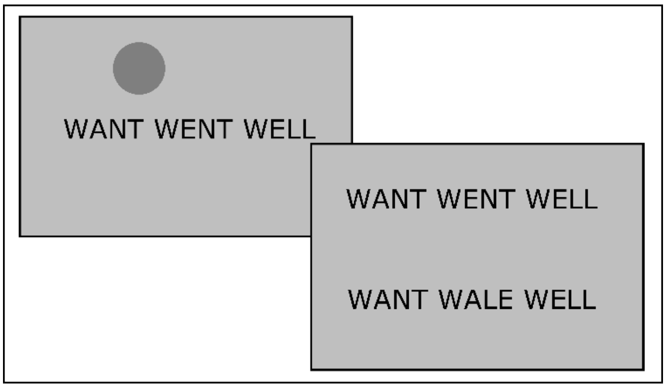

Fig 16: Example of the signage reading task. Subjects had to read the string of words under simulation of central scotoma for the time that they estimated necessary. Subjects pressed the space key to report that the task was completed and afterward they had to find the correct sting of words among two options.

Task 3: Performance of text reading task

Fig **17** shows an example of the text reading task. Subjects had to read a text under simulation of central scotoma for the time that they estimated necessary. The text was presented in five subsequently shown paragraphs. Each paragraph consisted of six lines. The paragraph was aligned to the left and every line had a different length. The paragraph extended 33 degrees of visual angle horizontally and was positioned centrally on the screen.

As resolution of retinal areas located more than 3 degrees of visual angle away from the fovea is decreased, the character size of the text was magnified. Chung et al., (1998), showed that the critical print size for 3° eccentricity, in which reading speed is not limited by print size, is approximately 0.5 degrees. Therefore, to avoid limitations on reading speed due to print size, the character size of our reading task was 0.5 x 0.7 degrees of visual angle. The spacing between lines was 1.9 degrees of visual angle. The subject had to read the text of the five paragraphs and once finished reading, answer questions about its content. The questions were performed verbally and they had to be answered with a yes or a no.

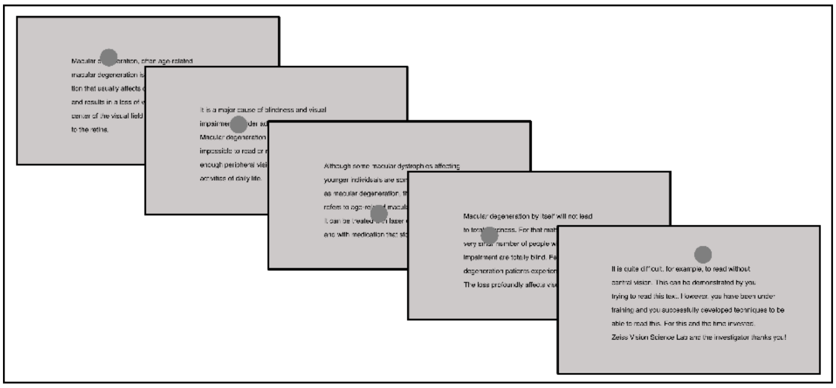

Fig 17: Example of the text reading task. Subjects had to read the sequence of paragraphs and at the end of the experiment, answer questions related to the text.

Retention of the developed PRL

For a fair comparison between the current PRL position and the baseline PRL position, retention was assessed by performing tasks already performed before. In the retention session performed six to seven weeks after session I, the same experiment performed in the assessment of the baseline PRL was followed. The only difference was that this time, the duration of the data acquisition was increased to 5 minutes. Additionally, the retention of the pursuit task was also evaluated following the same procedure for the pursuit task. In the retention session performed 1 and 25 month after Session I, the same experiment performed in the assessment of the baseline PRL was followed, but here the duration of data acquisition was 5 minutes.

4.3.5. Data analysis

Position of the PRL for saccade stimulus and smooth pursuit eye movements

Eye movement data were classified using the eye tracker internal algorithms. The algorithm classified saccades, fixation and blinks using a saccadic velocity threshold of 30°/s, a saccadic acceleration threshold of 8000°/s^2 and saccadic motion threshold of 0.1°. This allowed the capture of smooth pursuit eye movements under the category of fixations, as the speed of this eye movements under a simulated scotoma is typically below 25°/s (Aguilar et al., 2011) and the speed of the stimulus was also always in the range of 15°/s and 25°/s. The eye movement data were translated to maps that summarized the fixational behavior after the performance of each experimental task. They show the location of the stimulus relative to the simulated scotoma after the performance of the task. The maps were obtained by calculating the stimulus position relative to the center of scotoma for every fixation recorded in the experiment. Subsequently, a bivariate Gaussian kernel estimator (Botev et al., 2010) was used to calculate the density of the fixation maps. The position of the PRL was defined to be the point located at the highest density of the fixation map (Kwon et al., 2013).

This analysis was used in the baseline PRL assessment, smooth pursuit eye movements, signage reading task and retention. Fig **18** shows an example of a fixation map after density calculation. The gray center represents the area covered by the scotoma and the cross at the highest density of the fixation map represents the PRL location.

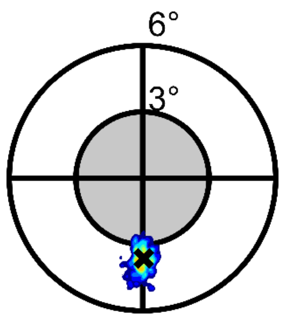

Fig 18: Example of a fixation map. After a collection of all fixations performed in the experiment, a bivariate Gaussian kernel estimator calculates the density of fixations. The figure shows the density of the distributions and the black cross shows the position of the PRL defined to be at the peak density of the map.

Radius of baseline PRL

The radius of the baseline PRL was based on the Euclidean distance between the baseline PRL location and every gaze position under fixation in the baseline task. The distance representing the 68th percentile of all measured gaze position distances from the baseline PRL location was defined to be the radius of the baseline PRL.

Distance between baseline PRL and transferred PRL

The distance between the baseline PRL and the transferred PRL was calculated using the Euclidean distance between both PRL locations.

Quantity for the transfer of the PRL

To quantify the PRL transfer, a Transfer Ratio R_T was introduced. R_T was calculated by dividing the distance between the PRLs PRL_d over the radius of the baseline PRL R_B, as shown in formula 4.

$$R_T = \frac{PRL_d}{R_B} \quad (4)$$

R_T values below 1 indicate that the transferred PRL was located within the radius of the baseline PRL extend, whereas R_T values above 1 indicate that the transferred PRL was not located within the radius of the baseline PRL extend.

Position of the PRL for text reading task

In the text reading task, we adapted a method used by Timberlake et al. (1987) to determine the location of the PRL. They divided the retina into several perceptual areas, forming a grid to determine the location of the PRL. They calculated the percentage of words hitting every area and defined the PRL to be at the area with the highest percentage. In our study, the grid was transformed to a radial perceptual grid with a size that spanned the visual perceptual area for reading.

For normally sighted people, the minimum reading perceptual area covers two degrees of visual angle to the right and to the left sides of the fixation and one degree of visual angle above and below the fixation (Aulhorn, 1953). The total perceptual span, or region of effective vision during eye fixations in reading, is known to be larger on the right side of the fixation point (Rayner et al., 2010). In this study, since the letters were magnified to ease the performance of the reading, we estimated the perceptual span window to be 3.7 degrees of visual angle.

Fig **19**, panel A shows the radial grid with a visual span out of the scotoma of 3.7 degrees of visual angle. In the analysis, the center of the grid was aligned at each fixation and the centroid of any letter that was lying within this grid, was saved as a reference stimulus position, Fig **19**, panel B. In panel C can be seen an example of the radial grid after the collection of all centroids for all fixations. Panel D shows the percentage of hits per radial block for the example presented in panel C. Additionally, the red dot in panel D shows the baseline PRL position for that sample subject.

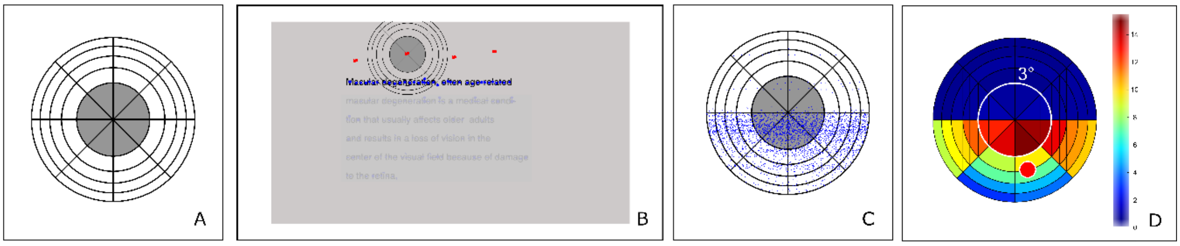

Fig 19: Panel A shows the radial grid used for the determination of the PRL on the text reading task. The grid is divided into blocks of equal areas. The distance between the edge of the scotoma and the edge of the grid spans 3.7 degrees of visual angle. Panel B shows an example of the grid located at the center of the second fixation (red dot). The blue dots correspond to the centroids of each letter. Panel C shows the centroid positions relative to the scotoma for all fixations after the performance of the task. Panel D shows the resultant percentage of hits per block once all the fixations are analyzed. Warm colors represent a relatively high percentage. Additionally, the red dot corresponds to the subject`s baseline PRL.

4.4. Results

4.4.1. Baseline: acquisition of PRL location

Prior to this study, ten out of fifteen subjects developed a PRL that was induced using systematic stimulus relocations, the other five subjects had a PRL developed without an inducement procedure (Barraza-Bernal et al., 2017). The baseline PRL position was acquired from fixation during the four saccade tasks. The position of highest fixation density was defined as the PRL location. Fig **20** shows the baseline PRL locations of every subject from left induced PRL (blue squares), right induced PRL (red squares) and not induced PRL (black diamonds) groups, which also correspond to the final performance assessment presented in Barraza-Bernal et al., 2017. These baseline PRL locations were compared to the PRL locations used during everyday life visual tasks.

Fig **20** shows that all but two subjects developed a PRL outside of the scotoma. Subjects 12 and 13 alternated the fixations between two locations (inside and outside of the scotoma) suggesting that right induced PRLs may be more difficult to develop.

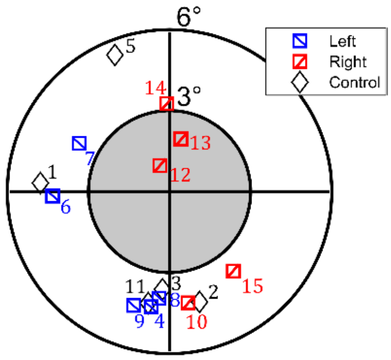

Fig 20: Baseline PRL positions of every subject. PRL positions of the left induced group are shown in blue, of the right induced group in red. The black diamonds show the PRL positions of the subjects without inducement. The numbers correspond to the subject number.

4.4.2. Transfer of PRL to smooth pursuit eye movements

The smooth pursuit fixation maps for every subject are shown in Fig S3. The PRL location was compared with the baseline PRL location. Fig **21** A shows bars that represent the radius of the baseline PRL, which was defined to be the 68th percentile of the distances obtained between the baseline PRL location and every gaze point during fixation. The black dot represents the Euclidean distance between baseline PRL and transferred PRL. This is shown for all subjects. The groups are distinguished by colors, where blue corresponds to the left induced group, red to the right induced group and gray to the naturally developed PRL group. A black dot within the bar indicates that the transferred PRL is located within the radius of the baseline PRL extend. For subject number 5 the mean radius of baseline PRL was large because the subject developed two PRLs, one above the scotoma and another one below the scotoma. The mean distance between baseline PRL and pursuit PRL positions for all subjects from the left induced group was 0.97 ± 0.26 degrees of visual angle, and for the subjects from the right induced group was 1.55 ± 1.35 degrees of visual angle. The mean Transfer Ratio R_T was calculated by dividing the distance between the PRLs over the radius of the baseline PRL. R_T was 0.29 ± 0.06 for the left induced group, 0.49 ± 0.55 for the right induced group and 0.57 ± 0.43 for the subjects without the inducement procedure. The R_T values obtained for all subject are significantly smaller than one (one sample t-test,

$t_{(14)} = -5.3$, $p < 0.01$). Thus, the results suggested a transfer from saccadic task to smooth pursuit eye movements.

Fig **21** B shows the PRL location for the pursuit task connected to their corresponding baseline PRL position for the three groups and illustrates the transfer of the PRL, as well as the maintenance of the induced hemifield.

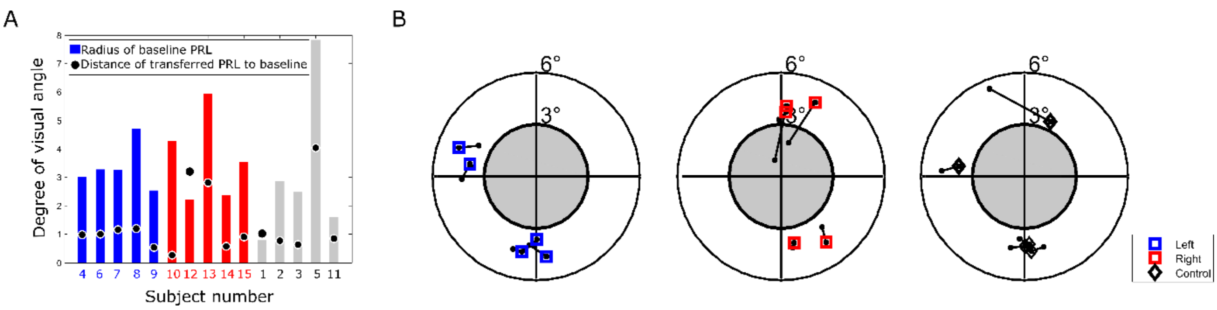

Fig 21: A: Radius of the baseline PRL for every subject (bars) and the distance between the pursuit PRL and the baseline PRL (black dot). B: PRL position for the pursuit PRL connected to the baseline PRL position (black dot) for the three groups.

In Barraza-Bernal et al., 2017, subjects 12 and 13 alternated the fixations between inside and outside of the scotoma. This behavior suggested that right induced PRLs may be more difficult to develop. However, Fig **21** B shows that the subjects brought the PRL from the scotoma region to a location out of the scotoma, indicating a further progression of PRL development. Subjects without the inducement procedure showed a mean distance between baseline PRL and pursuit PRL of 1.46 ± 1.44 degrees of visual angle and only one subject showed a pursuit PRL located out of the radius of the baseline PRL (subject 1). Thus, PRLs induced under a saccadic evoking paradigm transfer to a pursuit task.

4.4.3. Transfer of PRL to reading task

Signage reading task

Fig **22** A shows bars representing the radius of the baseline PRL together with a black dot that represents the distance of the signage reading PRL to the baseline PRL. The mean distance between the baseline PRL and the signage reading PRL for the subjects from the left induced group and the right induced group were 3.57 ± 1.78 degrees of visual angle and 1.62 ± 1.11 degrees of visual angle, respectively. Subjects from the control group showed a mean distance between baseline PRL and signage reading PRL of 2.8 ± 1.88 degrees of visual angle.

The mean Transfer Ratio R_T for the left induced group was 1.05 ± 0.50, for the right induced group was 0.42 ± 0.27 and for the subjects without the inducement procedure was 2.02 ± 3.08. Additionally, the R_T values obtained for all subject were not significantly smaller than one (one sample t-test, $t_{(14)} = 0.36$, $p = 0.72$). This suggested a general lack of PRL transfer for this task. The PRL positions change may be a change based on a functionality driven selection mechanism.

Fig **22** B shows the PRL location for the signage reading connected to their corresponding baseline PRL position for the three groups and confirm that subjects from the left induced group changed the PRL from the left hemifield to a point below the scotoma.

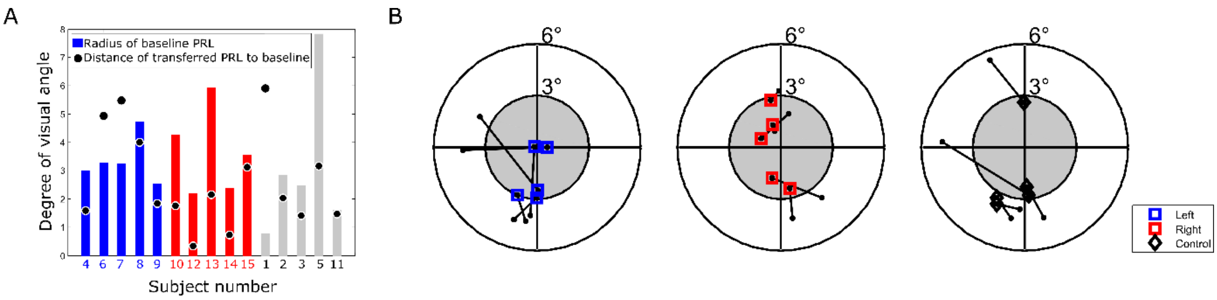

Fig 22: A: Radius of the baseline PRL for every subject (bars) and the distance between the reading PRL and the baseline PRL (black dot). B: PRL position for the signage reading task connected to the baseline PRL position (black dot) for the three groups.

Fig **22** B suggest that subjects locate the PRL inside the scotoma. But, considering the size of the stimulus, the pattern rather shows, that the subjects placed the text as centered as possible. At the chosen positions, the size of the stimulus was big enough to leave one part of the letters visible. One example text position is shown in Fig **23**. It demonstrates that a portion of the letters is visible.

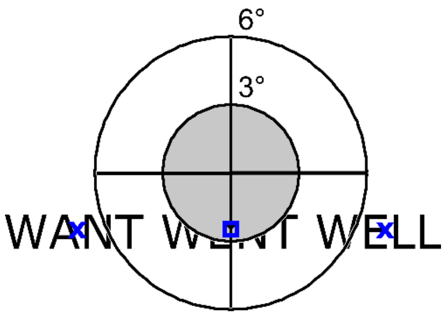

Fig 23: Example of a subject with a PRL location seemingly inside the scotoma. The example shows blue crosses corresponding to the center of mass of each word. When the center of mass of the word on the center is located at the PRL position, a portion of the word is still visible and can be used for the performance of the task.

Text reading task

The mean fixation duration of all subjects ranged between 212 and 314 ms and overall, the mean time spent during fixations was 272 ± 33 ms.

The percentage of hits per radial block was plotted together with the baseline PRL for every subject in Fig **24**.

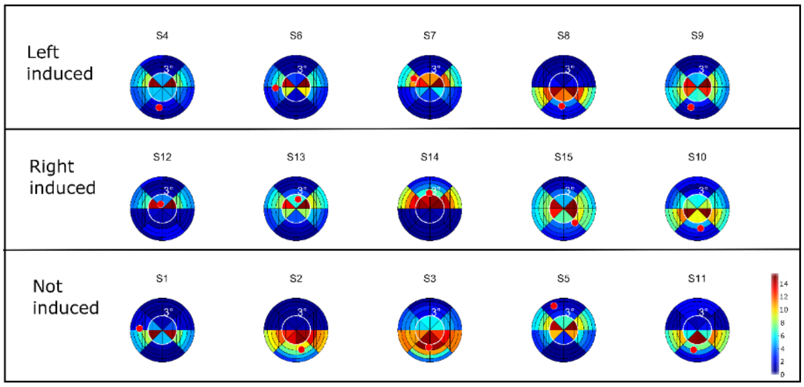

Fig 24: Areas used for the text reading task. Each diagram represents the reading pattern of a subject. The diagrams are divided into blocks of equal area. The color represents the percentage of times that a letter was located in the block. The red dot shows the baseline PRL position. The upper array corresponds to subjects from the left induced group, the middle to subjects from the right induced group and the lower to the subjects that developed a PRL without an inducement procedure.

Due to the distribution of words on the left and right of the scotoma, the exact fixated word is unknown, thus, only the vertical position of a PRL is assessable. Therefore, we compare this results to the baseline vertical position.

To distinguish between PRLs located above versus below the scotoma, the perceptual window was divided into four quadrants as shown in Fig **25**. Quadrant 2 and 4 were contrasted, leaving the influence of the words that were located on the left or right side of the scotoma unconsidered (quadrants 1 and 3). The total percentage of hits in quadrant 2 P_{Q2} and quadrant 4 P_{Q4} were calculated and subsequently, the ratio R (equation 5) was calculated.

$$R = \frac{P_{Q2} - P_{Q4}}{P_{Q2} + P_{Q4}} \tag{5}$$

This ratio classified the position of the PRL in terms of up or down; every value above 0 corresponded to a PRL located above the scotoma and every value below 0 corresponded to a PRL located below the scotoma.

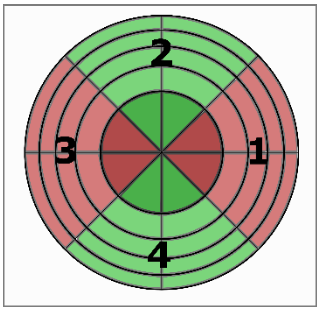

Fig 25: Division of quadrants for the calculation of ratio R.

Fig **26** shows the ratios for every subject (unfilled). For comparison, the vertical location of the baseline PRL is presented for each subject (filled). The diagrams show that subjects kept their PRL position close to the baseline position. Furthermore, all but two subjects (subject 6 and subject 1) maintained their vertical PRL location. This suggests that the vertical location of the PRL is maintained in a text reading task.

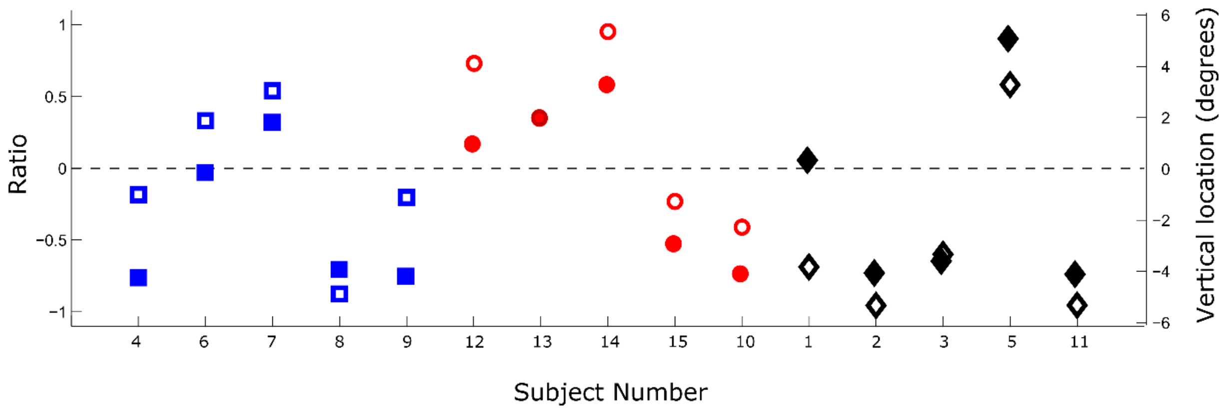

Fig 26: Ratio quantifying the vertical location of the PRL for text reading (unfilled points) and vertical location of the baseline PRL (filled points). Values above the zero line correspond to PRLs located on the upper visual field and values below the zero line to PRLs located on the lower visual field.

4.4.4. Retention of the PRL position

Short term retention

Short term retention of saccadic behavior

The retention was tested six to seven weeks after the initial PRL development. Fig **27** A shows bars representing the radius of the baseline PRL together with a black dot that represents the distance of the retention-saccade PRL to the baseline PRL. The mean distance between baseline PRL and saccade PRL for the subjects from the left induced group was 2.19 ± 1.77 degrees of visual angle, for the subjects from the right induced group it was 1.47 ± 1.42 degrees of visual angle. The mean distance between baseline PRL and retention PRL for the subjects without an induced PRL was 0.92 ± 0.98 degrees of visual angle.

The mean Transfer Ratio R_T for the left induced group was 0.67 ± 0.54, for the right induced group was 0.36 ± 0.18 and for the subjects without the inducement procedure was 0.32 ± 0.21. The R_T values were significantly smaller than one (one sample t-test, $t_{(14)} = -5.81$, $p < 0.01$). This suggested a transfer of PRL.

Fig **27** B shows the PRL location for the retention-saccadic task connected to their corresponding baseline PRL position for the three groups and confirm a general retention of PRL and also a maintenance of the induced hemifield.

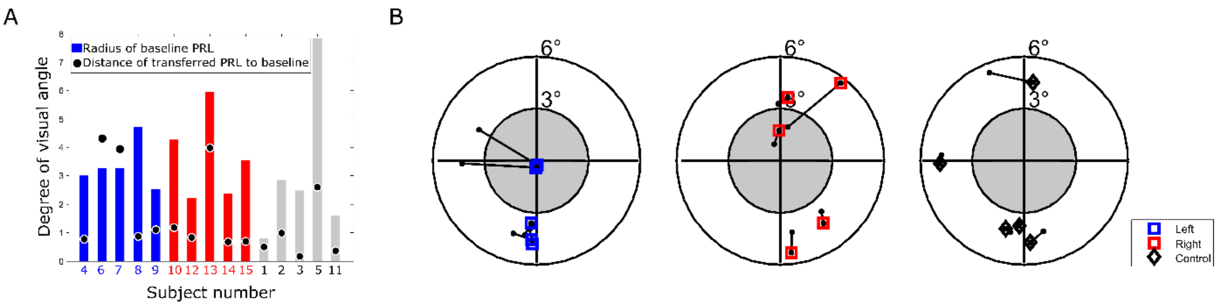

Fig 27: A: Radius of the baseline PRL for every subject (bars) and the distance between the retention-saccadic PRL and the baseline PRL (black dot). B: PRL position for the retention-saccadic task connected to the baseline PRL position (black dot) for the three groups.

Fig **27** B also shows that three subjects presented fixations inside the scotoma, two from the left induced group and one from the right induced group. The two subjects from the left induced group seemed to lose their developed PRL and moved it to the center of the scotoma whereas the subject from the right induced group had a baseline PRL inside the scotoma. In these cases, the subjects alternated the fixations between their baseline PRL location and the center of the scotoma. Fig **28** shows the fixations for both subjects (subjects 6 and 7) that were alternated between the PRL and the center of the scotoma, suggesting that the induced PRL was partially retained. Only for comparison, two subjects that retained the PRL are shown below (subjects 4 and 15).

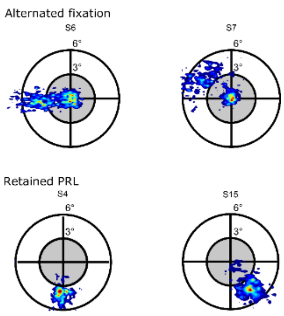

Fig 28: The fixation maps of subjects 6 and 7, alternating fixations between regions outside of the scotoma and the center of the scotoma. The regions outside of the scotoma corresponded to the regions of their trained PRL, suggesting that the induced PRL was partially retained. For comparison, two subjects that retained the PRL at their respective trained PRL location are shown below (Subjects S4 and S15).

Short-term retention of pursuit eye movements

Fig **29** A shows bars representing the radius of the baseline PRL together with a black dot that represents the distance of the retention-pursuit PRL to the baseline PRL. The mean distance between the baseline PRL and pursuit PRL was 1.26 ± 0.89 degrees of visual angle in the left induced group. In the right induced group it was 2.21 ± 1.52 degrees of visual angle. The subjects without an induced PRL showed a mean distance between the baseline PRL and pursuit PRL of 1.30 ± 1.33 degrees of visual angle.

The mean Transfer Ratio R_T for the left induced group was 0.38 ± 0.27, for the right induced group was 0.65 ± 0.43 and for the subjects without the inducement procedure was 0.55 ± 0.52. Additionally, the R_T values obtained for all subject were significantly smaller than one (one sample t-test, $t_{(14)} = -4.52$, $p < 0.01$), suggesting a transfer of PRL.

Moreover, Fig **29** B shows the PRL location for the retention-pursuit task connected to their corresponding baseline PRL position for the three groups and confirm the retention of the PRL as well as the maintenance of the induced hemifield.

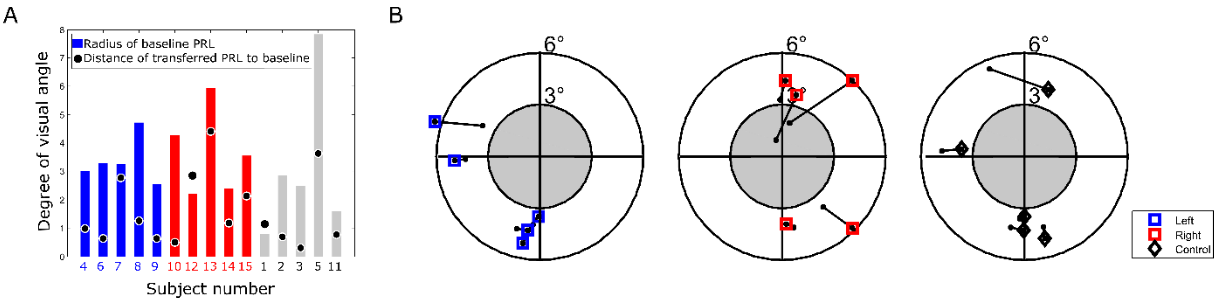

Fig 29: A: Radius of the baseline PRL for every subject (bars) and the distance between the retention-pursuit PRL and the baseline PRL (black dot) after six to seven weeks without simulation of central scotoma. B: PRL position for the retention-pursuit PRL connected to the baseline PRL position (black dot) for the three groups.

The same subjects that brought the PRL to a location outside of the scotoma in the pursuit task, kept the pursuit PRL 6 to 7 weeks after the task performance. These results showed retention of both left and right induced PRLs and suggest that inducing procedures using saccadic evoking tasks have long lasting effects.

Long term retention

A total of five subjects were recruited for the measurement of long term retention, one from the left induced group, two from the right induced group and two subjects with a freely developed PRL. The two subjects from the right induced group were recruited 11 month after the performance of Session I. The subject from the left induced group and not induced PRL were recruited 25 month after the performance of Session I. Fig **30** A shows bars representing the radius of the baseline PRL together with a black dot that represents the distance of the long term retention PRL to the baseline PRL. The distance between baseline PRL and retention PRL for the subject from the left induced group was 1.12 degrees of visual angle, whereas the mean distance between baseline PRL and retention PRL for the two subjects from the right induced group was 0.61 ± 0.15 degrees of visual angle. The two subjects with a self-chosen PRL showed a mean distance between the baseline PRL and long term retained PRL of 0.84 ± 0.04 degrees of visual angle.

The Transfer Ratio R_T for the subject from the left induced group was 0.34, for the both subjects from the right induced group was 0.16 ± 0.02 and for both subjects without the inducement procedure was 0.69 ± 0.58. Additionally, the R_T values obtained for all subject were significantly smaller than one (one sample t-test, $t_{(4)}$= -3.33, p = 0.02). This showed that even years after PRL development, some subjects retained the PRL.

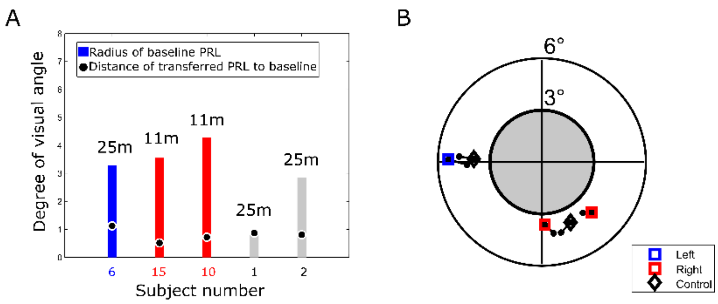

Fig 30: A: Radius of the baseline PRL (bars) for the subject recruited and the distance between the long term retention PRL and the baseline PRL (black dot). The retention time is shown above each bar (months). B: PRL position for the long term retention PRL connected to the baseline PRL position (black dot) for the three groups.

4.5. DISCUSSION

The way that individuals position their eye during eccentric fixation has been studied under different oculomotor visual tasks, for example, walking, doing sports, or making sandwiches and tea. Fixation locations are shown to optimize performance with respect to the spatio-temporal demand of the task (Land et al., 1994, 1997, 1999; Hayhoe et al., 2003; Turano et al., 2003). Already Yarbus's work (1967) revealed the intrinsic cognitive nature of eye movements and demonstrated the importance of the instructions in the determination of fixation location during the passive inspection of visual scenes. These specific patterns of eye movements were also reported to be idiosyncratic (Andrews et al., 1999) and suggest that fixational behavior during active visual tasks, like reading or visual search, differs from that during the performance of a passive inspection of a visual scene. In this study, PRL positions were studied under the performance of different visual tasks: pursuit, signage reading, and text reading.

The first visual task was pursuit eye movements. Pursuit depends on a number of stimulus parameters. Target luminance, size and position on the visual field can influence the latency and gain of pursuit (Westheimer et al., 1975). Also, pursuit ensures optimal vision only when the target is moving slowly, since the visual acuity starts to decrease when the retinal image velocity exceeds 3 deg/s (Westheimer et al., 1975). Furthermore, when the amplitude or frequency of the target is increased, the smooth moving eye starts to lag behind the target and its velocity becomes smaller (Fuchs et al., 1967; Collewijn et al., 1984; Yasui et al., 1984). All these influential parameters may have tuned the induced PRL location, however, our results showed a transfer of induced PRL to pursuit PRL. Furthermore, induced PRLs were maintained at their induced location. In two cases, the PRL was moved outside of the scotoma, which suggested that the pursuit task may be facilitating the performance of the eccentric fixation.

Our data also supports other studies that already demonstrated a fast and consistent oculomotor adaptation to a simulated central scotoma under pursuit eye movements (Pidcoe et al., 2006). Furthermore, it is known that the neuronal substrate of pursuit and saccades differ strongly. Nonetheless, transfer of PRLs induced by saccadic training to pursuit tasks was shown.

The second task tested was reading. Also in this task, a variety of influencing factors exist. When reading a text or paragraph, the eye movements are affected by the syntax of the sentence (Rayner et al., 1987) and the complexity of the words of interest (Pollatsek et al., 1985, 1986; Zola et al., 1984). These sets of visual parameters may influence even more significantly the visual behavior at the presence of the central scotoma.

Timberlake et al., (1987) examined fixation patterns in patients with macular scotoma and reported that a single retinal area was used for reading words composed of three letters, but when some of the patients were instructed to use another alternative region for fixation, there was a small improvement on reading speed. This suggested that the PRL used during signage reading might not be the best for reading a text. We investigated signage reading and found that the subjects from the left induced group did not transfer the PRL position. Some showed central fixation and a distance between the signage reading and the baseline PRLs that were out of the baseline PRL range. These changes hint towards difficulties to transfer the PRL into the word reading task and must be taken into account on the development of training procedures.

Moreover, some subjects changed the PRL location from the left side of the scotoma to a position below the scotoma. This result supports that a PRL for left-to-right reading will preferentially be below the central scotoma (Whittaker et al., 1993; Guez et al., 1993; Petre et al., 2000; Deruaz et al., 2002; Chung et al., 2004; Frennesson et al., 2007). However, this effect was observed on both, induced PRL and naturally developed PRL.

The subjects from the right induced group kept a distance between signage reading and baseline PRL always within the range of baseline PRL radius, however, unlike in the pursuit task, the subjects located the reading PRL mainly on the scotoma. This can be attributed to the size of the letters. Eccentric fixations left a portion of the letters visible and maybe subjects used this portion for the performance of the task. Another possible explanation is a noisy control of the eye movements that may be attributed to the different conditions in which the scotoma was simulated or to the different inducing paradigms. In Barraza-Bernal et al., 2017 we controlled the oculomotor change by means of a PRL value. The analysis showed that subjects from left induced group and subjects without an a PRL inducement improved the fixation behavior significantly after three training sessions, nevertheless, subjects from the right induced group did not show a significant improvement of oculomotor behavior. Perhaps, this deficit on oculomotor control was the factor reflected on the signage reading task.

We investigated text reading and found that all but two subjects maintained their vertical PRL location. Two subjects showed changes on their vertical location, these were the same subjects which did not transfer their PRL to signage reading. The maintenance of vertical position may suggests a transfer of baseline PRL to text reading.

70% of the subjects presented a Ratio R below 0, indicating a vertical PRL location situated below the simulated scotoma. These results again support that PRLs for left-to-right reading are preferentially below the scotoma.

In normal reading, the fixation duration occurs during an average time between 200 and 250 ms (Sereno et al., 2003; O'Regan, 1980). In the text reading task, subjects used a longer average information-processing time of 272 ± 33 ms. This might be attributed to the decrease of visual acuity that makes it harder to identify words presented in parafoveal regions.

We also investigated the retention of the learned behavior. When saccadic behavior was tested six to seven weeks after the first session, we observed that all but two subjects kept the PRL in a region within the baseline PRL. This result suggests that PRLs can be maintained for weeks without simulation. Specifically, the induced locations maintained, suggesting that the PRL position was successfully induced. The retention was also tested with a pursuit task and we observed that all but two subjects maintained their PRL location and in addition, all PRL locations observed were consistent with the induced PRL location. The two subjects that changed their PRL, moved it to eccentric locations, suggesting that the pursuit movements might facilitate the performance of eccentric fixations.

Additionally, we investigated retention of the saccade task in five subjects after eleven months and twenty five months. Every subject retained the PRL and kept the induced PRL location. Kwon et al. (2013) also showed retention in periods of time between one week and one month. In our study we showed an unreported and longer period of retention. These long lasting effects suggest that the learned behavior can be considered permanent.

Regarding the number of PRLs, only one of fifteen subjects showed a development of two eccentric PRLs, which corresponds to the 6% of the subjects tested. In contrast, other studies on patients showed that a larger portion used more than one PRL during a simple fixation task (39% in Whittaker et al., 1988 and 44% in Crossland et al., 2005). The main difference between the numbers of PRLs used may be attributed to the size of the scotoma. Crossland et al., 2005 showed that multiple PRLs were more likely to occur if the scotoma size exceeded 20° and attributed this to a decrease of fixation stability when the target is presented at such a large eccentricities of the fovea.

The results presented can be summarized as follows: the induced PRL transferred to the pursuit eye movement PRLs and to the vertical component of the text reading PRLs. However, the induced PRL was not transferred to the signage reading PRLs. The induced PRLs were retained after a short period of time (six to seven weeks) under the performance of pursuit eye movements and saccadic eye movements. For every subject available, the induced PRLs were also retained after a long-term period of time (one to two years) under the performance of saccadic eye movements. However, since only five subjects were recruited after such long time period, the conclusion on the long-term retention are limited.

Although the present results provide first evidence on a selective transfer behavior of eccentric fixations, the reality of patients with central scotomas differs from the simulated conditions in a variety of ways. Laboratory conditions do not represent everyday life situations of patients with maculopathies in all its detail. Furthermore, performance is an important indicator for final training success in real life conditions. Thus, further studies might focus on the evaluation of task performance in a broad variety of tasks, as well as on the transfer of the presented findings to clinical training procedures.

4.6. CONCLUSION

We show a maintenance of PRL location when pursuit eye movements were evoked. Furthermore, we show a vertical maintenance of PRL location when text reading was performed. In signage reading, PRL position were adjusted to the low demand of the task, allowing part of the stimulus to be covered by the scotoma. In addition, the retention of the trained PRL was studied weeks and months after the last training procedure and subjects showed a retention of their PRL, both for induced and freely chosen PRL positions.

Thus, learned behavior can be transferred to an untrained visual task. This allows the training of specific visual tasks using other alternative visual tasks. For example, reading efficiency may be improved using saccade-evoking tasks. However, we showed that in some cases PRLs are still subject to the demand of the task, suggesting that trained PRLs do not prevent other selection mechanisms to change the PRL location. Thus, the trained PRL can be considered as a starting point to enhance the visual performance.

4.7. SUPPLEMENTARY MATERIAL

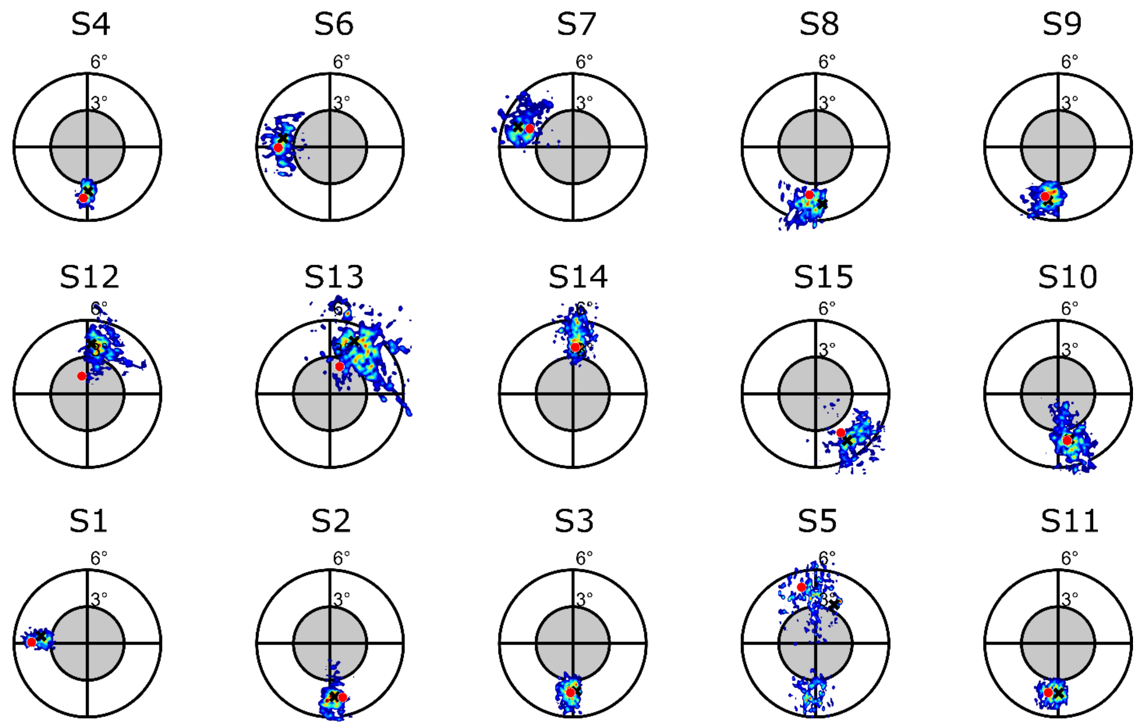

Fig S3: Fixation maps of every subject after the performance of the pursuit task. The black cross shows their respective PRL location. The red dot shows their baseline PRL. Subjects from the upper array corresponds to the subjects with the left induced PRL, from the middle array to the subjects with a right induced PRL and from the lower array to the subjects with a PRL developed without the inducement procedure.

5. CAN POSITIONS IN THE VISUAL FIELD WITH HIGH ATTENTIONAL CAPABILITIES BE GOOD CANDIDATES FOR A NEW PREFERRED RETINAL LOCUS?

Barraza-Bernal M.J.[1], Ivanov I. V. [1], Nill S.[1], Rifai K. [1], Trauzettel-Klosinski S.[2], & Wahl S[1]. (2017). Vision Research 140, 1-12.

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5.1. ABSTRACT

The sustained component of visual attention lowers the perceptual threshold of stimuli located at the attended region. Attentional performance is not equal for all eccentric positions, leading to variations in perception. The location of the preferred retinal locus (PRL) for fixation might be influenced by these attentional variations. This study investigated the relation between the placement of sustained attention and the location of a developed PRL using simulations of central scotoma. Thirteen normally sighted subjects participated in the study. Monocular sustained attention was measured in discrete eccentric locations of the visual field using the dominant eye. Subsequently, a six degrees macular scotoma was simulated and PRL training was performed during eight ten-minutes blocks of trials. After training, every subject developed a PRL. Subjects with high attentional capabilities in the lower hemifield generally developed PRLs in the lower hemifield (n = 10), subjects with high attentional capabilities in the upper hemifield developed PRLs in the upper hemifield (n = 2) and one subject with similar attentional capabilities in the upper and lower hemifield developed the PRL on the upper hemifield. Analyzed individually, the results showed that 70% of the subjects had a PRL location in the hemifield where high attentional performance was achieved. These results suggest that attentional capabilities can be used as a predictor for the development of the PRL and are of significance for low vision rehabilitation and for the development of new PRL training procedures, with the option for a preventive attentional training in early macular disease to develop a favorable PRL.

Keywords: sustained attention, preferred retinal locus, fixation

5.2. INTRODUCTION

Patients with maculopathies use undamaged retinal areas for fixation and other visual tasks. This shift of fixation to a peripheral retinal location is called “eccentric viewing” and the utilized area is called preferred retinal locus (PRL) for fixation (Cummings et al., 1985; Timberlake et al., 1987; Fletcher et al., 1997). It is defined as one or more circumscribed regions of functional retina that are repeatedly aligned with a target for a specific task. Researchers have extensively studied the PRL in terms of location, fixation stability, reading and cortical adaptations (Nilsson et al., 2003; Crossland et al., 2004, 2005; 2011; Cummings et al., 1985, 1992; Fine et al., 1999; Fletcher et al., 1997; Guez et al., 1993; Sunness et al., 1996; Trauzettel-Klosinski et al., 1996; Whittaker et al., 1988; Messias et al., 2007). However, the mechanisms responsible for a particular placement are not fully understood. Cheung (2005) summarized three hypotheses for the selection of the PRL. One of them is the function-dependent hypothesis. This hypothesis suggests that the selection of the PRL may be dictated by the suitability of the location to the specific visual task. It was shown that PRLs in the lower visual field are suitable in a range of important everyday tasks. For example, a PRL for left-to-right reading is preferred to be below the central scotoma, since only then the reader can estimate the amplitude of the eye movement towards the next word or towards the next line. Similarly, while navigating, important visual information to avoid obstacles is located in the lower visual field, and in this case PRLs in the lower visual field will be advantageous. Therefore, the function-dependent hypothesis predicts that the location of the new PRL will be positioned mostly in the lower visual field. Another hypothesis is the retinotopic hypothesis, which suggests that the selection of the PRL location is dependent on retinotopic reorganizations. In this case, neurons in the cortical area V1 remap to the inputs from retinal locations near the scotoma, leading to a selection of a PRL at the border of the central scotoma. This hypothesis predicts the PRL location at a region adjacent to the border of the scotoma. The last hypothesis corresponds to the performance-dependent hypothesis. It suggests that the PRL will be developed at retinal locations that can maximize visual performance. This hypothesis predicts that the PRL location is determined by regions of the retina with good visual acuity or, on the basis of visual attention, by regions of the retina with high attentional capabilities.

However, the three hypotheses might not be mutually exclusive and the same PRL location may be determined by different mechanisms. For example, in a large cohort of low vision patients with a macular scotoma, the PRL was observed to be near the scotoma and in the lower part of the visual field (Fletcher et al., 1997). In these cases, PRLs were developed at the proximity of the damaged retina as predicted by the retinotopic hypothesis and in the lower visual field as predicted by the function-dependent hypothesis for left-to-right reading. While this finding shows that the selection of the PRL might be explained by several mechanisms, the contribution of each mechanism to this selection is not yet understood.

In the present study, we investigated one of the hypotheses for the selection of the PRL. We addressed the question whether the locations with high attentional capabilities are candidates for this selection. The attentional capabilities were investigated using a sustained attention measurement. Sustained attention corresponds to a component of visual attention that allows individuals to deploy and keep attention on eccentric locations of the visual field by an effort of will. This component of visual attention lowers the perceptual threshold of stimuli located at the attended region (Nakayama et al., 1989). Altpeter et al. (2000) investigated the sustained attention in patients with macular disease at cued and attended discrete positions in the visual field. They reported that 57% of the tested subjects showed better performance in the lower hemifield, 16% of the subjects showed better performance in the upper hemifield, and 27% of the subjects showed similar performance in the upper and lower hemifields. In addition to these asymmetries, no differences in attentional performance between normally sighted people and patients suffering from small macular scotomas were found. Therefore, it was assumed that the attentional variations do not change from the pre-scotoma stage to the post-scotoma stage. They also compared the attentional performance of a centrally fixating eye with an eccentrically fixating fellow eye in patients with a macular scotoma and suggested a link between sustained attention and the placement of the PRL.

In the present study we investigated in the same eye of a subject if attentional performance and PRL selection are related. Sustained attention was measured using the procedure described by Altpeter et al. (2000) and the development of the PRL was studied using simulations of central scotomas. This kind of simulations lead to the development of a PRL (Pidcoe et al., 2006; Kwon et al., 2013). The bivariate contour ellipse area (BCEA) was used to express fixation stability, or variance (Steinman, 1965; Crossland et al., 2004). Thus, the BCEA allowed us to quantify the fixation quality of the subjects after the scotoma simulation. However, the BCEA does not provide an analysis of PRL location. Therefore, a separate analysis of the PRL location was used to show that significant changes of the BCEA were indeed due to the development of the PRL in eccentric locations and not due to refinements of foveal fixations. The location of the PRL was obtained using a bivariate kernel density estimator (Botev et al., 2010), where the location was defined to be at the peak density of the fixations (Kwon et al., 2013).

The prediction of PRL location based on attentional capabilities could be of significance for low vision rehabilitation. Patients with an early macular disease, who have an unfavorable distribution of their attentional capabilities, could receive an attentional or PRL training in order to develop a functionally favorable PRL location.

5.3. METHODS

5.3.1. Participants

Thirteen participants took part in the study, four males and nine females with ages between 20 and 30 years (mean 25.3 years). All subjects were naïve in regard to the purpose of the experiments. The study was performed with regard to the declaration of Helsinki and subjects gave their informed consent before their participation.

The subjects were required to have healthy eyes and visual acuity above or equal to 0.0 logMAR. Thus, subjects with a spherical ametropia higher than ± 0.75 D, or with an astigmatism higher than - 0.50 D were not eligible to participate in the study. Because of this limitation, none of the subjects had to be corrected to normal vision and therefore neither glasses nor contact lenses were worn. This was necessary to avoid unwanted reflections from glasses and contact lenses during the eye tracker data acquisition.

5.3.2. Study design

The experiment consisted of three sessions, each one separated by at least 24 hours. In the first session, objective refraction and a visual acuity measurement were performed to make sure that every participant had normal visual acuity. Subsequently, a measurement of sustained attention using the dominant eye was performed according to Altpeter et al. (2000).

In the second and third sessions, simulations of central scotoma were performed. A gaze contingent system was used for the simulation. This allowed to observe and study the development of the PRL (Bertera, 1988; Henderson et al., 1997; Whittaker et al., 1988; Fine et al., 1999; Sommerhalder et al., 2003; Cornelissen et al., 2005; Scherlen et al., 2008; Aguilar et al., 2011; McIlreavy et al., 2012; Kwon et al., 2013; Walsh et al., 2014; Pidcoe et al., 2006). Subjects had to solve a set of visual tasks while a gaze-contingent mask was presented at the prevailing eye position. Since the mask blocked central vision, subjects were forced to foveate eccentrically, and as a consequence, to develop a preferred retinal locus for fixation. Finally, the position of the newly developed PRL was compared with the positions of high attentional capabilities of each participant.

5.3.3. Apparatus

The objective refraction was carried out using an aberrometer (ZEISS i.Profiler plus; Carl Zeiss Vision GmbH, Germany). Visual acuity was measured using a standard Snellen chart (OCULUS Optikgeräte GmbH, Wetzlar, Germany) with a minimum contrast of 90% under a minimum luminescence of 300 cd/m^2.

The stimuli were presented on a ViewPixx/3D display with a vertical refresh rate of 100 Hz and a spatial resolution of 1920 x 1080 pixels.

Eye positional data were collected using the Eyelink 1000 Plus eye tracker for head fixed measurements (SR Research, Ltd., Ontario, Canada) and a gaze-contingent program written in MATLAB (MathWorks Inc, Natick, MA, USA). The program combined the Psychtoolbox (Brainard, 1997; Kleiner et al., 2007) and the Eyelink toolbox (Cornelissen et al., 2002) to present a set of gaze-dependent and gaze-independent stimuli. The gaze-dependent stimulus was a foveally centered circular mask, the repositioning of which was delayed by less than 20 ms after the eye position was detected. The gaze-independent stimulus was a saccade target. The saccade target had multiple components that were used in combination with a discrimination task to increase the fixation time of the subjects. Vertical and horizontal positions of the eye were recorded at 1 kHz.

A chin rest was used to minimize movements of the head and to hold the eyes at a distance of 66.6 cm from the display.

5.3.4. Stimuli and procedure

Preliminary visual assessment and sustained attention

The objective refraction, visual acuity measurement and determination of dominant eye were performed in an illuminated room, whereas every subsequent experiment was conducted in a dark room. Eye dominance was assessed by asking subjects to look through the pinhole at the biggest letter on a Snellen chart, located six meter away from them. The eye used to look through the hole was assumed to be the dominant eye. This eye was used to measure sustained attention and simulate the scotoma, while the other eye was patched.

The procedure for the sustained attention measurement can be seen in Fig **31**, left. A fixation cross was presented in the center of the screen for one second. Afterwards, a red cue appeared at an eccentricity of 8 degrees for one second, indicating the location in which the target will be presented. The locations tested were placed at 8 degrees eccentricity along different meridians in 45° increments from 0° to 315°. The red cue had been shown to improve the subjects' performance and activated the sustained component of visual attention (MacKeben, 1999). Subjects were asked to deploy their attention on the cued location while keeping fixation on the central cross. After a random time between 2.5 to 4 seconds, a Snellen E appeared in the cued location. The preliminary tests determined the size and duration of the Snellen E presentation (see paragraph below). In this study, the Snellen E presented in the sustained attention measurement was 40 arcmin for two subjects and 34 arcmin for eleven subjects. The presentation time obtained for all subjects ranged between 60 and 160 ms and the mean presentation time was 124.6 ± 29.6 ms (SD). Seven distractors were presented together with the Snellen E in all other locations. Finally, to avoid afterimage effects, eight masks were presented for 100 ms in all 8 locations.

The task was to use the arrow keys to report the orientation of the Snellen E, which was presented with the opening to the right, left, up or down. This procedure continued in a pseudo-random fashion until the stimulus was presented at each location 12 times. Eye movements were monitored using the eye tracker, and every time the participant performed an eye movement that broke fixation on the cross, the trial was aborted and repeated directly after the trial. The right panel of Fig **31** shows a schematic representing recognition performance of the subject at the eight tested locations. The percentage of correct responses is represented by the length of the radius for each tested location. Neighboring blue dots are connected linearly, using a blue dotted line. The connections stressed the performance differences between hemifields.

To ensure that the local differences in attentional performance reflected indeed the properties of sustained attention, two preliminary tests were performed according to Altpeter et al. (2000). Each test was performed following the procedure shown in Fig **31**. In the first test, we determined the size and presentation time of the stimulus for each subject. The initial stimulus size was 34 arcmin and the presentation duration was incremented in steps of 20 ms until the subject answered 75% of the times correctly in at least two of the eight tested locations. In case the subject did not perform well with that size and a maximum of 200 ms of duration time, the size of the target was increased to 40 arcmin. The second preliminary test was performed to ensure that the subject´s performance was not limited by spatial resolution. The stimulus was presented at a pre-determined size (see above) in all eight locations for a duration of 1s. The experiment continued only when all responses were correct.

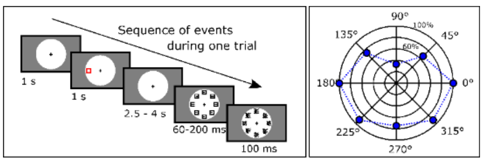

Fig 31: The left panel shows the events occurring during one trial of the sustained attention measurements. The right panel shows an example of a diagram resulting from the measurements. The diagram shows the recognition performance of the subject in the eight locations tested. The length of the radius to each position shows the percentage of correct responses.

Simulation of a central scotoma

The simulation consisted of a foveally presented circular disk of 6 degrees diameter. The background luminance of the screen and disk was 64 cd/m^2, and their color was identical (dark gray). The outline of the disk was drawn to help subjects to orient their saccades. In total, there were two simulation sessions, each divided into four training blocks. The main task was to discriminate the components of a stimulus that was presented at varying screen positions.

Fig **32** shows the events occurring during the simulation. At the beginning of the PRL development, subjects foveated the stimulus and, as a consequence, it disappeared behind the scotoma. After some training, subjects began to suppress the normal foveating mechanism and learned to fixate the stimulus eccentrically. The figures on the right show the collected fixations at the two different stages of the PRL development.

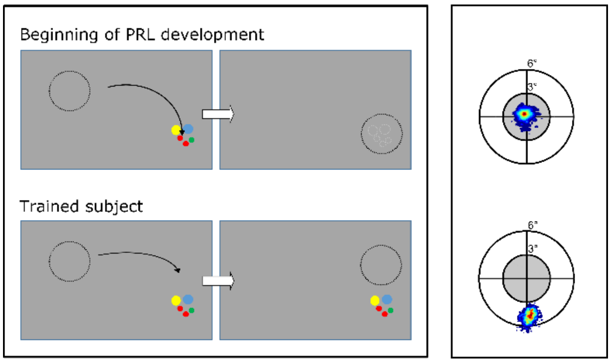

Fig 32: The figure on the left shows the simulation of a central scotoma. The upper half shows that, at the beginning of the PRL development, eye movements placed the scotoma on top of the stimulus. The lower half shows that after some training, the eye movements were re-directed and fixation was now performed eccentrically. The right panel shows examples of the fixations performed at different stages of the development. The upper figure shows the fixations when the subject was at the beginning of the training and the lower figure when the subject is already trained after 8 training blocks of 10 minutes.

A 13-point calibration was performed at the beginning of each training block. This calibration collected fixation samples from 13 known target points in order to map raw eye position data to gaze. Subsequently, a validation with 13 points was performed to provide information about the calibration accuracy. The experiments continued only if the validation was confirmed to be good by the eye tracker.

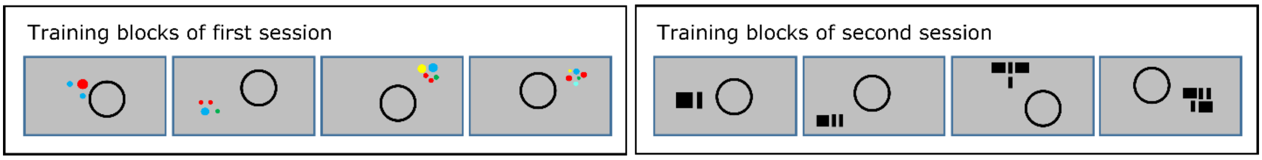

Fig 33: Example of stimuli presented during the first and second training sessions. Each training session was separated into four blocks of 10 minutes recording. In the first session, colored dots were presented and in each block a new color and dot was added. The location and size of the dots were randomized in every trial, but they were always distributed in an area spanning 1.5 degrees. Subjects had to judge whether there were more blue or more red dots. In the second session, squares and lines were presented. In each block, a new component (square or line) was added. The location of each component was randomly assigned. Subjects had to discriminate the components of the stimulus. For example, in the first block, they had to report whether the components were equal or different.

Fig 33 shows the stimuli for the first and second training sessions. In each session, a stimulus that evokes a saccade was presented (saccade stimulus). The stimulus consisted of a number of components that increased with the training block to introduce crowding effects. Given that crowding decreases the performance during eccentric viewing of a stimulus (Wallace et al., 2013) the new component increased the task complexity and therefore kept the subjects challenged. The main difference between the training sessions was that in session I the discrimination of the stimuli required a color discrimination, and in session II a shape discrimination. The different discriminations were selected in order to increase the complexity of the task over the training period. Overall, the distribution of the components spanned 1.5 degrees.

In session I, the colored dots were randomly distributed around a pre-determined center of mass. A new dot and color were added in each training block. The task was to differentiate between red and blue dots and report whether there were more red or blue dots. Subjects used the up and down arrow keys to report whether there were more red or blue dots.

In session II, the stimulus was a combination of squares and lines. In the first block, the components were a combination of either two lines, two squares or a square and a line. Subjects had to report whether the components were equal or different. In case they were equal (e.g., two squares), subjects used the space key to mark both components red and reported that they were equal using the up arrow key. In case they were different (a square and a line), subjects used the space key to mark only the square red and reported that they were different using the down arrow key. In the second block the stimulus was a combination of three components that were randomly assigned to be squares or lines. Subjects used the space key to mark all squares red and to report whether there were more squares or lines. They used the up arrow key to report more squares and the down arrow key to report the occurrence of more lines.

In the third block the stimulus had four components that were randomly assigned to be squares or lines. Subjects used the space key to mark all squares red and reported whether the components were two lines and two squares or whether the components had a different arrangement, for example, only one line and three squares. Finally in the last block the stimulus was a combination of four components that were randomly assigned to be squares or lines. Subjects used the space key to mark all squares red and reported whether there were more squares or lines. They used the up arrow key to report more squares and the down arrow key to report more lines.

Eye position data were collected during 10 minutes in each training block, but because a recalibration was performed between the trials and the eye positional data were not collected during this recalibration, the complete block lasted longer than 10 minutes. On average, subjects performed 116.4 ± 56.5 trials ranging between 26 and 279 trials.

5.3.5. Data analysis

Development of the preferred retinal locus of fixation

To study the PRL development, fixational stability and the location of the PRL were analyzed at different training stages. The fixations were separated from other events (blinks and saccades) using the Eyelink parsing algorithm. The algorithm classified fixations, saccades and blinks using a saccadic velocity threshold of 30°/s, a saccadic acceleration threshold of 8000°/s^2 and a saccadic motion threshold of 0.1° (Liu et al., 2016; Bethlehem et al., 2014; Lingnau et al., 2008; Smith et al., 2014; Van der Stigchel et al., 2013). Fixation stability or variance of the fixations was obtained by calculating the bivariate contour ellipse area (BCEA) of the fixation distributions (Steinman, 1965; Crossland et al., 2004) that encompassed 68% of fixations around the mean (Castet et al., 2012; Kwon et al., 2012; Liu et al., 2016). Small BCEAs corresponded to smaller fixation areas and therefore higher fixation stability. The location of the PRL was obtained from the kernel density estimation (Botev et al., 2010) of the fixations and was defined to be the one at the peak density (Kwon et al., 2012).

Sustained attention

The separation of groups based on the subjects' performance with cued attention was implemented using the ratio R_g between the performance levels at the 90° and at the 270° locations (per(90) and per(270)) for the percentage of correct responses. For comparison, this separation was performed using the methods of Altpeter et al. (2000).

$$R_g = \left(\frac{\mathrm{per}(90)}{\mathrm{per}(270)}\right) \tag{6}$$

G1: $R_g < 0.8$ reduced performance in the upper location.

G2: $R_g > 1.2$ reduced performance in the lower location.

G3: $1.2 \geq R_g \geq 0.8$ similar performance in the upper and lower location.

Development of the PRL combined with sustained attention

The number of eccentric fixations R_{fix} was quantified by calculating the number of fixations outside of the scotoma F_O divided by the total number of fixations F_T (equation 7).

$$R_{fix} = \left(\frac{F_O}{F_T}\right) \tag{7}$$

R_{fix} was obtained from all the fixations collected in a training block. This value was calculated for the eight performed training blocks and subsequently, the eight R_{fix} values were normalized to the subjects highest R_{fix}. In the normalized quantity R_{fixN}, values close to one represented training blocks in which the stimulus was fixated outside the scotoma. To compare the fixational behavior with the recognition performance mediated by sustained attention, three training sessions for each subject were selected. The selected training sessions corresponded to different stages of scotoma development. We investigated the first training session, in which R_{fixN} was equal or above 0.5, the first training session in which R_{fixN} was equal or above 0.75, and finally the training session in which R_{fixN} was 1. The number of training blocks needed to reach $R_{fixN} \geq 0.5$ was 1.3 ± 0.5 blocks, ranging between the 1st and 2nd block. The number to reach $R_{fixN} \geq 0.75$ was 2.3 ± 1.5 blocks, ranging between the 2nd and 5th blocks. This showed that most of the subjects reached the first level of performance ($R_{fixN} \geq 0.5$) at about the same time, however, to reach the second level of performance ($R_{fixN} \geq 0.75$), subjects needed different times. The best level of performance, when $R_{fixN} = 1$, was reached at 5.9 ± 1.3 blocks of training that ranged between the 3rd and 8th blocks.

The eccentric fixations at each stage of the development ($R_{fixN} \geq 0.5$, $R_{fixN} \geq 0.75$ and $R_{fixN} = 1$) were translated to angle histograms. In the histograms, bins were centered at the same directions tested during the performance of the sustained attention measurement (0°, 45°, 90°, 135°, 180°, 225°, 270° and 315°).

Fig **34** shows on the left an example of a kernel density map after the performance of a training block, and on the right it shows the translation of these data to an angle histogram. The length of a bin is proportional to the number of eccentric fixations located within the bin range. In the example of Fig **34**, the bin centered at 270°

includes fixations at angular positions between 247.5° and 292.5°. This translation allowed a comparison between the locations with high attentional capabilities and the location of PRL development.

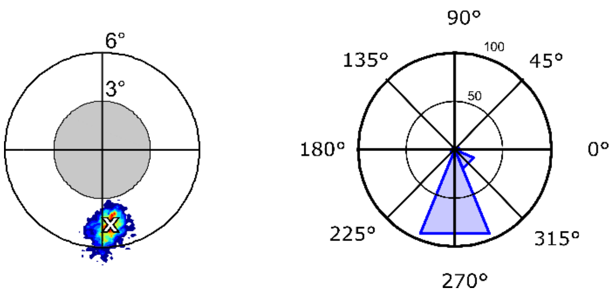

Fig 34: The diagram on the left shows an example of the fixations in a complete training block. The white cross shows the location of the PRL at the peak of the fixation density map. The gray circle at the center shows the area covered by the artificial scotoma. The figure on the right shows the angle histogram for the diagram presented on the left. In this case, the bin at 270° shows that most of the fixations were located in that direction. The angle histogram is divided into eight bins centered at the same angular locations tested on the sustained attention measurements.

Mean resultant vectors of the angle histograms were obtained to determine the direction of the mean PRL developed. The resultant vectors were calculated using the circular statistics toolbox (Berens, 2009).

5.4. RESULTS

Development of the preferred retinal locus for fixation, variance and location.

The mean variance (BCEA) of the fixations decreased significantly after eight training blocks of 10 minutes (Fig **35**, left). The mean variance of the fixations performed in the last training block was reduced by 55% in comparison to that of the first block (paired sample t-test, $t_{(12)} = 3.45$, $p < 0.01$). This result showed fast (80 minutes) adaptation of oculomotor behavior during the training.

To examine whether the significant decrease of the BCEA was combined with a re-direction of saccades in favor of eccentric locations, the location of the PRL was also determined. The location of the PRL was obtained by calculating the position in which the peak density of the fixations was located.

Fig **35** (right) shows the distance between the PRL to the center of the scotoma (or foveal location) as a function of the training blocks. We found a significant increase between the first training block and the last training block (paired sample t-test, $t_{(12)} = -3.12$, $p < 0.01$). Furthermore, the mean distance between fovea and PRL for all subjects at the end of the training was 4.87 ± 1.26 deg (standard deviation, SD), which shows that the newly acquired PRLs were located outside of the scotoma at the end of the training.

These results suggest that subjects located the scotoma on top of the stimulus at the beginning of the training. However, this behavior was suppressed as the training progressed and they learned to fixate eccentrically.

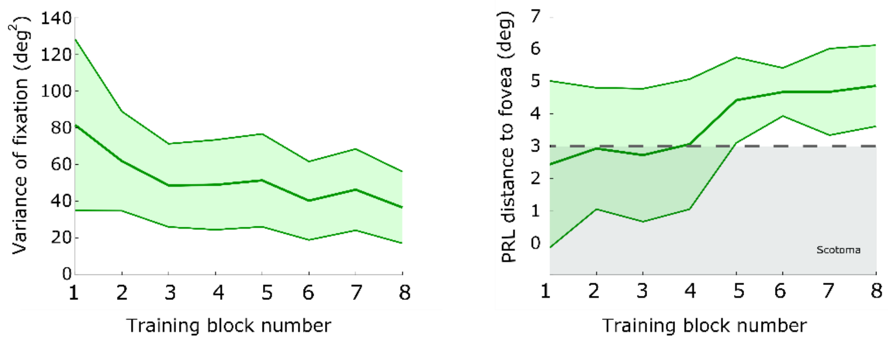

Fig 35: The diagram on the left shows the mean variance (BCEA) of fixations (y axis, deg2) as a function of the training block (x axis) for the 13 subjects. The right diagram shows the mean distance between fovea and PRL (y axis, deg) as a function of the training block (x axis). At the end of the training period, every subject had a significantly smaller BCEA and a mean PRL location situated outside of the scotoma.

Sustained attention and the development of the PRL, mean effects

The ratio R_g from the percentage of correct responses for the 90° and the 270° meridians was calculated. This allowed to separate the subjects into three groups: group one (G1) with ten subjects and a mean ratio R_g of 0.63 ± 0.17, group two (G2) with two subjects and a mean ratio R_g of 1.79 ± 0.30 (SD) and group three (G3) with one subject and a ratio R_g of 1. Results for each group were averaged and plotted in a single attention diagram. This helped to compare graphically the attentional trends with the distribution of the fixations around the scotoma.

Fig **36** shows the resultant attention diagrams for the different groups, G1, G2 and G3, where the mean percentage of correct response was calculated for every tested location. The distance between the center of the diagram and the blue dot represents the percentage of correct response for the eight tested locations at an eccentricity of 8 degrees. In addition, the blue arrow shows the mean resultant vector, which was calculated using the percentage of correct response for each orientation. To do so, the percentages of correct response for each orientation was transformed into a vector with the length indicating the percentage obtained and the angle indicating the orientation tested. The mean resultant vector was obtained using the circular statistics toolbox (Berens, 2009) which used the eight vectors as input. In the figure are shown the mean resultant vectors for G1, G2 and G3.

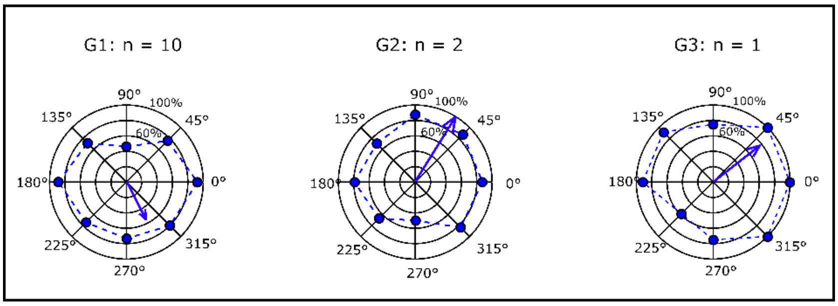

Fig 36: Recognition performance mediated by sustained attention for subjects from group 1 (G1: n = 10), group 2 (G2: n = 2) and group 3 (G3: n = 1). The distances between the blue dots and the center of the diagram represent the percentage of correct responses for the different locations tested. The separation of groups was performed using the ratio R_g between the location at 90° (per(90)) and the location at 270° (per (270)) for the percentage of correct responses. The blue vector shows the mean resultant for the respective attentional diagram.

In addition, the ratio of the mean percentage of correct responses on the vertical meridian (v = 90° + 270°) and the mean percentage of correct responses on the horizontal meridian (h = 0° + 180°) were calculated. The ratio (h/v) for all subjects was 1.48 ± 0.29 (SD), indicating better performance on the horizontal meridian.

Mean angle histograms of eccentric fixations were obtained for each group at the different stages of PRL development (Fig **37**). Histograms underlined red, green, and blue show the data for the stage when $R_{fixN} \geq 0.5$, $R_{fixN} \geq 0.75$, and $R_{fixN} = 1$, respectively. In the histograms, the red arrow represents the mean resultant vector obtained from the corresponding distributions. The length of the vector represents a measurement of circular spread. The longer the resultant vector, the more concentrated the data sample is around the mean direction.

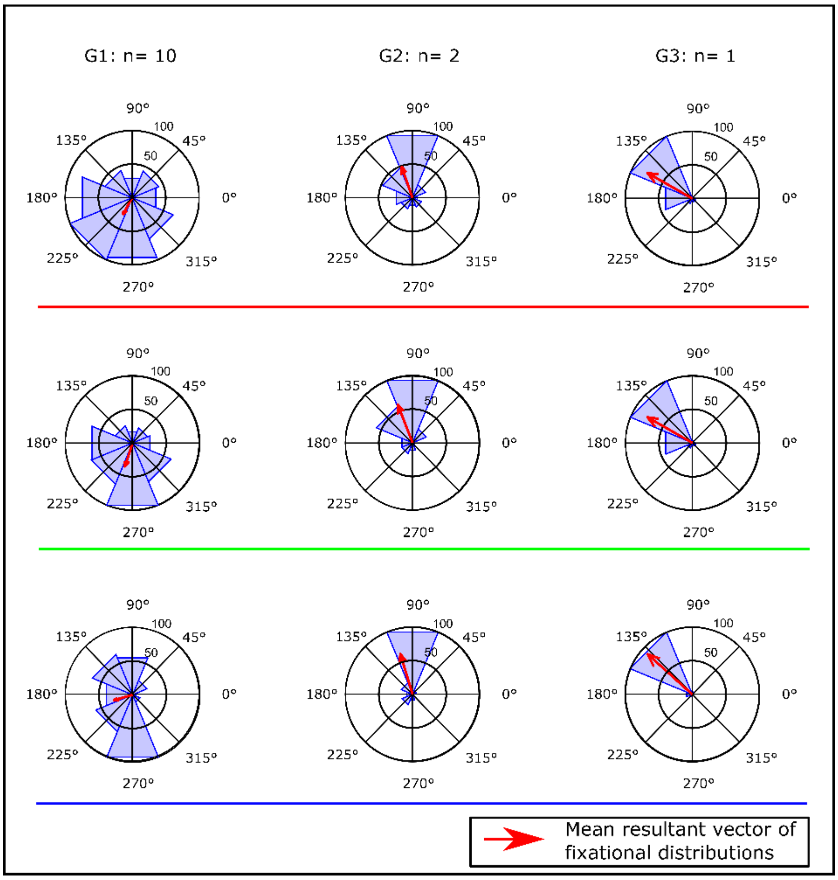

Fig 37: Mean distribution of eccentric fixations. The angle histograms were separated into three groups (G1, G2, and G3) based on the subject´s performance using cued sustained attention. Three different stages of the PRL development were analyzed (red, RfixN ≥ 0.5, green RfixN ≥ 0.75 and blue RfixN = 1). Red arrows show the mean resultant vector of the distribution of eccentric fixations. In G1 with 10 subjects, all vectors pointed to the lower hemifield, coinciding with the hemifield in which the higher recognition mediated by sustained attention was found. In G2 with 2 subjects, the vectors pointed to the upper hemifield, also coinciding with the hemifield where the higher recognition mediated by sustained attention was found. Finally in G3 with only one subject, the vectors also pointed to the hemifield where the best recognition mediated by sustained attention was found.

In G1, most of the eccentric fixations were distributed on the lower hemifield, independent of the stage of the development. The mean resultant vectors of the eccentric distributions pointed to the lower hemifield in all three stages, meaning that most of the eccentric fixations were located in the lower hemifield. Some eccentric fixations were also performed on the horizontal meridian during the first and second stage of development ($R_{fixN} \geq 0.5$ and $R_{fixN} \geq 0.75$). This behavior changed in the last stage ($R_{fixN} = 1$), where eccentric fixations were performed above the fixation cross. This was observed in four subjects who located the stimulus above the scotoma at the last stage of the PRL development.

In G2, most of the eccentric fixations were distributed in the upper hemifield, independent of the stage of the development. The mean resultant vectors of the eccentric distributions pointed to the upper hemifield in all three stages.

Finally, the eccentric fixations in the one subject with similar recognition performance above and below the fixation cross (G3) resulted in an oblique vector that pointed to the location at 135°.

The results for recognition performance mediated by sustained attention (Fig **36**) and fixation behavior (Fig **37**) are summarized in Fig **38**. The figure shows the mean resultant vector of performance with cued sustained attention (blue) and of the fixation behavior (red). The vector for the fixational behavior was obtained by averaging the vectors from the three different stages of PRL development. For subjects in G1, the absolute difference in direction between recognition performance and fixation vectors was 66.58°, while for G2 it was 49.34°, and for G3 it was 109.16°. These mean effects show that locations with high recognition performance and a newly developed PRL in group 1 and group 2 were found to be in the same hemifield of the visual field.

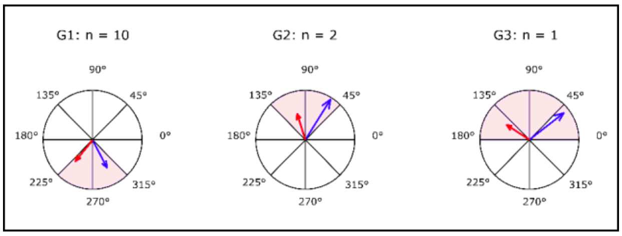

Fig 38: Summary of the mean recognition performance mediated by sustained attention and fixation distributions for subjects from the three groups. Red vectors represent the mean eccentric distributions for the three stages of the PRL development, while the blue vectors represent mean recognition performance mediated by sustained attention.

Sustained attention and the development of the PRL, individual differences

The results for the recognition performance mediated by sustained attention and for the development of the PRL were also analyzed separately in order to examine whether the mean effects were also reflected in each subject.

Fig **39** shows for each subject the diagram for recognition performance and the angle histogram for the eccentric fixations at the three different stages of the PRL development (red, $R_{fixN} \geq 0.5$, green $R_{fixN} \geq 0.75$ and blue $R_{fixN} = 1$). S1, S2, S3, S4, S5, S7, S9, S10, S11 and S13 correspond to subjects from G1 whereas S6 and S12 correspond to subjects from G2 and S8 is the subject from G3.

In the last stage of the PRL development, the fixational mean vector of nine subjects pointed to the hemifield where the subject's highest recognition performance was found (S2, S5, S6, S7, S8, S9, S11, S12 and S13), corresponding to approximately 70% of the participants. Four subjects from G1 showed distributions of eccentric fixations on the upper hemifield (S1, S3, S4 and S10).

The angular difference between the mean resultant vectors of attention and fixation distributions were calculated for all subjects at the three stages of the PRL development. For $R_{fixN} \geq 0.5$ it was 65.9 ± 38.1 degrees, for $R_{fixN} \geq 0.75$ it was 66.5 ± 38.2 degrees, and for $R_{fixN} = 1$ it was 86.0 ± 53.1 degrees. These values represent a portion of the circle that is lower than the 25%. Thus, they showed an overall relationship between attention and fixation at the three developmental stages.

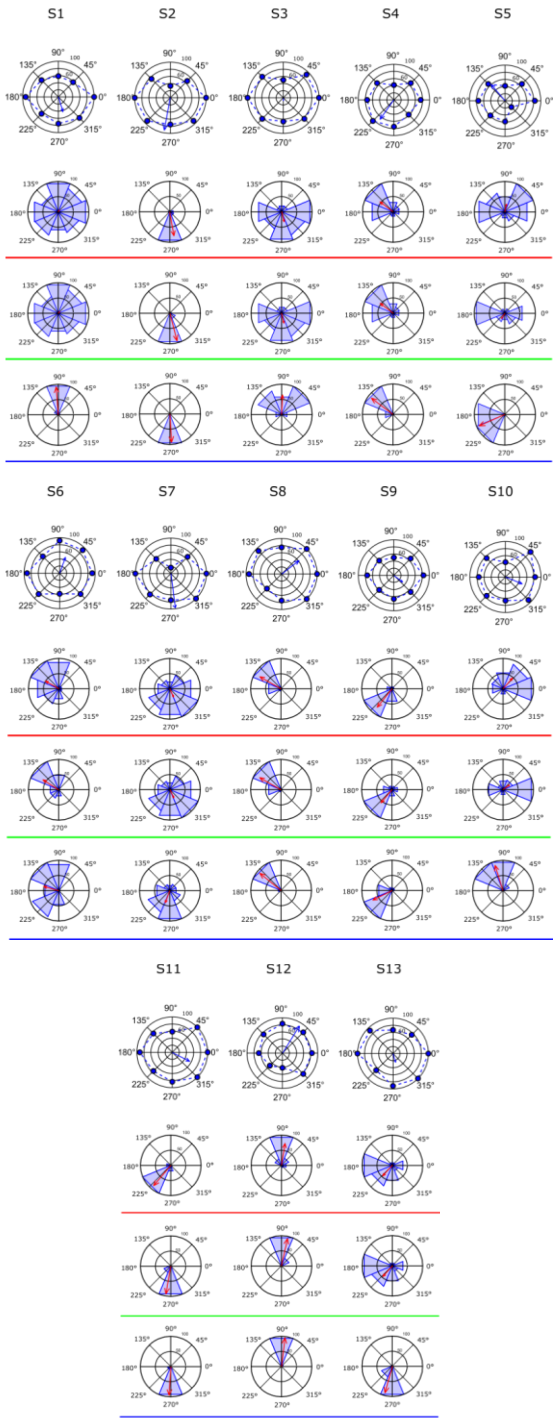

Fig 39: Individual results for the recognition performance mediated by sustained attention and the angle histogram at the three different stages of the PRL development (red, RfixN ≥ 0.5, green RfixN ≥ 0.75 and blue RfixN = 1). Blue vectors represent the mean resultant vector of the recognition performance and the red vectors represent the mean resultant vector of the distribution of eccentric fixations.

5.5. DISCUSSION

The measurements of recognition performance mediated by sustained attention showed that when the upper and lower hemifields are compared, ten subjects showed better attentional performance in the lower hemifield, whereas two showed better performance in the upper hemifield, and one showed similar levels of performance in the upper and lower hemifields. An analysis over all showed that the average distribution of eccentric fixations was consistent with the recognition performance mediated by sustained attention. Moreover, when the individual differences were analyzed, nine out of thirteen subjects turned out to relate recognition performance to the hemifield where the PRL was developed (six from G1, two from G2 and 1 from G3).

5.5.1. The horizontal versus vertical asymmetries in attention

Our results, in agreement with other studies (MacKeben, 1999; Altpeter et al., 2000; He et al., 1996), further demonstrate vertical asymmetries in the effectiveness of sustained attention, where better attentional capabilities were demonstrated in the lower than the upper visual field. Altpeter (2000) reported that 57% of the tested subjects with mostly juvenile maculopathies showed better performance in the lower hemifield, 16% of the subjects showed better performance in the upper hemifield and 27% of the subjects showed similar performance in both hemifields (upper and lower). This tendency was also observed in a study on healthy subjects, in which the sustained component of attention was used with a letter recognition paradigm (MacKeben, 1999). That study reported that 50% of the subjects showed difficulties to deploy the sustained attention on the upper hemifield, 33.3% of the subjects showed difficulties to deploy it in the lower hemifield, and 16.6% of the subjects showed difficulties to deploy it in the upper and lower hemifields. Furthermore, He (1996) found greater attentional resolution in the lower visual field in a total of 4 subjects. In the present study, the ratio R_g provided information about the hemifield with reduced attentional performance. The results showed that 76.9% of the subjects (n_{total} = 13) performed worse in the upper hemifield, 15.4% of the subjects performed worse in the lower hemifield and 7.7% of the subjects performed similarly in the upper and lower hemifield.

5.5.2. The development of the preferred retinal locus for fixation

Our results showed a significant decrease of variance of the fixations and a significant change in the PRL location. Moreover, at the end of the training, all subjects had developed a PRL outside of the scotoma.

The mean variance of the fixations (mean BCEA) obtained in the last block of training was 36.6 ± 19.5 (SD) deg^2. In contrast to our variance, other studies obtained lower variances when subjects performed with a simulated central scotoma. Kwon (2013) obtained variances below 10 deg^2 after 15 hours of explicit training. In the same way, Liu (2016) obtained BCEAs of the same size after only 6 to 10 hours of explicit training. The main difference in variance compared with our study can be attributed to the difference in training time. In the present study, eight training blocks were performed, which made a total time of 80 minutes. In addition, unlike in the previously mentioned studies, we did not instruct the subjects to use a specific region of the visual field using gaze cues. In the absence of such an explicit training, it was unlikely to obtain low variances and therefore high fixation stabilities. The low fixation stabilities at the end of the training constitute unstable PRLs. Given that one purpose of this study was to find out whether the performance-dependent hypothesis might explain the selection of the PRL location, the fixation stability did not play an important role. Moreover, explicit training only decreases the variance of the fixations, but does not influence the selection of the PRL location (Kwon et al., 2012; Liu et al., 2016). Thus, our training finished when the mean PRL position was located out of the scotoma and when we found a mean PRL position significantly different from the initial mean PRL position.

In addition, the rates of oculomotor learning were faster than those reported by Kwon et al. (2013). This might be attributed to the size of the simulated scotoma. The diameter of our scotoma was six degrees of visual angle, whereas the diameter of the scotoma simulated by Kwon et al. (2013) was ten degrees of visual angle.

These results supported previous findings that demonstrated that with a simulated central scotoma, the normal foveating behavior was replaced by a new saccadic behavior in favor of eccentric fixations. In addition, our results provide unreported evidence that a new PRL can be developed after only 80 minutes of training with a simulated scotoma.

5.5.3. Sustained attention and the development of the PRL, mean effects

Cheung (2005) summarized the three hypotheses for the development of the PRL as a function- dependent, performance-dependent and retinotopy-dependent hypothesis. The performance- dependent hypothesis postulated that the PRL selection might be triggered by the remaining retinal locations with good visual acuity or alternatively, with high attentional capabilities. In this study we provided data that compared the attentional performance of three groups (separated based on their attentional capabilities) with their selection of preferred retinal locus of fixation. The results showed that subjects with better attentional capabilities in the lower hemifield placed their PRL in that hemifield. This was supported by the mean resultant vectors obtained for both, fixational distributions around the scotoma and attentional mean direction. Both vectors were located in the same hemifield and their absolute directional difference was 66.58°. Besides that, subjects with better attentional deployment in the upper hemifield developed a PRL in the upper hemifield and the absolute difference between attentional and fixational vectors was 49.34°. This PRL development was in contradiction to the evidence reporting high prevalence to locate the PRL either below or on the left side of the scotoma (Guez et al., 1993; Trauzettel-Klosinski et al., 1996; Fletcher et al., 1997; Fletcher et al., 1994; Sunness et al., 1996; Cummings et al., 1992; Crossland et al., 2005), but was consistent with the performance-dependent hypothesis for the development of the PRL. Overall, the results showed that the mean distributions of eccentric fixations was consistent with the hemifield in which the high attentional performance was found.

The mean distance between fovea and PRL for all subjects at the end of the training was 4.87 degrees. Given that the radius of the scotoma was 3 deg, these results also support the retinotopic hypothesis for the development of the PRL, which predicts the selection of PRL at the border of the central scotoma.

The grouping of the subjects allowed an analysis based on the differences between the superior and inferior hemifields, but many subjects showed high attentional performance in the nasal and temporal hemifields. Thus, if the retinal locations with good attentional capabilities can indeed predict the PRL location, we would expect most of the PRLs to be to the left or right of the simulated scotoma. As this was not the case, we suggest that the selection of the PRL location might be influenced by the asymmetry of attentional capacity on the different meridians. If the attentional capability is symmetric on one meridian, which was the case for the horizontal meridian for most subjects, the PRL is unlikely to be located on that meridian. However, if the attentional capability is asymmetric on one meridian, which was the case for the vertical meridian, the PRL is likely to be developed at the location of that meridian with the higher attentional capability.

5.5.4. Sustained attention and the development of the PRL, individual differences

When the performance of the subjects was analyzed individually, the results showed that approximately 70% of the subjects (nine out of thirteen) presented a PRL location in the hemifield where high performance with consciously directed sustained attention was found. This result showed that, even if mean effects relate attentional capabilities to the development of the PRL, individual differences must be taken into account and suggest that attention may not be the only mechanisms that plays a role on the development of the PRL.

5.6. CONCLUSION

In the present study we used monocular simulations of central scotoma to address the question whether there is a relationship between the locations with high attentional capabilities in the visual field and the selection of the PRL. The results showed that overall, the development of the PRL was consistent with the attentional capabilities. Analyzed individually, nine of thirteen subjects presented a PRL location on the meridian with the highest asymmetry and at the location on that meridian where the highest attentional capability was achieved. These results supported previous findings that showed a link between locations with good attentional capabilities within the visual field and the development of the PRL. In addition, the findings supported the performance dependent hypothesis for the development of the PRL. Furthermore, it might help in the identification of future PRL locations and therefore individualized training strategies for patients with a developing maculopathy.

In the paper of Altpeter et al (2000) there was first evidence that there might be a correlation between locations of good attentional capabilities and PRL. Some open questions remained: in this previous study only the attention field of the centrically fixating eye could be compared with the eccentrically fixating fellow eye (in patients with maculopathy).

In the present study we were able to investigate in the same eye of a normally sighted subject and at the same time, if attention field and PRL are correlated. The finding of this study opens the possibility to select patients with early macular disease, who have an unfavorable distribution of their attentional capabilities for reading. Such patients on risk, i.e. with early macular changes or with macular pathology in the fellow eye, could receive early attention training in order to develop a functionally favorable location of best attentional performance and a later PRL. This would allow a preventive intervention to augment later rehabilitation.

6. SUMMARY

Patients with central vision loss use alternative retinal locations to compensate for the lack of visual input. This retinal location is referred to as preferred retinal locus of fixation. The mechanisms underlying the PRL development are not fully understood and patients may not always select the most beneficial PRLs for the performance of a specific visual task.

This work addressed the question whether the selection of PRL location can be influenced and whether the influenced PRL can be transferred to daily visual tasks. Furthermore, the relationship between the abilities to deploy attention in the visual field and the PRL development was investigated.

The participants were normally sighted subjects that underwent a simulation of central scotoma. To induce the PRL, a stimulus that evoked a saccade was presented and subjects had to perform a discrimination task while systematic stimulus relocation were applied to the stimuli. After four training sessions, the final PRL location was assessed. In addition, subjects performed a pursuit task, and two different reading tasks to address whether the induced PRL can be transferred to daily visual tasks. The attention hypothesis was addressed in the third study with a new cohort of participants. Sustained attention was compared to the PRL developed after two sessions of central scotoma simulation.

The results showed that systematic stimulus relocations can be used to influence the development of the PRL and that the induced PRL further transfers to some daily visual tasks. Furthermore, the attentional capabilities of the subjects were shown to be related to the PRL development. The relationship between attention and PRL development could be used as an indicator of potential PRL locations when patients are at early stages of their disease. This information would allow the prediction of beneficial PRL developments and can help for the decision on whether they need to be further trained. In case that training strategies are needed, systematical stimulus relocations can be a good starting point to induce the PRL. With the knowledge that induced PRLs can be transferred to other visual tasks, PRLs can be induced and be further used in everyday life situations.

7. ZUSAMMENFASSUNG

Patienten mit zentralem Sehverlust nutzen alternative Netzhautorte, um den Mangel an visuellem Input auszugleichen. Diese Netzhautposition wird als bevorzugter retinaler Locus der Fixierung bezeichnet. Die Mechanismen, die der PRL-Entwicklung zugrunde liegen, sind bisher nicht vollständig verstanden. Darüber hinaus kann es vorkommen, dass Patienten nicht immer die für die Durchführung einer bestimmten Sehaufgabe günstigsten PRLs auswählen.

Die Fragestellung der Arbeit ist, ob die Wahl der PRL-Position induziert werden und deren beeinflusste Position auf die täglichen Sehaufgaben übertragen werden kann. Darüber hinaus wurde eine Hypothese zur Auswahl des PRL untersucht, der die unterschiedlich stark entwickelte Aufmerksamkeit im Gesichtsfeld mit der PRL-Entwicklung korreliert.

Bei den Probanden handelte es sich um normalsichtige Probanden, die sich einer Simulation des Zentralskotoms unterzogen haben. Um den PRL zu induzieren, mussten die Probanden eine Diskriminierungsaufgabe erfüllen, während ein Stimulus, der Sakkaden hervorruft, systematischen Positionsveränderungen unterzogen wurde. Nach vier Trainingseinheiten wurde der endgültige PRL-Standort ermittelt. Darüber hinaus führten die Probanden eine Folgeaufgabe und zwei verschiedene Leseaufgaben durch, um zu klären, ob der induzierte PRL auf das tägliche Sehvermögen übertragen werden kann. Die Aufmerksamkeitshypothese wurde in der dritten Studie mit einer neuen Probandenkohorte adressiert. Die Richtung der maximalen visuellen Aufmerksamkeit wurde mit der Position des PRL verglichen. Der PRL wurde nach zwei Sitzungen zentraler Skotom-Simulation entwickelt wurde.

Die Ergebnisse zeigten, dass systematische Stimulusverlagerungen genutzt werden können, um die Entwicklung des PRL zu beeinflussen. Darüber hinaus konnte gezeigt werden, dass die induzierte PRL sich auf alltägliche Sehaufgaben übertragen lässt. Weiterhin wurde gezeigt, dass die Aufmerksamkeitsfähigkeiten der Probanden mit der PRL-Entwicklung zusammenhängen.

Die Beziehung zwischen Aufmerksamkeit und PRL-Entwicklung könnte als Indikator für potenzielle PRL-Standorte verwendet werden, wenn sich Patienten in einem frühen Stadium ihrer Erkrankung befinden. Diese Informationen würden die Vorhersage von vorteilhaften PRL-Entwicklungen ermöglichen und können bei der Entscheidung darüber, ob sie weitergebildet werden müssen, behilflich sein. Für den Fall, dass Trainingsstrategien benötigt werden, können systematische Stimulusverlagerungen ein guter Ausgangspunkt sein, um die PRL zu induzieren. Mit dem Wissen, dass induzierte PRLs auf andere Sehaufgaben übertragbar sind, können PRLs induziert und in Alltagssituationen weiterverwendet werden.

8. References

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9. PUBLICATIONS

9.1. PEER REVIEWED PAPERS

1. Barraza-Bernal M.J., Rifai K., & Wahl S. (2017). A preferred retinal location of fixation can be induced when systematic stimulus relocations are applied. Journal of vision, 17(2):11, 1-13.

2. Barraza-Bernal M.J., Rifai K., & Wahl S. (2017). Transfer of the induced preferred retinal locus of fixation to everyday visual tasks. Journal of Vision, 17(14):2, 1-16.

3. Barraza-Bernal M.J., Ivanov I. V., Nill S., Rifai K., Trauzettel-Klosinski S., & Wahl S. (2017). Can positions in the visual field with high attentional capabilities be good candidates for a new preferred retinal locus?. Vision Research 140, 1-12.

4. Barraza-Bernal M.J., Rifai K., & Wahl S. (2018). The retinal locus of fixation in simulations of progressing central scotomas. Journal of Vision, 18(1):7, 1-12.

5. Rifai K., Hornauer M., Buechinger R., Schoen R., Barraza-Bernal M.J., Habtegiorgis S., Glasenapp C., Wahl S. & Mappes T. (2018). Efficiency of ocular UV protection by clear lenses. Biomedical optics express, 9(4):1948

9.2. CONFERENCES

1. Barraza-Bernal M.J., Rifai K., & Wahl S. (2015). Inducing the preferred retinal locus of fixation, Perception, 44, 298-298. Presented at the 38th European Conference on Visual Perception, Liverpool, England.

2. Barraza-Bernal M.J., Rifai K., & Wahl S. (2015). Visual behavior in the presence of a simulated central vision loss and forcing a preferred retinal locus. Presented at the Young Researcher Vision Camp, Leibertingen, Germany.

3. Barraza-Bernal M.J., Nill S., Rifai K., Trauzettel-Klosinski S., & Wahl S. (2016). The role of local attentional variations during eccentric view on the development of the preferred retinal locus of fixation, Journal of Vision, 16(12), 419-419. Presented at the Sixteenth annual meeting of the Vision Science Society, St. Pete Beach, Florida, USA.

4. Barraza-Bernal M.J., Rifai K., & Wahl S. (2016). Transfer of induced PRL among visual tasks, Perception, 45, 297-298. Presented at the 39th European Conference on Visual Perception, Barcelona, Spain.

5. Barraza-Bernal M.J., Ivanov I., Nill S., Rifai K., Trauzettel-Klosinski S., & Wahl S. (2016). Positions in the visual field with good attentional capabilities are candidates for a new preferred retinal locus of fixation, Presented at the Young Researcher Vision Camp, Leibertingen, Germany.

6. Barraza-Bernal M.J., Ivanov I., Rifai K., & Wahl S. (2017). Sustained visual attention at different retinal eccentricities and its significance for the development of the preferred retinal locus, Journal of Vision, 17(10), 700-700. Presented at the Seventeenth Annual Meeting of the Vision Science Society, St. Pete Beach, Florida, USA.

7. Barraza-Bernal M.J., Rifai K., & Wahl S. (2017). The relocation of the preferred retinal locus under progression of a central scotoma, Perception, 46, 235-236. Presented at the 40th European Conference on Visual Perception, Berlin, Germany.

8. Barraza-Bernal M.J., Rifai K., & Wahl S. (2018). Fixation behavior in the presence of progressing scotoma. Presented at the New Horizons in Vision and Hearing Research, Tuebingen, Germany.

9.3. Patents

Rifai, K., Wahl, S., & Barraza-Bernal, M. J., (2017). U.S. Patent No. WO 2017001335 A1. Washington, DC: U.S. Patent and Trademark Office. Device and computer program for training a preferred retinal locus of fixation. Also under EP 3111828 A1.

9.4. Talks

Novel strategies to enhance the performance of the visually impaired using simulations of central vison loss. Young Researcher Vision Camp 2017, Leibertingen, Germany.

10. PERSONAL CONTRIBUTION

Publication 1 and Publication 2: A preferred retinal location of fixation can be induced when systematic stimulus relocations are applied. Journal of vision, 17(2):11, 1-13 and Transfer of the induced preferred retinal locus of fixation to everyday visual tasks. Journal of Vision, 17(14): 2, 1-16.

Authors: Barraza-Bernal M.J., Rifai K., & Wahl S.

I declare that my contributions to the academic work presented in the publications specified above, were to develop the initial idea, to develop the experimental methods, to conduct the experiment, to develop the analysis of data and to analyze the data. I also wrote the first version of the manuscript and improved it based on the inputs from the other authors.

The second author of the publication, Rifai K., also contributed with the principal idea, with ideas for the methods and data analysis and also reviewed the manuscript before and after submission.

The third author of the publication, Wahl S., contributed with material and with revisions of the manuscript before and after the submission.

Publication 3: Can positions in the visual field with high attentional capabilities be good candidates for a new preferred retinal locus?. Vision Research 140, 1-12.

Authors: Barraza-Bernal M.J., Ivanov I. V., Nill S., Rifai K., Trauzettel-Klosinski S., & Wahl S.

I declare that my contributions to the academic work presented in the publications specified above, were to develop the initial idea, to develop the experimental methods, to conduct the experiment, to develop the analysis of data and to analyze the data. I also wrote the first version of the manuscript and improved it based on the inputs from some of the other authors.

The author Ivanov I. V., and Rifai K., reviewed the manuscript before and after submission.

The author Nill S., performed the measurements of attention of a 30 percentage of the subjects and helped with the translation of subject’s informed consent from English to German.

The author Trauzettel-Klosinski S., contributed with the principal idea and reviewed the manuscript before and after submission.

The author Wahl S., contributed with material and with revisions of the manuscript before and after the submission.

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