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# Eye Movements in Macular Degeneration

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## Abstract

In healthy vision, the fovea provides high acuity and serves as the locus for fixation achieved through saccadic eye movements. Bilateral loss of the foveal regions in both eyes causes individuals to adopt an eccentric locus for fixation. This review deals with the eye movement consequences of the loss of the foveal oculomotor reference and the ability of individuals to use an eccentric fixation locus as the new oculomotor reference. Eye movements are an integral part of everyday activities, such as reading, searching for an item of interest, eye–hand coordination, navigation, or tracking an approaching car. We consider how these tasks are impacted by the need to use an eccentric locus for fixation and as a reference for eye movements, specifically saccadic and smooth pursuit eye movements.

### Keywords

macular degeneration; fixation stability; saccade; smooth pursuit; oculomotor reference; adaptation

## INTRODUCTION

In healthy vision, both the fovea and the periphery play critical roles in gathering information from the environment. The foveal region has a privileged status because it has the highest acuity and is used as the oculomotor reference—the origin of the reference system for saccadic eye movements. Thus, macular degeneration (MD), which primarily affects the central retina, can have a profound impact on tasks of daily living. MD, including age-related MD (AMD) and juvenile MD (JMD), is the leading cause of vision loss in industrialized countries. AMD affects approximately 170 million people worldwide and occurs in two forms—dry and wet. Dry AMD is more common (85–90% of cases) and often starts in the macular periphery and then closes in on the fovea with disease progression. Wet AMD is less common (10–15% of cases) but more disabling as it initially affects the fovea. Thus, it accounts for 90% of AMD cases with severe vision loss (Hubschman et al. 2009). Both types of AMD can lead to bilateral scotomata in the central 15–20° (Cheung & Legge 2005, Schuchard et al. 1999). JMD includes the variants Stargardt's disease, Best's vitelliform dystrophy, and X-linked retinoschisis (Altschwager et al. 2017). The prevalence of these forms is lower than that of AMD (ranging from 1 in 2,500 to 1 in 10,000), but they have a similar impact on visual function, primarily affecting the central visual field.

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In both AMD and JMD, the resultant binocular central field loss (CFL) that ensues when scotomata occur in both eyes can significantly impact daily life. If the affected region includes the fovea in both eyes, patients adopt an eccentric preferred retinal locus (PRL) for binocular fixation. Although the stability of fixation is profoundly compromised by the use of eccentric fixation (Kumar & Chung 2014), this review focuses on saccadic and pursuit eye movements in CFL.

## THE PREFERRED RETINAL LOCUS AS A REFERENCE FOR EYE MOVEMENTS

Saccades are rapid, ballistic movements that typically bring an object of interest onto the high-acuity fovea. Bilateral vision loss at and around the fovea not only impairs acuity but also introduces challenges for eye movements due to the loss of the foveal oculomotor reference. Renninger & Ma-Wyatt (2011) provided a compelling demonstration of the difficulty of directing the PRL to a saccade target. Participants viewed the display with their preferred eye and were asked to direct gaze at the central fixation marker and to make a saccade to a target flashed in one of eight locations around a circle with an eccentricity of 2–12°. While normal controls made radial saccades directly to the target, an individual with CFL had difficulty directing his PRL to the target (Figure 1a). The scan path of the eye was not direct even when the saccade target was visible, curving toward the target at the end of the saccade and requiring multiple small saccades to reach the target. Saccades to targets that fell within the scotoma in the upper-right quadrant (Figure 1a) were particularly tortuous. In addition to being misdirected, saccades in CFL have characteristics of nonfoveating saccades (Whittaker et al. 1988), with lower peak velocity and longer duration than saccades executed by the fovea.

### Adapting to a Nonfoveal Locus for Eye Movements

Some of the challenges of saccadic eye movements can be understood within the context of moving the oculomotor reference from the fovea to the PRL. Most individuals with MD use an eccentric locus for fixation within six months after the onset of bilateral foveal loss (Crossland et al. 2005), but they take much longer to use this locus as an oculomotor reference (White & Bedell 1990). Only one-third of the participants in White & Bedell's (1990) study moved their PRL directly to reacquire a saccadic target, and these were individuals who had had MD for over three years. A similar trend was observed in primate studies following lesions to the fovea. Heinen & Skavenski (1992) showed that adult macaques with 2° and 3° lesions to their central retina were able to fixate with an eccentric PRL the very next day after the retinal ablation, but the transition to using this locus for saccades was not complete at two months post-lesion. Two of the three animals were not able to bring the PRL directly to the saccade target at the end of the testing period (3.5 months).

### Training a Preferred Retinal Locus for Eye Movements

A more recent study has shown that demanding eye movement training can help rereference saccades to a newly formed PRL (Kwon et al. 2013). Young, healthy participants with an artificial scotoma that was designed to simulate vision loss in MD were allowed to freely view a display, practice visual search, and follow a target that was suddenly displaced. Most developed a single fixational PRL after approximately 3 h of training and were beginning to use this region to acquire targets of interest. However, the fixation stability and the ability to acquire saccadic targets of the newly formed PRL were much worse than those of the fovea in nonscotoma controls. To improve performance, the authors marked the developing PRL with a cross and had observers practice the same tasks by trying to land the marked PRL location on the target (explicit training). After 15 to 25 h of this training, fixation stability and the acquisition of targets with the PRL were similar to those of the fovea. This and other studies that implemented this training protocol (Chen et al. 2019, Liu & Kwon 2016, Tsank & Eckstein 2017) suggest that these methods could be used to improve oculomotor rereferencing in individuals with MD. However, the following caveat needs to be borne in mind. Oculomotor training was less effective when the scotoma boundary was invisible (Kwon et al. 2013, Walsh & Liu 2014), and the scotoma had the same luminance as the background. This consideration is significant for individuals with MD because their scotoma boundary is not visible, and its location is not easily discerned, much like the location of the optic disc in monocular viewing. We discuss this further in the section titled Challenges to Visual Search.

## CONSEQUENCES FOR READING

Reading is impacted by both the loss of visual acuity and poor oculomotor control (Chung 2011, 2020; Fine & Peli 1995; Fletcher et al. 1999; Legge et al. 2001). Increases in font size and magnification partially address the acuity problem, but resulting decreases in visual span (the number of letters that can be recognized in a single fixation) and slower processing of letters impact reading speed (Cheong et al. 2007, 2008). In this section, we focus primarily on the oculomotor challenges of using an eccentric retinal locus to fixate a word and to move the eye forward on the line. Rubin & Turano (1994) developed a method to present words at the same location, thereby reducing the need to make saccades. The rapid serial visual presentation (RSVP) method improved reading rate by a factor of 1.5 in individuals with CFL; however, this improvement was smaller than that in normally sighted individuals. This finding suggests that other factors such as poor fixation stability and reduced visual span might contribute to CFL (Rubin & Feely 2009). In fact, Crossland et al. (2004) showed that improvements in reading speed were strongly correlated to improvements in fixation stability in the first year following onset of MD, the period when individuals adopt and use an eccentric PRL following loss of foveal vision.

In conventional reading, poor oculomotor control also affects saccades to the next word. In addition to inaccurate forward saccades to the desired location in the line, the presence of the scotoma causes parts of words to be missed, resulting in a large number of backward regressive saccades (Bullimore & Bailey 1995, Rubin & Feely 2009). The presence of the scotoma may also complicate finding the next line. In an elegant study, Seiple et al. (2011) showed that a simple eye movement training protocol in which CFL participants shifted their gaze back and forth between two horizontally separated targets led to improvements in reading speed. The training started with simple dot targets and progressed to single letters, to pairs of letters, and finally to triplets. The authors found that this eye movement training protocol improved reading speed much more than did training that made participants more aware of their scotoma location or training with serial presentation of text at the same location (RSVP). Other studies have used a moving window that highlights a word at a time to guide eye movements in reading (Nguyen et al. 2011). Training with a moving window yields results similar to those of RSVP, implying that it is not as effective as the simple protocol that trains horizontal eye movements to targets of increasing complexity.

# CHALLENGES TO VISUAL SEARCH

In addition to the impact of poor oculomotor control on active visual search, aspects of a binocular scotoma also make visual search particularly challenging. Unlike reading, where the eye is moving mostly to a horizontal location, the target location in visual search is unknown and can be hidden by the scotoma. Two additional factors complicate visual search. First, individuals with CFL are often unaware of the location of their scotoma (Fletcher et al. 2012, Safran & Landis 1999). Second, they are unaware that they are missing information behind the scotoma due to filling in (Zur & Ullman 2003). Consider a person with CFL shopping for groceries and looking for her favorite cereal. She looks on the shelf, and the label of the desired cereal falls within her scotoma. She moves on to look at another location because she is unaware of the missing information. Thus, doing the simplest tasks is time consuming and frustrating. To address these challenges, Janssen & Verghese (2016) undertook a two-step training process to teach scotoma awareness and train individuals with CFL to make eye movements toward the scotoma to uncover information that they would miss otherwise.

The scotoma awareness training allowed participants to experience their scotoma by searching for a single target presented within their scotoma. They were free to explore eye movement strategies that uncovered the target in a self-paced manner. Each trial started with observers fixating a mark at the center of the screen. As the eyes moved, they naturally uncovered the target. A retention session (approximately two months post-training) showed that participants made saccades directly toward their scotoma when asked to find the single hidden target (Figure 1c). Janssen & Verghese (2016) tested whether this adaptive strategy could be used to uncover hidden information in a separate same-different task in which participants had to decide whether two stimuli were identical. One of these was presented within the binocular scotoma, while the other was on the opposite side of the scotoma from the PRL and clearly visible (Figure 1b). Observers were allowed to make eye movements to uncover the hidden target. As training progressed, display time was progressively shortened to allow approximately a single saccade, so observers had to move their PRL directly toward the hidden target to uncover it (Figure 1b). After two 240-trial training sessions, participants learned to direct their saccades toward their scotoma. Figure 1c shows that trained CFL participants moved their eyes directly toward their scotoma, even two months after the end of training. However, the scotoma awareness and eye movement strategy in the same-different task did not generalize to a search task on a natural scene background. Observers were asked to actively search the display and report the number of Gaussian blob targets subtending approximately 2°, which were small enough to be obscured by participants’ scotomata (between 5° and 30°). Janssen & Verghese found no evidence that training preferentially increased the number of saccades toward the scotoma, a strategy that would have revealed hidden targets in the proximity of the PRL.

## SACCADES IN VISUAL SEARCH

As indicated above, individuals with CFL often complain that they struggle to find objects, such as house keys or their favorite jam on the supermarket shelf. In recognition of this challenge, several studies have looked at visual search in CFL, focusing primarily on search time. MacKeben & Fletcher (2011) asked a group of low-vision participants, including those with MD, to search for a Landolt-C target with eye movements and identify the orientation of the opening. The target was twice the size of the acuity limit and was presented at a random location. Under these conditions, the presence of a central scotoma significantly increased the latency to identify the Landolt-C orientation. Across all participants in the study, latency was significantly correlated with reading speed, suggesting that integrity of the visual field and the ability to direct eye movements efficiently modulated performance in the search-and-identify task. Acuity was not correlated to latency to find and identify the target because the target size was set above each individual's acuity limit. However, in a natural scene search task where the targets were presented in a cluttered scene and varied considerably in size, Wiecek et al. (2012) found that for individuals with MD, acuity and scotoma size were significant predictors of search time to find the target.

Other studies have looked at characteristics of saccadic eye movements including fixation duration, number of saccades, saccadic amplitude, and scan path ratio (a metric of saccade efficiency that measures the total scan path to find the target relative to the shortest distance between the starting eye position and the target; Brockmole & Henderson 2006). Geringswald et al. (2013) used these saccade metrics to determine whether participants with CFL benefited from exposure to repeated stimulus configurations (the contextual cuing effect) in a task where they had to find a T among Ls. Participants with CFL showed a small facilitation with repeated (as opposed to novel) contexts for search time, number of fixations, and scan path ratio, although the effect of contextual cueing was not as strong as for normally sighted individuals. Boucart et al. (2015) analyzed eye movements in more realistic tasks, where participants were required to make a sandwich (familiar task) or replicate a model from a child's construction set (unfamiliar). Observers were required to search among relevant and irrelevant items and to select those necessary for the task. Compared to controls, individuals with MD had significantly more saccades, as well as longer total gaze duration on all items regardless of whether they were relevant to the task, particularly for the unfamiliar task. This result suggests that individuals with CFL take longer to extract information from an object in an unfamiliar context. Additional factors that affected object identification in CFL included shorter intersaccadic fixation duration and longer scan path ratios (Thibaut et al. 2016). Additionally, visual search in CFL was particularly impaired under crowded versus uncrowded conditions (Thibaut et al. 2020), suggesting that crowding at the eccentric PRL may impact the visibility of search targets in daily life (Wallace et al. 2017). Interestingly, performance was related to the size of the scotoma, but not to visual acuity. As individuals with MD do not preferentially direct their saccades toward their scotoma to uncover hidden objects (Janssen & Verghese 2016), it is unsurprising that scotoma size impacts the mean target search time. A similar effect of scotoma size was also found when individuals with an artificial scotoma were asked to look for spatial distortions in visual scenes (McIlreavy et al. 2012).

Interestingly, only a few studies have related the characteristics of eye movements during visual search to individual scotomata. Renninger et al. (2008) conducted a shape discrimination task to assess the efficiency of eye movement in CFL. Participants used their preferred eye to view and actively explore a silhouette for two seconds. They were then asked to discriminate the viewed shape from one that was slightly modified. As the shape was characterized by the orientation of its edges, fixating locations that provided the maximum information about the edge orientation was optimal. Efficiency was defined as the ratio of information gained across individual fixations relative to the optimal gain achieved by an information maximization model (Renninger et al. 2007), given the size and location of the individual's monocular scotoma. Renninger et al. observed that scotoma size had a dramatic effect on the efficiency of saccades in gathering information about shape. Individuals with scotoma diameters of less than 5° had saccadic efficiencies similar to those of control participants, but saccadic efficiency declined with larger scotomata.

Van der Stigchel et al. (2013) investigated eye movements in visual search in relation to a coarse map of the binocular scotoma for four individuals with JMD. In addition to having longer saccadic search latencies, participants made more saccades and had longer fixation dwell times. Two participants also had smaller-amplitude saccades toward the scotoma. Recently, Vullings & Verghese (2021) mapped the binocular scotoma in detail and used the Janssen & Verghese (2016) task to relate search performance to the shape and size of the binocular scotoma (C. Vullings, Z. Lively and P. Verghese, unpublished data). Vullings et al. observed that, similar to controls, participants with CFL made mostly horizontal saccades. The detailed map of the binocular scotoma (Vullings & Verghese 2021) revealed that participants with CFL actually made more saccades toward their scotoma (Figure 2) than did controls toward comparable directions (C. Vullings, Z. Lively and P. Verghese, unpublished data). Notably, CFL saccades had small amplitudes [consistent with the results of Van der Stigchel et al. (2013)] and were mostly directed toward the scotoma edge closest to the PRL for larger scotomata. These findings suggest that multiple saccades may be necessary to uncover the region hidden by a large scotoma.

## SACCADES IN FACE RECOGNITION

Individuals with CFL find it difficult to identify faces and facial expressions (Alexander et al. 1988, Bullimore et al. 1991, Tejeria et al. 2002) and to determine whether someone is looking at them (Sheldon et al. 2014), which significantly impairs their social interactions. Most people strongly rely on facial expressions in social contexts to read the room, often before anything is said. In the case of CFL, the difficulty in discriminating facial expressions hinders social interactions and makes watching television substantially less enjoyable.

Seiple et al. (2013) suggested that these difficulties could be due to altered scanning behavior. They used a scanning laser ophthalmoscope (SLO) to image the retina and track eye movements while simultaneously projecting the highly recognizable face of Leonardo da Vinci's *Mona Lisa*. The authors reported that participants with CFL fixated the internal features of the face (eyes, nose, and mouth) less frequently than did control participants (62% of fixations for CFL versus 87% for controls). Instead, those with CFL made more saccades toward external features (38% versus 13%). The investigators ruled out optical blur as a potential reason for this preference by blurring the image for control participants, who continued to look at the three main internal facial features. In this task, the authors found shorter saccadic amplitudes for control participants than for participants with AMD. Although this observation is opposite the typical trend, it is not surprising given that control participants looked more at the closely spaced eyes, nose, and mouth, whereas participants with AMD would switch between features, such as the cheek and forehead. Finally, the authors did not find any evidence for use of multiple PRLs when viewing a face image, as has been demonstrated in other tasks (e.g., Crossland et al. 2011, Duret et al. 1999).

Tsank & Eckstein (2017) specifically examined whether scanning behavior for faces was altered in the presence of a central scotoma. They tested the ability of observers with an artificial scotoma to recognize faces where the external features had been cropped. An ideal observer model that accounted for the scotoma and incorporated the decline of visibility with eccentricity for isolated stimuli predicted that the locations that maximized facial information in the presence of a scotoma were the tip of the nose and the top of the forehead. Observers in the study did not generally fixate these locations, leading Tsank & Eckstein (2017) to conclude that fixation patterns were not optimal in simulated CFL.

However, Bernard & Chung (2016) suggested that the altered patterns of saccades to external facial features was an adaptive strategy to avoid internal facial features, which are more prone to crowding (due to their closer spacing) when viewed with an eccentric PRL. This crucial variable was not taken into account in the Tsank & Eckstein (2017) model. In addition to replicating Seiple and colleagues' (2013) results with an eye tracker, Bernard & Chung showed that individuals with CFL were actually better at discriminating faces when shown only external features than when shown only internal features (66.8% versus 35.8% recognition accuracy). Participants were best at recognizing the face when it was a full-face image, using a combination of external and internal features [outcomes corroborated by Logan et al. (2020)]. Furthermore, Bernard & Chung highlighted that the scan paths were different within the CFL group, possibly due to the size and position of their scotomata. An individual with a PRL located on the left of the scotoma would likely benefit from looking at the right side of the face to keep the scotoma from obscuring the face. In general, their findings are consistent with those of Taylor et al. (2018) showing that face recognition performance in a match-to-sample task was determined by the size of the retinal lesion and whether the fovea was spared. Individuals with CFL rely more on external facial features that are less affected by crowding effects, suggesting that the alterations in their scanning behavior are driven by adaptive saccade strategies in the presence of a scotoma.

For tasks that require saccades, including visual search, reading, and face recognition, scotoma size appears to be the main factor that determines performance. Larger scotomata not only obscure a larger part of the visual field, but are also associated with a more eccentric fixation locus and increased fixation instability.

## PURSUIT IN MACULAR DEGENERATION

Eye movements are required not only to saccade to static targets, but also to acquire and follow moving objects. Humans constantly use smooth pursuit eye movements to follow motion in their visual field, such as that of people or approaching vehicles, or simply to help stabilize the retinal image due to self-motion. Central scotomata lead to significant impairments in the quality and control of smooth pursuit eye movements (Pidcoe & Wetzel 2006). The reasons for these deficiencies are complex. First, CFL is typically associated with the loss of the fovea, which is normally used to pursue small objects. Second, the retinal regions available to maintain smooth pursuit tend to be at greater eccentricities, making continuous visual tracking difficult due to the physical limitations of eye movement in the orbit. Third, foveal loss may be accompanied by the development of multiple PRLs (Crossland et al. 2005, Whittaker et al. 1988). Finally, scotomata develop relatively independently in the two eyes and are rarely symmetrical, potentially compromising binocular coordination.

The ability to continuously follow moving objects is essential in daily life. For normally sighted individuals, accurate tracking ensures correct estimation of self- and target motion (Land 1999) and also ensures that the object remains on the same portion of the retina, reducing retinal slip and thus visual information loss. In individuals with CFL, there is an added consideration—the slippage of an object across the retina can lead to the loss of that object in the scotoma. In natural contexts, this outcome can be dangerous; for example, during locomotion, a potential hazard—such as an oncoming bicyclist—may disappear from view.

Although smooth pursuit is considered to be primarily driven by a velocity signal (Rashbass 1961), it is commonly considered a foveal behavior, particularly for small spot targets (for a review, see Krauzlis 2004) where the area of highest visual acuity is used to acquire and track the moving object. Studies suggest a close synergy between saccades and smooth pursuit (Orban de Xivry et al. 2006), especially when targets require foveation. Under these circumstances, smooth pursuit is accompanied by catch-up saccades that place the fovea closer to the target during pursuit (Heinen et al. 2016). Studies of smooth pursuit in CFL suggest that pursuit-specific oculomotor limitations compound the deficits in saccade behaviors described in the previous section.

## DIRECTION DEPENDENCE OF SMOOTH PURSUIT GAIN

Smooth pursuit gain is defined as the ratio of eye velocity to target velocity. Previous literature suggested that pursuit in the periphery is feasible with only marginally lower gains as compared to the fovea (Winterson & Steinman 1978). Although CFL participants do pursue targets, they do so with lower smooth pursuit gains (González et al. 2018a,c; Shanidze et al. 2016b, 2017), even when accounting for age-related decline in pursuit (Sharpe & Sylvester 1978). These findings are also consistent with those in younger control participants pursuing a target with an artificial scotoma (Pidcoe & Wetzel 2006).

Given that smooth pursuit is a motion-driven behavior, one potential explanation for reduced gains in CFL is that motion perception is impaired in the damaged retina, providing a noisy or unreliable signal to the pursuit system. Indeed, when motion perception is tested at threshold, there is some evidence that it may be affected in AMD (Eisenbarth et al. 2008). However, when Shanidze & Verghese (2019) investigated the ability of participants with

CFL to discriminate direction and speed of large, high-contrast stimuli, akin to those used in pursuit studies in CFL, they did not find deficits compared to age-matched controls. This outcome is consistent with prior work that demonstrated similar speed discrimination in the periphery and the fovea (McKee & Nakayama 1984). Therefore, a closer examination of additional factors that might contribute to pursuit deficits in CFL is warranted.

Both speed and direction affect smooth pursuit gains in CFL. These individuals show a larger decrease in pursuit gain with increasing target speed than do controls (González et al. 2018c, Shanidze et al. 2017). However, these results are somewhat difficult to interpret given that both studies used a fixed target path length across all speeds, resulting in shorter durations for higher velocities. Therefore, one cannot distinguish whether lower pursuit gains in CFL reflect a true deficit in target tracking at higher speeds or a difficulty in acquiring the target and reaching steady-state pursuit within the shorter time available. This latter explanation is further supported by a known increase in pursuit latency in participants with CFL as compared to controls (Shanidze et al. 2016b).

In addition to speed, the target path relative to the scotoma is a significant determinant of smooth pursuit velocity in CFL (González et al. 2018c, Shanidze et al. 2016b). Shanidze et al. (2016b) looked at the relationship between PRL or scotoma location and target trajectory, using an SLO to first map participants' monocular scotomata and subsequently project pursuit targets directly onto the participants' retinas. The targets moved in a step-ramp (Rashbass 1961), jumping 6° in one direction and traveling smoothly back in the opposition direction for 12°. Using eight target directions (four cardinals and four obliques), Shanidze et al. were able to probe retinal regions with and without a scotoma. The amount of retinal damage along the target trajectory was compared with pursuit gain for that trajectory (Figure 3a). They found that pursuit gain was significantly lower for targets heading into the scotoma, as compared to those heading into healthier retina.

Shanidze et al.'s (2016b) approach using the SLO allowed them to precisely map the relationship between target trajectory and scotoma location; however, it also limited them to monocular viewing. In a subsequent study, González and colleagues (2018c) used a similar step-ramp paradigm to examine the effect of dominant-eye PRL location and target direction on pursuit gain during binocular viewing. They found that participants with MD showed significantly better pursuit for leftward and downward target motion, as compared to rightward and upward. No such relationship was seen in the age-matched controls. The authors speculated that the higher gain of leftward and downward motion is consistent with the higher prevalence of PRLs to the left of and below the scotoma (Fletcher & Schuchard 1997), although participants with PRLs on both sides of the scotoma were included in the study. This outcome is consistent with Shanidze et al.'s (2016b) findings, where pursuit gains tended to be higher for target trajectories toward healthier retina. The two sets of results cannot be compared directly, however, as González and colleagues did not visualize the retina during the pursuit experiment, making it impossible to map the relative locations of the target trajectory, PRL, and scotoma. Interestingly, normally sighted controls who pursued sinusoidally moving targets with an artificial scotoma were found to always place the target in the left visual field relative to the scotoma (Pidcoe & Wetzel 2006). The directional dependence of pursuit gain in CFL suggests that substantial target occlusion by the scotoma is a factor in participants' pursuit deficits (Ackerley & Barnes 2011b, Churchland & Lisberger 2002).

## IS THERE A PREFERRED RETINAL PURSUIT LOCUS?

Independent of eye velocity and pursuit gain is the question of the position of the fixational PRL or fovea relative to the target. González and colleagues (2018c) inferred that individuals with MD may not put the fixational PRL on the pursuit target. Shanidze et al. (2016b) used an SLO to directly visualize the retinal loci used for pursuit and showed that both participants with CFL and controls did not have their fixational PRL or fovea on the large annular pursuit target (1.7°) on more than 50% of the trials. Interestingly, they found evidence for the use of multiple PRLs: Two participants with CFL used a PRL switching strategy, typically using a more peripheral region with a larger region of intact retina to find the target and then switching to a preferred locus surrounded by a smaller region of intact retina to pursue the target. To determine whether the positional offset of the fovea or PRL to the target was due to its relatively large size and high visibility, they used the SLO to examine pursuit for small foveal targets (0.5°). Even with the smaller targets, young healthy control participants did not habitually use the fovea for pursuit (Shanidze et al. 2016a). These studies suggest that placement of the fovea on the target is not necessary to effectively pursue the target. Thus, the offset of the PRL from fixation is not in itself an explanation of pursuit deficits in CFL.

## BINOCULAR COORDINATION AND SCOTOMA OVERLAP IN SMOOTH PURSUIT

Any consideration of a single pursuit locus suggests a coordination between the eyes akin to that seen during fixation (Kabanarou et al. 2006), where the dominant or better eye determines the position of both eyes, regardless of whether the target falls on the intact retina of the nondominant or worse eye. The alternative is that the eyes use a hybrid strategy where the participant maximizes the amount of time that the target is tracked by either eye. To determine how the eyes are coordinated in CFL during pursuit, Shanidze et al. (2017) asked participants to track moving targets either binocularly or monocularly with the better or worse eye. All eye tracking was binocular, even for monocular viewing when the nonviewing eye was occluded with a filter that blocked visible but not infrared light. The authors found that, during binocular viewing, participants with CFL had significantly higher gains in the dominant than in the nondominant eye. They did not find the same relationship for control participants or for either participant group during monocular viewing. This finding suggests that, in monocular viewing, the gain of the nonviewing eye is set by the viewing eye, whereas in the binocular condition, the visual input in each eye influences pursuit velocity of that eye.

Differences in gain between the two eyes suggest a change in binocular coordination during pursuit in CFL. Shanidze et al. (2017) investigated how the two eyes are coordinated in time by cross-correlating the positions of the eyes across the duration of the trial on a trial-by-trial basis. They found significantly lower correlations between the eyes in CFL participants, as compared to age-matched controls (Figure 3c). Note that, for both groups, the highest correlations were associated with zero time delay between the two eyes. Binocular coordination was related to the degree of overlap of residual vision in the two eyes: In individuals with significantly overlapping PRLs, the eyes tended to be more correlated during pursuit. Individuals with nonoverlapping scotomata (Figure 3b) showed a decrease in binocular coordination that was present during monocular and binocular (Figure 3c) viewing of the pursuit target. Shanidze et al. also investigated which measures of visual function predicted a decrease in binocular correlation and found that the ratio of contrast sensitivities between the two eyes, and stereoacuity when measurable, was the best predictor of binocular coordination. This finding suggests that the existence of eyes with similar contrast sensitivity (Valberg & Fosse 2002) and of intact retina at corresponding locations to mediate stereo sensitivity (Verghese & Ghahghaei 2020) are important factors that determine binocular coordination. Taken together with the observation regarding overlap between the PRL and scotoma, these findings suggest that the difference in retinal damage between the eyes may be more significant for pursuit in CFL than the level of intact function in the better eye.

## DO SACCADES HELP KEEP THE EYE ON THE TARGET DURING PURSUIT IN CENTRAL FIELD LOSS?

Saccadic and pursuit eye movements are known to be effortful in CFL individuals, as parietal and frontal areas of the attention network are significantly more active during saccades and pursuit, respectively, in these individuals compared to controls (Little et al. 2008). In pursuit studies that use demanding task conditions with a small stimulus, controls make an increased number of catch-up saccades (Heinen & Watamaniuk 1998; Heinen et al. 2016, 2018; Madelain et al. 2005). Specifically, Madelain et al. (2005) showed that when participants were asked to attend to either the large or small ring of a compound stimulus to perform a discrimination task, attention to the small ring produced more catch-up saccades than attention to the large ring.

As pursuit gain is low in CFL, we wondered whether saccades may contribute to motion tracking. We reanalyzed the binocular pursuit data of Shanidze et al. (2017) to examine saccades during pursuit. Although participants with CFL had more saccades overall, the saccades were distributed more broadly, without a clear relation to target direction (Figure 4a), unlike those of control participants, who mainly exhibited saccades in one of the six target directions (or in the opposite direction to catch the target at the initial step; Figure 4b). This difference is clearly evident in the angular error of the saccade with respect to the target direction (Figure 4c,d). Controls mostly made small (<2°) and medium-sized (2–5°) saccades in the target direction (0°) or medium saccades opposite the target direction (180°) to first acquire the target, whereas participants with CFL made saccades in a broad range of directions around the target. Thus, while we clearly see that saccades help keep gaze on the target for controls, the benefit of saccadic eye movements is not as clear for CFL. It is possible that saccades are made to catch up with the target, but that fixational instability and poor oculomotor control result in misdirected saccades (Figure 1a).

Safi et al. (2020) also conducted an experiment to determine whether a more demanding task would recruit catch-up saccades in CFL. Specifically, we investigated whether smooth pursuit gain and saccade frequency change when the task requires discrimination of a moving target close to the acuity limit, as opposed to the larger, more visible target used by Shanidze et al. (2016b, 2017) and González et al. (2018a,c). The pursuit target was an annulus that changed briefly to a Landolt-C of the same diameter and moved leftward or rightward (Safi et al. 2020). Participants were asked to identify the orientation of the opening in the C after each trial. Even when the target was adjusted to each individual's acuity limit, participants with CFL had lower pursuit gains and poorer target discrimination than age-matched controls. They also did not make significantly more saccades during the presentation of the C versus the annulus. Thus, even under demanding conditions near the acuity limit, participants with CFL do not use catch-up saccades effectively.

## DO HEAD MOVEMENTS IMPROVE PURSUIT?

Findings using binocular eye tracking of smooth pursuit illuminate the importance of considering pursuit in participants with CFL in a natural setting, where the head is free to move, and viewing is binocular. Due to the eccentric position of the eyes in the orbit, head-free pursuit may provide individuals with CFL access to a larger oculomotor range than do head-restrained conditions. Furthermore, previous studies suggest that head movements do not require direct visual input for pursuit (see Ackerley & Barnes 2011b), allowing for pursuit to persist longer than for eye-only tracking after the target disappears. This consideration is important in CFL, where the target may enter into the scotoma unbeknownst to the individual due to perceptual filling-in.

To investigate this question, Shanidze & Velisar (2020) measured smooth pursuit in individuals with CFL in head-restrained and unrestrained conditions. Consistent with previous findings, individuals with CFL had significantly lower gains than controls in both head-restraint conditions. Interestingly, unlike González et al. (2018c), Shanidze & Velisar found pursuit gain to be lowest in the downward direction. Overall, pursuit gains were higher in the head-restrained condition. Because smooth pursuit gain in the head-unrestrained condition is a function of overall gaze (eye-in-head and head velocity together), they examined each independently. They found that age-matched controls had significantly higher eye velocities and displacements than did individuals with CFL in both head-restraint conditions. Some participants with CFL compensated for low eye velocities with an increased number of saccades, some of which contributed to displacing the eye in the target direction (Figure 5a). However, head velocity or displacement did not differ significantly between groups. The finding that observers with CFL have lower eye but similar head velocities was particularly evident for higher head velocities, where participants with CFL tended to move their eyes in the opposite direction of the target. Given that head velocities did not exceed those in controls, the difference in eye movement strategy is unlikely to be due to the need to cancel out higher head velocities that may exceed target speed.

Data showing that the eyes move opposite the target direction suggest that vestibulo-ocular reflex (VOR) cancellation may be deficient in CFL, and coordination of eye and head movements may be affected in those without foveal fixation. For example, for gaze to follow a moving target, the reflexive counterrotation of the eyes opposite the head (VOR) must be suppressed. Whether VOR is completely off, or whether it is countermanded by additional visual mechanisms during head-free movement, such as pursuit, are subjects of debate (Ackerley & Barnes 2011a, Johnston & Sharpe 1994). Prior studies do indicate that this suppression may be fovea dependent (for a review, see Barnes 1993), although it may be possible without the constant presence of the visual stimulus (Barnes & Grealy 1992). Thus, if VOR cancellation is not optimal in CFL, then head movements may prove disadvantageous during pursuit. Figure 5b shows an example pursuit trial in CFL where the participant moves her head with the target velocity but counterrotates the eyes relative to the head, thus canceling out head pursuit. Overall, when looking at combined eye and head motion, participants with CFL tend to have gaze velocities that are less consistent with pursuit (target velocity) and closer to VOR (gaze velocity = 0) than those of controls (Figure 5c).It should be noted that an eccentric PRL asymmetrically affects VOR gain (González et al. 2018b).

Furthermore, countering our initial hypothesis that head movements might improve pursuit by enhancing the available oculomotor range in CFL, Shanidze & Velisar (2020) found no significant relationship between fixation eccentricity and head contribution to smooth pursuit; they also found that participants with CFL and control participants covered a similar proportion of the target trajectory with head movements. Thus, although saccades may have been instrumental, head movements did not improve pursuit in either group (Figure 5a).

## CONCLUDING REMARKS

Saccadic and pursuit eye movements are clearly effortful in individuals with CFL. These issues are related to poor oculomotor control with an eccentric PRL and to the presence of scotomata that interfere with gathering information with saccades and with continuous smooth pursuit of a moving target. The interplay between oculomotor systems is evident. Although the saccadic system can provide an adaptation to mitigate pursuit deficits, saccades are often misdirected and thus do not help to keep gaze on the moving target. Concurrently, head movements that could potentially increase oculomotor range in pursuit are sometimes countermanded by the failure to suppress the VOR.

Despite these challenges, individuals with CFL show an amazing ability to adapt to their vision loss. Training protocols directed at the position-based saccadic system have improved fixation stability, have trained eye movements in reading, and have the potential to help rereference saccades to the PRL. The excellent sensitivity of the periphery to motion clearly helps in navigation, allowing individuals with large scotomata and poor acuity to be independent, to take public transport, and even to play squash (Sullivan et al. 2008).

Research to maximize residual vision in CFL will have greater translational impact if it emulates real-world conditions, where viewing is binocular, and the head and body are free to move. Importantly, CFL due to MD is heterogeneous, so it is essential to characterize the location and extent of the individual’s binocular scotoma relative to the location of one or more PRLs.

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## LITERATURE CITED

Ackerley R, Barnes GR. 2011a. Extraction of visual motion information for the control of eye and head movement during head-free pursuit. Exp. Brain Res 210(3–4):569–82 [PubMed: 21298423]

Ackerley R, Barnes GR. 2011b. The interaction of visual, vestibular and extra-retinal mechanisms in the control of head and gaze during head-free pursuit. J. Physiol 589(Pt. 7):1627–42 [PubMed: 21300755]

Alexander MF, Maguire MG, Lietman TM, Snyder JR, Elman MJ, Fine SL. 1988. Assessment of visual function in patients with age-related macular degeneration and low visual acuity. Arch. Ophthalmol 106(11):1543–47 [PubMed: 3190538]

Altschwager P, Ambrosio L, Swanson EA, Moskowitz A, Fulton AB. 2017. Juvenile macular degenerations. Semin. Pediatr. Neurol 24(2):104–9 [PubMed: 28941524]

Barnes GR. 1993. Visual-vestibular interaction in the control of head and eye movement: the role of visual feedback and predictive mechanisms. Prog. Neurobiol 41(4):435–72 [PubMed: 8210413]

Barnes GR, Grealy MA. 1992. Predictive mechanisms of head-eye coordination and vestibulo-ocular reflex suppression in humans. J. Vestib. Res 2(3):193–212 [PubMed: 1342395]

Bernard J-B, Chung STL. 2016. The role of external features in face recognition with central vision loss: a pilot study. Optom. Vis. Sci 93(5):510–20 [PubMed: 26829260]

Boucart M, Delerue C, Thibaut M, Szaffarczyk S, Hayhoe M, Tran THC. 2015. Impact of wet macular degeneration on the execution of natural actions. Investig. Ophthalmol. Vis. Sci 56(11):6832–38 [PubMed: 26513497]

Brockmole JR, Henderson JM. 2006. Using real-world scenes as contextual cues for search. Vis. Cogn 13(1):99–108

Bullimore M, Bailey IL. 1995. Reading and eye movements in age-related maculopathy. Optom. Vis. Sci 72(2):125–38 [PubMed: 7753526]

Bullimore MA, Bailey IL, Wacker RT. 1991. Face recognition in age-related maculopathy. Investig. Ophthalmol. Vis. Sci 32(7):2020–29 [PubMed: 2055696]

Chen N, Shin K, Millin R, Song Y, Kwon MY, Tjan BS. 2019. Cortical reorganization of peripheral vision induced by simulated central vision loss. J. Neurosci 39(18):3529–36 [PubMed: 30814310]

Cheong AMY, Legge GE, Lawrence MG, Cheung SH, Ruff MA. 2007. Relationship between slow visual processing and reading speed in people with macular degeneration. Vis. Res 47(23):2943–55 [PubMed: 17881032]

Cheong AMY, Legge GE, Lawrence MG, Cheung SH, Ruff MA. 2008. Relationship between visual span and reading performance in age-related macular degeneration. Vis. Res 48(4):577–88 [PubMed: 18191983]

Cheung S, Legge GE. 2005. Functional and cortical adaptations to central vision loss. Vis. Neurosci 22(2):187–201 [PubMed: 15935111]

Chung STL. 2011. Improving reading speed for people with central vision loss through perceptual learning. Investig. Ophthalmol. Vis. Sci 52(2):1164–70 [PubMed: 21087972]

Chung STL. 2020. Reading in the presence of macular disease: a mini-review. Ophthalmic Physiol. Opt40(2):171–86 [PubMed: 31925832]

Churchland AK, Lisberger SG. 2002. Gain control in human smooth-pursuit eye movements. J. Neurophysiol87(6):2936–45 [PubMed: 12037197]

Crossland MD, Crabb DP, Rubin GS. 2011. Task-specific fixation behavior in macular disease. Investig. Ophthalmol. Vis. Sci 52(1):411–16 [PubMed: 20811056]

Crossland MD, Culham LE, Kabanarou SA, Rubin GS. 2005. Preferred retinal locus development in patients with macular disease. Ophthalmology 112(9):1579–85 [PubMed: 16087239]

Crossland MD, Culham LE, Rubin GS. 2004. Fixation stability and reading speed in patients with newly developed macular disease. Ophthalmic Physiol. Opt 24(4):327–33 [PubMed: 15228511]

Duret F, Issenhuth M, Safran AB. 1999. Combined use of several preferred retinal loci in patients with macular disorders when reading single words. Vis. Res 39(4):873–79 [PubMed: 10341972]

Eisenbarth W, MacKeben M, Poggel DA, Strasburger H. 2008. Characteristics of dynamic processing in the visual field of patients with age-related maculopathy. Graefe's Arch. Clin. Exp. Ophthalmol 246(1):27–37 [PubMed: 17882447]

Fine EM, Peli E. 1995. Scrolled and rapid serial visual presentation texts are read at similar rates by the visually impaired. J. Opt. Soc. Am. A 12(10):2286–92

Fletcher DC, Schuchard RA. 1997. Preferred retinal loci relationship to macular scotomas in a low-vision population. Ophthalmology 104(4):632–38 [PubMed: 9111255]

Fletcher DC, Schuchard RA, Renninger LW. 2012. Patient awareness of binocular central scotoma in age-related macular degeneration. Optom. Vis. Sci 89(9):1395–98 [PubMed: 22863789]

Fletcher DC, Schuchard RA, Watson G. 1999. Relative locations of macular scotomas near the PRL: effect on low vision reading. J. Rehabil. Res. Dev 36(4):356–64 [PubMed: 10678458]

Geringswald F, Herbik A, Hoffmann MB, Pollmann S. 2013. Contextual cueing impairment in patients with age-related macular degeneration. J. Vis 13(3):28

González EG, Liu H, Tarita-Nistor L, Mandelcorn E, Mandelcorn M. 2018a. Smooth pursuit of amodally completed images. Exp. Eye Res 183:3–8 [PubMed: 30012507]

González EG, Shi R, Tarita-Nistor L, Mandelcorn ED, Mandelcorn MS, Steinbach MJ. 2018b. Image stabilization in central vision loss: the horizontal vestibulo-ocular reflex. Vision 2(2):19

González EG, Tarita-Nistor L, Mandelcorn E, Mandelcorn M, Steinbach MJ. 2018c. Mechanisms of image stabilization in central vision loss: smooth pursuit. Optom. Vis. Sci 95(1):60–69 [PubMed: 29252901]

Heinen SJ, Badler JB, Watamaniuk SNJ. 2018. Choosing a foveal goal recruits the saccadic system during smooth pursuit. J. Neurophysiol 120(2):489–96 [PubMed: 29668381]

Heinen SJ, Potapchuk E, Watamaniuk SNJ. 2016. A foveal target increases catch-up saccade frequency during smooth pursuit. J. Neurophysiol 115(3):1220–27 [PubMed: 26631148]

Heinen SJ, Skavenski AA. 1992. Adaptation of saccades and fixation to bilateral foveal lesions in adult monkey. Vis. Res 32(2):365–73 [PubMed: 1574851]

Heinen SJ, Watamaniuk SNJ. 1998. Spatial integration in human smooth pursuit. Vis. Res 38(23):3785–94 [PubMed: 9893807]

Hubschman JP, Reddy S, Schwartz SD. 2009. Age-related macular degeneration: current treatments. Clin. Ophthalmol 3(1):155–66 [PubMed: 19668560]

Janssen CP, Verghese P. 2016. Training eye movements for visual search in individuals with macular degeneration. J. Vis 16(15):29

Johnston JL, Sharpe JA. 1994. The initial vestibulo-ocular reflex and its visual enhancement and cancellation in humans. Exp. Brain Res 99(2):302–8 [PubMed: 7925810]

Kabanarou SA, Crossland MD, Bellmann C, Rees A, Culham LE, Rubin GS. 2006. Gaze changes with binocular versus monocular viewing in age-related macular degeneration. Ophthalmology 113(12):2251–58 [PubMed: 16996593]

Krauzlis RJ. 2004. Recasting the smooth pursuit eye movement system. J. Neurophysiol 91(2):591–603 [PubMed: 14762145]

Kumar G, Chung ST. 2014. Characteristics of fixational eye movements in people with macular disease. Investig. Ophthalmol. Vis. Sci 55(8):5125–33 [PubMed: 25074769]

Kwon M, Nandy AS, Tjan BS. 2013. Rapid and persistent adaptability of human oculomotor control in response to simulated central vision loss. Curr. Biol 23(17):1663–69 [PubMed: 23954427]

Land MF. 1999. Motion and vision: why animals move their eyes. J. Comp. Physiol. A 185(4):341–52 [PubMed: 10555268]

Legge GE, Mansfield JS, Chung ST. 2001. Psychophysics of reading: clinical predictors of low-vision reading speed. Vis. Res 41(6):725–43 [PubMed: 11248262]

Little DM, Thulborn KR, Szlyk JP. 2008. An fMRI study of saccadic and smooth-pursuit eye movement control in patients with age-related macular degeneration. Investig. Ophthalmol. Vis. Sci 49(4):1728–35 [PubMed: 18385097]

Liu R, Kwon MY. 2016. Integrating oculomotor and perceptual training to induce a pseudofovea: a model system for studying central vision loss. J. Vis 16(6):10

Logan AJ, Gordon GE, Loffler G. 2020. The effect of age-related macular degeneration on components of face perception. Investig. Ophthalmol. Vis. Sci 61(6):38

MacKeben M, Fletcher DC. 2011. Target search and identification performance in low vision patients. Investig.Ophthalmol. Vis. Sci 52(10):7603–9 [PubMed: 21873676]

Madelain L, Krauzlis RJ, Wallman J. 2005. Spatial deployment of attention influences both saccadic and pursuit tracking. Vis. Res 45:2685–703 [PubMed: 16005932]

McIlreavy L, Fiser J, Bex PJ. 2012. Impact of simulated central scotomas on visual search in natural scenes. Optom. Vis. Sci 89(9):1385–94 [PubMed: 22885785]

Mckee SP, Nakayama K. 1984. The detection of motion in the peripheral visual field. Vis. Res 24(1):25–32 [PubMed: 6695503]

Nguyen NX, Stockum A, Hahn GA, Trauzettel-Klosinski S. 2011. Training to improve reading speed in patients with juvenile macular dystrophy: a randomized study comparing two training methods. Acta Ophthalmol 89(1):82–88 [PubMed: 19764912]

Orban De Xivry JJ, Bennett SJ, Lefèvre P, Barnes GR. 2006. Evidence for synergy between saccades and smooth pursuit during transient target disappearance. J. Neurophysiol 95(1):418–27 [PubMed: 16162830]

Pidcoe PE, Wetzel PA. 2006. Oculomotor tracking strategy in normal subjects with and without simulated scotoma. Investig. Ophthalmol. Vis. Sci 47(1):169–78 [PubMed: 16384959]

Rashbass C 1961. The relationship between saccadic and smooth tracking eye movements. J. Physiol 159:326–38 [PubMed: 14490422]

Renninger L, Dang L, Verghese P, Fletcher DC. 2008. Effect of central scotoma on eye movement behavior. J. Vis 8(6):641

Renninger L, Ma-Wyatt A. 2011. Recalibration of eye and hand reference frames in age-related macular degeneration. J. Vis 11:954

Renninger LW, Verghese P, Coughlan J. 2007. Where to look next? Eye movements reduce local uncertainty. J. Vis 7(3):6

Rubin GS, Feely M. 2009. The role of eye movements during reading in patients with age-related macular degeneration (AMD). Neuro-Ophthalmology 33(3):120–26

Rubin GS, Turano K. 1994. Low vision reading with sequential word presentation. Vis. Res 34(13):1723–33 [PubMed: 7941378]

Safi M, Verghese P, Shanidze N. 2020. Effects of task demands on smooth pursuit gain in macular degeneration. Investig. Ophthalmol. Vis. Sci 61:1045

Safran AB, Landis T. 1999. From cortical plasticity to unawareness of visual field defects. J. Neuro-Ophthalmol 19(2):84–88

Schuchard RA, Naseer S, de Castro K. 1999. Characteristics of AMD patients with low vision receiving visual rehabilitation. J. Rehabil. Res. Dev 36(4):294–302 [PubMed: 10678452]

Seiple W, Grant P, Szlyk JP. 2011. Reading rehabilitation of individuals with AMD: relative effectiveness of training approaches. Investig. Ophthalmol. Vis. Sci 52(6):2938–44 [PubMed: 21296824]

Seiple W, Rosen RB, Garcia PMT. 2013. Abnormal fixation in individuals with viewing an image of a face. Optom. Vis. Sci 90(1):45–56 [PubMed: 23238260]

Shanidze N, Ghahghaei S, Verghese P. 2016a. Accuracy of eye position for saccades and smooth pursuit. J. Vis 16(15):23

Shanidze N, Heinen S, Verghese P. 2017. Monocular and binocular smooth pursuit in central field loss. Vis.Res 141:181–90 [PubMed: 28057580]

Shanidze N, Verghese P. 2019. Motion perception in central field loss. J. Vis 19(14):20

Shanidze NM, Fusco G, Potapchuk E, Heinen S, Verghese P. 2016b. Smooth pursuit eye movements in patients with macular degeneration. J. Vis 16(3):1

Shanidze NM, Velisar A. 2020. Eye, head, and gaze contributions to smooth pursuit in macular degeneration. J. Neurophysiol 124(1):134–44 [PubMed: 32519572]

Sharpe JA, Sylvester TO. 1978. Effect of aging on horizontal smooth pursuit. Investig. Ophthalmol. Vis. Sci17(5):465–68 [PubMed: 640792]

Sheldon S, Quint J, Hecht H, Bowers AR. 2014. The effect of central vision loss on perception of mutual gaze. Optom. Vis. Sci 91(8):1000–11 [PubMed: 25014364]

Sullivan B, Jovancevic-Misic J, Hayhoe M, Sterns G. 2008. Use of multiple preferred retinal loci in Stargardt's disease during natural tasks: a case study. Ophthalmic Physiol. Opt 28(2):168–77 [PubMed: 18339049]

Taylor DJ, Smith ND, Binns AM, Crabb DP. 2018. The effect of non-neovascular age-related macular degeneration on face recognition performance. Graefe's Arch. Clin. Exp. Ophthalmol 256(4):815–21 [PubMed: 29484559]

Tejeria L, Harper RA, Artes PH, Dickinson CM. 2002. Face recognition in age related macular degeneration: perceived disability, measured disability, and performance with a bioptic device. Br. J. Ophthalmol 86(9):1019–26 [PubMed: 12185131]

Thibaut M, Boucart M, Tran THC. 2020. Object search in neovascular age-related macular degeneration: the crowding effect. Clin. Exp. Optom 103(5):648–55 [PubMed: 31698519]

Thibaut M, Delerue C, Boucart M, Tran THC. 2016. Visual exploration of objects and scenes in patients with age-related macular degeneration. J. Fr. Ophtalmol 39(1):82–89 [PubMed: 26707755]

Tsank Y, Eckstein MP. 2017. Domain specificity of oculomotor learning after changes in sensory processing. J. Neurosci 37(47):11469–84 [PubMed: 29054879]

Valberg A, Fosse P. 2002. Binocular contrast inhibition in subjects with age-related macular degeneration. J. Opt. Soc. Am. A 19(1):223–28

Van der Stigchel S, Bethlehem RAI, Klein BP, Berendschot TTJM, Nijboer TCW, Dumoulin SO. 2013. Macular degeneration affects eye movement behavior during visual search. Front. Psychol 4:579. [PubMed: 24027546]

Verghese P, Ghahghaei S. 2020. Predicting stereopsis in macular degeneration. J. Neurosci 40(28):5465–70. [PubMed: 32487694]

Vullings C, Verghese P. 2021. Mapping the binocular scotoma in macular degeneration. J. Vis 21(3):9

Wallace JM, Chung STL, Tjan BS. 2017. Object crowding in age-related macular degeneration. J. Vis 17(1):33 [PubMed: 28129416]

Walsh DV, Liu L. 2014. Adaptation to a simulated central scotoma during visual search training. Vis. Res 96:75–86 [PubMed: 24456805]

White JM, Bedell HE. 1990. The oculomotor reference in humans with bilateral macular disease. Investig. Ophthalmol. Vis. Sci 31(6):1149–61 [PubMed: 2354915]

Whittaker SG, Budd J, Cummings RW. 1988. Eccentric fixation with macular scotoma. Investig. Ophthalmol. Vis. Sci 29(2):268–78 [PubMed: 3338884]

Wiecek E, Jackson ML, Dakin SC, Bex P. 2012. Visual search with image modification in age-related macular degeneration. Investig. Ophthalmol. Vis. Sci 53(10):6600–9 [PubMed: 22930725]

Winterson BJ, Steinman RM. 1978. The effect of luminance on human smooth pursuit of perifoveal and foveal targets. Vis. Res 18(9):1165–72 [PubMed: 716236]

Zur D, Ullman S. 2003. Filling-in of retinal scotomas. Vis. Res 43(9):971–82 [PubMed: 12676241]

### SUMMARY POINTS

1. Individuals with MD take a long time to adapt to using the PRL to acquire a saccadic target. Even saccades to targets outside the scotoma are not direct, impacting daily activities such as reading or visual search.
2. Targeted eye movement training improves reading, and scotoma awareness training helps direct saccades to regions previously hidden by the scotoma.
3. Abnormal eye movement scan patterns in face recognition may be an adaptive strategy to use residual vision effectively.
4. Smooth pursuit gain is lower in individuals with MD.
5. Target direction relative to the scotoma is a significant determinant of smooth pursuit gain. Pursuit gain is lower for targets heading into the scotoma, as compared to those heading into healthier retina.
6. Individuals with MD do not continuously place their PRL on the tracked target, a behavior similar to pursuit by individuals with an intact fovea.
7. Binocular coordination during smooth pursuit depends on the similarity of the monocular scotomata in the two eyes.
8. Pursuit gain continues to be low when the head is free to move. Head movements do not compensate for low pursuit gain, although saccades might.

## FUTURE ISSUES

1. The extent to which the PRL inherits the oculomotor properties of the old fovea needs to be investigated.
2. In addition to typical clinical metrics such as acuity, type of disease, and onset time, investigators need to take into account the individual scotoma characteristics that determine visual function during binocular viewing in the real world. These include the size of the binocular scotoma with respect to the PRL and the presence of multiple PRLs.
3. Studies in CFL need to include investigations of visual function in more natural settings such as binocular and head-free viewing during manual tasks and locomotion.

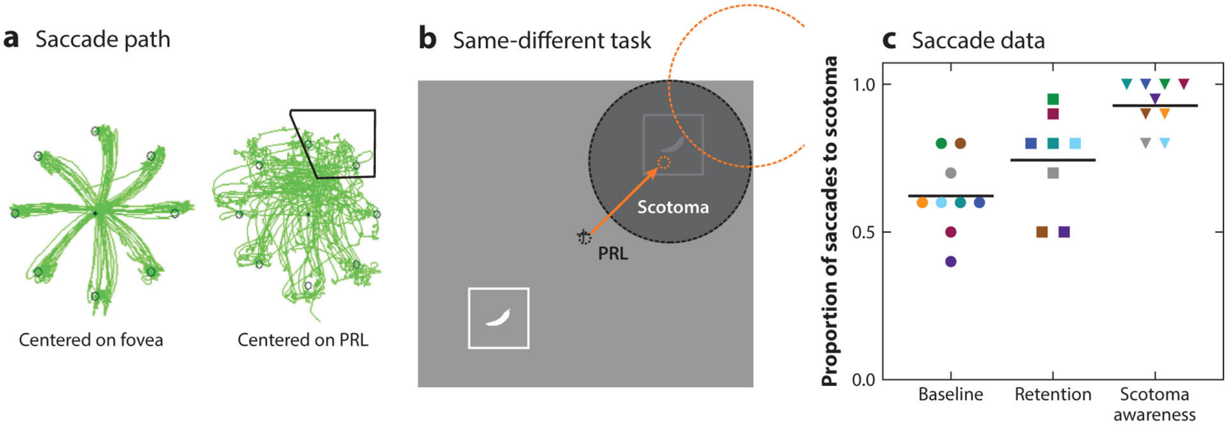

**Figure 1.**

(*a*) Scan paths to a target that appeared in one of eight positions in a healthy control (*left*) and a participant with CFL (*right*). The black outline represents the scotoma. The healthy control directed gaze close to the central fixation marker as directed, but the participant with CFL tended to place his PRL above and to the right of the fixation marker at the start of the trial (L. Renninger and A. Ma-Wyatt, unpublished conference data, used with permission; see also Renninger & Ma-Wyatt 2011). (*b*) Same-different task where CFL participants had to judge whether two stimuli were the same. Importantly, one stimulus was hidden behind their scotoma (*black disk*). Movement of the PRL (*dashed black circle*) toward the scotoma would uncover the hidden stimulus. PRL and scotoma location after this eye movement are shown in orange (based on principles from Janssen & Verghese 2016). (*c*) The proportion of saccades made toward the scotoma by CFL participants during baseline and retention for the same-different task and for a scotoma awareness task where a single target was placed behind the scotoma (C. Janssen and P. Verghese, unpublished data). Abbreviations: CFL, central field loss; PRL, preferred retinal locus.

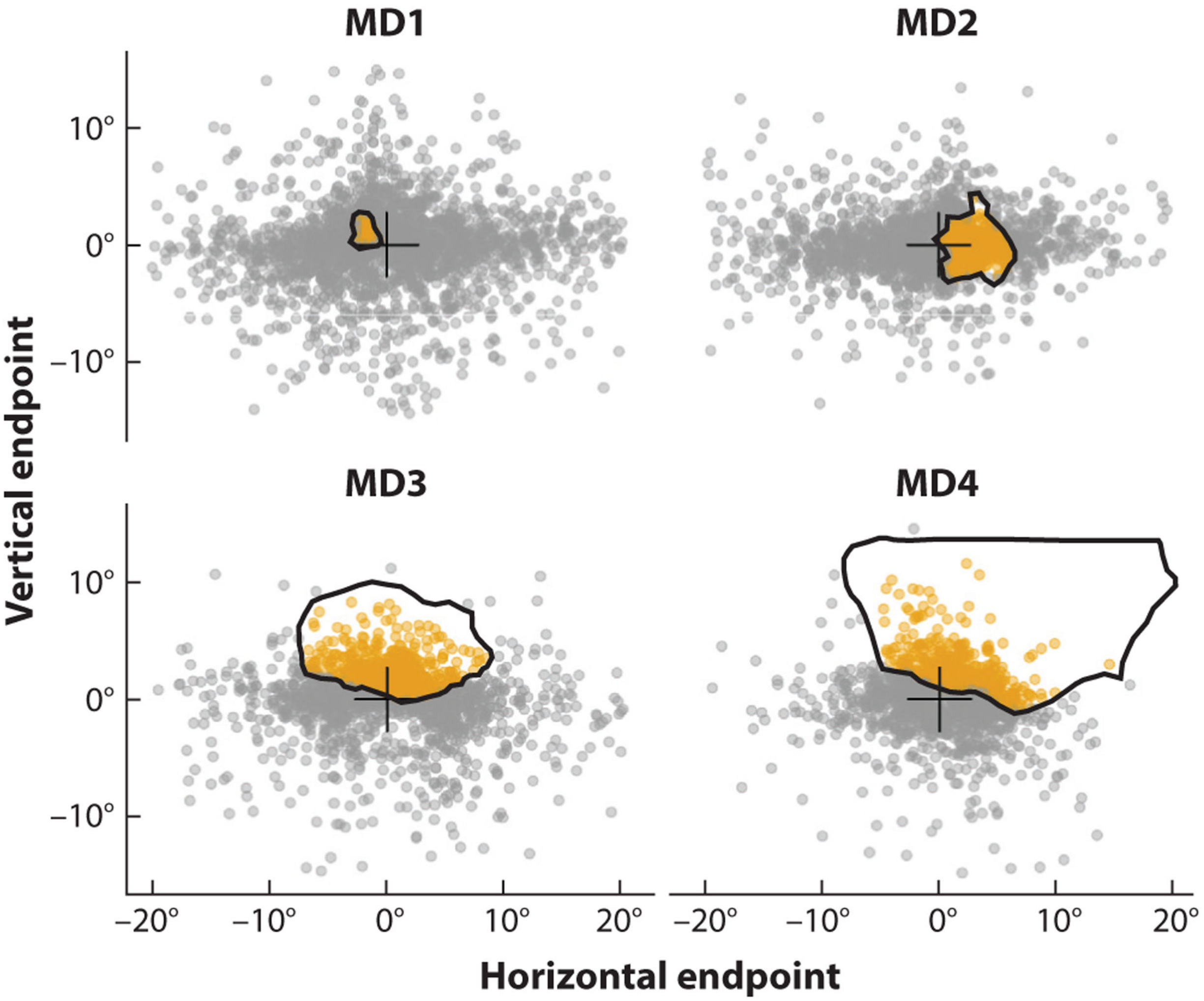

**Figure 2.**

Saccade endpoints relative to PRL for four participants with MD. Black crosses indicate PRL locations, orange dots indicate saccade endpoints directed toward the scotoma, and black outlines indicate binocular scotomata mapped with an eye tracker (C. Vullings, Z. Lively and P. Verghese, unpublished data). Abbreviations: MD, macular degeneration; PRL, preferred retinal locus.

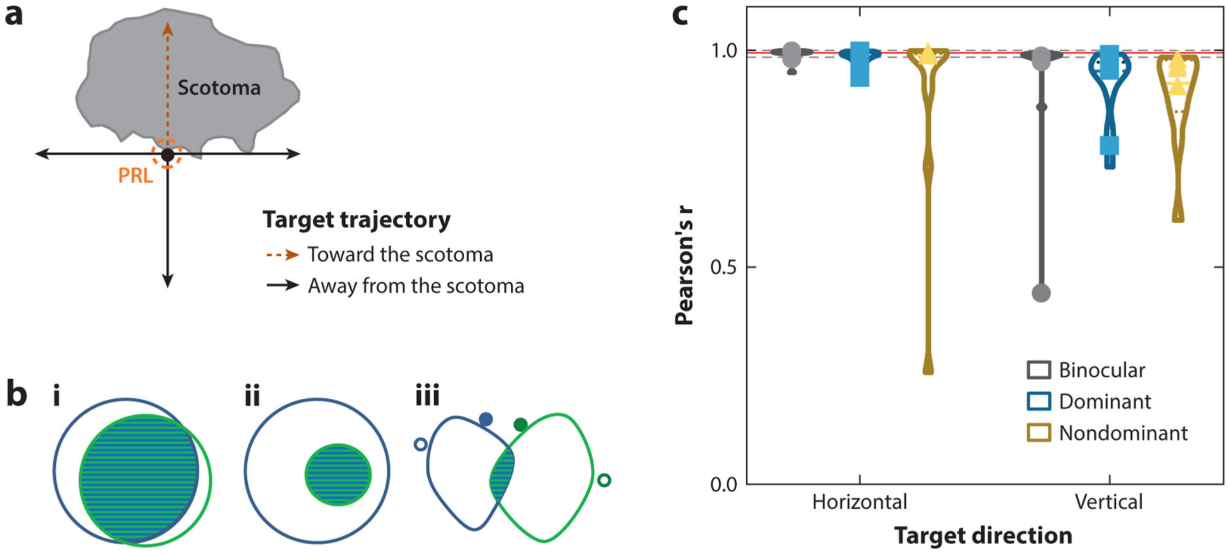

**Figure 3.**

(*a*) Schematic of pursuit directions relative to a monocular scotoma. (*b*) Relative size and overlap of monocular scotomata. (*i*) Large binocular scotoma resulting from similar scotomata in each eye. (*ii*) Small binocular scotoma resulting from a small scotoma in one eye that overlaps with a large scotoma in the other eye. (*iii*) Small binocular scotoma resulting from large nonoverlapping scotomata in each eye. Note that this scotoma is small in the static fixation case but can become larger as the relative position of the two eyes changes. Possible relative PRL locations are indicated with small circles. Neighboring PRLs are indicated with solid shading, and distant PRLs are indicated with hashed shading (left and right eyes and their corresponding PRLs are marked in blue and green, respectively). (*c*) Binocular coordination between the eyes in participants with CFL. Symbols show participants with overlapping PRLs and scotomata. The red horizontal line indicates mean correlation for controls; dashed gray lines indicate standard deviation. Figure constructed using data adapted from Shanidze et al. (2017). Abbreviations: CFL, central field loss; PRL, preferred retinal locus.

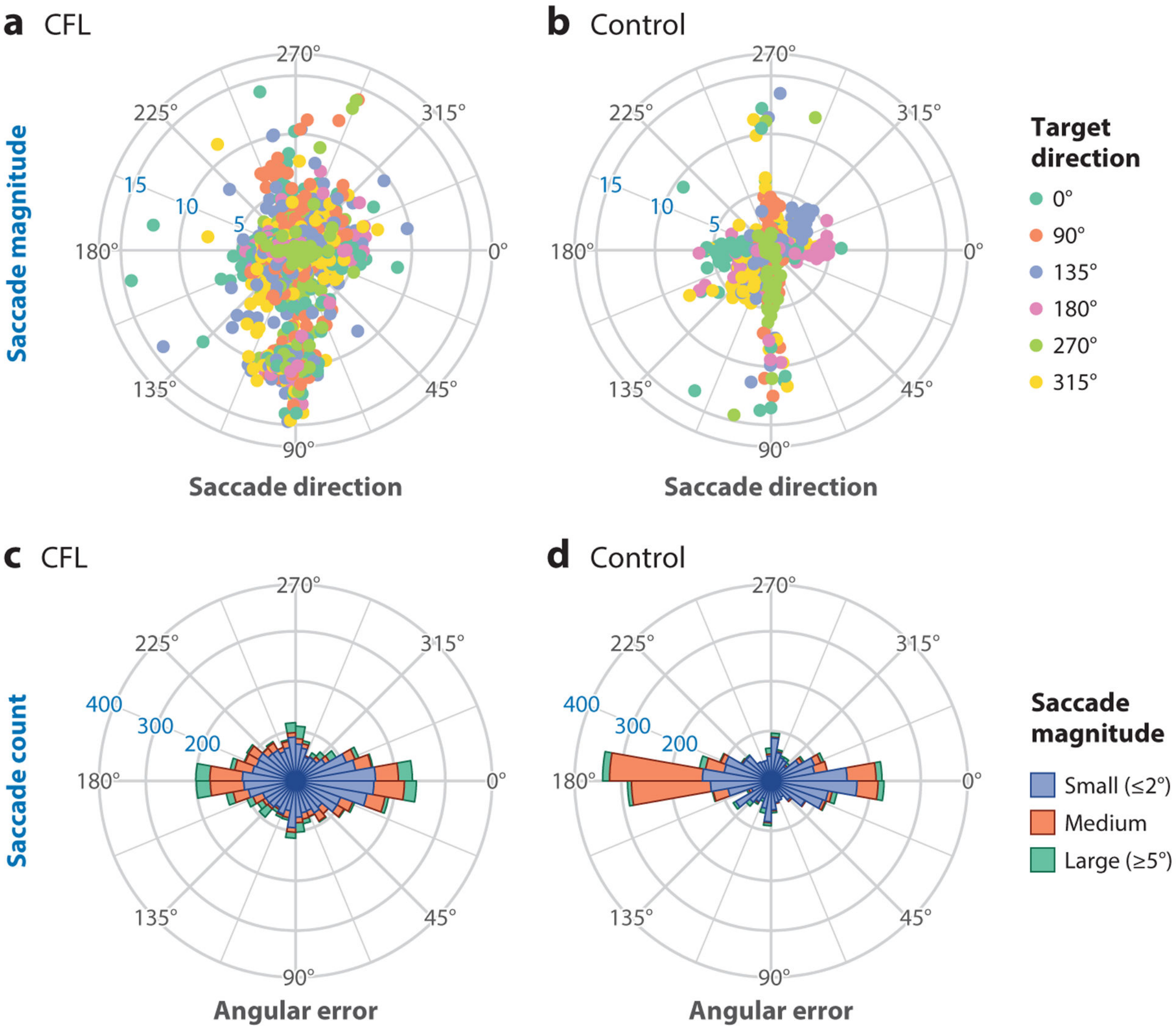

**Figure 4.**

(*a*,*b*) Distribution of raw saccade directions for six target directions, indicated by different colors. The radial axis indicates saccade magnitude. (*c*,*d*) Histogram of saccade directions relative to target direction, stacked by saccade magnitude. 0° indicates saccades in the target direction. The radial axis indicates saccade count. Data taken from NM Shanidze, Z Lively, R Lee, A Velisar and P Verghese, unpublished data. Abbreviation: CFL, central field loss.

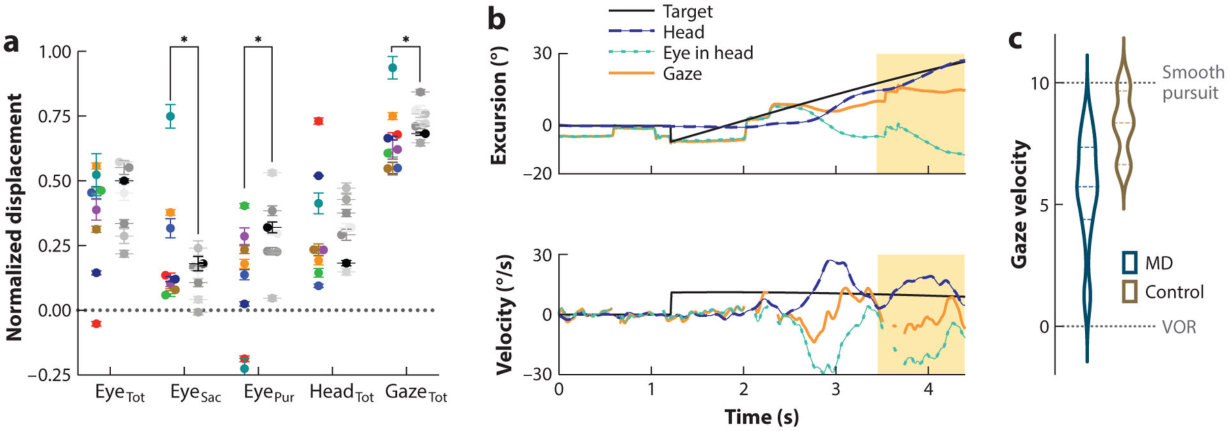

**Figure 5.**

Eye and head movements during smooth pursuit. (*a*) Mean eye and head displacement for the head-free condition. Participants with macular degeneration are represented by colored symbols, and controls are represented by grayscale symbols. Normalized eye displacement across the entire ramp portion of the pursuit trial is shown. Columns correspond to total eye displacement ($\text{Eye}_{\text{Tot}}$), eye displacement due to saccades only ($\text{Eye}_{\text{Sac}}$) and smooth pursuit only ($\text{Eye}_{\text{Pur}}$), head displacement ($\text{Head}_{\text{Tot}}$), and total displacement due to eye and head motion ($\text{Gaze}_{\text{Tot}}$). Each color corresponds to a given participant. Data are averaged across all trials and all directions; error bars are SE. Asterisks represent significant group differences between MD and controls. (*b*) Single head-free horizontal pursuit trial for one participant. The yellow box indicates the period where eye movement cancels head movement. The top panel shows position, and the bottom shows velocity. (*c*) Mean gaze (combined eye and head) velocity during pursuit of a 10°/s target. Ideal pursuit velocity and ideal VOR are marked with dotted lines. Figure adapted with permission from Shanidze & Velisar (2020). Abbreviations: MD, macular degeneration; SE, standard error; VOR, vestibulo-ocular reflex.