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The Effect of Structured Background on Smooth Pursuit with Real and Simulated Central Scotoma

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THE EFFECT OF STRUCTURED BACKGROUND ON SMOOTH PURSUIT WITH REAL AND SIMULATED CENTRAL SCOTOMA

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A THESIS

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VISION SCIENCE

ABSTRACT

The purpose of the study was to better understand the role of the fovea in smooth pursuit eye movements in human subjects. The research entailed a systematical study of a previously unstudied condition where the foveal inputs of both the background and the pursuit target were eliminated through simulation but the anatomic fovea was intact; and a comprehensive study of smooth pursuit eye movements of human subjects with real central scotoma.

Ten normally sighted subjects (NS) and three central scotoma subjects (CS) were asked to visually pursuit a 0.87^{o} yellow dot moving along either a horizontal or a vertical trajectory against a uniform grey or a binary random checkerboard structured background. The time-position waveform of the target was a sinewave with a 10^{o} amplitude and a frequency of either 0.15 or 0.40 Hz. NS tracked the target with the fovea or a 6.3˚ diameter simulated central scotoma. A high-speed eye tracker was used to track eye movements during pursuit in all subjects and to provide instantaneous gaze position data for implementing a central scotoma in NS subjects. Composite and smooth pursuit gains were obtained from raw eye position data using standard procedures.

A structured background caused a significantly larger proportional reduction in smooth gain when pursued with a simulated scotoma than with full foveal visual input. This was true under all conditions except in the horizontal direction at 0.40 Hz. In CS, the overall smooth gains were lower when pursuing a target on a structured background than a uniform background. When pursuing a target on a structured background, CS had a significantly larger proportional smooth gain reduction than NS with the fovea or a simulated scotoma. This was true in all conditions except in the vertical direction with a 0.15 Hz target.

Our results demonstrate that an anatomically intact fovea is required to perform quality smooth pursuit on a structured background even if it receives no visual input. A central scotoma disrupts the oculomotor control of smooth pursuit more profoundly than simply cutting off foveal visual inputs.

Keywords: smooth pursuit, fovea, central scotoma, background

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INTRODUCTION

Human beings explore their visual environment by moving their eyes so that the high acuity and high sensitivity fovea can be directed to and maintained on targets of interest to extract useful information. The efficiency of this system is greatly compromised when foveal vision is lost to diseases such as macular degeneration. Many studies have been devoted to understanding the impact of central field loss (CFL) on directing a functioning non-foveal retinal location to a target of interest (saccades without fovea), but little has been learned about how the functioning non-foveal retinal location can be kept on a moving target (smooth pursuit without fovea). This study explores smooth pursuit on different backgrounds with real and simulated CFL.

Normal Smooth Pursuit

Smooth pursuit eye movements are currently viewed as a response to motion, attention, cognitive expectations, and past experience (Kowler, 2011). Smooth pursuit allows one to continually maintain a moving target on the fovea, the retinal area of highest visual acuity; while saccades, or fast eye movements, allow quick and accurate targeting of the fovea from one point of interest to another (Hutton, 2000). Smooth pursuit works together with saccades to maintain a clear image of a moving object of interest on the fovea by constantly adjusting for target motion, background motion, and eye velocity throughout the execution of eye movement (Pack, 2001). A large volume of prior research has focused on eye movements and smooth pursuit specifically. For this reason, only previous literature related to the effects of a structured background on smooth pursuit of a sine wave stimulus in subjects with real and simulated scotoma is discussed herein.

In a typical smooth pursuit experiment, subjects are asked to follow a moving target with their eyes. In the simplest case, a target oscillates along a straight line with the velocity profile of a sine wave. This pursuit stimulus is quantified by two variables, the frequency, which is how fast the target oscillates (number of round-trips per second or Hz), and the amplitude, which is how far the target travels in each direction (in degrees of visual angle) (Figure 1).

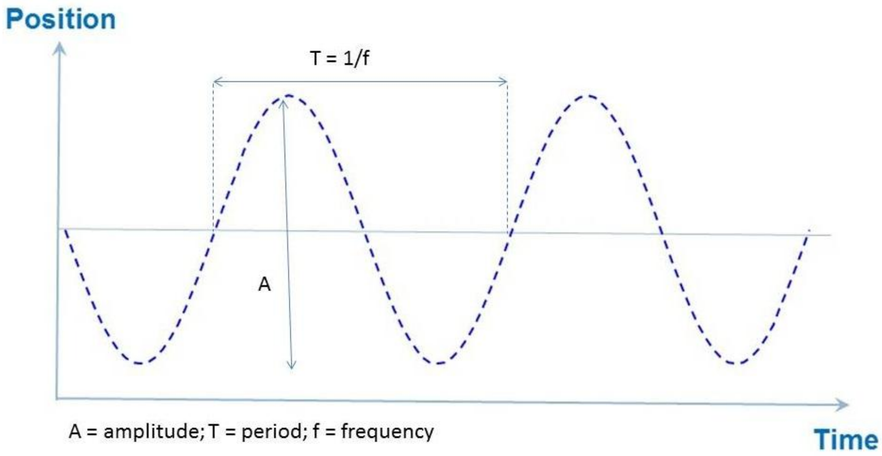

Figure 1. Example of a sine waveform.

The sine wave stimulus serves as the basis for more complicated waveforms because any waveform can be broken down into sinewaves of different frequencies, amplitudes and phases through Fourier Transform. The target can oscillate on a horizontal line, a vertical line, or a line in other directions to induce smooth pursuit in these directions.

Normal Smooth Pursuit on Uniform Background

The quality of smooth pursuit is commonly quantified by the gain and phase of the eye relative to the moving target. Eye gain is defined as the ratio of peak-to-peak amplitudes of the fundamental component of eye and target position (Collewijn, 1984). Eye phase is a measure of the difference in degrees that the eye leads or lags the target movement.

Under ideal conditions, normal subjects can almost perfectly smooth pursue a target using the fovea. For example, while pursuing a high contrast target on a dark, uniform background at frequencies less than 0.40 Hz, smooth pursuit gain is near unity, and phase shift remains near zero. As sinusoidal motion of a target exceeds 0.40 Hz, smoothness of pursuit is reduced and the insertion of saccades increases. When both smooth pursuit and saccades are used, a composite gain that describes the overall tracking quality can be derived (Figure 2). Smooth gain, which describes only the smooth pursuit component of tracking, is derived by removing the saccadic contribution from the composite gain (Collewijn, 1984).

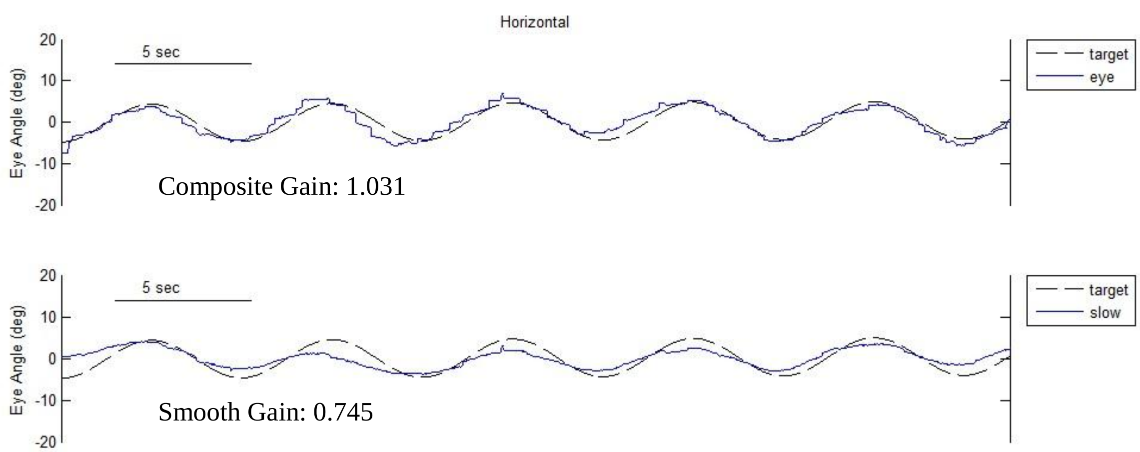

Figure 2. Example of eye position data with composite and smooth gain.

To maintain the fovea on the target when using smooth pursuit tracking, catch- up saccades made in the same direction as target motion may be inserted. Catch-up saccades may overshoot or undershoot the target. In the case of overshoot, smooth pursuit typically slows to allow the target to catch up, thus causing a reduction in smooth gain. If the catch-up saccade undershoots the target, smooth pursuit may exceed unity to realign the target on the fovea without an additional catch-up saccade. These adaptations are possible if the foveation error is small, and serve to minimize the insertion of additional saccades, which reduce target visibility (Grossberg, 2012). A result of catch-up saccades is that composite and smooth pursuit gains may exceed unity (Collewijn, 1984; Optican, 1985). Therefore a comprehensive understanding of smooth pursuit requires analysis of gains of both composite and smooth pursuit.

Normal Smooth Pursuit on a Structured Background

A structured background represents more of a real-world environment than the dark, uniform backgrounds typically used to study smooth pursuit (Kimming, 1992). Collewijn (1984) compared the effects of dark, diffuse and structured backgrounds on composite and smooth pursuit gains. Subjects were seated 1.5 m in front of a screen. A target of 7 minutes of arc diameter was projected on the screen. A scleral coil was used to record eye movements as subjects tracked the target on different types of backgrounds. The backgrounds used were room darkness (<1 cd/m^2), diffuse illumination (11 cd/m^2) or a structured background that could be horizontal and vertical sine-wave or square-wave gratings, or checkerboard patterns made up of random checks of 15 minutes of arc. The average luminance of the diffuse and structured backgrounds was the same. Target waveforms tested were single sine wave (0.15-0.52 Hz, amplitude 7-10˚), triangular (0.06-0.52 Hz, amplitude 7-10˚), and pseudorandom (made up of four summed non-harmonic sine waves of different amplitudes). To analyze the data, horizontal and vertical components of the eye movement were separated. For sine-wave stimuli, the smooth gain was calculated by first removing the saccades from the raw eye movement data and then reconnecting the smooth pieces into the smooth pursuit waveform.

Collewijn (1984) found that the dark and diffuse backgrounds had little effect on smooth pursuit. The gain of the horizontal and vertical composite component remained at or near unity (100%), and only decreased slightly at the highest frequency. The smooth component made up about 94% of the total eye movement, the remainder consisting of saccades. Smooth gain was slightly higher in the horizontal direction compared to the vertical, and decreased at the higher frequencies (range 0.15-0.52 Hz). Structured backgrounds caused a 10% reduction of smooth pursuit gain in the horizontal, and 20% in the vertical direction. This result did not change with the type of structured background used.

In a subsequent experiment testing smooth pursuit of a peripheral target, Collewijn (1986) used arrows aligned five degrees above and below the fovea to simulate eccentric tracking of single sinusoids of 0.15 or 0.52 Hz (amplitude 10˚) and various triangular or pseudorandom stimuli. Subjects were asked to follow an imaginary spot located midway between the arrows as they moved along a horizontal trajectory. Consistent with Collewijn's earlier work (1984), dark and diffuse backgrounds had little effect on smooth pursuit gain with tracking of sinusoidal targets. Horizontal pursuit of the same eccentric targets against a random dot structured background (that covered the fovea and periphery) reduced smooth gain by about 20%, as opposed to the 10% previously reported with foveally stimulated targets.

Normal Smooth Pursuit on Structured Background – Possible Mechanism

When pursuing a target moving over a structured stationary background, the movement of the eyes induces a motion of the retinal image of the background in the opposite direction. This large field background motion would result in an involuntary optokinetic nystagmus (OKN), which causes the eyes to move in the same direction of the background (i.e., opposite to the direct of the target) (Krauzlis, 2004). Therefore, in order to smooth pursue a target against a structured background one must maintain the target on the fovea while somehow discounting the induced background retinal image motion in the opposite direction. Pack (2001) proposed that the motion of the background, although in conflict with the smooth pursuit, can provide useful predictive information about eye velocity that helps control smooth pursuit. Based on prior research, Pack developed a model that uses target motion, background motion, and eye velocity to maintain smooth pursuit eye movements; and suggests how pursuit is performed on structured backgrounds. This model is only briefly discussed herein, as a thorough examination of the complexities of this topic is beyond the scope of this thesis.

The main areas of visual motion processing in primates are MT (middle temporal area; V5) and MST (medial superior temporal area) (Ilg, 2008). Area MT consists of small receptive field cells that respond to the direction and speed of target motion. MT contains cells that produce responses during pursuit of a foveal or parafoveal target. (Ilg, 2003) MST receives input from MT and is composed of two parts, MSTl (lateral) and

MSTd (dorsal). MSTl has neurons with small receptive fields and is used in the execution of smooth pursuit, whereas MSTd contains larger receptive fields and is thought to play a role in the analysis and compensation of structured background motion. (Pack, 2001; Inaba, 2011) MST contains neurons that respond to a variety of stimuli including foveal or parafoveal pursuit (termed "visual tracking" neurons), and eccentric or imaginary target motion. (Ilg, 2008)

In tracking a target with smooth pursuit against a structured background, MT and MST communicate with each other and with other brain centers to provide information about background motion, target motion, and eye velocity. This communication helps drive eye movements. (Pack, 2001; Grossberg, 2012)

Pack's model proposed that when tracking on a dark, uniform background, eye movement almost matches the target motion in space, and target motion on the retina is quite small. In this case, the output signal from MST is low. However, when tracking a target on a structured background, the background motion produces a larger signal from MST. Although the signal of MST cells in the direction of the target is stronger, cells preferring motion in the opposite direction are also stimulated. Pack (2001) hypothesized that, due to the background motion, this competing signal in MST cells to direct the eye in two opposite directions at the same time leads to suppression of the OKN response, but at the expense of a slight reduction in pursuit speed and smooth gain, as was observed in studies by Collewijn (1984, 1986).

Smooth Pursuit With Central Scotoma

Typically the fovea is used in fixation and smooth pursuit of a target of interest. Visual acuity decreases rapidly as distance from the fovea increases. When the fovea is severely damaged by diseases such as Stargardt's disease or macular degeneration, a central scotoma occurs. A central scotoma is an area in the center of the visual field where visual perception is severely impaired or completely abolished. Although a central scotoma is usually depicted as a blurry area that partially or completely conceals the image behind it, in reality, a lot of patients do not see a black or gray patch and are not consciously aware of the existence of a scotoma. However, they are aware of the consequences of the scotoma, for example, an object disappears, a line breaks, or a car suddenly jumps out from nowhere (Schuchard, 2005). To increase the patient's awareness of the scotoma is one of the first steps of rehabilitation.

Patients with central scotoma must utilize a peripheral retinal location to see. If the patient can consistently use one peripheral retinal location to see, this location is called a preferred retinal locus (PRL) (Crossland, 2011). Several PRLs may develop according to specific visual tasks (Cohen, 2005) or be dependent on illumination (Lei, 1997).

While much research has focused on saccadic movements with a central scotoma (Whitaker, 1991), to our knowledge no studies have investigated the effects of real central scotoma on smooth pursuit gain in humans. Parafoveal lesions in monkeys have been reported to cause markedly decreased eye velocity during smooth pursuit tracking of a small (20 arc min in diameter) red He-Ne laser (Roberts, 1986), though the type of background used in this study was not reported.

Smooth Pursuit on Structured Background With Central Scotoma

Skavenski (1993) proposed that foveal stimulation is needed to smoothly pursue a target in the presence of a structured background. He hypothesized that suppression of background motion caused by smooth pursuit of a peripheral target was not effective without the fovea. In that study, monkeys were trained to fixate and pursue a target when it moved. Then, a lesion three degrees arc in diameter was photocoagulated at the fovea. After a few days the monkeys had established a PRL and could maintain fixation against a dark background. Stationary or moving checkerboard or random dot backgrounds elicited minor deterioration of fixation. Saccades took longer than fixation to adapt but eventually recovered to a moderate degree. Initially saccades were made to the fovea, but over time increased in frequency to the PRL. Saccades showed similar results on dark and lighted backgrounds.

Smooth pursuit of sinusoidal or pseudorandom sine or triangular waveforms with a 0.1˚ target against a dark background was measured and found to be almost as good as that prior to foveal lesion. However, when the visibility of a sine-wave grating background whose orientation was perpendicular to the pursuit path was increased, the pursuit became more and more saccadic. The smooth gain decreased and eventually became immeasurable. Target size and color was adjusted in an attempt to compensate for any loss in target salience. The same sine-wave background had a slightly smaller effect when the target was 5 times larger. Smooth pursuit testing soon after photocoagulation, and again one year later, produced similar reductions in gain, demonstrating a failure of the system to recover. (Skavenski, 1993)

Summary

Skavenski noted that he was the first to report that the fovea may play a central role in enabling smooth pursuit of a peripheral target on structured backgrounds (1993). This is particularly important, as a structured background represents more of a real world condition for smooth pursuit. Research under these conditions may elicit more meaningful information about eye movements in subjects with central scotoma. Skavenski also noted the large difference between the pursuit eye movements of his monkeys and those of the subjects of Collewijn & Tamminga's (1984) experiment, even though a peripheral retinal location was used for pursuing in both cases. He raised the question "Why must the fovea be there even when it is not directly stimulated?" This study aims to achieve a better understanding of the effect of background on smooth pursuit by studying subjects with real and simulated scotomas.

RATIONALE OF THESIS

There is one monkey study that demonstrated that obliterating the fovea had only a mild effect on smooth pursuit against a uniform background, but had a devastating effect on smooth pursuit against a structured background (Skavenski, 1993). This differential effect was not due to the fact that a peripheral retinal location was used for pursuit because normal human subjects can perform pursuit of peripheral targets on both a uniform and structured background with only a mild reduction of smooth gain (Collewijn, 1986). The role of an intact fovea in smooth pursuit cannot be unequivocally determined from these studies because Skavenski's monkeys had damaged fovea and thus had no foveal input of the background, while Collewijn's human subjects had an intact fovea and had foveal input of the background. There are two possible causes for the strong effect of a structured background on smooth pursuit observed in Skavenski's monkeys – lack of foveal input of the background, and damage to the anatomic fovea. Therefore, it is not clear whether the foveal visual input related to smooth pursuit must be there or an anatomically intact fovea must be there or both in order to support good pursuit performance over a structured background. This study is designed to achieve a better understanding of the role of the fovea in smooth pursuit by, 1) using a gaze-contingent display to test smooth pursuit with intact fovea but with no foveal input of the background; and, 2) measuring smooth pursuit in patients with a central scotoma.

METHODS

Subjects

Ten adult normally sighted (NS) subjects (seven women and three men), and three subjects with central scotoma (CS; one woman and two men) were tested. Their ages ranged from 21 to 62 years. (Table 1)

Table 1

Age and Gender of Subjects by Group

Group	**Gender**	**Age**
Normally Sighted (NS); n=10	Female (7)	22, 27, 30, 35, 36, 45, 52
	Male (3)	21, 22, 44
Central Scotoma (CS); n=3	Female (1)	52
	Male (2)	27, 62

Three NS and one CS subject had previous exposure to eye tracking tasks, including smooth pursuit or simulated central scotoma. Two of the CS subjects were recruited from the UAB Center for Low Vision Rehabilitation. The other subjects were recruited from UAB students and staff and local communities through word of mouth and flyers.

Enrollment and Screening Tests

Prior to any testing, the purpose, procedure and any risks of the study were explained to the subject and an informed consent was obtained following protocols approved by the UAB Institutional Review Board. All subjects went through an enrollment and screening testing session by a low vision optometrist (author) that took one hour to complete. The subject's history was taken, to exclude any remarkable ocular or systemic history (such as strabismus, or schizophrenia) that might interfere with smooth pursuit. High contrast monocular and binocular acuities were tested of normally sighted subjects at 4 meters with a Bailey-Lovie acuity chart. The chart is standardized for 6 meters, so +0.1 logMAR was added to the measured acuities. NS subjects all had visual acuity that was correctable to Snellen 20/20 equivalent. For two of the CS subjects, visual acuity was obtained from their last examination at the UAB Center for Low Vision Rehabilitation. To ensure adequate color vision of NS subjects, Ishihara's Tests for Colour Deficiency, Concise Edition, 2006 was conducted.

CS subjects underwent scotoma and fixation mapping using a Nidek microperimeter (MP1 by Nidek Technologies, Vigonza, Italy), which allowed the examiner to observe a subject's fundus in real-time. Subjects were seated in front of the MP1 and asked to look into the objective of the device and to maintain steady fixation at a red fixation cross at the center of a dark field during the entire test. Cross size was adjusted depending on the subject's scotoma size. Subjects were asked if the cross was clear. If not, a built-in spherical error correction was adjusted to make the cross appear clear. The examiner then took an infrared picture of the fundus and selected two retinal landmarks, one at the center of the optic disk, and the other on a portion of the retinal vessels. These landmarks are used by the MP1 to track the movements of the eye so that the perimetry target could be delivered to the intended retinal location.

To map the scotoma, a semi-automatic screening protocol was used, in which the retinal area around the scotoma was demarked manually and was filled automatically with perimetric testing locations. The perimetry target was a white light spot that flashed on a dark background. Subjects were given a hand-held clicker and instructed to press the clicker when a flash of light was detected, while maintaining fixation on the cross.

Small manual adjustments of the MP1 camera position were made during perimetry testing. The device would temporarily halt testing when the eye and the device were not correctly aligned and eye tracking was lost. Depending on the size of scotoma and the subject's ability to maintain stable fixation, testing took between 5-15 minutes per eye. The subject could take short breaks during testing if needed. After completion of perimetry, a color fundus photo was taken and a registration procedure was used to superimpose the color photo with the infrared photo. This allows one to visualize the physical scotoma on the retina together with the visual field threshold results. Because the MP1 tracks eye movements during the examination, it records a history of fixation points used by the subject throughout the test. These points are also superimposed on the color fundus photo and can be used to determine PRL and to assess fixation stability.

Equipment

An EyeLink II eye tracker (SR Research, version 2.31), running at a sampling rate of 250 Hz, was used to record eye movements and to simulate a central scotoma. The EyeLink II is widely utilized in eye movement studies. It is a head-mounted system with dedicated hardware to monitor pupil and head movements. It consists of a headband with two eye cameras that monitor the movements of the two pupils, and a head motion camera that monitors four infrared illuminators attached to the stimulus computer monitor to register head movement. Pupil positions and head positions are used to calculate gaze positions.

The EyeLink II has two dedicated computers. A host computer is used to track the eyes, and a display computer is used to generate and display visual stimuli. Visual stimuli were shown on a 20” Dell Trinitron CRT color monitor running at a 120 Hz frame rate and 800x600 pixels resolution with a maximum luminance of 80 cd/m^2. At a viewing distance of 60 cm, the display area of the monitor subtends 34.0x26.9˚, and each pixel subtends 2.62 minutes of arc. The communication between the host and display computer allows the display computer to receive a set of eye position data every 4 ms with a delay of about 2 ms.

Stimulus

Pursuit Target

The pursuit stimulus was generated on the display computer using PsychToolbox (http://psychtoolbox.org/HomePage) on Matlab (The MathWorks, Natick, MA). The pursuit target was a 0.87˚ diameter yellow circle with a 0.29˚ diameter grey diamond in the center. While the traditional stimulus used for smooth pursuit is usually a small 0.1˚ bright laser spot projected on a screen (Collewijn, 1984; Heinen, 1998), a larger stimulus is needed to accommodate for the reduced vision of CS subjects. For example, Little (2008) used a dot stimulus subtending 2˚ of visual angle to investigate brain area activation during smooth pursuit in macular degeneration subjects. This stimulus size was chosen to ensure that subjects with vision better than 20/600 could follow the target. The

CS subjects in our study had visual acuity of 20/200 (1.0 logMAR), therefore a 0.87˚ target was considered appropriate. During pilot testing, a participating CS subject demonstrated that high smooth pursuit gains could be obtained using this target under optimal pursuit conditions.

The color of stimuli used in smooth pursuit experiments is typically red (Collewijn, 1984). While target salience plays a role in smooth pursuit (Miura, 2001), reduction in smooth pursuit gain against structured backgrounds is not simply due to target contrast (Kimmig, 1992). Pilot testing revealed that for a CS subject, red targets were difficult to track and tended to blend into the background. Compared to red, blue and green target demonstrations, a yellow target with a luminance of 142 cd/m^2 was subjectively perceived as easiest to follow on uniform and structured backgrounds; and thus was used in this study.

The target moved smoothly along either a horizontal or a vertical straight line. The velocity profile of the target was a sine-wave with a 10˚ peak-to-peak amplitude. Once the amplitude of the target motion was fixed, the velocity of the target was determined by the frequency of the target waveform. Two frequencies, 0.15 and 0.40 Hz, were tested. A sine waveform is frequently used in smooth pursuit eye movement studies. One of the reasons is that any target waveform can be decomposed into sums of sinewaves of different amplitudes and phases using Fourier transform. In this study, a sinewave was selected because more complex waveforms, such as unpredictable waveforms made of the sum of several random sinewaves, might not elicit measurable smooth pursuit under some of the study conditions in which severe impairment of visual input, either from a simulated or a real central scotoma, were studied. A sinewave would also facilitate comparison with results of classic studies, such as those of Collewijn (1984) and Skavenski (1993). The amplitude and frequencies of 0.15 and 0.40 Hz were also chosen based partly on Collewijn's studies of smooth pursuit that tested target velocities of 0.15-0.52 Hz (1984, 1986). Based on pilot testing of NS subjects with simulated scotoma and CS subjects, higher frequencies such as 0.52 Hz, were not included in the study design because of their tendency to reduce smooth gain to a point that might not provide meaningful results under both real and simulated scotoma conditions.

Background

The stimulus was presented on either a uniform grey or a binary random checkerboard background made up of black and white square checks 0.87^{o} in size. Both backgrounds had mean luminance of 127 cd/m^2. Traditionally, smooth pursuit experiments utilize a dark (< 1 cd/m^2) uniform background (Collewijn, 1984). A bright target on such a dark background has significantly higher average contrast compared to the same stimulus on a structured background, and thus may put pursuit on a structured background in an inferior position. Collewijn found that smooth pursuit was slightly improved on a dark background as compared to a diffuse background. For this reason we chose to equalize the mean luminance of the uniform and structured backgrounds in this study so that the contrast effect between target and background would be minimized.

Simulated Central Scotoma

A gaze-contingent, 6.3˚ diameter, circular, grey spot was generated with the Psychtoolbox to simulate a central scotoma in NS subjects. This was achieved by blending a transparency-adjustable sheet with the underlying background image (α-blending). The profile of the simulated scotoma was a circular pit whose bottom was completely opaque (no background information was visible) on a flank plain which was completely transparent (background information 100% visible). There was a smooth Gaussian transition from complete opaque to complete transparent, giving the simulated scotoma a fuzzy look on a structured background. The diameter of the scotoma was defined at the half-height of the Gaussian transition. On the mid-gray uniform background, the scotoma was not visible unless the pursuit target fell into or emerged from it. On the structured background, the scotoma appeared as a circular gray spot where the background image was completely wiped out in its center and became gradually visible toward its edge. The position of the simulated scotoma was updated on every screen frame using the most recent gaze position data from the eye tracker in a way that the stimulus, target and background, was obscured from the foveal viewing of the subject, effectively producing a central scotoma. In order to visualize the target during pursuit trials with the simulated central scotoma, subjects had to look away from the target so that the target fell on a retinal region not covered by the scotoma.

Procedure

Normally Sighted Subjects

Prior to any testing, subjects were told that their task was to follow a moving target as accurately and smoothly as possible without anticipating the target motion while keeping their head as still as possible. Subjects were informed that the testing would include a grey or checkerboard-type background, a yellow target, and a horizontally or vertically moving target at slow or faster speed. Subjects were also told that under some conditions their central view of the target would be obscured by a simulated central scotoma or “blob”. It was explained to subjects that, in trials with scotoma:

> *“…wherever you look, there will be an area that is greyed out. Therefore, you have to use your side or peripheral vision to view the target. You may have a reflex to use your central vision to see the target, but again, that will only make the target disappear, or grey out. It may take a little while to get used to using your side vision to follow the target. To keep the target in your side vision you may try to look above or to the side of the target. The goal of the task is the same as that without the scotoma, that is, to mirror, or follow, the movement of the target as accurately and smoothly as possible, without anticipating the target motion or moving your head, but using your side vision only.”*

In between trials, subjects were asked to confirm that the target was always in their side vision, or that the scotoma did indeed cover the target when an attempt to directly view the target was made. During blinks, eye tracking would be temporarily lost and the monitor would grey out, providing no visual information. This was instituted to prevent the subject from intentionally defeating the gaze-contingent display by causing eye tracking loss by narrowing the eye opening or moving the eyes to extreme positions. Trials in which subjects reported they could see the target with their fovea were excluded from analysis and retested. This occurred in less than ten trials.

The laboratory had fluorescent lighting. Subjects were seated 60 cm from the display monitor and used a chin rest to maintain a constant viewing distance. This helped stabilize the head for more accurate eye tracking. The headband of the EyeLink II eye tracker was first fit on the subject's head snuggly. Then the positions of eye cameras were adjusted so that they lined up with the eyes. Next, camera focus was adjusted to form clear images of the subject's pupils. Tracking of the pupils at extreme eye positions were checked to ensure reliable tracking over the pursuit field. The real time images of the eyes provided by the eye tracker made these adjustments easy. Subjects were instructed to inform the researcher if at any time the head band felt too tight, or if they needed a break from testing.

Each pursuit experimental session started with a five-point calibration, followed by a similar validation procedure to confirm the accuracy of the calibration. Calibration and validation was repeated if neither eye received a designation of "GOOD", as determined by the eye tracker host computer. Each pursuit experimental session consisted of two or four pursuit trials. Each pursuit trial started with the pursuit target appearing at the starting position of the target trajectory (5˚ to the left of or above the center of the screen). The subject was instructed to fixate directly on the target. The fixation was monitored by the researcher by viewing the relative positions between gazes of the two eyes and the fixation target on the host display. The trial was started by pressing the space bar when the subject's eyes were on the target. This "drift correction" was used to adjust for any slight changes of headband or camera position. If the measured error was correctable, it would be corrected and the trial started. If not, calibration and validation was repeated. Based on Collewijn's (1984) study, each trial consisted of a 35-second pursuit. The subject pursued the target using both eyes.

There were four experimental factors for normally sighted subjects: viewing condition (foveal vs. simulated scotoma), background (uniform vs. structured), pursuit direction (horizontal vs. vertical) and target velocity (0.15 vs. 0.40 Hz) (Table 2). A full factorial design was used, in which all combinations of all factors were tested 8 times. The first 5-7 trials were conducted without the simulated scotoma. This provided subjects the opportunity to become familiar with the pursuit task under the different conditions. Before the first scotoma condition, subjects were reeducated on the consequences of simulated scotoma and the goal of the task (as described above). Then the order of testing conditions was randomized. In between sessions, subjects were allowed to sit back from the chinrest and rest while the researcher set up the next condition. For NS subjects, the testing took between 5-7 hours to complete.

Table 2

Testing Conditions for Normally Sighted Subjects

Group	Background	Scotoma	Target Direction	Target Frequency	Target Color	Number of Trials
Normally Sighted; n=10	Uniform	None	Horizontal	0.15 Hz	Yellow	8
	Uniform	None	Vertical	0.15 Hz	Yellow	8
	Uniform	None	Horizontal	0.40 Hz	Yellow	8
	Uniform	None	Vertical	0.40 Hz	Yellow	8
	Structured	None	Horizontal	0.15 Hz	Yellow	8
	Structured	None	Vertical	0.15 Hz	Yellow	8
	Structured	None	Horizontal	0.40 Hz	Yellow	8
	Structured	None	Vertical	0.40 Hz	Yellow	8
	Uniform	Simulated	Horizontal	0.15 Hz	Yellow	8
	Uniform	Simulated	Vertical	0.15 Hz	Yellow	8
	Uniform	Simulated	Horizontal	0.40 Hz	Yellow	8
	Uniform	Simulated	Vertical	0.40 Hz	Yellow	8
	Structured	Simulated	Horizontal	0.15 Hz	Yellow	8
	Structured	Simulated	Vertical	0.15 Hz	Yellow	8
	Structured	Simulated	Horizontal	0.40 Hz	Yellow	8
	Structured	Simulated	Vertical	0.40 Hz	Yellow	8

Central Scotoma Subjects

Central scotoma subjects had varying macular disorders (Figure 3; Table 3).

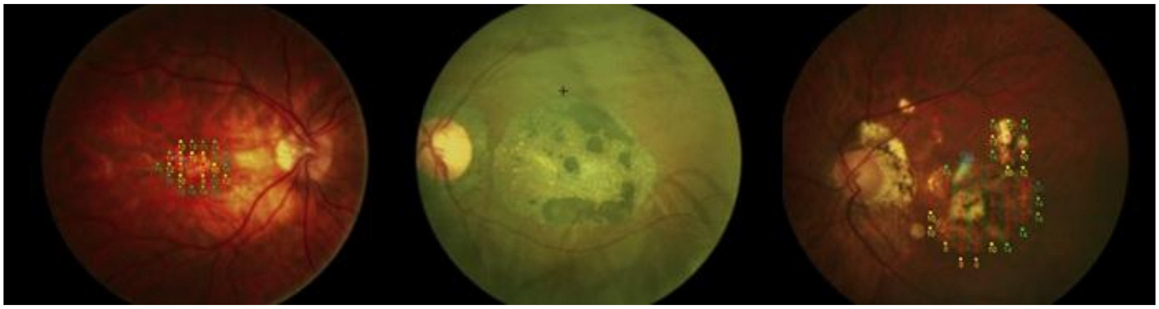

Figure 3. Photographs of retinal lesions in central scotoma subjects (11, 13, and 12 respectively).

The procedure for testing of central scotoma subjects differed only slightly from NS subjects. CS subjects were tested monocularly using an eye patch to occlude the non-tested eye. The eye to be tested for CS subjects 11 and 13 was chosen based history of using bioptic telescopes to drive. The eye for sighting through the telescope is typically the dominant or better eye. Subject 12 had a smaller central lesion in the left eye, and pilot testing had established the left eye as the better tracking eye.

Table 3

Ocular Conditions of Central Scotoma Subjects

Group	**Subject**	**Retinal Disorder**	**Visual Acuity**	**Central Scotoma**	**Fixation During MP1**	**Color Vision**
Central Scotoma n=3	11	OD: Congenital, Undetermined	20/200	3-4˚	Superior temporally	1/14
	12	OS: Idiopathic CNVM	20/225	12˚	Superiorly	1/14
	13	OS: Stargardt’s Disease	20/200	18-20˚	Superiorly	1/14

CNVM = choroidal neovascular membrane; OD = right eye; OS = left eye

Prior to each experimental session, a three-point calibration and validation was performed for CS subjects. Three-point calibration was used because it was more difficult to calibrate subjects with central scotoma and less stable fixation. Calibration and validation were repeated if they were rated “FAIR” or worse by the host system. Drift correction was performed as with NS subjects. CS subjects were instructed similarly to NS subjects using foveal pursuit, that is, to follow the target as accurately and smoothly as possible without moving their head. There were 3 experimental factors for CS subjects: background (uniform vs. structured), pursuit direction (horizontal vs. vertical) and target velocity 0.15 vs. 0.40 Hz). A full factorial designed was used in which all combinations of all factors were tested 8 times (Table 4). The testing order was randomized. Testing took 2-3 hours to complete.

Table 4

Testing Conditions for Central Scotoma Subjects

Group	**Background**	**Scotoma**	**Target Direction**	**Target Frequency**	**Target Color**	**Number of Trials**
Central Scotoma; n=3	Uniform	None	Horizontal	0.15 Hz	Yellow	8
	Uniform	None	Vertical	0.15 Hz	Yellow	8
	Uniform	None	Horizontal	0.40 Hz	Yellow	8
	Uniform	None	Vertical	0.40 Hz	Yellow	8
	Structured	None	Horizontal	0.15 Hz	Yellow	8
	Structured	None	Vertical	0.15 Hz	Yellow	8
	Structured	None	Horizontal	0.40 Hz	Yellow	8
	Structured	None	Vertical	0.40 Hz	Yellow	8

Data Analysis

Pursuit Eye Movement Analysis

Historically, there is a lack of standardization in the quantification of smooth pursuit used in research studies. Different investigators have used different methods to quantify pursuit quality, and thus the results are not always comparable. The raw eye movement recordings were first inspected for data integrity. Approximately 30 individual trials from various subjects were omitted due to simulated scotoma misalignment or if more than 8 trials per condition were collected in a subject. This represented less than 5% of the collected trials. The smooth pursuit data analysis method used by Collewijn was customized for this study. The composite gain and phase of the pursuit were computed using raw eye movement recordings. To calculate the composite gain, a sinewave of the same frequency as the target waveform was fitted to the raw eye position data. The amplitude of the fitted curve was divided by the amplitude of the target waveform to obtain the composite gain. The phase was determined by the difference in degrees between the fitted and target waveforms.

Then, the results of Eyelink's online parsing was used to partition eye movement recording into fast (saccadic) and slow (pursuit) movements. The criteria for saccade detection were amplitude > 0.1^{o}, velocity > 30°/s and acceleration > 8,000°/s. To compute smooth gain, the saccades were removed from the eye position data and the remaining smooth pieces were connected to produce the smooth component waveform. Then a sinewave of the same frequency as the target waveform was fitted to the smooth component. The smooth gain was calculated by dividing the amplitude of the fitting curve by the amplitude of the target waveform.

Instead of using Fourier transform to determine the smooth pursuit amplitude and phase, a fitting of the spatiotemporal waveform of the composite and smooth eye movement was performed to determine the amplitude and phase of the best-fitting sinewave at the stimulus frequency. This choice was a practical one. This study included some very challenging conditions under which only very slow smooth pursuit eye movements might be reliably recorded. For example, if 0.10 Hz target frequency was used for the CS subjects, the 35-second pursuit would result in only 3.5 cycles of pursuit eye movements. When this heavily truncated waveform was Fourier transformed, its representation in the frequency domain would consist of only a few points, which would have made the estimation of the height of the peak (gain) highly variable. We found spatiotemporal waveform fitting much more robust, and it agreed very well with the result from the Fourier method when there were a large number of cycles to make frequency domain calculation precise.

Statistical Analysis of the Effects of Background and Scotoma

The main interest of this research was the effect of a structured background on smooth pursuit in the presence of a central scotoma. At this moment, only the composite and smooth gains under the tested conditions were analyzed. Other eye movement parameters, such as the initiation of pursuit, the phase, and the retinal position used in pursuit in the presence of a simulated or real central scotoma, will be analyzed in future reports. Repeated measures ANOVA with BACKGROUND (uniform vs. structured) as the within-subject (repeated) variable and SCOTOMA (NS with fovea, NS with simulated central scotoma, and CS), DIRECTION (horizontal vs. vertical) and FREQUENCY (0.15 and 0.40) as the between-subject factors was used to analyze the interplay between study factors. Separate analyses were also made to test the background effect, which was the difference between smooth gains obtained when pursuing on a uniform background (G_u) and on a structured background (Gs). The background effect was quantified either as the linear difference between G_u and G_s and (G_u – G_s) or as a proportional change (G_u / G_s -1). A one-way ANOVA was used to compare the impacts of scotoma on background effects in different groups.

RESULTS

Normally Sighted Subjects

A repeated measures ANOVA analysis with BACKGROUND (uniform gray background and black and white binary random checkerboard background as the within-subject variable and SCOTOMA (no simulated scotoma and simulated scotoma), pursuit DIRECTION (horizontal vs. vertical) and target movement FREQUENCY (0.15 vs. 0.40 Hz) as the between-subjects factors was used to analyze the data obtained from the ten normally sighted subjects. Composite and smooth pursuit gains are analyzed separately.

Composite Gain

The main effect of BACKGROUND was not significant ($F=3.368$, $p=0.067$). This was not surprising, because composite gain, which included the contributions of both smooth and saccade components, were close to unity under most conditions. Even though adding a structured background reduced the overall composite gain slightly (1.115 ± 0.2991 vs. 1.093 ± 0.2392), this change was not significant. The main effects of SCOTOMA and DIRECTION were significant ($F=64.711$ and 15.573, $p<0.0005$). The composite pursuit gains were higher with a simulated scotoma than without (1.038 vs. 1.171), and higher in the horizontal direction than vertical (1.137 vs. 1.072). The FREQUENCY main effect was not significant ($F=1.630$, $p=0.202$). The overall composite gain was slightly higher when pursuing a 0.15 Hz sinusoidal target than pursuing a faster, 0.40 Hz target (1.115 vs. 1.094), but the difference was not significant.

The SCOTOMA*DIRECTION (F=34.915, p<0.0005) was significant. There was little difference between horizontal and vertical composite gains when NS subjects pursued a target with the fovea (1.022 vs. 1.054), but there was a large horizontal difference when a simulated central scotoma was in place (1.252 vs. 1.089).

All other interactions were not significant.

Smooth Gain

The main effects of BACKGROUND, SCOTOMA, DIRECTION and FRQUENCY were all highly significant (F=169.4, 1027, 87.63 and 28.78, p<0.0005). The overall smooth gains were higher on a uniform background than on a structured background (0.666±0.296 vs. 0.577±0.304), higher when pursuing with fovea than with a simulated central scotoma (0.837 vs. 0.406), higher in the horizontal than the vertical direction (0.684 vs. 0.558), and higher with a slower, 0.15 Hz target than a faster 0.40 Hz target (0.658 vs. 0.585).

The BACKGROUND*SCOTOMA interaction was significant (F=21.32, p<0.0005), indicating that the effect of a structured background on smooth pursuit was different with and without a simulated scotoma. More specifically, the background effect (the difference in overall smooth gains obtained on a uniform and structured background) was 0.898-0.776=0.122 when NS subjects pursued with the fovea and was 0.435-0.377=0.058 when NS subjects pursued with a simulated scotoma. In other words, although a simulated scotoma in general caused a large reduction of smooth gain, it resulted in a smaller background effect.

The BACKGROUND*DIRECTION interaction was significant (F=35.14, p<0.0005), indicating that the effect of a structured background on smooth pursuit was different in horizontal and vertical directions. The difference in overall smooth gains obtained on a uniform and structured background was 0.709-0.660=0.049 when NS subjects pursued in the horizontal direction and was 0.624-0.493=0.131 in the vertical direction. Therefore, a structured background caused a larger reduction in smooth gain in the vertical direction than in the horizontal direction.

The BACKGROUND*FREQUENCY interaction was not significant (F=3.560, p=0.060). Although increasing the target velocity (from 0.15 to 0.40 Hz) in general caused a significant reduction in smooth pursuit gains, the background effect at 0.15 Hz (0.709-0.606=0.103) was not significantly different from that at 0.40 Hz (0.624-0.547=0.077).

The BACKGROUND*SCOTOMA*DIRECTION interaction was significant (F=8.589, p=0.004). The background effects were 0.947-0.886=0.061 and 0.471-0.434=0.037 when NS subjects pursued with the fovea and with a simulated scotoma in the horizontal direction. The corresponding background effects were 0.849-0.667=0.182 and 0.398-0.320=0.078 in the vertical direction. Therefore, the impact of the pursuing condition (foveal vs. simulated scotoma) on the background effect was stronger in the vertical direction than in the horizontal direction. Similarly, when pursuing with a simulated scotoma, a 3.6% background effect was observed in the horizontal direction, compared to a 7.8% effect in the vertical direction.

The BACKGROUND*SCOTOMA*FREQUENCY interaction was also significant (F=12.938, p<0.0005). The background effects were 0.943-0.833=0.110 and

0.475-0.379=0.096 when NS subjects pursued a 0.15 Hz target with the fovea and with a simulated scotoma, respectively. The corresponding background effects were 0.853-0.720=0.133 and 0.398-0.320=0.078 for pursuing a faster 0.40 Hz target, respectively.

The SCOTOMA*DIRECTION interactions were significant (F=0.593, p=0.015). The scotoma effects (the difference between smooth pursuit gains obtained with fovea and with a simulated central scotoma) were 0.917-0.452=0.465 and 0.758-0.359=0.399 in horizontal and vertical directions, respectively. A simulated central scotoma produced a larger smooth gain loss in the horizontal than the vertical direction.

The SCOTOMA*FREQUENCY interactions were significant (F= 4.773, p= 0.029). The scotoma effects were 0.888-0.427=0.461 and 0.786-0.384=0.402 for pursuing a 0.15 Hz and a 0.40 Hz target, respectively. A simulated central scotoma produced a larger smooth gain loss when pursuing a slower target than a faster target.

The DIRECTION*FREQUENCY interaction was also significant (F=11.988, p=0.001). The frequency effect (the difference between smooth pursuit gains observed with a 0.15 Hz and a 0.40 Hz target) were 0.697-0.672=0.025 in the horizontal direction and 0.618-0.499=0.117 in the vertical direction, respectively. This was consistent with previous foveal smooth pursuit studies in normal subjects (Collewijn, 1984).

Other interactions were not significant.

Simulated Scotoma and Background Effect

In the analysis above, the BACKGROUND*SCOTOMA interaction was significant because pursuit with fovea suffered more from a structured background than pursuit with a simulated scotoma (background effects 0.122 and 0.058). The

BACKGROUND*SCOTOMA*DIRECTION interaction was significant because the background effects for foveal and simulated scotoma pursuit were 0.061 and 0.037 in the horizontal direction and 0.182 and 0.078 in the vertical direction. Again, the results seemed to suggest that pursuit with fovea suffered more from a structured background than pursuit with simulated scotoma. However, these analyses averaged the effects of slower and faster (0.15 and 0.40 Hz) target. There was also concern that comparing the difference between smooth pursuit gains on uniform and structured backgrounds (G_u - G_s) may not be an appropriate measurement when the effect of a simulated scotoma was considered, because pursuit with central scotoma drastically reduced the smooth gain. For example, the same 0.1 gain loss from 1.0 to 0.9 represents a much larger proportional gain loss than from 0.5 to 0.4.

When the proportional change of smooth gains obtained with a uniform and a structured background, (G_u/G_s-1) was used and the effect of slow and fast target was taken into consideration separately, the following pattern emerged (column 6, Table 5).

Table 5

Linear and Proportional Background Effect With Fovea and Simulated Scotoma

Pursuit Type	**Direction**	**Velocity**	**Linear**	**Paired t-test**	**Proportional**	**Paired t-test**
Foveal	Horizontal	Slow (0.15 Hz)	0.0538	t = -1.461 p = 0.148	0.0740	t = -4.816 p = <0.0005*
Simulated Scotoma	Horizontal	Slow (0.15 Hz)	0.0894		0.4789	
Foveal	Vertical	Slow (0.15 Hz)	0.1654	t = 2.642 p = 0.010*	0.3038	t = -2.127 p = 0.037*
Simulated Scotoma	Vertical	Slow (0.15 Hz)	0.1065		0.4532	
Foveal	Horizontal	Fast (0.40 Hz)	0.0670	t = 3.010 p = 0.004*	0.1104	t = -1.362 p = 0.177
Simulated Scotoma	Horizontal	Fast (0.40 Hz)	-0.0104		0.2098	
Foveal	Vertical	Fast (0.40 Hz)	0.1992	t = 7.575 p = <0.0005*	0.4359	t = 2.125 p = 0.037*
Simulated Scotoma	Vertical	Fast (0.40 Hz)	0.0505		0.2955	

When the velocity of the pursuit target was low (0.15 Hz), a larger proportional background effect was found in pursuit with a simulated scotoma than that with the fovea. This was true for both horizontal (0.479 vs. 0.074; $p<0.0005$) and vertical (0.453 vs. 0.304; $p=0.037$) pursuits. This proportional background effect was also seen with 0.40 Hz target velocity in the horizontal direction (0.210 vs. 0.110; $p=0.177$). In other words, compared to a uniform background, a structured background caused a proportionally larger reduction of smooth gain when pursued with a simulated scotoma than without. However, a larger proportional background effect was found in pursuit with a fovea than that with a simulated scotoma when the velocity of the pursuit target was high (0.40 Hz) in the vertical direction (0.436 vs. 0.296; $p=0.037$). (Figure 4)

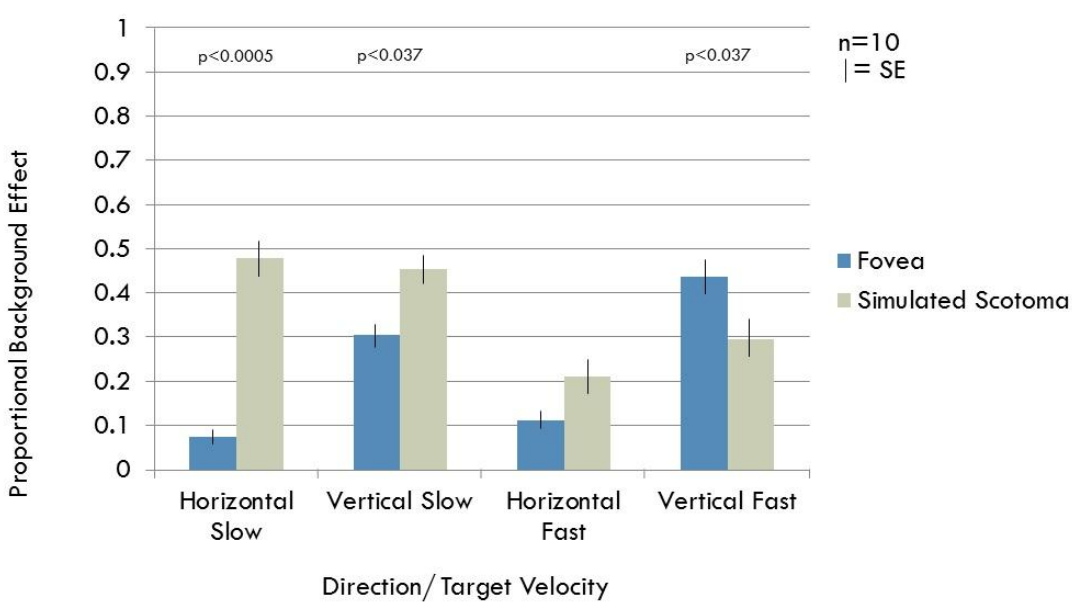

Figure 4. Proportional background effect with fovea and simulated scotoma.

When the linear difference in smooth gains with a uniform and a structured background was used (G_u - G_s), (column 4 in Table 5) a larger background effect was found in pursuit with fovea than with a simulated scotoma. This was true with target velocity of 0.15 Hz in the vertical direction (0.1654 vs. 0.1065; $p=0.010$), as well as with a target velocity of 0.40 Hz in the horizontal (0.0670 vs. -0.0104; $p=0.004$) and vertical direction (0.1992 vs. 0.0505; $p<0.0005$). When the velocity of pursuit was 0.15 Hz in the horizontal direction, the background effect was larger in pursuit with a simulated scotoma than with fovea (0.0894 vs. 0.0538; $p=0.148$).

Central Scotoma Subjects

A repeated measures ANOVA analysis with BACKGROUND (uniform gray background and black and white binary random dot background) as the within-subject variable and pursuit DIRECTION (horizontal vs. vertical) and target movement FREQUENCY (0.15 vs. 0.40 Hz) as the between-subjects factors was used to analyze the data obtained from the three central scotoma subjects. Composite and smooth pursuit gains are analyzed separately.

Composite Gain

The main effect of BACKGROUND was not significant ($F=3.265$, $p=0.074$). Composite gains included the contributions of both smooth and saccade components, and were slightly less than unity under most conditions. Adding a structured background reduced the overall composite gain slightly (0.966±0.190 vs. 0.923±0.236), but this change was not significant. The main effects of DIRECTION, and FREQUENCY were significant ($F=13.630$ and 11.376, $p<0.0005$ and $p=0.001$). The composite pursuit gains were higher in the horizontal direction than vertical (1.006 vs. 0.883) and higher when pursuing a 0.15 Hz sinusoidal target than when pursuing a 0.40 Hz target (1.001 vs. 0.888).

All other interactions were not significant.

Smooth Gain

The main effects of BACKGROUND, DIRECTION and FRQUENCY were all highly significant (F=456.82, 26.84, 113.36, $p<0.0005$). The overall smooth gains were higher on a uniform background than on a structured background (0.588±0.134 vs. 0.322 ±0.100), higher in the horizontal than the vertical direction (0.484 vs. 0.426), and higher with a slower, 0.15 Hz target than a faster 0.40 Hz target (0.515 vs. 0.395). (Figure 5)

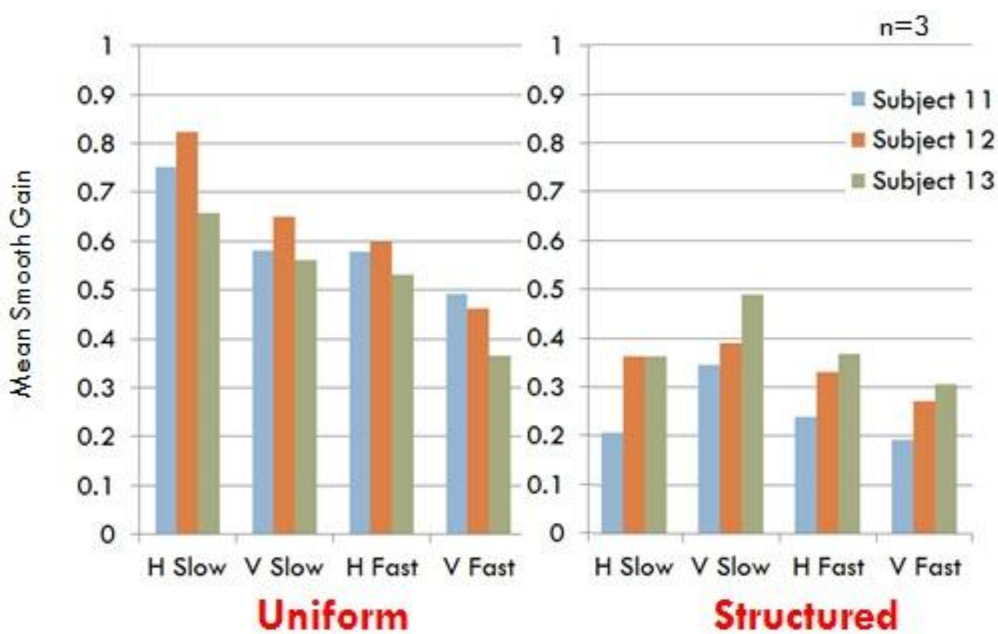

Figure 5. Comparison of mean smooth gain in real central scotoma subjects.

The BACKGROUND*DIRECTION interaction was significant (F=40.943, p<0.0005), indicating that the effect of a structured background on smooth pursuit was different in horizontal and vertical directions. The difference in smooth gains obtained on a uniform and structured background was 0.657-0.311=0.346 when CS subjects pursued in the horizontal direction and was 0.519-0.332=0.187 in the vertical direction, respectively. Therefore, a structured background caused a larger reduction in smooth gain in the horizontal direction than in the vertical direction.

The BACKGROUND*FREQUENCY interaction was significant (F=13.719, p<0.0005). The background effect on smooth pursuit differed significantly when pursuing a target at 0.15 Hz (0.671-0.359=0.312) as compared to when pursuing a target at 0.40 Hz (0.505-0.285=0.220). The background caused more gain reduction when tracking a slower target.

The BACKGROUND*DIRECTION*FREQUENCY interaction was significant (F=11.497, p=0.001). The background effects were 0.744-0.311=0.433 and 0.598-0.408=0.190 when CS subjects pursued a 0.15 Hz target in the horizontal and vertical direction, respectively. The corresponding background effects were 0.570-0.312=0.258 and 0.439-0.257=0.182 at a target frequency of 0.40 Hz. Therefore, the impact of the pursuing direction (horizontal or vertical) on the background effect was stronger when pursuing a 0.15 Hz target than a 0.40 target.

The DIRECTION*FREQUENCY interaction was also significant. The frequency effects were 0.527-0.441=0.086 in the horizontal direction and 0.503-0.348=0.155 in the vertical direction.

Normally Sighted Subjects and Central Scotoma Subjects

A repeated measure ANOVA analysis with BACKGROUND (uniform gray background and black and white binary random dot checkerboard background) as the within-subject variable and SCOTOMA (NS no simulated scotoma, NS simulated scotoma, and CS), pursuit DIRECTION (horizontal vs. vertical) and target movement FREQUENCY (0.15 vs. 0.40 Hz) as the between-subjects factors was used to analyze the data obtained from the ten normally sighted subjects and three central scotoma subjects. Composite and smooth pursuit gains are analyzed separately.

Composite Gain

The main effect of BACKGROUND, 1.065±0.326 for uniform background and 1.037±0.271 for structured background, was significant ($F=5.200$, $p=0.023$). The main effects of SCOTOMA, DIRECTION and FREQUENCY were also significant ($F=59.761$, 23.352, $p<0.0005$; and $F=8.721$, $p=0.003$). The composite pursuit gains of NS pursued with a simulated scotoma had the highest composite gain (1.171), followed by NS pursued with fovea, (1.038) and followed by CS subjects pursued with real scotoma (0.945). Composite gains were higher in the horizontal direction than vertical (1.093 vs. 1.009) and higher when pursuing a 0.15 Hz sinusoidal target than pursuing a faster, 0.4 Hz target (1.077 vs. 1.025).

The SCOTOMA*DIRECTION ($F=19.211$, $p<0.0005$) was significant. There was little difference between horizontal and vertical composite gains when NS subjects pursued a target with the fovea in horizontal and vertical directions (1.022 vs. 1.054), but there was a large difference when pursuing with a simulated central scotoma (1.252 vs.

1.089). CS subjects' composite gain was near unity when pursuing in the horizontal direction but decreased in the vertical direction (1.006 vs. 0.883).

The SCOTOMA*FREQUENCY interactions were significant (F=3.412, p=0.033). The scotoma effects for NS pursuing a 0.15 Hz and a 0.40 Hz target were small (1.036-1.194= -0.158 and 1.040-1.147= -0.107), and were higher with simulated scotoma than with fovea. CS subjects had a gain of unity when tracking a 0.15 Hz target, and a reduction in gain when pursuing a target at 0.40 Hz (1.001 vs. 0.888).

All other interactions were not significant.

Smooth Gain

The main effects of BACKGROUND, SCOTOMA, DIRECTION and FRQUENCY were all highly significant (F=419.30, 624.21, 56.32 and 40.94, p<0.0005). The overall smooth gains were higher on a uniform background than on a structured background (0.640±0.190 vs. 0.577±0.217), highest when NS pursuing with fovea, followed by CS pursuing with real scotoma and followed by NS pursuing with a simulated central scotoma (0.837, 0.455 vs. 0.406), higher in the horizontal than the vertical direction (0.618 vs. 0.514), and higher with a slower, 0.15 Hz target than a faster 0.40 Hz target (0.610 vs. 0.522) (Figure 6).

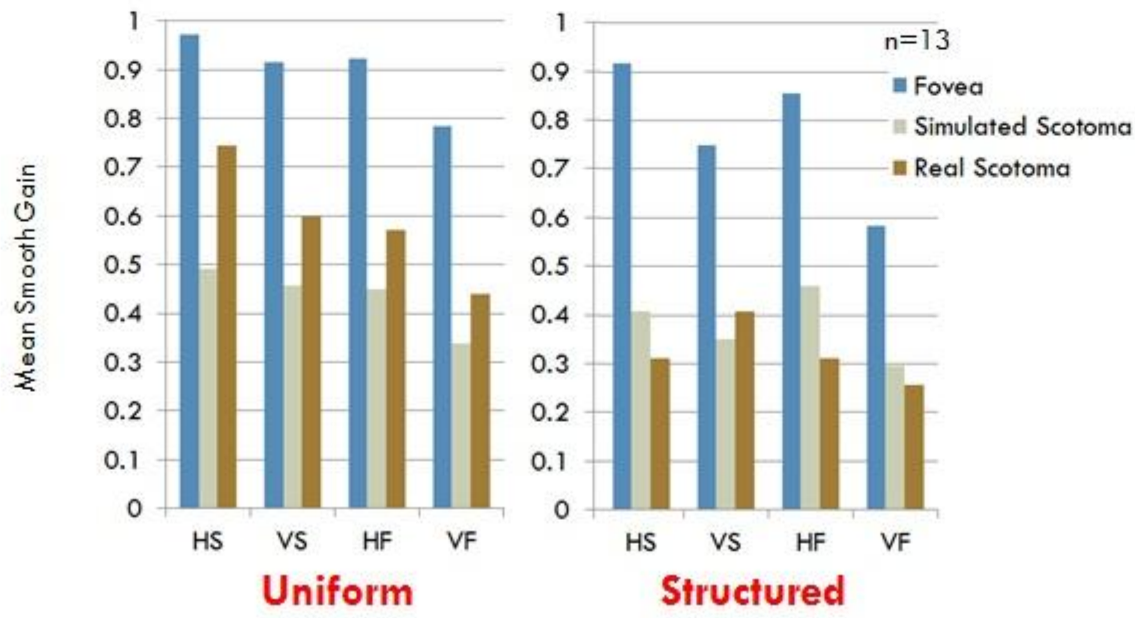

Figure 6. Comparison of mean smooth gain in normally sighted subjects with fovea and simulated scotoma, and real central scotoma subjects.

The BACKGROUND*SCOTOMA interaction was significant (F=57.183, p<0.0005), indicating that the effect of a structured background on smooth pursuit was different with foveal pursuing and with simulated and real scotoma. The background effect was 0.898-0.776=0.122 when NS subjects pursued with the fovea, 0.435-0.377=0.058 when NS subjects pursued with a simulated scotoma, and 0.588-0.322=0.266 in CS subjects. As shown in Figure 6, CS subjects with real scotoma always had higher gains than NS subjects with simulated scotoma on a uniform background, but had lower with similar gains on a structured background. The overall result was a much larger background effect in the real scotoma than in the simulated scotoma.

The BACKGROUND*DIRECTION interaction was not significant (F=0.008, p=0.927), Although pursuing a target in the horizontal direction in general caused a reduction in smooth pursuit gains, the background effect in the horizontal direction

(0.692-0.544=0.148) was not significantly different compared to the vertical direction (0.589-0.440=0.149).

The BACKGROUND*FREQUENCY interaction was significant ($F=10.989$, $p=0.001$), indicating that the effect of a structured background on smooth pursuit was different at frequencies of 0.15 Hz and 0.40 Hz. The difference in overall smooth gains obtained on a uniform and structured background was 0.696-0.524=0.172 when subjects pursued a target at 0.15 Hz and 0.584-0.460=0.124 when pursuing a target at 0.40 Hz, indicating that background effect at 0.15 Hz was greater than at 0.40 Hz.

The BACKGROUND*SCOTOMA*DIRECTION interaction was significant ($F=25.939$, $p<0.0005$). The background effects in the horizontal direction were 0.061, 0.037 and (0.657-0.311=0.346) when NS subjects pursued with the fovea and simulated scotoma, and CS subjects pursued with real scotoma. The corresponding background effects in the vertical direction were 0.182, 0.078 and (0.519-0.332=0.187). In NS subjects, the impact of the pursuing condition (foveal vs. simulated scotoma) on the background effect was stronger in the vertical direction than in the horizontal direction. CS subjects with real scotomas showed a response more similar to NS subjects pursuing with fovea in the vertical direction, but suffered a much larger reduction in smooth gain when pursuing in the horizontal direction on a structured background.

The BACKGROUND*SCOTOMA*FREQUENCY interaction was also significant ($F=8.530$, $p<0.0005$). The background effects were 0.110, 0.096 and (0.671-0.359=0.312) when NS subjects with fovea and with a simulated scotoma and CS subjects with real scotoma pursued a 0.15 Hz target. The corresponding background effects were 0.133, 0.078, and (0.505-0.285=0.220) for pursuing a faster 0.40 Hz target.

CS subjects had a much more significant background effect at both 0.15 Hz and 0.40 Hz target frequencies than NS subjects.

The BACKGROUND*DIRECTION*FREQUENCY interaction was significant (F=6.922, p=0.009). The background effects were 0.736-0.545=0.191 and 0.656-0.503=0.153 when pursuing a 0.15 Hz target in the horizontal and vertical direction. The corresponding background effects were 0.647-0.542=0.105 and 0.521-0.377=0.144 at target frequency of 0.40 Hz. Thus, the impact of the pursuing direction (horizontal or vertical) on the background effect was stronger when pursuing a 0.15 Hz target than a 0.40 target.

The SCOTOMA*DIRECTION interactions were significant (F=5.189, p=0.006). The scotoma effects in NS subjects were 0.465 and 0.399 in horizontal and vertical directions, producing a larger smooth gain loss in the horizontal than the vertical direction. CS subjects also had a larger reduction in the horizontal (0.484) as compared to vertical direction (0.426).

The SCOTOMA*FREQUENCY interactions were significant as well (F= 3.636, p= 0.027). The scotoma effects of pursuing a 0.15 Hz and a 0.40 Hz target were 0.461 and 0.402 for NS subjects, and 0.515 and 0.395 for CS subjects. A simulated central scotoma produced a larger smooth gain loss when pursuing a slower target than a faster target. This was true in CS subjects as well, though the loss for CS subjects was greater at 0.15 Hz, and slightly less at 0.40 Hz.

The DIRECTION*FREQUENCY interaction was also significant (F=9.452, p=0.002). The frequency effects were 0.641-0.595=0.046 in the horizontal direction and 0.579-0.449=0.130 in the vertical direction. Other interactions were not significant.

Scotoma and Background Effect

A one-way ANOVA was used to investigate the interaction between different backgrounds and scotoma in smooth pursuit. Linear and proportional background effects were the dependent variables and viewing conditions (NS subjects with fovea(0), NS with simulated scotoma (1), and CS subjects with real scotoma (2)) were the factors. Pursuit orientations were horizontal vs. vertical and target velocities were 0.15 and 0.40 Hz. The results were summarized in Table 6 and Table 7. Bonferroni test was used in Post Hoc analysis among viewing conditions.

Table 6

Linear Background Effect Comparison Among Conditions

Condition	**Direction**	**Velocity (Hz)**	G_u	G_s	G_u-G_s	**F**	**p**	**Post hoc**	**Sig**
Foveal (0)	Horizontal	Slow 0.15	0.971	0.918	0.054	58.307	<0.0005	0 vs. 1	0.439
Simulated Scotoma (1)	Horizontal	Slow 0.15	0.492	0.407	0.089			0 vs. 2	<0.0005
Real Scotoma (2)	Horizontal	Slow 0.15	0.744	0.311	0.434			1 vs. 2	<0.0005
Foveal (0)	Vertical	Slow 0.15	0.914	0.749	0.165	5.770	0.004	0 vs. 1	0.016
Simulated Scotoma (1)	Vertical	Slow 0.15	0.457	0.351	0.106			0 vs. 2	1.000
Real Scotoma (2)	Vertical	Slow 0.15	0.598	0.407	0.190			1 vs. 2	0.021
Foveal (0)	Horizontal	Fast 0.40	0.922	0.855	0.067	26.051	<0.0005	0 vs. 1	0.008
Simulated Scotoma (1)	Horizontal	Fast 0.40	0.449	0.460	-0.010			0 vs. 2	<0.0005
Real Scotoma (2)	Horizontal	Fast 0.40	0.570	0.312	0.257			1 vs. 2	<0.0005
Foveal (0)	Vertical	Fast 0.40	0.783	0.584	0.199	24.682	<0.0005	0 vs. 1	<0.0005
Simulated Scotoma (1)	Vertical	Fast 0.40	0.339	0.289	0.051			0 vs. 2	1.000
Real Scotoma (2)	Vertical	Fast 0.40	0.440	0.257	0.182			1 vs. 2	<0.0005

Table 7

Proportional Background Effect Comparison Among Conditions

Condition	**Direction**	**Velocity (Hz)**	**G_u**	**G_s**	**G_u/G_s -1**	**F**	**p**	**Post hoc**	**Sig**
Foveal (0)	Horizontal	Slow 0.15	0.971	0.918	0.074	41.455	<0.0005	0 vs. 1	0.010*
Simulated Scotoma (1)	Horizontal	Slow 0.15	0.492	0.407	0.479			0 vs. 2	<0.0005*
Real Scotoma (2)	Horizontal	Slow 0.15	0.744	0.311	1.907			1 vs. 2	<0.0005*
Foveal (0)	Vertical	Slow 0.15	0.914	0.749	0.304	3.694	0.027	0 vs. 1	0.081
Simulated Scotoma (1)	Vertical	Slow 0.15	0.457	0.351	0.453			0 vs. 2	0.083
Real Scotoma (2)	Vertical	Slow 0.15	0.598	0.407	0.523			1 vs. 2	1.000
Foveal (0)	Horizontal	Fast 0.40	0.922	0.855	0.110	28.026	<0.0005	0 vs. 1	0.597
Simulated Scotoma (1)	Horizontal	Fast 0.40	0.449	0.460	0.210			0 vs. 2	<0.0005*
Real Scotoma (2)	Horizontal	Fast 0.40	0.570	0.312	0.948			1 vs. 2	<0.0005*
Foveal (0)	Vertical	Fast 0.40	0.783	0.584	0.436	11.790	<0.0005	0 vs. 1	0.250
Simulated Scotoma (1)	Vertical	Fast 0.40	0.339	0.289	0.296			0 vs. 2	0.001*
Real Scotoma (2)	Vertical	Fast 0.40	0.440	0.257	0.872			1 vs. 2	<0.0005*

Horizontal direction. In the horizontal direction, the linear background effects (G_u - G_s) were significantly different among the three viewing conditions with both slow and fast (0.15 and 0.40 Hz) targets ($F=58.307$, $p<0.0005$; $F=26.051$, $p<0.0005$). CS subjects had a much larger reduction of smooth gain when pursuing on structured background at these target velocities (0.434, 0.257) than NS with fovea (0.054, 0.067) and with simulated scotoma (0.089, -0.010). Post hoc comparisons showed significant differences ($p<0.0005$) between CS with real scotoma and the other two conditions when pursuing a target at 0.15 and 0.40 Hz, The linear background effects for NS with fovea and with simulated scotoma were also significantly different at 0.40 Hz (0.008).

The proportional background effects (G_u / G_s -1) were also significantly different among the three viewing conditions in the horizontal direction with both slow and fast (0.15 and 0.40 Hz) targets (F=41.455, p=<0.0005; F=28.026, p<0.0005). CS subjects demonstrated a larger proportional reduction in smooth gain on a structured background, compared to NS with simulated scotoma and with fovea (1.907, 0.479 and 0.074 for 0.15 Hz target; 0.948, 0.210 and.0.110 for 0.40 Hz target). Post hoc comparisons found significant differences at 0.15 and 0.40 Hz target frequencies between CS subjects and NS with fovea and with simulated scotoma (p<0.0005). NS subjects with simulated scotoma were found to have a larger reduction in smooth gain on structured background compared to NS with fovea (p=0.010) at 0.15 Hz.

Vertical direction. In the vertical direction, the linear background effects were significantly different among the three viewing conditions when pursing a target with a velocity of 0.15 Hz (F=5.770, p=0.004). CS with real scotoma showed a larger reduction in gain (0.190) compared to NS with fovea (0.165) and NS with simulated scotoma (0.106). Post hoc comparison showed significant differences between NS with fovea and simulated scotoma (0.016), and between NS with simulated scotoma and CS with real scotoma (0.021). The proportional background effects were also significantly different among the three viewing conditions when pursuing a slow target (0.15 Hz) (F=3.694, p=0.027). CS subjects suffered the largest background effect (0.523), followed by NS with simulated scotoma (0.453) and foveal pursuit (0.304). Post hoc comparisons of foveal pursuit, simulated scotoma, and real scotoma were not significant. (Figure 7)

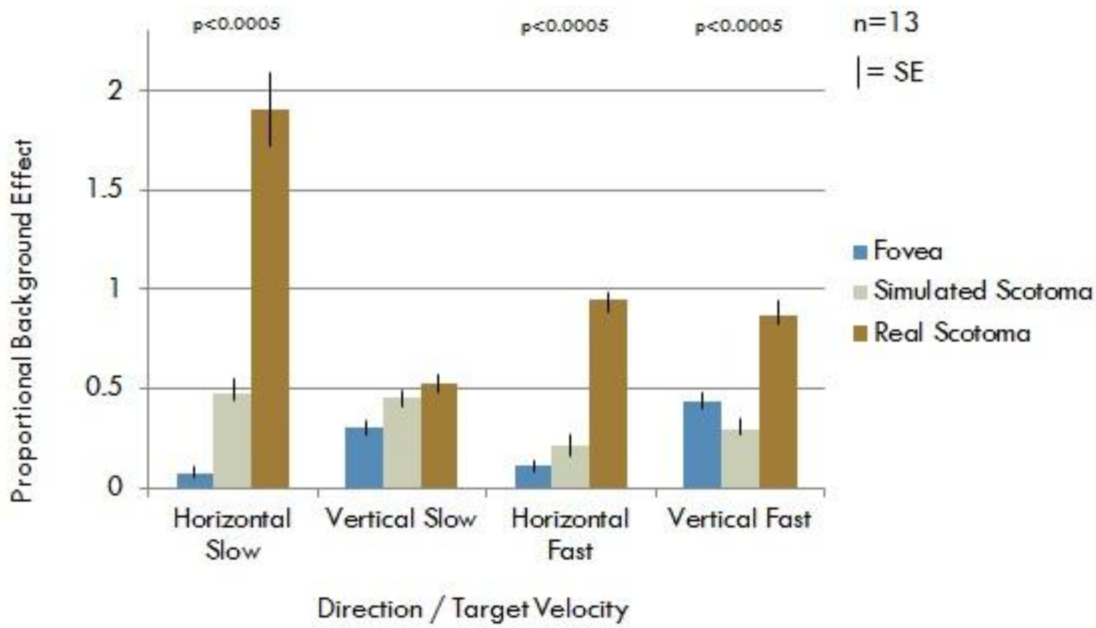

Figure 7. Proportional background effect with fovea, simulated scotoma, and real scotoma.

A statistically significant difference among the groups was found in the linear background effect while pursuing a target at 0.40 Hz in the vertical direction (F=24.682, p=<0.0005). Linear background effect found foveal pursuit had larger reduction in smooth gain (0.199), followed by CS subjects with real scotoma (0.182) and simulated scotoma pursuit (0.051). In a pairwise comparison of the linear differences, NS subjects with simulated scotoma were statistically different from NS with fovea and CS subjects with real scotoma (<0.0005). The proportional background effects were also significantly different among the three viewing conditions when pursuing a fast target (F=11.790, p<0.0005). CS subjects had a larger reduction in smooth gain (0.872) compared to NS with fovea (0.436) and NS with simulated scotoma (0.296). Pairwise comparison of the proportional change revealed a significant difference between NS with fovea and CS with real scotoma ($p=0.001$), and NS with simulated scotoma and CS with real scotoma ($p<0.0005$).

Analysis with the linear background effect showed CS subjects as having greater reduction in smooth pursuit gain in all cases except when pursuing a 0.40 Hz target in the vertical direction. Pursuit of a 0.15 Hz target in the horizontal showed the most dramatic reduction. Smooth gain reduction in the vertical direction was generally more similar among the groups. Considering the proportional background effect, CS subjects with real scotoma showed larger background effects than NS with simulated scotoma and NS with fovea in all conditions. This difference was more pronounced in the horizontal direction, especially at the low target velocity of 0.15 Hz

DISCUSSION

A better understanding of the role of the fovea in smooth pursuit has both theoretical and practical importance. Research approaches to deprive foveal input during pursuit have included presenting a pursuit target in the peripheral vision or by damaging the fovea (Collewijn, 1986; Skavenski, 1993). While some interesting findings have been obtained, especially in terms of the effects of pursuing on a structured background, the question Skavenski posed as to why the fovea is a requirement for smooth pursuit against a structured background has not been properly answered. The contribution of this research is twofold, a systematic study of a previously unstudied condition where the foveal inputs of both the background and the pursuit target are eliminated but the anatomic fovea is intact, and a comprehensive study of smooth pursuit eye movements of human subjects with real central scotoma.

Smooth Pursuit – The Role of the Fovea

Our study examined the importance of foveal input in smooth pursuit. It was inspired by three important empirical findings involving smooth pursuit on a structured background: 1) moderate reduction of smooth gain when pursuing with an intact fovea (Collewijn, 1984); 2) moderate reduction of smooth gain when pursuing with peripheral retinal locations while the fovea was intact (Collewijn, 1986); and 3) severe reduction of smooth gain when pursuing with peripheral retinal locations with a damaged fovea (Skavenski, 1993). Skavenski (1993) stated “Why the fovea must be there even when it is not directly stimulated is not clear." However, this question was asked prematurely, because neither Skavenski's study nor those of Collewijn's had established what might have happened if the fovea was intact but not receiving visual input during pursuit on a structured background. This study contributes to the understanding of the fovea's role by studying smooth pursuit with a simulated central scotoma that blocked the foveal visual input while leaving the anatomic fovea intact. Our finding that a simulated central scotoma caused significantly less background effect than that observed in patients with real central scotoma suggested that cutting off foveal visual input was not likely the cause of the devastating background effect observed in patients. In other words, the existence of an intact fovea, receiving or not receiving visual input, assures high pursuit performance on a structured background. With this missing piece in place, we can now explore why the fovea must be there even when it is not directly stimulated. One possible role of an intact fovea is to invoke a more precise cortical map, probably through attention deployment, for the purpose of pursuing target even though there is no foveal visual input. When the fovea is damaged, attention can no longer be deployed to the fovea and a more inferior cortical map, typically related to peripheral vision, has to be used. This proposition, however, will be proved or disproved in future studies.

Comparison between the Current and Previous Studies

The proportional background effects in normally sighted subjects pursing with the fovea were similar to Collewijn's 1984 study (Table 8). Our simulated scotoma subjects showed a larger proportional change than Collewijn's 1986 study subjects in the horizontal slow condition but similar performance in the horizontal fast condition (Table

8). Could the difference be due to the fact that Collewijn's subjects had foveal access to the background, whereas our subjects had no foveal input due to a simulated scotoma (i.e., foveal input only to a simulated scotoma)? This distinction is small but it could be possible that even though peripheral targets are used in both cases, there is a difference. As previously mentioned, there is only moderate reduction in smooth pursuit due to structured background in both cases, but a more thorough investigation of the degree of foveal attention to the background or the simulated scotoma itself may reveal additional information about the role of the fovea. Unlike previous studies, the current study reported on smooth pursuit in the vertical direction as well.

Table 8

Results Comparison of Current and Previous Studies

Study	**Condition**	**Target**	**Proportional Background Effect**			
			Horizontal Slow	Vertical Slow	Horizontal Fast	Vertical Fast
Collewijn 1984	Fovea	Central	**11.8**	**28.6**	**14.3**	**36.4**
Collewijn 1986	Fovea	Peripheral	17.9		20.0	
Skavenski 1993	Real Scotoma	Peripheral	60.0			
Keith 2012	Fovea	Central	**7.40**	**30.4**	**11.0**	**43.6**
	Simulated Scotoma	Peripheral	47.9	45.3	21.0	29.6
	Real Scotoma	Peripheral	190	52.3	94.8	87.2

Simulated Scotoma Visibility

Interestingly, we observed that the visibility of a simulated scotoma may play a role in smooth pursuit performance. In our study, the scotoma was implemented by a mask of variable transparency. When the background was uniform, there was nothing in the transparent or the opaque areas to see, and the scotoma blended completely into the background. The only time the scotoma was noticeable to the subjects was when the target fell into the opaque area of the mask and disappeared or when it moved into the transparent area and became visible again. Therefore, the position and spatial extent of the mask was very uncertain to the subject. On a structured background, however, the features of the background were obscured in the opaque area of the mask, and gradually became visible toward the transparent area. This transition from non-seeing to seeing, though it happened only in peripheral vision, clearly defined the scotoma as a fuzzy patch of gray over the structured background. We observed only a slight background effect under the simulated scotoma condition, which we believe may to be attributable to scotoma visibility. This visibility cue may allow compensatory mechanisms, such as aligning of the scotoma with elements of the structured background, or with the edge of the monitor screen, which assist smooth pursuit. One possible control experiment would be smooth pursuit on a uniform background with a visible simulated scotoma, for example a scotoma lighter or darker than a uniform background. It would be informative to determine if smooth pursuit improves with increasing scotoma visibility.

Smooth Pursuit in Normally Sighted and Simulated Scotoma Subjects

A larger background effect was observed in NS with simulated scotoma in the slower target conditions compared to the faster conditions. One possible explanation is that in the slower condition the retinal image motion of the structured background is reduced compared to the faster condition (Collewijn, 1984). Even though the target velocities used in our study were within the range of normal smooth pursuit, a slower background motion opposite to target motion may produce a stimulus that is more difficult for the brain to "ignore", and thus act to reduce smooth pursuit.

We also found that in the condition with a vertical fast target, foveal pursuit was more affected than simulated scotoma by the structured background. This condition represents the most difficult task in our study. Subjects tracking using the fovea performed most poorly in this condition. One possibility for foveal tracking having a larger background effect could be due to a floor effect, where the true detriment in pursuit with simulated scotoma in this condition cannot be adequately measured because tracking quality was so poor.

In NS subjects, the composite gain for foveal pursuit was close to unity (1.038) while the composite gain for pursuit with a simulated scotoma was consistently larger than unity (1.171) and the difference was significant. On the other hand, the smooth gain for pursuit with fovea was consistently higher than that for pursuit with a simulated central scotoma (0.837 vs. 0.406). One possible explanation for the hypermetric composite gain may be the relatively low sensitivity to motion in peripheral vision (Tyler, 1972). When a NS subject pursued with a simulated scotoma, a peripheral retinal location was used to view the moving target. If motion sensitivity was low at that location, the subject might not notice the target had moved to the end of its trajectory and had started to turn back, and thus might overshoot the target's position until they noticed a large positional error and made a large saccadic eye movement to catch up. The effect of poor sensitivity to motion might be more pronounced when the target followed a sine wave, in which the target speed approach zero at the turn-around point. Collewijn (1986) found increased composite gain of 10-20% in tracking of eccentric targets, which was attributed to the overshoot of saccades. Further analysis of the data may help to test the validity of this explanation.

Smooth Pursuit With Real Scotoma

In all conditions but one CS subjects suffered a larger proportional background effect than foveal or simulated scotoma tracking. The effect was most pronounced in the horizontal slow target condition.

While each of the central scotoma subjects had similar visual acuity, their scotoma sizes were 3˚, 12˚ and 18˚. Despite this large variation in scotoma size, pursuit ability appeared to be comparable under the conditions tested (Figure 5). Interestingly, all three subjects showed better tracking in the vertical slow target condition against a structured background than in the horizontal condition. Horizontal tracking typically produces higher smooth gain (Collewijn, 1984), and did so in our study on a uniform background. To our knowledge, our study is the first to report smooth gain in vertical directions in subjects with real central scotoma. Skavenski's experiments only measured smooth pursuit in the horizontal direction. It is possible that different retinal locations might be used in pursuing target moving in different directions in our central scotoma subjects. For example, while a retinal location superior to the scotoma is ideal for horizontal pursuit because the whole target trajectory falls in the functioning portion of the retina, the same retinal location would not be desirable for vertical pursuit because the target trajectory now passes through the scotoma. Further examination of our eye movement data in the direct perpendicular to the target trajectory may reveal possible strategies our CS subjects used.

The overall smooth gain of the CS subjects (0.455) was significantly higher than that of the NS subjects with a simulated central scotoma (0.406). CS subjects had higher mean gain compared to simulated scotoma in every condition on a uniform background, but in only one condition on a structured background. One reason for the advantage may be that the CS subjects had optimized their strategies in pursuing using peripheral retinal locations while the NS subjects had yet to develop a proficient eye movement strategy using peripheral visual input. When a simulated central scotoma was in place, the subject might have used saccades to chase the target or pursue with multiple peripheral retinal locations depending on which was closer to the target. Both strategies would result in lower smooth gain.

Smooth Pursuit on a Structured Background – Mechanism

Existing research on brain areas MT and MST highlights the complex network of communication regarding smooth pursuit initiation, maintenance, and adaptation. MT has neurons that respond to foveal and parafoveal stimulation (Ilg, 2003). MT passes information not only to MST, but to other brain areas. Similarly, MST sends on information regarding background motion and extra-retinal signals (Ilg, 2008). We speculate that in subjects with real scotoma this information cascade may be disrupted due to damage to the fovea, and cause conflict in a system that would normally balance conflicting signals to enable smooth pursuit despite the background effect. Were it not for this built-in system redundancy, any tracking of a target in space may be all but impossible with a damaged fovea. It is perhaps the remaining cross communication across the system that allows smooth pursuit, albeit with diminished effectiveness. Further research is needed in this area.

Conclusion

NS subjects with no foveal input due to simulated scotoma suffered much less of a background effect than CS subjects who have no foveal input due to damaged fovea. This finding suggests that to maintain high pursuit performance on a structured background, an intact anatomic fovea is crucial, even if it is not receiving any visual input. A damaged fovea not only cuts off foveal visual input but disrupts the oculomotor control of smooth pursuit in a more profound way. Further investigation of this disruption will better our understanding of normal oculomotor control and provide guidance to rehabilitation training that may improve quality of life of patients with central scotoma.

Limitations and Future Studies

The simulated central scotoma used in our study differed from real scotoma in several ways. First, the extent and position of the simulated scotoma was different from any of the real scotomas. This difference may have implications when results of simulated and real scotoma are compared. Although the pursuit gains of our three CS patients were quite comparable, despite the large size difference in their scotoma, future studies should simulate the profile of scotoma more closely, for example, by using the sensitivity map of real scotoma as the transparency map. Second, our CS patients had had years of experience with their scotoma and had mastered the skill of using peripheral retinal locations for various tasks. The experience of using peripheral retinal locations in our simulation subjects was very limited. Interestingly, our results indicated that smooth pursuit with a simulated scotoma was not always worse than that with a real one. There were conditions where simulated scotoma was systematically and significantly better than real scotoma while under other conditions were significantly worse. This suggests that the difference in experience with peripheral pursuing might not be used simply to dismiss the use of simulation study. Due to the time constraint, it was not possible to conduct an extensive adaptation study to reduce the gap in experience, but future studies may incorporate this element. The simulation based on gaze contingent display technique is by nature binocular (two eyes seeing the same mutilated image). Patients with bilateral central scotoma seldom have identical scotoma in the two eyes. The oculomotor behavior is thus likely to be determined by input from both eyes with scotomas in complicated ways. Monocular simulation (cover one eye) may make testing more comparable.

A target with a sinusoidal waveform is known to induce predictive pursuit quickly. This adaptation results in very high gains but may obscure the underlying oculomotor strategy. Some researchers take pains to avoid predictive pursuit by using pseudorandom waveforms. Another advantage of using pseudorandom waveforms is high output. If four non-harmonic sinewaves are used to produce a pseudorandom waveform, it is possible to obtain four sets of gains and phases from one pursuit trial. Future study should consider carefully planned pseudo-random waveforms. To our knowledge this is the first study to report on the effects of smooth pursuit on uniform and structured backgrounds in humans with real central scotoma. While our sample size was small, a substantial amount of data has been collected, thanks to the cooperation of our subjects.

Only the gains are analyzed and reported here. A more comprehensive picture about the smooth pursuit behavior of patients with central scotoma will emerge after other aspects of the data, which include the phase, initial saccades, retinal positions used for pursuit of different directions and pursuit strategies have been analyzed. Other types of visual field loss may also interfere with smooth pursuit, especially those in the parafoveal region. These can provide excellent material to understand normal and impaired visual systems in controlling eye movements, especially when the field loss clearly interferes with one direction but not another.

Finally, our study only paves the way for the further quests into why the fovea has to be intact to perform good smooth pursuit. More studies are needed to achieve a better understanding of how the fovea contributes to smooth pursuit. There are existing models postulating the brain pathways involved in smooth pursuit control and how they may support pursuit on structured background, but none have addressed the effect of a real central scotoma. This research may lead to the development of assistive technologies that serve to enhance the visual information available to those with central scotoma.

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APPENDIX

INSTITUTIONAL REVIEW BOARD APPROVAL FORM

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on January 24, 2017. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator:	KEITH, THOMAS A
Co-Investigator(s):	
Protocol Number:	**E120224012**
Protocol Title:	*Effect of Structured Background on Smooth Pursuit in Subjects with Real and Simulated Central Scotoma*

The above project was reviewed on 3/20/12. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This project qualifies as an exemption as defined in 45CF46.101, paragraph 4.

This project received EXEMPT review.

IRB Approval Date: 3/20/12

Date IRB Approval Issued: 3/20/12

Cari Oliver
Assistant Director, Office of the Institutional Review Board for Human Use (IRB)

Investigators please note:

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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