Saccadic adaptation in the presence of artificial central scotomas

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Abstract

Age-related macular degeneration (AMD) is characterized by the degradation of the macula resulting in poor central vision and difficulty performing daily tasks. Helping AMD patients optimally utilize their residual visual function is the focus of current rehabilitative strategies. Here we test whether saccadic adaptation is possible in the presence of an artificial central scotoma and if so, to what extent. The ultimate goal is to use saccadic adaptation to train patients in performing saccade re-referencing to better utilize their intact peripheral vision; patients would learn to make saccades to direct their preferred peripheral locus to the object of interest rather than the inutile fovea. We measured saccadic adaptation in healthy young participants using a central gaze-contingent artificial scotoma in two experiments, using a conventional double-step paradigm for both experiments, testing twelve and thirteen subjects respectively. Experiment 1 tested backward adaptation using a visible as well as an invisible 3° diameter scotoma. Experiment 2 consisted of forward adaptation using a 2° and a 4° invisible scotoma. We thus explored both backward and forward adaptation (known to involve different mechanisms), different-sized central scotomas, and different visibilities of scotomas. We found that in all scotoma conditions, participants adapted to similar amounts compared to control conditions without scotomas. We conclude that saccadic adaptation can occur sufficiently with central scotomas. Our results support the idea that central vision of the target is unnecessary for adaptation and that saccadic adaptation is driven primarily by peripheral retinal error.

Keywords: plasticity, age-related macular degeneration, central vision, eye movements

Introduction

Age-related macular degeneration (AMD) affects 170 million people in the world, a number projected to reach 288 million by 2040 (Jonas, 2014; Pennington & DeAngelis, 2016). As one of the leading causes of visual impairment and blindness, AMD will continue to become more prevalent within the world's aging population (Lutz, Sanderson, & Scherbov, 2001; Pascolini & Mariotti, 2012). Deterioration of the macula impedes visual acuity by affecting central vision, which can appear blurry or distorted (Cacho, Dickinson, Smith, & Harper, 2010). The fovea, the central area of the macula which we use to perceive details, is dysfunctional, so patients need to use their intact peripheral vision to access visual information. Patients can be trained to or can spontaneously learn to consistently use one or more peripheral regions, known as the preferred retinal locus (PRL) (Cheung & Legge, 2005; Chung, 2013; Crossland, Culham, Kabanarou, & Rubin, 2005; Fletcher & Schuchard, 1997).

One avenue of rehabilitation for AMD patients is to help them improve their use of the PRL through more efficient saccades. Saccades direct the fovea, a small region of the retina with the clearest vision, to an object of interest. Saccade re-referencing in which the eye movement directs instead the PRL to the object would greatly improve visual abilities (Cheung & Legge, 2005; Nilsson, Frennesson, & Nilsson, 1998; Sunness, Applegate, Haselwood, & Rubin, 1996; Walsh & Liu, 2014; White & Bedell, 1990), speeding up visual discrimination in the periphery. However, directing the PRL to the object instead has shown to be extremely difficult and if successful, can take years (Cheung & Legge, 2005; Krauzlis, Goffart, & Hafed, 2017). One possibility to achieve saccade re-referencing is through training using saccadic adaptation. Here, we investigate whether saccadic adaptation can occur in the presence of a central scotoma, and if so to what extent.

Saccades continue to be accurate even as one ages and extraocular muscles weaken, because the brain monitors and adjusts the accuracy of saccades (Herman, Blangero, Madelain, Khan, & Harwood, 2013). This is known as saccadic adaptation. For example, saccades that undershoot or overshoot a target are adjusted over a short period of time so that subsequent saccades to the same target will have an amplitude that is closer to the target's distance. This is easily demonstrable in a lab setting using a double step paradigm (McLaughlin, 1967), where a target's

position is repeatedly shifted during the saccade. Gradually, saccades land closer to the shifted target position.

Despite the multitude of studies on saccadic adaptation, the nature of the error signal that drives saccadic adaptation is not fully resolved. For example, if central vision is necessary for saccadic adaptation, then saccadic adaptation is unlikely to occur with a central scotoma. Many studies have indirectly shown that central vision is unnecessary for adaptation. For instance, multiple studies have shown that similar amounts of adaptation occurred even when the task was modified to elicit very few corrective saccades (Noto & Robinson, 2001; Wallman & Fuchs, 1998). Thus, feedback based on central vision after the corrective saccade is not necessary for adaptation. Similarly, other studies have suggested that adaptation occurs in response to a *peripheral* retinal error after the 1st saccade (Noto & Robinson, 2001; Wallman & Fuchs, 1998) or a difference between the post-saccadic retinal image and the predicted image, again based entirely on *peripheral vision* of the desired target (Bahcall & Kowler, 2000). For example, Bahcall and Kowler (2000) demonstrated backward saccadic adaptation during a task where participants were instructed to saccade partway to a target (75% of the distance from initial fixation point), which could not be based on retinal error. Further, recent evidence has shown that even intra-saccadic visual feedback received mid-flight during a saccade is sufficient to result in saccadic adaptation (Muriel Panouillères et al., 2016; Muriel Panouillères, Gaveau, Socasau, Urquizar, & Pélisson, 2013). These findings support the idea of peripheral visual information being used for adaptation rather than central. However, notably, it has not yet been demonstrated that occlusion of central vision does not impact adaptation in any way. It may be that central vision (for example after the corrective saccade or when adaptation has occurred) plays a role in adaptation, such as determining when to stop adapting. Occlusion of the target after the corrective saccade might be interpreted as a change in the external visual scene, which might also impact saccadic adaptation.

In addition, is it unclear whether there are limits to the eccentricity of peripheral visual information that can drive adaptation? If so, different sized scotomas may have different influences on adaptation. Robinson et al. (2003) tested saccadic adaptation in monkeys and showed that adaptation was most consistent for target shifts of 20 to 60% of the target eccentricity, with a decrease in adaptation for greater eccentricities (although not for forward adaptation), as well as inconsistent adaptation for smaller target shifts (<20%). Two things to

note are that 1) this has not been tested in humans, who show some differences from monkeys, such as quicker adaptation as well as stronger effects (Albano & King, 1989; Deubel, Wolf, & Hauske, 1986; Andreas Straube, Fuchs, Usher, & Robinson, 1997) and 2) the number of adaptation trials were extensive (400 to 2,800). With human participants and with fewer trials, it is unclear whether for example, larger central scotomas, resulting in the shifted target being occluded sooner during the saccade, would reduce the amount of adaptation. We therefore tested whether changing the size of the artificial central scotoma influenced adaptation.

While saccadic adaptation has been shown to occur for both backward and forward target shifts, there are many differences between backward and forward adaptation. For one, forward adaptation is less efficient, takes longer and results in less gain change compared to backward adaptation (Ethier, Zee, & Shadmehr, 2008; Hernandez, Levitan, Banks, & Schor, 2008; Muriel Panouillères et al., 2009; Andreas Straube & Deubel, 1995). But more importantly, there is both behavioural and neurological evidence that forward and backward adaptation have different underlying neuronal mechanisms (Pélisson, Alahyane, Panouillères, & Tilikete, 2010). A largely supported model is that while backward adaptation is caused by a decrease in saccade gain, forward adaptation relies on a remapping mechanism (Ethier et al., 2008; Hernandez et al., 2008; Semmlow, Gauthier, & Vercher, 1989). Neurological evidence also suggests a difference in mechanism, such as Purkinje cells in the cerebellum firing differently in forward and backward adaptation (Catz, Dicke, & Thier, 2008) and has demonstrated that forward adaptation is more affected by cerebral lesions than backward (Golla et al., 2008). Therefore, we tested both forward and backward adaptation paradigms with central scotomas to determine if there were any differences in the amount of adaptation.

Finally, it is reported that patients with AMD tend to be unaware of the presence of their scotoma (Fletcher, Schuchard, & Renninger, 2012). This unawareness leads to major difficulties in achieving daily tasks because patients are unable to determine how to move their eyes toward strategic locations to make an optimal use of their peripheral vision (Walsh & Liu, 2014). Scotoma awareness is a possible tool for rehabilitation for patients with central vision loss (Scheiman, Scheiman, & Whittaker, 2007; Walsh & Liu, 2014). One means of achieving awareness is by using gaze-central artificial scotomas that are slightly larger than the actual scotoma. In the present study, we aim to test whether saccadic adaptation is impacted by the

visibility of the scotoma. A visible scotoma provides continuous feedback of the eye position during the adaptation task and may negatively impact adaptation, since it provides more accurate information about the target position and shifts relative to the eye position.

Here we investigated whether adaptation can occur in response to only peripherally viewed targets in the presence of an artificial central scotoma. In experiment 1, we used a backward adaptation paradigm and varied the visibility of the scotoma (visible and invisible). In experiment 2, we used a forward adaptation paradigm and tested invisible scotomas of two different sizes (2° and 4° diameters). We found that in both experiments with central scotomas, saccadic adaptation occurred to a similar degree to those in the control conditions.

Experiment 1

Methods

Participants

Twelve participants took part in this study (three male, age range: 19-40, M = 22.92, SD = 5.52, including two authors AK and LO). All participants had normal or corrected-to-normal vision and no known neurological impairments. All gave written informed consent to participate in the experiment. All procedures were pre-approved by the Health research ethics committee at the University of Montreal. (16-129-CERES-D)

Apparatus

Participants sat in a dark room facing a VIEWPixx LCD monitor (VPixx Technologies, Montreal, QC), its center aligned horizontally with the participant's mid-sagittal plane and vertically at eye level. The screen dimensions were 52.1 cm by 29.2 cm. The screen was at a distance of 62 cm from the participant's eyes. The participants' heads were immobilized via a chin and forehead support placed at the edge of the table on which the monitor was located. Eye-movements were recorded using an infrared-emitting video-based eye tracker (EyeLink 1000 Plus, SR Research, Mississauga, ON, Canada). The backlight on the screen was set to a very low setting to ensure that the monitor frame was not easily visible (ViewPixx, back light setting: 5).

The position of the right eye was recorded at 1000 Hz using Eyelink 1000 video-based eye tracker (SR Research).

Procedure

Stimuli used are shown in Figure 1**.** A white oval fixation stimulus was used instead of a small dot or cross to ensure that participants would be able to fixate even in the presence of the scotoma. It was located 4.9° left of the center horizontally, at the centre of the screen vertically and was 0.9° by 4.8° in size. The target for the first saccade (referred to as T1) was located 9.7° right of the center (14.6° right of fixation), and the second target (referred to as T2) was located 4.9° to the left of T1 (9.7° right of fixation). Both targets were white filled circles with a diameter of 0.5° (*Fig. 1A*).

In the scotoma conditions, a black (invisible) or grey (visible) artificial circular central scotoma (3° in diameter) was present. The invisible scotoma was the same colour as the background (i.e. black), and so, was not visible (*Fig. 1B*). Its presence was perceived only when it occluded stimuli such as the fixation oval. The grey scotoma was visible due to the contrast difference from the background (*Fig. 1C*). Therefore, it provided information about current eye position to the participant. A custom written Experimental Builder (SR Research, Kanata, Canada) experiment was used to ensure real-time gaze-contingent central scotoma presentations. Prior to each experimental block, eye position was calibrated and validated using a standard 13-point calibration sequence.

Participants took part in three sessions for the saccadic adaptation task, completing one of the three conditions (control, invisible scotoma and visible scotoma) each week, in random order. Each session was performed at least one week apart to ensure that there was no retention of adaptation (Alahyane & Pélisson, 2005).

Each session comprised three consecutive blocks. The first block was a pre-adaptation block of 20 trials, where only T1 was illuminated and extinguished at saccade onset. There was therefore no visual feedback after the 1st saccade was completed. The second block was the adaptation block, consisting of 180 trials with the presentation of both T1 and T2. The last block was the post-adaptation block, which was identical to the pre-adaptation block. The three blocks were

run continuously in sequence with no interruption or breaks. In total participants performed 220 trials per session.

In the adaptation block, each trial began with the presentation of the fixation oval which participants were asked to look at (*Fig.1*). After 1500 ms, T1 appeared and participants were instructed to look at it as soon as it appeared. When a saccade was detected, T1 was extinguished and T2 was displayed. T2 remained visible for 500 ms. After an inter-trial interval of 500 ms the fixation oval re-appeared and the next trial was initiated.

Data Analysis

We collected a total of 7,920 trials from 12 participants. Saccade timing and position were automatically calculated offline using a saccade detection algorithm with a velocity criterion of 15°/s, and verified visually. Manual inspection involved removing trials where saccades were made before the first target appeared, where there was a blink during the saccade, where the tracker lost eye position, and where subjects made eye movements not directed toward T1. In total, there were 744 trials removed (9.4% of total trials). We also removed trials where saccades reactions times were too short (less than 80 ms) or too long (more than 500 ms); there were 127 such trials (1.6% of all trials). Then, we normalized trials in each block by adjusting them by how much the mean saccade start point deviated from fixation point. This was to account for any errors in the calibration process. We removed 28 trials (0.4%) where participants' saccades did not begin near the fixation stimulus center (more than 2° horizontally or 2° vertically away) and 2 trials (0.03%) with extremely large saccade amplitude (20 degrees or more). We additionally removed 128 outlier trials (1.6%) where the amplitude of the first saccade was more than 2.5 standard deviations away from the mean for each session for each participant.

Gain was calculated as the actual saccade amplitude divided by the desired saccade amplitude. The actual saccade amplitude was the difference between horizontal start and end positions of the first saccade. The desired saccade amplitude was the difference between horizontal start position of the first saccade and T1 target position (9.7°). Thus a gain of one would indicate that the saccade reached T1, and a gain less or greater than one would mean that the participant undershot or overshot the target respectively. We removed 103 gain outlier trials (1.3%) where gain was more than 2.5 standard deviations away from the mean for each session for each participant. In total, there remained 6,788 trials (85.7%).

We calculated the mean gain for the pre-adaptation block and the post-adaptation block for each participant for each condition. We also calculated the change in gain as follows:

$$\Delta \text{ Gain} = \text{Mean gain in post-adaptation trials} - \text{Mean gain in pre-adaptation trials}$$

Percent gain change was determined as follows:

$$\text{Percent gain change} = \frac{(\text{mean post-adaptation gain} - \text{mean pre-adaptation gain})}{\text{mean pre-adaptation gain}} \times 100$$

We calculated the percentage of trials with corrective saccades in the adaptation blocks. Corrective saccades were determined using the following criteria: 1) the start position of the 2nd saccade was less than 1deg from the end position of the 1st saccade, 2) the endpoint of the 2nd saccade was within 5 deg horizontally of T2 and 3) the amplitude of the saccade was greater than 0 and was directed towards T2.

Data were analyzed using MATLAB (MATLAB and Statistics Toolbox Release 2018a) and statistical analyses were performed with SPSS (SPSS Statistics for Windows, Version 25.0).

Results

Figure 2 shows the first saccade endpoints of a typical participant for all three conditions. As can be observed, in all three conditions, there was a shift in saccade endpoints away from T1 (dotted line) to T2 (solid line), demonstrating saccadic adaptation. Moreover, this was similar across the conditions. In addition, we also observed that the participant tended to undershoot T1(dotted line) in the pre-adaptation block in all conditions. Finally, interestingly, in the invisible (*Fig. 2B*) and visible (*Fig. 2C*) conditions, the participant's first saccade endpoints landed so that T2 was occluded by the scotoma (gray region) relatively early within the adaptation block. Nevertheless, adaptation appeared to be the same. These observations are quantified across all participants below.

Degree of saccadic adaptation

In *Fig. 3A* is depicted the mean gains in the pre and post- adaptation blocks for each condition. We performed a 2-way repeated measures ANOVA with condition (control, invisible and visible) and block (pre and post) as factors. As can be seen, there was a decrease in gain from pre to post adaptation blocks in all three conditions, confirmed by a significant main effect for block ($F(1,11)=18.7$, $p<0.001$). In addition, we also found a significant main effect of condition ($F(2,22)=5.99$, $p=0.008$), and a significant interaction effect ($F(2,22) = 6.84$, $p=0.005$). Post-hoc tests showed that there was a significant decrease in gain for each of the three conditions. We confirmed that adaptation occurred for the control condition (*Fig. 3, left bars*). A paired t-test between mean gain in the pre-adaptation trials ($M = 0.86$, $SD = 0.05$) and post-adaptation ($M = 0.73$, $SD = 0.05$) trials was significant ($t(11) = 9.49$, $p<0.001$). There was a 14% decrease between the mean gains of pre- and post-adaptation trials, which was an adaptation of about half the amount of the target shift (33% decrease). There was also a significant decrease in the invisible condition (invisible pre $M = 0.84$, invisible post $M = 0.68$, $t(11)=13.5$, $p<0.001$) as well as the visible condition (visible pre $M = 0.81$, visible post $M = 0.71$, $t(11)=8.29$, $p<0.001$).

In addition, we performed two one-way ANOVAs for the pre and post blocks separately. For the pre block, the ANOVA was significant ($F(2,22) = 4.8$, $p=0.018$). Post-hoc t-tests revealed significant differences between the control condition ($M = 0.86$) and the visible condition ($M=0.81$, $t(11)=3.32$, $p=0.007$, Bonferoni-Holm familywise error rate), but no other differences. For the post block, the ANOVA was also significant ($F(2,22) = 8.03$, $p=0.002$). Post-hoc t-tests revealed significant differences between the control ($M = 0.73$) and the invisible condition ($M=0.68$, $t(11)=3.9$, $p=0.002$), and between the visible ($M=0.71$) and the invisible condition ($M=0.68$, $t(11) = 2.8$, $p=0.018$). There was no significant difference between the control and visible conditions ($p=0.16$). In summary it appears that participants had smaller gains in the visible condition in the pre block, possibly due to them having visual feedback of their eye position. This difference did not remain in the post-block but this may be related to differences in adaptation for the three conditions, which is examined next.

To compare difference in adaptation, we compared change in gain between pre and post blocks for the three conditions (*Fig. 3B*). First, we confirmed that there was significant saccadic adaptation through one-sample t-tests. All three conditions showed gain changes that were significantly different from 0 (all $p<0.001$). A one-way repeated-measures ANOVA on gain change with condition as a factor was significant ($F(2,22)=6.83$, $p=0.005$). Post-hoc testing

revealed that gain reduced to a greater degree for the invisible condition (M=-0.15) compared to the visible condition (M=-0.12, t(11)=3.3, p=0.007), but there were no differences between invisible and control (M=-0.12, p=0.043, Holm-Bonferoni family-wise error rate was 0.025), nor between control and visible (p=0.13). In summary, adaptation was largest for the invisible scotoma condition and smallest for the visible condition, with no significant differences from control, whose gain was in between the two.

Occlusion of the 2nd target by the scotoma

As can be seen in *Fig. 2A* and *B*, around midway in the adaptation block, many saccade endpoints landed within the scotoma occlusion zone. In other words, in the scotoma adaptation block conditions, for any saccade endpoint that landed at 6.35° or less, the scotoma occluded T2. It appeared that this did not impact adaptation however. We calculated the percentage of saccade endpoints that landed within this zone for all participants. The amounts of occlusion were quite substantial, ranging from 47% to 96% for the invisible condition (M=84%, SD = 15.7%) and from 34% to 98% for the visible condition (M=73%, SD = 25.5%). We compared each individual's amount of gain change to the percent of occlusion for each condition to investigate whether increased occlusion led to decreased adaptation. As expected given that the invisible condition showed more adaptation with more occlusion, we did not find a significant relationship for either condition (p>0.05). Thus, it appears that for the backward condition, viewing T2 during the later stages of the saccade was sufficient to drive adaptation (Muriel Panouillères, Gaveau, Socasau, Urquizar, & Pélisson, 2013).

Corrective saccades

We investigated whether there was a relationship between the number of corrective saccades were performed and the amount of adaptation. We observed that across all conditions, half (6) the participants made no corrective saccades. Two more participants made minimal corrective saccades in one of the conditions (participant 5, baseline condition, 5%; participant 6, invisible condition, 8%). For the 4 remaining participants, on average 69% of all trials comprised corrective saccades (SD = 23%) for the baseline condition, 41% (SD = 31%) for the invisible condition and 41%(SD = 41%) for the visible condition.

There were no significant differences overall across the conditions ($F(2, 22)=3.29$, $p=0.06$). Moreover, there was no significant relationship between mean change in gain and the percentage of corrective saccades in any of the 3 conditions ($p>0.05$). These results show that corrective saccades did not play a role in adaptation.

Experiment 1 Summary

Participants performed backward saccadic adaptation in three conditions: a control condition, in the presence of an invisible 3° diameter central scotoma, and in the presence of a 3° invisible central scotoma. Overall, the amount of adaptation was similar across the three conditions. These results show that central vision occlusion does not affect adaptation.

However, a concern with the backward adaptation paradigm is that fatigue may have caused a large proportion of saccade gain decrease. Although extraocular muscles tend to be relatively resistant to fatigue (Fuchs & Binder, 1983; Saito, 1992), it has been shown in both humans (De Gennaro, Ferrara, Curcio, & Bertini, 2001; De Gennaro, Ferrara, Urbani, & Bertini, 2000; Rowland et al., 2005; Sprenger, Zils, Heide, Born, & Gais, 2005) and monkeys (A Straube, Robinson, & Fuchs, 1997; Andreas Straube et al., 1997) that fatigue can affect saccade metrics. Therefore, it could be that the equal amounts of adaptation during the scotoma conditions might be related to fatigue rather than adaptation per se.

In addition, our results for backward adaptation may not be generalizable to forward adaptation. It must be noted that backward and forward adaptation are fundamentally different, likely based on different mechanisms (Catz et al., 2008; Ethier et al., 2008; Golla et al., 2008; Hernandez et al., 2008; Pélisson et al., 2010; Semmlow et al., 1989). Therefore, it would be difficult to make conclusions about forward adaptation based on results from this first experiment.

In order to address these outstanding issues, we performed a second experiment, where were tested forward adaptation. In this experiment, we used two different-sized invisible central scotomas. By varying the diameter of scotoma, we can investigate how the eccentricity of the viewed peripheral T2 affects adaptation: a larger scotoma results in larger eccentricities of T2 relative to the fovea, being occluded.

Experiment 2

Methods

The experiment was almost identical to experiment 1, with a few changes that are outlined below.

Participants

Thirteen participants took part in this study (four male, age range: 19-42 years, M = 24.38 years, SD = 5.84, including the author AK). All participants had normal or corrected-to-normal vision, no known neurological impairments, and gave written informed consent to participate in the experiment.

Procedure

Stimuli were presented with custom code using Matlab (MATLAB, The Math Works Inc., Natick, MA) with Psychtoolbox (Brainard, 1997; Pelli, 1997) and EyeLink toolboxes (Cornelissen, Peters, & Palmer, 2002).

There were three conditions in total: a control condition, a 2°, and a 4° diameter scotoma condition. Aside from the presence of a scotoma and its size, all conditions were identical.

Prior to each session, eye position was calibrated first using a standard 9-point calibration window (EyeLink 1000 Plus, SR Research, Mississauga, ON, Canada). A second 15-point calibration was used to calculate correction values in X and Y to precisely align the scotoma on participants' fovea (MATLAB, The Math Works Inc., Natick, MA). During this procedure, participants fixated on 15 dots presented in random order, equally spaced across a grid spanning 4/5th of the screen, then pressed a button. Fixation dots were a shape combining the bullseye and cross hair to enhance fixation stability and precision (Thaler, Schütz, Goodale, & Gegenfurtner, 2013). A custom Matlab script mapped eye positions to the fixation dot locations using a polynomial fit with 6 parameters. Then, these parameters were used to adjust eye position from the EyeLink's parameters for accurate scotoma presentation and eye position recording; the standard EyeLink calibration resulted in a mean error of 2.21° in absolute distance (distance between recorded position and the actual target positions), while the 2nd calibration reduced this error to 0.53°.

Stimuli used are shown in *Figure 4***.** The white fixation oval was identical to experiment 1. The target for the first saccade (referred to as T1) was located 5° right of the center (10° right of

fixation), and the second target (referred to as T2) was located 5° at the right of T1 (15° right of fixation). Both targets were white filled circles with a diameter of 0.5°.

In the scotoma conditions (*Fig. 4B & C*), a black artificial circular central scotoma (2° or 4° in diameter) was present. It was the same colour as the background (i.e. black), and so, was not visible. Its presence was perceived only when it occluded stimuli such as the fixation oval.

Participants took part in three sessions completing each at least a week apart, in random order. Each session was comprised of three blocks. The first block was a pre-adaptation block, comprised of 25 trials. In this block, only T1 was illuminated and extinguished at saccade onset. The second block was the adaptation block, consisting of 200 trials with the presentation of both T1 and T2. The last block was the post-adaptation block, which was identical to the pre-adaptation block. In total participants performed 250 trials per session, which took 12 to 15 minutes. We increased the number of trials from the 1st experiment as forward adaptation typically takes longer than backward adaptation (Lévy-Bencheton, Khan, Pélisson, Tilikete, & Pisella, 2016).

Each trial began with the presentation of the fixation oval at which participants were asked to look. After 2000 ms, T1 appeared and participants were instructed to look at it as soon as it appeared. When a saccade was detected, T1 was extinguished and T2 was displayed. The average time of T2 onset relative to saccade peak time was 2.25 ms. T2 remained visible for 400 ms. For the two scotoma conditions, T2 was also presented for 400 ms, although often it was not visible after the corrective saccade as it was covered by the central scotoma. After an inter-trial interval of 400 ms the fixation oval re-appeared and the next trial was initiated.

Data Analysis

The same parameters and analysis methodology was used as for Exp. 1. We collected a total of 9,747 trials from 13 participants. Trials were removed 1) in which saccades were made before the first target appeared, where there was a blink during the saccade, where the tracker lost eye position, and where subjects made eye movements not directed toward T1 (1,247 trials, 12.8% of total trials), 2) where saccades reaction times not between 80 and 500 ms (214 trials, 0.2%), 3) where participants' normalized saccades did not begin near fixation stimulus center (122 trials, 0.13%), 4) where 1st saccade amplitude was more than 2.5 standard deviations away from the mean for each session for each participant (144 trials, 0.15%), and 5) where gain was more than

2.5 standard deviations away from the mean for each session for each participant (107 trials, 0.11%). In total, there remained 7,913 trials (81.2%).

Results

Figure 5 depicts saccade endpoints for a typical participant for all three conditions, again showing similar amounts of adaptation across the three conditions.

Saccadic adaptation

In *Fig. 6A* can be seen the mean gain for the pre (white bars) and the post (gray filled bars) for each condition as well as individual gains (thin black lines). We observed that participants were less consistent in demonstrating forward adaptation compared to backward adaptation in experiment 1. Some individual participants even showed a decrease in gain. Nevertheless, the increase in gain, though smaller than backward, was similar across conditions. We performed a two-way repeated measures ANOVA with condition (control, 2° scotoma, 4° scotoma) and block (pre, post) as factors. The ANOVA revealed a significant main effect of condition ($F(2,24)=3.8$, $p=0.037$) and a significant main effect of block ($F(1,12)=22.7$, $p<0.001$) but no interaction effects ($p>0.05$). These results suggest that there was a significant increase in gain in the post block compared to the pre block for all three conditions (mean pre gain = 0.99, mean post gain = 1.06). Bonferroni-corrected pairwise comparisons also revealed that the overall gain (collapsed across pre and post) was largest for the 2° scotoma condition ($M=1.05$), which was significantly different from the 4° scotoma condition ($M=1$, $p=0.01$), but not from control ($M=1.02$).

In *Fig. 6B* can be seen the mean (bars) and individual (dots) change in gain for the three conditions from pre to post. Interestingly, we did observe with one-sample t-tests that the change in gain was not significantly different from 0 for the 4° scotoma condition ($t(12)=1.8$, $p=0.09$), while it was significantly different for the other two conditions (control; $t(12)=5.3$, $p<0.001$, 2°; $t(12)=3.2$, $p=0.008$). Nevertheless, the change in gain was not significantly different across conditions, as shown by a one-way ANOVA ($F(2,24)=0.6$, $p=0.5$, control M = 0.089, 2° M = 0.064, 4° M = 0.055).

Scotoma occlusion

Unlike experiment 1, very few saccade endpoints landed such that the scotoma occluded T2. For the 2° scotoma, 12 out of 13 participants had no saccades landing within this zone during the adaptation block and one participant had 0.5% of saccades. For the 4° scotoma, only 3 out of 13 participants had saccades landing within the zone (M = 2.12%, SD =0.63%).

Corrective saccades

Like in exp. 1, we compared corrective saccade proportions with the change in gain. Overall, there was a wide range in the percentage of adaptation trials with corrective saccades overall (M = 76.3%, SD = 34.8%), ranging from 100% to 1.4%, but a few participants were responsible for most of the variability. In particular, participant 6 made very few corrective saccades (<14% in the three conditions) as did participant 13 (<15%). The remaining 11 participants made a corrective saccade the majority of the time. This was in contrast to the backward paradigm results, where the majority of participants did not make corrective saccades.

However, similar to the 1st experiment, there were no significant differences overall across the conditions (Control, M = 76.3%, SD = 38.6%; 2° scotoma, M = 77.2%, SD = 35.6%; 4° scotoma, M = 75.2%, SD = 32.7%; $F(2.24)=0.098$, $p=0.9$). Moreover, there was no significant relationship between mean change in gain and the percentage of corrective saccades in any of the 3 conditions ($p>0.05$). These results show that corrective saccades also did not play a role in adaptation for forward adaptation.

Experiment 2 summary

We observed that the presence of the scotoma (both 2° and 4° diameters) resulted in similar amounts of adaptation compared to the control condition, confirming results from experiment 1 that central vision occlusion does not affect saccadic adaptation. Unlike for backward adaptation in experiment 2, we observed that there was almost no occlusion of T2 after the 1st saccade during adaptation trials. This was due to the fact that most saccades tended to undershoot T1, as is the general tendency for saccades (Becker & Fuchs, 1969; de Bie, van den Brink, & van Sonderen, 1987; Deubel, Wolf, & Hauske, 1982; Kapoula, 1985).

Discussion

We measured the extent to which saccadic adaptation occurred in the presence of artificial central scotomas of different visibilities and sizes and with different adaptation directions. We observed similar amounts of adaptation to control conditions in all cases. In the backward adaptation paradigm, we observed adaptation even when the scotoma occluded the shifted target the majority of the time at the end of the saccade, suggesting that adaptation took place in response to the shifted target during the ongoing saccade. In addition, we observed similar amounts of adaptation whether the scotoma was visible to the participant (thus providing visual feedback of eye position) or invisible. In the forward adaptation paradigm, we also observed similar amounts of adaptation compared to control for two differently sized invisible scotomas. We conclude that saccadic adaptation occurs equally well in the presence of a central scotoma and that peripheral peri- and post- saccadic visual feedback of the shifted target location are sufficient to drive adaptation.

We observed comparable adaptation with central scotomas, regardless of the size of the scotoma or its visibility. These results support the idea that saccadic adaptation would be possible in patients with AMD as a means of training. We propose to use saccadic adaptation to adapt eye position such that the desired target lands on the PRL after the 1st saccade after training over the course of numerous trials. The effects of saccadic adaptation have been shown to remain for a short duration, typically under a week (Alahyane & Pélisson, 2005). But, this could be attributed to the fact that saccades which direct the object of interest outside the fovea are not ideal for healthy participants. It could be possible that if AMD patients are trained so that saccades direct targets to the PRL, this would be beneficial to their visual function, and therefore the effects of adaptation would be better maintained.

We observed no difference in adaptation between visible and invisible central scotomas, demonstrating that adaptation could occur even when patients are unaware of the presence of the scotoma itself (Fletcher et al., 2012). Importantly, our results support that idea that that a visible scotoma is not detrimental to adaptation. Moreover, awareness of the scotoma would likely be beneficial in maintaining adaptation, which could be achieved through the use of a gaze-contingent visible scotoma, that is the shape of the patient's scotoma but slightly larger. This would aid patients in reinforcing adaptation to make an optimal use of their peripheral vision (Walsh & Liu, 2014). Along these lines, it has been suggested that scotoma awareness is a

possible tool for rehabilitation for patients with central vision loss (Scheiman et al., 2007; Walsh & Liu, 2014).

For backward adaptation, it was often the case that the central scotoma occluded the shifted target at the end of the 1st saccade, thus theoretically impeding saccadic adaptation. However, we observed that this was not the case and that adaptation occurred equally well. Indeed, we observed that there was equal adaptation across the 3 backward conditions, confirming previous findings (M. Panouillères et al., 2016; Muriel Panouillères et al., 2013). Specifically, it has been shown that intra-saccadic visual feedback received mid-flight during a saccade can also cause saccadic adaptation (Muriel Panouillères et al., 2016; Muriel Panouillères, Gaveau, Socasau, Urquizar, & Pélisson, 2013). The effect of visual feedback timing was tested by comparing an intra-saccadic condition, where the shifted target was displayed only during the saccade and a post-saccadic condition, where the shifted target was displayed after the saccade (Muriel Panouillères et al., 2013). Both conditions produced equal amounts of adaptation, for both backward and forward target shifts. In an additional experiment using backward target shifts, the researchers showed that even 10ms and 2ms durations were sufficient to cause adaptation in the same manner as a post-saccadic presentation, but only during the deceleration phase of the saccade and not during the acceleration phase or at peak velocity (M. Panouillères et al., 2016). To summarize, it appears that even intra-saccadic *peripheral* presentation of T2 is sufficient for adaptation and that post-saccadic foveal or peri-foveal information does not increase the amount of adaptation.

While we found relatively consistent decreases in gain across all three conditions for the backward paradigm, in the forward paradigm we observed overall less consistent gain change, with individual participants showing little or even backward adaptation. This is consistent with previous findings that show that forward adaptation does not always result in gain increases, particularly for target shifts of less than 50% of target eccentricity (Robinson, Noto, & Bevans, 2003). Other studies have also demonstrated that a larger number of trials are needed to elicit gain increases (equal to gain decreases in backward adaptation) in forward adaptation (Deubel et al., 1986; Miller, Anstis, & Templeton, 1981; Andreas Straube et al., 1997) It has been proposed that forward and backward adaptation are based on different mechanisms in the brain (Ethier et

al., 2008; Hernandez et al., 2008; Pélisson et al., 2010; Semmlow et al., 1989) which would likely lead to different behaviour patterns.

We also investigated whether there were differences in the number of corrective saccades across conditions and whether this was related to the amount of adaptation. In both cases, we found no differences and no relationship, confirming that corrective saccades did not play a role in adaptation. Specifically, it appears that making a corrective saccade to T2 after the 1st saccade to T1 did not play a role in determining the error for which the saccade must compensate. In addition, the lack of difference across control and scotoma conditions in both backward and forward adaptation experiments also demonstrate that the scotoma did not influence behaviour. As for how corrective saccades would influence saccade gain adaptation, most research concludes they are insignificant: removing corrective saccades has almost no effect on saccade gain and changing the direction of corrective saccades has no influence either (Noto & Robinson, 2001; Wallman & Fuchs, 1998).

For both backward and forward adaptation, we observed that foveal feedback of T2 was not important; there was no significant difference between the scotoma conditions, while foveal feedback did differ. While it is well established that foveal feedback of the shifted target is not necessary for adaptation, the nature of the error signal that drives adaptation is still unresolved. It was proposed that a visual retinal error (how far off the fovea is from the target after the saccade) drove adaptation (Noto & Robinson, 2001; Wallman & Fuchs, 1998). However, other researchers suggested that adaptation is caused not by retinal error per se, but by the difference between the retinal image (post-saccade) and the predicted image (pre-saccade), which they named the visual comparison model (Bahcall & Kowler, 2000). They believed that retinal error is not an adequate error signal in a real world scenario, such as scanning scenery in nature, where it would be difficult to determine retinal error because of the numerous visual objects that can take on a variety of shapes (Bahcall & Kowler, 2000). In support of this proposal, Bahcall and Kowler (2000) also demonstrated saccadic adaptation during a task where participants were instructed to saccade partway to a target (75% of the distance from initial fixation point). In this case, the retinal error would always be positive. However, the target was shifted backwards and this resulted in backward saccadic adaptation rather than forward as would be predicted if retinal error drove adaptation. This visual comparison model is analogous to the more general sensory

prediction error hypothesis (SPE) proposed by some researchers to drive adaptation, defined as the discrepancy between the predicted and actual sensory signals (Herman et al., 2013; Shadmehr, Smith, & Krakauer, 2010). There is much support for sensory prediction errors in the visuomotor system (Mazzoni & Krakauer, 2006; Shadmehr et al., 2010; Tseng, Diedrichsen, Krakauer, Shadmehr, & Bastian, 2007) as well as in visual perception (Alink, Schwiedrzik, Kohler, Singer, & Muckli, 2010; Den Ouden, Kok, & De Lange, 2012; Meyer & Olson, 2011).

In conclusion, we showed that both backward and forward adaptation occurred equally as well in the presence of an artificial gaze-contingent central scotoma as with normal vision. These findings support our proposal of using saccadic adaptation as a means of training for saccade re-referencing for people with central vision loss.

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Figure legends

Fig 1. Stimuli and procedure (Experiment 1). In all conditions, each trial began with the fixation stimulus displayed for 1500 ms, followed by the first target (T1). A white oval fixation stimulus was used so that participants would be able to fixate even with the scotoma. Both T1 and T2 were white circles with a diameter of 0.5°. At saccade onset, T1 was extinguished and T2 was illuminated coincidentally. In the (A) control and (B), (C) scotoma conditions, T2 was displayed for 500 ms. The red cross represents the participant's gaze position. In (B) and (C), the black dotted circle outlines the scotoma. As a result, T2 would be covered by the scotoma after the 2nd saccade and thus not visible to the participant. The black background of the screen is depicted as dark grey for visibility.

Fig 2. Saccade endpoints of a typical participant (Experiment 1). First saccade endpoints are denoted by a black empty circle. In all conditions there was a shift in saccade endpoints from T1 (dotted line) to T2 (solid line), demonstrating adaptation. Note that the participant undershot T1 (dotted line) even during the pre-adaptation block across all conditions. Filled in grey is the scotoma occlusion zone, which is 1.5 degrees or less away from T2.

Fig 3. Mean saccade gain by block and condition (Experiment 1). (A) shows the mean gain for the pre (white bars) and the post-adaptation blocks (gray bars) for each condition as well as individual gains from each participant (thin black lines). (B) shows a bar graph of the change in mean gain between pre and post-adaptation blocks for each condition. Open dots represent individual mean gains for each participant.

Fig 4. Stimuli and procedure (Experiment 2). In all conditions, each trial began with the fixation stimulus displayed for 2000 ms, followed by the first target (T1). Trial sequence was almost identical to that described for experiment 1. In all conditions, T2 was displayed for 400 ms. In the 2° scotoma (B) and 4° scotoma (C) conditions, the black dotted circle outlines the scotoma.

Fig 5. Saccade endpoints of a typical participant (Experiment 2). First saccade endpoints are denoted by black empty circles. In all conditions there was a shift in saccade endpoints from T1 (dotted line) to T2 (solid line), demonstrating adaptation. Filled in grey is the scotoma occlusion zone, which is 1 degree or less away from T2 in (B) and 2 degrees or less away from T2 in (C).

Note that in both (B) and (C) there were no endpoints in the occlusion zone, in contrast to Experiment 1.

Fig 6. Mean saccade gain by block and condition (Experiment 2). Data are presented in the same manner as in Fig. 3.

References

Alahyane, N., & Pélisson, D. (2005). Long-lasting modifications of saccadic eye movements following adaptation induced in the double-step target paradigm. *Learning & Memory (Cold Spring Harbor, N.Y.)*, *12*(4), 433–443. https://doi.org/10.1101/lm.96405

Albano, J. E., & King, W. M. (1989). Rapid adaptation of saccadic amplitude in humans and monkeys. *Investigative Ophthalmology & Visual Science*, *30*(8), 1883–1893.

Becker, W., & Fuchs, A. F. (1969). Further properties of the human saccadic system: Eye movements and correction saccades with and without visual fixation points. *Vision Research*, *9*(10), 1247–1258. https://doi.org/10.1016/0042-6989(69)90112-6

Cacho, I., Dickinson, C. M., Smith, H. J., & Harper, R. A. (2010). Clinical impairment measures and reading performance in a large age-related macular degeneration group. *Optometry and Vision Science□: Official Publication of the American Academy of Optometry*, *87*(5), 344–349. https://doi.org/10.1097/opx.0b013e3181d9515c

Catz, N., Dicke, P. W., & Thier, P. (2008). Cerebellar-dependent motor learning is based on pruning a Purkinje cell population response. *Proceedings of the National Academy of Sciences*, *105*(20), 7309. https://doi.org/10.1073/pnas.0706032105

Cheung, S., & Legge, G. E. (2005). Functional and cortical adaptations to central vision loss. *Visual Neuroscience*, *22*(2), 187–201. https://doi.org/10.1017/S0952523805222071

Chung, S. T. L. (2013). Cortical Reorganization after Long-Term Adaptation to Retinal Lesions in Humans. *The Journal of Neuroscience*, *33*(46), 18080. https://doi.org/10.1523/JNEUROSCI.2764-13.2013

Crossland, M. D., Culham, L. E., Kabanarou, S. A., & Rubin, G. S. (2005). Preferred Retinal Locus Development in Patients with Macular Disease. *Ophthalmology*, *112*(9), 1579–1585. https://doi.org/10.1016/j.ophtha.2005.03.027

de Bie, J., van den Brink, G., & van Sonderen, J. F. (1987). THE SYSTEMATIC UNDERSHOOT OF SACCADES: A LOCALIZATION OR AN OCULOMOTOR PHENOMENON? In J. K. O'REGAN & A. LEVY-SCHOEN (Eds.), *Eye Movements from Physiology to Cognition* (pp. 85–94). https://doi.org/10.1016/B978-0-444-70113-8.50013-8

De Gennaro, L., Ferrara, M., Curcio, G., & Bertini, M. (2001). Visual search performance across 40 h of continuous wakefulness: Measures of speed and accuracy and relation with oculomotor performance. *Physiology & Behavior*, *74*(1), 197–204. https://doi.org/10.1016/S0031-9384(01)00551-0

De Gennaro, L., Ferrara, M., Urbani, L., & Bertini, M. (2000). Oculomotor impairment after 1 night of total sleep deprivation: A dissociation between measures of speed and accuracy. *Clinical Neurophysiology*, *111*(10), 1771–1778. https://doi.org/10.1016/S1388-2457(00)00393-X

Deubel, H., Wolf, W., & Hauske, G. (1982). Corrective saccades: Effect of shifting the saccade goal. *Vision Research*, *22*(3), 353–364. https://doi.org/10.1016/0042-6989(82)90151-1

Deubel, H., Wolf, W., & Hauske, G. (1986). Adaptive gain control of saccadic eye movements. *Human Neurobiology*, *5*(4), 245–253. Retrieved from PubMed. (3818374)

Ethier, V., Zee, D. S., & Shadmehr, R. (2008). Changes in Control of Saccades during Gain Adaptation. *The Journal of Neuroscience*, *28*(51), 13929. https://doi.org/10.1523/JNEUROSCI.3470-08.2008

Fletcher, D. C., & Schuchard, R. A. (1997). Preferred Retinal Loci Relationship to Macular Scotomas in a Low-vision Population. *Ophthalmology*, *104*(4), 632–638. https://doi.org/10.1016/S0161-6420(97)30260-7

Fletcher, D. C., Schuchard, R. A., & Renninger, L. W. (2012). Patient awareness of binocular central scotoma in age-related macular degeneration. *Optometry and Vision Science: Official Publication of the American Academy of Optometry*, *89*(9), 1395–1398. https://doi.org/10.1097/opx.0b013e318264cc77

Fuchs, A. F., & Binder, M. D. (1983). Fatigue resistance of human extraocular muscles. *Journal of Neurophysiology*, *49*(1), 28–34. https://doi.org/10.1152/jn.1983.49.1.28

Golla, H., Tziridis, K., Haarmeier, T., Catz, N., Barash, S., & Thier, P. (2008). Reduced saccadic resilience and impaired saccadic adaptation due to cerebellar disease. *European Journal of Neuroscience*, *27*(1), 132–144. https://doi.org/10.1111/j.1460-9568.2007.05996.x

Hernandez, T. D., Levitan, C. A., Banks, M. S., & Schor, C. M. (2008). How does saccade adaptation affect visual perception? *Journal of Vision*, *8*(8), 3–3. https://doi.org/10.1167/8.8.3

Jonas, J. B. (2014). Global prevalence of age-related macular degeneration. *The Lancet Global Health*, *2*(2), e65–e66. https://doi.org/10.1016/S2214-109X(13)70163-3

Kapoula, Z. (1985). Evidence for a range effect in the saccadic system. *Vision Research*, *25*(8), 1155–1157. https://doi.org/10.1016/0042-6989(85)90105-1

Krauzlis, R. J., Goffart, L., & Hafed, Z. M. (2017). Neuronal control of fixation and fixational eye movements. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *372*(1718), 20160205. https://doi.org/10.1098/rstb.2016.0205

Lévy-Bencheton, D., Khan, A. Z., Pélisson, D., Tilikete, C., & Pisella, L. (2016). Adaptation of Saccadic Sequences with and without Remapping. *Frontiers in Human Neuroscience*, *10*, 359. https://doi.org/10.3389/fnhum.2016.00359

Lutz, W., Sanderson, W., & Scherbov, S. (2001). The end of world population growth. *Nature*, *412*(6846), 543–545. https://doi.org/10.1038/35087589

Miller, J. M., Anstis, T., & Templeton, W. B. (1981). Saccadic plasticity: Parametric adaptive control by retinal feedback. *Journal of Experimental Psychology: Human Perception and Performance*, *7*(2), 356–366. https://doi.org/10.1037/0096-1523.7.2.356

Nilsson, U., Frennesson, C., & Nilsson, S. (1998). Location and stability of a newly established eccentric retinal locus suitable for reading, achieved through training of patients with a dense central scotoma. *Optometry and Vision Science: Official Publication of the American Academy of Optometry*, *75*(12), 873–878. Retrieved from PubMed. (9875992)

Noto, C. T., & Robinson, F. R. (2001). Visual error is the stimulus for saccade gain adaptation. *Cognitive Brain Research*, *12*(2), 301–305. https://doi.org/10.1016/S0926-6410(01)00062-3

Panouillères, M., Gaveau, V., Debatisse, J., Jacquin, P., LeBlond, M., & Pélisson, D. (2016). Oculomotor Adaptation Elicited By Intra-Saccadic Visual Stimulation: Time-Course of Efficient Visual Target Perturbation. *Frontiers in Human Neuroscience*, *10*(91). https://doi.org/doi:10.3389/fnhum.2016.00091

Panouillères, Muriel, Gaveau, V., Socasau, C., Urquizar, C., & Pélisson, D. (2013). Brain Processing of Visual Information during Fast Eye Movements Maintains Motor Performance. *PLOS ONE*, *8*(1), e54641. https://doi.org/10.1371/journal.pone.0054641

Panouillères, Muriel, Weiss, T., Urquizar, C., Salemme, R., Munoz, D. P., & Pélisson, D. (2009). Behavioral Evidence of Separate Adaptation Mechanisms Controlling Saccade Amplitude Lengthening and Shortening. *Journal of Neurophysiology*, *101*(3), 1550–1559. https://doi.org/10.1152/jn.90988.2008

Pascolini, D., & Mariotti, S. P. (2012). Global estimates of visual impairment: 2010. *British Journal of Ophthalmology*, *96*(5), 614. https://doi.org/10.1136/bjophthalmol-2011-300539

Pélisson, D., Alahyane, N., Panouillères, M., & Tilikete, C. (2010). Sensorimotor adaptation of saccadic eye movements. *Neuroscience & Biobehavioral Reviews*, *34*(8), 1103–1120. https://doi.org/10.1016/j.neubiorev.2009.12.010

Pennington, K. L., & DeAngelis, M. M. (2016). Epidemiology of age-related macular degeneration (AMD): Associations with cardiovascular disease phenotypes and lipid factors. *Eye and Vision (London, England)*, *3*, 34–34. https://doi.org/10.1186/s40662-016-0063-5

Robinson, F. R., Noto, C. T., & Bevans, S. E. (2003). Effect of Visual Error Size on Saccade Adaptation in Monkey. *Journal of Neurophysiology*, *90*(2), 1235–1244. https://doi.org/10.1152/jn.00656.2002

Rowland, L. M., Thomas, M. L., Thorne, D. R., Sing, H. C., Krichmar, J. L., Davis, H. Q., … Belenky, G. (2005). Oculomotor Responses During Partial and Total Sleep Deprivation. *Aviation, Space, and Environmental Medicine*, *76*(7), C104–C113.

Saito, S. (1992). Does fatigue exist in a quantitative measurement of eye movements? *Ergonomics*, *35*(5–6), 607–615. https://doi.org/10.1080/00140139208967840

Scheiman, M., Scheiman, M., & Whittaker, S. (2007). *Low Vision Rehabilitation: A Practical Guide for Occupational Therapists*. Retrieved from https://books.google.ca/books?id=xGKXuM7H6SMC

Semmlow, J. L., Gauthier, G. M., & Vercher, J.-L. (1989). Mechanisms of short-term saccadic adaptation. *Journal of Experimental Psychology: Human Perception and Performance*, *15*(2), 249–258. https://doi.org/10.1037/0096-1523.15.2.249

Sprenger, A., Zils, E., Heide, W., Born, J., & Gais, S. (2005). Differential Effects of Sleep Deprivation on Saccadic Eye Movements. *Sleep*, *28*(9), 1109–1115. https://doi.org/10.1093/sleep/28.9.1109

Straube, A, Robinson, F. R., & Fuchs, A. F. (1997). Decrease in saccadic performance after many visually guided saccadic eye movements in monkeys. *Investigative Ophthalmology & Visual Science*, *38*(13), 2810–2816.

Straube, Andreas, & Deubel, H. (1995). Rapid gain adaptation affects the dynamics of saccadic eye movements in humans. *Vision Research*, *35*(23), 3451–3458. https://doi.org/10.1016/0042-6989(95)00076-Q

Straube, Andreas, Fuchs, A. F., Usher, S., & Robinson, F. R. (1997). Characteristics of Saccadic Gain Adaptation in Rhesus Macaques. *Journal of Neurophysiology*, *77*(2), 874–895. https://doi.org/10.1152/jn.1997.77.2.874

Sunness, J. S., Applegate, C. A., Haselwood, D., & Rubin, G. S. (1996). Fixation Patterns and Reading Rates in Eyes with Central Scotomas from Advanced Atrophic Age-related Macular Degeneration and Stargardt Disease. *Ophthalmology*, *103*(9), 1458–1466. https://doi.org/10.1016/S0161-6420(96)30483-1

Wallman, J., & Fuchs, A. F. (1998). Saccadic Gain Modification: Visual Error Drives Motor Adaptation. *Journal of Neurophysiology*, *80*(5), 2405–2416. https://doi.org/10.1152/jn.1998.80.5.2405

Walsh, D. V., & Liu, L. (2014). Adaptation to a simulated central scotoma during visual search training. *Vision Research*, *96*, 75–86. https://doi.org/10.1016/j.visres.2014.01.005

White, J. M., & Bedell, H. E. (1990). The oculomotor reference in humans with bilateral macular disease. *Investigative Ophthalmology & Visual Science*, *31*(6), 1149–1161.

Figure 1

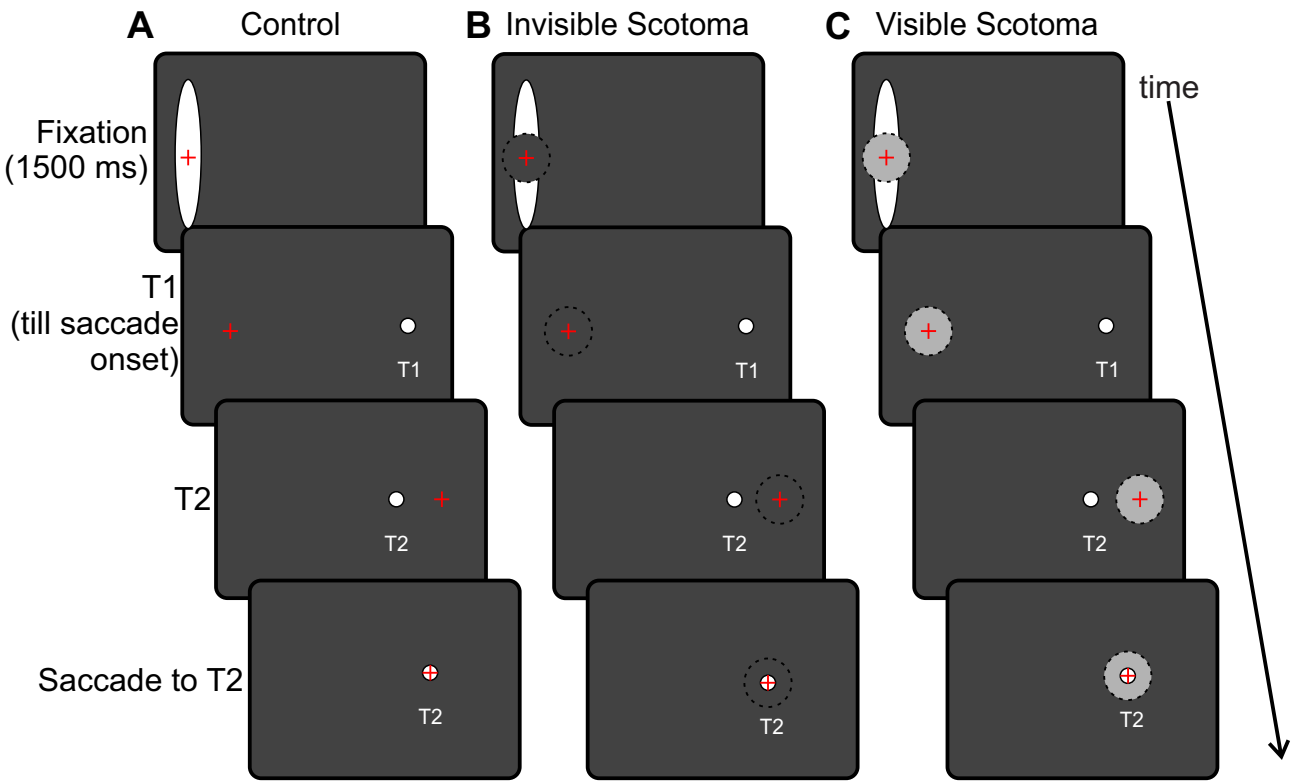

A
Control
B
Invisible Scotoma
C
Visible Scotoma
time
Fixation
(1500 ms)
T1
(till saccade
onset)
T2
Saccade to T2
T1
T2
T2

Figure 2

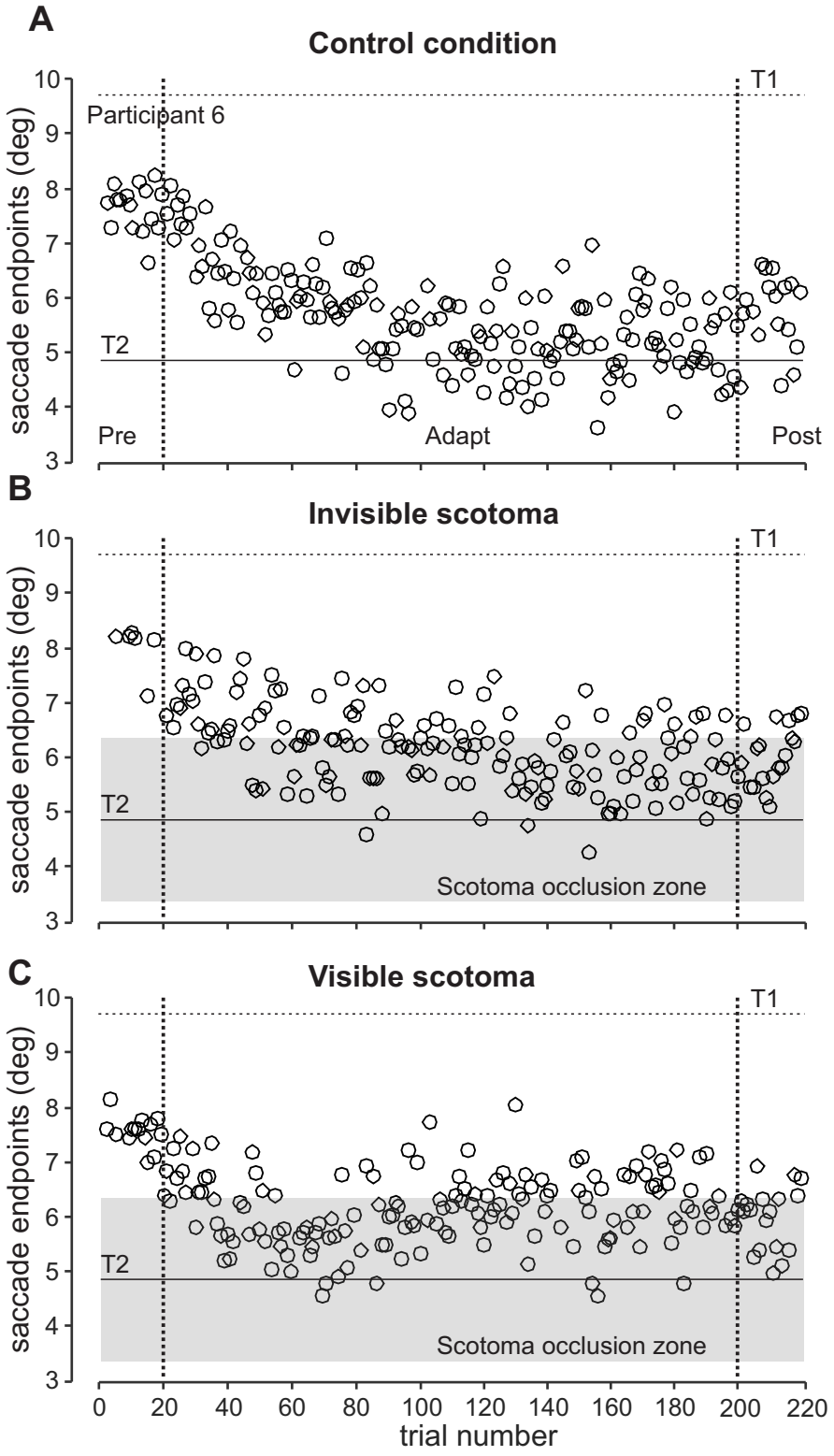

A
Control condition
Participant 6
T1
T2
Pre
Adapt
Post
saccade endpoints (deg)
B
Invisible scotoma
Scotoma occlusion zone
C
Visible scotoma
trial number

Figure 3

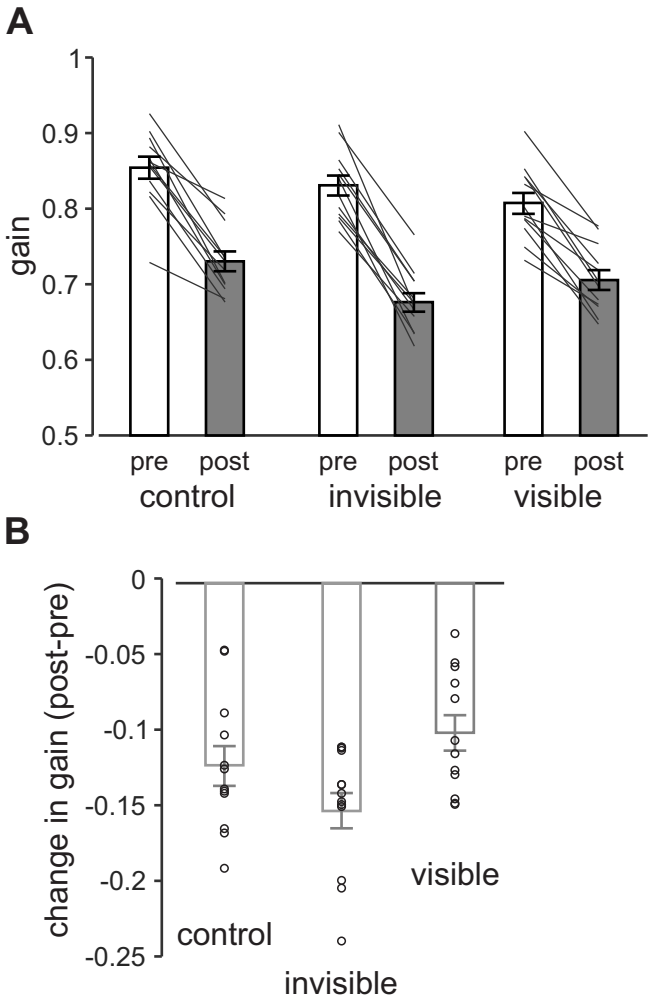

A
gain
1
0.9
0.8
0.7
0.6
0.5
pre
post
control
pre
post
invisible
pre
post
visible
B
change in gain (post-pre)
0
-0.05
-0.1
-0.15
-0.2
-0.25
control
invisible
visible

Figure 4

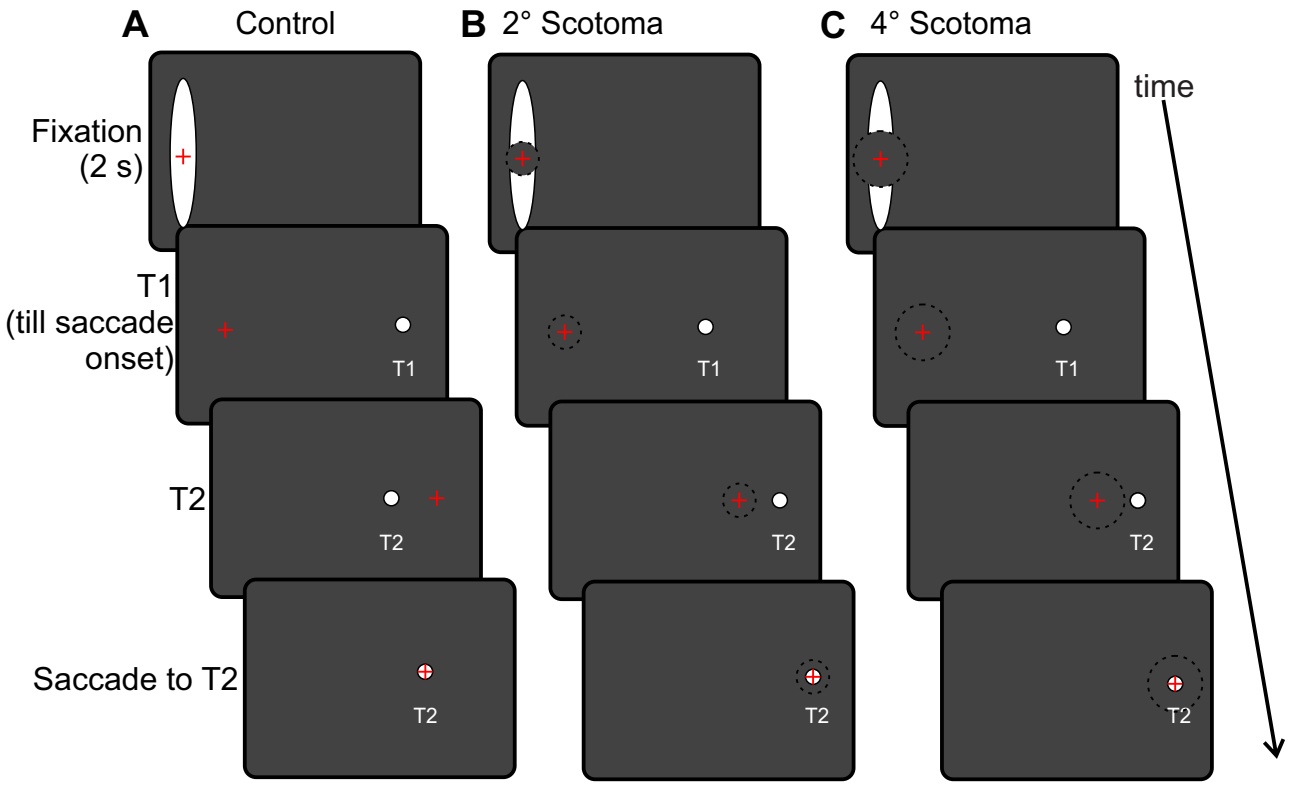

A
Control
B
2° Scotoma
C
4° Scotoma
time
Fixation
(2 s)
T1
(till saccade
onset)
T2
Saccade to T2
T1
T2
T2

Figure 5

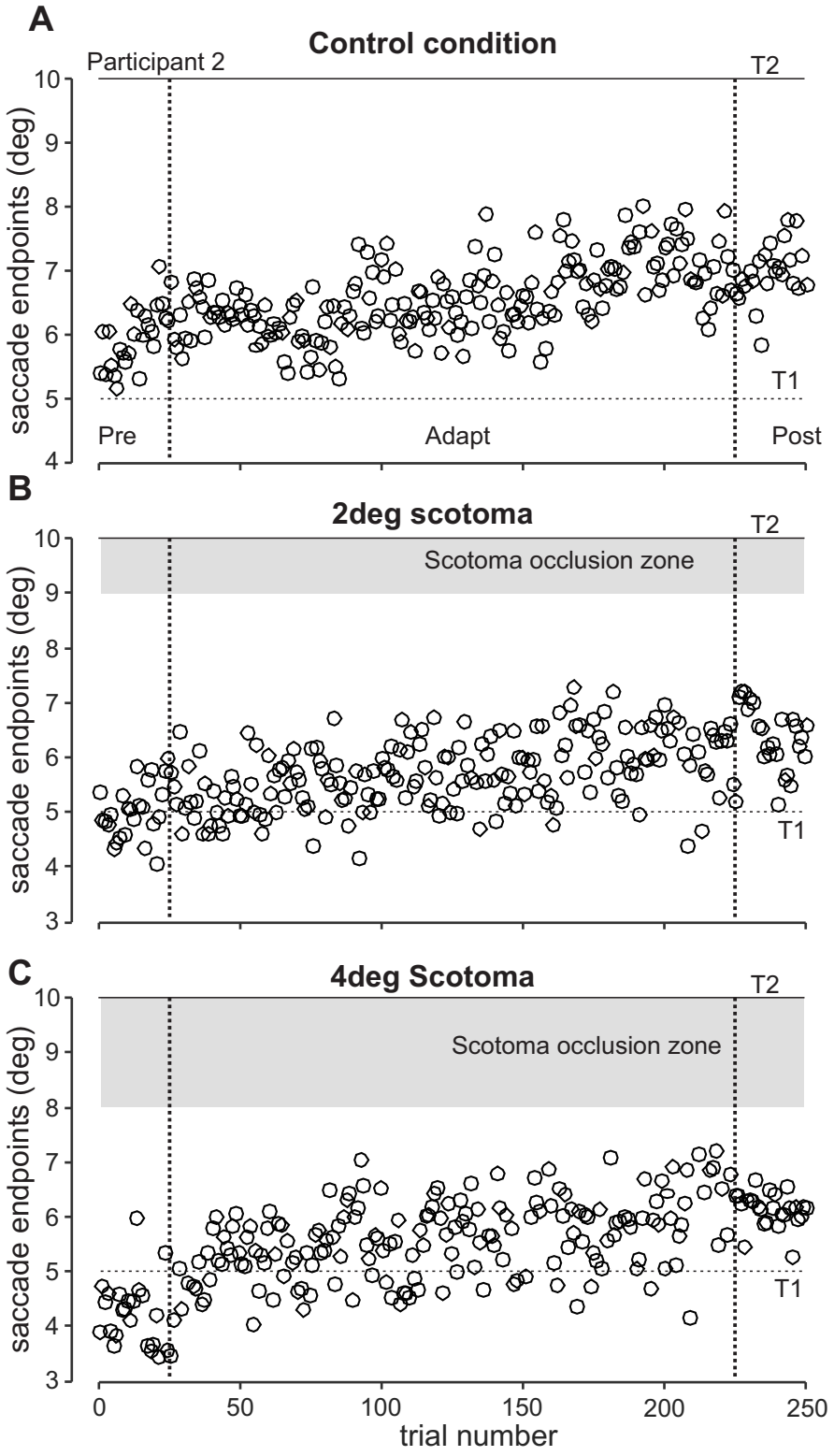
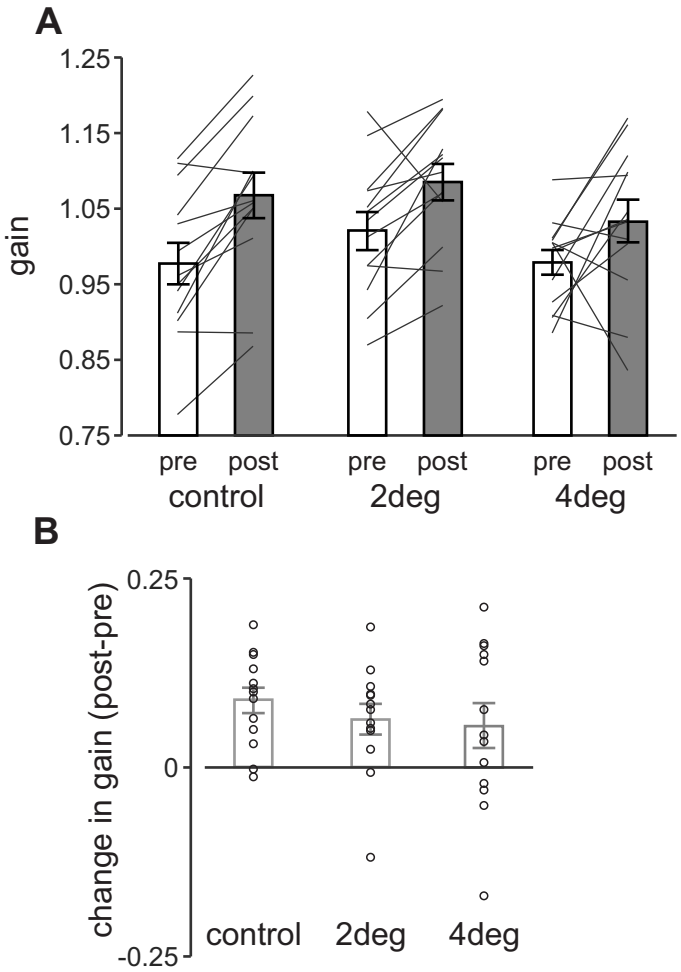

A
Control condition
Participant 2
T2
T1
Pre
Adapt
Post
saccade endpoints (deg)
B
2deg scotoma
Scotoma occlusion zone
T2
T1
saccade endpoints (deg)
C
4deg Scotoma
Scotoma occlusion zone
T2
T1
saccade endpoints (deg)
trial number

Figure 6


A
1.25
1.15
1.05
0.95
0.85
0.75
gain
pre
post
pre
post
pre
post
control
2deg
4deg
B
0.25
0
-0.25
change in gain (post-pre)
control
2deg
4deg