Investigating Unstable Fixation in Patients with Macular Disease

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Purpose. To assess the effect on visual acuity of compensating fixation instability by controlling retinal image motion in people with macular disease.

Methods. Ten patients with macular disease participated in this study. Crowded and noncrowded visual acuity were measured using an eye tracking system to compensate for fixation instability. Four conditions, corresponding to four levels of retinal image motion, were tested: no compensation (normal motion), partial compensation (reduced motion), total compensation (no motion), and overcompensation (increased motion). Fixation stability and the number of preferred retinal loci were also measured.

Results. Modulating retinal image motion had the same effect on crowded and noncrowded visual acuity ($P = 0.601$). When fixation instability was overcompensated, acuity worsened by 0.1 logMAR units ($P < 0.001$) compared with baseline (no compensation) and remained equal to baseline for all other conditions.

Conclusions. In people with macular disease, retinal image motion caused by fixation instability does not reduce either crowded or noncrowded visual acuity. Acuity declines when fixation instability is overcompensated, showing limited tolerance to increased retinal image motion. The results provide evidence that fixation instability does not improve visual acuity and may be a consequence of poor oculomotor control. (*Invest Ophthalmol Vis Sci.* 2011;52:1275–1280) DOI:10.1167/iovs.09-4334

Macular degeneration is the leading cause of legal blindness in Western countries.[1–3] In advanced macular disease patients change their fixation from the center to the periphery of the retina, in a process known as eccentric viewing.[4,5] The part of the peripheral retina most commonly used during visual tasks is known as the preferred retinal locus (PRL).[6–10] When using the peripheral retina, many visual tasks such as reading become very difficult or impossible.

Difficulties faced by people with macular disease are partially explained by the poor resolution of the peripheral retina. Resolution declines in part because receptive fields of the visual responsive neurons in the periphery are wider than in the center of the retina.[11–17] However, in people with macular disease even when the visual task is scaled to account for the reduced resolution, visual performance is still reduced.[18] A further factor that might limit peripheral vision in people with central vision loss is fixation instability.

In normal vision some amount of fixation instability is beneficial. In the central retina, tolerance of retinal image motion is relatively low: Resolution starts to decline for velocities above 2.5° s^{-1}.[19,20] Despite this low tolerance, motion imposed by normal fixation instability enhances central vision.[21–23] In the peripheral retina fixation instability is of greater importance than in the central retina to prevent image fading. Linear velocities of up to 10° s^{-1} can improve resolution.[24–26]

Troxler fading exemplifies the difference between central and peripheral retina. Troxler fading refers to the fading of images presented in the peripheral retina during sustained fixation. This happens because image motion imposed by normal fixation is insufficient to prevent the decline of the response given by the peripheral visual-responsive neurons.[21,27] This finding has led to speculation that fixation instability might be beneficial for patients who must use eccentric viewing. In a study by Deruaz et al.[28] participants reported enhancement of peripheral presented targets when they voluntarily increased instability. The authors recommended caution when training fixation control in patients because instability would be part of a beneficial adaptation mechanism to prevent fading of the image in peripheral retina. Two recent studies have shown that when retinal image speed falls below a critical level at the fovea a dynamical triggering mechanism increases eye instability to avoid perceptual fading.[21,29] If a similar mechanism exists during eccentric viewing, eye instability would be beneficial, and instability would increase when retinal motion is reduced. In a previous study, with simulated scotomas, we found that instability reduced visual acuity for crowded letters but increased acuity for noncrowded letters.[30]

Evidence for a detrimental effect of fixation instability in eccentric viewing comes from several sources. For example, there is a strong correlation between instability and slower reading speeds in people with either newly[31] or well-established macular degeneration.[32]

Training to achieve better control of fixation is part of many rehabilitation programs for people with macular scotomas. Thus, an understanding of the implications of fixation instability is important. In this study we investigated the effect of fixation instability on visual acuity for crowded and noncrowded letters in patients with central scotomas caused by macular disease. The amount of retinal image motion was controlled by an eyetracker. We anticipated that acuity would improve by reducing the amount of retinal image motion caused by fixation instability, and the effect would be more pronounced for crowded letters. Additionally, if fixation instability is caused by a mechanism triggered by low retinal image motion, eye stability would change under different conditions. We measured fixation stability to explore that question.

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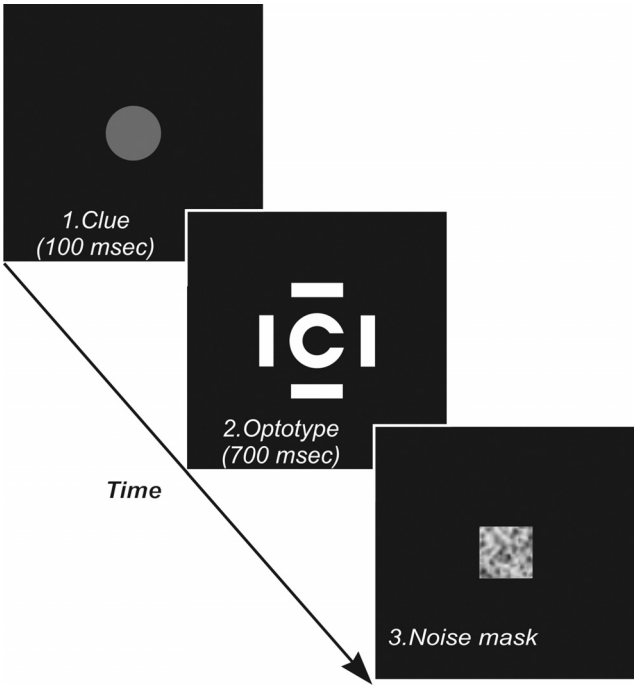

FIGURE 1. Sequence of stimuli in each trial. The optotype was preceded by a cue reducing spatial uncertainty and followed by a noise mask, visible until a response was given.

METHODS

Participants were recruited from the Low Vision Clinic at Moorfields Eye Hospital in London. All subjects gave their informed consent to participate. The study was approved by the Moorfields & Whittington Research Ethics Committee and conformed to the tents of the Declaration of Helsinki. All participants had a long-term diagnosis of bilateral macular degeneration, and none had any secondary eye condition or neurologic disease. All participants had a central scotoma identified by microperimetry (MP-1 microperimeter; Nidek Technologies, Padova, Italy). The microperimeter was also used to determine the location of the preferred retinal locus.

Visual acuity was measured in a crowded or noncrowded visual display (Landolt C) under different conditions of retinal image stabilization. The size of the optotype was under control of a Quest staircase,[33,34] written in a computing language programming environment (MATLAB; MathWorks, Natick, MA) using elements of commercially available toolboxes.[33,35,36] Stimuli were displayed as white targets on a black background on a 21-inch computer monitor (Trinitron GDM-F500R; Sony, Tokyo, Japan), with peak luminance of 98 cd/m^2, resolution of 1280 × 1024 pixels, and 100 Hz refresh rate. The system had a Michelson contrast of 80% and was presented for 700 msec, without surrounding bars (noncrowded) and with surrounding bars (crowded). The separation between the boundaries of the device and the bars was equal to two strokes of the "C" (Fig. 1).

Observers sat 50 cm from the monitor and viewed the display monocularly with their better eye. An infrared eyetracker (Eyelink I; SR Research Ltd., Mississauga, Ontario, Canada) using commercial software (Eyelink, v. 2.11) was used to record eye position and to change the level of retinal image motion. Control of retinal image motion was achieved by moving the stimulus with the eye. The position (x,y) of the eye was transferred, without filtering, from the eyetracker personal computer (PC) to a second PC displaying the stimulus. Eye velocity and acceleration were calculated using the time between samples. Before data collection, calibration (using a five-point grid) and drift correction were performed.

Velocity of the optotype during fixations was modulated by a gain factor: gain = v_{target}/v_{eye}, where v_{target} is target velocity and v_{eye} is eye velocity. Four gains were used: gain 0 (no compensation of retinal image motion), gain 0.1 (partial compensation leading to reduced retinal image motion), gain 1 (total compensation resulting in no retinal image motion), and gain 10 (overcompensation resulting in increased retinal image motion). Gain 0 corresponds to the baseline condition; that is, the target was simply displayed in the center of the screen. A saccade was defined as an eye velocity greater than 30° s^{-1} and/or acceleration greater than 8500° s^{-2}. These detection criteria allowed the target to be exposed during microsaccades, but during saccades the screen was blanked. The optotype position was updated continuously, and it reappeared when the next fixation started.

There was an estimated 20 msec[35] delay from the eye movement to the update of the target position on the screen. That delay includes the time the samples took to travel from the eyetracker PC to the PC displaying the stimuli, plus the time of monitor refresh. This delay reduced the accuracy with which each gain could be achieved when the eye was moving. Further information on our experimental setup has been published previously.[30]

Visual acuity was measured in 16 blocks: 4 gains × 2 crowding conditions × 2 repetitions, in random order. Each block consisted of 40 trials. Before the first session of data collection, practice was provided by measuring crowded and noncrowded visual acuity for at least two different gains per visual acuity. In the remaining sessions, one block of practice with a randomly chosen gain was performed.

Eye movements were analyzed offline to measure fixation stability. Periods when the optotype was visible were isolated from raw data; trials containing blinks or outliers (data collected outside the calibration area) were excluded from analysis. Eye positions from intersaccadic intervals were used to calculate the bivariate contour ellipse area (BCEA) in min arc^2 containing 68% of the eye positions.[8,37]

For the analysis of acuity thresholds, all visual acuities were normalized against noncrowded visual acuity for gain 0. Linear mixed models run in standard statistical software (SPSS v.14; SPSS, Chicago, IL) were used to analyze repeated measures.

RESULTS

Eleven subjects were recruited. Ten finished the study, and one withdrew because of the difficulties imposed by the task. Two subjects had been diagnosed with juvenile macular degeneration, and the remainder had age-related macular degeneration. The condition was bilateral in all participants, and all subjects had dense central scotomas on microperimetry, with the exception of S9, who had a relative central scotoma. Age ranged from 25 to 89 years old, and visual acuity in the better eye was between 0.7 and 1.2 logMAR. No patient had more than one PRL identified on either the eyetracker or the MP1 fixation data. A summary of the

TABLE 1. Characteristics of Participants in This Study

Subject	Age (y)	Diagnosis	Eye	Visual Acuity	PRL Location
1	84	AMD	L	0.7 logMAR	L
2	87	AMD	R	1.0 logMAR	A
3	89	AMD	R	1.0 logMAR	L
4	72	AMD	R	1.0 logMAR	L
5	54	JMD	L	0.7 logMAR	B
6	73	AMD	R	1.2 logMAR	*
7	88	AMD	R	1.1 logMAR	B
8	89	AMD	R	1.0 logMAR	B
9	81	AMD	R	0.4 logMAR	Central
10	24	JMD	L	0.8 logMAR	B

PRL, preferred retinal locus. The PRL location is defined in visual field space: B, below; A, above; L, left; R, right. VA, visual acuity; AMD, age-related macular disease; JMD, juvenile macular disease.

* PRL was not clearly defined.

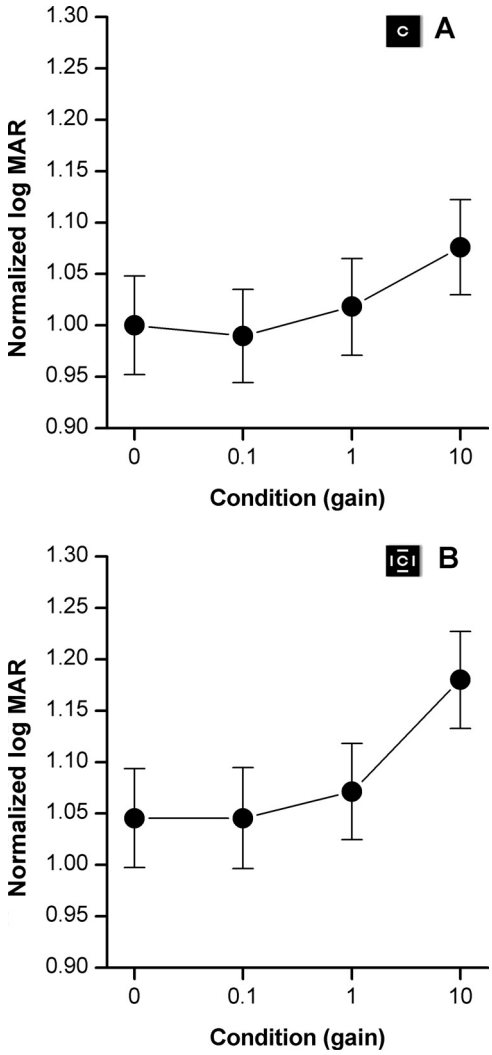

FIGURE 2. Variation of noncrowded (**A**) and crowded (**B**) visual acuity with gain. Symbols show the mean for all participants for each gain as estimated by mixed models; error bars, 95% confidence interval. All acuities were normalized before statistical analysis against noncrowded acuity obtained with gain 0.

clinical characteristics of the participants is given in Table 1. Visual acuity and fixation stability were not different between the two subjects with juvenile macular disease and those with age-related macular degeneration (visual acuity, $P = 0.06$; fixation stability, $P = 0.49$).

Variation of Visual Acuity with Gain

Figure 2 shows visual acuity obtained for each condition. Figure 2A displays noncrowded acuity, and Figure 2B displays crowded acuity. Both crowding ($P < 0.001$) and gain ($P < 0.001$) had significant effects on visual acuity, but the interaction gain×crowding was not significant ($P = 0.601$).

Noncrowded visual acuity was better than crowded acuity for all gains, with mean difference of 0.071 logMAR ($P < 0.001$).

Acuity for the overcompensation condition (gain 10) was reduced compared with the no compensation condition by 0.10 logMAR ($P < 0.001$), for both crowded and noncrowded stimuli. These results show that reducing retinal image motion (gains 0.1 and 1) had no effect on patients' visual acuity; however, increased retinal image motion (gain 10) had a detrimental effect on acuity.

Variation of Fixation Stability with Gain

Figure 3 shows the variation of fixation stability with gain during visual acuity measurements. Figure 3A shows noncrowded acuity, and Figure 3B shows crowded acuity. Gain had a significant effect on fixation stability ($P < 0.001$), but there was no effect of crowding ($P = 0.23$) or interaction of gain×crowding ($P = 0.18$).

Fixation stability for crowded and noncrowded stimuli gain 0 (mean BCEA: 9795 min arc^2) was significantly better than all other gains (mean BCEA: 21,230 min arc^2, $P = 0.001$ for gain 0.1; mean BCEA: 21,750 min arc^2; $P < 0.001$ for gain 1; mean BCEA: 17,780 min arc^2; $P = 0.014$ for gain 10). There was no significant difference in fixation stability between gain 0.1, 1.0, and 10. BCEA values were in the same range as those found in previous studies (mean: 20,360 min arc^2, 95% confidence interval: 10,160–30,560 min arc^2).[9,38–40]

Effect of Gain on Retinal Image Speed

Figure 4 shows the variation of the eye speed and retinal image speed calculated offline during a typical trial for gain 10. In this

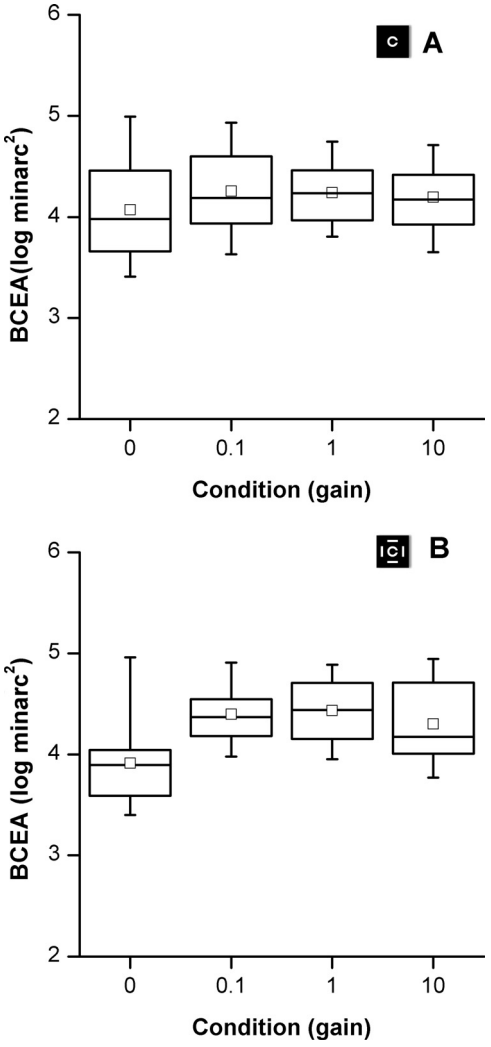

FIGURE 3. Variation of fixation stability with gain during noncrowded (**A**) and crowded (**B**) visual acuity measurements. Length of the box, interquartile range (25th–75th percentiles); whiskers, 5th–95th percentiles. Inside the box, squares show the means, and the horizontal lines show the median. BCEA was calculated in min arc^2 and log10 transformed before statistical analysis to approximate a normal distribution.

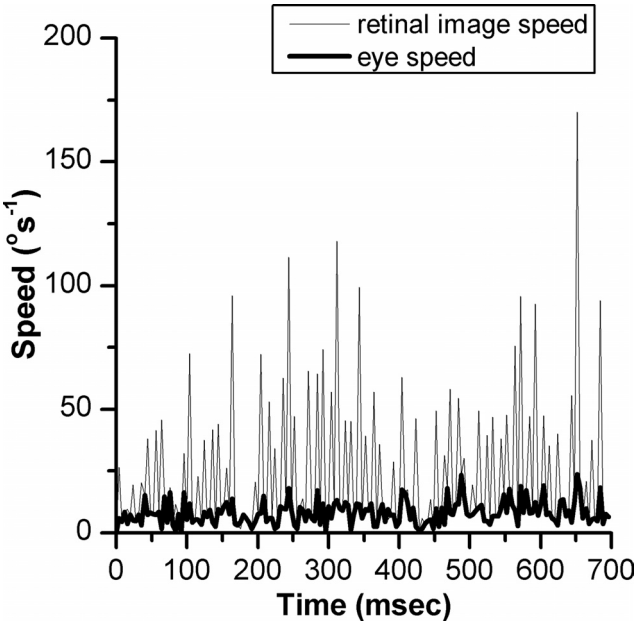

FIGURE 4. Profile of the eye velocity (thick line) and retinal image velocity (thin line) of the target during a typical trial for gain 10.

trial no saccades were detected by our criteria. Frames when the retinal image speed was very high correspond to large overshoots of the target on the monitor, which sometimes caused the perception of multiple targets.

Retinal image speed was calculated for the intersaccadic periods (including microsaccades). The baseline retinal image speed (gain 0) was 8.7° s^{-1}, which was significantly higher than the retinal image speed for gain of 0.1 (4.8° s^{-1}) and gain 1 (3.0° s^{-1}), but significantly lower than the retinal image speed for gain 10 (12.4° s^{-1}).

DISCUSSION

In this study we measured crowded and noncrowded visual acuity while compensating for fixation instability by controlling retinal image motion in the better eye of patients with macular scotomas. The effects of controlling retinal image motion on visual acuity and on fixation stability are discussed separately. These effects are likely to be applicable when viewing binocularly because binocular oculomotor behavior is thought to be driven by the better eye.[41,42]

Effect of Gain on Visual Acuity

Compensating for fixation instability in people with macular disease failed to improve visual acuity on our task: no compensation (gain 0), partial compensation (gain 0.1) and total compensation (gain 1) all produced similar acuity. These results suggest that fixation instability of these patients does not reduce visual acuity for briefly exposed stimuli.

These results are in agreement with studies showing no reduction or some improvement in normal peripheral visual acuity for moving targets. In these studies retinal image motion was caused by normal fixational eye movements or was increased by manipulating the target's velocity.[24,25,43] In people with macular scotomas we expected improvement of acuity when motion was compensated because retinal image motion is naturally increased due to their fixation instability. This was not the case. The lack of a difference in visual acuity across gain 0, gain 0.1, and gain 1 under both crowded and uncrowded conditions might indicate the following:

1. Patients have adapted to the amount of retinal image motion caused by their "normal" fixation instability;
2. Independently of any adaptation, fixation instability in patients is within the tolerance of the part of the retina they use during eccentric viewing (and that might be part of the reason why that area is used as the PRL);
3. Limitations of our stabilization system reduced the size of any observed effect (see below).

Crowded visual acuity was worse than noncrowded visual acuity. The difference of 0.071 logMAR units between acuities is within values found in previous studies. In other studies involving patients, the reduction for crowded acuity varied from 0.06 logMAR units[44] to 0.11 logMAR units.[45] Other studies found higher differences, up to 0.15 logMAR units, in healthy peripheral retinas.[46]

Contrary to our findings for control subjects,[30] the effect of gain did not differ between crowded and noncrowded acuity. We know from previous studies that acuity measured with isolated letters would be minimally affected by very high levels of retinal image motion.[28,47] However, we expected higher variation between gains under crowded conditions because crowding would increase blur for high levels of retinal image motion.[20] In a study measuring peripheral acuity in healthy retina with jittering targets, Falkenberg et al.[24] failed to find any interaction between jitter and crowding. In the same study, reading speed for sequentially presented words reduced when jitter increased. That might happened because words caused increased crowding.

Another contribution to the lack of interaction between gain and crowding is likely to be the characteristics of our participants. The group was small and heterogeneous regarding the PRL location. PRLs were in different directions relative to the fovea and at different eccentricities, and it is known that retinal location changes the effect of crowding.[48,49] The number of participants was not sufficient to test the interaction between gain, PRL eccentricity, and PRL direction.

Effect of Gain on Fixation Stability

When retinal image motion was controlled by our technique, the magnitude of eye movements during fixation increased when compared with no compensation (gain 0). However, it remained constant under all compensation conditions (gains 0.1, 1.0, and 10). Reduction in eye stability under compensation conditions was probably caused by target's motion on the monitor. Atypical smooth pursuit can occur when the target is perceptually moving despite the retinal image speed being null, for example, when following an after-image.[50–52]

Under the three compensation conditions eye instability (BCEA) remained constant. If fixation instability was caused by a mechanism to increase retinal image motion to prevent perceptual fading, the three gains should yield variation in eye stability. Accordingly, reduced retinal motion (gain 0.1 and gain 1) would increase eye instability, and increased retinal motion (gain 10) would reduce eye instability. Based on their results, Deruaz et al.[28] argued that training fixation control, leading to a reduction in retinal image motion, might reduce patients' vision. They considered that fixation instability could be part of a mechanism to maintain the visual target moving between adjacent or separated loci in the retina. Our results show that eye instability was independent of the retinal image motion imposed by our three conditions. This argues against such a mechanism and against benefits of fixation instability for patients' vision. Recently Reinhard et al.[53] observed that patients with macular disease tend to use separated or adjacent loci during visual tasks, but they attributed that to patients' poor adaptation to the disease. Our results add evidence that

fixation instability is a consequence of poor oculomotor control and not a strategy to enhance eccentric viewing.

Limitations of the Study

Our stabilization system has limitations due to the delay between the real eye movement and the time its effect is visible in the screen. Because of this delay the mean retinal image speed for gain 0, gain 0.1, and gain 1 was always below 10° s^{-1}, which might have reduced the difference between gains. Also, unstable fixation is likely to affect the overall effect of stabilization because relatively widely separated retinal areas might have been used for different eyetracker calibrations and/or drift corrections. This would lead to the optotype's being stabilized in the peripheral retina but not always in the same area. Finally, our sample size was too small to elicit differences between subjects with juvenile macular disease and those with age-related macular degeneration.

Conclusions

Our study shows that compensating for fixation instability does not improve visual acuity in patients with macular disease. In other words, their typical fixation instability does not appear to be a cause of their reduced visual acuity. However, increasing instability reduces acuity for crowded and noncrowded targets. This study gives further evidence that fixation instability is a consequence of impaired oculomotor control rather than an adaptation made to improve visual function.

Training oculomotor control can improve reading speed without a significant improvement in acuity.[54] Future work should investigate the effects of correcting fixation instability on more "real world" tasks such as reading or recognizing faces. Controlling retinal image motion might help to reduce positional uncertainty in the peripheral retina and consequently lead to a significant improvement of other visual abilities such as visual scanning.

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