

# Fixation Stability during Binocular Viewing in Patients with Age-Related Macular Degeneration

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**PURPOSE.** The authors examined the fixation stability of patients with age-related macular degeneration (AMD) and large interocular acuity differences, testing them in monocular and binocular viewing conditions. The relationship between fixation stability and visual performance during monocular and binocular viewing was also studied.

**METHODS.** Twenty patients with AMD participated. Their monocular and binocular distance acuities were measured with the ETDRS charts. Fixation stability of the better and worse eye were recorded monocularly with the MP-1 microperimeter (Nidek Technologies Srl., Vigonza, PD, Italy) and binocularly with an EyeLink eye tracker (SR Research Ltd., Mississauga, Ontario, Canada). Additional recordings of monocular fixations were obtained with the EyeLink in viewing conditions when one eye viewed the target while the fellow eye was covered by an infrared filter so it could not see the target.

**RESULTS.** Fixation stability of the better eye did not change across viewing conditions. Fixation stability of the worse eye was 84% to 100% better in the binocular condition than in monocular conditions. Fixation stability of the worse eye was significantly larger ( $P < 0.05$ ) than that of the better eye when recorded monocularly with the MP-1 microperimeter. This difference was dramatically reduced in the binocular condition but remained marginally significant (95% confidence interval,  $-0.351$  to  $-0.006$ ). For the better eye, there was a moderate relationship between fixation stability and visual acuity, both monocular and binocular, in all conditions in which this eye viewed the target.

**CONCLUSIONS.** Fixational ocular motor control and visual acuity are driven by the better-seeing eye when patients with AMD and large interocular acuity differences perform the tasks binocularly. (*Invest Ophthalmol Vis Sci.* 2011;52:1887-1893) DOI:10.1167/iovs.10-6059

Age-related macular degeneration (AMD) is a degenerative eye disease that destroys central vision and is recognized as a disabling factor in an aging population.<sup>1</sup> In developed

countries, AMD is the leading cause of legal blindness in people 65 years or older and represents a substantial economic burden on the health systems of these countries.<sup>2,3</sup>

Central vision damage results in a sharp drop in visual functions such as acuity, contrast sensitivity, stereopsis, and color discrimination.<sup>4-8</sup> In addition, the ocular motor system loses its reference position—which is at the fovea in the normal eye and damaged in patients with AMD—leading to difficulties in ocular motor control. However, patients adapt to this loss by developing “pseudofoveae” in the healthy eccentric parts of the retina. These are called preferred retinal loci (PRLs) and may serve as the new reference position for the ocular motor system.<sup>9-13</sup>

The precision (i.e., fixation stability) of ocular motor control with a PRL is often evaluated by how variable eye fixations are when one fixates intently on a stimulus for a certain period.<sup>14</sup> Fixation stability of patients with AMD is poor and decreases with retinal eccentricity, affecting visual performance.<sup>15-18</sup> Another important feature of the PRL is its retinal location. It has been suggested that different PRL locations (e.g., a PRL located to the right or to the left of scotoma in the visual field) elicit different ocular motor problems during tasks such as reading.<sup>10,19-22</sup> The PRL is not consciously chosen, and, to date, it is still unknown what factors determine the location of a PRL (see Ref. 23 for review).

It is difficult to establish what the reference position of the ocular motor system is during binocular viewing. Fixation stability can be recorded concomitantly for the two eyes with eye trackers, but this method is limited by the fact that the absolute location of the PRLs cannot be determined. On the other hand, recordings of fixation stability and absolute location of the PRL can be obtained with instruments such as the scanning laser ophthalmoscope (SLO) or the microperimeter (MP-1; Nidek Technologies Srl., Vigonza, PD, Italy), but these are monocular instruments. The MP-1 is the newest generation of microperimeters, which allow for the rapid recording of fixation stability and PRL location.

Monocular recording of the PRL may not accurately reflect the properties of the PRL during binocular viewing. When the monocular PRLs are in corresponding positions in the two eyes (Fig. 1A), it is reasonable to assume that the same PRLs are used during binocular viewing. But there are reports that more than one PRL may occur, depending on the viewing conditions and the duration of the disease.<sup>11,19,24-28</sup> However, this phenomenon seems to be the exception rather than the rule in patients with well-established PRLs tested in conditions using the same viewing distances and under the same illumination.<sup>20,28</sup>

The problem of binocular viewing with PRLs becomes more complicated, however, in patients with AMD in whom one eye is more affected than the other (Fig. 1B) or in whom monocular PRLs are not in corresponding positions (Fig. 1C). Studies have shown that some patients with central vision loss who have unequal damage to the retinas of the two eyes experience binocular inhibition.<sup>5,29,30</sup> That is, for these patients visual

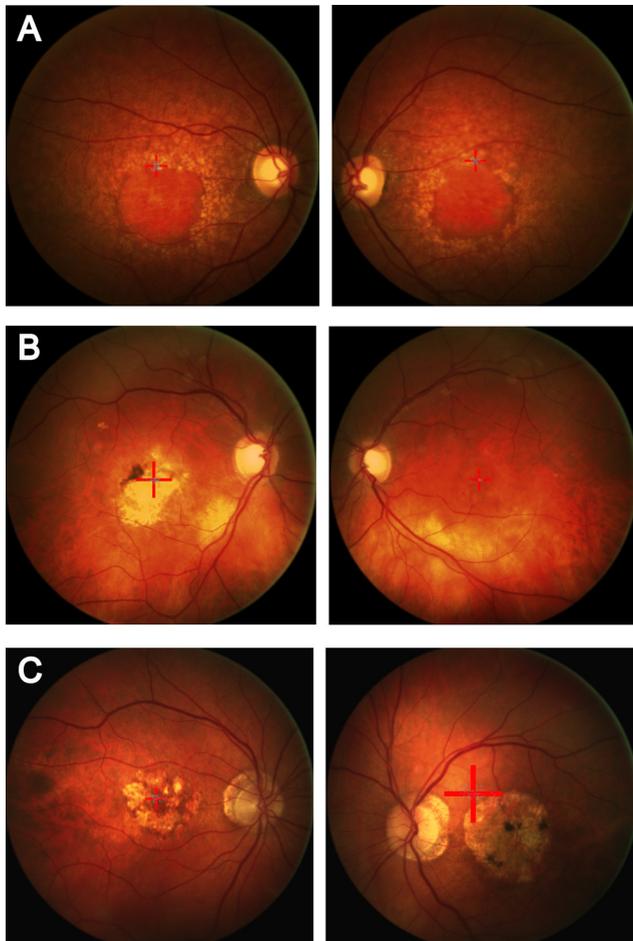
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**FIGURE 1.** PRL of the left and right eye recorded monocularly with the MP-1 and shown on the fundus photographs for three patients with AMD. (A) Patient with monocular PRLs in corresponding retinal positions. (B) Monocular PRLs of a patient whose right eye was more affected than the left eye. (C) Patient with monocular PRLs in noncorresponding retinal positions.

performance when using only the better eye is superior to that when using both eyes. One explanation of binocular inhibition may be that the ocular motor control during binocular viewing is influenced by the poor control of the worse-seeing eye. For example, fixation stability of the worse-seeing eye could affect binocular fixation, making it poorer than the fixation of the better-seeing eye alone. In addition, when the PRLs are not in corresponding positions, the visual system may have to bring the PRL of the two eyes into correspondence during binocular viewing, and it is possible that in such cases one PRL may land on the scotoma. Indeed, Kabanarou et al.<sup>31</sup> reported that the PRL of patients with AMD may shift location when monocular viewing changes to binocular viewing, but these changes happen predominantly in the worse eye. More than half the patients participating in their study showed a shift in gaze position when the viewing condition changed from monocular to binocular.

It is not known whether fixation stability also changes with monocular versus binocular viewing conditions in these patients and, if changes do occur, what their influence was on visual performance. These are important questions for several reasons. First, conclusions about the function of the visual system of patients with central vision loss is sometimes based on the assumption that the properties of the PRL identified with an SLO or MP-1 are the same as the one used to perform

tasks under different viewing conditions.<sup>20,32</sup> Second, the most sophisticated efforts in optimizing vision for patients with AMD focus on ocular motor training and, although patients use their binocular vision in their day-to-day life, some of these methods involve only monocular training.<sup>20,22,33</sup> Thus, the aims of this study are to examine: 1) the binocular fixation stability of patients with AMD and large interocular acuity differences; and 2) the influence of fixation stability on visual performance.

## METHODS

### Participants

Twenty patients with confirmed diagnoses of AMD (10 women, 10 men; mean age,  $79.4 \pm 8.3$  years) participated in the study. Eighteen patients had bilateral AMD, and two had the disease only in the left eye. The patients had no history of neurologic diseases, cognitive impairment, or other significant ocular diseases with the exception of mild cataract. Their monocular and binocular visual acuities were measured at 6 m using a computerized version of the ETDRS chart (single line). The better- and worse-seeing eyes were identified as the eyes with the best and worst acuity, respectively. (The better-seeing eye and the worse-seeing eye are referred to as the better and the worse eye, respectively, throughout the paper). Patients were recruited from referrals to the Eye Clinic at the Toronto Western Hospital, where they underwent ophthalmological assessment before enrollment in the study. Informed consent was obtained from all participants, and the research was approved by the University Health Network Research Ethics Board and conducted in accordance with the tenets of the Declaration of Helsinki.

### Monocular Fixation Stability Recorded with the MP-1 Microperimeter

Monocular fixation stability and the PRL location of the better and worse eye were recorded with the MP-1 microperimeter in a dark room. This instrument can rapidly perform computerized microperimetry and record fixation stability. It uses an auto eye-tracking system that registers horizontal and vertical eye position relative to an anatomical landmark (i.e., a retinal blood vessel) while compensating for stimulus projection location at a sampling rate of 25 Hz. The black and white image of the fundus is captured with an infrared camera, and its movements are recorded while the patient fixates on a target projected on a graphics screen. The fixational eye movements can then be registered with a color fundus photograph offline.

The fixation stimulus was a red cross. The standard size of the cross was  $3^\circ$ , but this size was occasionally enlarged for the worse eye when the patient could not easily find the cross. Patients were seated with their head steadied in the headrest of the instrument and were instructed to keep their gaze in the middle of the fixation cross. Testing was conducted one eye at a time while the other eye was patched. During fixation examination, the patient's eye positions were recorded for 15 to 30 seconds, after which a color fundus photograph was taken. No mydriatic drops were used during this procedure.

### Binocular Fixation Stability Recorded with the Eye Tracker

Binocular recordings of fixation stability were obtained with the eye tracker (EyeLink 1000; SR Research Ltd., Mississauga, Ontario, Canada) at a sampling rate of 250 Hz. This instrument employs a high-speed infrared camera system to record eye positions using the pupil/corneal reflection eye tracking principle. Recording can be done both monocularly and binocularly; during binocular recording, the eye tracker records eye positions independently for the two eyes.

In a well illuminated room, each patient was seated with his or her head steadied on a headrest, 60 cm in front of a monitor (Sync Master 900 NF; Samsung, Seoul, South Korea) with a useful field of view of

34.4 × 26 cm. Calibration was made binocularly using a standard five-point grid. The calibration stimulus was a nine-cycle radial grating black stimulus that subtended 4.3° of visual angle; the properties of this stimulus were described elsewhere.<sup>14</sup> During calibration, the patients were instructed to fixate in the middle of the radial grating and to move their eyes when the stimulus moved so that they would see the center of the stimulus. Only if the eye tracker classified the calibration as “good” were the recording trials initiated.

After a successful calibration, a 3° red cross was presented in the middle of the monitor, on a white background with a luminance of 240 cd/m<sup>2</sup>. In all trials, the patients were given the same instructions: to look at, and keep their gaze as steady as possible in the middle of the red cross. Binocular recordings of the eye position during fixation were obtained in three different conditions. The first was binocular viewing, when both eyes viewed the target. The second was right eye monocular viewing, when the right eye viewed the target while the left eye was covered by a double infrared (IR) filter (Wratten #87 IR; Eastman Kodak, Rochester, NY). These two filters were overlapped to prevent the covered eye from seeing the target, but the eye tracker could record the eye positions of the covered eye. The third was left eye monocular viewing condition, when the left eye viewed the target while the right eye was covered by the IR filter. The experimenter pressed a button to start a 15 second recording of eye position in each trial.

### Statistical Analysis

Fixation stability was evaluated with the 68% bivariate contour ellipse area (BCEA), which is described elsewhere.<sup>34</sup> In short, this measure is based on the values of the standard deviations of the horizontal and vertical eye positions and the correlation coefficient of the horizontal and vertical eye positions. Analysis was carried out in accordance with the guidelines described in Tarita-Nistor et al.<sup>18</sup> to reduce instrument artifacts (for data recorded with the MP-1) and any undue influence of outliers (for data recorded with both the MP-1 and the EyeLink).

All analyses were performed referring to better and worse eye rather than to left and right eye. In cases where repeated-measures analyses of variance were performed, the effects were tested using a univariate criterion with a Greenhouse-Geisser correction, and the familywise error rate across the pairwise comparisons was controlled with a Bonferroni approach. Alpha level was set at 0.05 for all tests. Given the a priori knowledge of the direction of the relationship, the *P* value of the correlation coefficients between acuity and fixation stability were based on one-tailed tests. Acuity values were expressed in logMAR units and BCEA values in degrees squared.

## RESULTS

### Acuity

One-way repeated-measures analysis of variance revealed that the patients had large interocular acuity differences ( $F(2,38) = 33.33$ ;  $P < 0.01$ ), and pairwise comparisons showed that binocular acuity was driven by the better eye. That is, acuity of the better eye (mean,  $0.37 \pm 0.20$  logMAR) was not significantly different from binocular acuity (mean,  $0.37 \pm 0.21$  logMAR) and was significantly better than that of the worse eye (mean,  $0.99 \pm 0.50$  logMAR). The average interocular acuity difference was 0.6 logMAR. Box plots of acuities of the better, worse, and both eyes are shown in Figure 2. There were three cases with visual acuity of 2 logMAR in the worse eye. The three outlying cases shown in the graph were not far outliers (each had a *z* score of 2.01).

### Fixation Stability

**Better Eye.** Two-way repeated-measures analysis of variance was conducted to examine the effect of viewing condition on fixation stability using BCEA as the dependent variable.

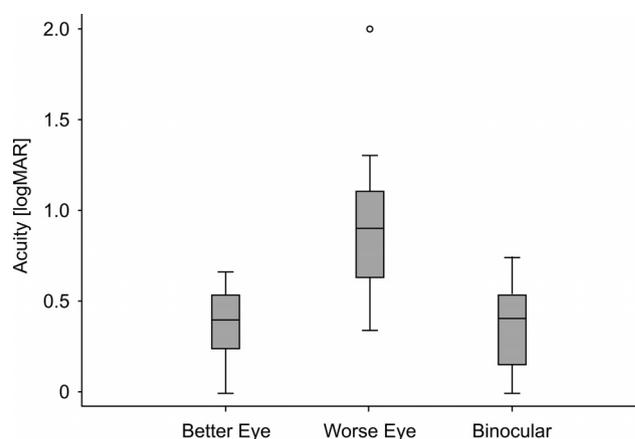


FIGURE 2. Box plots of acuity of the better eye, worse eye, and both eyes.

This analysis included all the conditions in which the better eye viewed the target. The fixation stability of the worse eye was also reported, regardless of whether this eye viewed the target or not. The within-subject factors were Eye with two levels or not (better, worse) and Viewing Condition with three levels (MP-1 Monocular, EyeLink Binocular, EyeLink Better Eye Viewing). In this last viewing condition, only the better eye viewed the fixation target while the worse eye was covered by the IR filter, but fixation stability was recorded for both eyes.

In this analysis, we found three BCEA values—one in each viewing condition—that were far outliers (their standardized values were larger than  $\pm 3$ ) and that had the potential of inflating the results. These data were generated by the worse eye of two patients with very poor vision in that eye. One way of dealing with far outliers is to delete these cases, but this approach decreases the sample size. Another way is to apply a logarithmic transformation to the data, but then the conclusions drawn will be about log BCEA rather than BCEA and this is more difficult to interpret. Alternatively, the influence of the outliers can be reduced by changing their scores. In such cases, Tabachnick and Fidell<sup>35</sup> recommend assigning the outlying case a raw score that is one unit larger than the next most extreme score in the distribution. Thus, this case comes closer to the mean but maintains its rank order. Given that we know these cases are sampled from our target population, we decided to adopt the latter option. As a result, the outlying scores of the worse eye changed as follows: from 8.24 to 6.95 deg<sup>2</sup> in the MP-1 Monocular condition, from 5.55 to 3.90 deg<sup>2</sup> in the EyeLink Binocular condition, and from 11.36 to 5.56 deg<sup>2</sup> in the EyeLink Better Eye Viewing condition. The outlying cases are further analyzed in the Analysis of the Outlying and Missing Data Group section.

Results of the two-way repeated-measures analysis of variance using cleaned data showed that the Eye main effect was significant ( $F(1,19) = 13.68$ ;  $P < 0.01$ ) as was the Condition main effect ( $F(2,38) = 4.39$ ;  $P < 0.05$ ). The Eye × Condition interaction failed to reach significance ( $F(2,38) = 1.84$ ;  $P = 0.18$ ). Pairwise comparisons showed that the BCEA of the better eye had similar values in all three viewing conditions. In addition, the BCEA of the worse eye was 84% smaller in the EyeLink Binocular condition than in the MP-1 Monocular condition. This difference was statistically significant ( $P < 0.05$ ). Moreover, for the worse eye, the BCEA in the MP-1 condition was similar to that in the EyeLink when this eye was covered by the IR filter and only the better eye viewed the target.

The mean BCEA difference between the better and worse eye was only 0.18 deg<sup>2</sup> in the EyeLink Binocular condition but 0.88 deg<sup>2</sup> in the MP-1 Monocular condition and 0.74 deg<sup>2</sup> in

**TABLE 1.** Mean  $\pm$  SD of the BCEA of the Better and Worse Eye in Three Conditions: MP-1 Monocular, EyeLink Binocular, and EyeLink Better Eye Viewing

	MP-1 Monocular	EyeLink Binocular	EyeLink Better Eye Viewing
Better eye BCEA, deg <sup>2</sup>	0.77 $\pm$ 0.84	0.71 $\pm$ 1.06	0.79 $\pm$ 0.97
Worse eye BCEA, deg <sup>2</sup>	1.64 $\pm$ 1.97	0.89 $\pm$ 1.05	1.53 $\pm$ 1.78

the EyeLink Better Eye Viewing condition. These differences were significant in all three conditions but only marginally in the EyeLink Binocular condition (95% CI,  $-0.351$  to  $-0.006$ ). The means and standard deviations of the BCEA in each condition are shown in Table 1, and the results of this analysis are shown in Figure 3.

The results were also confirmed using nonparametric tests that included the outliers. Friedman's two-way ANOVA by ranks was significant ( $\chi^2 = 57.81$ ;  $P < 0.001$ ). A planned Friedman test for three related samples showed that there were no significant differences in fixation stability in the conditions in which the better eye saw the target ( $\chi^2 = 2.7$ ;  $P = 0.26$ ). Wilcoxon signed ranks test revealed that fixation stability of the worse eye was significantly better in the binocular than in the MP-1 condition ( $z = -2.58$ ;  $P < 0.05$ ). Wilcoxon tests also confirmed the differences between the better and worse eye within each condition.

**Worse Eye.** This analysis was similar to that of the Better Eye but included all the conditions in which the worse eye viewed the target. The fixation stability of the better eye was also reported, regardless of whether this eye viewed the target or not. The three levels of the Viewing Condition factor were MP-1 Monocular, EyeLink Binocular, and EyeLink Worse Eye Viewing. In this last viewing condition, only the worse eye viewed the fixation target while the better eye was covered by the IR filter, but the eye tracker recorded the positions of the two eyes. Fixation stability in the latter condition could not be recorded for five patients with very poor vision, including the two who generated the outliers in the first analysis. These specific cases are discussed in Analysis of the Outlying and Missing Data Group section. Therefore, this analysis is based on a sample size of  $n = 15$ .

The Eye main effect ( $F(1,14) = 6.92$ ;  $P < 0.05$ ), the Condition main effect ( $F(2,28) = 7.71$ ;  $P < 0.05$ ), and the Eye  $\times$  condition interaction ( $F(2,28) = 8.74$ ;  $P < 0.05$ ) were all significant. In the EyeLink Binocular condition, the BCEA of the worse eye was 85% smaller than that in the MP-1 Monocular

**TABLE 2.** Mean  $\pm$  SD of the BCEA of the Better and Worse Eye in Three Conditions: MP-1 Monocular, EyeLink Binocular, and EyeLink Worse Eye Viewing

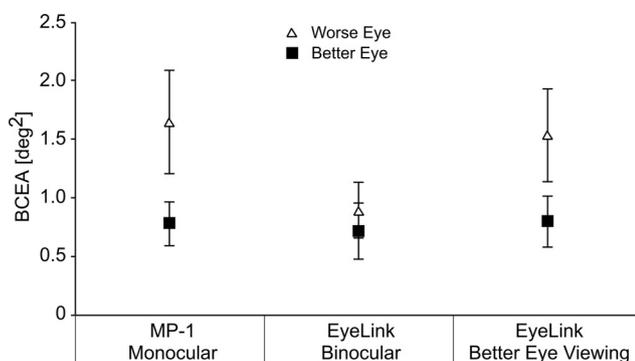
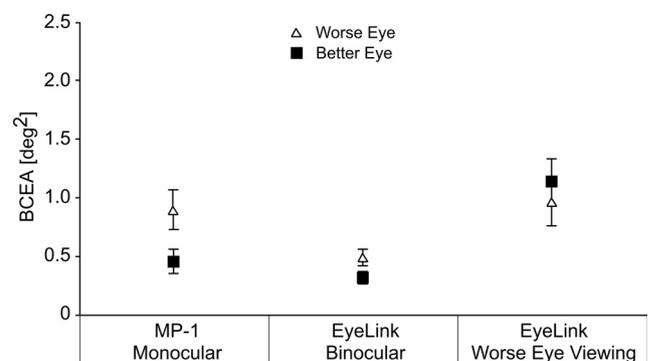
	MP-1 Monocular	EyeLink Binocular	EyeLink Worse Eye Viewing
Better eye BCEA, deg <sup>2</sup>	0.45 $\pm$ 0.39	0.31 $\pm$ 0.19	1.13 $\pm$ 0.77
Worse eye BCEA, deg <sup>2</sup>	0.89 $\pm$ 0.65	0.48 $\pm$ 0.26	0.96 $\pm$ 0.81

condition and 100% smaller than that in the EyeLink Worse Eye Viewing condition. These differences were statistically significant only for the latter comparison ( $P < 0.05$ ). The difference between the BCEAs of the better and worse eyes was significant in the MP-1 condition ( $P < 0.01$ ), but not in the EyeLink Worse Eye Viewing condition. Despite the fact that the mean difference between the BCEAs of the two eyes was very small ( $0.17$  deg<sup>2</sup>) in the EyeLink Binocular condition, this difference was statistically significant (95% CI,  $-0.293$  to  $-0.045$ ). In addition, when the worse eye viewed the target in the EyeLink, fixation stability of the better eye covered by the IR filter was significantly worse ( $P < 0.05$ ) than its fixation in the MP-1 Monocular and EyeLink Binocular conditions. The means and standard deviations of the BCEA from each condition are shown in Table 2, and the results of this analysis are plotted in Figure 4.

#### Analysis of the Outlying and Missing Data Group

Five patients with very poor vision were not included in the previous analysis (see Worse Eye) because their fixation stability could not be recorded in the EyeLink Worse Eye Viewing condition. These five patients included the two who generated the outliers in the analysis of the fixation stability of the Better Eye. To determine whether their pattern of results was different, we repeated the Better Eye analysis for this subgroup.

The results show that these patients generated highly variable data, but the pattern of results was similar to that of the whole group. That is, acuity of the better eye (mean =  $0.53 \pm 0.07$  logMAR) was similar to binocular acuity (mean =  $0.50 \pm 0.06$  logMAR) and better than that of the worse eye (mean =  $1.22 \pm 0.48$  logMAR). In addition, because this small sample size did not allow us to run a two-way repeated measures analysis of variance, we reported only the means of the BCEAs of both eyes in the three conditions in which the data could be recorded: MP-1 Monocular, EyeLink Binocular, and EyeLink Better Eye Viewing. These means include the three outlying values and are reported in Table 3 and plotted in Figure 5. Once

**FIGURE 3.** Means (SE) of fixation stability recorded with the MP-1 and the EyeLink (binocular and better eye viewing conditions) ( $n = 20$ ).**FIGURE 4.** Means (SE) of fixation stability recorded with the MP-1 and the EyeLink (binocular and worse eye viewing conditions) ( $n = 15$ ).

**TABLE 3.** Mean ± SD of the BCEA of the Better and Worse Eye in Three Testing Conditions for the Outlying and Missing Data Group: MP-1 Monocular, EyeLink Binocular, and EyeLink Better Eye Viewing

	MP-1 Monocular	EyeLink Binocular	EyeLink Better Eye Viewing
Better eye BCEA, deg <sup>2</sup>	1.72 ± 1.13	1.92 ± 1.66	1.80 ± 1.54
Worse eye BCEA, deg <sup>2</sup>	4.12 ± 3.29	2.46 ± 2.10	4.23 ± 4.55

again, the means of their BCEAs were much larger, but the pattern of results was similar to that of the whole group for this analysis (see Better Eye). BCEA of the better eye was similar in all three conditions, while that of the worse eye was much better in the EyeLink Binocular condition than in the MP-1 Monocular and the EyeLink Better Eye Viewing conditions.

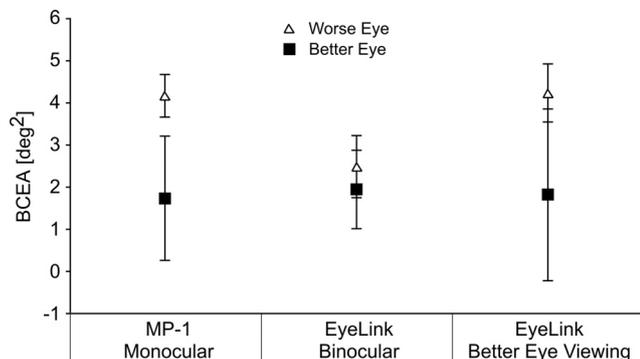
**Relationship between Visual Acuity and Fixation Stability**

**Better Eye.** Fixation stability of the better eye in the three conditions in which this eye was viewing the target (MP-1 Monocular, EyeLink Binocular, EyeLink Better Eye Viewing) was correlated with this eye’s acuity and with binocular acuity. Pearson’s correlation coefficients are shown in Table 4. The results show that fixation stability of the better eye had a moderate correlation with this eye’s visual acuity and with binocular acuity in all three viewing conditions.

**Worse Eye.** Similar analyses were carried out for the worse eye, in the three conditions in which this eye was viewing the target (MP-1 Monocular, EyeLink Binocular, EyeLink Worse Eye Viewing). Because of the outliers and missing data, as explained in the previous section, the correlations in the last condition were based on *n* = 15. Correlation coefficients are presented in Table 5. Results show that fixation stability of the worse eye did not correlate with this eye’s visual acuity in any of the three conditions, and it correlated only marginally with binocular acuity in the EyeLink Binocular condition.

**DISCUSSION**

The ocular motor system of patients with AMD is forced to acquire a new reference position, usually in the healthy retina at the border of the scotoma.<sup>12</sup> A large body of research has been dedicated to studying ocular motor control with a PRL, but many of these studies focused on the PRL of the better eye in monocular viewing conditions.<sup>12,15–18,20,22,24,33,36</sup> Binocu-



**FIGURE 5.** Means (SE) of fixation stability recorded with the MP-1 and the EyeLink (Binocular and Better Eye Viewing conditions) for the five people with missing and/or outlying data.

**TABLE 4.** Pearson’s *r* Correlation Coefficients between Acuity (Monocular and Binocular) and Fixation Stability of the Better Eye in the Three Conditions in Which This Eye Was Viewing the Target

	Fixation Stability of the Better Eye ( <i>n</i> = 20)		
	MP-1 Monocular	EyeLink Binocular	EyeLink Better Eye Viewing
Better eye acuity	0.46*	0.41*	0.41*
Binocular acuity	0.51*	0.38†	0.39*

\* *P* < 0.05, one tail; † *P* = 0.05, one tail.

lar viewing is more ecologically valid, but little is known about ocular motor control of these patients when both eyes are used.<sup>31,37</sup> The main goal of this study was to shed more light on fixation stability during binocular viewing in patients with AMD and large interocular acuity differences. The results showed that, when viewing binocularly, fixational ocular motor control is driven by the better eye.

The fixation stability of the better eye was similar across viewing conditions. We found that fixation stability of the better eye essentially did not change from the monocular to the binocular condition nor under different light levels and viewing distances. This finding is consistent with reports that eye movements during reading with the better eye are similar to those during binocular reading in patients with AMD.<sup>31</sup> We also found that the fixation stability of the worse eye was 84% to 100% better in binocular than in monocular conditions. These results suggest that binocular viewing improves the fixation stability of the worse eye and has no effect on that of the better eye.

The similarity between fixation stability values recorded with the MP-1 and the EyeLink (one eye viewing condition) may seem surprising because it has been reported that, for control participants, the SLO gives significantly lower estimates of these values than the EyeLink.<sup>38</sup> In that study, the differences between the SLO and the EyeLink estimates of fixation stability were most likely caused by differences in testing conditions: the participant’s head was restrained by the headrest in the SLO and was unrestrained in the EyeLink. In the present study, however, recordings were done using a headrest with both the MP-1 and the EyeLink, which may explain the similarities.

We found that, when recorded monocularly with the MP-1, the fixation stability of the worse eye was poorer than that of the better eye. This is not surprising because the worse eye most likely has a larger scotoma, and fixation stability decreases with retinal eccentricity.<sup>16,18</sup> The magnitude of the difference between the fixation stability of the worse eye and the better eye was dramatically reduced when the patients viewed the fixation target binocularly. Although this difference

**TABLE 5.** Pearson’s *r* Correlation Coefficients between Acuity (Monocular and Binocular) and Fixation Stability of the Worse Eye in the Three Conditions in Which This Eye Was Viewing the Target

	Fixation Stability of the Worse Eye		
	MP-1 Monocular	EyeLink Binocular	EyeLink Worse Eye Viewing*
Worse eye acuity	0.26	0.15	0.13
Binocular acuity	0.24	0.38†	0.21

\* Sample size, *n* = 15.

† *P* = 0.05, one tail.

was very small and probably of no clinical importance, it remained statistically significant in the binocular condition. Given that the microsaccades elicited during fixation are conjugate in binocular viewing,<sup>39</sup> this difference could have been caused by larger drifts of the worse eye during binocular fixation.<sup>40</sup> Our preliminary data on fixation coordination show that indeed this may be the case. Detailed analysis of the fixation coordination of patients with AMD will be reported in a subsequent paper.

It is difficult to predict ocular motor control with a PRL in a binocular condition when the monocular PRLs are not in corresponding retinal locations or when there is a large difference in the retinal damage of these patients. It is reasonable to assume that the ocular motor control is driven by the better eye, but two situations could occur: 1) the same PRL of the better eye that is used in monocular condition drives the control in the binocular condition; or 2) the better eye uses a different PRL in the binocular condition. When the viewing condition changed from monocular to binocular, Kabanarou et al.<sup>37</sup> reported a shift in the gaze position in a large proportion of patients, but only in the worse eye. This suggests that the PRL of the better eye does not shift, in most cases, when viewing conditions change from monocular to binocular. The same authors reported a shift of the gaze position in both eyes only in three cases (approximately 10% of the patients). This means that in a small proportion of patients, the better eye uses at least two PRLs: one in the monocular condition and one in the binocular condition. Moreover, it has been shown that people with AMD and relative scotomas may use different PRLs as a function of background luminance,<sup>24</sup> and our testing conditions could have facilitated this situation to occur (i.e., testing performed under different light level conditions with the MP-1 and EyeLink). Only one study investigated whether fixation stability changes with different PRLs for the same eye.<sup>20</sup> These authors trained a new PRL in a different location; at the end of training, fixation stability was the same for both the trained and untrained PRL. Therefore, even if the better eye uses a different PRL during binocular viewing, fixation stability may be similar to that of the monocular PRL. Taken together, all these reports further reinforce our findings that binocular control is driven by the better eye.

The binocular advantage shown by people with normal vision is not always observed in people with AMD and with unequal damage to the two eyes.<sup>5,6,29,30,41</sup> On the contrary, some patients experience binocular inhibition, possibly because the function of the worse eye affects the function of the better eye during binocular viewing.<sup>5,29,30</sup> Two of our patients showed binocular acuity inhibition of one line, and one patient showed binocular acuity inhibition of two lines on the ETDRS charts. Even in these cases, however, fixation stability of the better eye during binocular viewing was as good as that during monocular viewing. That is, the worse eye did not influence the fixational control of the better eye during binocular viewing. The same pattern of results was found for the two patients with AMD in only one eye.

The practical implication of these findings is that, if a rehabilitation plan includes techniques for fixation stability improvement, these techniques can be applied to the better eye only. Based on the results of the present study, it is expected that gains in fixation stability of the better eye would be reflected in binocular fixation as well. Further studies are needed to confirm this prediction.

Another goal of this study was to explore the relationship between visual acuity and fixation stability during monocular and binocular viewing. We have previously reported a moderate relationship between visual acuity and monocular fixation stability for the better eye,<sup>18</sup> but others have not found this relationship when using a much smaller sample size or patients

with early stages of AMD.<sup>15,17</sup> In the present study, we correlated fixation stability of the better eye recorded in the three conditions in which this eye viewed the target (i.e., MP-1 Monocular, EyeLink Binocular, EyeLink Better Eye Viewing) with this eye's visual acuity as well as with binocular acuity. We found a moderate relationship between fixation stability and visual acuity, both monocular and binocular, in all three conditions. Interestingly, this was not the case when fixation stability of the worse eye was correlated with monocular and binocular acuity, with only one exception: binocular acuity and fixation stability of the worse eye had a marginal correlation in the binocular viewing condition. The implication of these results is that, when a differentiation between the better and the worse eye is not made, the relationship between fixation stability and visual acuity could be weaker than that when only the better eye is considered.

In conclusion, this study showed that the fixation stability of people with AMD and large interocular acuity differences is driven by the better eye. Fixation stability of the worse eye dramatically improves during binocular viewing. The implications of these findings are that rehabilitation techniques that involve efforts to stabilize fixation could focus on the better eye only. Moreover, when one is interested in the relationship between visual acuity and fixation stability, differentiating between the worse eye and the better eye is necessary for meaningful conclusions.

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### References

- Bunce C, Wormald R. Causes of blind certifications in England and Wales: April 1999–March 2000. *Eye*. 2008;22:905–911.
- Owen CG, Fletcher AE, Donoghue M, Rudnicka AR. How big is the burden of visual loss caused by age related macular degeneration in the United Kingdom? *Br J Ophthalmol*. 2003;87:312–317.
- Coleman AL, Yu F. Eye-related medicare costs for patients with age-related macular degeneration from 1995 to 1999. *Ophthalmology*. 2008;115:18–25.
- Schuchard RA, Naseer S, de Castro K. Characteristics of AMD patients with low vision receiving visual rehabilitation. *J Rehabil Res Dev*. 1999;36:294–302.
- Faubert J, Overbury O. Binocular vision in older people with adventitious visual impairment: sometimes one eye is better than two. *J Am Geriatr Soc*. 2000;48:375–380.
- Tarita-Nistor L, González EG, Markowitz SM, Steinbach MJ. Binocular interactions in patients with age-related macular degeneration: acuity summation and rivalry. *Vision Res*. 2006;46:2487–2498.
- Mones J, Rubin GS. Contrast sensitivity as an outcome measure in patients with subfoveal choroidal neovascularisation due to age-related macular degeneration. *Eye*. 2004;19:1142–1150.
- Lovie-Kitchin J, Feigl B. Assessment of age-related maculopathy using subjective vision tests. *Clin Exp Optom*. 2005;88:292–303.
- von Noorden GK, Mackensen G. Phenomenology of eccentric fixation. *Am J Ophthalmol*. 1962;53:642–661.
- Guez J-E, Le Gargasson J-F, Rigaudiere F, O'Regan JK. Is there a systematic location for the pseudo-fovea in patients with central scotoma? *Vision Res*. 1993;33:1271–1279.
- Schuchard RA. Preferred retinal loci and macular scotoma characteristics in patients with age-related macular degeneration. *Can J Ophthalmol*. 2005;40:303–312.
- White JM, Bedell HE. The oculomotor reference in humans with bilateral macular disease. *Invest Ophthalmol Vis Sci*. 1990;31:1149–1161.
- Fletcher DC, Schuchard RA. Preferred retinal loci relationship to macular scotomata in a low vision population. *Ophthalmology*. 1997;104:632–638.

14. González EG, Teichman J, Markowitz SN, Lillakas L, Steinbach MJ. Fixation stability using radial gratings in patients with age-related macular degeneration. *Can J Ophthalmol*. 2006;41:333-339.
15. Timberlake GT, Mainster MA, Peli E, Augliere RA, Essock EA, Arend LE. Reading with a macular scotoma, I: retinal location of scotoma and fixation area. *Invest Ophthalmol Vis Sci*. 1986;7:1137-1147.
16. Timberlake GT, Sharma MK, Grose SA, Gobert DV, Gauch JM, Maino JH. Retinal location of the preferred retinal locus relative to the fovea in scanning laser ophthalmoscope images. *Optom Vis Sci*. 2005;82:177-185.
17. Crossland MD, Culham LE, Rubin GS. Fixation stability and reading speed in patients with newly developed macular disease. *Ophthalmic Physiol Opt*. 2004;24:327-333.
18. Tarita-Nistor L, González EG, Markowitz SM, Steinbach MJ. Fixation characteristics of patients with macular degeneration recorded with the microperimeter microperimeter. *Retina*. 2008;28:125-133.
19. Deruaz A, Whatham AR, Mermoud C, Safran AB. Reading with multiple preferred retinal loci: implications for training a more efficient reading strategy. *Vision Res*. 2002;42:2947-2957.
20. Tarita-Nistor L, González EG, Markowitz SM, Steinbach MJ. Plasticity of fixation in patients with central vision loss. *Vis Neurosci*. 2009;26:487-494.
21. Nilsson UL, Frennesson C, Nilsson SE. Location and stability of a newly established eccentric retinal locus suitable for reading, achieved through training of patients with a dense central scotoma. *Optom Vis Sci*. 1998;75:873-878.
22. Nilsson UL, Frennesson C, Nilsson SE. Patients with AMD and a large absolute central scotoma can be trained successfully to use eccentric viewing, as demonstrated in a scanning laser ophthalmoscope. *Vision Res*. 2003;43:1777-1787.
23. Cheung SH, Legge GE. Functional and cortical adaptations to central vision loss. *Vis Neurosci*. 2005;22:187-201.
24. Lei H, Schuchard RA. Using two preferred retinal loci for different lighting conditions in patients with central scotomas. *Invest Ophthalmol Vis Sci*. 1997;38:1812-1817.
25. Duret F, Issenhuth M, Safran AB. Combined use of several preferred retinal loci in patients with macular disorders when reading single words. *Vision Res*. 1999;39:873-879.
26. Crossland MD, Sims M, Galbraith RF, Rubin GS. Evaluation of a new quantitative technique to assess the number and extent of preferred retinal loci in macular disease. *Vision Res*. 2004;44:1537-1546.
27. Crossland MD, Culham LE, Kabanarou SA, Rubin GS. Preferred retinal locus development in patients with macular disease. *Ophthalmology*. 2005;112:1579-1585.
28. Reinhard J, Messias A, Dietz K, et al. Quantifying fixation in patients with Stargardt disease. *Vision Res*. 2007;47:2076-2085.
29. Quillen DA. Effect of unilateral exudative age-related macular degeneration on binocular visual function. *Arch Ophthalmol*. 2001;119:1725-1726.
30. Valberg A, Fosse P. Binocular contrast inhibition in subjects with age-related macular degeneration. *J Opt Soc Am*. 2002;19:223-228.
31. Kabanarou SA, Rubin GS. Reading with central scotoma: is there a binocular gain? *Optom Vis Sci*. 2006;83:789-796.
32. Baker CI, Dilks DD, Peli E, Kanwisher N. Reorganization of visual processing in macular degeneration: replication and clues about the role of foveal loss. *Vision Res*. 2008;48:1910-1919.
33. Seiple W, Szlyk JP, McMahon T, Pulido J, Fishman GA. Eye-movement training for reading in patients with age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2005;46:2886-2896.
34. Steinman RM. Effect of target size, luminance, and colour on monocular fixation. *J Opt Soc Am*. 1965;55:1158-1165.
35. Tabachnick BG, Fidell LS. *Using Multivariate Statistics*. 4th ed. Needham Heights, MA: Allyn & Bacon; 2001:67-71.
36. Bellmann C, Feely M, Crossland MD, Kabanarou SA, Rubin GS. Fixation stability using central and pericentral fixation targets in patients with age-related macular degeneration. *Ophthalmology*. 2004;111:2265-2270.
37. Kabanarou SA, Crossland MD, Bellmann C, Rees A, Culham LE, Rubin GS. Gaze changes with binocular versus monocular viewing in age-related macular degeneration. *Ophthalmology*. 2006;113:2251-2258.
38. Crossland MD, Rubin GS. The use of an infrared eyetracker to measure fixation stability. *Optom Vis Sci*. 2002;79:735-739.
39. Martinez-Conde S, Macknik SL, Hubel DH. The role of fixational eye movements in visual perception. *Nat Rev Neurosci*. 2004;5:229-240.
40. Martinez-Conde S. Fixational eye movements in normal and pathological vision. *Prog Brain Res*. 2006;154:151-176.
41. Tarita-Nistor L, González EG, Markowitz SM, Steinbach MJ. Binocular function in patients with age-related macular degeneration: a review. *Can J Ophthalmol*. 2006;41:327-332.