Uncorrected Myopic Refractive Error Increases Microsaccade Amplitude

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Submitted: October 15, 2014
Accepted: February 9, 2015

Citation: Ghasia FF, Shaikh AG. Uncorrected myopic refractive error increases microsaccade amplitude. *Invest Ophthalmol Vis Sci*. 2015;56:2531–2535. DOI:10.1167/iovs.14-15882

Purpose. Human brain generates miniature eye movements, such as microsaccades, to counteract image fading due to visual adaptation. Generation of microsaccade relies on the amount of retinal error or acuity demand for a desired visual task. The goal of this study was to assess the influence of visual blur, induced by uncorrected refractive error on microsaccades and saccades.

Methods. Ten subjects with myopia held their gaze on a visual target during two experiment conditions: corrected refractive error and uncorrected refractive error. Eye movements were measured with high-resolution video oculography under binocular viewing conditions during both tasks. Gaze holding function, microsaccades, and visually guided saccades were analyzed and compared during both tasks.

Results. We found an increase in the amplitude of microsaccades in the presence of uncorrected refractive error, but the microsaccade frequency and velocity remained unchanged. The microsaccade amplitude systematically increased with an increase in uncorrected refractive error. The main sequence relationship relating the saccade amplitude with respective peak velocity was not significantly different between two conditions. The onset latency, peak velocities, and accuracy of visually guided saccades also were unchanged between the two conditions.

Conclusions. These results suggest that visual blur, hence the precision of an image on the fovea, has an important role in calibrating the amplitude of fixational eye movements, such as microsaccades.

Keywords: visual acuity, saccade, gaze, microsaccades, blur, visual fading

Investigative Ophthalmology & Visual Science

The primate visual system is heavily dominated by sensory adaptation. Constant stimulation at a given location on fovea causes progressively weaker neural responses and visual fading.[1–5] Fortunately, our brain has overcome adaptation by constantly changing the foveal position of the object image. Such a task is accomplished by virtue of head movements, eye position drifts, and miniature eye movements called microsaccades.[6–8] The microsaccades also are necessary to direct the gaze back to fovea after eye position drifts, which are inherent to human eye movement system.[1,9,10]

A number of factors modulate microsaccades. In the absence of vision, the microsaccades become larger.[10,11] High acuity tasks also increase the rate of microsaccades.[12] Microsaccades also facilitate an accurate fixation, such that sudden onset of a stimulus promptly captures our attention.[13–17] We asked whether compromise in foveal image accuracy due to suboptimal refraction affects microsaccades. Therefore, we assessed the effects of visual blur induced by uncorrected refractive error on microsaccades and saccades.

Methods

Eye movements were measured and analyzed from 10 myopic healthy subjects (five female and five male, age range, 25–37). A high-resolution video-based eye tracker (EyeLink 1000; SR Research, Ontario, Canada) was used to noninvasively measure horizontal and vertical eye positions. This technology allows identification of saccades as low as 0.15°. The spatial resolution of the system is 0.01°; hence, allowing possibility to find minute differences with 2-decimal accuracy. The experiment protocols complied with the tenets of the Declaration of Helsinki, and was approved by the Cleveland Clinic institutional review board. All subjects provided written informed consent.

Eye Movement Recordings

The subject's head was supported on a chin-rest 55 cm away from the liquid crystal display (LCD) screen. The subjects were instructed to fixate their gaze on a red visual target projected on the LCD screen with a white background in a completely dark room for 45 seconds. The target was circular; the diameter subtended 0.5° visual angle with the same contrast for all experimental sessions. A similar target was used to record horizontal (0°, ±5°, ±10°, and ±15°) and vertical (0°, ±5°, and ±10°) saccades in a separate trial. Each subject did two identical trials, thus ,making 40 visually guided saccades (24 horizontal and 16 vertical). The horizontal and vertical eye positions were measured as the subject attempted to fixate the gaze on the visual target. Binocular eye positions were measured at temporal resolution of 500 Hz. The digital output from EyeLink and the distance between the LCD screen and the subject's nasion was used to compute the

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Table 1. Refractive Error and Uncorrected Visual Acuity at 55 cm in Study Participants

Subject #	OD SE	OD logMAR Acuity Uncorrected	OS SE	OS logMAR Acuity Uncorrected
1	−3.25	0.33	−3	0.3
2	−2.5	0.	−2.5	0
3	−4.75	0.75	−4.5	0.7
4	−3.25	0.33	−2.25	0.3
5	−8	1.3	−8	1.3
6	−7.5	1.0	−7.5	1.0
7	−1.25	0	−1.25	0
8	−2.5	0	−2.5	0
9	−4.5	0.7	−4.5	0.7
10	Plano	0	−1.25	0

visual angle. Further analysis was done offline on calibrated visual angle vectors.

All 10 subjects had best corrected visual acuity of 20/20 with appropriate strengths of contact lenses. Table 1 summarizes the refractive error and uncorrected visual acuity at 55 cm of all the subjects. None of the subjects had more than 0.50 of astigmatic correction. In addition, for all the subjects, the spherical equivalent was similar in both eyes except one subject who was plano in one eye (Table 1). In the latter subject, the eye movements were recorded while viewing monocularly with the affected eye. The experiment was conducted in the presence of corrected and uncorrected refractive error on the same day, but in randomly determined sequence. Calibration was performed separately for corrected and uncorrected refractive error conditions.

Data Analysis

Eye position data were used for further analysis. All eye position epochs were smoothened with a Savitzky-Golay filter (frame length, 11). Eye position was differentiated and smoothed with a Savitzky-Golay filter (polynomial order, 3; frame length, 21) to compute eye velocity. Microsaccades were identified with the algorithm of Engbert and Kliegl.[14] This algorithm implements three strategies to detect microsaccades. It first transforms the eye positions into eye velocities. Then, during fixation it generates the velocity vectors whose mean is effectively zero. In this representation the microsaccades are identified as "outliers" in the velocity space. Then, this algorithm independently computes the horizontal and vertical velocity threshold using the multiples of the standard deviation of the velocity distribution. The algorithm uses these thresholds to determine the onset of microsaccades. Finally, the algorithm uses binocularly synchronous events to determine whether they were microsaccades. Data were analyzed on binocular eye positions. The analysis excluded saccades that were larger than 4°. The variables of interest were amplitudes, frequencies, and peak velocities. We used composite vector of horizontal and vertical components for further analysis.

We used 10° per second velocity threshold for visually guided saccade detection. Saccade amplitude was the absolute difference between the eye positions at the start and end of the saccade. Visually guided saccade latency was defined as the time difference between the shift in target location and initiation of saccade. Data analysis was performed using custom prepared software in MATLAB programming language (MathWorks, Natick, MA, USA).

Results

Uncorrected refractive error causes visual blur. We assessed the impact of such visual blur on microsaccades. Figure 1A illustrates an example of visual fixation with best-corrected visual acuity. Examples of microsaccades (arrows), either following a drift in the eye position or as part of (physiological) square-wave jerk, are shown. Figure 1B illustrates an example of visual fixation from the same subject, but with uncorrected refractive error creating visual blur on the fovea. Microsaccades appeared to have larger amplitudes in the presence of visual blur.

Figure 1C depicts the influence of uncorrected refractive error on the distribution of the microsaccade amplitude in one subject. The median amplitude of microsaccades was 0.56°, but it decreased to 0.37° when the refractive error was corrected. The distributions of amplitudes of all microsaccades were compared, and they were significantly different (Kolmogorov-Smirnov test, $P = 0.02$). Similar comparison of effects of refractive error on the amplitudes of microsaccades was done in all subjects. Uncorrected refractive error consistently increased the amplitude of microsaccades in all but one subjects.

Histograms in Figure 1D summarize the distribution of amplitudes of microsaccades measured from all subjects. The population median was 0.7° (interquartile range, 0.38°) when refractive error was corrected. The median was 0.8° (interquartile range, 0.45°) in the presence of uncorrected visual blur. The two distributions were significantly different (Kolmogorov-Smirnov test, $P = 3e\text{-}6$). Scatterplot in Figure 1E depicts the effects of visual blur on the median amplitude of microsaccade with each data point representing one subject. Most data points fall above equality line, suggesting an increase in the microsaccade amplitude in the presence of uncorrected refractive error. Refractive error causing visual blur did not affect the median frequency of microsaccades as all data points scattered on both sides of the equality line in Figure 1F. Box plots in Figure 1G summarize the effects of refractive error on the frequencies of all microsaccades collated from all subjects. In the presence of visual blur, median frequency of microsaccade was 1.8 Hz, interquartile range was 0.9 to 2.7 Hz, and the range of 95% confidence interval was 1.66 to 1.84 Hz. The median frequency was unchanged with comparable interquartile interval (1.01 and 2.65 Hz) and 95% confidence interval between 1.69 and 1.86 Hz after correction of refractive error. Two populations were not significantly different (1-way ANOVA, $F = 0.37$; df = 1; $P = 0.52$). We asked whether visual blur affects the amplitude–velocity relationship (the main sequence) of microsaccades. The cluster of data points depicting the main sequence in the presence of visual blur overlapped with the cluster representing normal vision. The difference was not statistically significant (ANCOVA, $P > 0.05$).

We then assessed whether the severity of visual blur induced by refractive error determines the amplitude of microsaccade. Figure 2 depicts the relationship of severity of refractive error and increase in the amplitude of microsaccades. In this figure, each data point depicts one subject; the refractive error is plotted on the *x*-axis while the corresponding percent increase in the median microsaccade amplitude is plotted on the *y*-axis. A summary from all, except one, subjects is illustrated in Figure 2. The goal of this analysis was to assess whether severity of refractive error correlates with the change in microsaccade amplitude. The excluded subject had normal vision in one eye and mild refractive error in the other, and had no change in the microsaccade amplitude. In all other subjects, the values of percent increase in the microsaccade amplitude proportionately increased with

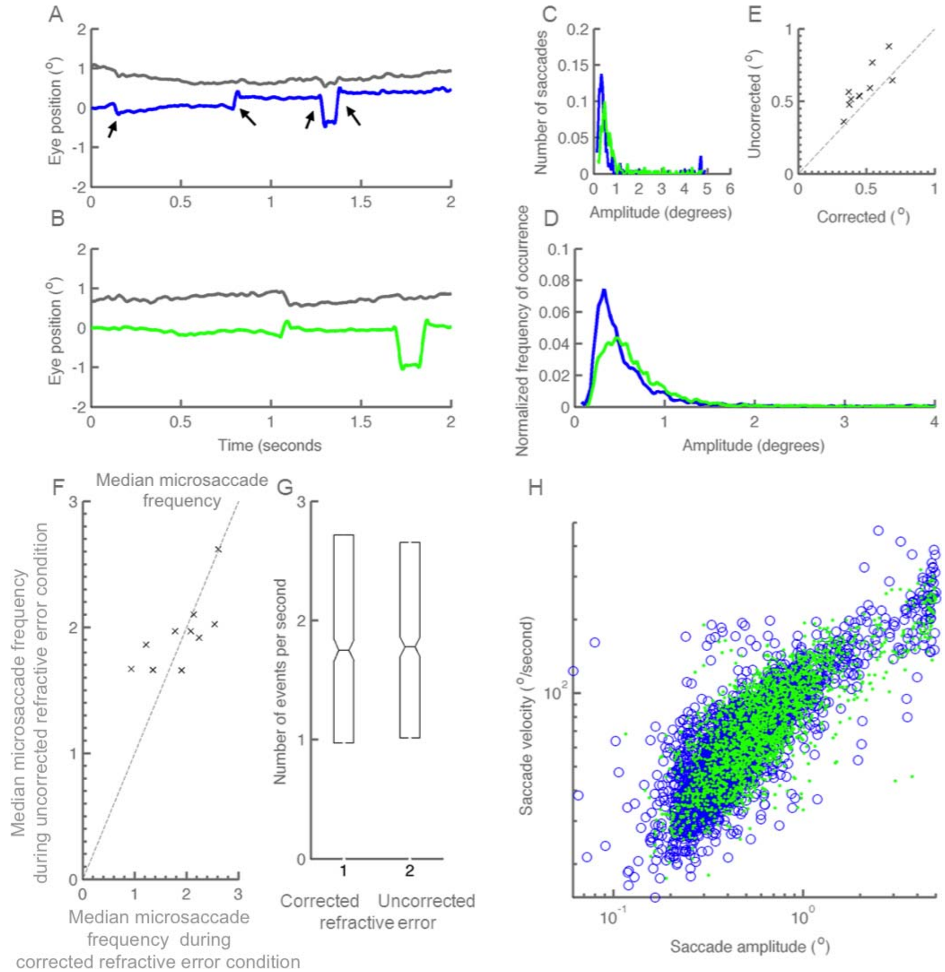

FIGURE 1. Example of visual fixation in one subject when refractive error was corrected (**A**) or in absence of such correction (**B**). (**A**, **B**) The eye position is plotted on the *y*-axis while the *x*-axis depicts corresponding time. The *colored line* depicts horizontal eye position, while *gray lines* illustrate vertical eye position. *Arrows* represent microsaccades. (**C**) Histograms depict the comparison of distribution of microsaccade amplitude and the influence of uncorrected refractive error. Number of samples are normalized and plotted on the *y*-axis, while the *x*-axis is corresponding bin-values. *Green line* depicts values when refractive errors were present, while *blue line* is after the correction of refractive errors. (**D**) Histograms illustrate the summary of the distribution of amplitudes of all microsaccades from all subjects. Normalized numbers of events in a given bin are plotted on the *y*-axis, while the *x*-axis represents the bins of microsaccade amplitude. The histogram plotted with the *blue line* show distribution of microsaccades recorded in the absence of refractive error. The *green line* depicts the distribution of microsaccade amplitude in the presence of refractive error. (**E**) Summary of the effects of refractive error on the median amplitude of microsaccades. Each *symbol* depicts one subject. The median amplitude from given subject in the presence of uncorrected refractive error is plotted on the *y*-axis, while the median amplitude from the same subject when refractive error is corrected is plotted on the *x*-axis. *Gray line* is an equality line. (**F**) Effects of refractive error on the microsaccade frequency are summarized. Each data point represents one subject. Median value of the microsaccade frequency during uncorrected refractive error condition from a given subject is plotted on the *y*-axis, while the *x*-coordinate depicts the median frequency during corrected refractive error condition. The *dashed line* is an equality line. All data points fall around the equality line suggesting no influence of refractive error on the microsaccade frequency. (**G**) The effect of refractive error on the frequency of all microsaccades from all subjects is illustrated. Each *box* depicts microsaccade frequency in the uncorrected refractive error condition or during condition when refractive error is corrected. The length of each *box* depicts the interquartile interval, *notch* suggests 95% confidence interval, and the *horizontal line* in the *center* of the *notch* is the median value. *Overlapping notches* suggest lack of difference in the median values of two populations. (**H**) The effect of refractive error on the main sequence relationship of microsaccades was assessed. The main sequence relationship is depicted. Each data point depicts one microsaccade; *blue* data points represent microsaccade during corrected refractive error condition, while *green* data points are microsaccades captured when refractive error was uncorrected. Amplitude of each microsaccade is plotted on the *x*-axis; corresponding velocity is plotted along the *y*-axis. The clusters of data points overlap suggesting a lack of influence of refractive error on main sequence relationship.

the severity of refractive error. The relationship between refractive error and increase in the microsaccade amplitude had a correlation coefficient of 0.67. The correlation was statistically significant ($P = 0.02$).

We also assessed the influence of uncorrected refractive error on the accuracy of visually guided horizontal and vertical saccades, their onset latency, and peak velocities. There was no statistically significant difference in these parameters of visually guided saccades measures between the two conditions (Table 2).

Our results suggested that the visual blur on the fovea induced by uncorrected refractive error increases the amplitude of microsaccades. The increase in the microsaccade amplitude significantly correlates with the severity of refractive error. The visual blur due to refractive error, however, neither affects the frequency nor the velocity of

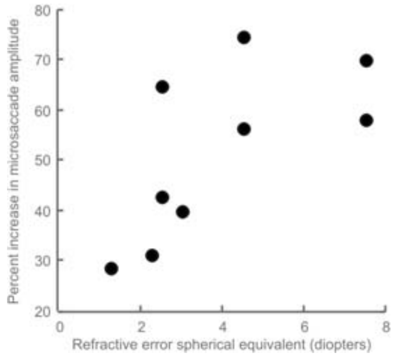

FIGURE 2. Relationship between the percent increase in microsaccade amplitude and the severity of refractive error is shown. Each data point depicts one subject. Refractive error is plotted on the *x*-axis, while the *y*-axis depicts corresponding value of percent increase in microsaccade amplitude. The dependence had significant correlation (correlation coefficient = 0.67; $P = 0.02$).

microsaccades as depicted in the main sequence relationship.

DISCUSSION

Microsaccades are miniature eye movements triggered by visual fading due to neural adaptation as well as by retinal errors induced by drifts in the eye position.[9,18] We saw an increase in microsaccade amplitude in uncorrected refractive error state. The properties of visual fixation target are known to affect microsaccades, viewing of bigger target elicits microsaccades with larger amplitude.[19] One possibility is that blurring of the foveal image due to uncorrected refractive error is equivalent to viewing a larger target resulting in an increase in microsaccade amplitude.[1,9,10] Hence, we suggest that an increase in the amplitude of microsaccade without any change in the frequency in the presence of uncorrected refractive error is possibly a neural compensatory mechanism to counteract peripherally induced visual blur.

Lack of increase in the frequency of microsaccades in presence of visual blur due to refractive error, unlike increasing microsaccade frequency from visual adaptation, can be described by the fundamental difference in the cause of blur. Visual adaptation results in saturation of the neural activity in the afferent visual system. Such changes serve as a trigger for microsaccades. In contrast, refractive error–induced visual blur does not lead to saturation of retinal neural activity, hence lacking the trigger to increase the frequency of microsaccades. It is possible that chronically persistent visual blur due to refractive error might induce adaptive changes in the central nervous system. Such changes lead to increased amplitude of microsaccades, but without affecting its frequency when the target is viewed without correcting the refractive error.

Theoretically, mounting contact lenses on the surface of the eyes can increase its mass. Although small, such increase in the mass of the moving eyeball might reduce peak acceleration and subsequently the peak velocity. Changes in these parameters would affect the time taken to achieve the desired amplitude movement, but not the actual saccade amplitude. If there is any effect of change in mass of the eyes due to contact lens, it should affect the main sequence relationship. We did not find any effect of contact lens on the main sequence (Fig. 1H). We found no difference in accuracy, latency, or peak velocities of visually-guided saccades during corrected versus uncorrected refractive error conditions. Our findings are in agreement with prior studies showing the lack of effect of artificially induced monocular blur with contact lens on saccade dynamics in healthy subjects.[20] A recent study investigating gaze holding in patients with progressive supranuclear palsy had two groups of healthy controls.[21] Microsaccades in one group of healthy controls was measured with scleral search coils, while the other group of healthy subjects had measurements with video oculography (Eyelink II; SR Research). There were no differences in the dynamic properties of microsaccades between two groups of healthy subjects.[21] The search coil technique requires the use of a contact lens. Thus, our conclusion for the effects of

TABLE 2. Saccadic Accuracy, Velocity, and Latency in Corrected and Uncorrected Refractive Error Conditions

	Corrected Refractive Error	Uncorrected Refractive Error	*P* Value, *t*-Test
Horizontal saccades, 5° target			
Accuracy, eye amp/target amp	1.05 ± 0.3	0.98 ± 0.15	0.27
Velocity, deg/sec	206.8 ± 57.1	199.1 ± 44.3	0.57
Latency, msec	0.13 ± 0.05	0.12 ± 0.04	0.71
Horizontal saccades, 10° target			
Accuracy, eye amp/target amp	0.93 ± 0.09	0.96 ± 0.11	0.23
Velocity, deg/sec	327.3 ± 47.1	322.0 ± 43.2	0.64
Latency, msec	0.14 ± 0.05	0.14 ± 0.03	0.49
Horizontal saccade, 15° target			
Accuracy, eye amp/target amp	0.9 ± 0.07	0.92 ± 0.10	0.3
Velocity, deg/sec	385.7 ± 51.6	389.0 ± 65.0	0.85
Latency, msec	0.13 ± 0.06	0.14 ± 0.06	0.51
Vertical saccades, 5° target			
Accuracy, eye amp/target amp	0.94 ± 0.2	1.03 ± 0.19	0.16
Velocity, deg/sec	183.4 ± 39.8	195.0 ± 51.0	0.38
Latency, msec	0.13 ± 0.04	0.15 ± 0.05	0.23
Vertical saccades, 10° target			
Accuracy, eye amp/target amp	0.94 ± 0.13	1.03 ± 0.19	0.69
Velocity, deg/sec	310.3 ± 57.8	195.0 ± 51.0	0.55
Latency, msec	0.13 ± 0.04	0.15 ± 0.03	0.13

contact lens on microsaccades received further support from a study from two independent laboratories.[21]

Precision, defined as the ability to reliably reproduce a measurement in a fixating eye, is critical to interpret eye-tracking data. Spatial resolution, measured as RMS, is very important for algorithms detecting saccades or microsaccades. Lower value of the RMS ensures better reliability of microsaccades detection. Contact lens does not reduce the precision of an eye tracker. An investigation from an independent laboratory showed that calibration, accuracy, and precision of eye tracking data while wearing eyeglasses were much less precise, but the contact lens ensured significantly better precision, even more accurate compared to no visual aids at all.[22] Another independent study also showed comparable outcome of video-based eye tracking (without any visual aid) compared to the gold standard scleral search coil technique that requires wearing of a contact lens.[23]

The contact lenses are not fixed, but could have minor slip on the surface of the eye. We asked whether such slip could affect our results. It is noteworthy that a video-based eye tracker takes into account corneal light reflection and pupil detection models. Hence, possible minor contact lens slip on the eye surface could potentially affect the amplitude measured with corneal light reflex. In our experiments, we used corneal light reflex and pupil detection algorithms; thus, it is unlikely to have influenced the measured amplitude. Although unlikely in our experiment, even if present, any influence of contact lenses on increase in microsaccade amplitude would shift the microsaccade distribution, but not change the shape of distribution. We found not only a shift in microsaccade distribution, but also a change in the distribution curve (Fig. 1B). Such effect further suggests the physiological role of refractive error on modulating the amplitude of microsaccade.

It also is possible that a minor slip of the contact lens might shift the image position on the fovea leading to image blur. In light of our findings, such blur might underestimate improvement in saccade amplitude when contact lenses are mounted. In other words, the effects of visual acuity on saccade amplitude should be even stronger than what our experiments revealed. It also is possible that retinal image may vary depending on the alignment of the optical axis of the contact lens with the optical axis of the eye. We must emphasize that only one of our subjects had astigmatism of 0.75 diopter (D); all other subjects had astigmatism of 0.25 D or less; hence, requiring only spherical correction in their contact lenses. The changes seen in the subject who had 0.75 D of astigmatism were comparable to those without it. Finally, if there is any influence of contact lens shift on our results, it should be independent of the severity of refractive error. In contrast, we found the saccade amplitudes were larger in subjects with higher refractive error.

To summarize, we found uncorrected refractive error increases the amplitude of microsaccade. Percent increase in the microsaccade amplitude is proportional to the severity of refractive error; hence, the amount of visual blur. The visual blur due to refractive error, unlike visual fading due to neural adaptation, does not affect the microsaccade frequency. This study suggested an increase in the amplitude of microsaccade as a single adaptive change to myopia during short-term assessments.

Acknowledgments

The authors thank R. John Leigh, MD (RJL) for providing technical equipment.

Supported by the Knights Templar Eye Foundation (FG), Fight-for-Sight (FG), and Blind Children's Center (FG) research grants; and a Dystonia Medical Research Foundation Grant (AS) and Research to Prevent Blindness Unrestricted Grant.

Disclosure: **F.F. Ghasia**, None; **A.G. Shaikh**, None

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