Title
Saccadic latency in amblyopia

Journal
Journal of Vision, 16(5)

ISSN
1534-7362

Authors
McKee, Suzanne P
Levi, Dennis M
Schor, Clifton M
et al.

Publication Date
2016-03-04

DOI
10.1167/16.5.3

Peer reviewed

Saccadic latency in amblyopia

Suzanne P. McKee Smith-Kettlewell Eye Research Institute, San Francisco, CA, USA

Dennis M. Levi School of Optometry, University of California, Berkeley, CA, USA

Clifton M. Schor School of Optometry, University of California, Berkeley, CA, USA

J. Anthony Movshon Center for Neural Science, New York University, New York, NY, USA

We measured saccadic latencies in a large sample (total $n = 459$) of individuals with amblyopia or risk factors for amblyopia, e.g., strabismus or anisometropia, and normal control subjects. We presented an easily visible target randomly to the left or right, 3.5° from fixation. The interocular difference in saccadic latency is highly correlated with the interocular difference in LogMAR (Snellen) acuity—as the acuity difference increases, so does the latency difference. Strabismic and strabismic-anisometropic amblyopes have, on average, a larger difference between their eyes in LogMAR acuity than anisometropic amblyopes and thus their interocular latency difference is, on average, significantly larger than anisometropic amblyopes. Despite its relation to LogMAR acuity, the longer latency in strabismic amblyopes cannot be attributed either to poor resolution or to reduced contrast sensitivity, because their interocular differences in grating acuity and in contrast sensitivity are roughly the same as for anisometropic amblyopes. The correlation between LogMAR acuity and saccadic latency arises because of the confluence of two separable effects in the strabismic amblyopic eye—poor letter recognition impairs LogMAR acuity while an intrinsic sluggishness delays reaction time. We speculate that the frequent microsaccades and the accompanying attentional shifts, made while strabismic amblyopes struggle to maintain fixation with their amblyopic eyes, result in all types of reactions being irreducibly delayed.

Introduction

It has long been known that reaction times are slower to stimuli presented to amblyopic eyes than to normal eyes (Mackensen, 1958; von Noorden, 1961). Hamasaki and Flynn (1981) related the interocular difference in manual reaction time, to stimuli presented to each eye of amblyopic subjects, to the Snellen acuity of the amblyopic eye. They found a systematic increase with decreasing acuity—the worse the acuity, the larger the difference in reaction time. Saccadic latency is also longer in amblyopic eyes than in normal eyes (Ciuffreda, Kenyon, & Stark, 1978a, 1978b; Mackensen, 1958; Niechwiej-Szwedo, Chandrakumar, Goltz, & Wong, 2012; Niechwiej-Szwedo, Goltz, Chandrakumar, Hirji, & Wong, 2010;). Once initiated, the dynamics of amblyopic saccades are normal, indicating that their longer latency is due to sensory or cognitive factors rather than low-level motor problems (Ciuffreda et al., 1978a, 1978b; Ciuffreda, Levi, & Selenow, 1991; Niechwiej-Szwedo et al., 2010; Niechwiej-Szwedo et al., 2012; Perdziak, Witkowska, Gryncewicz, Przekoracka-Krawczyk, & Ober, 2014).

One might suppose that the amblyopic eye is slow just because it is less sensitive than the fellow (non-amblyopic) eye or than normal eyes. Reaction time decreases as a power function of stimulus intensity (Piéron, 1914, 1952), so if the effective stimulus were weaker in the amblyopic eye than in the fellow eye, one would predict a slower response (Cuiffreda et al., 1991; Pianta & Kalloniatis, 1998). In the studies described above, the targets were small luminous features presented on a dark background, i.e., high contrast

Citation: McKee, S. P., Levi, D. M., Schor, C. M., & Movshon, J. A. (2016). Saccadic latency in amblyopia. *Journal of Vision*, *16*(5):3, 1–15, doi:10.1167/16.5.3.

doi: 10.1167/16.5.3 Received August 23, 2015; published March X, 2016 ISSN 1534-7362

targets. Hamasaki and Flynn (1981) thought that their targets might be too small for the amblyopic eyes so they doubled the target size and repeated the measurements on two particularly slow observers; their reaction times did improve with the larger target, but their amblyopic eyes were still significantly slower than their fellow eyes.

Levi, Harwerth, and Manny (1979) measured manual reaction time as a function of the contrast of centrally fixated sinusoidal gratings in four amblyopes. Reaction time fell with contrast in conformance with Piéron's law. The top graph of Figure 1 plots a representative data set from this study for the amblyopic and fellow eyes of a strabismic anisometrope. These data were fitted with a power law (Equation 1), where α and β determine the slope of the function and γ sets the asymptotic floor:

$$RT = \alpha C^{-\beta} + \gamma \quad (1)$$

The reaction time function in the amblyopic eye is systematically slower than the function of the fellow eye; it is displaced leftward, along the contrast axis, by an amount roughly equal to the ratio of the contrast thresholds for the two eyes (Palmer, Huk, & Shadlen, 2005; Pianta & Kalloniatis, 1998). In the bottom graph of Figure 1, we replot the data in multiples of contrast threshold. The lateral separation between the two functions is almost eliminated. However, there remains a significant difference between the two functions at asymptote; the asymptotic floors (γ), based on the fitted functions (shown by the arrows), is 241 ms for the nonamblyopic eye and 287 ms for the amblyopic eye—a difference of 46 ms. We conclude that there is a delay in the amblyopic eye of this subject that cannot be overcome by increasing target contrast.

In normal observers, saccadic latency decreases with increasing contrast, following the same power law (Piéron's law) as manual reaction time (Ludwig, Gilchrist, & McSorley, 2004; White, Kerzel, & Gegenfurtner, 2006). Thus, in amblyopic observers, we might anticipate an interocular difference in saccadic latency based on differences in interocular sensitivity plus some other factor that affects the asymptotic levels, following the pattern shown in Figure 1.

It is somewhat surprising that Hamasaki and Flynn (1981) found that reaction time correlated with acuity, because acuity measures are not measures of contrast sensitivity. Contrast thresholds do increase gradually with the loss in acuity in amblyopia (McKee, Levi, & Movshon, 2003), but the targets used in the Hamasaki-Flynn study were high contrast, like those of Levi et al. (1979) at asymptote, so it appears that the worse the acuity, the longer the irreducible delay. The correlation between saccadic latency to highly visible peripheral stimuli and visual acuity in central vision (Gerin, Peronnet, & Magnard, 1973) is even more puzzling,

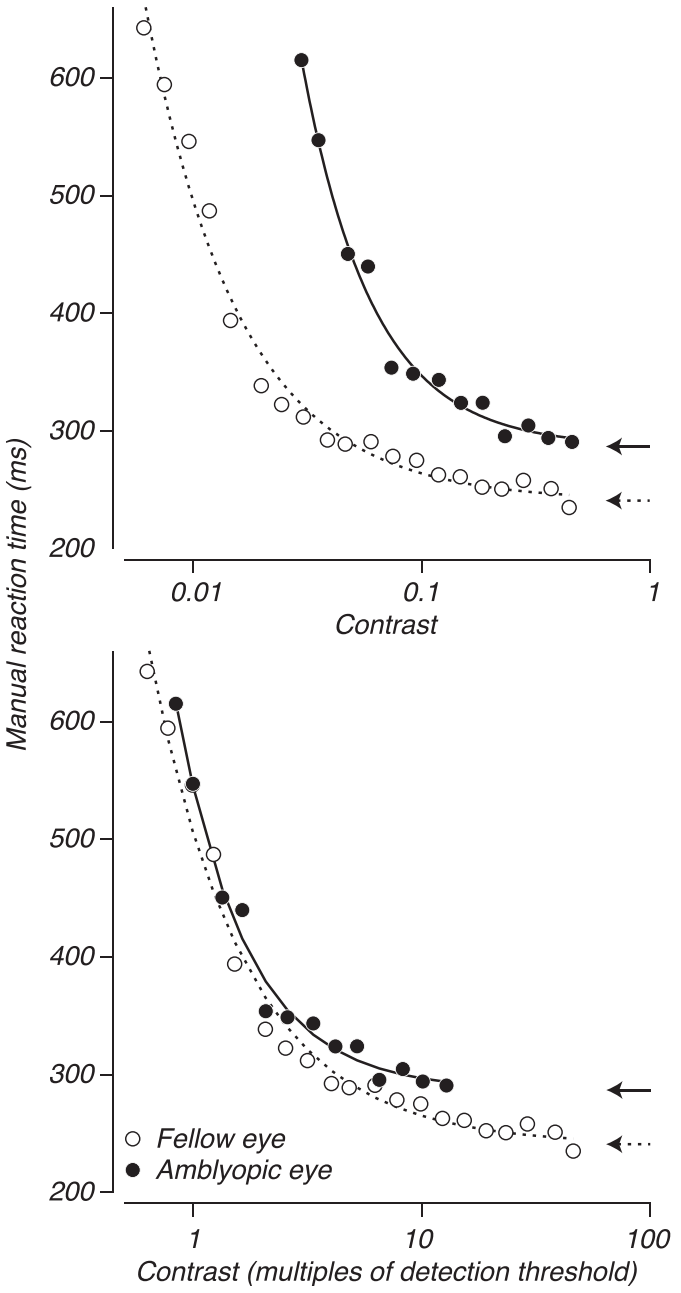

Figure 1. Manual reaction time to a 2 c/° grating. Nonamblyopic (open symbols) and amblyopic eyes (filled symbols) of a strabismic anisometrope. The curves are best-fitting power functions. Data from figure 2 in Levi, Harwerth, and Manny (1979). Top: Data plotted as a function of contrast. Bottom: Data plotted a function of contrast in multiples of threshold. Arrows point to asymptotes estimated from fitted power functions.

since acuity is often normal or nearly so in the amblyopic periphery, particularly in strabismic amblyopes (Hess & Jacobs, 1979; Hess & Pointer, 1985; Katz, Levi, & Bedell, 1984; Levi, Klein, & Aitsebaomo, 1984). This correlation suggests that in amblyopes either resolution influences saccadic latency, or that some

other factor, correlated with Snellen acuity, delays the onset of saccades.

The data presented here were taken more than two decades ago, along with numerous clinical, psychophysical and other oculomotor measurements. The results of the psychophysical tests and other oculomotor measurements have been previously described in three earlier publications (Levi, McKee, & Movshon, 2011; McKee et al., 2003; Schor, Fusaro, Wilson, & McKee, 1997). However, we have not reported the saccadic latencies from this group.

We propose to use this large data base to explore three questions: (1) Does saccadic latency in all types of amblyopes have a dependence on the LogMAR (Snellen) acuity of the amblyopic eye similar to that observed for manual reaction time by Hamasaki and Flynn (1981)? (2) Do the psychophysical measurements of grating acuity and, particularly, contrast sensitivity, made concurrently with the oculomotor measurements, provide an explanation for the longer saccadic latencies found in amblyopia? (3) Are there differences in saccadic latency associated with different types of amblyopia, i.e., with strabismus, anisometropia, or strabismus-anisometropia?

Methods

We measured saccadic latency for a target presented either to the left or right of fixation. The target was a large bright "X," 1° high by 1° wide that was increased in size to 2° for observers with acuity worse than 20/40. The "X" initially appeared in the center of the monitor and then abruptly jumped right 3.5°, remaining in this position for 1 s. The "X" returned to center and remained at the central position for a variable duration ranging from 1–2 s.; it then shifted 3.5° right or left at random. The whole sequence was repeated until the target had appeared 10 times in each of the right and left positions. Observers were asked to follow the movements of the *center* of the X as quickly as possible.

The stimuli were presented on a Princeton MAX-15 monitor (P4 Phosphor; Princeton Graphic Systems, Princeton, NJ) with screen dimensions of 19.7 × 25.5 cm (11° × 14°). The mean luminance for the targets was 90 cd/m^2. Stimuli were viewed monocularly, while the other eye was covered by an opaque occluder. Observers' heads were stabilized with a head holder. Viewing distance was 1 m. For the latency measurements and for all the psychophysical measurements described below, observers wore their best optical corrections, based on the clinical examination that preceded laboratory testing.

Saccades were measured with an Eye-Trac Model 210 Limbus Tracker (Applied Science Laboratories, Waltham, MA). This apparatus consisted of two infrared trackers for each eye that responded to the amount of light reflected from the limbal-scleral boundary; the difference in light signaled by the detectors was converted into degrees of eye rotation per volt. Before the oculomotor measurements, the tracker was calibrated for each eye by asking the observer to look at the large "X" presented first in the center of the monitor and then 4.5° to the left and right of center.

Saccadic analysis

Eye position was sampled every 5 ms and stored for subsequent analysis offline. The raw data were smoothed by averaging with a moving window 11 samples wide. The change in position was calculated between adjacent samples and also samples three steps apart. Our criteria for a saccade were (a) a velocity exceeding 30°/s at the next sample and for the next six samples; (b) an amplitude $> 1°$ at sample points 50, 100, 150, 200, and 250 ms after the initial velocity threshold was exceeded. Latency was defined as the time between target onset and saccade initiation minus 15 ms (halfway through saccadic window); it was rejected if it were greater than 500 ms or less than 125 ms. As a check for stability, we also rejected any saccade if a change in amplitude greater than 1° occurred 100 ms prior to the latency measurement or a change greater than 2° occurred 75 ms after the measurement.

Observers

These saccadic latency measurements were part of a large-scale study of the psychophysical and oculomotor characteristics of individuals with amblyopia or with risk factors for amblyopia, e.g., strabismus or anisometropia. We chose an age range, 8 to 40, so that only individuals falling between posttreatment and prepresbyopic ages were included in our study. The average age of our sample was 25.8 years, with a standard deviation of 9.3 years; the median age was 27. Each adult signed a consent form that described the purpose of the study and the testing procedures; a parent or guardian of each minor signed the consent form. This research followed the tenets of the World Medical Association Declaration of Helsinki, and was approved by the appropriate Institutional Review Boards.

The clinical examination that assessed the refractive and oculomotor abnormalities of each participant has been described in detail in three previous publications (Levi et al., 2011; McKee et al., 2003; Schor et al., 1997). This examination was performed by ophthalmologists and optometrists who had been trained in

the special diagnostic protocol associated with the study. In brief, it measured refractive error under both dry and cycloplegic conditions, established the presence of strabismus with unilateral and alternating cover tests at two distances with each eye occluded for a least 5 s, quantified the presence of horizontal and vertical angles of deviation with a prism-cover test, and included numerous other clinical observations on oculomotor stability and binocular function. All subsequent psychophysical measurements, including acuity measured with the Bailey-Lovie LogMAR chart, were made with the observers wearing best optical correction.

For their data to be included in the current study, each observer had to complete at least two latency measurements for each position (left and right). Observers failed to meet this criterion either because they could not perform the task or more commonly because we were unable to obtain calibration or saccadic data on their eyes due to technical limitations. Those who failed came from all clinical designations, including two from the normal subgroup. Thus, the numbers of observers in the abnormal subgroups shown below do not match the numbers in previous publications based on this same large-scale study. The original sample contained 427 abnormal observers and 68 normal controls, but 36 of these observers failed to meet our saccadic criterion for inclusion. The sample used here included 393 abnormal observers and 66 normal controls for a total of 459 participants. Note that only Figure 2 includes the data from all 393 abnormal observers (82 anisometropes, 39 strabismics, 85 strabismic-anisometropes, plus 187 observers with other abnormalities).

Based only on the clinical assessment, we had divided the original abnormal sample into ten different subgroups. However, in the current study, our third objective was to compare differences in saccadic latency among the subgroups with the conditions that are most commonly associated with amblyopia—strabismus, anisometropia, and strabismus-anisometropia. The characteristics of these three subgroups are described in detail below. We also explored whether amblyopia associated with any kind of strabismus (e.g., inconstant strabismus) affected latency, so the characteristics of these three groups are described in detail below as well.

We have not listed the detailed characteristics of the other four abnormal subgroups (deprivationals, refractives, eccentric fixators, and other abnormals) because their specific sensory characteristics, e.g., contrast sensitivity, were not used to analyze the cause of slow saccadic latency in amblyopia. We have however included the data from these other four groups in Figure 2 to show the general dependence of interocular latency differences on interocular differences in acuity among all types of amblyopes—our first objective in this study.

Pure Anisometropes (Total n = 82; 49 amblyopes)
- •Unequal refractive error, with a difference in refractive error between the eyes of 1D or more at the most anisometropic meridian
- •No ocular deviation
- •No eccentric fixation
- •No history of deprivation
- •No history of surgery

Pure Strabismics (Total n = 39; 26 amblyopes)
- •Constant ocular deviation
- •No history of deprivation
- •Less than 1D difference in refractive error between the eyes

Strabismic-anisometropes (Total n = 85; 70 amblyopes)
- •Constant ocular deviation
- •Unequal refractive error with a difference between the eyes of 1D or more at the most anisometropic meridian
- •No history of deprivation

Inconstant Strabismics (n = 23; 8 amblyopes)
- •Less than 1D difference in refractive error between the eyes.
- •No history of deprivation
- •Ocular deviation that is not consistently present under all testing conditions

Inconstant Strabismic-Anisometropes (n = 38; 20 amblyopes)
- •Unequal refractive error with a difference between the eyes of 1D or more at the most anisometropic meridian
- •No history of deprivation
- •Ocular deviation that is not consistently present under all testing conditions

Former Strabismics (n = 18; 7 amblyopes)
- •Surgical history
- •No detectable constant or inconstant deviation
- •No history of deprivation
- •Less than 1D difference in refractive error between the eyes

Normal (n = 66)

Psychophysical measurements

We used psychophysical measurements of acuity, contrast sensitivity, and binocularity to interpret the latency results in this study. Note that in all figures we are plotting the interocular difference in saccadic latency versus an interocular difference in a log measurement (LogMAR, log grating acuity, Pelli-Robson contrast sensitivity), i.e., the interocular ratio of acuities or contrast sensitivities.

To assess acuity, we measured both grating and LogMAR (Snellen) acuity. For the grating acuity measurements, we used a high-contrast (80%) horizontal sinusoidal grating, generally viewed at 6 m. We decreased the viewing distance to 3 m for observers with Snellen acuities between 20/200 and 20/600 and to 1 m for observers with acuity worse than 20/600. The grating segment was windowed by an elliptical two-dimensional Gaussian that subtended $\sim 1.7° \times 1.2°$ at 6 m. The contrast was ramped on over 200 ms, and after a 500 ms plateau, was ramped off over 200 ms. The starting spatial frequency was set at roughly two thirds of the cut-off frequency as estimated from LogMAR acuity. Spatial frequency was varied by a staircase procedure that increased spatial frequency following three correct responses and decreased it after one incorrect response. Observers responded "grating present (Yes)" or "absent (No)"; no feedback was given. One third of the trials were blanks. The staircase was terminated after six reversals; threshold was estimated as the geometric mean of the last four reversals.

To measure optotype (Snellen) acuity, we used the modified Bailey-Lovie (LogMAR) chart, which was used in the early treatment diabetic retinopathy study (ETDRS Report, 1985). Observers viewed the chart with their best visual correction at a distance of 3 m. Background luminance was 61 cd/m^2. The test was scored on a letter-by-letter basis. In the current study, we define amblyopia as a difference of two lines (LogMAR = 0.2) or more between the eyes—a common clinical definition (Ciuffreda et al., 1991) and one that is used by contemporary studies of amblyopia treatment (Gunton, 2013). The three previous publications based on this same large sample defined amblyopia as a visual acuity of 20/40 (LogMAR = 0.3) or worse in one eye. However, the definition of amblyopia was not critical to data analysis in those publications, except incidentally as a descriptor.

We measured contrast sensitivity with a Pelli-Robson chart, viewed at 1 m. This chart uses letters of the same size (3°) but with decreasing contrast. In each row of the chart, the letters decrease in contrast in proportional steps from left to right, and also from top to bottom. Each observer identified as many letters as possible; his or her performance was scored according to the standard method proposed by the test designers (Pelli, Robson, & Wilkins, 1998).

We also made two measurements of binocularity. The first was a standard clinical test for stereopsis—the Randot "Circles" test (Stereo Optical Co., Chicago, IL), which was administered according to instructions supplied by the manufacturer. Observers viewed the test circles with best optical correction, but without prisms. The second test used the dichoptic quadrature motion stimulus devised by Shadlen and Carney (1986) to evaluate binocular motion integration (BMI). This test is described in detail in McKee et al. (2003). Briefly, each eye viewed a horizontal sinusoidal grating whose contrast was modulated sinusoidally at 2 Hz. The stimuli in the two eyes were spatially and temporally 90° out of phase; the direction of the phase shift determined whether the gratings appeared to move up or down. Observers were asked to judge the direction of motion for four different spatial frequencies. Prior to motion testing, the observers adjusted Risley prisms to align horizontal nonius lines at the edges of the dichoptic displays; they also matched dichoptically the contrasts of gratings presented to the two eyes.These two tests (Circles and BMI) were scored as pass-fail. If an observer had any measureable stereopsis based on the Circles test, he or she was given a pass. In the BMI test, an observer was given a pass if he or she correctly judged the direction of motion 75% of the time at the coarsest tested spatial frequency (0.38 c/°). All normal observers passed both tests. Generally, there was remarkably good agreement between the two binocular measures; 81% of abnormal observers either passed both tests or failed both tests. Abnormal observers who passed both tests were designated "binocular," while those who failed both tests were "non-binocular." This criterion was used to distinguish between binocular ($n = 21$) and nonbinocular ($n = 15$) anisometropic amblyopes for the data presented in Figure 5. Thirteen anisometropic amblyopes failed one binocular test and passed the other, so their data are not shown in Figure 5.

Statistical analysis

In each of the figures, we have fitted weighted regression lines to the scatter-plots using the iterative procedure described by Press, Flannery, Teukolsky, and Vetterling (1992); this procedure takes account of the variance of the two dependent measures being plotted, and finds those values of a and b that minimize a X^2 sum of the squared random variables, each normalized by its variance. We assumed a 20 ms standard deviation for the interocular latency difference, and a 0.1 log unit standard deviation for the interocular differences in the psychophysical measures. We explored the effect of using other standard deviation values; changes in the standard deviation produced changes in the absolute values of slopes, but did not affect our estimates of statistical significance, which are based on the ratio of the slopes, not the absolute values.

To determine whether the slopes of a pair of these best fitting lines were significantly different, we used permutation analysis (Efron & Tibshirani, 1993), to estimate the probability that the measured ratio could have arisen by chance. We first combined the data from two test groups, e.g., strabismics and anisometropes, into a single pool and then randomly assigned members

of the pool to two groups of the same size as the original test groups. We estimated the ratio of the slopes for the two randomly chosen groups and repeated this resampling process a thousand times, estimating the slope ratio for every randomly-generated pair of groups. The resulting distribution of slope ratios is an instantiation of the sampling distribution of the null hypothesis, namely that the true ratio of the slopes is 1. If our observed ratio lay outside the distribution generated by random assignment, then we assert that the probability of the observed ratio could have arisen by chance is less than 0.001 (1/1000). If the observed ratio lay within the range of ratios generated by random assignment, then we estimated how frequently a ratio this large or larger would occur by chance, e.g., if 4/1000 were as large—or larger—than the observed ratio, we assigned a probability of 0.004. All statements of significance are based on these permutation computations. The ratio of the slopes for strabismic observers and strabismic-anisometropic observers was not significantly different from 1 for any of the psychophysical measurements. So, we combined the strabismic and strabismic anisometropic groups into one group and estimated the slope for the combined strabismic group for comparison to the slope of the anisometropic group. Our permutations tested whether the slope ratio of all strabismics to anisometropes differed significantly from 1. The slopes, the natural logs of the ratios, and the p values from each of the permutation tests are shown in Appendix 1, Table 2; the relevant p value for each comparison of strabismic and anisometropic observers is cited at appropriate places within the Results section.

Results

Our observers made saccades to a bright "X" presented at one of two different eccentric (3.5°) locations while viewing monocularly with either their strong or weak eyes; targets were presented at random to the left or right of fixation. As there was no significant difference in the latencies for the two directions, we averaged the measurements from both directions for each eye. In the graphs that follow, we plot the latency difference between the eyes, rather than the average latency of the nondominant eye, to control for variables, such as age, that could affect latency independently of visual status. To parallel our use of latency differences, we used interocular log differences, i.e., the interocular ratio, of the psychophysical variables (LogMAR, log grating acuity and Pelli-Robson contrast) rather than the acuity or sensitivity of the nondominant eye, for the x axis. Generally, there is a very high correlation between the acuity or sensitivity of the nondominant eye and the acuity or sensitivity difference between the eyes, so our conclusions are not much affected by this choice. For example, the correlation between the LogMAR acuity of the nondominant eye and the interocular difference in logMAR acuity is 0.9.

The scatter plot in Figure 2 shows the interocular difference in saccadic latency as a function of the difference in LogMAR acuity for the whole abnormal population. The three abnormal subgroups, strabismics, anisometropes, and strabismic-anisometropes, that represent most amblyopes in the general population, are shown by red, green, and blue circles, and all the other abnormal observers ($n = 187$) by small gray circles. Normal observers show no mean interocular latency or acuity difference (black circle in the inset of Figure 2). As shown in Appendix 1, Table 1, the latencies of the fellow eyes of the amblyopic observers are not, on average, different from the latencies of the normal preferred eyes, so the interocular differences shown in the scatter plot primarily reflect the latencies of the amblyopic eyes. Saccadic latency increases with the increasing loss of acuity in the weaker eye, just like manual reaction time (Hamasaki & Flynn, 1981). The correlation coefficient between latency and Snellen acuity in the Hamasaki-Flynn study was 0.82, comparable to 0.75 that we obtained here for the whole abnormal sample ($n = 393$).

Figure 2 also shows best-fitting regression lines for the strabismic, anisometropic, and strabismic-anisometropic observers. The slopes for the strabismic and strabismic-anisometropic observers are virtually identical, so the two strabismic groups were combined for a statistical comparison to the anisometropic group; the slope for the combined strabismic group was significantly steeper ($p < 0.001$) than the slope for the anisometropic group. This finding indicates that saccadic latency in anisometropes has a different dependence on acuity than in strabismics, echoing our earlier conclusion, based on the psychophysical data, that strabismic and anisometropic observers show different patterns of visual loss in amblyopia (McKee et al., 2003).

The mean data (inset Figure 2) provide compelling evidence that what primarily determines the mean interocular latency difference is the mean difference in LogMAR acuity. When the acuity difference is close to zero, so is the latency difference. The mean latency differences for the nonamblyopic strabismics, anisometropes, and strabismic-anisometropes (triangles), who have a negligible interocular difference in acuity, are nearly identical to that for the normal observers, as other studies have found (Ciuffreda et al., 1978a, 1978b; Niechwiej-Szwedo et al., 2010; Niechwiej-Szwedo et al., 2012). On average, the strabismic and strabismic anisometropic amblyopes (red and blue

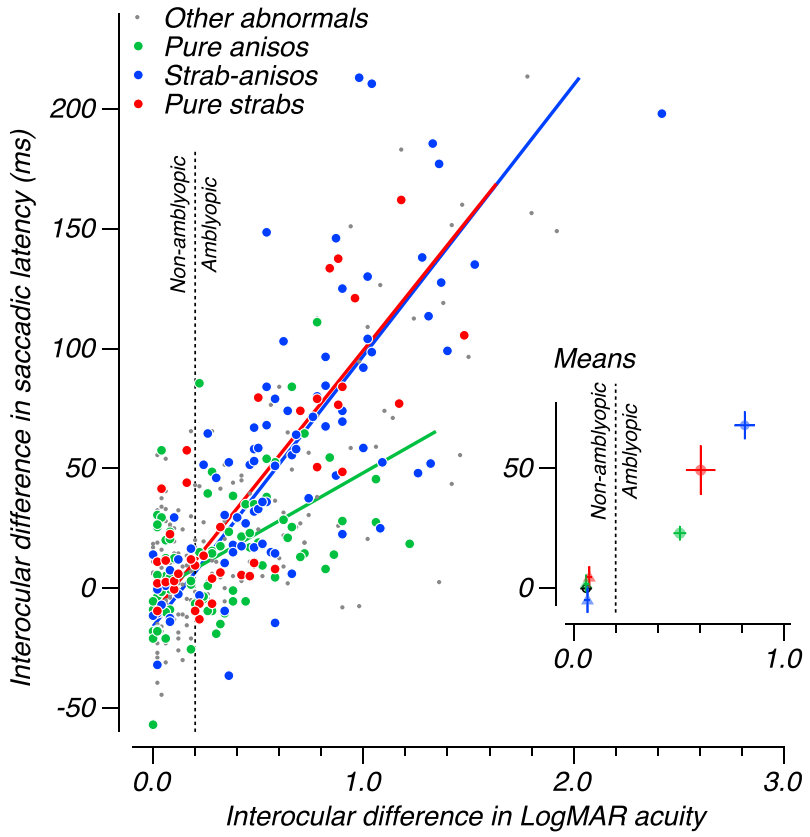

Figure 2. Interocular difference in saccadic latency plotted versus the interocular difference in LogMAR acuity (the ratio of acuities). Anisometropic observers (green circles; $n = 82$); strabismic observers (red symbols; $n = 39$); strabismic-anisometropic observers (blue symbols; $n = 85$); other abnormal observers (gray symbols; $n = 187$). The slope for all strabismic observers (strabismic and strabismic-anisometropic combined) is significantly different from the slope for the anisometropic observers ($p \leq 0.001$). Inset graph shows mean values, ± one standard error, for the nonamblyopic and amblyopic members of these three subgroups. Nonamblyopic strabismic, anisometropic, and strabismic-anisometropic observers, like normal observers (black circle; $n = 66$), have, on average, no interocular difference in latency.

symbols) have a larger difference between their eyes in LogMAR acuity than the anisometropic amblyopes (green symbols), and consequently, a larger difference in saccadic latency.

Does the strong correlation between the interocular differences in LogMAR acuity and saccadic latency mean that *resolution* affects latency? Although optotype tests, such as LogMAR and Snellen, are the standard clinical measures of resolution, they introduce a complexity into the assessment of visual resolution in amblyopes. All optotype tests rely on letter identification to estimate resolution. The measured acuity depends on the observer's ability to resolve the lines forming the letters, but it also depends on the ability to discriminate the relative orientations and positions of the lines. Because the orientation and position information need not be very precise to support letter recognition, LogMAR acuity is largely limited by resolution in normal observers. Grating acuity is a pure measure of resolution, because there is no requirement to detect anything about the grating, except its presence. In normal observers, LogMAR acuity and grating acuity give similar estimates of acuity, but in strabismic amblyopes, the loss in grating acuity is considerably less than the loss in optotype acuity (Gstalder & Green, 1971; Hess, Campbell, & Greenhalgh, 1978; Levi & Klein, 1982a, 1982b; 1985; McKee et al., 2003; Rentschler, Hilz, & Brettel, 1980). This discrepancy in strabismic amblyopes between optotype acuity and grating acuity is undoubtedly due to the additional requirements—position and orientation discrimination—required for letter identification.

To determine the contribution of resolution, per se, we examined the relationship between grating acuity and latency; Figure 3 shows the interocular differences in saccadic latency versus differences in *log* grating acuity, i.e., the ratio of acuities, for the three major abnormal subgroups (note that both amblyopic and nonamblyopic members are included in our scatterplots). Here again, there are highly significant differences ($p < 0.001$) between the slope for the combined strabismic group and the slope for the anisometropic

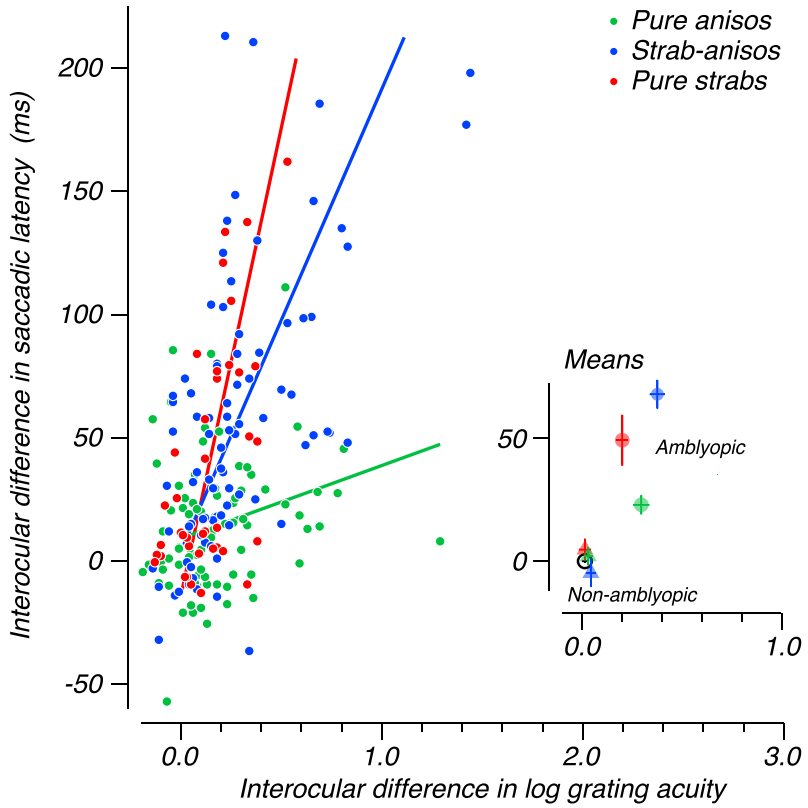

Figure 3. Interocular difference in saccadic latency plotted versus the interocular difference in log grating acuity (the ratio of acuities). Anisometropic observers (green circles; $n = 82$); strabismic observers (red symbols; $n = 39$); strabismic-anisometropic observers (blue symbols; $n = 85$). Inset shows mean values, $\pm$ 1 standard error, for the nonamblyopic and amblyopic members of these three subgroups plus the mean for normal observers. The interocular difference in log grating acuity does not predict the interocular difference in latency.

group. The latency differences for the anisometropes show only a shallow dependence on the log grating acuity difference, whereas the latency differences for the strabismics and strabismic-anisometropes increase steeply with the loss of grating acuity in the weak eye, again supporting a functional distinction between anisometropes and strabismics.

The mean data, shown by the inset in Figure 3, reveal that the latency difference for the strabismic amblyopes is roughly 23 ms longer than for the anisometropic amblyopes, although their mean interocular difference in grating acuity is slightly less than that of the anisometropes. The strabismic-anisometropic amblyopes have, on average, an interocular latency difference of more than 65 ms, about 40 ms longer than the anisometropic amblyopes. Generally, the mean latency difference does not appear to track the mean log grating acuity difference between the eyes. Thus, the strong relation between saccadic latency and LogMAR acuity shown in Figure 2 does not reflect the declining resolution (as measured by grating acuity) of the amblyopic eye, but rather a coincidental relationship between two separable characteristics of strabismic amblyopes: an abnormally long saccadic latency and their inability to identify the letters of a LogMAR chart because of poor foveal position and orientation acuity (Hess & Holliday, 1992; Levi & Klein, 1982a, 1982b; 1985; Wang, Levi, & Klein, 1998).

As we noted in the Introduction, manual reaction time and saccadic latency should depend primarily on contrast sensitivity, not acuity. One plausible explanation for the sluggish latency in strabismic amblyopes is that they are intrinsically less sensitive to contrast than anisometropic amblyopes. As shown by the scatter plot in Figure 4, contrast sensitivity is quite variable in this population. Nevertheless, there are significant differences between the slopes of the regression lines for the combined strabismic groups and the anisometropic group ($p = 0.004$). The interocular differences in log contrast sensitivity, i.e., the ratio of sensitivities, for the anisometropic, strabismic, and strabismic-anisometropic amblyopes span roughly the same range, meaning that all three groups have roughly the same contrast sensitivity. The mean values (inset Figure 4) confirm that the average differences in interocular contrast sensitivity among these groups are similar and too small to explain the large difference in interocular saccadic latency between the strabismic and anisometropic groups.

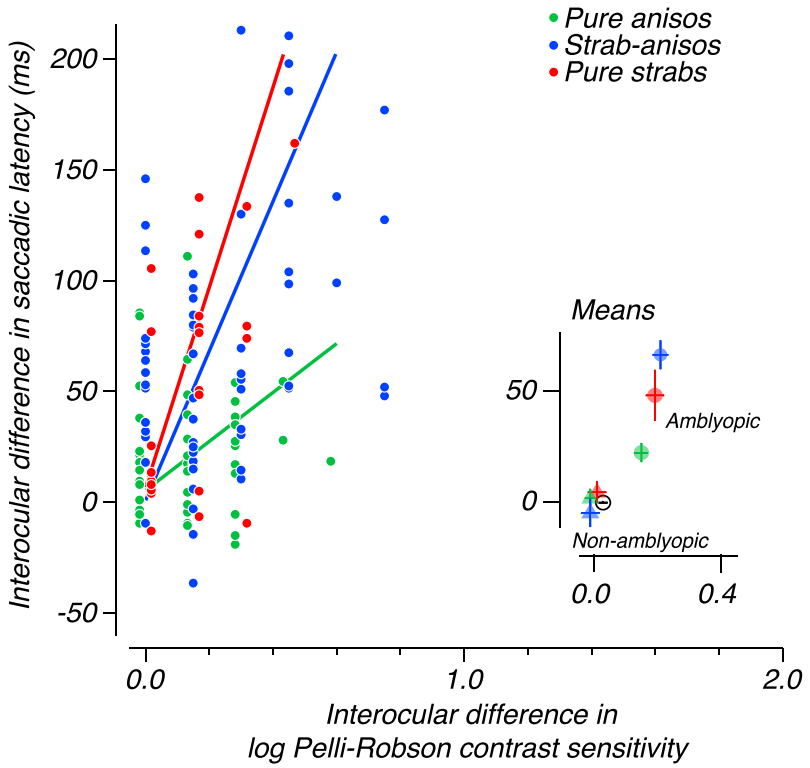

Figure 4. Interocular difference in saccadic latency plotted versus the interocular difference in log Pelli-Robson contrast sensitivity (the ratio of sensitivities). Anisometropic observers (green circles; $n = 82$); strabismic observers (red symbols; $n = 39$); and strabismic-anisometropic observers (blue symbols; $n = 85$). Inset shows mean values, ± one standard error, for the nonamblyopic and amblyopic members of these three subgroups plus the mean for normal observers. The interocular difference in log Pelli-Robson contrast sensitivity does not predict the interocular difference in latency.

Recall that the stimulus for these saccadic measurements was a large, high contrast (>40%) target that would surely lie on the asymptotic part of the reaction time functions shown in Figure 1. Near asymptote, a large decrease in contrast produces only a small change in reaction time. For example, a decrease from 40% to 20% contrast increases reaction time by only about 15 ms. Saccadic latency follows the same function of contrast as manual reaction time in normal observers (Ludwig et al., 2004; White et al., 2006). Assuming that, in amblyopes, the contrast dependence of saccadic latency resembles the manual reaction time function, the *effective* target contrast in the amblyopic eye would have to be reduced about 10-fold to increase saccadic latency by 50–70 ms. It is apparent from the means shown in Figure 4 that the interocular difference in log contrast sensitivity is far less than a log unit in the two strabismic groups, making it unlikely that poor contrast sensitivity is responsible for their prolonged saccadic latency.

We have other evidence that interocular differences in contrast sensitivity do not account for interocular latency differences. Our large study included other types of strabismic amblyopes: inconstant pure strabismics, inconstant strabismic-anisometropes, and former strabismics. To determine if amblyopia associated with any kind of strabismus affected latency, we have added these other types of strabismic amblyopes to Figure 5. Except for the inconstant strabismic-anisometropes (blue triangle), the mean latency differences of the strabismic groups are between 50–80 ms, substantially higher than the anisometropic amblyopes. Thus the increase in the saccadic latency of strabismic amblyopes is not determined by contrast sensitivity alone, since the mean differences in contrast sensitivity among the various types of amblyopes fall within a narrow range and largely overlap.

One of the main conclusions from our previous analysis of the psychophysical data was that the presence or absence of binocular vision altered the pattern of visual abnormalities in amblyopia (McKee et al., 2003). Whereas only a tiny proportion of strabismics, whether amblyopic or not, have residual binocular function, most anisometropes have binocular function as defined by our tests. Indeed, about half of anisometropic *amblyopes* passed both of our binocular tests. Nonbinocular anisometropic amblyopes tend to resemble strabismic amblyopes (Agrawal, Conner, Odom, Schwartz, & Mendola, 2006; Levi et al., 2011; McKee, 1998). To explore whether binocularity affected their saccadic latency, we divided the anisometropic

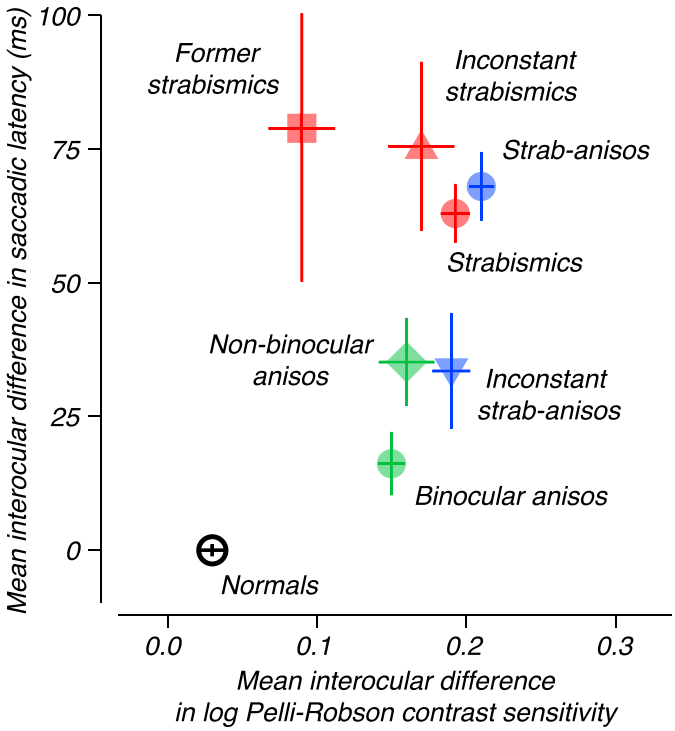

Figure 5. Mean difference in saccadic latency versus mean difference in log Pelli-Robson contrast. Except for the normal group ($n = 66$, black circle), all other groups are composed of *amblyopic* observers. In addition to strabismic amblyopes ($n = 26$, red circle), strabismic-anisometropic amblyopes ($n = 70$, blue circle), binocular anisometropic amblyopes ($n = 21$, green circle) and nonbinocular anisometropic amblyopes ($n = 15$, green diamond), we have added the means for formerly strabismic amblyopes ($n = 7$, red square) inconstant strabismic amblyopes ($n = 8$, red triangle) and inconstant strabismic-anisometropic amblyopes ($n = 20$, blue triangle). The error bars correspond to ± 1 standard error.

amblyopes into binocular and nonbinocular groups. The mean for the binocular anisometropic amblyopes (green circle) shows a small, but significant, increase in the interocular latency difference of about 15 ms compared to the normal observers—a value that is small enough that it may arise from their interocular difference in contrast sensitivity (see Pianta & Kalloniatis, 1998). However, with the loss of binocular vision, the latency difference for the anisometropic amblyopes (green diamond) doubles to roughly 30 ms, and is now roughly equal to the interocular latency difference of one of the strabismic groups. The average interocular contrast sensitivity difference for the binocular and nonbinocular anisometropes is about the same, providing additional evidence that the observed interocular differences in saccadic latency are not entirely dependent on interocular differences in contrast sensitivity.

Discussion

Compared to normal observers, strabismic amblyopes have significantly longer latencies when making a saccade with their amblyopic eyes. All types of strabismic amblyopes, whether constant or inconstant, have a latency that is, on average, 40–80 ms longer in their amblyopic eyes than in their fellow eyes. Anisometropic amblyopes also have longer latencies, but the mean difference between their eyes is about 25 ms—much less than that of the strabismic amblyopes. Interestingly, this difference in interocular latency for anisometropic amblyopes is almost identical to that found by Perdziak et al. (2014), who used a delayed saccade task to targets presented at 10° eccentricity; thus, the exact experimental paradigm is not critical to our findings. Other studies based on smaller samples have also noted that saccadic latency is longer in the amblyopic eye of strabismics than in that of anisometropes (Fukushima & Tsutsui, 1984; Mimura, Kato, Kani, & Shimo-oku, 1981; Niechwiej-Szwedo et al., 2010, 2012). The long saccadic latency in strabismic amblyopes cannot be attributed primarily to poor resolution (as measured by grating acuity) or insensitivity to contrast because anisometropic amblyopes have, on average, about the same interocular difference in grating acuity and contrast sensitivity as strabismic amblyopes (Figures 3 and 4). What then accounts for the long saccadic latency in strabismics?

Under everyday binocular viewing conditions, an amblyope would almost never initiate a saccade toward a target seen in the amblyopic eye (Popple & Levi, 2008). For one thing, there is not much to be gained by shifting the amblyopic fovea to a peripheral target. The nonamblyopic eye selects which features are of interest and where the eyes should look. The nonamblyopic eye initiates saccades, and the conjugate control of eye movements brings the amblyopic eye "along for the ride." Saccades are generally preceded by a shift in selective attention from the fovea to the saccadic target (Kowler, Anderson, Dosher, & Blaser, 1995). Because the amblyopic eye does not determine the saccadic target, it probably has little influence on selective attention during binocular viewing, and may suffer from inadequate command of attention even during monocular viewing. Several studies have found abnormalities in the control of attention by the amblyopic eye (Farzin & Norcia, 2011; Kiorpes, Pham, & Carrasco, 2012; Popple & Levi, 2008; Sharma, Levi, & Klein, 2000). Lai, McKee, Hou, and Verghese (2013) found that the amblyopic eye could use cued attention to enhance contrast sensitivity, but that the shift in attention to the cued site was delayed, compared to normal observers. Thus, the longer saccadic latencies found in amblyopes may be due to the slow shift in attention prior to saccadic initiation.

Yet, an explanation based only on poor control of attention by the amblyopic eye does not distinguish between anisometropic and strabismic amblyopes. Moreover, in the rare cases of unilateral strabismus with good vision in both eyes, the dominant eye would almost always determine the saccadic target and thus, the nondominant eye should also have poor control over attention, but saccadic latency in the nonpreferred eye of nonamblyopic unilateral strabismics is essentially normal. We require an explanation specific to strabismic amblyopes.

Strabismic amblyopes suffer from a variety of oculomotor abnormalities, other than saccadic latency. For example, the two eyes make saccades that differ in size and direction both in strabismic humans (Bucci, Kapoula, Yang, Roussat, & Bremond-Gignac, 2002; Maxwell, Lemij, & Collewijn, 1995) and strabismic monkeys (Fu, Tusa, Mustari, & Das 2007; Walton, Ono, & Mustari, 2014). The most striking oculomotor feature of a strabismic amblyope is the degree of unsteadiness when fixating with the amblyopic eye (Cuiffreda, Kenyon, & Stark, 1979; Gonzalez, Wong, Niechwiej-Szwedo, Tarita-Nistor, & Steinbach, 2012; Maxwell et al., 1995; Schor & Hallmark, 1978; Zhang et al., 2008).

Recently, Chung, Kumar, Li, and Levi (2015) used a scanning laser ophthalmoscope to measure the slow drifts and microsaccades of 28 anisometropic and strabismic amblyopes, quantifying the probable range and area of instability by a conventional metric, the bivariate contour ellipse (BCEA). They found that the BCEA in the amblyopic eye of strabismics was significantly larger than in the amblyopic eye of anisometropes, which was not significantly different from normal fixation instability. Note, however, that anisometropic amblyopes are a somewhat heterogeneous group; the absence of binocularity makes anisometropic amblyopes more similar to strabismic amblyopes (see Figure 5). Chung et al. (2015) did not distinguish between binocular and non-binocular anisometropic amblyopes, but among anisometropic children, a much greater instability (larger BCEA) is found among those who lack stereopsis than among those with stereopsis (Birch, Subraminian, & Weakley, 2012).

In a typical eye movement trace measured during fixation by a strabismic amblyope, the eye drifts away from fixation, a microsaccade follows to correct the drift, and then other microsaccades occur to correct the error generated by the first microsaccade. Normal observers also use microsaccades to correct for drift and/or microsaccade error (Wang, Yuval-Greenberg, & Heeger, 2016), but both the drift and the size of the errors in normals are much smaller than in strabismic amblyopes.

Perhaps the many microsaccades made by strabismic amblyopes (and possibly non-binocular anisometropes) during attempted fixation could explain our results (Perdziak et al., 2014). As with larger saccades, there is a refractory period between microsaccades of 150–200 ms (Carpenter, 1977; Otero-Millan, Troncoso, Macknik, Serrano-Pedraza, & Martinez-Conde, 2008). In normal observers, microsaccades, occurring shortly ($<$150 ms) before a saccadic target is presented increase the mean latency of the subsequent saccade by about 40 ms (Rolfs, Laubrock, & Kliegl, 2006). Thus, if the designated target appears within the refractory period following a microsaccade, the initiation of a subsequent saccade would be delayed. Given the increased frequency of microsaccades in the strabismic amblyope, the chance of the target appearing during a refractory period is higher.

Yet, manual reaction time shows the same correlation with the Snellen acuity of the amblyopic eye as saccadic latency (Hamasaki & Flynn, 1981), and the motor component of the refractory period of a saccade would not affect the timing of hand movements. However, the refractory period for a saccade involves a shift in attention prior to initiation (Kowler et al., 1995). Microsaccades, like larger saccades, also involve attentional shifts before initiation (Chen, Ignashchenkova, Their, & Hafred, 2015; Yuval-Greenberg, Merriam, & Heeger, 2014). Divided attention increases reaction time (Ninio & Kahneman, 1974), so perhaps when microsaccades are made immediately before the target appears, visual attention is divided between the attentional shifts accompanying the microsaccades and the attention directed to monitoring target onset, resulting in longer manual reaction times. There is evidence that, in normal observers, faster manual reaction times are

associated with a reduction in the frequency of microsaccades (Betta & Turatto, 2006; Kliegl, Rolfs, Laubrock, & Engbert, 2009). We speculate that, for the strabismic amblyope, the numerous microsaccades, made while struggling to maintain fixation, result in all types of reactions being delayed by a fluctuating wave of refractoriness and the accompanying shifts in attention. Because the degree of unsteadiness is correlated with LogMAR acuity (Birch, 2013; Chung et al., 2015), it follows that manual reaction time and saccadic latency are also correlated with LogMAR acuity.

Keywords: amblyopia, saccades, reaction time, attention, acuity

Acknowledgments

This project was initiated in 1983 by John Flynn, who assembled a group of clinical and basic scientists to consider the use of psychophysical and oculomotor measurements to classify different types of amblyopia. In 1989, we obtained NEI support for a full-fledged study of visual functions in amblyopia. Nance Wilson coordinated and directed the two data collection centers (University of California, Berkeley, and the Smith-Kettlewell Eye Research Institute). We are grateful for the continuous technical support provided by Douglas Taylor during the data collection phase. We acknowledge the invaluable contribution of Kaiser Foundation Research Institute in finding many amblyopic and at-risk observers suitable for this study, and for performing their clinical examinations. We thank Dr. Susan Day for her many contributions to the design of the clinical protocol, and for performing many of the clinical examinations. We also thank Eileen Kowler for suggesting that fixation instability might affect shifts in attention. This project was supported by National Eye Institute Grant U10 EY07657.

Commercial relationships: none.
Corresponding author: Suzanne P. McKee.
Email: suzannemckee4@gmail.com.
Address: Smith-Kettlewell Eye Research Institute, San Francisco, CA, USA.

References

Agrawal, R., Conner, I. P., Odom, J. V., Schwartz, T. L., & Mendola, J. D. (2006). Relating binocular and monocular vision in strabismic and anisometropic amblyopia. *Archives of Ophthalmology*, *124*, 844–850.

Betta, E., & Turatto, M. (2006). Are you ready? I can tell by looking at your microsaccades. *Neuroreport*, *17*, 1001–1004.

Birch, E. E. (2013). Amblyopia and binocular vision. *Progress in Retinal and Eye Research*, *33*, 67–84.

Birch, E. E., Subraminian, V., & Weakley, D. R. (2012). Is the 'flick' in anisometropia a sign of microstrabismus or fixation instability? *Journal of AAPOS*, *16*, e2.

Bucci, M. P., Kapoula, Z., Yang, Q., Roussat, B., & Bremond-Gignac, D. (2002). Binocular coordination of saccades in children with strabismus before and after surgery. *Investigative Ophthalmology & Visual Science*, *43*, 1040–1047. [PubMed] [Article]

Carpenter, R. H. S. (l977). *Movements of the eyes*. London: Pion Limited.

Chen, C. Y., Ignashchenkova, A., Their, P., & Hafed, Z. M. (2015). Neuronal response gain enhancement prior to microsaccades. *Current Biology*, *25*, 2065–2074, doi.org/10.1016/j.cub.2015.06.022.

Chung, S. T. L., Kumar, G., Li, R. W., & Levi, D. M. (2015). Characteristics of fixational eye movements in amblyopia: Limitations on fixation stability and acuity? *Vision Research, 114*, 87–99, doi.org/10.1016/j.visres.2015.01.016.

Ciuffreda, K. J., Kenyon, R. V., & Stark, L. (l978a) Increased saccadic latencies in amblyopic eyes. *Investigative Ophthalmology & Visual Science*, *17*, 697–702. [PubMed] [Article]

Ciuffreda, K. J., Kenyon, R. V., & Stark, L. (l978b) Processing delays in amblyopic eyes: Evidence from saccadic latencies. *American Journal of Optometry and Physiological Optics*, *55*, 187–196.

Ciuffreda, K. J., Kenyon, R. V., & Stark, L. (l979). Fixational eye movements in amblyopia and strabismus. *Journal of the American Optometry Association*, *50*, 1251–1258.

Ciuffreda, K. J., Levi, D. M., & Selenow, A. (l991). *Amblyopia: Basic and clinical aspects*. Boston: Butterworth-Heinemann.

Efron, B., & Tibshirani, R. J. (l993). *An introduction to the bootstrap*. New York: Chapman & Hall.

ETDRS Report. (1985). Photocoagulation for diabetic macular edema. *Archives of Ophthalmology*, *103*, 1796.

Farzin, F., & Norcia, A. M. (2011). Impaired visual decision-making in individuals with amblyopia. *Journal of Vision*, *11*(14):6, 1–10, doi:10.1167/11.14.6. [PubMed] [Article]

Fu, L., Tusa, R. J., Mustari, M. J., & Das, V. E. (2007). Horizontal saccade disconjugacy in strabismic monkeys. *Investigative Ophthalmology & Visual Science*, *48*, 3107–3114. [PubMed] [Article]

Fukushima, M., & Tsutsui, J. (1984). Visually and

auditory evoked saccadic reaction time in amblyopia. In R. Reinecke (Ed.) *Strabismus II* (443–449). New York: Grune & Stratton.

Gerin, P., Peronnet, F., & Magnard, P. (1973). Relation entre temps de reaction et alteration de la perception visuelle dans l'amblyopie fonctionnelle. [Translation: Relation between reaction time and the alteration of visual perception in functional amblyopia]. *Electroencephalography and Clinical Neurophysiology*, *35*, 49–57.

Gonzalez, E. G., Wong, A. M. F., Niechwiej-Szwedo, E., Tarita-Nistor, L., & Steinbach, M. J. (2012). Eye position stability in amblyopia and in normal binocular vision. *Investigative Ophthalmology & Visual Science*, *53*, 5386–5394. [PubMed] [Article]

Gstalder, R. J., & Green, D. G. (1971). Laser interferometric acuity in amblyopia. *Journal of Pediatric Ophthalmology*, *8*, 251–256.

Gunton, K. B. (2013). Advances in amblyopia: What have we learned from PEDIG trials? *Pediatrics*, *131*, 540–547, doi:10.1542/peds.2012-1622.

Hamasaki, D. I., & Flynn, J. T. (l981). Amblyopic eyes have longer reaction times. *Investigative Ophthalmology & Visual Science*, *21*, 846–853. [PubMed] [Article]

Hess, R. F., Campbell, F. W., & Greenhalgh, T. (1978). On the neural abnormality in human amblyopia: Neural aberrations and neural sensitivity loss. *Pflügers Archive: European Journal of Physiology, 377*, 201–207.

Hess, R. F., & Holliday, I. E. (l992). The spatial localization deficit in amblyopia. *Vision Research*, *32*, 1319–1339.

Hess, R. F., & Jacobs, R. J. (1979). A preliminary report of acuity and contour interactions across the amblyope's visual field. *Vision Research*, *19*, 1403–1408.

Hess, R. F., & Pointer, J. S. (1985). Differences in the neural basis of human amblyopia: the distribution of the anomaly across the visual field. *Vision Research*, *25*, 1577–1594.

Katz, L. M., Levi, D. M., & Bedell, H. E. (1984). Central and peripheral contrast sensitivity in amblyopia with varying field size. *Documenta Ophthalmologica*, *58*, 351–373.

Kiorpes, L., Pham, A., & Carrasco, M. (2012). Effects of attention on visual performance in amblyopic macaque monkeys [Abstract]. *Society for Neuroscience Abstracts*, 469.08.

Kliegl, R., Rolfs, M., Laubrock, J., & Engbert, R. (2009). Microsaccadic modulation of response times in spatial attention tasks. *Psychological Research*, *73*, 136–146.

Kowler, E., Anderson, E., Dosher, B., & Blaser, E. (1995). The role of attention in the programming of saccades. *Vision Research*, *35*, 1897–1916.

Lai, X., McKee, S., Hou, C., & Verghese, P. (2013). Cuing attention takes more time in strabismic amblyopes [Abstract]. *Journal of Vision*, *13*(9): 470, doi:10.1167/13.9.470. [Abstract]

Levi, D. M., Harwerth, R. S., & Manny, R. E. (1979). Suprathreshold spatial frequency detection and binocular interaction in strabismic and anisometropic amblyopia. *Investigative Ophthalmology & Visual Science*, *18*, 714–725. [PubMed] [Article]

Levi, D. M., & Klein, S. A. (l982a). Differences in Vernier discrimination for gratings between strabismic and anisometropic amblyopes. *Investigative Ophthalmology and Visual Science*, *23*, 398–407. [PubMed] [Article]

Levi, D. M., & Klein, S. A. (l982b). Hyperacuity and amblyopia. *Nature*, *298*, 268–270.

Levi, D. M., & Klein, S. A. (l985). Vernier acuity, crowding and amblyopia. *Vision Research*, *25*, 979–991.

Levi, D. M., Klein, S. A., & Aitsebaomo, P. (1984). Detection and discrimination of the direction of motion in central and peripheral vision of normal and amblyopic observers. *Vision Research*, *24*, 789–800.

Levi, D. M., McKee, S. P., & Movshon, J. A. (2011). Visual deficits in anisometropia. *Vision Research*, *51*, 48–57, doi:10.1016/j.visres.2010.09.029.

Ludwig, C. J. H., Gilchrist, I. D., & McSorley, E. (2004). The influence of spatial frequency and contrast on saccade latencies. *Vision Research*, *44*, 2597–2604.

Mackensen, G. (1958). Reaktionszeitmessungen bei Amblyopia [Translation: Reaction time in amblyopia]. *Graefes Arch Ophthalmol*, *159*, 636–642.

Maxwell, G. F., Lemij, H. G., & Collewijn, H. (l995). Conjugacy of saccades in deep amblyopia. *Investigative Ophthalmology & Visual Science*, *36*, 2514–2522. [PubMed] [Article]

McKee, S. P. (1998). Vision screening in the preschool child. In *Binocular functioning and visual acuity in amblyopia* (pp. 206–228). Bethesda, MD: Health Resources and Services Administration, HHS.

McKee, S. P., Levi, D. M., & Movshon, J. A. (2003). The pattern of visual deficits in amblyopia. *Journal of Vision*, *3*(5):5, 380–405, doi:10.1167/3.5.5. [PubMed] [Article]

Mimura, O., Kato, H., Kani, K., & Shimo-oku, M. (l98l). Saccadic latencies in amblyopia using infrared television fundus camera with two-dimensional stimuli. *Japanese Journal of Ophthalmology*, *25*, 248–257.

Niechwiej-Szwedo, D., Chandrakumar, M., Goltz, H.

C., & Wong, A. M. F. (2012). Effects of strabismic amblyopia and strabismus without amblyopia on visuomotor behavior I: Saccadic eye movements. *Investigative Ophthalmology & Visual Science*, *53*, 7458–7468. [PubMed] [Article]

Niechwiej-Szwedo, D., Goltz, H. C., Chandrakumar, M., Hirji, Z. A., & Wong, A. M. F. (2010). Effects of anisometropic amblyopia on visuomotor behavior, I: Saccadic eye movements. *Investigative Ophthalmology & Visual Science*, *51*, 6348–6354. [PubMed] [Article]

Ninio, A., & Kahneman, D. (1974). Reaction time in focused and in divided attention. *Journal of Experimental Psychology*, *103*, 394–399.

Otero-Millan, J., Troncoso, X. G., Macknik, S. L., Serrano-Pedraza, I., & Martinez-Conde, S. (2008). Saccades and microsaccades during visual fixation, exploration, and search: Foundations for a common saccadic generator. *Journal of Vision*, *8*(14):21, 1–18, doi:10.1167/8.14.21. [PubMed] [Article]

Palmer, J., Huk, A. C., & Shadlen, M. N. (2005). The effect of stimulus strength on the speed and accuracy of a perceptual decision. *Journal of Vision*, *5*(5):1, 376–404, doi:10.1167/5.5.1. [PubMed] [Article]

Pelli, D. G., Robson, J. G., & Wilkins, A. J. (1988). The design of a new letter chart for measuring contrast sensitivity. *Clinical Vision Sciences*, *2*, 187–199.

Perdziak, M., Witkowska, D., Gryncewicz, W., Przekoracka-Krawczyk, A., & Ober, J. (2014). The amblyopic eye in subjects with anisometropia show increased saccadic latency in the delayed saccade task. *Frontiers in Integrative Neuroscience*, *8*, 1–13, doi:10.3389/fnint.2014.00077.

Pianta, M. J., & Kalloniatis, M. (l998). Characteristics of anisometropic suppression: Simple reaction time measurements. *Perception & Psychophysics*, *60*, 491–502.

Piéron, H. (1914). Recherches sur les lois de variation des temps de latence sensorielle en fonction des intensités excitatrices [Translation: Research on the laws of variation of sensory latency as a function of stimulus intensity]. *Année Psychol*, *22*, 17–96.

Piéron, H. (1952). *The sensations: Their functions, processes and mechanisms*. London: Frederick Muller Ltd.

Popple, A. V., & Levi, D. M. (2008). The attentional blink in amblyopia. *Journal of Vision*, *8*(13):1, 1–9, doi:10.1167/8.13.12. [PubMed] [Article]

Press, W. H., Flannery, B. P., Teukolsky, S. A., & Vetterling, W. T. (1992). *Numerical recipes in C: The art of scientific computing*. Cambridge: Cambridge University Press.

Rentschler, I., Hilz, R., & Brettel, H. (l980). Spatial tuning properties in human amblyopia cannot explain the loss of optotype acuity. *Behavioural Brain Research*, *1*, 433–443.

Rolfs, M., Laubrock, J., & Kliegl, R. (2006). Shortening and prolongation of saccade latencies following microsaccades. *Experimental Brain Research*, *169*, 369–376.

Schor, C. M., Fusaro, R. E., Wilson, N., & McKee, S. P. (l997). Prediction of early-onset and esotropia from components of the infantile squint syndrome. *Investigative Ophthalmology & Visual Science*, *38*, 719–740. [PubMed] [Article]

Schor, C. M., & Hallmark, W. (l978). Slow control of eye position in strabismic amblyopia. *Investigative Ophthalmology & Visual Science*, *17*, 577–581. [PubMed] [Article]

Shadlen, M. N., & Carney, T. (1986). Mechanisms of human motion perception revealed by a new cyclopean illusion. *Science*, *232*, 95–97.

Sharma, V., Levi, D. M., & Klein, S. A. (2000). Undercounting features and missing features: evidence for a high level deficit in strabismic amblyopia. *Nature Neuroscience*, *3*, 496–501.

Von Noorden, G. K. (l961) Reaction time in normal and amblyopic eyes. *Archives of Ophthalmology*, *66*, 695–699.

Walton, M. G., Ono, S., & Mustari, M. (2014). Vertical and Oblique Saccade Disconjugacy in strabismus. *Investigative Ophthalmology & Visual Science*, *55*, 275–290. [PubMed] [Article]

Wang, H., Levi, D. M., & Klein, S. A. (1998). Spatial uncertainty and sampling efficiency in amblyopic position acuity. *Vision Research*, *38*, 1239–1251.

Wang, H. X., Yuval-Greenberg, S., & Heeger, D. J. (2016). Suppressive interactions underlying visually evoked fixational saccades. *Vision Research*, *118*, 70–82, doi.org/10.1016/j.visres.2015.01.009.

White, B. J., Kerzel, D., & Gegenfurtner, K. R. (2006). The spatio-temporal tuning of the mechanisms in the control of saccadic eye movements. *Vision Research*, *46*, 3886–3897.

Yuval-Greenberg, S., Merriam, E. P., & Heeger, D. J. (2014). Spontaneous microsaccades reflect shifts in covert attention. *Journal of Neuroscience*, *34*, 13693–13700.

Zhang, B., Stevenson, S. S., Cheng, H., Laron, M., Kumar, G., Tong, J., & Chino, Y. M. (2008). Effects of fixation instability on multifocal VEP (mfVEP) responses in amblyopes. *Journal of Vision*, *8*(3):16, 1–14, doi:10.1167/8.3.16. [PubMed] [Article]

Appendix 1

Category	Preferred eye	Nonpreferred eye
Normal ($n = 66$)	223 ± 3	223 ± 3
Anisometropic amblyopes ($n = 49$)	219 ± 3	242 ± 4
Strabismic amblyopes ($n = 26$)	215 ± 4	264 ± 9
Strab-Aniso amblyopes ($n = 70$)	215 ± 3	284 ± 5
Former Strab amblyopes ($n = 7$)	211 ± 15	290 ± 26
Inconstant strabismic-amblyopes ($n = 8$)	222 ± 9	298 ± 19

Table 1. Mean latencies (±1 *SE*) in milliseconds for horizontal saccades.

Type	All anisometropic	All strabismic	ln (ratio)	*p* value
LogMAR acuity	50 ± 8.4	111.1 ± 5.1	0.80	< 0.001
Grating acuity	29.6 ± 9.9	205.9 ± 12.8	1.94	< 0.001
Pelli-Robson	110.5 ± 26.1	350.9 ± 29.7	1.16	0.004

Table 2. Slopes and ratios.