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# Characteristics of fixational eye movements in amblyopia: Limitations on fixation stability and acuity?

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ABSTRACT

Persons with amblyopia, especially those with strabismus, are known to exhibit abnormal fixational eye movements. In this paper, we compared six characteristics of fixational eye movements among normal control eyes ($n = 16$), the non-amblyopic fellow eyes and the amblyopic eyes of anisometropic ($n = 14$) and strabismic amblyopes ($n = 14$). These characteristics include the frequency, magnitude of landing errors, amplitude and speed of microsaccades, and the amplitude and speed of slow drifts. Fixational eye movements were recorded using retinal imaging while observers monocularly fixated a 1° cross. Eye position data were recovered using a cross-correlation procedure. We found that in general, the characteristics of fixational eye movements are not significantly different between the fellow eyes of amblyopes and controls, and that the strabismic amblyopic eyes are always different from the other groups. Next, we determined the primary factors that limit fixation stability and visual acuity in amblyopic eyes by examining the relative importance of the different oculomotor characteristics, adding acuity (for fixation stability) or fixation stability (for acuity), and the type of amblyopia, as predictive factors in a multiple linear regression model. We show for the first time that the error magnitude of microsaccades, acuity, amplitude and frequency of microsaccades are primary factors limiting fixation stability; while the error magnitude, fixation stability, amplitude of drifts and amplitude of microsaccades are the primary factors limiting acuity. A mediation analysis showed that the effects of error magnitude and amplitude of microsaccades on acuity could be explained, at least in part, by their effects on fixation stability.


## 1. Introduction

Amblyopia is a developmental abnormality resulting from physiological alternations in the visual cortex that impairs form vision (Ciuffreda, Levi, & Selenow, 1991). It affects 2–4% of the population, and is usually associated with anisometropia, strabismus, or both conditions concurrently. Besides impaired form vision, amblyopia, especially when it is associated with strabismus, is often accompanied by oculomotor anomalies that include eccentric and unsteady fixation (Schor & Hallmark, 1978; Zhang et al., 2008), low pursuit gain (Bedell, Yap, & Flom, 1990; Schor, 1975) and abnormal saccadic eye movements (reduced saccadic amplitudes, increased saccadic latencies and increased number of corrective saccades: Ciuffreda, Kenyon, & Stark, 1978; Schor, 1975). In this study, our focus is on fixational eye movements.

For people with normal vision and normal oculomotor control, their eyes are constantly in motion even when they attempt to maintain stable fixation on a visual target. These involuntary eye movements during fixation comprise of tremors, slow drifts and microsaccades. Tremors are high-frequency oscillatory motion of the eye and are difficult to measure with most of the conventional eye movement measuring devices. However, tremors are generally considered to serve no functional purpose. Slow drifts are slow movements of the eyes, usually with an amplitude <10 arc min (e.g. Ditchburn & Ginsborg, 1953; Krauskopf, Cornsweet, & Riggs, 1960; Nachmias, 1961; Ratliff & Riggs, 1950; Steinman et al., 1975). Microsaccades are miniature saccades, or the fast eye movements that are interspersed among the slow drifts. They usually occur between 0.5 and 3 per second, with an amplitude <30 arc min (e.g. Cherici et al., 2012; Ditchburn & Ginsborg, 1953; Ratliff & Riggs, 1950; Sansbury et al., 1973; Steinman et al., 1975).

For people with amblyopia, it is well known that the speed of slow drifts is higher than in normal eyes (Bedell, Yap, & Flom, 1990; Ciuffreda, Kenyon, & Stark, 1979; Schor & Hallmark, 1978) and that the amplitude of slow drifts is also larger (Ciuffreda, Kenyon, & Stark, 1979; Schor & Hallmark, 1978). As for microsaccades, Ciuffreda et al. (who referred to them as *saccadic intrusions*) reported a frequency of occurrence of ~1 per second (range: 0.3–2

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per second), with an increased frequency and amplitude when the amblyopic eye monocularly fixates a visual target. Schor and Hallmark (1978) and Schor and Flom (1975) also reported similar ranges of frequency of microsaccades, which too, were higher than the values observed in normal controls. In contrast, a recent study reported no difference in the frequency or the amplitude of microsaccades among amblyopic and the non-amblyopic fellow eyes of amblyopes and normal control eyes (González et al., 2012). However, these studies examining the characteristics of fixational eye movements span several decades and used different techniques and devices (with different precision and resolution capabilities) for measuring fixational eye movements, thus it is unclear how comparable the findings are across different studies. Therefore, the *first goal* of this study was to use a novel method of measuring eye movements, *viz.*, retinal imaging, combined with a cross-correlation technique (Kumar & Chung, 2014; Stevenson & Roorda, 2005) to evaluate the various characteristics of fixational eye movements in amblyopic observers.

A characteristic of fixational eye movements that is not captured by the properties of slow drifts and microsaccades is the variability of eye positions during fixation, or, the *fixation stability*. It has long been documented that amblyopic eyes have poor fixation stability (Schor & Hallmark, 1978; Zhang et al., 2008). However, to date, it is unclear what factors limit fixation stability in amblyopic eyes. González et al. (2012) claimed that the fixation instability in amblyopic eyes is due to slow drifts, as they found no difference in terms of the frequency and amplitude of microsaccades between their amblyopic and control groups. However, our recent work examining the relationship between fixation stability and fixational eye movements in people with macular disease suggests that the amplitude of microsaccades is the primary contributor to fixation instability (Kumar & Chung, 2014). Therefore, it is conceivable that fixation stability in persons with amblyopia is limited by the amplitude of microsaccades, just as in people with macular disease. As the *second goal* of this study, we sought to determine the primary factors that limit fixation stability in amblyopic eyes. This information is important if fixation stability is found to limit functional vision (see below). In this case, an effective treatment protocol to improve functional vision in amblyopic eyes should target the specific oculomotor components that are the major factors limiting fixation stability.

Form vision is impaired in the amblyopic eyes. Given that fixational eye movements are abnormal in amblyopic eyes, a logical question is whether the abnormal fixational eye movements limit form vision in persons with amblyopia. Many aspects of vision in the amblyopic eyes are reported to be affected by fixational eye movements, including but are not limited to: positional acuity (Demanins & Hess, 1996; Hess & Holliday, 1992; Levi & Klein, 1982; 1983; 1985), displacement thresholds (Levi, Klein, & Aitsebaomo, 1984), contour integration (Hess & Demanins, 1998; Levi et al., 2007), and crowding (Bonneh, Sagi, & Polat, 2007; Flom, Weymouth, & Kahneman, 1963; Hess & Jacobs, 1979; Levi & Klein, 1985; Song, Levi, & Pelli, 2014). However, since reduced visual acuity is the sine qua non of amblyopia, we were most interested in examining which characteristic(s) of fixational eye movements (if any) is the primary factor limiting acuity in persons with amblyopia. In addition, we were interested to determine whether there exists a positive correlation between visual acuity and fixation stability. Such a correlation is observed in people with macular disease (Reinhard et al., 2007; Tarita-Nistor et al., 2011), and there are some recent attempts to test whether such a relationship also exists in amblyopic eyes, with inconsistent results. On one hand, based on the results of 13 adult amblyopes (strabismic [$n = 5$], anisometropic [$n = 4$] and mixed [$n = 4$]), González et al. (2012) concluded: "For the amblyopia group, visual acuity and fixation stability did not exhibit significant correlations." (p. 5391). On the other hand, Subramanian, Jost, and Birch (2013) obtained measurements from a large sample of children with amblyopia and found a significant positive correlation between visual acuity and fixation stability when data were considered for all groups together. The correlation was the strongest for the strabismic amblyopia group ($p = 0.002$, $n = 7$), followed by the mixed amblyopia group ($p = 0.04$, $n = 24$), but was not significant for the anisometropic amblyopia group ($p = 0.26$, $n = 20$). The question of whether a positive correlation exists between visual acuity and fixation stability is important because if such a correlation really exists, then treatment for amblyopia may benefit from procedures aimed at improving fixation stability. We note that correlation does not imply causation, and that several previous studies have addressed the role of fixational eye movements in limiting acuity (Ciuffreda, Kenyon, & Stark, 1979; Hess, 1977; Schor & Flom, 1975) in a handful of amblyopic observers. The *third goal* of the study was to determine the oculomotor parameters (including fixation stability) that are the primary factors limiting visual acuity. To achieve this goal, we used robust statistical tools that go beyond simple correlational measurements.

## 2. Methods

Forty-four adults participated in this study. Twenty-eight of them had amblyopia, defined as a difference in the best-corrected visual acuity between the two eyes of $\geqslant 0.2$ logMAR (the logarithm of the minimum angle of resolution) and that the better-seeing eye (the *fellow eye*) had an acuity of at least 0.0 logMAR (equivalent to 20/20 Snellen acuity) or better. The other 16 were control observers with normal vision (acuity in each eye at least 0.0 logMAR and normal stereoacuity). Among the 28 observers with amblyopia, 14 had amblyopia due to anisometropia (defined as a difference in refractive corrections of >0.75D spherical equivalent) with no strabismus; and 14 had amblyopia due to strabismus (four of them also had anisometropia), as revealed using the standard cover test procedure. Details of the observers' characteristics are given in Table 1. All observers gave written informed consent before the commencement of data collection. This research followed the tenets of the Declaration of Helsinki and was approved by the Committee for Protection of Human Subjects at the University of California, Berkeley.

We elicited fixational eye movements by asking observers to maintain steady fixation on the center of a highly visible 1° cross, presented in the primary gaze of the observers, using a scanning laser ophthalmoscope (SLO, Rodenstock, Germany). The SLO, with a field of view of 32° by 24°, uses laser beams (a red Helium–Neon [632 nm] and a near-infrared wavelength that is invisible to human eyes) to present stimuli and to image the retina simultaneously, thus the fixation cross appears as a high-contrast red cross on a dimmer background. Observers were instructed to look at the center of the fixation cross while keeping the eye as still as possible, for a duration of 30 s. Although both eyes of observers remained open throughout testing, only the tested eye could see the fixation cross. Regardless of which eye was the amblyopic eye, we adhered to the same testing order. We first tested the right eye for 10 s as a practice trial (data of which were excluded for analysis). Then we began the actual data acquisition according to the following order: right eye, left eye, left eye, right eye, right eye and left eye, such that three 30-s trials were obtained from each eye. Retinal images were captured continuously at 30 Hz for the duration of each trial using a frame grabber (Meteor-II PCI Frame Grabber, Matrox Electronic Systems Ltd., Canada) interfaced with a TV-One CORIO scan converter (CS-450 Eclipse, Erlanger, KY). Software for generating and presenting the fixation cross, and controlling the flow of the experiment was custom-written in MATLAB