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Publication Date

2025-05-01

DOI

10.1016/j.visres.2025.108588

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The impact of eye movements on amblyopic vision: A mini-review

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ARTICLE INFO

Keywords:

Amblyopia
Eye Movements
Eye-tracking
Fixation Instability
Visual acuity
Strabismus
Anisometropia

ABSTRACT

Our eyes move constantly to search for and inspect objects of interest, to track moving objects, to read along a line of text and to prevent image fading. However, persons with amblyopia (PWA), in addition to a broad array of visual deficits, have abnormal eye movements. This review briefly describes the types of eye movements deficits in persons with amblyopia and how they are measured. We then go on to discuss what is known about how abnormal eye movements in persons with amblyopia affect their vision. Finally, we ask whether the abnormal eye movements are amenable to amblyopia treatment and whether they can be used to diagnose/classify amblyopia.

1. Introduction

Our eyes are in constant motion. We shift our gaze to search for and inspect objects of interest in our peripheral visual field, to track moving objects, to read along a line of text and to prevent image fading. Even when we try to fixate an object intently, our eyes are in motion. Over the last decade or so there has been a major re-thinking about the role of eye movements (EMs) in visual perception in persons with normal vision (Martinez-Conde, Otero-Millan, & Macknik, 2013; Rucci & Victor, 2015; Scholes, McGraw, Nystrom, & Roach, 2015).

Amblyopia, a neurodevelopmental condition that results in physiological alterations in the visual pathways and impaired vision in one eye, less commonly in both, and is characterized by abnormal eye movements and a broad range of neural, perceptual, oculomotor and clinical abnormalities (Levi, 2020). How do these eye abnormalities impact amblyopic vision? This is not a trivial question; it's a chicken and egg problem. Persons with amblyopia have impaired vision. Do the visual impairments affect their eye movements or do the abnormal eye movements affect their vision? There is a long history of studying eye movements in amblyopia, with a host of studies in the 1970's and 80's. There seems to have been a resurgence of interest over the last 20 years or so. In this review we briefly describe how eye movements are measured, the types of eye movements and how these are affected in persons with amblyopia. We then go on to discuss what is known about how abnormal eye movements in persons with amblyopia affect their vision. Finally, we ask: (1) Are the abnormal eye movements amenable to amblyopia treatment?; and (2) Can EMs be used to diagnose/classify

amblyopia? We note that there are several excellent recent reviews of specific eye movement abnormalities in persons with amblyopia (e.g., Ghasia & Wang, 2022; Niechwiej-Szwedo, Colpa, & Wong, 2019; Verghese, McKee, & Levi, 2019; Wong, 2023). Our aim in this review is to provide a broad and comprehensive assessment of the extant studies and to try to provide some insights into how the abnormal eye movements may influence vision in persons with amblyopia.

2. Measuring eye movements in Humans

Interest in understanding how the eyes move and their effects on visual perception can be dated back to the time of Aristotle (Wade, 2010), although the method for evaluating eye movements was limited to direct observation of the eyes back then. A complete review of all the methods that scientists have used to track changes in eye or gaze position is outside the scope of this paper, but some of the prehistoric methods include the use of afterimages (Brock & Givner, 1952), the use of mercury for imaging the front of the eye (Barlow, 1952) and the optical lever contact lens system (Ratliff & Riggs, 1950). The earliest precise non-invasive method was described by Dodge (1901) and Worth (1921) who used the reflection of a light from the cornea onto a photographic plate to record the eye movement on the plate.

The earliest measurements in relation to oculomotor responses in persons with amblyopia were first described by Claude Worth, the pioneering British ophthalmologist (Worth, 1921). "He suggested a very simple and direct method for this observation: Place the patient in a dark room. Throw the light of an ophthalmoscope first into his good eye while

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he is looking at this light. Note the reflection of the ophthalmoscope light on the cornea of the good eye. Then cover this eye and note whether the amblyopic eye can now fixate the light so as to bring the corneal reflection into a corresponding position. By means of this method, eccentricities of 2 degrees or more can readily be detected" (Brock & Givner, 1952). Worth suggested that fixation with the amblyopic eye might be non-foveal, a condition described clinically as eccentric fixation. Von Noorden & Burian (1958) followed up on this idea using electro-oculography (EOG). This method was also employed by Mackensen (1957a) and others. (We discuss eccentric fixation further below). The following is a brief summary of the methods that are currently in use for research, and many of the studies that we cite in this paper used one of these methods.

2.1. Methods to measure eye movements in Humans

In this section we briefly describe the various noninvasive methods for measuring eye movements and their advantages and disadvantages (Table 1). For amblyopia, Table 1 includes "retinal locus", i.e., the ability of the method to determine whether the individual uses the fovea for fixation, or whether they fixate eccentrically. Additionally, other issues may be important for use in amblyopia, e.g., the ease of use for clinical applications and the ability to stabilize the retinal image to address research questions.

2.1.1. Electro-oculography (EOG)

EOG measures the electrical potential difference between the front (cornea) and back (retina) of the eye. The technique involves placing electrodes at the outer canthi of the two eyes to detect the voltage changes that occur when the eyes make conjugate movements horizontally. Horizontal eye vergence could also be detected with a third electrode placed on the forehead as a reference. However, it's not very good for measuring vertical eye movements because of difficulty in identifying a proper location for electrodes. It is non-invasive, relatively inexpensive, simple and easy to use in children or poorly cooperative patients, and does not require a bite bar. However, its resolution can

only be as good as about 1 deg (Leigh, 2015; Cornsweet & Crane, 1973) and is limited by electrical and electromyographic noise. Moreover, it requires frequent calibration and the measurements are affected by ambient light levels.

2.1.2. Infra-red limbus tracking

This method tracks the position of the limbus (the border between the sclera and the cornea) and compares the differential amount of light reflected by the sclera and the iris as the eye moves. Infra-red light is usually used as the source of illumination. The source(s) of illumination and the detectors can be mounted on a spectacle frame. This method is non-invasive, simple and easy to set up, and is an excellent option for measuring horizontal eye movements, but not for vertical eye movements because the upper eyelids often cover part of the iris, making it impossible to track the position of the upper limbus. An alternative solution is to track the position of the upper or the lower eyelid.

2.1.3. Dual Purkinje image tracker

The dual Purkinje image tracker derives eye position by comparing the first and the fourth Purkinje images. Its spatial resolution can reach 1–1.5 arc min (Holmqvist & Blignaut, 2020), with an accuracy of approximately 1 arc min (Cornsweet & Crane, 1973). However, it is expensive, difficult to use and maintain, susceptible to the lens wobbling effect and often requires subjects to use a bite bar.

2.1.4. Magnetic search coil technique

This has been considered as the gold standard for measuring eye movements because of its high spatial (< 0.1 deg) and temporal (> 1 kHz) resolution, and its capability to measure torsional rotations of the eyes, in addition to simply horizontal and/or vertical eye movements. The cons of the magnetic search coil technique are subjects' discomfort in wearing a scleral annulus (which limits the duration of data collection), the cost of the magnetic field coils and the scleral annulus, the need to use topical anesthetic drops on the cornea, potential slippage of the annulus and corneal abrasions. While this method has been used in amblyopic monkeys (Foeller & Tychem, 2002), we are not aware of any

Table 1
Noninvasive methods for measuring eye movements.

Method	Spatial resolution	Accuracy	Temporal resolution	Retinal locus	Image stabilization	Ease of use	Remarks
EOG	1–2 deg	1–2 deg	250–1000 Hz	X	X	✓	Relatively easy to use, and is widely used in clinical environment
IR limbus tracking	0.5–1 deg (can get down to a few arc min when head is restrained)	1 deg	50–500 Hz	X	X	✓	
Dual Purkinje Image tracker	1 arc min (0.0167 deg)	1 arc min (0.1–0.5 deg?)	500–1000 Hz	X	✓	X	Head immobilization (bite bar) is often required
Magnetic search coil	1 arc min (0.0167 deg)	< 0.1 deg	1000–2000 Hz	X	X	X	Excellent for measuring torsional eye movements
Video-based systems	0.1–1 deg	0.1–1 deg	Depends on the model, but most operate at 60–120 Hz, high-end systems up to 1000–2000 Hz	X	X✓	✓	video-based systems are used for gaze contingent studies; but stabilization is imperfect because the system needs time to update the screen after the completion of a saccade. Typical values of the delay reported in the literature ranges between 10 and 30 ms. Participants reported that they could "cheat" by blinking rapidly and repeatedly to break the stabilization.
Research-grade scanning laser ophthalmoscopes (SLO)	0.1–1 arc min (depends on field size)	0.1–1 arc min	Depends on the analysis method, but 480 to 960 Hz have been reported in the literature	✓	✓	X	Head immobilization (bite bar) is often required, especially with adaptive-optics SLO (AO-SLO) that has a field size of ~ 1 deg
Commercial microperimeters	2–3 arc min (<0.05 deg)	2–3 arc min (<0.05 deg)	25–30 Hz (unless special methods are used to analyze data)	✓	X	✓	Unless special methods are used to interface with the device, otherwise only fixation stability can be measured, but not eye movements

X's = Negative, ✓ = Positive.

studies using this method to measure eye movements in humans with amblyopia, likely because of the cons mentioned above.

2.1.5. Video-based systems

Video-based systems have gained popularity and are currently widely used in basic science and applied research (e.g. marketing research). They are simple to use, relatively more affordable than other systems, cause minimal discomfort to subjects, and have reasonably good resolution (0.5° or better). These systems operate by tracking the corneal reflex and/or the pupil center of subjects. Therefore, they are prone to artifacts caused by changes in pupil size (e.g. when illumination changes) or shape. Some systems also compare the relative movement of the pupil center with respect to the first Purkinje image (the reflex of the anterior surface of the cornea); however, such comparisons may not be linearly related to eye position because the corneal surface is not spherical and the center of the rotation of the eye does not coincide with the center of curvature of the cornea. Some of these systems are head-mounted and are often bulky, heavy and could cause slippage; however, on the other hand, they can be used in mobile settings. Recently, a company (Pupil Labs) offers a new line of eye trackers that do not require calibration, are easy to use, portable and low-cost, but, as a trade-off, the resolution of their eye trackers is lower. In one study comparing the accuracy of eye tracking, the average spatial accuracy of eye tracking was found to be 0.82 deg for the Pupil Labs glasses, in comparison to 0.57 deg for the Eyelink 1000 eye-tracker (Ehinger, Gross, Ibs, & Konig, 2019).

2.1.6. Research-grade scanning laser ophthalmoscopes (SLO)

SLO was originally developed as an ophthalmic device to capture detailed images of the retina. It uses a laser beam to scan the retina point by point, therefore, each point is essentially imaged at a different time, and any eye motion during scanning will be embedded in the retinal image, causing distortions to the veridical retinal image. If the relative position of each scanned point or line of points with respect to the veridical retinal image (the “ground truth”) is known, then the eye motion that is embedded during scanning can be recovered. This is the principle of strip-based analysis of eye position using SLO (Mulligan, 1997; Stevenson & Roorda, 2005). In other words, the SLO can be used as an eye tracker, especially for studying fixational eye movements. An advantage of using SLO as an eye tracker is that it does not require eye position calibration. Research-grade SLOs are usually custom-built, allowing the export of videos, and often offering the option for stabilizing the image of a visual target on a specific location on the retina, making them ideal for conducting retinal stabilization studies to examine the effect of eye motion on visual functions. The resolution of custom-built SLOs depends on the desired field of view but usually is very high, for example, the resolution of an adaptive-optics SLO (AOSLO) with an imaging field of 1 deg could reach 0.12 arc min, much smaller than the diameter of a single cone at the fovea, although this comes at the expense of the field of view. Using the strip-based analysis, eye positions can be extracted at high sampling frequencies (published studies have used frequencies ranging from 480 to 960 Hz, but higher sampling frequencies are possible). However, the captured retinal images are prone to movements of the head, especially when the field of view is tiny. Therefore, if very high resolution is desired, often subjects would have to be placed on a bite bar. Also, because the SLO cannot capture retinal images outside its field of view, it is not an ideal device for measuring larger eye movements such as saccades larger than a few degrees in amplitude. SLOs are expensive and custom-built ones are difficult to operate and data analyses require good technical skills and could be time consuming. Also, almost all SLOs are monocular devices and thus cannot be used to study binocular eye movements (there are a few binocular units). Note that there is a new commercial SLO that is marketed as a retinal eye movement monitor (TSLO, C. Light Technologies) which might mitigate some of the cons of using a SLO as an eye tracker.

2.1.7. Commercial microperimeters

There are many commercially available ophthalmic retinal imaging devices that make use of the SLO technology, including the optical coherence tomographer (OCT) and microperimeters. The advantages of these commercial systems are that they are easy to use, offer a large field of view (30 deg or larger) with spatial resolution as fine as 2–3 arc min (although not as good as research-grade SLOs). On the other hand, because the sampling frequency of these devices is usually only 25–30 Hz, and users cannot program the devices to present a moving or a jumping target, commercial microperimeters are not useful for measuring eye movements, except for fixation stability. Indeed, most microperimeters include some measures of fixation stability. However, because manufacturers almost never provide a built-in function for users to export the videos of the captured retinal images, commercial systems cannot take advantage of the brute-force strip-based analysis to sample eye positions at a much higher sampling frequency than what the systems offer. Fig. 1 shows examples of fixation locations superimposed on the fundus of a normal observer and each eye of an observer with strabismic amblyopia, while attempting steady fixation obtained using a MAIA (Centervue, Padova, Italy) microperimeter. Additional details are provided below.

A survey of the literature reveals that almost all studies on eye movements in persons with amblyopia used one of these methods to measure eye movements: EOG, infra-red limbal tracking, video-based systems, SLOs and microperimeters. We are not aware of studies that used the Dual Purkinje Image tracker or the search coil method in amblyopia, most likely because of the difficulty in using them and that they are not as widely used as other methods because of their costs.

3. Types of eye movements and how they are affected in persons with amblyopia (PWA)

The abnormal eye movements of PWA have been widely studied and many of these abnormalities have been comprehensively discussed in chapters (Ciuffreda, Levi & Selenow, 1991; Schapero, 1971) and in more recent focused reviews on specific topics (e.g., Ghasia & Wang, 2022; Niechwiej-Szwedo et al., 2019; Verghese et al., 2019; Wong, 2023). Table 2 below provides a (simplified and somewhat selective) compilation of the different types of eye movement abnormalities that have been reported in the extant literature, and we briefly discuss these below. We note that many older studies often did not differentiate between the eye movements of individuals with anisometropic vs strabismic amblyopia. We attempt to clarify differences where they have been reported. An additional complication is that patients with early onset esotropia frequently have abnormal eye movements regardless of whether they are amblyopic or not, and often the age of onset is unknown or unreported.

3.1. Saccades

These rapid movements of the eyes shift the gaze from one point to another. We use saccades to read or to search for and inspect objects of interest in our peripheral visual field.

In PWA, when fixating with the amblyopic eye, saccadic movements may:

- i) be delayed (i.e., have increased latency relative to their fellow eye or that of controls: (Chow, Nallour Raveendran, Erkelens, Babu, & Thompson, 2022; Ciuffreda, Kenyon, & Stark, 1978a, 1978b; Gambacorta, Ding, McKee, & Levi, 2018; Mackensen, 1958; Niechwiej-Szwedo, Goltz, Chandrakumar, Hirji, & Wong, 2010; Niechwiej-Szwedo, Goltz, Colpa, Chandrakumar, & Wong, 2017). The interocular difference in saccadic latency is found to increase with larger differences in acuity between the two eyes (McKee, Levi, Schor, & Movshon, 2016). Increased latencies are not limited to saccadic eye movements. PWA also demonstrate

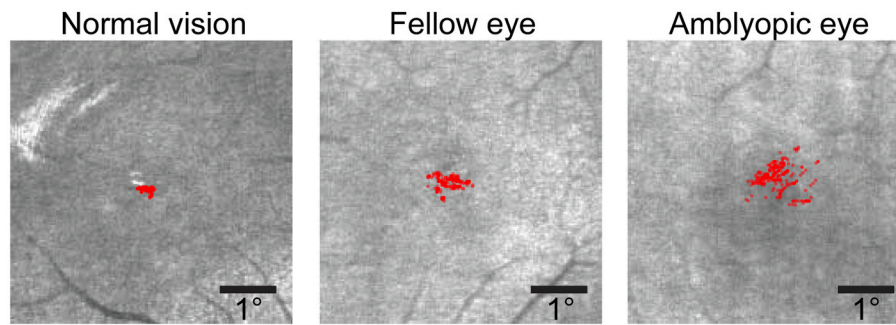


Fig. 1. Fixation locations (red dots) superimposed on the fundus of a normal observer (V.A. 20/16 left panel), and the dominant (V.A. 20/16–2 center panel) and amblyopic eye (20/64 right panel) of a strabismic amblyope, while attempting steady fixation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

prolonged manual reaction times (([Hamasaki and Flynn 1981](#)); [Gambacorta et al., 2018](#); [Levi, Harwerth, & Manny, 1979](#); [Mackensen, 1958](#); [Pianta & Kalloniatis, 1998](#); [Roberts, Cyerman, Smith, Kiorpes, & Carrasco, 2016](#)). Interestingly, in a small sample, [Gambacorta et al. \(2018\)](#) found that when the “effective contrast” of the stimuli to the two eyes was equalized (i.e., scaled in threshold units), the asymptotic reaction time of anisometropic but not strabismic amblyopes were similar in the two eyes. These authors hypothesized that there may be two separable effects on saccadic reaction time: (i) difficulty with directing actions to a target, related to disengagement of attention at the fovea, resulting in delays in both saccadic and manual reaction times, and (ii) an additional delay in saccadic reaction times when viewing with the amblyopic eye of strabismics, because of the motor refractory period from a previous fixational eye movement. An additional potential source of delay is the increased latency or sluggish neural responses of the amblyopic eye, as commonly seen in visually evoked cortical responses ([Levi & Harwerth, 1978](#); [Levi et al., 1979](#); [Levi & Walters, 1977](#); [Manny & Levi, 1982](#)).

- ii) follow the normal “main sequence” once initiated (i.e., saccadic amplitude/duration/peak velocity relationship), indicating normal motor control of saccadic eye movements ([Ciuffreda et al., 1978a, 1978b](#); [Ciuffreda, Levi & Selenow, 1991](#); [Niechwiej-Szwedo, Chandrakumar, Goltz, & Wong, 2012](#); [Niechwiej-Szwedo et al., 2010](#); [Perdziak, Witkowska, Grynciewicz, Przekoracka-Krawczyk, & Ober, 2014](#)), although it has been reported that the saccadic response gains (saccadic amplitude/target displacement) are lower and the peak velocity on the plateau region of “main sequence” is slightly higher when compared with controls ([Chow et al., 2022](#)).
- iii) show dysmetria (i.e., undershooting or overshooting the target). While saccadic dysmetria may occur in patients with cerebellar damage ([Kim, Kim, & Lee, 2023](#); [Xu-Wilson, Chen-Harris, Zee, & Shadmehr, 2009](#)), it has also been reported in patients with amblyopia ([Ciuffreda, Kenyon, & Stark, 1979b](#); [Mackensen, 1957b](#); [Schor, 1975](#)), possibly due to fixation instability or perceptual distortions of perceived visual space ([Barrett, Pacey, Bradley, Thibos, & Morrill, 2003](#); [Bedell & Flom, 1981](#); [Fronius, Sireteanu, & Zubcov, 2004](#)). Interestingly, PWA may also exhibit abnormal auditory localization ([Richards, Goltz, & Wong, 2019](#); [Wong, 2023](#)).
- iv) under binocular viewing conditions, [Maxwell, Lemij and Colle-wijn \(1995\)](#) reported that persons with “deep” amblyopia (acuity in the amblyopic eyes was reduced to counting fingers in 10 out of 11 of their participants) exhibited an apparent disconjugacy of saccades (with the maximum difference in saccade amplitude of the 2 eyes less than 10 % of the target amplitude). These authors postulated that the disconjugacy does not happen haphazardly,

instead, it is the result of “incoherent” oculomotor adaptation. We are uncertain as to what the authors mean by incoherent, however, an alternate view may be that the apparent disconjugacy is a consequence of non-linear interactions between the version and vergence movements ([Ciuffreda, K., personal communication](#)).

3.2. Smooth Pursuits

These are slow continuous movements of the eye. The primary function of pursuits is to keep the image of a moving stimulus on (or near) the fovea. We use pursuit eye movements to track a speeding car or a fast-moving baseball, which allow us to (almost) stabilize the image on the retina. In PWA, when viewing with the amblyopic eye, several abnormalities have been reported:

- i. Delayed initiation: Given the prolonged manual and saccadic reaction times, it is perhaps not surprising that when attempting to pursue a moving target, PWA show a delay in initiating the pursuit eye movement. Adults with anisometropic amblyopia show an approximately 20 msec delay when attempting to track a bright red target with their amblyopic eye relative to the nondominant eye of a normal control group. However, the stimuli were not matched for effective contrast (i.e., relative to the detection threshold). For these anisometropic amblyopes, other aspects of pursuit (discussed further below) were normal although steady-state gain was more variable ([Raashid, Liu, Blakeman, Goltz, & Wong, 2016](#)). We are not aware of reports of pursuit initiation latencies in strabismic amblyopes, but given the delays they exhibit in manual and saccadic reaction times, even when effective contrast is taken into account, this would not be surprising. As noted below, strabismic (but not anisometropic) amblyopes show other pursuit anomalies. To date, we do not yet know whether or not the cause underlying the prolonged manual and saccadic reaction times is the same as that underlying the latency in pursuit initiation.
- ii. Reduced gain (i.e., the eye movement lags behind the moving target): A common finding, dating back to [Von Noorden & Mackensen \(1962\)](#), and replicated by others, is that individuals with strabismic amblyopia begin to substitute rapid “catch up” saccadic jumps for smooth pursuit at lower velocities compared to their fellow eye (which was shown to be lower than that of normal control subjects: [Ciuffreda, Levi & Selenow, 1991](#); [Fukai, 1974](#)). This differs from the findings in anisometropic amblyopes, who show a normal pursuit velocity profile once pursuit has been initiated ([Raashid et al., 2016](#)).
- iii. Directional Asymmetries: Another common finding in individuals with strabismic amblyopia is asymmetric pursuit; i.e., with near normal pursuit gain in the direction of nasalward motion, but

Table 2
Consensus summary of eye movement abnormalities in PWA .

EM	Abnormality	References
Pursuit	Delayed initiation	Raashid, Liu, Blakeman, Goltz, & Wong, 2016
	Reduced Gain	Von Noorden & Mackensen, 1962; Raashid, Liu, Blakeman, Goltz, & Wong, 2016
	Asymmetric pursuit	Schor, 1975; Tychsen, Hurtig, & Scott, 1985; Von Noorden & Mackensen, 1962
	Saccadic substitution	Ciuffreda et al., 1979a, Ciuffreda et al., 1979b)
Saccade	Increased Latency	Chow, Nallour Raveendran, Erkelens, Babu, & Thompson, 2022; Ciuffreda, Kenyon, & Stark, 1978a, 1978b; Gambacorta, Ding, McKee, & Levi, 2018; Mackensen, 1958; Niechwiej-Szwedo, Goltz, Chandrakumar, Hirji, & Wong, 2010; Niechwiej-Szwedo, Goltz, Colpa, Chandrakumar, & Wong, 2017
	Normal Peak Velocity and Amplitude (follows “main sequence”)	Ciuffreda et al., 1978a, 1978b; Ciuffreda, Levi & Selenow, 1991; Niechwiej-Szwedo, Chandrakumar, Goltz, & Wong, 2012; Niechwiej-Szwedo et al., 2010; Perdziak, Witkowska, Grynciewicz, Przekoracka-Krawczyk, & Ober, 2014
	Dysmetria	Ciuffreda, Kenyon, & Stark, 1979b; Mackensen, 1957b; Schor, 1975
	Disconjugacy of saccades under binocular-viewing conditions; mainly in strabismic amblyopia	Maxwell, Lemij and Collewyn (1995)
Fixation	Eccentric fixation and/or increased instability	Altinbay, Sahli, Bingol Kiziltunc, & Atilla, 2023; Birch, Subramanian, & Weakley, 2013; Chung, Kumar, Li, & Levi, 2015; Gonzalez, Wong, Niechwiej-Szwedo, Tarita-Nistor, & Steinbach, 2012; Subramanian, Jost, & Birch, 2013
	Increase fixational saccade frequency	Chung et al., 2015
	Increased fixational saccade amplitude	Chung et al., 2015; Shaikh et al., 2016
	Increased fixational saccade speed	Chung et al., 2015
	Increased drift amplitude	Ciuffreda et al., 1980; Chung et al., 2015
	Increased drift Speed	Ciuffreda et al., 1980
	Correlation with Visual Acuity	Subramanian, Jost, & Birch, 2013; Chung et al., 2015
	Saccadic intrusions	Ciuffreda et al., 1979
	Disconjugacy	Ghasia, Otero-Millan, & Shaikh, 2018; Irsch et al., 2022
	Correlation with stereoacuity	Birch et al. (2013)
Nystagmus	Latent Nystagmus (LN) also referred to as Fusional Maldevelopment Nystagmus (FMN)	(Ghasia and Wang 2022; Ghasia and Tychsen 2024)
OKN	Reduced and/or asymmetric OKN	Nicolai, 1959; Schor & Levi, 1980; Mein, 1983; Flynn et al., 1984; Westall & Schor, 1985b; Schor, Fusaro, Wilson, & McKee, 1997; Brosnahan et al. 1998; Westall et al., 1998
VOR	Reduced and/or asymmetric VOR	Schor & Westall, 1984; Sharifi, Jafarzadeh, Kiarudi, Hassanzadeh, & Rostami, 2024
Vergence	Vergence instability	Kelly, Cheng-Patel, Jost, Wang, & Birch, 2019
	Inaccurate coordination of binocular vergence during saccades	Kenyon et al., 1978, 1980, 1981
	Abnormal central disparity vergence	Quere, 1979
	Reduced accommodative vergence in severe amblyopia	Kenyon et al., 1978, 1980, 1981
	Correlation with stereoacuity	Ukwade, Bedell, & Harwerth, 2003; McKee, Levi & Movshon, 2003

MS = microsaccade; OKN = Optokinetic Nystagmus; VOR = Vestibular Ocular Reflex.

with strongly reduced gain and saccadic interruptions in the temporalward direction (Schor, 1975; Tychsen, Hurtig, & Scott, 1985; Von Noorden & Mackensen, 1962).

iv. Abnormal Saccadic Substitution: Unlike normal observers, when some PWA attempt to track a target smoothly moving over a relatively short distance, saccades larger than the target amplitude were substituted for the pursuit movements. Ciuffreda et al. (1979a, b) called this “abnormal saccadic substitution”, and reported that it was specific to amblyopia but not strabismus. A plausible explanation is the high degree of positional uncertainty and spatial distortions seen in PWA (Bedell & Flom, 1981; Levi & Klein, 1982a, 1982b; Levi, Klein, & Yap, 1987).

3.3. Fixational eye movements (FEMs)

These are miniature eye movements during attempts at steady fixation of a stationary stimulus. The primary functions of FEMs include countering visual fading, enhancing high-acuity tasks and reformatting visual input into a spatio-temporal format that is most appropriate for analysis. FEMs comprise fixational saccades (or, microsaccades), slow drifts and tremors. Previous studies showed that fixational saccades, often referred to as microsaccades in people with normal vision because their amplitudes are usually smaller than 1 deg, also serve the purpose of putting objects of interest onto the center of the fovea (Ko, Poletti, & Rucci, 2010; Poletti, Listorti, & Rucci, 2013).

The following properties of FEMs have been reported in relation to

amblyopia:

i) Fixation stability.

Fixation stability is conventionally quantified by the area of the bivariate contour ellipse (BCEA) that encompasses a certain percentage of the eye positions during a fixation task, such as 68 % (± 1 standard deviation from the mean) and 95 % (± 2 standard deviations from the mean). More recently, the isoline method which does not assume a normal distribution of eye positions (Castet & Crossland, 2012), has gained popularity as a measurement of fixation stability. However, most of the literature reporting fixation stability in PWA used BCEA, thus most of the results reported here were based on BCEA. Note that we are not citing absolute values of BCEA here, because the absolute values could change depending on many factors, including stimulus size, the methods used to measure eye movements (see Table 1) and the measuring duration (Chung, Agaoglu & Krishnan, 2018). Fig. 1 shows examples of fixation locations superimposed on the fundus of a normal observer (V.A. 20/16 left panel), and the dominant (V.A. 20/16–2 center panel) and amblyopic eye (20/64 right panel) of a strabismic amblyope, while attempting steady fixation (unpublished data). Fixation stability was measured using a MAIA microperimeter (Centervue, Padova, Italy). Subjects were tested monocularly, with the other eye covered. They were instructed to keep their eyes as steady as possible at the center of a small red circle (0.76 deg diameter). Eye positions were sampled at 25 Hz for 10 s, and are shown as red dots superimposed on the central 5° of their retina. Fixation stability was quantified using both the BCEA and ISOA methods. For the normal observer, BCEA is 0.026 deg², ISOA is

0.0196 deg²; for the amblyopic observer: dominant eye: BCEA is 0.386 deg², ISOA is 0.240 deg²; amblyopic eye: BCEA is 1.122 deg², ISOA is 0.814 deg²).

It is almost universally true that fixation stability is worse (larger BCEA) in the amblyopic eyes than in the fellow eyes, or when compared with normal controls. This has been reported for adults (Altinbay, Sahli, Bingol Kiziltunc, & Atilla, 2023; Birch, Subramanian, & Weakley, 2013; Chung, Kumar, Li, & Levi, 2015; Gonzalez, Wong, Niechwiej-Szwedo, Tarita-Nistor, & Steinbach, 2012; Subramanian, Jost, & Birch, 2013) and for children with amblyopia (Subramanian et al., 2013; Altinbay et al., 2023). The ratio of BCEA between the amblyopic eyes and their fellow counterparts during monocular fixation (measurements made on the monocularly viewing eye) ranges between 1.7 and 2.4 (González et al., 2012; Subramanian et al., 2013; Altinbay et al., 2023). There is evidence that the ratio is higher in strabismic amblyopic eyes than in anisometropic amblyopic eyes (3.7× vs 1.5×: Chung et al., 2015). The instability of fixation appears to be more along the horizontal axis of the ellipse than along the vertical axis (Subramanian et al., 2013). When comparing fixation stability between the fellow eyes of PWA with that in normal controls, some studies reported that the BCEA were very comparable (Chung et al., 2015; Ghasia & Tychsen, 2024) while others showed that fixation stability was ~ 1.2× worse in the fellow eyes of PWA than in normal (Gonzalez et al., 2012; Subramanian et al., 2013), possibly due to Fusional Maldevelopment Nystagmus (FMN – discussed below).

Several studies have compared fixation stability of the amblyopic and the fellow eyes of PWA under binocular- vs. monocular-viewing conditions. While fixation stability of the amblyopic eyes was worse under monocular-viewing conditions (especially when the non-amblyopic eyes were covered) than under a binocular-viewing condition, the effect was much larger in the fellow eyes, i.e. fixation stability became much worse when the fellow eyes were covered and the amblyopic eyes were the viewing eyes, compared with the binocular-viewing condition (Gonzalez et al., 2012; Ghasia & Tychsen, 2024). Viewing conditions also influence fixational eye movements under binocular/dichoptic viewing: for example, when the fellow eye's target has lower contrast than that of the amblyopic eye, strabismic and mixed amblyopes may switch fixation to the amblyopic eye, and patients with anisometropic amblyopia show increased fixational instability at low contrast levels (Murray et al., 2022).

The BCEA quantifies the variability of fixation; however, patients with amblyopia, particularly strabismic amblyopia, frequently also have inaccurate fixation (i.e., the preferred retinal locus (PRL) used for fixation is extrafoveal). This is often referred to in the literature as eccentric fixation (Ghasia and Wang, 2022). While the PRL in individuals with normal vision “rarely coincides with the retinal location with the highest cone density” (Kilpelainen, Putnam et al. 2021); the fixation errors are tiny (on average < 5 arc min), whereas those in strabismic amblyopia are much larger (several degrees).

ii) Rate of fixational saccades.

Gonzalez et al. (2012) found that the rate of fixational saccades in the amblyopic eyes did not differ under a binocular-viewing condition (0.62 ± 0.49) or during monocular viewing using the amblyopic eyes (0.85 ± 0.39); and that the rate also did not differ from that in the normal control eyes. In their study, they did not examine whether there was any difference in the rate of fixational saccades between strabismic and anisometropic amblyopia. Chung et al. (2015) showed that strabismic amblyopic eyes exhibited approximately 1.7× more fixational saccades than in the anisometropic amblyopic eyes or in normal control eyes. On the other hand, Shaikh, Otero-Millan, Kumar, & Ghasia (2016) did not find any difference in the rate of fixational saccades between strabismic and anisometropic amblyopic eyes. The difference in the results between the studies of Chung et al. (2015) and Shaikh et al. (2016) could be due to either the method used to detect fixational saccades — Chung et al. (2015) used a fixed-velocity criterion whereas Shaikh et al. (2016) used an unsupervised clustering method — and/or adult (Chung et al., 2015)

vs. children (Shaikh et al., 2016) participants. Also, note that fixational saccades can be suppressed by instructions (Schor & Hallmark, 1978), e.g. whether the instructions were to simply fixate a target or to keep the eyes steady, therefore, differences in results reported by different studies could also be due to the instructions given to participants.

iii) Amplitude of fixational saccades.

Gonzalez et al. (2012) reported no difference in the amplitude of fixational saccades between controls and amblyopic eyes of PWA, and no difference between binocular- and monocular-viewing conditions. When data were separately analyzed for PWA due to strabismus or anisometropia, Chung et al. (2015) found that the amplitude of fixational saccades was larger (~2×) in the amblyopic eyes than in the fellow eyes or in normal control eyes only for PWA with strabismus, but not for PWA with anisometropia. Shaikh et al. (2016) also showed significantly larger amplitude of fixational saccades for PWA with amblyopia, with the amplitude increasing with the severity of amblyopia.

iv) Speed of fixational saccades.

Fixational saccades were faster in the amblyopic eyes of PWA than in the normal control eyes (1.4–1.8× faster), more so for strabismic than for anisometropic amblyopes (Chung et al., 2015). Fixational saccades were also faster in the fellow eyes of PWA than in the normal control eyes, but were only statistically significant for those with strabismic amblyopia (Chung et al., 2015). In general, fixational saccades in PWAs follow the main sequence (i.e., the monotonic increase in the peak velocity with the amplitude of the saccade; e.g. Shaikh et al., 2016), implying that there is a positive correlation between speed and amplitude of fixational saccades.

v) Amplitude of slow drifts.

Ciuffreda et al. (1980) showed that the amplitude of slow drifts was larger in the amblyopic eyes than in the fellow eyes during monocular viewing. These authors suggested that amplitude of drifts might adversely affect acuity in the amblyopic eyes, although the authors did not go as far as proving their suggestion. Chung et al. (2015) also reported larger amplitudes of slow drifts in amblyopic eyes than in fellow eyes during monocular viewing, but only for strabismic amblyopic eyes and not for anisometropic amblyopic eyes. Further, Chung et al. (2015) reported that the amplitude of slow drifts were larger in amblyopic eyes than in normal control eyes by 1.3–1.8×, with strabismic amblyopic eyes showing even larger amplitudes than anisometropic amblyopic eyes.

vi) Speed of slow drifts.

Ciuffreda et al. (1980) showed that the speed of slow drifts was higher in amblyopic eyes than the fellow eyes, by up to 3 deg/s. However, Chung et al. (2015) did not find any statistically significant difference in drift speed among amblyopic eyes, fellow eyes and the normal control eyes. The values of the drift speed in the amblyopic eyes are in fact similar (~3 deg/s) in the studies of Ciuffreda et al. (1980) and Chung et al. (2015), but they are much smaller in the normal control eyes and in the fellow eyes of people with amblyopia in Ciuffreda et al. (1980) than in Chung et al. (2015). The higher values of drift speed reported in normal controls in Chung et al. (2015) could be because their observers were all untrained. Cherici et al. (2012) reported a 3× increase in drift speed for untrained observers, compared with trained observers, as well as larger individual variability in untrained observers, and that they did not use a bite bar to stabilize the head movements of their observers. In contrast, Ciuffreda et al. (1980) used trained observers as their normal controls who were placed on a bite-bar during their experiment.

vii) Relationship between fixation stability and characteristics of fixational eye movements.

Given that the magnitude of fixation instability and many of the parameters of fixational eye movements are larger in the amblyopic eyes of PWA than in their fellow eyes, and in normal control eyes, it is logical to ask whether there exists any causal relationship between fixation instability and some of the parameters of fixational eye movements. A

multiple linear regression analysis showed that the error magnitude (difference in the end point of a fixation saccade from the mean fixation location), amplitude and frequency of fixational saccades, and visual acuity, are the important factors limiting fixation stability in adults with amblyopia (Chung et al., 2015).

3.4. Vestibular-Optokinetic eye Movements

These eye movements include optokinetic nystagmus (OKN) and the vestibular-ocular reflex (VOR). The following responses have been observed in PWA:

i. Asymmetric OKN responses: When viewing small field stimuli with the amblyopic eye, and in some, with the fellow eye as well, OKN is frequently asymmetric, with reduced velocity of the slow phase in response to temporalward and upward motion (Nicolai, 1959; Schor & Levi, 1980; Mein, 1983; Flynn, 1984; Westall & Schor, 1985b). Asymmetric OKN in the amblyopic eye may be a consequence of incomplete development of binocular vision (Schor & Levi, 1980; Schor, 1983); specifically decreased cortical input to subcortical areas and cortical suppression of the amblyopic eye (Westall & Schor, 1985b). Asymmetric OKN in the fellow eye is strongly predictive of early-onset esotropia (Schor, Fusaro, Wilson, & McKee, 1997; Brosnahan, Norcia et al. 1998; (Westall, Eizenman et al. 1998)). Similar asymmetries are evident in threshold measures of motion coherence in children with deprivation amblyopia due to unilateral cataracts (Giaschi, Asare, Jost, Kelly, & Birch, 2024).

ii. Reduced VOR responses: Rotation of the head results in compensatory counter rotation of the eyes. This VOR reflects the integration of visual, vestibular and somatosensory systems, and is critical for balance. Interestingly, abnormal binocular vision due to strabismus and/or amblyopia during development may impact balance, possibly implicating the VOR. However, early studies of VOR in amblyopia were somewhat contradictory. For example, Westall & Schor (1985a) reported asymmetric adaptation in strabismic amblyopes, and Schor & Westall (1984) reported that during head rotation in the dark, the VOR of their amblyopic subjects showed a directional preference related to that found when fixating in the dark. However, Tychsen et al. (1985) found normal VOR responses to body rotation at 0.3 Hz in the dark in infantile strabismics when there was no contamination from the pursuit system. More recent studies suggest that the VOR may be affected in PWA. For example, Sharifi, Jafarzadeh, Kiarudi, Hassanzadeh, & Ros-tami (2024) measured the ocular vestibulo-evoked myogenic potential to assess the VOR in 42 amblyopic patients, and reported that regardless of the type of amblyopia, the VOR with the amblyopic eye was reduced relative to the fellow eye.

3.5. Torsion

As far as we know, torsional eye movements in response to a steady or moving target have not been studied in PWA, although there are anecdotal observations that PWA might exhibit larger torsional eye movements than in normal controls (Otero-Milan, Personal communication, 2024), and this is an area that may be ripe for future research.

3.6. Vergence

Vergence eye movements help to direct the foveas of the two eyes toward objects at varying distances. Unlike the other types of eye movements discussed above, which are conjugate or versional movements of the two eyes, vergence movements are disconjugate (or disjunctive), meaning that the two eyes move in different directions. To focus on objects at near, the two eyes turn inward toward each other (convergence). When the focus shifts from a near object to one further away, the eyes turn outward (divergence). Under normal viewing conditions, changes in vergence are accompanied by commensurate changes in accommodation, except in older adults with presbyopia.

Under these conditions, both accommodative and disparity vergence play a role. “Vergences are found to be much more brittle and vulnerable to amblyopia than versions, and amblyopia is often accompanied by anomalies of fusional, accommodative, and fast vergence movements.” (Quere, 1979) – mainly in strabismic amblyopia. Similar results were reported in a series of studies by Kenyon et al. (1978, 1980, 1981), using small targets at different physical distances. Specifically they noted that in contrast to normal observers, strabismic patients (with or without amblyopia) made a saccadic movement with the dominant eye to foveate the stimulus, which was followed by an unequal vergence movement using accommodative rather than disparity vergence. However, with large stimuli (40–50 deg), strabismic patients (with or without amblyopia) do make normal disparity vergence responses (albeit with reduced amplitude) (Boman & Kertesz, 1985). It is also unclear whether these strabismic patients had undergone surgery. The abnormal disparity vergence in these patients may be a consequence of a reduced complement of disparity sensitive neurons in visual cortex, and binocular suppression (Kiorpes & Daw, 2018; Hallum et al., 2017; Bi et al., 2011; Sengpiel & Blakemore, 1996).

Additionally, in patients with deep amblyopia (>20/400), there may also be a reduction in accommodative vergence (Kenyon et al., 1978, 1980, 1981). More recent work has shown that some patients have reduced ability to make the appropriate vergence movements to fuse targets binocularly (Raveendran, Bobier & Thompson, 2019b), and that both amblyopic and non-amblyopic children, who are treated for anisometropia and/or strabismus, exhibit large vergence instability (Kelly, Cheng-Patel, Jost, Wang, & Birch, 2019).

Persons with normal vision show a pattern of divergence for upward and horizontal saccades as well as convergence with downward saccades (Gibaldi & Banks, 2019). These vergence biases are consistent with environmental statistics (Sprague et al., 2015). This pattern of vergence movements may be absent or highly variable in PWA (Aizenman, Gibaldi, Banks & Levi – in Prep).

3.7. Versions

3.7.i. Disconjugacy

Normal binocular eye movements during fixation are conjugate – i. e., the two eyes move together in the same direction and by the same amount, however a recent small scale study (4 PWA, 3 normal control subjects and one “successfully treated amblyope”) found that the 4 PWA displayed higher disconjugacy (interocular position instability) when attempting to fixate binocularly compared with the other 4 subjects (Irsch et al., 2022). They suggest that disconjugacy may be a “single sensitive test for the presence of amblyopia”; however, previous work found that patients with amblyopia and no nystagmus may also have increased disconjugacy of fixational saccades during binocular viewing (Kang, Beylergil, Otero-Millan, Shaikh, & Ghasia, 2019). Additionally, patients with strabismus but no amblyopia also demonstrate increased disconjugacy during fixation (Ghasia, Otero-Millan, & Shaikh, 2018).

3.7.ii. Latency and gain

Individuals with normal binocular vision have an advantage under binocular compared to monocular conditions in that they exhibit shorter saccadic latencies. However, patients with strabismus both with or without amblyopia, show no such advantage; moreover, a small number of patients with severe amblyopia and no measurable stereopsis showed reduced gain when viewing with the amblyopic eye (Niechwiej-Szwedo, Chandrakumar et al. 2012). Saccadic adaptation gain is reported to be lower both when viewing with the amblyopic eye and during binocular viewing (Raashid et al., 2013).

3.8. Early onset of esotropia affects eye movements in PWA

A large-scale study of 200 strabismic subjects (almost all amblyopic or ‘recovered’ amblyopes) was able to predict early onset esotropia

based largely on the pattern of eye-movement abnormalities (Schor et al., 1997). They report that the best oculomotor predictors of early onset esotropia were Dissociated Vertical Deviation (DVD where, when covered, each eye deviates vertically in the same direction, in contrast to a vertical strabismus where the two eyes deviate in opposite directions) and the speed of monocular smooth pursuit abnormalities in the preferred eye. Another oculomotor feature commonly associated with early onset of esotropia and/or visual deprivation is Fusional Maldevelopment Nystagmus (FMN) or Latent Nystagmus (Tychsen & Boothe, 1996; Tychsen et al., 2010; Murray et al., 2022; Scaramuzzi et al., 2019). FMN is characterized by showing a nasally directed slow phase under monocular viewing with the reversal in the direction of the quick phase toward the uncovered eye. FMN is thought to occur when there is decorrelated input to the two eyes during a sensitive period when stereopsis is emerging, and consequently, the nasalward bias evident in infancy persists (Hasany, Wong, Foeller, Bradley, & Tychsen, 2008; Murray et al., 2022; Ghasia & Tychsen, 2024). Amblyopic patients with strabismus are more likely to have FMN than those without strabismus (Ghasia & Tychsen, 2024). This “latent” nystagmus, which is evident only when one eye is covered, is also associated with an early onset of amblyopia and/or strabismus, a loss of binocular vision and dissociated vertical deviation (DVD) (Guyton, 2000). While latent nystagmus can result in reduced acuity, some individuals with early onset esotropia and latent nystagmus can achieve good visual acuity during the low velocity period of their slow phase nystagmus (Dell’Osso et al., 1995).

4. What do we know about how each of these affect different tasks in PWA?

Amblyopia is associated with difficulties or deficits in performing a broad range of tasks, not only when viewing with the amblyopic eye, but for some, with the fellow eye and both eyes simultaneously. These include a loss of visual acuity, relative position acuity and contrast sensitivity, particularly at high spatial frequencies, as well as increased internal noise and prolonged manual and saccadic reaction times to visual stimuli (McKee et al., 2016; see Levi (2020) for a review). Additionally, they have difficulty processing stimuli defined by contrast or motion, in contour integration, temporal and spatial problems, and reduced attentional capacity (Poppel & Levi, 2008), and have increased random noise (Levi & Klein, 2003; Levi, Klein, & Chen, 2008). Under normal everyday viewing conditions with both eyes open, the most common deficit in amblyopia is reduced stereoscopic depth perception. Reducing the vision of one eye (in neurotypical persons) by blurring, filtering or reducing contrast degrades stereoacuity (Westheimer & McKee, 1980; Donzis, Rappazzo, Burde, & Gordon, 1983; Legge & Gu, 1989; Menon, Bansal, & Prakash, 1997), and degrading vision in one eye has a more deleterious effect on stereopsis than by degrading both eyes (Westheimer & McKee, 1980; Legge & Gu, 1989).

Persons with amblyopia frequently manifest deficits in reading (Bhutada et al., 2022; Birch & Kelly, 2017; Kelly, Jost, De La Cruz, & Birch, 2015; Kelly et al., 2017; Stifter, Burgasser, Hirmann, Thaler, & Radner, 2005a, 2005b), visual search (Neri & Levi, 2006; Tsirlin, Colpa, Goltz, & Wong, 2018; Black, Wood, Hoang, Thomas, & Webber, 2021; Nagarajan, Luo, Narasimhan, & Satgunam, 2022), visually-guided hand movements (Grant & Conway, 2015, 2023; Grant, Melmoth, Morgan, & Finlay, 2007; Grant & Moseley, 2011; Grant, Suttle, Melmoth, Conway, & Sloper, 2014; Suttle, Melmoth, Finlay, Sloper, & Grant, 2011; Melmoth, Finlay, Morgan, & Grant, 2009; Niechwiej-Szwedo, Goltz, Chandrakumar, & Wong, 2012; Niechwiej-Szwedo, Kennedy, et al., 2012; Subramanian et al., 2013), and walking across complex terrains (Bonnen et al., 2021). Below we consider whether and how the eye movement deficits of PWA may affect their performance on some of these tasks.

4.1. Contrast sensitivity

PWA have substantially reduced contrast sensitivity for high spatial

frequency grating stimuli (Levi & Harwerth, 1977; Hess & Howell, 1977) in their amblyopic eyes, compared with the fellow eyes. Higgins, Daugman, & Mansfield (1982) found essentially no difference between stabilized and unstabilized contrast sensitivity in their amblyopic eyes, despite their marked fixation instability. Moreover, they report that superimposing the pattern of image motion recorded from the amblyopic eye on the eye of a normal observer does not reduce contrast sensitivity.

4.2. Visual acuity and relative position discrimination

Unsurprisingly, PWA have reduced visual resolution (acuity) in the amblyopic eyes, when compared with the fellow eyes or normal control eyes. Hess (1977a) reported that visual resolution for squarewave gratings in 4 adults with strabismic amblyopia was similar under normal (unstabilized) and stabilized viewing (stabilization was achieved by creating afterimages of the gratings). However, in PWA, optotype visual acuity and other fine spatial position discrimination thresholds (e.g., Vernier acuity and bisection) are often much more compromised than would be predicted from their grating acuity, especially in strabismic amblyopia (Levi & Klein, 1982a, 1982b; Levi et al., 1987). There are a number of plausible explanations for this; these optotypes are local and the critical features for identification are highly localized whereas gratings are extensive and provide redundant information. Eccentric fixation would result in an optotype being viewed extrafoveally, whereas an extended grating might be imaged on the fovea as well as the eccentric location. Moreover, because of the very localized features of optotypes, fixational eye movements (especially fixational saccades) might be expected to have a larger impact on optotype identification than on grating resolution. Indeed, a number of studies have shown a significant correlation between the visual acuity and fixational stability of PWA (Subramanian et al., 2013; Chung et al., 2015; Wang et al., 2021). In Fig. 2, we replotted measurements of fixation stability and visual acuity of individual participants from the studies of Subramanian et al. (2013) and Chung et al. (2015). In both studies, fixation stability was quantified by the area of the bivariate contour ellipse (BCEA) that enclosed 68 % of the eye positions during fixation. Note that the original data in Subramanian et al. (2013) reported BCEA for 95 % of the eye positions. Here, we adjusted their BCEA values for 68 % of eye positions.

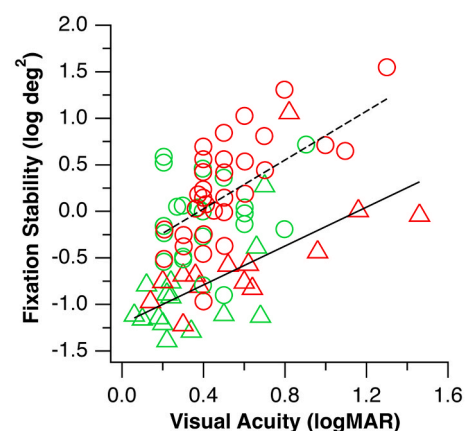


Fig. 2. Fixation stability, quantified by the BCEA (in $\log \text{deg}^2$) that enclosed 68 % of the eye positions, is plotted as a function of visual acuity (in $\log \text{MAR}$) for the amblyopic eyes of participants in the studies of Subramanian et al. (2013) and Chung et al. (2015). Subramanian et al. reported BCEA for 95 % of eye positions in their paper; in this figure, values plotted are adjusted for 68 %. Symbols (circles for Subramanian et al. and triangles for Chung et al.) are color coded — green for anisometropic amblyopes and red for strabismic or mixed (strabismic + anisometropic) amblyopes. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

The vertical offset between the two sets of data, implying different magnitudes of fixation stability, is likely due to the different methods used and the ages of the participants in the two studies (children in Subramanian et al. (2013) and adults in Chung et al. (2015)). Fig. 2 clearly illustrates a significant relationship between acuity and fixation stability (worse acuity is associated with higher fixation instability), but fixation (in)stability is not the only limiting factor on acuity. A multiple linear regression analysis revealed that the error magnitude, fixation stability, amplitude of drifts and amplitude of microsaccades were the main eye movement components limiting visual acuity in adults with amblyopia (Chung et al., 2015). Also, note that the reduced fixation stability in PWA is not mimicked by reducing visual acuity in people with normal vision using optical defocus (Raveendran, Bobier, & Thompson, 2019a).

4.3. Visual search

Finding an object, a familiar face or a needle in a haystack requires efficient visual search. Several studies have shown that visual search is compromised when searching with the amblyopic eye (Neri & Levi, 2006; Tsirlin et al., 2018; Black et al., 2021; Nagarajan et al., 2022). Chen and colleagues (Chen, Otero-Millan, Kumar, Shaikh, & Ghasia, 2018) measured eye movements during a simple search task in children with amblyopia and reported that they performed worse than controls with each eye. When viewing with the amblyopic eye they took longer, performed worse, and spent less time with gaze directed near the search target than control subjects. They exhibited lower fixational saccade and saccade frequencies during both fixation and free-viewing search, and these deficits were more marked in patients with latent nystagmus (which is often indicative of an early onset of amblyopia). Similar deficits have been reported in children with anisometropic amblyopia, even when viewing binocularly (Nagarajan et al., 2022).

In normal adults, the frequency of fixational saccades increases with more complex scenes and near the search target (Otero-Millan, Troncoso, Macknik, Serrano-Pedraza, & Martinez-Conde, 2008; Mengenthaler & Engbert, 2010). Recent work in our lab shows that when performing visual search, saccadic latency was longer with the amblyopic eye than with either the fellow eye or compared with either eye of controls. Saccade landing at the peripheral target was less accurate in both eyes of PWA than controls, and was correlated with fixational instability. Additionally, binocular viewing reduced fixational instability in both controls and anisometropic amblyopes, but not in strabismic amblyopes. These results are not simply a direct consequence of reduced visual acuity due to defocus (Kwon, Belen, Lien, Yeritsyan, Do, & Levi, 2024; Kwon & Levi, 2023). Indeed, as noted above, the reduced fixation stability in PWA is not mimicked by reducing visual acuity using optical defocus (Raveendran et al., 2019a).

4.4. Reading

With small, closely spaced print, PWA read slowly, even when eye movements are not required. Levi, Song & Pelli (2007) used rapid serial visual presentation (RSVP) to measure reading speed in adults with amblyopia. Under these conditions (where eye movements are not required), crowding (the deleterious influence of nearby contours), not visual acuity or letter size, limits reading speed. They concluded that in PWA (as in the normal fovea and periphery), crowding limits reading solely by determining the uncrowded span: the number of characters that are not crowded and can be identified during a single fixation.

Do eye movement deficits impact reading in PWA? Several studies have shown that the maximum reading speed is slower when reading with the amblyopic eye or with both eyes than it is in age matched controls (Stifter et al., 2005a, 2005b; Bhutada et al., 2022; Birch & Kelly, 2017; Kelly et al., 2017). When reading regular text (e.g. excerpts from the Oxford First Encyclopedia), reading speed of adults with strabismic amblyopia is slower with the amblyopic eye than age matched controls

for a wide range of font sizes. Reading with the non-amblyopic eye or with both eyes was also slower than controls, but only for small font sizes (Kanonidou, Gottlob, & Proudlock, 2014; Kanonidou, Proudlock, & Gottlob, 2010). These authors report that strabismic amblyopes made more saccades per line than controls irrespective of font size and viewing conditions. Specifically, they made more regressive saccades and longer fixation durations, but the number of progressive saccades and the amplitude of progressive saccades were not different. We note that these small fonts are not representative of typical reading, where font size is larger than 0.3 logMAR, and only occurred during amblyopic eye viewing. Bhutada and colleagues (Bhutada et al., 2022), used a fixed print size corresponding to logMAR = 1 in 23 patients with amblyopia and 9 control subjects. They reported that the amblyopic patients had reduced reading speeds with increased fixation duration and saccades (both progressive and regressive) during binocular, fellow eye and amblyopic eye viewing compared to controls. Fixation instability of the amblyopic eye was increased during both monocular and binocular viewing. Additionally, they found that when viewing with both eyes, there was increased vergence instability compared to controls. Aside from the educational consequences of slow reading, self-perception may be lower in amblyopic children who read slowly and have poor motor skills (Birch et al., 2019).

4.5. Stereopsis

Normal stereopsis requires the two eyes to be reasonably well aligned, functional and well matched in resolution, contrast sensitivity etc. Additionally, normal stereopsis requires a neural mechanism to combine the images from the two eyes and compute depth from binocular disparity (and combine it with other depth cues) (Levi, 2022). In adults with normal binocular vision, the perception of large (36 arc min) disparity in an extended (30 × 30 deg) display is remarkably tolerant to disparities between the two eye's images of as much as 2 degrees (Erkelens & Collewijn, 1985). However, stereo thresholds are impacted by vergence errors that exceed about 1.5 arc min (Ukwade, Bedell, & Harwerth, 2003). Not surprisingly, stereopsis is absent or severely disrupted in patients with strabismic amblyopia who have vergence misalignment exceeding that required for good stereovision, and to a lesser extent in those with anisometropic amblyopia (McKee, Levi, & Movshon, 2003), when the acuity and contrast sensitivity of the amblyopic eye are worse than that of the fellow eye. McKee et al. (2003) suggested that PWA, who failed to detect large stereoscopic disparities (mainly, but not exclusively, strabismic), show a disproportionate loss in optotype and relative position acuity. How do eye movements influence stereopsis in PWA? Birch et al. (2013) measured fixational instability and stereopsis in children with anisometropic amblyopia. They report a strong correlation between stereo acuity and fixational instability; children with normal stereo vision all demonstrated normal fixational stability while those who failed the stereoacuity test (nil stereo) showed the largest instability. Two thirds of the children with reduced stereoacuity had Fusional Malformation Nystagmus (FMN) waveforms and those with nil stereo all had FMN waveforms. Scaramuzzi et al. (2021) evaluated the fixational eye movements of amblyopic children following treatment (part time occlusion of the non-amblyopic eye). About half of their patients showed improvement in stereoacuity; two-thirds of those who improved were anisometropic and the rest were strabismic or mixed. Almost 80 % of the patients with no nystagmus improved whereas only 1/8 with FMN improved.

4.6. Eye-Hand coordination

PWA may have deficits in visually guided hand movements such as reaching and grasping a static object, e.g., a coffee cup (Grant et al., 2007; Melmoth et al., 2009; Suttle et al., 2011; Niechwiej-Szwed et al., 2012; Niechwiej-Szwed, Kennedy, et al., 2012; reviewed in Levi, Knill, & Bavelier, 2015). As noted above, lower self-perception is associated

with poor motor skills. However, evidence suggests that these deficits are not a consequence of fixation instability (Subramanian et al., 2013), or poor vergence control (Melmoth, Storoni, Todd, Finlay, & Grant, 2007). On the other hand, eye movements may be especially important in intercepting moving objects, for example, catching a flyball, especially when the motion trajectory is difficult to predict and when there is a high degree of visual uncertainty (reviewed by Fookien, Kreyenmeier, & Spering, 2021). Fookien et al. conclude that “Eye movements are functionally linked to interceptive hand movements via shared retinal and extraretinal signals”. PWA often have difficulties with such tasks. It would be interesting to determine what role, if any, the eye movement abnormalities in PWA affect their ability to quickly and accurately intercept moving objects.

4.7. Locomoting and balance

Normal binocular vision is important for the developing and maintaining good balance. Zipori and colleagues (2018) evaluated balance in strabismic patients both with and without amblyopia as well as in normal controls. Their results suggest that balance was compromised in both patient groups and they conclude that “even mild binocular discordance/dysfunction may lead to postural instability”.

Normal binocular vision is also important for determining where to step when walking in complex terrain. Interestingly, PWA (as well as individuals with reduced stereo vision due to strabismus or imposed monocular blur on normal participants) have been shown to bias their gaze towards closer footholds (Bonnen et al., 2021). Interestingly, in adults 65 and older, binocular vision disorders (including strabismus and amblyopia) have a significantly higher risk of falling and sustaining a musculoskeletal injury or fracture (Pineles et al., 2015).

To the extent that their stereovision is impacted by vergence errors, eye movement deficits may contribute to the gaze-gait strategies of PWA.

5. The chicken and egg problem

While there is a clear relationship between the visual acuity of PWA and their fixational stability (Fig. 2), the question remains: does poor fixation limit visual perception in amblyopia, or vice-versa? Some have attempted to address this question, either by stabilizing the retinal image (Hess, 1977; Higgins et al., 1982), or by recording the amblyopic eye's fixation pattern and examining the effect of superimposing the amblyopic eye's retinal image motion on the performance of a normal eye (Higgins et al., 1982), while others (us included) have tried to mitigate the effects of retinal image motion by using horizontal stimuli or brief exposures. Based on our current understanding of fixational eye movements, we hypothesize that it is not the retinal image motion per se, but rather, the frequent fixation saccades made while fixating with their amblyopic eyes, that result in shifts in attention leading to a broad range of visual abnormalities: reduced perceptual sensitivity and visual acuity, increased crowding and positional uncertainty, mapping distortions and prolonged saccadic reaction times (because of the motor refractory period from a previous saccade or fixation saccade (Gambacorta et al., 2018; Verghese et al., 2019)).

Previously, we examined fixational eye movements in a large group of amblyopic ($N = 28$) and normal ($N = 16$) subjects using a Rodenstock Scanning Laser Ophthalmoscope (Chung et al., 2015). Our results showed that fixation stability is markedly affected in strabismic amblyopic eyes, and that the error magnitude, amplitude, and frequency of microsaccades are the primary ocular motor factors contributing to their fixation stability. Importantly, we found a significant correlation ($r = 0.67$) between the reduced visual acuity and fixation stability (Fig. 2 above). While it is difficult to tease apart whether acuity is the limiting factor on fixation stability, or vice versa, there are several reasons that lead us to believe that fixation stability may place some limits on acuity, instead of the other way round. First, simply blurring the retinal image

in a normal eye does not mimic the effects of amblyopia on eye movements when fixating (Raveendran et al., 2019a; Kwon, Belen, Lien, Yeritsyan, Do & Levi, 2024) or searching (Kwon & Levi, 2023). Second, it has been shown that random jittering of an acuity target degrades acuity in observers with normal vision (Chung & Bedell, 1995). When fixation is unsteady or when the acuity target is jittered, from moment to moment, the image lands on different retinal loci, introducing uncertainty and interfering with the spatio-temporal integration required to form a global percept of the target – critical for letter identification. This random jitter hypothesis is also consistent with the largest contributors to reduced acuity being error magnitude and fixation stability. Increased error magnitude means that the fixation saccades are less accurate in their landing positions, resulting in the eye landing further away from the intended location. Third, fixation instability also places the acuity stimulus on different extrafoveal locations, thus further degrading acuity. Acuity correlates with the eccentricity of the preferred retinal locus in amblyopic eyes (Flom & Weymouth, 1961; Kandel, Grattan, & Bedell, 1977). Crowding also increases rapidly with increasing eccentricity, so it is likely that the eccentric fixation evident in strabismic amblyopia would result in increased crowding. There are good reasons to suspect that abnormal fixational eye movements might impact the resolution of amblyopic observers, particularly at high spatial frequencies and could also contribute to slow reading (discussed further below).

The potential effects of fixational eye movements described above are all consequences of the abnormal retinal image motion. However, there are good reasons to consider the role of abnormal fixational eye movements per se. In normal observers, fixation saccades can lead to shifts in attention (Martinez-Conde et al., 2013; Binda & Morrone, 2018). To the extent that similar attentional shifts occur when strabismic amblyopes make large fixation saccades, this may result in increased crowding and substitution errors (because attention is erroneously directed at a flanker rather than the target). For example, in a crowded acuity task with a 20/100 letter (25 arcmin), a large (25°-20') fixation saccade could result in fixation (and/or attention) on an abutting flanker.

A very recent attempt to unscramble the role of eye movements on motion perception (published after submission of this Review) argues that fixation instability (as indicated by the mean BCEA) does not account for elevated motion coherence thresholds for slowly moving dots when viewing with the amblyopic eye (Meier et al., 2025). Specifically, they measured fixational stability during the 600-msec presentation of the moving dots. However, it is now clear that fixational eye movements result in shifts in attention and reduced visual sensitivity prior to and at specific times during stimulus presentation (Kowler 2024; Martinez-Conde et al., 2013; Chen, Ignashchenkova et al., 2015; Yuval-Greenberg et al., 2014). Averaging the gaze data over the 600-msec stimulus presentation may have obscured any influence of the FEMs on thresholds.

Why are EMs abnormal in persons with amblyopia? A number of studies point to attentional deficits in both children (Black et al., 2021) and adults with amblyopia (for a review, see (Verghese et al., 2019)). These attention deficits could lead to eye movement deficits as well. In PWA with FMNS, the binocular deficits that originate in V1 are passed on downstream to extrastriate areas that drive conjugate gaze (Tychsen et al., 2010), and potentially sensory abnormalities that contribute to the abnormal eye movements.

6. Can abnormal EMs be improved in persons with amblyopia?

The current standard clinical treatment for amblyopia consists primarily of correcting any refractive error, followed by occlusion of the fellow eye, sometimes referred to as direct occlusion, for several hours per day (depending on the patients age) with the goal of improving the visual acuity of the amblyopic eye. While this approach results in improved visual acuity in many cases, it may not result in normal acuity or stereopsis in a substantial proportion of amblyopic children (Birch &

Stager, 2006; Birch, Stager, Berry, & Leffler, 2004; Holmes et al., 2003; Pediatric Eye Disease Investigator Group Writing et al., 2010; Repka et al., 2003; Repka et al., 2004; Repka et al., 2005; Stewart, Moseley, Stephens, & Fielder, 2004; Wallace et al., 2006; Woodruff, Hiscox, Thompson, & Smith, 1994), and even when visual acuity improves to normal, it regresses in about 25 % of patients within the first year of treatment (Holmes et al., 2004; Holmes & Levi, 2018). Unsurprisingly, there have been many reports, and controversies, about the effects of direct occlusion on the abnormal eye movements in PWA, especially regarding eccentric fixation, dating back to the middle of the last century. The controversy was over the belief by some, that direct occlusion might stabilize and “embed” eccentric fixation (Duke-Elder, 1949; Lyle, 1959; Wybar, 1961), summarized in Ciuffreda et al. (1991). This belief led its proponents to advocate indirect (or reverse) occlusion, i.e., patching the amblyopic eye rather than the fellow eye. However, clinical studies (Von Noorden, 1965; Parks & Friendly, 1966; Mackensen, Kroner, Postic, & Kelck, 1967; VerLee & Iacubucci, 1967) suggest that direct occlusion is more effective in improving both visual acuity and fixation stability than indirect occlusion, and that it does not stabilize the eccentric fixation. Interestingly, indirect occlusion for amblyopia has recently been resurrected, not as a method for treating eccentric fixation, but for reducing suppression (Zhou et al., 2019; Zhou, Thompson, & Hess, 2013; Lunghi et al., 2019).

A different approach to the treatment of eccentric fixation was the introduction of pleoptics (Cuppers, 1956; Bangerter, 1960, 1969), often used in conjunction with indirect occlusion. The key idea was to “dazzle” the perifoveal retina of the amblyopic eye with a very bright flash of light while shielding the fovea, and then having the patient use the afterimage to guide the (undazzled) fovea to read letters on a chart. While this approach became fairly popular in the UK and Europe, patients were generally hospitalized (often for months), and it was less frequently adopted in North America because it required multiple in-office visits and patient cooperation. While it is clear that the approach was effective in some patients (Garzia, 1987), a randomized clinical trial showed no statistical difference between patients undergoing conventional patching and those undergoing pleoptic treatment in addition to conventional treatment (Fletcher et al., 1969), and this approach is no longer in wide use (Zurevinsky, 2019; Godts & Mathysen, 2019). Similarly, the use of a red filter in front of the amblyopic eye (Brinker & Katz, 1963) based on the questionable assumption that the foveal cones are more sensitive to long wavelengths than the photoreceptors in the surrounding retina, has fallen out of favor.

More recent approaches to training fixation are based on biofeedback. This approach has been successful in patients with nystagmus (Ciuffreda, Goldrich, & Neary, 1982; Ciuffreda & Goldrich, 1983). Flom, Kirschen, & Bedell (1980) used auditory biofeedback to assist amblyopic subjects to improve fixation — when the subject’s eye position drifted outside of a “deadband”, defined by the experimenters, a tone was presented to the corresponding ear. Over time, subjects learned to fixate more accurately allowing the deadband to be narrowed. Following training, subjects were able to fixate more accurately even with no feedback. However, these authors did not report whether or not acuity or other visual functions improved following the biofeedback training. Recently, Maneschg, Barboni, Nagy, & Nemeth (2021) reported that fixation stability did not improve following surgical alignment of the eyes of four patients with strabismic amblyopia, but that two of these four patients (one with central fixation and the other had extra-foveal fixation) had better fixation stability after biofeedback training applied to the amblyopic eye. These authors also did not report whether or not acuity improved as a result of biofeedback training. More work is required to establish whether or not fixation training is indeed beneficial to people with amblyopia, and if so, whether or not the benefits also come at a cost, for instance, whether fixation training would lead to reduced suppression in the amblyopic eyes, which may in turn, cause diplopia especially in adults with amblyopia. All of these would need to be understood before fixation stability training could be used as an

effective treatment option for amblyopia.

Another recent approach (Nemes-Drăgan, Tipcu, Hapca, Pascualau, & Nicoara, 2024) takes advantage of the fact that the Visually Evoked Cortical Potential is most strongly driven by foveal stimulation. Specifically, they performed fixation training in a group of 16 anisometropic amblyopes, ages 15 – 57 years, and 16 (somewhat younger) control subjects, using the Retimax Vision Trainer (CSO, Florence, Italy). Participants viewed a variable size fixation target (the outline of a circle) superimposed on a checkerboard pattern that reversed 15 times/second, and the Steady State Visual Evoked Potential (SSVEP) amplitude at the reversal frequency was measured and was used to modulate the frequency of an auditory signal and the size of the fixation target. The larger the amplitude (indicating more foveal fixation and attention), the smaller the target. After 10 sessions (10 min/session), they report that visual acuity in the anisometropic amblyopic group improved by about 2 LogMar lines, consistent with previous studies using this approach (Esposito Veneruso, Ziccardi, Magli, Falsini, & Magli, 2014; Lapajne et al., 2020) which was largely maintained over the 12 month followup period. The improvement in visual acuity over the course of treatment was correlated with the increase in SSVEP amplitude. Both groups also showed increased contrast sensitivity and a highly variable increase in reading speed. We note that while the Nemes-Drăgan (2024) study had a “control group”, they had normal vision. Moreover, they did not actually measure eye movements, so we do not know which aspects of fixation (if any) actually changed. To date there has not been a comparison with a matched, active control group that, for example performed the same fixation training but with sham biofeedback. It would also be interesting to include subjects with strabismic amblyopia who are much more likely to have poor and eccentric fixation than purely anisometropic amblyopes.

7. Can EMs be used to diagnose/classify amblyopia?

There is no single diagnostic test for amblyopia. Currently amblyopia is diagnosed by (i) reduced visual acuity (usually in one eye) with the best optical correction, (ii) a history of an “amblyogenic” risk factor (strabismus, anisometropia, cataract) early in life, and (iii) by excluding any observable ocular pathology (i.e., clear media, normal retina, etc.). However, given the need for early diagnosis, this is not always possible, e.g., in infants and young children (see Hunter & Cotter, 2018 for a review), so a single clear, unambiguous objective marker for amblyopia would be a genuine step forward, both for diagnosis and for monitoring the effect of treatment. Could eye movements be used to screen for, diagnose and/or classify amblyopia, particular in infants and young children? One approach to early screening is the Pediatric Vision Scanner (PVS) which is based on the detection of alignment of the two eyes using retinal birefringence. This device was developed to detect strabismus, but it appears to be sensitive to anisometropic amblyopia, perhaps as a consequence of fixation instability or undetected microstrabismus (Loudon, Rook, Nassif, Piskun, & Hunter, 2011).

Based on the discussion in this review, a potential biomarker that is relatively easy to measure is fixation stability. Fixation stability can be measured using research equipment or clinical devices such as microperimeters, thus facilitating early detection of amblyopia in clinical settings. Many studies have shown that fixation stability can be measured in children as young as 3 years old (Ghasia et al., 2024). Previous reports showed that the ratio of fixation stability measurements (BCEA) between the amblyopic and the fellow eyes is between 1.7 to $2.4\times$. Therefore, in the clinic, if the fixation stability measurement obtained in the two eyes separately differs by about $1.7\text{--}2.4\times$, that could be another “risk factor” to consider when a clinician makes a diagnosis. Further, if binocular measurements of fixation stability could be made, perhaps the observation of substantial vergence instability can also be used as another “risk factor” for amblyopia. Note that, recently, more clinical trials have incorporated the measurement of fixation stability as an outcome measure, in addition to the more traditional measurement of

acuity, contrast sensitivity and stereopsis. If fixation stability proves to be a sensitive biomarker for the early detection of amblyopia, low-cost options such as smartphone apps may be developed to measure fixation stability in the future.

7.1. Could Artificial Intelligence (AI) be helpful?

AI is now being widely used to improve diagnosis and classification of many diseases, including those affecting the retina (e.g. [Sánchez-Morales et al., 2022](#); [Kim et al., 2022](#); [Zou, 2022](#)). For example, by ‘learning’ from thousands of retinal photographs, AI can be helpful in diagnosing glaucoma, age related macular degeneration, etc. It would be interesting to determine whether AI could be similarly helpful in the diagnosis and classification of amblyopia, after learning the fixational eye movement patterns of PWA and age matched controls. Additionally, AI may be helpful for patients and/or their caregivers seeking information about amblyopia. As a test, we asked ChatGPT ‘What is

amblyopia and how is it treated?’ The response from ChatGPT is shown in [Fig. 3](#).

AI may even be useful for researchers. Indeed, a recent study found that AI LLMs (large language models) trained on neuroscience literature are able to predict neuroscience experiment outcomes more accurately than human neuroscience experts ([Luo et al., 2024](#)).

8. Summary

Amblyopia is not just a sensory deficit, as some of the literature suggested ([Hess, 1977](#); [Higgins et al. 1982](#)); instead, it is also associated with motor (including oculomotor and eye-hand coordination) deficits. In this paper, we briefly summarized how the characteristics and dynamics of various types of eye movements differ between the amblyopic eyes and their fellow eyes and also with respect to normal control eyes. We note that there is not uniform consensus in the literature, for a number of reasons: the amblyopic population is not homogeneous,

ChatGPT’s response:

“Amblyopia, often referred to as “lazy eye,” is a visual impairment where one eye has reduced vision that is not correctable by glasses or contact lenses. It occurs when the brain and the affected eye do not work together properly, leading to a preference for the stronger eye. This condition typically develops during childhood, often before the age of 7, and can lead to permanent vision problems if not treated early.

Causes of Amblyopia

There are several common causes of amblyopia:

1. **Strabismus (misalignment of the eyes):** When the eyes are not aligned properly, the brain may ignore input from the misaligned eye, leading to amblyopia in that eye.
2. **Refractive errors (anisometropia):** Significant differences in the refractive power (focusing ability) of the two eyes, such as one eye being much more nearsighted or farsighted than the other, can result in amblyopia in the weaker eye.
3. **Deprivation (e.g., cataracts):** If something obstructs the vision of one eye, like a congenital cataract or ptosis (drooping eyelid), the brain may suppress the input from that eye, leading to amblyopia.
4. **Visual deprivation:** Conditions that restrict vision in one eye, such as trauma or disease, can also lead to amblyopia.

Symptoms

- Reduced vision in one eye
- Difficulty with depth perception
- Squinting or closing one eye to see better
- Eyes that appear misaligned (in cases of strabismus)
- Discomfort or difficulty focusing on objects with both eyes

Treatment Options

Early detection and treatment are crucial for the best outcomes. Treatment methods aim to force the brain to use the weaker eye more effectively, allowing the vision to develop more normally.

1. **Corrective lenses:** Glasses or contact lenses may be prescribed to correct any refractive errors, such as nearsightedness or farsightedness. This can help ensure both eyes are working together.
2. **Patch therapy:** The most common treatment for amblyopia involves patching the stronger eye for several hours a day. This forces the brain to rely on the weaker eye, encouraging its development. The duration and intensity of patching depend on the severity of the amblyopia and the age of the patient.
3. **Atropine eye drops:** Sometimes, atropine drops are used in the stronger eye to temporarily blur the vision, forcing the brain to use the weaker eye. This is an alternative to patching, especially in cases where patching is not well-tolerated.
4. **Vision therapy:** Vision therapy includes a series of exercises designed to improve the coordination and function of both eyes. This can help in cases where the eyes are misaligned or there are other coordination issues.
5. **Surgical intervention:** In cases where strabismus is the underlying cause, surgery may be needed to correct the alignment of the eyes. Surgery may also be needed if there is a cataract that obstructs the vision.
6. **Binaural vision therapy:** For certain cases, specialized therapies using computer programs or activities (such as playing video games designed to treat amblyopia) may help improve eye-brain coordination.

Best Outcomes

Treatment is most effective when started early, ideally before the age of 7, when the brain is still highly adaptable. However, even older children and adults can experience some improvement, though it may be more limited the longer the condition has been untreated.

Regular follow-up appointments with an eye care professional (usually a pediatric ophthalmologist or optometrist) are important to monitor progress and adjust treatments as needed.

Summary

Amblyopia is a condition in which one eye has reduced vision that can't be corrected with traditional means like glasses, often due to strabismus, refractive errors, or deprivation. Treatment primarily involves encouraging the weaker eye to develop better vision, using methods like patching, eye drops, vision therapy, and sometimes surgery. Early detection and treatment are key.”

Fig. 3. ChatGPT 4 Response to the question: ‘What is amblyopia and how is it treated?’.

differing in presumed cause (e.g., strabismus vs. anisometropia), age of onset and both psychophysical and motor consequences (McKee, Levi, and Movshon, 2003). Moreover, many of the extant studies have relatively small (and inhomogeneous) N's, limiting generalization. We also summarized how the eye movement deficits of persons with amblyopia may affect their performance on a variety of visual tasks. Unfortunately, to date, it remains unclear whether the abnormal eye movements exhibited by people with amblyopia are consequences of the poor functional vision, for example, as a compensatory mechanism; or whether the poor functional vision is the result of the abnormal eye movements (e.g. substantial retinal image motion). Clarifying this "chicken and egg" issue would be essential in developing effective treatment that aims at the underlying cause of the sensory and oculomotor deficits of amblyopia. Based on our discussion, some aspects of eye movements, such as fixation stability, are evolving as a biomarker for amblyopia. To capitalize on this, quick, low-cost and sensitive methods are needed to provide these measurements. Smartphone apps may offer a solution to this and future studies would need to solve some of the technical issues in using the built-in cameras of the smartphones for eye movement measurements. Undoubtedly, AI will be part of our daily lives and it is foreseeable that it would be used in the detection, diagnosis and even treatment of amblyopia, whether it is in clinical or the research environment.

CRedit authorship contribution statement

Dennis M. Levi: Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Susana T.L. Chung:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Supported by a grants from the National Eye Institute (NEI) R21EY030609 and R01EY034370. We are grateful to Ken Ciuffreda, Angela Gomez-Tomaz, Suzanne McKee and Cliff Schor and Gene Switkes for their thoughtful comments and suggestions on an earlier version of this manuscript.

Data availability

No data was used for the research described in the article.

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