CHAPTER 8

Fixational eye movements in normal and pathological vision

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Abstract: Most of our visual experience is driven by the eye movements we produce while we fixate our gaze. In a sense, our visual system thus has a built-in contradiction: when we direct our gaze at an object of interest, our eyes are never still. Therefore the perception, physiology, and computational modeling of fixational eye movements is critical to our understanding of vision in general, and also to the understanding of the neural computations that work to overcome neural adaptation in normal subjects as well as in clinical patients. Moreover, because we are not aware of our fixational eye movements, they can also help us understand the underpinnings of visual awareness. Research in the field of fixational eye movements faded in importance for several decades during the late 20th century. However, new electrophysiological and psychophysical data have now rejuvenated the field. The last decade has brought significant advances to our understanding of the neuronal and perceptual effects of fixational eye movements, with crucial implications for neural coding, visual awareness, and perception in normal and pathological vision. This chapter will review the type of neural activity generated by fixational eye movements at different levels in the visual system, as well as the importance of fixational eye movements for visual perception in normal vision and in visual disease. Special attention will be given to microsaccades, the fastest and largest type of fixational eye movement.

Fixational eye movements in normal vision

Eye movements during fixation are necessary to overcome loss of vision due to adaptive neural mechanisms that normalize responses across neurons in the face of unchanging or uniform visual stimulation. Thus, the goal of oculomotor fixational mechanisms may not be retinal stabilization, but rather controlled image motion adjusted so as to overcome adaptation in an optimal fashion for visual processing (Skavenski et al., 1979). In the early 1950s, it was shown that all eye movements could be eliminated in the laboratory, causing visual perception to fade to a homogeneous field (Ditchburn and Ginsborg, 1952; Riggs and Ratliff, 1952; Yarbus, 1967). Although this may seem counterintuitive at first, it is a common experience in all sensory modalities: we do not generally notice that our shoes are on for 16 hours a day. When the eyes were released from artificial stabilization, or if the stabilized image was changed, visual perception reappeared (Krauskopf, 1957; Ditchburn et al., 1959; Gerrits and Vendrik, 1970; Sharpe, 1972; Drysdale, 1975), just as, if we wiggle our toes, we once again notice that our shoes are on. Coppola and Purves (1996) found that images of entoptic vascular shadows (which are very stable) disappear in as little as 80 ms, suggesting that normal visual processing entails a rapid mechanism for image creation and erasure.

Even though retinal stabilization is most easily achieved under laboratory conditions, fading of objects in our visual periphery occurs quite often in normal vision: we are usually unaware of this.
Peripheral fading of stationary objects was first noticed by Troxler (see Fig. 3A). Troxler (1804) reported that, under voluntary fixation, stationary objects in the periphery of vision tend to fade out and disappear. In the late 1950s, Clarke related Troxler fading to the fading of stabilized images in the laboratory (Ditchburn and Ginsborg, 1952; Riggs and Ratliff, 1952), and was the first to attribute both phenomena to neural adaptation (Clarke, 1957, 1960, 1961; Clarke and Belcher, 1962).

The three main types of fixational eye movements are tremor, drift and microsaccades. See Tables 1–4 of Martinez-Conde et al. (2004) for a review of fixational eye movement parameters in humans and primates.

Overall fixation stability does not appear to be affected significantly by age, although older observers show greater variability in their fixations along the horizontal meridian compared to the vertical meridian (Kosnik et al., 1986). Abadi and Gowen (2004) found that age is positively correlated with the amplitude, but not the frequency, of saccadic intrusions during fixation. The range of fixation for upward gaze may decrease somewhat with age (Ciuffreda and Tannen, 1995), whereas younger observers present more equivalent fixation variabilities along the two meridians (Kosnik et al., 1986).

Fixation instability is greater in the dark: microsaccades tend to become larger (Ditchburn and Ginsborg, 1953; Cornsweet, 1956; Snodderly, 1987), and drifts are both larger and more frequent (Ditchburn and Ginsborg, 1953; Nachmas, 1961). Deprivation of vision, whether congenital or acquired, can lead to severe fixation instability (Leigh and Zee, 1980; Leigh et al., 1989), reflecting an ocular motor system that has not been calibrated by experience. In the presence of severe foveal damage, a preferred retinal location or pseudo fovea may be developed (Barrett and Zwick, 2000). Fixation instability may also be greater in patients with attention-deficit/hyperactivity disorder than in normal subjects (Gould et al., 2001).

**Tremor**

Tremor is an aperiodic, wave-like motion of the eyes (Riggs et al., 1953), with a bandwidth of ~90 Hz (Carpenter, 1988) and an amplitude of ~8.5 s of arc (Eizenman et al., 1985). Tremor is the smallest of all eye movements (amplitudes are about the diameter of a cone in the fovea (Ratliff and Riggs, 1950; Yarbus, 1967; Carpenter, 1988)), making it difficult to record accurately: tremor amplitudes and frequencies are usually near the level of the recording system’s noise. The contribution of tremor to the maintenance of vision is unclear. It has been argued that tremor frequencies are well over the flicker fusion frequencies in humans, and so the tremor of the visual image may be ineffective as a stimulus (Ditchburn, 1955; Gerrits and Vendrik, 1970; Sharpe, 1972). But some studies suggest that tremor frequencies can be below the flicker fusion limit (Spauschus et al., 1999). Greschner et al. (2002) have shown that low frequencies (5 Hz) of tremor-like motion generate strong synchronous firing in the turtle’s retina. Furthermore, early visual neurons can follow high-frequency flickering that is above the perceptual threshold for flicker fusion (Martinez-Conde et al., 2002). Thus it is possible that even high-frequency tremor is adequate to maintain activity in the early visual system, which may then lead to visual perception. Hennig and colleagues have proposed that noise in the range of ocular tremor improves spatial resolution and may partly underlie the hyperacuity properties of the visual system (Hennig et al., 2002).

Tremor is generally thought to be independent in the two eyes. This imposes a physical limit to the ability of the visual system to match corresponding points in the retinas during stereovision (Riggs and Ratliff, 1951; Spauschus et al., 1999).

Patients with brainstem damage and alteration in their level of consciousness present tremor with lower frequencies than normal individuals (Shakhnovich and Thomas, 1977; Coakley, 1983; Ciuffreda and Tannen, 1995).

**Drift**

Drifts occur simultaneously with tremor and are slow motions of the eye that take place between microsaccades. During drifts, the image of the object being fixated moves across approximately a
dozen photoreceptors (Ratliff and Riggs, 1950). Drifts appear to be random motions of the eye (Ditchburn and Ginsborg, 1953), generated by the instability of the oculomotor system (Cornsweet, 1956). Also, the orbital mechanics impose elastic restoring forces that pull the eye back to the center from eccentric positions. Drifts to the center at the end of saccades are actively avoided by the neural integrator through the sustained firing of ocular motoneurons (Leigh and Zee, 2006).

Drifts may have a compensatory role in maintaining accurate visual fixation when microsaccades are absent, or when compensation by microsaccades is poor (Nachmias, 1959, 1961; Steinman et al., 1967; St Cyr and Fender, 1969). Drifts have been reported to be both conjugate (Ditchburn and Ginsborg, 1953; Spauschus et al., 1999) and disconjugate (Krauskopf et al., 1960; Yarbus, 1967). As with tremor, drifts may result from the noise and variability of neural firing processes to the ocular muscles (Eizenman et al., 1985; Carpenter, 1988). However, if drifts and tremor are indeed conjugate in the two eyes, this may suggest a central origin (at least in part) for drifts and tremor. This agrees with observations of reduced or absent tremor in patients with brainstem lesions (Shakhnovich and Thomas, 1977).

Drifts have usually been characterized as the eye position change that occurs during the periods in between microsaccades. This categorization method has the potential complication that one may unintentionally attribute non-drift activity (such as activity produced by undetected tremor) to drifts. Gur et al. (1997) found drifts to cause less variability in neuronal responses in V1 than a combination of drifts and microsaccades.

**Microsaccades**

Microsaccades are involuntary jerk-like fixational eye movements that occur 3–4 times per second. They are the largest and fastest of the three fixational eye movements. They carry the retinal image across a range of several dozen (Ratliff and Riggs, 1950) to several hundred photoreceptor widths (Martinez-Conde et al., 2000, 2002, 2004; Hafed and Clark, 2002; Moller et al., 2002; Engbert and Kliegl, 2003a, b, 2004) and are about 25 ms in duration (Ditchburn, 1980). Microsaccades cannot be defined according to magnitude alone, as the magnitude of voluntary saccades can be as small as that of fixational microsaccades. The one critical aspect that differentiates microsaccades from regular saccades is that microsaccades are produced involuntarily while the subject is attempting to fixate. Microsaccades in the macaque monkey are very similar to those in the human (Skavenski et al., 1975; Snodderly and Kurtz, 1985; Snodderly, 1987) (Fig. 1A) and they have been described in several other species (Carpenter, 1988), although they seem to be most important in species with foveal vision. Microsaccade velocities are parametrically related to microsaccade magnitudes, following the “main sequence” (Zuber and Stark, 1965; Martinez-Conde et al., 2000; Moller et al., 2002) (Figs. 3C–E). This is also true of large voluntary saccades, and therefore it has been proposed that microsaccades and voluntary saccades may be generated by the same oculomotor mechanisms (Zuber and Stark, 1965). Van Gisbergen and colleagues found that the activity of burst neurons is similar for saccades and microsaccades (Van Gisbergen and Robinson, 1977; Van Gisbergen et al., 1981). Microsaccades in the two eyes are generally conjugate (Lord, 1951; Ditchburn and Ginsborg, 1953; Yarbus, 1967; Moller et al., 2002). The fact that microsaccades are involuntary suggests a subcortical control mechanism for microsaccade production (Moller et al., 2002).

Recent studies suggest that microsaccades may increase the retinal refresh to counteract receptor adaptation on a short time-scale and help to correct fixation errors on a longer time-scale (Engbert and Kliegl, 2004). It must be noted that the concept of “refreshing” the retinal images is mainly metaphorical. It does not imply that the same region of a visual scene will stimulate the same set of photoreceptors over and over due to microsaccades (as if one were to flash a stationary stimulus on the retina). On the contrary, microsaccades are expected to produce retinal slippage. Consecutive microsaccades will generally shift any given set of photoreceptors to a slightly different region of the visual scene. However, sequential pairs of horizontal
Microsaccades may sometimes be coupled in a square-wave pattern that moves the eye along one vector and then back along the reverse vector.

Several statistics of microsaccades are indicative of cognitive processes. During an attentional task, microsaccade rates transiently decrease and then increase to a higher than baseline level. Moreover, the direction of microsaccades is biased toward the spatial locus of attention (Hafed and Clark, 2002; Engbert and Kliegl, 2003b).
Neural responses to microsaccades

The neural responses to microsaccades have been studied in the lateral geniculate nucleus (LGN) (Martinez-Conde et al., 2002; Reppas et al., 2002), area V1 (Leopold and Logothetis, 1998; Martinez-Conde et al., 2000; Snodderly et al., 2001; Martinez-Conde et al., 2002), and extrastriate cortex (Bair and O'Keefe, 1998; Leopold and Logothetis, 1998). Presumably, microsaccades first generate neural signals at the level of retinal photoreceptors by moving the receptive fields (RFs) of less adapted photoreceptors over otherwise stationary stimuli. This photoreceptor activity may then be transmitted to subsequent levels in the visual hierarchy.

In our experiments, macaque monkeys were trained to fixate their gaze on a small fixation spot while a stationary stimulus of optimal characteristics was placed over the RF of the recorded neuron (for instance, a bar with optimal dimensions and orientation when recording from area V1). Microsaccades were then correlated with subsequent neural activity. Because the visual stimulus did not move and the head was fixed, modulation of neural activity only occurred when fixational eye movements moved the visual RF over the stationary stimulus.

We found microsaccades to be predominantly excitatory in the LGN and area V1 (Martinez-Conde et al., 2002) (Fig. 1A–D). Neuronal responses following microsaccades were purely visual in nature: microsaccades led to an increase in neural activity when a stationary bar of light was centered over the neuron's RF. However, when the bar was removed from the RF (and the monitor facing the monkey was blank except for the fixation spot) microsaccades did not lead to changes in neural activity (Fig. 1C). This demonstrated that microsaccade-induced activity in early visual neurons was visual (rather than motor) in nature. The neurons were excited only when their RFs swept across stimuli, and they were not excited during equivalent action by the motor system in the absence of a visual stimulus (Martinez-Conde et al., 2000, 2002).

Increases in firing rate after microsaccades were clustered in bursts of spikes. These bursts of spikes were better correlated with previous microsaccades than either single spikes or instantaneous firing rate (Fig. 2). Bursts that were highly correlated with previous microsaccades had large spike numbers and short inter-spike intervals (Martinez-Conde et al., 2000). Therefore long, tight bursts of spikes are the type of activity most effective in sustaining a visible image during fixation (Martinez-Conde et al., 2000, 2002). It is important to note that those bursts that were best indicators of previous microsaccades are not defined in terms of their biophysical properties, and may not share a common biophysical mechanism. Burst definitions that are solely based on specific biophysical parameters are unavoidably arbitrary, and they are not necessarily meaningful from a perceptual standpoint. On the contrary, when we correlate all possible burst parameters to previous microsaccades, we have the great advantage that we are letting perception tell us what an optimal burst is. The next section will establish that microsaccades are directly correlated with visibility; therefore bursts that are well correlated with previous microsaccades must encompass the neural code for visibility.

The optimality of the stationary visual stimulation had an effect on the size of bursts following microsaccades: when the stationary stimulus covering the neuron's RF had optimal characteristics (for instance, a bar of light with optimal orientation), microsaccades during fixation generated long bursts. When the stimulus centered on the RF had non-optimal characteristics, microsaccades produced shorter bursts. Thus long bursts were correlated with salient optimal stimuli, whereas short bursts were correlated with non-optimal visual stimulation (Martinez-Conde et al., 2002). Figure 1B plots the correlation between microsaccades and bursts for optimal vs. non-optimal stimuli in area V1.

To address the effectiveness of microsaccades in generating neural activity, we compared neural responses induced by microsaccades to neural responses induced by flashing bars. Onset responses to flashing bars in the LGN and area V1 were about 7 times larger than the responses to stationary bars moved across the neurons' RFs by microsaccades, perhaps because of the relative abruptness of flashes as stimuli (Martinez-Conde et al., 2002) (Fig. 1D, E). This experiment demonstrated that changes in retinal stimulation (which may or may not be due to retinal slippage)
are critical to generating neuronal responses in the visual system, thereby counteracting fading. Flashes (for which there is a low probability of slippage) are even more effective than microsaccades in generating neural responses in the LGN and V1.

Microsaccades could enhance spatial summation by synchronizing the activity of nearby neurons (Martinez-Conde et al., 2000). By generating bursts of spikes, microsaccades may also enhance temporal summation of responses from neurons with neighboring RFs (Martinez-Conde et al., 2000). Moreover, microsaccades may help disambiguate latency and brightness in visual perception, allowing us to use latency in our visual discriminations (Martinez-Conde et al., 2000). Changes in contrast can be encoded as changes in the latency of neuronal responses (Albrecht and Hamilton, 1982; Albrecht, 1995; Gawne et al., 1996). Since the brain knows when a microsaccade is generated, differential latencies in visual responses could be used by the brain to indicate differences in contrast and salience.

Suppression of perception and neural firing during large saccades is well known to exist (Wurtz, 1968, 1969; Macknik et al., 1991; Burr et al., 1994; Bridgeman and Macknik, 1995; Ross et al., 1996, 1997, 2001), but the existence of microsaccadic suppression is more controversial. Some studies have reported elevation of visual thresholds during microsaccades (Ditchburn, 1955; Beeler, 1967), but others have found little or no threshold elevation (Krauskopf, 1966; Sperling, 1990). In the early visual system (LGN and area V1), microsaccades generate increases in neural activity, but not suppression (Martinez-Conde et al., 2000, 2002). Murakami and colleagues have proposed that the extrastriate cortex, especially area MT (Murakami and Cavanagh, 2001; Sasaki et al., 2002) could be the locus for microsaccadic suppression. However, electrophysiological studies in macaque MT indicate that microsaccades induce strong excitatory responses in this area (Bair and O’Keefe, 1998). This seems to contradict a specific role of MT in microsaccadic suppression, although one cannot
rule out that neural responses in MT may drive a microsaccadic suppression system later in the visual hierarchy: the question remains open.

Perceptual responses to microsaccades
The role of microsaccades during visual fixation was first discussed 50 years ago. Cornsweet (1956) originally proposed that microsaccades return the eyes to the fixation target, and thus serve to correct the intersaccadic drifts of the eye. It was also postulated that microsaccades may play an “important role in maintaining vision by counteracting retinal fatigue” (Ditchburn et al., 1959; Nachmias, 1961). Carpenter (1988) postulated that, of the three types of fixational eye movements, only microsaccades may contribute significantly to the maintenance of vision, as drift velocities are too low and the magnitude and frequency of tremor would make it more detrimental than otherwise. Not all studies agreed, however. Starting in the late 1960s, and through the 1970s, a lively discussion on the importance of microsaccades for the maintenance of vision took place. Its main representatives were Ditchburn (microsaccades play an essential part in normal vision) and Steinman (microsaccades serve no useful purpose). The strongest evidence against the role of microsaccades in preserving visual perception was as follows: (1) trained subjects can suppress their microsaccades for several seconds when asked to hold their gaze on a visible target (Fiorentini and Ercoles, 1966; Steinman et al., 1967, 1973), and (2) Microsaccades are naturally suppressed while subjects perform high-acuity tasks, such as when sighting a rifle or threading a needle (Winterson and Collewijn, 1976; Kowler and Steinman, 1979), and (2) Troxler fading tends to occur during precise fixation (Winterson and Collewijn, 1976; Kowler and Steinman, 1979), and (2) Troxler fading tends to occur during precise fixation (Troxler, 1804). It followed that microsaccades may counteract Troxler fading.

To establish the correlation between microsaccades and visibility, we conducted a continuously sampled two-alternative forced choice (2-AFC) task in which the subject fixated a small spot, and simultaneously reported the visibility of a peripheral target (Fig. 3B), via button press (Martinez-Conde et al., 2006). Every millisecond of the experiment was coded as either visible (or intensifying) or invisible (or fading), according to the subject’s report. A naïve subject later reported that she had thought the stimulus was modulating in brightness physically: she did not realize that her fixation behavior was in fact driving the perceptual alternations.

Eye position was simultaneously measured, and microsaccades automatically identified with an objective algorithm (Martinez-Conde et al., 2000, 2002, 2006). We found that microsaccade probabilities, rates, and magnitudes increased before transitions to a more visible state (Fig. 4A–C, black lines), and decreased before transitions into a period of invisibility (fading) (Fig. 4A–C, gray lines). Moreover, binocular microsaccades were more effective than monocular microsaccades (Fig. 4D–F). The results revealed, for the first time, a direct correlation between microsaccades and visibility during fixation, and suggested that microsaccades may cause the bi-stable dynamics seen during Troxler Fading.

The psychophysical link found between microsaccades and visibility matched the predictions from our previous primate studies, in which microsaccades generated visual responses in V1
and LGN neurons (Martinez-Conde et al., 2000, 2002). Our combined psychophysical and physiological data indicate that microsaccades drive the perception of visibility during Troxler fading, and that they increase the responses of neurons in the early visual system. We can therefore conclude that the neuronal responses produced by microsaccades in the LGN and V1 (and presumably also in the retina) are the neural correlates of the perception of visibility during Troxler fading. When microsaccades are produced, early visual neurons fire and the stimulus appears visible. When microsaccades are suppressed, early visual neurons fall silent, and the stimulus becomes invisible, due to neural adaptation processes. Thus the neural adaptation necessary for the perception of Troxler fading takes place in the very first stages of the visual system.

Having shown that microsaccades contribute significantly to the maintenance of visibility, an
open question remains: does the role of microsaccades differ from the role of drifts and tremor? Microsaccades may be more important for peripheral vision, whereas drifts/tremor may maintain foveal vision (Clowes, 1962; Gerrits and Vendrik, 1974) when microsaccades are suppressed during specific tasks. Foveal RFs may be so small that drifts and tremor could be sufficient to prevent visual fading in the absence of microsaccades. RFs in the periphery may be so large that only microsaccades are large and fast enough (compared to drifts and tremor) to prevent visual fading, especially with low-contrast stimuli (Gerrits and Vendrik, 1974; Gerrits, 1978; Ditchburn, 1980; Martinez-Conde et al., 2000). But one should keep in mind that, if one could eliminate drifts and tremor altogether, while preserving microsaccades, microsaccades alone might then

Fig. 4. Microsaccade dynamics before transitions toward perceptual intensification vs. fading. (A) Average probability of microsaccades before transitions toward perceptual intensification (black) vs. fading (gray). The horizontal dashed line indicates average probability of microsaccades during the recording session. (B) Average rate of microsaccades before perceptual transitions. (C) Average microsaccade magnitude before perceptual transitions. The combined results in (A–C), indicate that a reduction in microsaccade rates and magnitudes leads to perceptual fading, whereas increases in microsaccade rates and magnitudes lead to perceptual intensification, confirming our predictions. (D) Average percentage increase in microsaccade probabilities before transitions toward perceptual intensification vs. fading. All microsaccades (same data as in panel A). (E) Binocular microsaccades (all other details as in (D)). (F) Monocular microsaccades (all other details as in (D)). Thin lines indicate SEM between subjects (n = 8 subjects). Modified from Martinez-Conde et al. (2006), with kind permission from Elsevier.
suffice to sustain both peripheral and foveal vision during fixation. In summary, all fixational eye movements may contribute to the maintenance of vision to some degree, and their relative contributions may depend on the specific task and stimulation conditions (Martinez-Conde et al., 2004).

Microsaccades may also drive perceptual flips in binocular rivalry (Sabrin and Kertesz, 1983) and other bi-stable percepts. Because microsaccades are correlated to visibility (Martinez-Conde et al., 2006) and they are suppressed during precise fixation, it follows that microsaccades must contribute (at least partially) to the perception of those classes of visual illusions that vary in strength depending on the accuracy of fixation. The experiments above demonstrate that Troxler fading is counteracted by microsaccades (Martinez-Conde et al., 2006). Second-order adaptation (such as the filling-in of artificial scotomas (Ramachandran and Gregory, 1991; Spillmann and Kurtenbach, 1992; Ramachandran et al., 1993)) is also facilitated by precise fixation. It therefore follows that microsaccades may similarly counteract filling-in of dynamic textures.

Many visual illusions attenuated when the observer fixates his/her gaze carefully (thus suppressing microsaccades), suggesting that microsaccades drive (completely or partially) the generation of the illusory percept. Such illusions include the illusory motion of static patterns (Fermuller et al., 1997), such as Leviant’s “Enigma” (Leviant, 1996), the Ouchi illusion (Ouchi, 1977), or Kitaoka’s “Rotating Snakes” (Kitaoka and Ashida, 2003), and even some classical brightness illusions such as the Hermann grid (Hermann, 1870). A recent study has proposed that microsaccades can be ruled out as a contributor to the Enigma illusion (Kumar and Glaser, 2006). However, no eye movement measurements were carried out, and so the question remains open.

The fact that microsaccades can be transiently suppressed by carefully fixating our gaze provides us with a very useful tool to predict the potential involvement of microsaccades in a variety of percepts.

Head-unrestrained microsaccades
Steinman and Kowler proposed that microsaccades were a laboratory artifact: i.e. that microsaccades do not occur in normal viewing conditions, but only after prolonged fixation in the laboratory when the subject’s head is restrained (for instance, with a bite bar) (Kowler and Steinman, 1980). They reasoned that during natural viewing conditions, normal head movements should suffice to maintain vision during fixation, and therefore very few or no microsaccades need be produced (Skavenski et al., 1979; Kowler and Steinman, 1980; Steinman and Collewijn, 1980). However, even if microsaccades have no significant effect on the visibility of moving stimuli (i.e. moving either on their own or due to head movements), they may be generated nevertheless. Indeed, it is possible that microsaccades could serve to enhance the visibility of a moving stimulus when the dynamics of head movements or the intrinsic stimulus motion do not have the ideal parameters to invoke visibility.

This is a critical issue to resolve: if microsaccades are a laboratory artifact, then their significance to normal and clinical vision is vastly diminished, even if they are correlated with visibility and neural activity. To address this possibility, we repeated the above experiment in head-unrestrained conditions (i.e. without the chinrest). We found that that microsaccade characteristics and functional properties were equivalent with heads restrained and unrestrained (Fig. 5A–C). Thus microsaccades are a natural oculomotor behavior, and not a laboratory artifact of head fixation.

Moreover, evidence from a clinical subject (A.I.), who is unable to make eye movements, shows that in the absence of eye movements, normal head movements alone do not suffice to maintain vision. Although the authors of the A.I. studies did not address microsaccades per se, they established that A.I. learned to move her head in a “saccadic” fashion, in order to conduct visual tasks such as reading, and visuomotor tasks such as pouring tea (Gilchrist et al., 1997, 1998; Land et al., 2002). Therefore saccadic movements, either of the head or of the eye, may represent an optimal sampling strategy for the visual system. Microsaccades may thus provide us with a window into the visual sampling mechanisms used by the brain during fixation.
Microsaccades during visual exploration

Steinman et al. (1973) and Kowler and Steinman (1979, 1980) reported that microsaccades are not helpful in tasks requiring complex visual information processing, and therefore they are much less common during brief fixations interposed between large saccades (in activities such as reading or counting) than during prolonged fixation. Winterson and Collewijn (1976) also reported that microsaccades are far less frequent during fine visuomotor tasks than during maintained fixation.

In the last decade, several laboratories have developed objective and automatic algorithms for microsaccade detection (Martinez-Conde et al., 2000; Engbert and Kliegl, 2003b). Current objective algorithms allow the identification of hundreds of thousands of microsaccades in a fast and automatic manner. Thus, the results obtained in the 1970s with subjective microsaccade identification techniques must now be re-evaluated with modern and objective methods. Figure 6 plots the eye movements of a human subject during the visual exploration of a static image. We found that the periods of fixation accounted for approximately 80% of the time spent in free-viewing, with either restrained or unrestrained heads. During the other 20% of the time we are virtually blind, due to saccadic suppression mechanisms. Since fixational eye movements sustain visibility during fixation, it follows that fixational eye movements may drive up to 80% of our visual experience. Microsaccades were prominent during the fixation periods that naturally occur during visual exploration. Moreover, the dynamics of microsaccades

Fig. 5. Head-unrestrained microsaccade dynamics. (A) Average probability of microsaccades before perceptual transitions under head unrestrained conditions. Thin lines indicate SEM between subjects (n = 7 subjects). Modified from Martinez-Conde et al., 2006, with kind permission from Elsevier. (B, C) Microsaccade main sequences for visual fixation with restrained vs. unrestrained head. (B) Microsaccades (n = 515; rate = 4.27 Hz) from a human subject during 2 min of visual fixation, with head supported by a chinrest. (C) Microsaccades (n = 444; rate = 3.7 Hz) from the same subject during 2 min of visual fixation with head unrestrained. Dashed lines indicate the 95% confidence intervals.
produced during visual exploration were similar to microsaccades produced during prolonged fixation. Since microsaccades counteract peripheral fading during fixation (Martinez-Conde et al., 2006), it may be that microsaccades drive a large fraction of our visual experience. Future research will quantify the fraction of visual experience driven by microsaccades vs. the other fixational eye movements during various visual tasks.

We have also observed that microsaccades occur in untrained monkeys during spontaneous free-viewing, and in trained monkeys during guided-viewing (i.e. with the fixation point appearing at random locations over the image; Figs. 7 and 8). Livingstone et al. (1996) also reported, anecdotally, that microsaccades occur in fixations during free- and guided-viewing in monkeys.

Abnormal eye movements during fixation

Impaired fixational eye movements are observed in patients with a variety of central and peripheral pathologies (Shakhnovich and Thomas, 1974, 1977; Ciuffreda and Tannen, 1995). Although we spend about 80% percent of our waking lives fixating our gaze, the contribution of impaired fixational eye movements to vision loss is generally overlooked. This gap in knowledge has prevented the field from developing new treatments and early diagnostic tools to ameliorate those visual deficits that are due to impaired fixational eye movements. The evaluation of fixational eye movements may prove useful in the differential diagnosis of disorders of the oculomotor system (especially at early stages) and their quantitative measurement (Yamazaki, 1968; Filin and Okhotsimskaya, 1977; Okhotsimskaia, 1977; Hotson, 1982). The clinical evaluation of fixational eye movements may also help to determine their potential role in therapies for visual deficits such as amblyopia, and in establishing the optimal duration of a given treatment (von Noorden and Burian, 1958; Ciuffreda et al., 1979a).

A non-exhaustive classification of abnormal eye movements during fixation follows below (Table 1). I have addressed the perceptual consequences of these abnormal eye movements when possible. See Leigh and Zee (2006) for detailed discussion on the pathophysiology of the various disorders of fixation. As the next several pages illustrate, the fixational eye movement system must achieve a very delicate balance: insufficient fixational eye movements lead to adaptation and visual fading, whereas excessive motion of the eyes produces blurring and unstable vision during fixation.
Increased drift and paucity of microsaccades in amblyopia

Amblyopia is defined as a visual acuity loss that is not attributable to detectable pathology or uncorrected refractive error. It is generally associated with strabismus, anisometropia, or both (Bedell et al., 1990). It has a known relationship with unsteady fixation and impaired fixational eye movements. Amblyopes exhibit decreased microsaccades and increased drifts in the amblyopic (non-dominant) eye 75% of the time spent during fixation (Ciuffreda and Tannen, 1995). However, fixation in the dark-adapted state is normal or close to normal (Wald and Burian, 1944; von Noorden and Burian, 1958). The dominant eye

Fig. 7. Responses of a V1 cell to a white circle during guided-viewing. The upper left inset shows the fixation point (and 2 x 2 degree fixation window) in relationship to the cell's RF and the stimulus (large circle). In (A, B) the fixation spot jumped randomly to each location in a square grid around the stimulus and each dot represents the foveal position at the time of each spike (accounting for a 35 ms response latency); (C, D) same data filtered so that each dot represents a burst of 4 or more spikes within a 20 ms interval. (B, D) are the same as (A, C), with stimulus removed. The large responses in (C) and (D) are to microsaccades and show preference at the cell's orientation. Reprinted from Martinez-Conde et al. (2000), with kind permission from Nature Publishing Group.

Fig. 8. Correlation of microsaccades to neural activity during a guided-viewing task in an awake monkey. (A) Visual stimulus scanned by a V1 RF during the guided-viewing task. (B) Responses (spike densities) of the V1 cell as a function of eye position. (C) Correlation of microsaccades to spikes from the data in (B).

Increased drift and paucity of microsaccades in amblyopia

Amblyopia is defined as a visual acuity loss that is not attributable to detectable pathology or uncorrected refractive error. It is generally associated with strabismus, anisometropia, or both (Bedell et al., 1990). It has a known relationship with unsteady fixation and impaired fixational eye movements. Amblyopes exhibit decreased microsaccades and increased drifts in the amblyopic (non-dominant) eye 75% of the time spent during fixation (Ciuffreda and Tannen, 1995). However, fixation in the dark-adapted state is normal or close to normal (Wald and Burian, 1944; von Noorden and Burian, 1958). The dominant eye
presents normal fixational eye movements, and binocular fixation is also normal (Ciuffreda et al., 1980). Fixation errors produced in amblyopes by excessive drift of gaze position are usually corrected by subsequent drifts in the opposite direction, rather than by microsaccades. Although strabismus often results in amblyopia, the abnormal fixational eye movement pattern described here is correlated to amblyopia irrespective of whether strabismus is present (Ciuffreda et al., 1979b, d, 1980; Srebro, 1983).

Increased drift and suppression of microsaccades in patients with severe amblyopia are often associated with rapid fading of the “small fixation spot, small and large acuity targets, and even portions of the laboratory” during monocular fixation with the amblyopic eye (Lawwill, 1968; Hess et al., 1978; Ciuffreda et al., 1979b, c). According to one patient’s report, he “made saccades to revive the faded or blanked-out portions” of the image during fixation with the amblyopic eye (Ciuffreda et al., 1979b). Visual fading in amblyopic eyes (in which drifts, but not microsaccades, are common) is likely related to Troxler fading during suppression of microsaccades in normal eyes (Martinez-Conde et al., 2006) (Fig. 4). The prevalence of perceptual fading in amblyopia also lends support to the theory that microsaccades may provide more optimal visual sampling dynamics than drifts.

Increased fixational drift can produce perceptual shifting of visual targets (Srebro, 1983). Increased drift amplitudes may also reduce visual acuity in amblyopia by moving the retinal images onto more eccentric positions, as well as contribute to increased variability in visual acuity measurements (Ciuffreda et al., 1979a, 1980). However, not all studies agree that increased drift leads to visual acuity loss (von Noorden and Burian, 1958; Srebro, 1983).

Increased drift velocities and amplitudes in amblyopia may be due to at least three factors: ineffectiveness of the microsaccadic system, ineffectiveness of the smooth pursuit velocity-correcting system, and/or normal drift characteristics for non-foveal fixation, as amblyopic patients often fixate on eccentric locations (Ciuffreda et al., 1979b). Patients with macular scotomas, and other pathologies that lead to prolonged deprivation of vision from one

Table 1. Abnormal eye movements during fixation

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eye, may also exhibit increased drift, with similar characteristics to drift in amblyopes (Leigh et al., 1989; Ciuffreda and Tannen, 1995).

Fixational eye movements in amblyopia tend to normalize during the course of successful orthoptics therapy (von Noorden and Burian, 1958; Ciuffreda et al., 1979a). However, all visual and oculomotor functions in the amblyopic eye may not improve concurrently (Ciuffreda et al., 1979a), bringing into question the relative importance of the sensory vs. motor deficit in amblyopia (von Noorden and Burian, 1958; Ciuffreda et al., 1978). It follows that amblyopic therapies should not be discontinued upon normalization of visual acuity and centralization of fixation, but should be extended until fixational eye movements are normalized or reach a stable state (Ciuffreda et al., 1979a). Ciuffreda et al. have suggested that the “critical period” for certain aspects of oculomotor plasticity in amblyopia may extend into adulthood. The lack of normalization of fixational eye movements in amblyopia may be responsible for some of the patients reverting to their former condition after the termination of the therapy (Ciuffreda et al., 1979a).

**Saccadic intrusions and oscillations**

Saccadic intrusions are abnormal horizontal saccades that “intrude” or interrupt accurate fixation (Ciuffreda and Tannen, 1995). Saccadic intrusions are biphasic: although one phase may be a smooth eye movement, the phase that takes the fovea away from its intended target is always a saccade (Sharpe and Fletcher, 1986). Saccadic intrusions tend to be 3–4 times larger than physiological microsaccades (Abadi and Gowen, 2004) and they may cause perceptual instability during fixation (Feldon and Langston, 1977).

Although saccadic intrusions are found in a variety of neurological disorders (Leigh and Zee, 2006), it is important to note that they also occur in normal subjects, with no adverse effect (although their frequency and amplitude are generally smaller than in patients). Abadi and Gowen (2004) found that, in a population of 50 healthy subjects, all 50 individuals presented saccadic intrusions during fixation.

Strabismus without amblyopia is often characterized by normal drift accompanied by saccadic intrusions during fixation (Ciuffreda et al., 1979c, 1980). These saccadic intrusions consist of an error-producing saccade followed (150–500 ms later) by an error-correcting saccade. Intrusion amplitudes usually range from 0.5 to 3.0°, and occur 1–4 times per second. Saccadic intrusions in strabismus without amblyopia do not appear to affect visual acuity (Ciuffreda et al., 1979b). Moreover, the production of saccadic intrusions in strabismus may result from local adaptation, and their occurrence may prevent and/or counteract visual fading (Ciuffreda et al., 1979c).

Saccadic oscillations are bursts of disruptions of fixation, and they may be thought of as salvos of saccadic intrusions (Sharpe and Fletcher, 1986). They may occur in normal subjects during blinks, vergence movements, or large vertical saccades, and moreover they may be produced voluntarily by some individuals (Ramat et al., 2005). Sustained high-frequency oscillations may give rise to oscillopsia (i.e. oscillating vision), due to the excessive motion of the retinal images (Leigh et al., 1994).

A key aspect to the identification of the various types of saccadic intrusions and oscillations is whether they present an intersaccadic interval, or not. Saccadic oscillations with an intersaccadic interval include square-wave jerks, macro square-wave jerks, square-wave oscillations, saccadic pulses, double saccadic pulses, and macro saccadic oscillations. Saccadic oscillations without an intersaccadic interval include microsaccadic oscillations, opsoclonus, microsaccadic opsoclonus, ocular flutter, microsaccadic flutter, and voluntary nystagmus (also called voluntary flutter). See Table 2 for a classification of saccadic intrusions and oscillations. Figure 9 illustrates several types of saccadic intrusions and oscillations.

**Saccadic intrusions and oscillations with an intersaccadic interval**

Saccadic intrusions and oscillations with saccadic intervals may share a common pathogenesis, usually involving dysfunction of saccade control due
to lesions of the frontal eye field, the superior colliculus, or disruption of the inputs to the superior colliculus (Leigh and Zee, 2006).

Square-wave jerks. Square-wave jerks are the most common type of saccadic intrusion (Sharpe and Fletcher, 1986; Abadi and Gowen, 2004). Monophasic square-wave jerks are couplets of unconscious, involuntary, conjugate microsaccades that occur in opposite horizontal directions (a microsaccade moving away from the fixation target, and a corrective microsaccade about 200 ms later) (Ciuffreda and Tannen, 1995). Their name comes from their “square-wave” appearance on the electro-oculogram (Feldon and Langston, 1977). Biphasic square-wave jerks are microsaccade triplets: the first microsaccade moves the eye away from the fixation target; the second microsaccade is twice as large as the first one and travels toward the fixation target, but then takes the eye beyond its original position; the third and final microsaccade has an amplitude equivalent to the initial microsaccade, and it returns the eye to its original position (Abadi and Gowen, 2004).

Square-wave jerks usually range in amplitude from 0.5 to 5° (Ciuffreda and Tannen, 1995), follow the main sequence, and their frequency is equivalent to that of microsaccades (Feldon and Langston, 1977). Because square-wave jerk dynamics are so similar to microsaccade dynamics, and because normal microsaccades are absent in some square-wave jerk patients, it has been proposed that square-wave jerks are abnormal microsaccades (Feldon and Langston, 1977; Ohtsuka et al., 1986). It is known that even a minimal enlargement of horizontal microsaccades tends to

Table 2. Saccadic intrusions and oscillations

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produce square-wave coupling in normal subjects (Ditchburn and Ginsborg, 1953; Feldon and Langston, 1977), and so it follows that square-wave jerks may be abnormally enlarged microsaccades (Shallo-Hoffmann et al., 1989).

Although square-wave jerks are common in certain diseases, they also occur in most normal subjects, without adverse effect (Shallo-Hoffmann et al., 1990; Ciuffreda and Tannen, 1995; Abadi and Gowen, 2004). Square-wave jerks are produced in all conditions of illumination, and also with closed eyes (Shallo-Hoffmann et al., 1989; Abadi et al., 2000). Just as with microsaccades, mild occurrences of square-wave jerks may be voluntarily and transiently suppressed during strict fixation (Ciuffreda et al., 1979d; Herishanu and Sharpe, 1981).

Shallo-Hoffmann and colleagues proposed that more than 16 square-wave jerks per minute during fixation, and over 20 square-wave jerks per minute in the dark or with closed eyes should be considered abnormal (Shallo-Hoffmann et al., 1989). However, Abadi and Gowen have recently reported that normal subjects may present up to 42.5 square-wave jerks per minute during fixation in mesopic conditions (Abadi and Gowen, 2004).

Frequent square-wave jerks are common in patients with functional strabismus, and they may precede the postnatal appearance of congenital nystagmus (Hertle et al., 1988; Ciuffreda and Tannen, 1995).

Square-wave jerks may occur almost continuously in progressive supranuclear palsy, cerebellar, and local cerebral lesions (Sharpe and Fletcher, 1986; Leigh and Zee, 2006). Cerebral lesions lead to square-wave jerks that are usually smaller than square-wave jerks of cerebellar origin, but their rates are equivalent in both conditions (Sharpe and Fletcher, 1986; Leigh and Zee, 2006). Frequent square-wave jerks may reflect a disorder of the saccadic pause cells, or a dysfunctional cerebellar-related saccadic gain control system (Ciuffreda and Tannen, 1995).

Macro square-wave jerks. Macro square-wave jerks (also called square-wave pulses) are rare (Leigh and Zee, 2006). They are larger than square-wave jerks (5–15° or more) (Ciuffreda and Tannen, 1995). However, they may not be simply enlarged square-wave jerks, as they have shorter intersaccadic intervals (50–150 ms) between sequential saccades and they take place on just one side of the fixation target (right or left) (Sharpe and Fletcher, 1986). Macro square-wave jerks are produced in bursts and they vary in amplitude. They occur in light or darkness, but they may be suppressed during monocular fixation (Leigh and Zee, 2006). Macro square-wave jerks are associated with cerebellar disease and multiple sclerosis (Leigh and Zee, 2006).

Square-wave oscillations. Square-wave oscillations are characterized by horizontal oscillations, in which each half cycle is indistinguishable from a sporadic square-wave jerk. The eyes typically...
oscillated to just one side of the fixation position (Sharpe and Fletcher, 1986). This disorder can be found in Parkinson’s disease combined with alcoholic cerebellar degeneration (Sharpe and Fletcher, 1986) and in progressive supranuclear palsy (Abel et al., 1984).

**Saccadic pulses and double saccadic pulses.** Saccadic pulses are high-frequency saccades that take the eyes away from the intended position. After each saccadic pulse, negative exponential smooth eye movement returns the eyes to the position previous to the saccade. Saccadic pulses are the least frequently observed type of saccadic intrusion in normal human subjects, although they can occur about once per minute (Abadi and Gowen, 2004).

Double saccadic pulses are intermittent and closely spaced saccadic couplets. They may occur in normal subjects sporadically (once every 2.5 min, Abadi and Gowen, 2004), especially in miniature form (Sharpe and Fletcher, 1986). Double saccadic pulses are the second most prevalent saccadic intrusion in normal subjects (after square-wave jerks) (Abadi and Gowen, 2004). Frequent saccadic pulses occur in patients with internuclear ophthalmoplegia (Leigh and Zee, 2006).

**Macrosaccadic oscillations.** Macrosaccadic oscillations look like bursts of conjugate, horizontal saccades, separated by intersaccadic intervals of about 200 ms (Sharpe and Fletcher, 1986). The saccades are so hypermetric that they overshoot the intended fixation target in both directions (Zee and Robinson, 1979; Sharpe and Fletcher, 1986; Leigh and Zee, 2006). The oscillations occur with increasing, then decreasing amplitudes, in a crescendo–decrescendo pattern (Selhorst et al., 1976). Saccade amplitudes may reach 40° or more (Selhorst et al., 1976; Sharpe and Fletcher, 1986). The bursts of oscillations last for several seconds and they are usually evoked by attempts to shift visual fixation (Selhorst et al., 1976). However, they may also occur during attempted fixation, or in the dark. Macrosaccadic oscillations may interfere with visual perception by changing the direction of gaze (i.e. losing one’s place during reading; R. John Leigh, personal communication).

Saccadic intrusions and oscillations without an intersaccadic interval

The pathogenesis of oscillations without saccadic intervals (such as flutter and opsoclonus) remains controversial, as no animal model exists. They probably reflect an inappropriate, repetitive, and alternating discharge pattern of different groups of burst neurons (Leigh and Zee, 2006). Ramat and colleagues have recently proposed a theoretical model for saccadic oscillations based on: (a) the coupling of excitatory and inhibitory burst neurons in the brainstem, and (b) the hypothesis that burst neurons show postinhibitory rebound discharge (Ramat et al., 1999, 2005).

Normal subjects present transient horizontal conjugate oscillations without an intersaccadic interval during vergence movements, combined saccade–vergence movements, vertical saccades, pure vergence, and blinks (Ramat et al., 2005).

**Microsaccadic oscillations.** Microsaccadic oscillations appear as bursts or spindles of horizontal microsaccades without an intersaccadic interval, in a crescendo–decrescendo pattern and with amplitudes under 1°. They may occur in normal subjects about twice per minute. They are also found in cerebellar patients with similar characteristics but higher rates (about eight times a minute) (Sharpe and Fletcher, 1986).

**Opsoclonus and microsaccadic opsoclonus.** Opsoclonus is characterized by multi-directional saccades of varying amplitudes, without an intersaccadic interval. The saccades are usually conjugate (Sharpe and Fletcher, 1986) and they occur in all three planes (horizontal, vertical and torsional) (Foroozan and Brodsky, 2004). Opsoclonus may result from a combination of uncontrolled saccades and microsaccades (Ellenberger et al., 1972). It may occur during smooth pursuit, convergence or blinks, and it often persists during

Macrosaccadic oscillations are associated with lesions affecting the fastigial nucleus and its output in the superior cerebellar peduncles, and they may also occur in some forms of spinocerebellar ataxia (Leigh and Zee, 2006).
eyelid closure or sleep (Leigh and Zee, 2006). Opsoclonus is typically associated with brainstem encephalitis (Ashe et al., 1991), diencephalic lesions (Ashe et al., 1991), and cerebellar lesions (Ellenberger et al., 1972; Sharpe and Fletcher, 1986; Ashe et al., 1991). Opsoclonus may also occur without evident cause (Leigh and Zee, 2006).

Microsaccadic opsoclonus can be described as a 1°-saw-tooth pattern of microsaccades in all three planes, without intersaccadic intervals (Leigh et al., 1994; Foroozan and Brodsky, 2004). Microsaccadic opsoclonus can be associated with blurred vision and oscillopsia. The etiology is currently unknown (Foroozan and Brodsky, 2004).

Ocular flutter and microsaccadic flutter. Unlike opsoclonus, ocular flutter is limited to one plane (typically the horizontal plane) and it consists of 1–5° saccades without intersaccadic intervals (Sharpe and Fletcher, 1986; Foroozan and Brodsky, 2004). On rare occasions, ocular flutter may be observed on the vertical plane (Hotson, 1982; Sharpe and Fletcher, 1986). Ocular flutter may be intermittent (Leigh and Zee, 2006) and it is often precipitated by a change in gaze (Ashe et al., 1991). It occurs in the dark as well as in the light, and it is typically conjugate (Cogan et al., 1982).

Opsoclonus and flutter appear closely related, and they may be seen in the same patient at different stages of an illness (Ellenberger et al., 1972; Sharpe and Fletcher, 1986; Ashe et al., 1991). However, opsoclonus is usually observed in the sickest patients (Ellenberger et al., 1972). Patients with multiple sclerosis and with signs of cerebellar and brainstem dysfunction often have flutter (Ellenberger et al., 1972; Sharpe and Fletcher, 1986). Opsoclonus and flutter are also associated with neuroblastoma and tumors of the lung, breast, and uterus (Ashe et al., 1991).

Opsoclonus and flutter may produce blurred vision (Zee and Robinson, 1979) and they frequently generate oscillopsia, due to the high frequency of the oscillations (which generates large retinal slip velocities), even when the oscillations themselves are of small amplitude (Leigh et al., 1994). Opsoclonus and flutter cannot be suppressed by voluntary effort (Leigh and Zee, 2006), but they diminish with eyelid closure (Ellenberger et al., 1972).

Microsaccadic flutter is characterized by abnormal microsaccadic oscillation, comprised of back-to-back horizontal microsaccades in a saw-tooth pattern, ranging from 15 to 50 Hz in frequency and with amplitudes of 0.1–0.5° (Carlow, 1986; Sharpe and Fletcher, 1986; Ashe et al., 1991). It usually causes disruptive oscillopsia (Sharpe and Fletcher, 1986; Ashe et al., 1991). The etiology is unknown (Sharpe and Fletcher, 1986; Ashe et al., 1991).

Voluntary nystagmus or flutter. About 8% of the population has the ability to generate (usually by making a vergence effort) bursts of high-frequency horizontal oscillations of back-to-back saccades, about 2–5° in amplitude (Sharpe and Fletcher, 1986; Ashe et al., 1991). Although this pattern (often used as a party trick) is usually referred to as voluntary nystagmus, it is not truly nystagmus, since slow eye movements are absent (Sharpe and Fletcher, 1986). Voluntary nystagmus causes oscillopsia; however it is not a clinical condition as it is generated voluntarily (Ashe et al., 1991). Voluntary nystagmus has equivalent dynamics and characteristics to pathological involuntary flutter, and it can be mistaken with it (Sharpe and Fletcher, 1986; Ashe et al., 1991). Thus by studying voluntary nystagmus we may gain insight into the nature of some disorders, such as involuntary flutter. Voluntary nystagmus may be an intrinsic and normally undeveloped capability that can be learned by most people (Hotson, 1984), potentially creating an untapped resource for the study of visual disorders.

Nystagmus during attempted fixation

This is a type of pathological oscillation that increases in size when the patient attempts to fixate (Sharpe and Fletcher, 1986). It is unaffected by illumination conditions and/or eyelid closure (Dell’osso and Daroff, 1975). It is characterized by a repetitive, to-and-fro motion of the eyes, initiated by a slow phase (Leigh et al., 1994), and it is often accompanied by impaired vision and oscillopsia (Sharpe and Fletcher, 1986; Leigh and Zee, 1991 #11788). However, the magnitude of the oscillopsia is usually smaller than the magnitude of the nystagmus (Leigh et al., 1994).
Nystagmus during attempted fixation commonly arises due to disturbance of the three main gaze-holding mechanisms: vestibular, neural integrator, and visual fixation. With nystagmus that is due to disturbance of the vestibular mechanism, the imbalance of the vestibular drives often causes constant velocity drifts. With nystagmus that is due to disturbance of the neural integrator, the eyes cannot be held in an eccentric position and thus drift back to the center of the orbit, giving rise to gaze-evoked nystagmus. With nystagmus that is due to disturbance of the visual fixation mechanism, the ability to suppress drifts (for example of vestibular origin) during attempted fixation may be deteriorated (Leigh and Zee, 2006).

Other forms of nystagmus are less well understood. Acquired pendular nystagmus (due, e.g., to multiple sclerosis) has a quasi-sinusoidal waveform (Sharpe and Fletcher, 1986; Leigh and Zee, 2006) and it is most visually distressing, impairing clear vision, and causing oscillopsia (Sharpe and Fletcher, 1986; Leigh and Zee, 1991; Leigh et al., 1994; Ciuffreda and Tannen, 1995; Leigh and Zee, 2006).

Congenital nystagmus may also disrupt steady fixation. One type is due to visual disorders, such as congenital retinal disorders and albinism. Another type of congenital nystagmus is not associated with visual disorders: these individuals often show brief foveation periods when the eyes are relatively still and on target. Such individuals usually have near-normal vision and no illusion of oscillopsia (Leigh and Zee, 2006).

Congenital fixation nystagmus can occur in a variety of jerk and pendular waveforms. In pendular (i.e. sinusoidal) nystagmus, both phases of the oscillation are smooth movements. In jerk nystagmus, the second phase of the oscillation is a correcting saccade (Sharpe and Fletcher, 1986). However, some patients have complex waveforms that are not easy to characterize as either jerk or pendular (Dell’osso and Daroff, 1975; Yee et al., 1976), and many sub-varieties have been described (Dell’osso and Daroff, 1975). Also, the nystagmus may change from pendular to jerk for different gaze directions (Ciuffreda and Tannen, 1995).

Psychological factors such as fatigue, stress, and especially attention can exert a strong influence on the intensity and waveform shape of the nystagmus (Abadi and Dickinson, 1986). Figure 10 illustrates four common nystagmus waveforms.

About 50% of strabismic patients have nystagmus, and 15% of patients with congenital nystagmus have strabismus (Ciuffreda and Tannen, 1995). See Leigh and Zee (2006) for further details and discussion on the various nystagmus types.

**Superior oblique myokymia**

Superior oblique myokymia is a rapid, small amplitude, non-saccadic, rotatory ocular oscillation limited to one eye (Susac et al., 1973). Attacks usually last less than 10 s, but may occur many times a day (Leigh and Zee, 2006). Superior oblique myokymia can be distinguished from microsaccadic flutter because it is always monocular and has a strong torsional component (Ashe et al., 1991). Superior oblique myokimia is accompanied by monocular blurring (Leigh and Zee, 2006), monocular oscillopsia, and sometimes torsional diplopia (Susac et al., 1973). Although the causes are obscure, the clinical course is benign (Susac et al., 1973). An abnormality of the trochlear motor units may underlie this disorder (Leigh et al., 1994).

**Ocular paralysis**

Filin and Okhotsimskaya examined the dynamics of fixational eye movements in a large population of patients with orbital paralysis (including myasthenia, myopathy, and malignant exophthalmia), basal paralysis (including patients with isolated paresis and paralysis of the III and VI nerves and patients with total or incomplete ophthalmoplegia), and nuclear paralysis (Filin and Okhotsimskaya, 1977; Okhotsimskai and Filin, 1977; Okhotsimskaia, 1977). In myasthenia and myopathy the rate and speed of saccades decreased, and in a number of cases drift also decreased in frequency and amplitude, resulting in considerable stabilization of the eyes. In patients with incomplete basal paralyses of the III and IV nerves, the frequency of microsaccades decreased, whereas drift increased in frequency and amplitude. In cases of mild paresis, fixational eye movements of the affected eye were comparable to the normal eye. The most
pronounced changes in fixational eye movements occurred in patients with complete paralysis of the oculomotor nerves. None of these patients produced microsaccades and the drift was of small amplitude or completely absent: the eye was stabilized.

Stabilization of the eyes due to complete or incomplete paralysis presumably leads to decrease in visibility and ultimately visual fading, as it is the case with the fading of stabilized images in the laboratory (Ditchburn and Ginsborg, 1952; Riggs and Ratliff, 1952).

Slow refixation saccades

Slow saccades of restricted amplitude may reflect abnormalities in the oculomotor periphery, whereas slow saccades of normal amplitude are usually caused by central neurological disorders (Leigh and Zee, 2006). Refixation saccades can be pathologically slow in progressive nuclear palsy, (Garbutt et al., 2003, 2004) especially when the disease is severe (Boghen et al., 1974; Troost et al., 1976).

The velocity–amplitude relationship of microsaccades in progressive nuclear palsy may be similarly affected (R. John Leigh, personal communication). If so, several questions need to be addressed: are slow microsaccades as effective in preventing adaptation and counteracting fading as normal microsaccades? If not, how effective are they? In our previous experiments, we found that both microsaccade amplitudes and microsaccade velocities were positively correlated with visibility during fixation. However, as microsaccade amplitude and microsaccade velocity covary in the main sequence, it is difficult to determine which of these two variables, amplitude or speed, is more critical to visibility. Future experiments that examine the effects on visibility of microsaccades with an abnormal velocity–amplitude slope should help answer these questions.

Conclusions

Approximately 80% of our visual experience happens during fixation. During the other 20% of the time we are virtually blind, due to saccadic suppression mechanisms. Therefore, understanding

Fig. 10. Common slow-phase waveforms of nystagmus during attempted fixation. (A) Constant velocity drift of the eyes ("saw-tooth" nystagmus), due to peripheral or central vestibular disease, or to cerebral hemisphere lesions. (B) Drift of the eyes from an eccentric orbital position back to the center of the orbit (gaze-evoked nystagmus), with decreasing velocity. The unsustained eye position is caused by an impaired neural integrator. (C) Drift of the eyes away from the central position, with increasing velocity. The unsustained eye position suggests an unstable neural integrator. This disorder is found in the horizontal plane in congenital nystagmus and in the vertical plane in cerebellar disease. (D) Pendular nystagmus (either congenital or acquired). Reprinted from Leigh and Zee (2006). Courtesy of R. John Leigh.
the neural and perceptual effects of fixational eye movements is crucial to understanding vision.

Fixational eye movements were first measured in the 1950s, but sometime during the 1970s, the field arrived at an impasse due to difficulties in data collection, discrepancies in results by different laboratories, and disagreements over the interpretation of the available data. A revival in interest in the late 1990s was ushered in by the development of very accurate non-invasive eye movement measurement techniques, in addition to the advent of single-unit recording techniques in alert monkeys, and new computational approaches for eye-movement characterization and modeling. Research in fixational eye movements is one of the newest and fastest-moving fields in visual and oculomotor neuroscience today.

The evaluation of fixational eye movements may be critical to the early and differential diagnosis of oculomotor disease, to the assessment of ongoing treatments, and to develop therapies to restore visual function in patients who cannot produce normal eye movements during fixation. Many visual and oculomotor diseases include fixational eye movement defects that have gone untreated. Correcting these fixational eye movement deficiencies may provide a novel way to ameliorate some of the debilitating effects of these pathologies.

Finally, a large amount of psychophysical and physiological visual research has been carried out while subjects were engaged in visual fixation. Therefore, understanding the precise physiological and perceptual contributions of fixational eye movements may moreover be critical to the interpretation of previous and future vision research.

Abbreviations

LGN  lateral geniculate nucleus of the thalamus
RF    receptive field
V1    primary visual cortex

Acknowledgments

Drs. R. John Leigh, Stephen Macknik, and Xoana Troncoso helped with data analysis and figure formatting, and Dr. Xoana Troncoso read the manuscript and made helpful comments. I am very grateful to Dr. R. John Leigh for graciously providing Figs. 9 and 10, and for his insights and discussion of slow saccades, square-wave jerks, and many other concepts addressed here. Thanks also to Dr. David Sparks for helpful discussion and for pointing me to the Van Gisbergen and colleagues' studies on the generation of microsaccades. Thomas Dyar and Dr. Xoana Troncoso acquired the data for Figs. 5b, c and 6. This study was supported by the Barrow Neurological Foundation.

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