

Mechanisms for generating and compensating for the smallest possible saccades

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Abstract

Microsaccades are small eye movements that occur during gaze fixation. Although taking place only when we attempt to stabilize gaze position, microsaccades can be understood by relating them to the larger voluntary saccades, which abruptly shift gaze position. Starting from this approach to microsaccade analysis, I show how it can lead to significant insight about the generation and functional role of these eye movements. Like larger saccades, microsaccades are now known to be generated by brainstem structures involved not only in compiling motor commands for eye movements, but also in identifying and selecting salient target locations in the visual environment. In addition, these small eye movements both influence and are influenced by sensory and cognitive processes in various areas of the brain, and in a manner that is similar to the interactions between larger saccades and sensory or cognitive processes. By approaching the study of microsaccades from the perspective of what has been learned about their larger counterparts, we are now in a position to make greater strides in our understanding of the function of the smallest possible saccadic eye movements.

Introduction

When we attempt to fix our gaze at a specific object in our environment, our eyes paradoxically continue to move, no matter how hard we attempt to stabilize them (Ratliff & Riggs, 1950; Barlow, 1952; Ditchburn & Ginsborg, 1953; Martinez-Conde *et al.*, 2004; Rolfs, 2009). Such fixational eye movements often include fast phases or flicks, called microsaccades (Barlow, 1952; Zuber *et al.*, 1965; Steinman *et al.*, 1973; Martinez-Conde *et al.*, 2004; Rolfs, 2009). As their name suggests, microsaccades appear, at least kinematically, as scaled-down versions of larger voluntary saccades. Specifically, these movements are characterized by brief, almost instantaneous step-like changes in eye position, with stereotypical patterns of rapid eye acceleration followed by rapid eye deceleration. Moreover, descriptive statistics about the metrics of these eye movements are essentially extrapolations of the known relationships that exist for larger saccades. For example, microsaccades fall on the small-amplitude extension of the same 'main sequence' relationship between movement amplitude and peak velocity for saccades (Zuber *et al.*, 1965).

Despite the resemblance between microsaccades and larger voluntary saccades, most research on microsaccades has not paralleled that on saccades. For example, even though saccade generation has been well studied at the behavioral (e.g. Findlay & Walker, 1999; Findlay, 2009), neurophysiological (e.g. Sparks & Mays, 1990; Wurtz & Optican, 1994; Schall & Thompson, 1999) and computational modeling (e.g. Girard & Berthoz, 2005) levels, the mechanisms for microsaccade generation remain relatively unexplored (Van Gisbergen

et al., 1981; Hafed *et al.*, 2009a). Instead, most early research on microsaccades has concentrated on questions as to why these eye movements occur at all. In this review, I first provide a brief history of microsaccades, highlighting some of these early questions and the ongoing debates that they have spurred (Martinez-Conde *et al.*, 2004; Collewijn & Kowler, 2008; Melloni *et al.*, 2009). I then summarize advances made in understanding the neurophysiological mechanisms associated with microsaccades, from the perspective both of how they are generated as well as how they may modulate visual processing. I argue that a clear understanding of the neural mechanisms for microsaccade generation is a necessary prerequisite for answering the question of why these eye movements occur. Moreover, I show that using the well-studied 'saccadic' system as the starting point for understanding microsaccade generation, one can make significant progress in answering this and other questions.

A brief history of microsaccades

After a flurry of behavioral studies on microsaccadic eye movements in the mid-1900s, the field of microsaccade research had almost completely dried up by around 1980 (see review by Rolfs, 2009). The reason for this was that microsaccades were deemed unnecessary for the two main functions initially hypothesized for them: (i) maintaining precise ocular fixation (Adler & Fliegelman, 1934; Ratliff & Riggs, 1950; Ditchburn & Ginsborg, 1953; Ginsborg, 1953; Doesschate, 1954; Ditchburn, 1955; Cornsweet, 1956) and (ii) supporting stimulus visibility in the face of image fading due to steady retinal stimulation (Ditchburn & Ginsborg, 1952; Ginsborg, 1953; Yarbus, 1957, 1967; Pritchard, 1961). In terms of the first of these functions, slow control in the form of ocular drift was often found to be capable of holding

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eye position during fixation fairly well, and correcting for possible positional errors of eye orientation (Nachmias, 1959; Steinman *et al.*, 1973; Winterson & Collewijn, 1976; Kowler & Steinman, 1980). In addition, it was found that only approximately 30% of microsaccades appear to correct for position errors caused by previous drift (Boyce, 1967). Thus, by around 1980, microsaccades were considered at the very least to be supportive of, but not absolutely necessary for, oculomotor control during precise gaze fixation. [A recent study by Ko *et al.* (2010) is among evidence that microsaccades do in fact precisely direct gaze, as we discuss shortly.]

In terms of the second main reason for the almost complete loss of interest in microsaccades, namely their putative role in maintaining visibility, it was argued that different sources of retinal image motion can and do prevent visual fading (Steinman *et al.*, 1973; Skavenski *et al.*, 1979; Kowler & Steinman, 1980; Steinman, 2003; Collewijn & Kowler, 2008). For example, small body movements are associated with retinal image motion that is sufficient to prevent perceptual fading (Skavenski *et al.*, 1979). In fact, some early behavioral studies have even found that microsaccades may under some circumstances be detrimental to vision because of the suppressed visual sensitivity associated with them (a phenomenon referred to as ‘microsaccadic suppression’) (Zuber & Stark, 1966; Beeler, 1967; Rattle & Foley-Fisher, 1968). As a result, by the 1980s, microsaccades were largely considered to be a curiosity as to why they occur, and research on them had all but completely stopped.

In the 20 years that ensued after the initial collapse of microsaccade research, two major developments in brain and cognitive sciences occurred, and the insights from these developments could have (in hindsight) enriched the questions concerning microsaccades beyond just their role in maintaining ocular fixation and preventing image fading. The first of these developments was that neurophysiological studies on awake, behaving monkeys became a mainstay of neuroscience research aimed at linking brain circuits to behavior. The advent of the fixating monkey was used to great promise in studying vision, action and decision-making among other topics. However, as there was little interest left in microsaccades, there were virtually no studies on the neural mechanisms associated with microsaccade generation or their influences on vision. In fact, when microsaccades were considered in visual neuroscience experiments at all, they were often viewed as a nuisance that has to be controlled for (e.g. Read & Cumming, 2003). Thus, by the end of the twentieth century, new developments in neurophysiology placed us at a renewed position to study microsaccades from an alternative perspective – namely, how neuronal activity may be modulated by the occurrence of these movements (e.g. Martinez-Conde *et al.*, 2000, 2002; Bosman *et al.*, 2009; Herrington *et al.*, 2009; Hafed & Krauzlis, 2010).

The second development that occurred since the 1980’s was the birth of modern-day ‘cognitive neuroscience’. Through pioneering experiments on human performance, Posner and his colleagues virtually jump-started modern-day quantitative research on cognitive processes such as visual attention (e.g. Posner, 1980). These authors, now considered among the founding fathers of this field, have championed the idea that ‘mental chronometry’ (e.g. reaction time measurements) allows concrete measurements of internal psychological processes. Visual attention became one of the most well-studied cognitive phenomena in the 20 years that followed. However, despite significant efforts in relating visual (and other forms of) attention to saccades (Posner, 1980; Remington, 1980; Rizzolatti, 1983; Rizzolatti *et al.*, 1994; Sheliga *et al.*, 1994, 1997; Deubel & Schneider, 1996; Schall & Thompson, 1999), similar studies on microsaccades were not considered. Thus, by the end of the twentieth century, microsaccade

research stood a renewed chance for revival with the benefit of what had been learned about cognitive processes, such as visual attention, and their relationship to eye movements (e.g. Hafed & Clark, 2002).

Eventually, microsaccade research caught up with these two developments. At the neurophysiological level, studies of the influences of microsaccades on sensory representations emerged. Specifically, several groups investigated how visual activity in the brain is transiently modulated after the occurrence of microsaccades (Leopold & Logothetis, 1998; Martinez-Conde *et al.*, 2000, 2002; Snodderly *et al.*, 2001). Significant emphasis was placed on the observation of increases in visual responses after microsaccades in the lateral geniculate nucleus (LGN), the first relay channel for visual information arriving from the retina, and area V1, the primary visual cortex (Martinez-Conde *et al.*, 2000, 2002). Thus, these studies were effectively a continuation of one of the original questions concerning the function of microsaccades, namely whether they are necessary for maintaining vision in the face of retinal image fading. At the behavioral level, however, investigations of the relationships between microsaccades and attention, benefiting from the new field of cognitive neuroscience and theories linking attention and action (Posner, 1980; Remington, 1980; Rizzolatti, 1983; Rizzolatti *et al.*, 1994; Sheliga *et al.*, 1994, 1997; Deubel & Schneider, 1996; Schall & Thompson, 1999), were made (Hafed & Clark, 2002; Engbert & Kliegl, 2003). In these studies, the question was no longer whether microsaccades are necessary for vision or for oculomotor control, but whether similar interactions between cognition and saccades could be found at the level of microsaccades. These results ushered in a new array of queries about the brain mechanisms associated with microsaccades. Thus, the hallmark of the first decade of the twenty-first century was a renewed interest in microsaccadic eye movements, and the emergence of new questions about these movements, questions that benefited from the earlier advances in understanding cognitive phenomena such as visual attention.

With the dawning of the second decade of the twenty-first century, an opportunity now exists to increase our understanding of microsaccades, and therefore constrain our interpretation of microsaccade function and how these movements may influence behavior. The opportunity lies in the fact that we still know relatively little about the neural mechanisms for generating microsaccades. Recent results have brought to light the importance of going after these mechanisms, and it stands to reason that understanding how microsaccades are generated can help constrain our interpretation of why these eye movements occur, and how they may affect vision and behavior when they do. This is particularly important now because the resurgence of microsaccade research in the last decade has also meant the appearance of often-extreme over-interpretation of some experimental observations concerning these movements. In what follows, I provide a review of our understanding of the brain mechanisms for generating microsaccades, as well as the mechanisms for compensating for these eye movements in visual sensory representations. The hallmark of these mechanisms is their similarity to those associated with larger saccades.

Neural mechanisms for microsaccade generation

Saccade generation at a glance

To approach the study of microsaccade generation, much can be gained from what we have learned so far about generating the larger, but kinematically similar, voluntary saccades. The process of saccade generation can functionally be viewed as a hierarchical cascade of information from areas that perform visual analysis and interpretation, to areas that select the saccade target from among many alternatives,

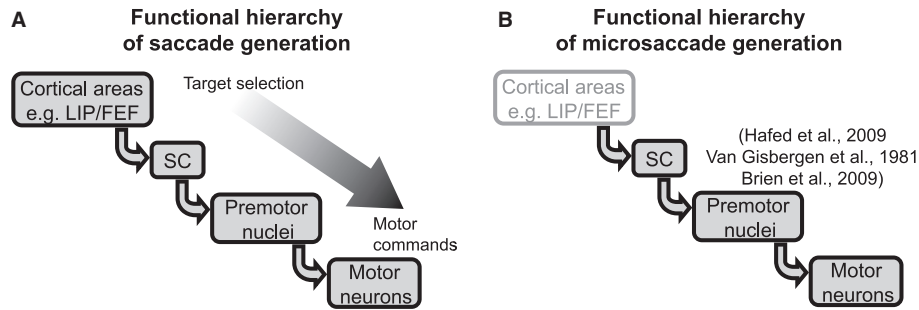


FIG. 1. Functional hierarchy of saccade and microsaccade generation. (A) The process of saccade generation may be viewed as a cascade of stages that use sensory and other information to select a saccade target from among alternative distractors and then convert the information about the target's location to the appropriate motor commands. Low-level motor command compilation is generally implemented in the brainstem, whereas higher-level selective processes are generally implemented by the midbrain superior colliculus (SC) and cortical areas (e.g. LIP and FEF). This general functional hierarchy highlights important areas needed for saccade generation, and includes areas probably involved in microsaccade generation (B), but it is not exhaustive. (B) Current knowledge about the neural mechanisms for microsaccade generation is limited to sub-cortical areas.

and finally to areas that compile the motor commands for innervating the eye muscles and rotating the eyes (Fig. 1A). At the bottom of the hierarchy, sub-cortical involvement in saccade generation is predominant, with the existence of more and more machine-like activity patterns that culminate in shaping motor neuron discharge for innervating the eye muscles (Sparks, 1986; Hepp *et al.*, 1989; Sparks & Mays, 1990; Krauzlis, 2005). As one progresses higher up in the hierarchy, cortical involvement in saccade generation becomes more prevalent, and this involvement may be viewed as being more supervisory in nature, playing a role in filtering out unwanted saccade targets and defining the currently relevant goal for the single upcoming movement (as well as when to initiate such a movement) (Schall & Thompson, 1999; Krauzlis, 2005; Bisley, 2011; Bisley & Goldberg, 2010).

Among the sub-cortical areas involved in saccade generation, the superior colliculus (SC) plays a primary role. This structure interfaces sensory processing and cognition to motor generation by implementing a 'priority' map, which contributes to defining the locations of behaviorally relevant stimuli in the environment (Wurtz *et al.*, 1982; Kustov & Robinson, 1996; Cavanaugh & Wurtz, 2004; Fecteau *et al.*, 2004; Ignashchenkova *et al.*, 2004; Muller *et al.*, 2005; Fecteau & Munoz, 2006; Hafed & Krauzlis, 2008; Lovejoy & Krauzlis, 2010; Nummela & Krauzlis, 2010). Besides being useful for possibly modulating sensory representations for perceptual decisions (Ignashchenkova *et al.*, 2004; Muller *et al.*, 2005; Cavanaugh *et al.*, 2006; Lovejoy & Krauzlis, 2010; Nummela & Krauzlis, 2010), this priority map identifies potential targets for saccades and therefore plays a role in the decision to select a given saccade endpoint (Carello & Krauzlis, 2004; McPeck & Keller, 2004). The SC also contains neurons with pure movement-related discharge patterns (Wurtz & Optican, 1994; Munoz & Wurtz, 1995a; Moschovakis, 1996), and inactivation of the SC impairs saccade generation, suggesting that it plays a role in the motor control of saccades (Aizawa & Wurtz, 1998; Quaia *et al.*, 1998). Finally, the SC projects to lower-level areas in the brainstem (Sparks & Hartwich-Young, 1989), such as the reticular formation, which constitute the final motor pathway for saccades (Leigh & Zee, 2006). Thus, starting from the SC and downstream, saccade generation is primarily concerned with identifying target location and translating this information into motor commands for moving the eyes. As I describe in more detail shortly, this scheme of processing appears to be identical in many respects for microsaccades (Fig. 1B).

Of particular importance to saccade generation at the cortical level are the lateral intraparietal area (LIP) and frontal eye fields (FEF) (Schall & Thompson, 1999; Krauzlis, 2005; Goldberg *et al.*, 2006).

These areas are implicated in visual attention, decision-making and target selection (Schall & Thompson, 1999; Krauzlis, 2005; Goldberg *et al.*, 2006; Bisley, 2011; Bisley & Goldberg, 2010; Gottlieb & Balan, 2010; Gottlieb & Snyder, 2010), and they also possess descending projections to brainstem areas, such as the SC (Pare & Wurtz, 1997, 2001; Sommer & Wurtz, 2000). Both LIP and FEF again define 'priority' or 'saliency' maps for behaviorally relevant locations (Schall & Thompson, 1999; Krauzlis, 2005; Goldberg *et al.*, 2006; Bisley, 2011; Bisley & Goldberg, 2010; Gottlieb & Balan, 2010; Gottlieb & Snyder, 2010). These maps, in addition to their role in modulating selective attention and perception, allow the oculomotor system to make the decision to commit to one particular saccade target location from among many alternatives (Schall & Thompson, 1999). The information represented in these maps may be considered as a source of top-down cognitive control over voluntary eye movements (Krauzlis, 2004, 2005).

Therefore, to generate a saccade, a series of cortical and sub-cortical patterns of discharge convert sensory information about the location of the saccade endpoint into motor commands that move the eyes to this endpoint.

Microsaccade generation – pre-motor and motor nuclei

Turning to 'microsaccade' generation, almost all we know about the involvement of pre-motor and motor nuclei in controlling these eye movements was described in the seminal paper by Van Gisbergen *et al.* (1981). In this paper, Van Gisbergen and colleagues marched up the hierarchy described above for saccade generation (Fig. 1), and they quantified the discharge properties of abducens nucleus motor neurons and reticular formation burst neurons for saccades of different sizes, including movements as small as 15 min arc (0.25°).

Van Gisbergen *et al.* (1981) found that putative motor neurons exhibit modulated activity for microsaccades. As is known, motor neurons show burst-tonic changes in firing rate at the time of saccades (Fuchs & Luschei, 1970; Robinson, 1970, 1973; Schiller, 1970; Robinson & Keller, 1972; Van Gisbergen *et al.*, 1981). Initially, a burst of activity starts immediately before saccade onset in the on-direction of the neuron (i.e. the direction in which the innervated muscle needs to be driven in order for the eye to move to its intended orientation). This burst is what gives saccades the stereotypical pattern of rapid eye acceleration followed by rapid eye deceleration. After the saccade, when the eye has landed at its new orbital position, the tonic discharge of the motor neurons reflects this new position and serves to hold the eye at that position until the next movement. Van Gisbergen

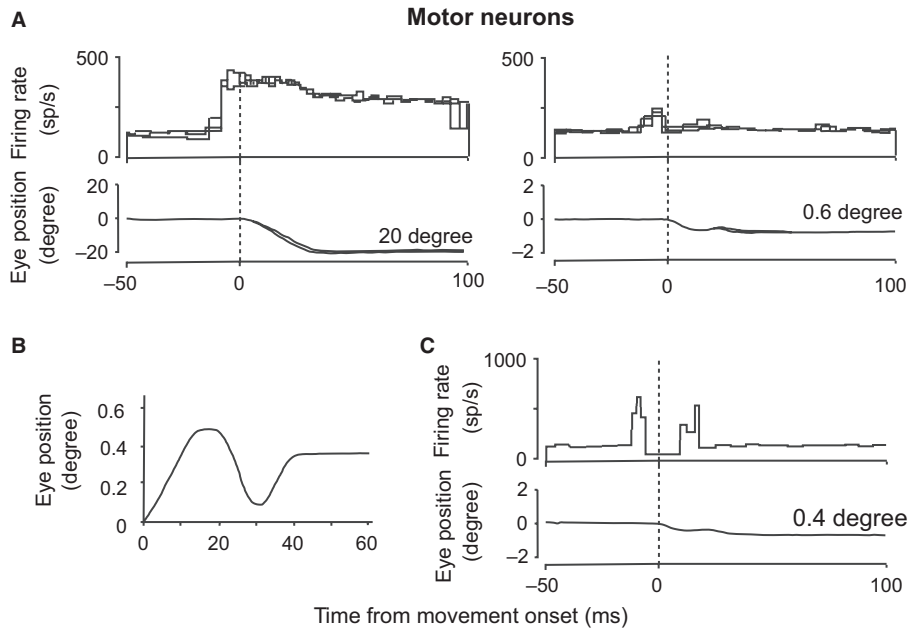


FIG. 2. Motor neuron activity associated with microsaccades is similar to that associated with larger voluntary saccades. (A) Activity of an example motor neuron for a 20° saccade and a much smaller approximately 0.6° saccade. For both movements, there is a burst immediately prior to movement onset and then a tonic level of activity to hold the eye at its new orbital position. (B) Example of a composite eye movement in which a microsaccade in one direction is followed by a couple of oscillatory movements in opposing directions. (C) Activity of a motor neuron for a composite movement like that in B. The first microsaccade in the composite movement is in the on-direction of the neuron. The neuron exhibits a burst prior to the movement, as expected. Then, for the subsequent oscillatory movements, the neuron pauses if the movement is in its off-direction and bursts if the subsequent movement is in its on-direction. Thus, the oscillatory movements of the eye are not mechanical artifacts of the eye plant, but reflect changes in motor neuron discharge, even for the smallest movements. Adapted, with permission, from Van Gisbergen *et al.* (1981).

et al. (1981) found that abducens nucleus motor neurons also exhibit a burst immediately prior to microsaccades in the neuron's on-directions (Fig. 2A). Although based on recordings from only six neurons, these results constituted the first neurophysiological evidence that microsaccades reflect changes in activity at the level of brainstem motor neurons that drive the eye muscles. In more recent work, Van Horn & Cullen (2009) extended and supported this evidence by quantitatively characterizing the discharge dynamics of ten more motor neurons during slightly larger fixational saccades (having peak velocities in the range 50–150°/s).

Motor neuron discharge during microsaccades appears to be highly specific. Van Gisbergen *et al.* (1981) also considered the cases in which microsaccades, and some saccades of small amplitude (less than approximately 3°), exhibit dynamic overshoots and oscillations (Fig. 2B). A microsaccade with dynamic overshoot and/or oscillations has a series of eye movements in either the on- or off-direction of a given motor neuron. Remarkably, the motor neurons investigated by Van Gisbergen *et al.* (1981) exhibited bursts for on-direction microsaccades, but were also modulated by the individual eye oscillation components within these larger composites of oscillatory movements. This is illustrated in Fig. 2C for a sample neuron, which burst for the first and last components of a composite movement and paused for the middle one (being in the neuron's off-direction). Thus, not only are microsaccades generated by motor neuron activity modulations, but the eye position oscillations that may be observed for these movements are not merely mechanical artifacts of the eye plant; instead, they reflect activity at the level of motor neurons.

Proceeding one level higher in the saccade generation hierarchy of Fig. 1A, Van Gisbergen *et al.* (1981) also recorded the activity of medium-lead burst neurons (MLBNs) in the paramedian pontine reticular formation. For saccades, these neurons exhibit bursts that

start approximately 12 ms prior to saccade onset, and they act in a push–pull manner to define the metrics of the upcoming eye movement (Van Gisbergen *et al.*, 1981; Buttner-Ennever & Buttner, 1988; Leigh & Zee, 2006). That is, for a given saccade, motor neurons driving a given eye muscle receive excitatory bursts from one side of the brainstem and inhibitory bursts from the other side. The difference in firing rate between these excitatory and inhibitory bursts shows modulation with saccades, loosely resembling the eye velocity profile, and Van Gisbergen *et al.* (1981) found that it also does so for microsaccades (Fig. 3). Moreover, this rate difference seems to play an important role in defining the metrics of the movements because eye trajectory can be predicted, or modeled, based on these data (Van Gisbergen *et al.*, 1981; Scudder *et al.*, 1988; Cullen & Guitton, 1997a,b,c). This allowed Van Gisbergen and colleagues (1981) to develop one of the textbook models of saccade generation, which can replicate saccade and microsaccade generation metrics by brainstem neurons. Thus, MLBNs in the brainstem reticular formation have also been shown to be involved in microsaccade generation, and in a manner that is consistent with their putative role in defining the metrics of saccadic eye movements. [Van Gisbergen *et al.* (1981) also found that long-lead burst neurons (LLBNs) in the brainstem are modulated during microsaccades. For both saccades and microsaccades, these neurons seem to be further from providing a definition of the kinematics of movements than MLBNs. For example, they exhibit a long prelude period of neuronal discharge even before the eye has begun to move (Buttner-Ennever & Buttner, 1988; Leigh & Zee, 2006).]

Another class of pre-motor neurons in the brainstem, that of omnipause neurons (OPNs), again seems to behave for microsaccades as it does for larger saccades. As their name suggests, OPNs are neurons that are tonically active during fixation and pause during

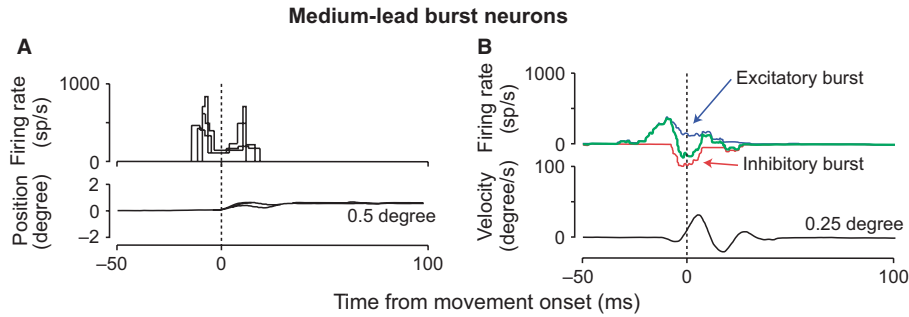


FIG. 3. Burst neuron discharge around microsaccades. (A) Example medium-lead burst neuron (MLBN) showing modulation prior to a small 0.5° saccadic eye movement. The neuron shows a burst prior to movement onset, and also shows a subsequent burst for subsequent eye movements in the same direction (as in the case of the motor neuron of Fig. 2C). (B) Demonstration of how the activity of excitatory and inhibitory burst neurons is related to instantaneous eye velocity during a 0.25° microsaccade. The bottom panel shows eye velocity, with oscillations like those in Fig. 2B. The top panel shows the firing rate of an MLBN during two movements. The blue curve is for a movement in the on-direction of the neuron and is used to estimate the contribution of the excitatory burst activity to the generation of the microsaccade of the bottom panel. The red curve shows the activity of the neuron (flipped to the negative y-axis) for a similar movement in the opposite direction. This second curve is used to estimate the contribution of the inhibitory burst activity that would putatively influence the microsaccade of the bottom panel. The difference between the excitatory and inhibitory bursts (green) resembles instantaneous eye velocity, and is believed to contribute to the dynamics of such velocity. Adapted, with permission, from Van Gisbergen *et al.* (1981).

saccades in all directions (Leigh & Zee, 2006). Moreover, saccade-related pauses in the activity of these neurons are well synchronized with eye movement onset and end (Everling *et al.*, 1998). As a result, these neurons are generally considered to be part of the gating mechanism for saccade generation (Girard & Berthoz, 2005; Leigh & Zee, 2006). In fact, models of saccade generation with high feed-forward burst gains (like the model of Van Gisbergen *et al.*, 1981) are inherently unstable control systems that are rendered stable by such a gating mechanism. Van Gisbergen *et al.* (1981) managed to record the activity of a single OPN and found that it paused during microsaccades. The neuron stopped firing 25 ms prior to microsaccade onset and resumed firing 30 ms later for a movement amplitude of 0.5° . Given the typical duration of a 0.5° movement, these numbers appear similar to those found for larger saccades (Everling *et al.*, 1998). Brien *et al.* (2009) analysed the activity of 18 additional OPNs during saccades smaller than 2° . These authors also found a lower firing rate during these movements than during a fixation interval shortly prior to them (Fig. 4). Thus, even though these studies did not analyse the detailed temporal pattern of OPN activity around microsaccade onset and end, the emerging picture is that OPN function for microsaccades is similar to that for larger eye movements.

The finding that pre-motor and motor brainstem nuclei are involved in microsaccade generation, and to a similar extent to larger saccades, is sufficient to explain why microsaccade kinematics are similar to the kinematics of larger voluntary saccades (Zuber *et al.*, 1965; Van

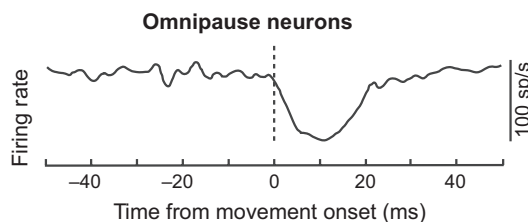


FIG. 4. Omnipause neuron (OPN) activity for small saccades. The figure shows the average firing rate of 18 OPNs during saccades smaller than 2° in amplitude. The neurons reduce their activity around movement onset, as might be expected from a gating mechanism for microsaccades, although the inclusion of a large range of amplitudes precludes learning about the exact timing of firing rate modulations around the smallest movements. Adapted, with permission, from Brien *et al.* (2009).

Gisbergen *et al.*, 1981). However, these findings may also have significant implications in explaining other microsaccade characteristics that have been studied extensively in recent years, and that may have been interpreted in light of high-level influences on these movements. For example, even though microsaccades typically occur at some steady rate during fixation (e.g. 1–3 movements per second), when a stimulus transient occurs, like a visual target onset, microsaccade rate drops to zero shortly after that event and then recovers. This phenomenon, referred to as ‘microsaccadic inhibition’ (Engbert & Kliegl, 2003; Rolfs, 2009), might be thought of, at first glance, as being related to the putative role of microsaccades in refreshing retinal images (Martinez-Conde *et al.*, 2004). In other words, if a visual stimulus appears suddenly in the visual environment, this induces transient sensory activity in the brain, which reduces the need for microsaccades to cause such sensory transients by jittering retinal images. Thus, microsaccadic inhibition could be thought of as a top-down or active influence on microsaccades to modulate the quality of sensory signals in the face of fading (Rolfs, 2009). As can be seen, this interpretation is colored by the putative role of microsaccades in enhancing visibility through jittering retinal images (Martinez-Conde *et al.*, 2004, 2009; Melloni *et al.*, 2009; Rolfs, 2009). However, an alternative, plausible mechanism for microsaccadic inhibition, based on our understanding of the role of brainstem structures in microsaccade generation, could be related to OPN activity. Specifically, even though OPNs are tonically active during fixation, when a visual stimulus appears in the environment, approximately 50% of all OPNs exhibit a visual sensory response to this onset, in the form of increased activity (Everling *et al.*, 1998; Missal & Keller, 2002; Boehnke & Munoz, 2008). The timing of this increase in OPN activity is similar to the timing of microsaccadic inhibition. Thus, if OPN activity implements a threshold for whether a microsaccade or saccade occurs, then this stimulus-induced increase in OPN activity would be expected to reduce the probability of microsaccades (and saccades). In fact, visual onsets also inhibit larger voluntary saccades in much the same way as they do for microsaccades [the phenomenon referred to as ‘saccadic inhibition’ (Reingold & Stampe, 2002, 2004; Stampe & Reingold, 2002)]. In both cases, it then takes time to generate the subsequent stimulus-induced saccades or microsaccades, due in part to the buildup of movement-related activity that is needed in structures such as the SC (see below), explaining the prolonged period of inhibition followed by subsequent rebound in saccade and microsaccade

frequency. Thus, microsaccadic inhibition (like saccadic inhibition) could reflect a low-level mechanism of saccade gating at the level of OPN. Further experimental and modeling work is necessary to elucidate this possibility, especially exploring the influence of other sensory modalities on OPN (e.g. audition, which can also cause microsaccadic inhibition; Rolfs *et al.*, 2008), and to evaluate how the visual system may make use of the ensuing period of reduced saccade and microsaccade probability as a result of such gating.

Microsaccade generation – superior colliculus

Almost 30 years after Van Gisbergen and colleagues' investigation of the pre-motor and motor nuclei's involvement in microsaccade generation, we (Hamed *et al.*, 2009a) turned our attention to the SC. Our motivation was mainly twofold. If the SC does play a role in microsaccade generation, then this would provide an ideal neural substrate for understanding the influences of cognitive processes, such as visual attention, on microsaccades (Hamed & Clark, 2002; Engbert & Kliegl, 2003). This is so because the SC's 'priority map' reflects attentional allocation (Kustov & Robinson, 1996; Cavanaugh & Wurtz, 2004; Ignashchenkova *et al.*, 2004; Muller *et al.*, 2005; Cavanaugh *et al.*, 2006; Lovejoy & Krauzlis, 2010). Second, given the known ascending projections from the SC to cortical areas that help evaluate and interpret visual signals, such as middle temporal area (MT) and FEF (Sommer & Wurtz, 2002, 2004a,b, 2008; Berman & Wurtz, 2010), involvement of the SC in microsaccade generation would also raise the possibility that internal, 'corollary', information about these small eye movements may be used by other brain areas, possibly to modulate perceptual processing [as is the case for larger saccades (Sommer & Wurtz, 2002, 2004a,b)]. We thus explored the role of the SC in microsaccade generation as a necessary first step to investigate these possibilities.

The SC contains a distributed representation of retinotopic space that is useful for identifying saccade endpoints (Lee *et al.*, 1988). Neurons located caudally in this structure represent peripheral eccentricities, and neurons located more rostrally represent foveal and parafoveal locations (Fig. 5A) (Robinson, 1972). For a typical saccade to a peripheral target, peripheral (caudal) neurons in the intermediate and deep layers of this structure exhibit firing rate increases prior to movement onset, a peak of discharge during the movement, and then firing rate decreases back to baseline after movement end (Fig. 5B) (Wurtz & Optican, 1994; Munoz & Wurtz, 1995a). Not all neurons in the SC would be activated for such a saccade, however, because individual neurons possess individual 'response fields' that are generally confined to a particular region of retinotopic space (Fig. 5C) (Goldberg & Wurtz, 1972; Wurtz & Goldberg, 1972; Lee *et al.*, 1988; Wurtz & Optican, 1994; Munoz & Wurtz, 1995a,b; Marino *et al.*, 2008). Thus, for a given saccade, a subset of SC neurons exhibits elevated activity, and there is a 'hill' of activation in the SC map whose center of mass could be thought of as coding the saccade endpoint (Lee *et al.*, 1988). Moreover, the low-level activity appearing long before saccade onset is generally believed to reflect the increasing behavioral relevance of the spatial location as a potential saccade target (Basso & Wurtz, 1997, 1998; Dorris & Munoz, 1998). As the time of saccade onset nears, and the region represented by these neurons emerges as the clear 'winner' for committing to the saccade, this activity increases and often includes a burst during the movement itself [by these and another class of so-called burst neurons in the SC (Wurtz & Optican, 1994; Munoz & Wurtz, 1995a)]. Thus, the SC contains a spatial map of locations in which activity in one portion of this map rises for a saccade to the corresponding location in space, identifying the goal of the

movement and contributing to its initiation and control (Lefevre *et al.*, 1998).

The distributed spatial representation in the intermediate and deep layers of the SC also extends down to the smallest detectable saccades (Hamed *et al.*, 2009a). Given the apparent continuity of the map representation of Fig. 5A, we (Hamed *et al.*, 2009a) probed for microsaccade-related activity in the SC by recording the activity of neurons in the rostral portion of this structure, representing foveal regions of space. We hypothesized that microsaccades would be represented in this portion of the SC because of their small movement amplitudes, and we found neurons with movement-related discharge patterns that are almost identical to those observed for larger saccades (Fig. 5D). That is, for each such neuron, there existed a set of microsaccade directions and amplitudes for which the neuron increased its firing rate in the period prior to microsaccade onset, exhibited a peak discharge during the movement and then decreased its activity after the movement. Moreover, the neuron was specific in terms of which microsaccades caused such activity patterns, and thus possessed a 'response field' just like caudal neurons do for larger saccades (Fig. 5E). So, prior to a given microsaccade, a hill of activity appears in the rostral SC that is centered on the neurons coding the microsaccade amplitude and direction to be generated. Eventually, the activity builds up and a microsaccade is triggered. Given the small size of microsaccades, these results suggest that there is remarkable selectivity in the spatial representation within the foveal/parafoveal zone of the SC, with individual neurons not merely responding to all possible tiny eye movements but in fact exhibiting a preference for a subset of such movements (Fig. 5E). This neuronal specificity is reminiscent of the selectivity of motor neurons and burst neurons that Van Gisbergen *et al.* (1981) found for individual movement components (Figs 2 and 3), and it suggests that individual microsaccades (and kinematic components of them) are encoded precisely, at least in the brainstem. Thus, SC involvement in microsaccade generation is consistent with its involvement in saccade generation.

As with larger saccades, the involvement of the SC in microsaccade generation appears more detached from (and, in the functional hierarchy of Fig. 1, higher than) defining the exact kinematics of the upcoming eye movement. For example, in the specific intermediate and deep layer neurons we investigated, movement-related activity in the SC for microsaccades (and saccades) shows a gradual increase in firing rate even fairly long before movement onset. What might the role of the SC in microsaccade generation be, then, and how different is this role from that of pre-motor and motor brainstem nuclei? One possibility is that the SC, its entire spatial map including the foveal representation covering microsaccades, represents at any one moment in time the behavioral relevance of different spatial locations (Krauzlis *et al.*, 2004; Hamed & Krauzlis, 2008; Hamed *et al.*, 2008; Lovejoy & Krauzlis, 2010). Thus, a hill of activation on the SC map indicates that the spatial location represented by this population activity is behaviorally relevant. During steady fixation, the fixated 'goal' is foveal and results in activity centered around the rostral SC on either side of the brainstem (Fig. 6). This is conceptually no different from the population activity that would exist in the caudal SC immediately prior to a large saccade; in this case, the saccade endpoint is the 'goal' and its location is represented by a hill of activity in the corresponding SC location (Carello & Krauzlis, 2004; Krauzlis *et al.*, 2004; McPeck & Keller, 2004). Now, if the activity associated with the fixated goal becomes biased to one side or the other, the center of mass of this activity shifts to a non-zero eccentricity. This may be sufficient to trigger a microsaccade (Hamed & Krauzlis, 2008; Hamed *et al.*, 2008, 2009a). This model allows predictions about the effects of reversible SC inactivation on eye position and microsaccade generation, which

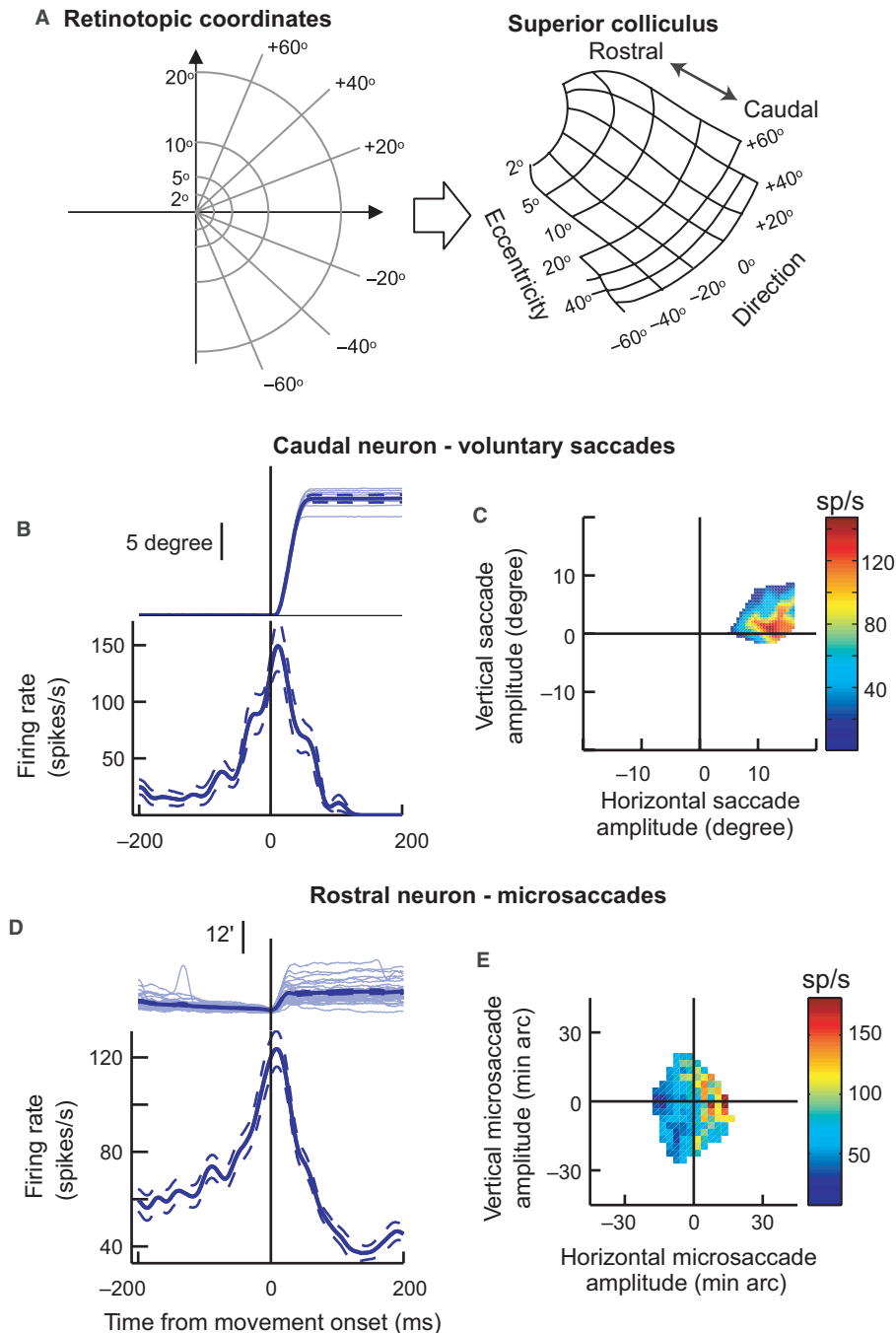


FIG. 5. A neural correlate for microsaccade generation in the primate superior colliculus (SC). (A) Retinotopic representation of space in the SC. Neurons in the SC form a topographic representation with caudal neurons corresponding to peripheral eccentricities and rostral neurons corresponding to central locations. The figure shows iso-eccentricity and iso-direction lines to illustrate the anatomical mapping (right) of the visual coordinates on the left. (B) Activity of a sample SC neuron around saccades larger than approximately 10° directed to the neuron's preferred location in space. The top panel shows eye position aligned on saccade onset, and the bottom panel shows firing rate. The neuron exhibited expected movement-related activity patterns. (C) Activity of the same neuron in B during saccades to different locations. A subset of saccade endpoints was associated with higher activity than others, demonstrating the spatial specificity of the neuron, or its 'response field'. (D) Activity of a sample rostral SC neuron for its preferred 'microsaccades'. Note the great similarity to B except for the different eye movement amplitudes (12 min arc is equivalent to 0.2°). (E) Activity of the same neuron in D during microsaccades of different directions and amplitudes. Again, the neuron was similar to C except for the change in movement scale. That is, it possessed a 'response field' preference for a subset of microsaccades. D and E adapted from Hafed *et al.* (2009a).

have been tested and validated using smooth pursuit (Hafed *et al.*, 2008) and microsaccades (Hafed *et al.*, 2009a). For example, the model predicts that artificially biasing the hill of activity by inactivating one side of the SC should cause an offset in eye position,

which moves the retinotopic representation of the goal to rebalance the activity bilaterally, and which results in a lower overall amplitude for the hill (and thus a lower likelihood of microsaccades) (Hafed *et al.*, 2008, 2009a).

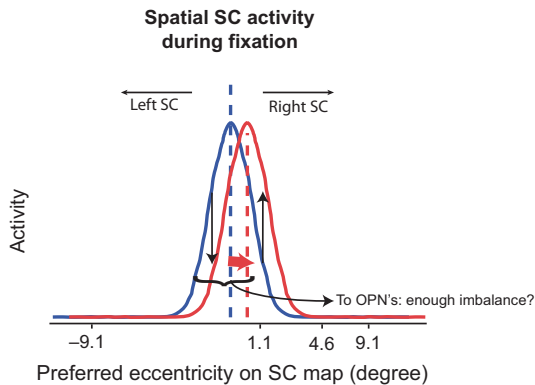


FIG. 6. Model explaining how the rostral SC can contribute to microsaccade generation, through increases in activity (Hafed *et al.*, 2008, 2009a), despite having excitatory projections to OPNs, which reduce their activity at the same time. The figure shows a one-dimensional representation of the SC map. During fixation, activity is centered bilaterally on the rostral SC representing foveal and parafoveal regions. Due to the spatial specificity of individual rostral SC neurons for individual microsaccades (Hafed *et al.*, 2009a), prior to a given movement, a set of neurons coding the movement's endpoint will increase their activity whereas others preferring other spatial locations will decrease (vertical black arrows). This results in an effective spatial shift in the locus of the entire population of activity during fixation (red population profile with horizontal red arrow). If a microsaccade were to occur as a result of this shift, OPNs would pause (Fig. 4), but clearly the rostral SC would not be entirely inhibited. Thus, the excitatory projections from the SC to OPNs (black curved arrow) do not necessarily gate the onset and offset of OPN activity. Instead, they may allow OPNs to apply a threshold on whether sufficient biases in SC activity exist to justify triggering a movement.

Involvement of the SC in microsaccade generation also raises a question concerning anatomical evidence of excitatory connections between the SC (which are strongest from the rostral region but also extend caudally) and OPNs (Gandhi & Keller, 1997; Buttner-Ennever *et al.*, 1999). Historically, these projections have been suggested to imply that the rostral SC contributes to the gating of saccades by OPNs – if the rostral SC is active, OPNs are active; if it is not, OPNs can pause and allow saccades to be triggered (Pare & Guitton, 1994; Everling *et al.*, 1998; Bergeron & Guitton, 2001, 2002). The problem with this view, however, is that during microsaccades (as well as smooth pursuit), there are neurons in the rostral SC that increase their activity [e.g. Hafed *et al.* (2009a) for microsaccades and Krauzlis *et al.* (1997) for pursuit] even though OPNs reduce theirs (Van Gisbergen *et al.*, 1981; Missal & Keller, 2002; Keller & Missal, 2003; Brien *et al.*, 2009). In fact, many of the SC neurons that were tested for possessing excitatory connections to OPNs, whether these SC neurons were rostral or not, were found to exhibit saccade-related increases in activity, rather than decreases like the OPNs that they were connected to (Gandhi & Keller, 1997). Thus, an alternative possibility that reconciles these observations is that the projections from the SC to OPNs allow the latter to detect deviations in the balance of activity across the two SCs, rather than merely to reflect whether the rostral SC population is active or not (Fig. 6). When the hill of activity is biased in one direction or the other, OPNs use the SC projections to implement a threshold on whether the imbalance is enough to trigger a movement (pause to allow for saccades that rebalance activity) or not. Besides being consistent with behavioral observations of eye movements with small target steps (de Bie & van den Brink, 1984), the advantage of this model is that it can also explain microsaccadic inhibition (Rolfs *et al.*, 2008; Rolfs, 2009), as alluded to above. This is so because an increase in OPN activity [due to a stimulus onset, for example (Boehnke & Munoz, 2008)] can be thought of as an increase in the threshold to trigger movement (Hafed

et al., 2009a). This possibility needs to be tested explicitly using experimental and modeling techniques, and it demonstrates how investigating the neural mechanisms for microsaccade generation can also help clarify structure–function relationships in the oculomotor system.

Finally, future neurophysiological studies of various microsaccade-related behavioral phenomena can benefit from the discovery that the SC is involved in microsaccade generation. First, as mentioned earlier, the SC is now a strong candidate for investigating how and why microsaccade onset times and directions can be modulated by covert shifts of visual attention (Hafed & Clark, 2002; Engbert & Kliegl, 2003). Even though several hypotheses have been made about such involvement (e.g. Hafed & Clark, 2002; Rolfs *et al.*, 2006, 2008; Hafed *et al.*, 2009a), exhaustive studies of microsaccade occurrence dynamics during covert attentional allocation in the monkey, and neurophysiological studies investigating such modulation, remain to be performed (but see Hafed *et al.*, 2009b, 2011). Second, the specificity of the representation of microsaccade endpoints within the SC can explain recent evidence that microsaccades precisely relocate gaze during high-acuity visual tasks (Ko *et al.*, 2010). It would be interesting to investigate whether similar specificity exists in other classes of neurons in the SC, such as superficial layer visual neurons or pure saccade-related burst neurons (Goldberg & Wurtz, 1972; Wurtz & Optican, 1994; Munoz & Wurtz, 1995a), for the small eccentricities associated with microsaccades. This specificity also raises the possibility that microsaccades, despite being referred to almost universally as involuntary movements, may be under voluntary control just like their larger counterparts. That is, if these movements precisely relocate gaze (Ko *et al.*, 2010), and are represented precisely in the brain (Van Gisbergen *et al.*, 1981; Hafed *et al.*, 2009a), then it may be that individual voluntary saccades of the size of microsaccades are possible (evidence for this exists: Steinman *et al.*, 1967; Haddad & Steinman, 1973). Finally, the role of the SC in visual processing and the influence of large saccades on such processing are both areas that have been well studied (Robinson & Wurtz, 1976; Sommer & Wurtz, 2002, 2006). Thus, similar involvement of the SC in microsaccade generation allows us to study the sensory consequences of microsaccades in such a light, as I allude to shortly.

Microsaccade generation – cortical control of microsaccades?

It is currently not known whether cortical areas, such as the FEF or LIP, contribute to microsaccade generation. This is important to pursue, however, because it can allow us to answer the question of whether microsaccades are voluntary. As mentioned above, even though evidence for voluntary control over these eye movements has been presented (Steinman *et al.*, 1967; Haddad & Steinman, 1973), the predominant assumption in even the most recent studies on microsaccades (e.g. Rolfs, 2009; Bonneh *et al.*, 2010) is that these eye movements are involuntary. Given our knowledge so far about the neural mechanisms for microsaccade generation, coupled with recent behavioral findings such as those of Ko *et al.* (2010), one is tempted to think that the similarity between microsaccades and saccades at the neural generation and behavioral levels implies that microsaccades, like larger saccades, can be under voluntary control. If so, cortical areas may be involved in such voluntary control, but this remains to be seen.

Microsaccade generation – the view so far

To summarize, our current understanding of microsaccade generation is limited to brainstem structures. Pre-motor and motor nuclei appear

to compile the motor commands for microsaccades in a manner that is consistent with how they would do so for larger saccades. In addition, a distributed spatial representation of microsaccade endpoints exists in the topographic map of the SC, and it seems to be an extension of the same representation for larger eye movements. Thus, microsaccades may be associated with a representation of foveal 'goal' locations at the level of the SC, just like larger saccades.

Despite this evidence, the rarity of more detailed studies of microsaccade generation mechanisms, and with larger neuronal populations, leaves open several opportunities for further understanding. For example, as mentioned earlier, the detailed time course of OPN activity around microsaccades is unknown. Moreover, the extent of voluntary control over these eye movements, and whether signatures of this control can be observed in the brainstem, remains to be determined. It would thus be interesting to study the physiological mechanisms associated with small saccades that are 'instructed' experimentally, perhaps through small steps in target position, and compare them with the mechanisms associated with microsaccades during steady fixation. It would also be interesting to understand how microsaccades may interact with slow drift components during fixation. For example, it was suggested in behavioral experiments that microsaccades are less frequent if slow drift spans large distances in the inter-microsaccadic intervals and more frequent if it does not (Engbert & Mergenthaler, 2006). Can knowledge of physiological microsaccade generation mechanisms explain the functional significance of this finding?

Finally, the apparent similarity between microsaccades and large saccades raises questions about whether other structures involved in saccade generation may also be involved in microsaccade generation. In addition to the FEF and LIP, which I discussed briefly above, areas such as the supplementary eye field (SEF) (Krauzlis, 2005; Schall & Boucher, 2007; Johnston & Everling, 2008; Nachev *et al.*, 2008), basal ganglia (Shires *et al.*, 2010) and several cerebellar nuclei (Pelisson *et al.*, 2003; Goffart *et al.*, 2004; Krauzlis, 2004; Girard & Berthoz, 2005) also contribute to saccade generation. It is currently unknown to what extent these same areas may be involved in microsaccades (but see Guerrasio *et al.*, 2010). However, if they are involved, it is likely that their roles in saccades are somehow preserved for microsaccades. For example, basal ganglia involvement in saccade generation may be associated with learning and the influence of reward. It would be interesting to know whether such processes are also related to microsaccades. Future behavioral and neurophysiological experiments can answer these questions.

Sensory consequences of microsaccade generation

Like larger saccades, microsaccades cause retinal image shifts and therefore alter the inputs to visual sensory areas in the brain. How might microsaccade-induced changes in retinal inputs be reflected in the activity of visual sensory and sensori-motor areas? Most of the early neurophysiological studies of microsaccades first investigated this aspect of these movements, and specifically probed their modulatory influences on striate and extrastriate cortices (Bair & O'Keefe, 1998; Leopold & Logothetis, 1998; Martinez-Conde *et al.*, 2000, 2002; Snodderly *et al.*, 2001). In these early studies, area V1 proved to be the most contentious. Leopold & Logothetis (1998) reported suppression of V1 activity after microsaccades, whereas Martinez-Conde *et al.* (2000, 2002) emphasized the observation of bursts. These authors used this observation as evidence for how microsaccades are necessary for preventing image fading during fixation (Martinez-Conde *et al.*, 2004). Snodderly *et al.* (2001) also studied V1 activity, and classified a variety of neuronal response types

associated with microsaccades; they often found suppression followed by subsequent enhancement in the same V1 neurons. In the years that followed, the prevalent view that persisted about the sensory consequences of microsaccades was the view of Martinez-Conde *et al.* (2004), which has been the inspiration for many behavioral studies of microsaccades (e.g. Engbert & Mergenthaler, 2006; Martinez-Conde *et al.*, 2006; Otero-Millan *et al.*, 2008; Troncoso *et al.*, 2008a,b). As a result, the hallmark of the past 10 years has been an emphasis on the role of microsaccades in enhancing vision (Martinez-Conde *et al.*, 2004, 2009; Collewijn & Kowler, 2008; Melloni *et al.*, 2009; Rolfs, 2009).

In later experiments, visual areas MT, V1 and visual area V4 were revisited (Bosman *et al.*, 2009; Herrington *et al.*, 2009), and areas LGN, LIP, ventral intraparietal area and SC were investigated anew (Martinez-Conde *et al.*, 2002; Herrington *et al.*, 2009; Haged & Krauzlis, 2010). The prevalent result from these more recent experiments was the observation of suppression of activity before and during microsaccades, with a subsequent increase in activity well after the movement in a subset of these areas (e.g. LGN, V1, V4) (Martinez-Conde *et al.*, 2002; Bosman *et al.*, 2009). Thus, it now appears that microsaccadic suppression, rather than enhancement, is the more widespread phenomenon, being observed in several sensory and sensori-motor areas in the brain.

Given our current understanding of the neural mechanisms for microsaccade generation, is it possible to reconcile such a multitude of evidence about the sensory consequences of these eye movements? Here again, the answer seems to lie in looking at larger saccades for inspiration. The influence of larger, voluntary saccades on vision has been studied extensively and using several techniques, from behavior (Ross *et al.*, 1997, 2001) to neurophysiology (Duhamel *et al.*, 1992; Sommer & Wurtz, 2002, 2006; Ibbotson *et al.*, 2008; Bremmer *et al.*, 2009; Crowder *et al.*, 2009) and modeling (Hamker *et al.*, 2008). The generally accepted view about these eye movements is that they move retinal images and are thus associated with two main influences on vision. First, shortly after each saccade, visual reafference is expected to drive early sensory areas with the newly appearing retinal images after movement end (Reppas *et al.*, 2002; Royal *et al.*, 2006; Ibbotson *et al.*, 2008; Kagan *et al.*, 2008; MacEvoy *et al.*, 2008; Bosman *et al.*, 2009; Bremmer *et al.*, 2009; Melloni *et al.*, 2009). Second, because saccades cause such dramatic changes in the input retinal image stream (for a review see Wurtz, 2008), saccades are also associated with mechanisms that ensure the perception of a stable world despite these changes. One such mechanism is the suppression of visual sensitivity before and during saccades, which can be observed behaviorally and in a variety of sensory and sensori-motor areas (Robinson & Wurtz, 1976; Ibbotson *et al.*, 2008; Bremmer *et al.*, 2009; Crowder *et al.*, 2009).

By extending the analogy between microsaccades and saccades from the realm of generation mechanisms (Fig. 1) to that of sensory consequences on neural activity, it is reasonable to argue (based on current understanding of saccadic influences on vision) that both increases and decreases in visual activity may be expected around the time of microsaccades. Specifically, areas closely connected to the sensory input may be expected to exhibit visual reafference after microsaccades, in addition to 'microsaccadic suppression' before and during the movement itself; areas less closely related to the sensory input may exhibit 'microsaccadic suppression' but not necessarily the strong visual reafference that is a direct sensory response. According to this view, LGN, V1, V2 and V4 are expected to increase their activity shortly after microsaccades, because of their proximity to retinal afferents, and this is what is generally observed. However, prior to and during the movements, these same areas may exhibit reduced

sensitivity, because they also exhibit suppression for larger saccades (Reppas *et al.*, 2002; Royal *et al.*, 2006; Ibbotson *et al.*, 2008; MacEvoy *et al.*, 2008; Bremmer *et al.*, 2009; Crowder *et al.*, 2009). Similarly, higher level sensori-motor areas, such as LIP, which are less closely linked to direct retinal input, may not exhibit direct reafference but are still expected to exhibit suppression in order to ensure perceptual stability [for example, of spatial representations (Duhamel *et al.*, 1992)] in the face of eye movement, again like larger saccades. Thus, the modulatory influences of microsaccades on sensory and sensori-motor structures described above are not necessarily controversial in light of their similarity to the influences of saccades.

Using the same approach, Hafed & Krauzlis (2010) exploited the well-studied phenomenon of 'saccadic suppression' in the SC (Goldberg & Wurtz, 1972; Robinson & Wurtz, 1976; Richmond & Wurtz, 1980), as well as the observation of similarity between saccade and microsaccade generation in the same structure (Hafed *et al.*, 2009a), to demonstrate an almost identical phenomenon of 'microsaccadic' suppression in SC neurons. It was found that stimulus-induced visual bursts in peripheral SC neurons are suppressed when stimulus onset coincides with microsaccade generation (Hafed & Krauzlis, 2010). Moreover, the time course of this suppression is similar to that of saccadic suppression (Zuber & Stark, 1966; Diamond *et al.*, 2000). This result is a direct correlate of classic observations in the SC for larger saccades (Goldberg & Wurtz, 1972; Robinson & Wurtz, 1976; Richmond & Wurtz, 1980), and it shows that part of the normal trial-to-trial variability in SC visual responses could be explained by microsaccades. This is similar to observations in cortical areas (Herrington *et al.*, 2009). Moreover, microsaccadic suppression in the SC appears to be reflected in reduced behavioral performance efficiency (measured as reaction time increases) even for stimuli that are high in contrast and continuously present (Hafed & Krauzlis, 2010). Thus, by using knowledge about microsaccade generation circuitry and how this circuitry has been used in the past to study the sensory consequences of larger saccades, it has become possible to clarify the interpretation of the sensory consequences of microsaccades (and, ultimately, the potential influences of these movements on behavior).

Future investigations of the sensory consequences of microsaccades can benefit from additional existing knowledge about the changes to visual perception that take place at the time of larger saccades. For example, peri-saccadic updating of spatial representations takes place in several areas (Duhamel *et al.*, 1992; Ross *et al.*, 2001; Sommer & Wurtz, 2006), and it is believed that such updating plays a role in ensuring perceptual stability in the face of image motion caused by these eye movements. It would be interesting to investigate whether a similar phenomenon occurs for microsaccades, and why such a phenomenon may be functionally useful. Saccades also influence the perception of time (Burr *et al.*, 2010). These are all areas of active investigation, and they will clarify our understanding of the complete set of mechanisms associated with microsaccades, and the functional role of these eye movements. More importantly, these investigations will help in facilitating the interpretation of visual neuroscience experimental results that are not necessarily concerned with eye movements, but that have to deal with the fact that such eye movements occur in any awake, fixating subject.

Conclusion

Recent results have shown that the functional organization of microsaccade generation is similar to that of saccades. At the level of the SC and downstream of it, in pre-motor and motor brainstem

circuits, microsaccade generation is almost identical to saccade generation. Even though much remains to be learned about other aspects of microsaccade generation in the brain (for example, whether cortical control of these movements takes place), current understanding of the neural mechanisms for controlling microsaccades clarifies the existing evidence of the sensory consequences of these eye movements. Moreover, such understanding provides testable predictions about the influence of sensory transients, voluntary control and cognitive processes on microsaccades. By approaching microsaccades from the perspective of their similarities to larger voluntary saccades, much can be learned about the mechanisms associated with these small eye movements, as well as their physiological consequences on input retinal image streams.

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Abbreviations

FEF, frontal eye field; LGN, lateral geniculate nucleus; LIP, lateral intraparietal area; LLBN, long-lead burst neuron; MLBN, medium-lead burst neuron; MT, middle temporal area; OPN, omnipause neuron; SC, superior colliculus; SEF, supplementary eye field; V1, primary visual area; V4, visual area V4; VIP, ventral intraparietal area.

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