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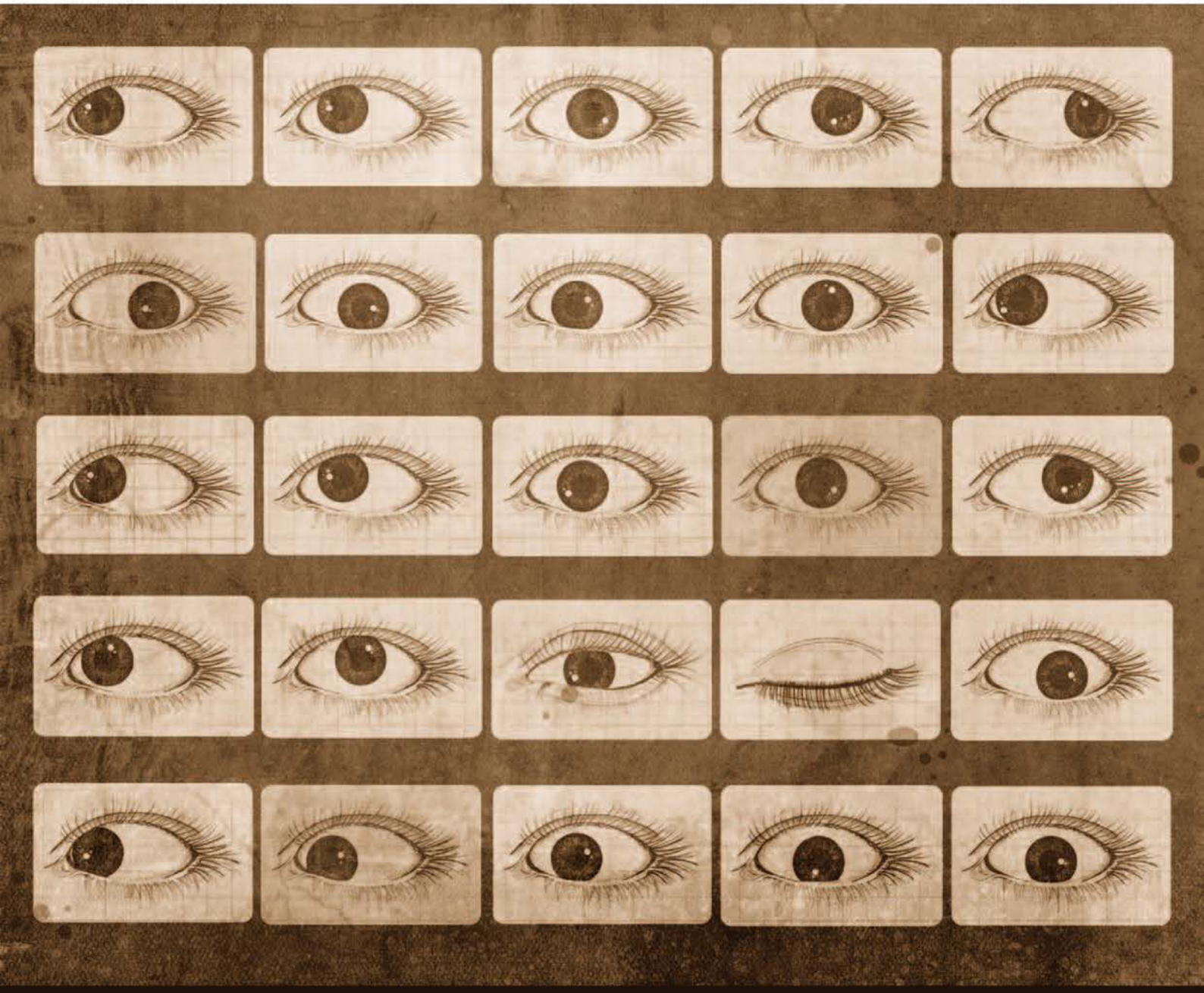

AN UNSTEADY GAZE
The neural mechanisms and functions of microsaccades

Traumatic brain injury
How could animal models be improved?

The impact of microsaccades on vision: towards a unified theory of saccadic function

Susana Martinez-Conde[1], Jorge Otero-Millan[1,2] and Stephen L. Macknik[1,3]

Abstract | When we attempt to fix our gaze, our eyes nevertheless produce so-called 'fixational eye movements', which include microsaccades, drift and tremor. Fixational eye movements thwart neural adaptation to unchanging stimuli and thus prevent and reverse perceptual fading during fixation. Over the past 10 years, microsaccade research has become one of the most active fields in visual, oculomotor and even cognitive neuroscience. The similarities and differences between microsaccades and saccades have been a most intriguing area of study, and the results of this research are leading us towards a unified theory of saccadic and microsaccadic function.

Our eyes are never still. Even when we attempt to fix our gaze, small ocular motions — generally undetectable to the naked eye — shift our eye position[1]. In the 1950s, studies reported that stationary objects vanished perceptually in the absence of so-called 'fixational eye movements'[2–4]. The following decades of research strived to identify the roles served by the three types of fixational eye movements: microsaccades, drift and tremor. Much of the research, and ensuing debate, focused on microsaccades — small saccades produced 1–2 times per second during fixation. Polar opposite positions as to the importance of microsaccades (or lack thereof) arose[5,6]. The dispute abated with an influential paper asserting that microsaccades "serve no useful purpose"[6].

The turn of the millennium saw a tentative resurgence in microsaccade research[1,7,8], which was facilitated by methodological advances in the simultaneous recordings of neural responses and eye positions in awake primates, progress in the computational modelling of eye movements and technological improvements leading to the manufacture of high-resolution and high-speed video-oculography systems for human eye tracking. The development of objective microsaccade-detecting algorithms[9] further contributed to the proliferation of human studies and rapid replication of results.

Research in the past decade linked microsaccades to perception[10–14] and determined key interactions between microsaccade dynamics and cognitive processes, especially in regard to the allocation of attention[9,15]. Concurrent milestones included the concept of a microsaccade–saccade continuum, which is sustained by evidence that saccades of all sizes share a common generator[16–21].

The proposal that microsaccades and saccades are the same type of eye movement has theoretical and practical implications. It simultaneously expands and places limits on the functional roles of microsaccades, and it helps to dispel the once popular notion that microsaccades should have one fundamental purpose versus another. The state-of-the-art theory is that microsaccades may serve as varied functions during fixation as saccades do during exploration[14].

The continuum from microsaccades to saccades may extend to 'saccadic intrusions'[17,22] — that is, saccades that intrude or interrupt accurate fixation — which are prevalent in various neurological disorders. A functional continuum spanning microsaccades, saccades and saccadic intrusions offers testable predictions that are significant not only to healthy vision and oculomotor control but also to the pathogenesis of neural disease[23].

Here, we discuss the latest findings on the neural bases of microsaccade generation and the perceptual consequences of microsaccades — two areas of research that were all but absent from the microsaccade landscape just a few years ago. We also present the latest findings on the physiological responses to microsaccades along the ascending visual pathway, the growing body of work demonstrating the interaction between microsaccades and cognition, and the budding research on pathological microsaccades. In doing so, we aim to elucidate several key concepts that have evaded consensus, such as the very

[1]*Department of Neurobiology, Barrow Neurological Institute, 350 W. Thomas Rd., Phoenix, Arizona 85013, USA.*
[2]*Department of Signal Theory and Communications, University of Vigo, Vigo 36310, Spain.*
[3]*Department of Neurosurgery, Barrow Neurological Institute, Phoenix, Arizona 85013, USA.*
Correspondence to S.M.-C.
e-mail: smart@neuralcorrelate.com
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definition of a microsaccade, the meaning of microsaccades during visual exploration and the potential effects of microsaccades in preserving versus restoring visibility during fixation.

The past decade of research has brought forth some of the most exciting discoveries in the history of the field. Today, microsaccade studies continue to grow rapidly, extending to visual, oculomotor and cognitive neuroscience. A unified theory of microsaccadic and saccadic function is on the horizon and, with it, an improved understanding of visual and oculomotor function in health and in disease.

What is a microsaccade?

Microsaccades (also known as fixational saccades) are small saccades that are produced during attempted fixation[24]. This operational definition, albeit useful for practical purposes[25], poses two important challenges: to establish the amplitudes corresponding to 'small' saccades and to determine whether the subject is 'attempting' to fixate. We address the issue of amplitude first.

How long is a piece of string? Until the 1990s, microsaccades were defined as having amplitudes smaller than 12 arc min. This cut-off value originated in earlier studies finding that the distribution of saccadic sizes during fixation declined sharply around 12 arc min[26]. However, later studies found that microsaccade sizes frequently exceed this value[27,28] (instead, current microsaccade magnitude distributions often asymptote around 1 degree[25]). Thus, most contemporary researchers have adopted the convention of using a 1-degree upper magnitude threshold (which captures more than 90% of saccades produced during attempted fixation)[18,25].

The mysterious shift to larger microsaccadic magnitudes in the past two decades remains unexplained[27]. Some researchers have argued that contemporary videooculography is noisier than the optical lever recordings of the 1960s and 1970s. However, this reasoning is unsatisfactory; a noisy instrument might account for the loss of the smallest microsaccades but not for the shift to larger amplitudes[26]. Indeed, a recent study conducted with a dual Purkinje image tracker (which is considered the most accurate and precise of the optical and feature recognition methods[29]) found that microsaccade magnitudes reached an asymptote at around 1 degree[30].

Current and former experimental conditions, including illumination, display type, means of head fixation and fixation effort, might differ[26,27]. Another suggestion is that older studies relied on highly trained observers, usually the authors themselves, whereas modern experiments prefer naive participants with little or no fixation experience[27] (although microsaccade magnitude distributions seem to be similar in experienced fixators and naive subjects[10,11]).

A further difference is that contemporary human eye tracking is usually non-invasive, whereas early contact lens-based techniques, such as the optical lever method[31], required direct and potentially unsafe contact with the eye[29]. (Young and Sheena[32] pointed out that fitting a contact lens with negative pressure (as in the optical lever method) posed significant dangers to the eye, including the "possibility of deforming the cornea and (…) damaging the accommodation muscles as a result of the pressure stress".) Thus, the recording apparatus could have hindered eye motion and thereby reduced the size of microsaccades in the early studies. Because non-contact eye trackers leave the eye unencumbered, microsaccades may be free to reach their natural (that is, larger) amplitude ranges in contemporary studies. Supporting this possibility, optical lever studies conducted in the 1980s[33,34] found microsaccade amplitudes resembling those in the earlier work (that is, 3–20 arc min). Microsaccades measured with a piezoelectric sensor (requiring direct ocular contact) also had decreased magnitudes. Sensor removal restored normal microsaccade magnitudes (which were measured with a video tracker)[35]. Last, both video tracking and the search coil technique (which is considered a gold standard in eye tracking owing to its excellent signal-to-noise ratio[29]) measured microsaccade magnitudes reaching around 1 degree[17] (FIG. 1). Lens-mounted search coils are arguably less invasive and hazardous than contact lens methods that require negative pressure

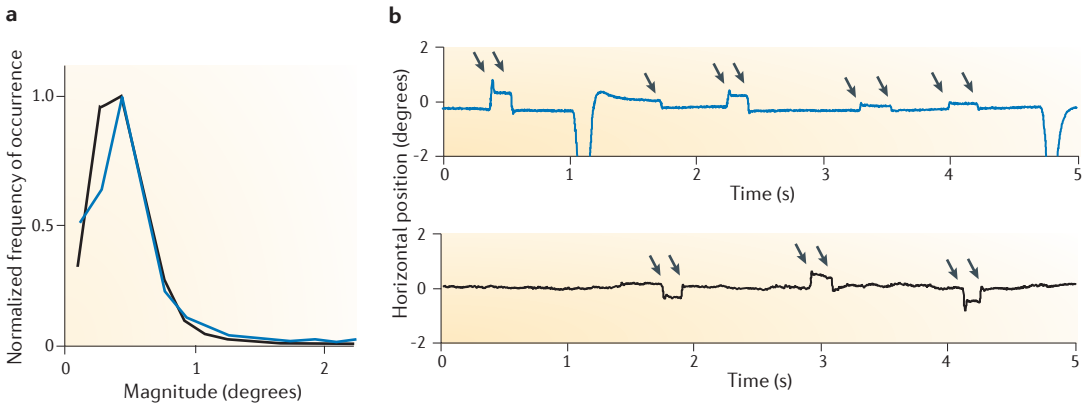

Figure 1 | **Microsaccade magnitudes.** **a** | Distribution of human microsaccade magnitudes obtained with video (black) and search coil recordings (blue). Microsaccade magnitudes, which are often in excess of 12 arc min, are comparable for both eye tracking methods. **b** | Examples of the corresponding eye position traces. Arrows identify microsaccades. The figure is modified, with permission, from REF. 17 © (2011) Society for Neuroscience.

(even though both techniques involve direct eye contact), and so the former might impose a lesser restriction on eye motion than the latter, given the same experimental conditions and amount of fixation effort. This possibility remains to be tested.

Whatever the explanation behind the recent shift towards larger microsaccades, the combined evidence indicates that setting a cut-off value of 12 arc min is both conceptually and experimentally unjustified. It is ironic that, for a field historically laden with questions about what constitutes natural versus unnatural oculomotor behaviour[29], the traditional definition of a microsaccade may turn out to be fundamentally artificial.

What are your intentions? Defining microsaccades as saccades that occur during the attempt to fixate poses the challenge of determining the subject's intent. During a fixation task in the laboratory, one can assume that most saccades produced will be microsaccades by definition, although some exploratory saccades may occur occasionally[18]. The situation becomes more complex when the subject carries out tasks other than prolonged fixation. Some authors have argued that microsaccades are absent from free viewing, but their stance has depended on microsaccades being smaller than 12 arc min, a view most researchers now reject (see above). Thus, non-fixation tasks (free viewing or visual search) allow us to distinguish between microsaccades and saccades according to the observer's intent; saccades produced during active exploration may be considered 'regular saccades', and saccades produced in the fixation periods between exploratory saccades may be considered 'microsaccades'. The predicament is that we are typically unaware of our eye movements; most saccades produced during normal exploration and search are involuntary, regardless of size. Subjects could continuously indicate their intent to fixate or shift their gaze, but this requirement would complicate the task and result in artificial viewing conditions. An alternative possibility that precludes interference with the subject's task is to determine the characteristics of saccades during prolonged fixation (most of these saccades are microsaccades by definition; see above) and use those parameters to identify microsaccades during free viewing. Accordingly, several recent studies have adopted the convention of considering microsaccades as saccades smaller than 1 degree, even during non-fixation conditions, including free viewing, visual search and visuomotor tasks[18,36] (FIG. 2a).

Neural bases of microsaccade generation

Behavioural studies have built a solid case showing that microsaccades and saccades share most, perhaps all, physical and functional properties. Among these, it is notable that both saccades and microsaccades are typically binocular and conjugate[37–39] (but see REF. 40) and that they follow the main sequence[18,41] (FIG. 2b). Visual changes transiently inhibit saccadic production during search, reading and other tasks[42], and microsaccadic production during maintained fixation[9,43]. Attending to peripheral stimuli while fixating can bias microsaccade[9,15] and saccade[44] direction (see 'Cognitive modulation of microsaccades'). Volitional control can affect microsaccades and saccades in comparable ways; although microsaccades are often described as involuntary[37,45,46], careful attempts to fixate markedly reduce the rate of microsaccades[47], and voluntary saccades can be the size of microsaccades[48]. Conversely, observers are not ordinarily aware of their exploratory saccades[45].

Temporal interactions between saccades and microsaccades further suggest a common triggering mechanism. Latency is increased for saccades that occur shortly after microsaccades[19,20]. Moreover, equivalent time intervals between microsaccades and saccades during exploration and search[18] indicate that saccades and microsaccades share timing constraints, supporting the hypothesis of a shared saccade and microsaccade generator[18].

Neural recordings from primate oculomotor structures have provided an increasingly clear picture of the pathway that leads to microsaccade generation (FIG. 3). Burst neurons in the pontomedullary reticular formation (downstream from the superior colliculus (SC)) and putative motor neurons in the nearby abducens nucleus are active during both microsaccades and saccades[49,50]. Similarly, some neurons in the SC rostral pole (which represents foveal goal locations) are as active for small saccades as neurons in the SC caudal region (which represents peripheral goal locations) are for large saccades[51]. For several decades, these pioneering studies provided the main physiological evidence for a shared generator.

In recent years, a flurry of studies have found comparable neural activity around saccades and microsaccades in multiple brain structures[16]. The activity of omnipause neurons in the pontine raphe decreases during microsaccades[40,52], and there is a continuous representation of saccade directions and amplitudes through the SC, down to the smallest microsaccades[21] (with microsaccade representation in the SC rostral pole, which is in agreement with previous observations[51]). Neural activity during microsaccades sometimes extends to small-amplitude voluntary saccades, which is consistent with behavioural evidence of a microsaccade–saccade continuum, and rostral SC inactivation results in decreased microsaccade rates[21]. Unilateral inactivation of the fastigial oculomotor region in the cerebellum likewise affects the metrics of visually guided saccades[53,54] and microsaccades[55].

Despite mounting evidence for a common generator for microsaccades and saccades[16–19,21,43], the precise mechanism that triggers microsaccades is unclear[16]. Current findings support a combined role of neural noise and fixation error in triggering microsaccades, with the contribution of each signal depending on the magnitude of the gaze position error[16]. For example, if a subject's gaze deviates from the target by around 0.5 degrees or more, corrective microsaccades might rectify the error[17,56], whereas if the fixation error is small or insignificant, neural noise might trigger microsaccades instead[17].

Microsaccades and fixation correction. Microsaccadic involvement in the control and correction of fixation position has been controversial for over 50 years[1,27]. It was originally proposed that microsaccades serve to re-foveate the target after intersaccadic drifts[56], but this idea was

Peak velocities and durations of microsaccades and saccades are parametrically related to microsaccadic and saccadic amplitudes.

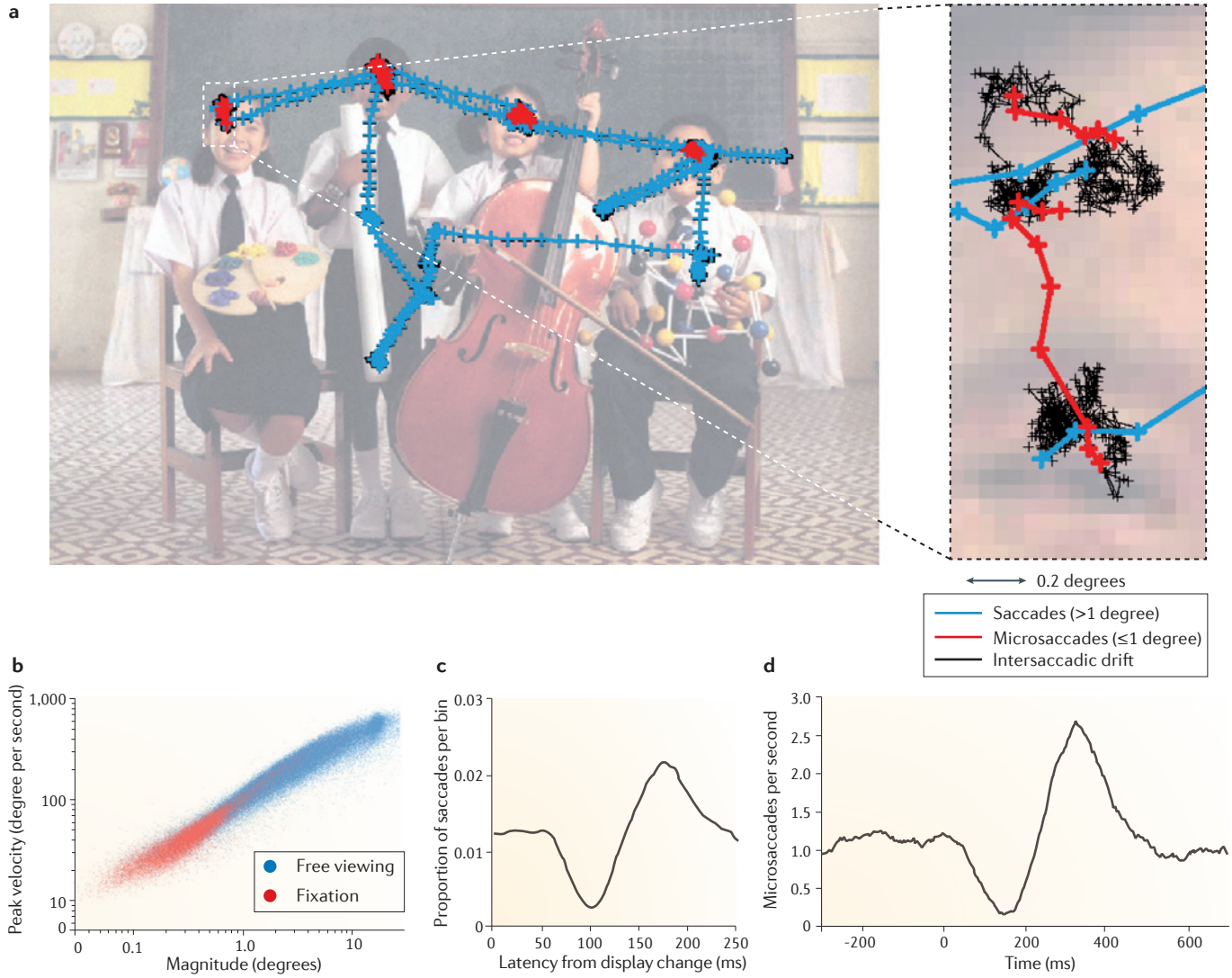

Figure 2 | **Equivalent functional dynamics in microsaccades and saccades.** **a** | Microsaccades and saccades during free viewing. The left panel shows a subject's eye positions during free visual exploration. The right panel shows a 10-second period of the same subject's eye position from the left panel in more detail. Faces were a primary focus of microsaccades. **b** | Microsaccades and saccades during free viewing (blue) follow the same main sequence as during attempted fixation (red). Some of the red dots are obscuring the blue dots underneath ($N = 8$ subjects). **c** | Saccadic inhibition after changes in peripheral stimuli. **d** | Microsaccadic inhibition after changes in peripheral stimuli. Parts **a** and **b** are modified, with permission, from REF. 18 © (2008) Association for Research in Vision and Ophthalmology. Part **c** is modified, with permission, from REF. 42 © (2000) Elsevier. Part **d** is modified, with permission, from REF. 9 © (2003) Elsevier.

subsequently challenged (see REF. 27 for a review). By the end of the 1970s, most of the field disregarded a potential role of microsaccades in the control of fixation position, while concluding that drift (also called slow control) served that very purpose. This notion remained uncontested until the early 2000s, when new analyses indicated that microsaccades both introduce (on a short timescale) and correct (on a longer timescale) fixation errors[57].

Research into the mechanisms of microsaccade generation has helped to clarify the role of microsaccades in fixation correction. Microsaccades triggered by fluctuations in SC activity might introduce fixation errors, but if these are large enough, they will trigger a subsequent corrective microsaccade[16]. Consistent with this idea, large microsaccades tend to be followed by subsequent microsaccades in the opposite direction, resulting in square-wave jerks (SWJs)[17]. Microsaccades can also correct eyeblink-induced fixation errors[58].

Cognitive modulation of microsaccades. A shared oculomotor generator helps to explain how saccades and microsaccades are affected by covert attention and distracters (FIGS 2c,d). The link between microsaccades and attention stems from the extensive overlap between the neural system that controls attention and the system that generates saccadic eye movements[59]. For instance, the SC — which has a causal role in microsaccade production[21] — targets saccades in connection with attentional

Square-wave jerks
(SWJs). Microsaccades that distance the eye from the fixation target, which are shortly followed by microsaccades that return the eye to the target.

Covert attention
Attention that is localized away from the centre of gaze.

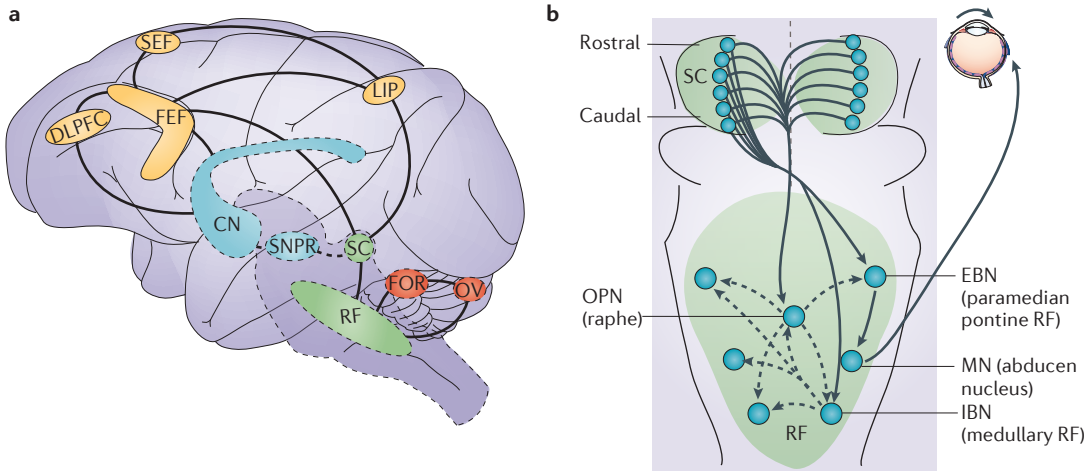

Figure 3 | **Microsaccade generation circuit.** **a** | Main brain areas implicated in the generation of saccades. Cortical areas (orange) related to the voluntary control of gaze include: the lateral intraparietal area (LIP), frontal eye fields (FEF), supplementary eye fields (SEF) and the dorsolateral prefrontal cortex (DLPFC). Basal ganglia are shown in blue; the caudate nucleus (CN) receives a projection from the FEF. The substantia nigra pars reticulata (SNPR) inhibits the superior colliculus (SC) to avoid unwanted eye movements and to control the initiation of saccades. Areas of the brainstem are shown in green; the SC projects to the reticular formation (RF) to produce the final motor command. Areas of the cerebellum are shown in red; the oculomotor vermis (OV) and the fastigial oculomotor region (FOR) provide a feedback loop to control saccade accuracy. **b** | Brainstem circuitry underlying the generation of a rightwards microsaccade. Activity during saccades and microsaccades is equivalent in all of the neuronal populations that have been identified in the saccade generation circuit, except in the case of inhibitory burst neurons (IBNs), in which no studies to date have conducted recordings in connection with microsaccades. SC neurons present two gradients of connectivity: one that is strongest between rostral SC and omnipause neurons (OPNs), and one that is strongest between caudal SC and excitatory burst neurons (EBNs). During fixation, the SC rostral poles drive OPNs, which in turn inhibit IBNs and EBNs. Small shifts in rostral activity trigger microsaccades, whereas large shifts (to the caudal region) give rise to saccades. Shifts in SC activity increase the drive to burst neurons and/or decrease the drive to OPNs. Sufficient inhibition to the OPNs (by the IBNs) allows the EBNs to drive the motor neurons (MNs), producing an eye movement. Solid lines correspond to excitatory connections and dashed lines to inhibitory connections.

shifts[60]. The location of covert attention might influence microsaccade direction by biasing the SC activation map[16,21,43]. Consistent with this proposition, studies have found that the spatial location indicated by an attentional visual cue can bias microsaccade directions towards or away from the cue[9,15,22,61–71]. Experimental differences concerning the use of endogenous (centrally presented) versus exogenous (peripherally presented) attentional cues might help to explain discrepancies in results[22]. Endogenous attentional cues tend to bias microsaccade directions towards the cue[9,15,22,69,71], which is consistent with saccade planning[15,65], whereas exogenous attentional cues often bias microsaccade directions away from the cue[61–64,68,70], which is consistent with inhibition of return[61,62,68,72].

There is debate on how reliably microsaccades indicate covert attention[63,67,69,73–75]. The link between spatial attention and microsaccade direction can depend on microsaccade timing with respect to cue onset[69]. In a recent study, microsaccades produced 200–400 ms after the cue were strongly biased towards the target, as long as they were the first or only microsaccades produced in the attentional cue–target interval.

Attentional cues also modify microsaccade rate. Microsaccade production falls at around 100–200 ms after the onset of an attentional cue and is then transiently enhanced[9,13,15,61,63,64,73,76–80] (FIG. 2d). Working memory[70,78] and task difficulty[71] can also influence microsaccade production. In a recent study, high cognitive load lowered microsaccade rates, but the directions of the remaining microsaccades were highly informative as regards to the spatial location of attention focus. Recently, it has been proposed that visual attention and perceptual input integration at the SC level can explain the range of effects on microsaccade rate and direction observed across various cueing tasks[81].

Inhibition of return
A stimulus presented at a location attended recently evokes a weaker response than a stimulus presented at a previously unattended location.

Physiological effect of microsaccades

At the onset of the twenty-first century, single-neuron studies reported that microsaccades triggered spike rate increases in area V1 and the lateral geniculate nucleus of the awake primate, often in the form of burst firing[82,83]. More recently, observations of microsaccade-triggered neural activity have extended to multiple areas of the extrastriate cortex[84–86] and to various recording techniques, including multineuron recordings[86], voltage-sensitive dye imaging[85], human electroencephalography [87] and human functional MRI[84] (FIG. 4; TABLE 1). Examination of the neural responses evoked by microsaccades (FIG. 4) allows us to draw a number of conclusions.

First, most recordings from retinotopic areas report that neural activity increases in response to microsaccades in the presence of stationary stimuli. Such increases, which are consistent with microsaccade-induced

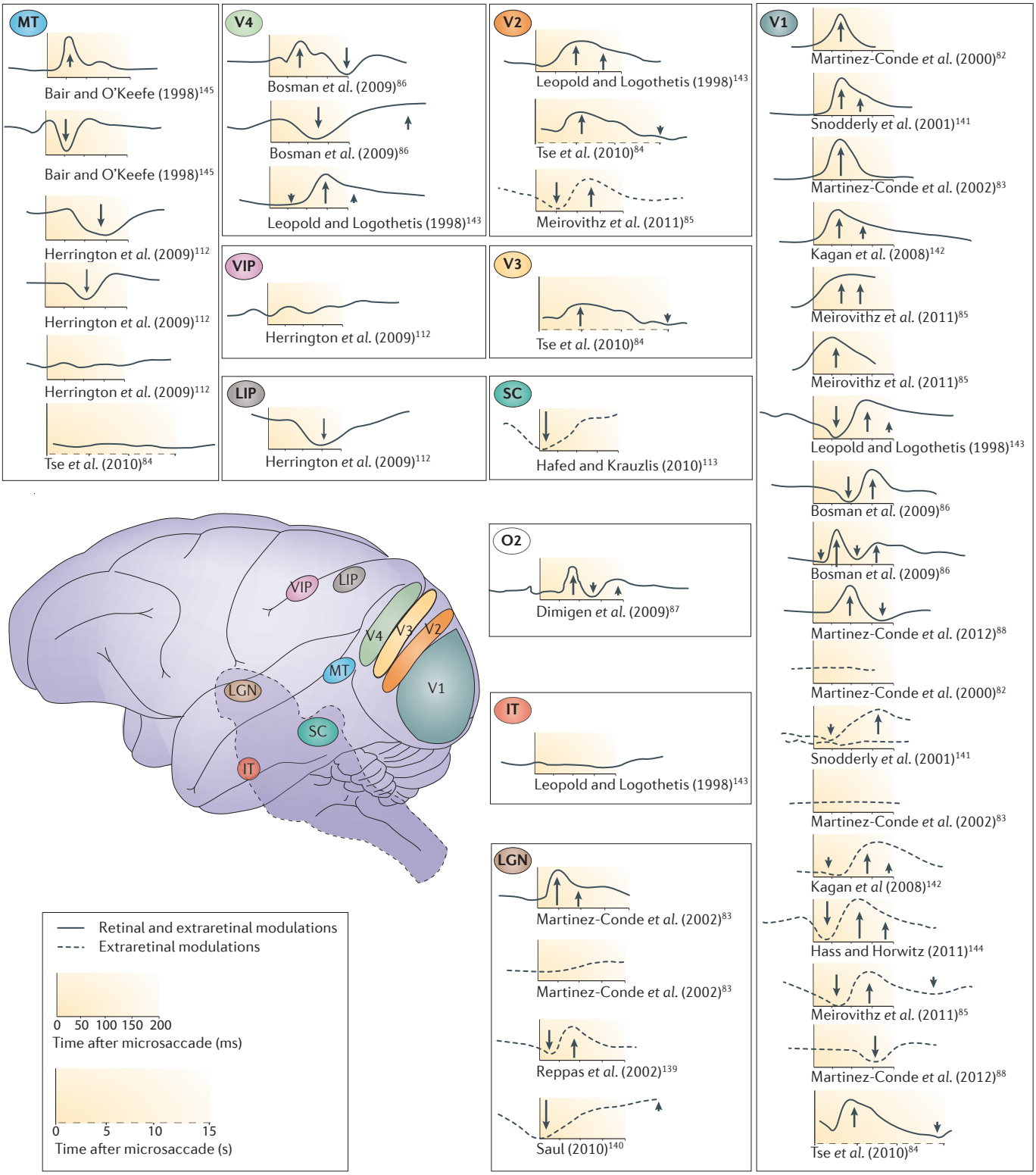

Figure 4 | **Neural responses to microsaccades along the visual pathway.** Insets indicate neural activity around microsaccade onsets according to different studies. Most experiments recorded responses to microsaccades in the presence of a visual stimulus (which was usually stationary and with optimal characteristics). Such responses might include retinal as well as extraretinal modulations (solid lines). Other experiments aimed to identify extraretinal modulations only (dashed lines) and typically recorded responses to microsaccades in the absence of visual stimulation or in the presence of a uniform stimulus. In the presence of optimal stimulation, microsaccade-triggered increases tend to prevail over decreases in neural activity. In the absence of visual stimulation, microsaccades often trigger decreases in neural activity. TABLE 1 provides experimental details for each study. IT, inferior temporal cortex; LGN, lateral geniculate nucleus; LIP, lateral intraparietal area; MT, middle temporal area; O2, right occipital cortex; SC, superior colliculus; VIP, ventral intraparietal area.

receptive field displacements over static visual objects, are probably comparable with the increases in neural responses that might result from equivalent object motion over static receptive fields. Thus, the interplay between the receptive field (or the receptive field conglomerate) and visual stimulus can explain microsaccade-driven retinal activity (which is conveyed to cortical areas by stimulation of the retinogeniculate pathway).

Second, in the absence of stimulation, or in the presence of uniform full-field stimulation (extending well beyond the borders of the receptive fields of the neurons recorded), microsaccade-triggered responses often take the form of decreases in neural activity. These might be the product of extraretinal brain activity triggered by the microsaccade generation circuit (FIG. 3) and/or visual stimulation of non-classical receptive fields.

Third, microsaccade-triggered increases in neural activity tend to be substantially larger than microsaccade-triggered decreases. Thus, despite some discrepancies across studies — which are probably caused by a combination of differences in visual stimuli, tasks used, recording techniques, neuronal sampling biases and so on — the pattern that emerges is that microsaccades modulate neural activity in retinotopic areas primarily through retinal motion and that extraretinal responses, albeit often present, are generally smaller than the visual responses driven by retinal activation.

One obstacle to quantifying the contribution of retinal versus non-retinal inputs to microsaccade-triggered neural responses is that, whenever a visual stimulus is present, microsaccade-driven activity can combine both retinal and extraretinal elements. A study recently compared the responses produced by real microsaccades with the responses generated by stimulus motion mimicking microsaccades in area V1 (REF. 88). Neuronal responses to real microsaccades were generally biphasic; a quick and marked increase over baseline was typically followed by a smaller and slower trough below baseline, whereas responses to simulated microsaccades included an excitatory peak but no trough. Thus, excitatory responses to real microsaccades might result from the displacement of the visual stimulus over the classical receptive field, with the subsequent inhibition reflecting non-retinal sources. The differential responses to real versus simulated microsaccades further suggest that area V1 neurons can distinguish between internally and externally generated motion (that is, visual displacements due to eye movements versus actual motion in the world). This distinction could help to disambiguate latency and contrast perceptually[1,82]. Contrast changes can be encoded as neural response latency changes[89,90], but one question that arises is how changes in latency can represent contrast without the brain first having knowledge of the timing of events. Given that the brain 'knows' when it generates microsaccades, it could use differences in response latencies to indicate contrast differences.

Microsaccades might enhance spatial summation by synchronizing neighbouring neurons, and microsaccade-triggered bursts of spikes[82,83] could facilitate temporal summation of responses[1]. Furthermore, recent research indicates that microsaccades modulate stimulus-induced gamma-band synchronization, as well as related behavioural responses[86].

Owing to the technical difficulty of conducting neural recordings in a moving eye, there is no direct evidence of neuronal responses to microsaccades in the primate retina. A modelling study concluded that microsaccades might enhance retinal sensitivity to edges[91] and supported the prediction that visual responses to microsaccades might start with photoreceptors[1,82,83].

What are the functions of microsaccades?

Saccades have multiple roles in vision: they correct gaze errors, foveate targets and search for and integrate information to stitch together each visual scene[29]. Recent research suggests that microsaccades might also serve various visual functions[14] (see 'Microsaccades and fixation correction' for the role of microsaccades in oculomotor control).

Microsaccades counteract foveal and peripheral fading. In the early 2000s, neurophysiological experiments showed microsaccade-triggered activity in primate visual neurons[82,83] (FIG. 4), but evidence that microsaccades had a perceptual effect was lacking[1]. In experiments to address this, subjects reported the visibility of peripheral and parafoveal targets that faded and intensified perceptually during fixation (Troxler fading (BOX 1))[10]. Microsaccade onsets led to visual restoration of faded targets, establishing a potentially causal relationship between microsaccades and visibility. Contrary to the proposal that microsaccades are a laboratory artefact resulting from head immobilization[6], lack of head-restraint did not alter the connection between microsaccade production and target restoration. Subsequent studies extended these conclusions to other fading paradigms[11,92] and connected microsaccades to perceptual transitions in binocular rivalry[93] and illusory motion[13,76] (FIG. 5).

Recent research indicated that microsaccades are the most important eye movement contributor to restoring faded vision during fixation, for both foveal and peripheral targets[14] (FIG. 5a). Furthermore, microsaccades and saccades generated a continuum of visual restoration as a function of their size, which is in agreement with the idea of a common underlying generator[16–21]. Multiple microsaccades within a short interval restored faded vision more effectively than single microsaccades[14], perhaps owing to temporal summation[1]. Microsaccades of all directions restored target visibility[14], which is consistent with previous analyses of microsaccade direction with regard to area V1 firing[82] and with the aperture problem (the inability of a receptive field to distinguish between motion speed and direction[82]).

Microsaccades might restore faded vision more efficiently than drift because they move receptive fields more quickly and over larger distances. New stimuli that microsaccades bring onto a receptive field will have little correlation to the stimulus to which the neuron has previously adapted. Accordingly, larger microsaccades have a stronger perceptual effect than smaller microsaccades,

Table 1 | **Neural responses to microsaccades along the visual pathway**

Brain area	Result	Stimulus	Analysis	Recording technology	Refs
Lateral geniculate nucleus	Enhancement	Optimal bar	MS-triggered average	Single-neuron	83
	No modulation	Black or white screen			
	Weak suppression followed by strong enhancement	Uniform stimulus modulated by temporal white-noise	MS modulation of responses to visual stimulation	Single-neuron	139
	Suppression	Fields of small bars modulated independently in time	Non-stationary first-order response	Single-neuron	140
V1	Enhancement	Optimal bar	MS-triggered average	Single-neuron	82
	Mix of transient and sustained enhancement	Optimal bar	MS-triggered average. Only MSs that bring stimulus into RFs of 'mixed position and saccade' neurons	Single-neuron	141
	Enhancement	Optimal bar	MS-triggered average	Single-neuron	83
	Mix of transient and sustained enhancement	Optimal bar	MS-triggered average. Only MSs that caused an increase in firing	Single-neuron	142
	Sustained enhancement	Small gabor patch or yellow spot (0.125° or 0.3°)	Imaging signal triggered by MSs. Only area activated at the end of the MS	Voltage-sensitive dye imaging	85
	Transient enhancement	Small gabor patch or yellow spot (0.125° or 0.3°)	Imaging signal triggered by MSs. Only area activated during the MS		
	Suppression followed by weak enhancement	Oriented grating (<1°)	MS-triggered average. Only MSs that kept RF inside stimulus	Single-neuron	143
	Phase-locked potential after MS	Dynamic grating (2–3° diameter)	MS-triggered average. Only MSs that were not preceded by other MSs	Local field potentials	86
	Rapid post-MS dynamics	Dynamic grating (2–3° diameter)	MS-triggered average. Only MSs that were not preceded by other MSs	Multineuron	
	Enhancement followed by suppression	Optimal bar	MS-triggered average	Single-neuron	88
	No modulation	Black or white screen	MS-triggered average	Single-neuron	82
	Enhancement (monkey A) No modulation (monkey B)	Uniform screen	MS-triggered average	Single-neuron	141
	No modulation	Black or white screen	MS-triggered average	Single-neuron	83
	Small suppression followed by sustained enhancement	Uniform screen or dark screen	MS-triggered average. Only saccades not preceded or followed by another saccade	Single-neuron	142
	Suppression followed by enhancement	Dynamic white noise (10°)	Normalized MS-triggered spike-density	Single-neuron	144
	Suppression followed by enhancement	Large stimulus activating the entire imaged area	Imaging signal triggered by MSs	Voltage-sensitive dye imaging	85
	Suppression	Black screen	MS-triggered average	Single-neuron	88
	Initial enhancement followed by suppression	22° × 16° polar grating	Deconvolution functions corrected for autocorrelation following MSs	fMRI	84
V2	Enhancement or no modulation	Oriented grating (<1°)	MS-triggered average. Only MSs that kept RF inside stimulus	Single-neuron	143
	Initial enhancement followed by suppression	22° × 16° polar grating	Deconvolution functions corrected for autocorrelation following MSs	fMRI	84
	Suppression followed by enhancement	Large stimulus activating the entire imaged area	Imaging signal triggered by MSs	Voltage-sensitive dye imaging	85
V3	Initial enhancement followed by suppression	22° × 16° polar grating	Deconvolution functions corrected for autocorrelation following MSs	fMRI	84
V4	Phase-locked components after the MS	Dynamic grating (2–3° diameter)	MS-triggered average. Only MSs that were not preceded by other MSs	Local field potentials	86
	Rapid post-MS dynamics	Dynamic grating (2–3° diameter)	MS-triggered average. Only MSs that were not preceded by other MSs	Multineuron	
	Enhancement	Oriented grating (<1°)	MS-triggered average. Only MSs that kept RF inside stimulus	Single-neuron	143

Table 1 (cont.) | **Neural responses to microsaccades along the visual pathway**

Brain area	Result	Stimulus	Analysis	Recording technology	Refs
Middle temporal area	Enhancement of weak activity	Drifting gratings of optimal size and location	MS-triggered average. Only MSs with preferred direction during low firing rate condition	Single-neuron	145
	Suppression of stimulus-evoked activity	Drifting gratings of optimal size and location	MS-triggered average. Only MSs with unpreferred direction during high firing rate condition		
	Suppression	Coherent motion in preferred direction	MS-triggered average	Single-neuron	112
	Small suppression	0% coherent motion before a test stimulus			
	No modulation	0% coherent motion before a test stimulus			
	No modulation	22° × 16° polar grating	Deconvolution functions corrected for autocorrelation following MSs	fMRI	84
Lateral intraparietal area	Suppression	Coherent motion in preferred direction	MS-triggered average	Single-neuron	112
Ventral intraparietal area	No modulation	0% coherent motion before a test stimulus	MS-triggered average	Single-neuron	112
Superior colliculus	Suppression	Flashed white bar	MS modulation of responses to visual stimulation	Single-neuron	113
Inferior temporal cortex	Weak enhancement or no response	Photographs of animate objects and two-dimensional geometrical patterns	MS-triggered average. Only MSs that kept RF inside stimulus	Single-neuron	143
Right occipital cortex	Large potential after MSs	Checkerboard 1 cycle per degree	Grand average ERP, time-locked to MS onsets	EEG	87

EEG, electroencephalography; ERP, event-related potential; fMRI, functional MRI; MS, microsaccade; RF, receptive field.

which may be due to their increased ability to bring receptive fields to uncorrelated stimulus regions[14]. Conversely, drift moves receptive fields slowly, often over smaller distances. Because nearby visual regions are highly correlated with each other[94], the stimuli that drift brings onto a given receptive field might be well correlated to stimuli the neuron has already adapted to, thereby failing to generate a vigorous response.

Microsaccades help to perform high-acuity tasks. Contrary to the classic conclusion that microsaccades are not helpful in high-acuity tasks[95,96], a recent study found that microsaccades precisely relocate the eye during the simulated threading of a needle[30]. Computational modelling of retinal responses to microsaccades further suggests that microsaccades may improve spatial resolution[91].

Microsaccades during free viewing. Do microsaccades occur during free viewing? The answer to this question depends critically on how one defines microsaccades (see 'What is a microsaccade?'). During free viewing of natural scenes and visual searches, the average microsaccade rate was 0.6 Hz[18] (FIG. 2a). Microsaccade rates near identified targets in the search task went up to 1.3 Hz (comparable with those during attempted fixation). In this study, saccades up to 1 degree were considered microsaccades, which is consistent with the distribution of microsaccade magnitudes during attempted fixation (see FIG. 1a for similar examples of microsaccade magnitude distributions). Another study found equivalent rates of microsaccades (also defined as less than 1 degree) in a naturalistic driving task[36]. Studies that have concluded that microsaccades are rarer during free viewing have applied more restrictive maximum microsaccade magnitudes (for example, 30 arc min in REF. 97) than those typically observed during fixation.

Microsaccades as an optimal sampling strategy. Saccades and microsaccades might reflect an optimal sampling strategy by which the visual system discretely acquires information[25,98]. A patient who could not move her eyes was found to produce head saccades with similar characteristics to eye saccades. The patient could perform complicated visuomotor tasks, such as making a cup of tea, without difficulty. The findings suggested that saccadic sampling might be a superior strategy to smooth visual scanning[99,100].

Microsaccades evoke transient responses in visual neurons[82,83] (FIG. 4), with or without sustained firing during intersaccadic periods. Transient burst firing has been related to visibility in several experimental paradigms[82,101–103]. Furthermore, transient oculomotor events (including microsaccades, saccades and blinks) rather than continuous drift triggered illusory motion

Box 1 | **Fading everywhere**

In 1804, Swiss philosopher Troxler documented that fixated images tend to fade away during normal vision[126]. The phenomenon, which is known as Troxler fading, came to be equated to peripheral fading. Ironically, Troxler had reported that even centrally fixated targets can disappear after prolonged observation (corroborating an earlier account by E. Darwin[125]). Brewster (in 1818)[133] later disregarded Troxler and Darwin's claims, however, and maintained that fixated objects never disappear, whereas peripheral objects do (see REF. 134 for a historical account). The later view has permeated contemporary beliefs about the limitations of Troxler fading, with a recent review asserting that foveal images do not fade "with or without microsaccades"[135].

However, foveal fading has been observed by numerous researchers in various experimental set-ups[14,125,126,136–138], and recent work suggests that microsaccades can restore any targets that have faded perceptually, including foveal targets[14] (FIG. 5a). The blurred picture on the right demonstrates full-field Troxler fading[138]. To experience it, fixate precisely on the centre of the image, while attending to the whole scene. Careful fixation over the course of several seconds will minimize your eye movements, causing the entire image to fade to grey. Stop fixating to revive the scene. Non-blurred images will similarly fade in the laboratory when eye movements are completely suppressed (for instance, with retinal stabilization techniques[2–4]). The figure is modified from REF. 138.

in a static pattern[13], perhaps because neural responses to transient stimuli are stronger than those to drifting stimuli[104,105]. Discrete temporal sampling might be an optimal strategy for information processing across sensory systems. Rodent sniffs sample olfactory information every 200–300 ms[106]; thus, they exhibit similar time dynamics to primate saccades and microsaccades[18]. Discrete sensory sampling might speed up information processing and therefore could be evolutionarily advantageous[106].

Microsaccadic suppression. Perceptual suppression during saccades, called 'saccadic suppression', is thought to be essential for maintaining visual stability as we explore the world with our eyes. Behavioural studies have found a comparable increase in visual thresholds for microsaccades, which is known as 'microsaccadic suppression'[107–109] (but see REFS 110,111). This might contribute to perceptual stability during fixation. Recent neurophysiological research has identified putative neural correlates of microsaccadic suppression (FIG. 4). Microsaccades near the onset of a test stimulus decreased detection and suppressed activity in middle temporal, lateral intraparietal and ventral intraparietal areas[112]. Stimulus onsets that were temporally close to microsaccades elicited visual bursts in the SC less effectively than stimuli that were presented in the absence of microsaccades[113]. This suppressive influence of microsaccades is complementary to their positive perceptual effect (for instance, their ability to restore faded vision) through retinal motion[25,113]. Future research should determine the potential temporal interactions of microsaccade-triggered increases and decreases in visibility[25].

Accidental versus fundamental roles of microsaccades. Microsaccade research has been hampered by attempts to determine the 'purpose' of microsaccades[6], as well as their 'accidental' (that is, incidental or epiphenomenal) versus 'fundamental' roles in vision[114,115]. One argument has been that for A (microsaccades) to have a fundamental effect on B (visibility), A must not only cause B, but the absence of B (that is, fading) must also cause A. Thus, upon finding that microsaccade production did not increase after fading, a recent study concluded that restoring faded vision is not a fundamental role of microsaccades[115]. This logic is problematic when applied to any number of physiological functions, but perhaps more importantly, to call some functional properties fundamental and others accidental (or to debate their purpose) goes counter to the evidence of random (that is, accidental) mutations in the evolution of nervous systems through natural selection[14]. The lack of a mechanism to trigger microsaccades in response to fading does not disprove that microsaccades restore faded vision during fixation. Therefore, the available evidence indicates that counteracting fading is a function of microsaccades[14].

Pathological microsaccades

The oculomotor system must calibrate how much the eyes move during fixation. Too little movement can lead to fading, and too much motion can lead to blurred and unstable vision. Impaired fixational eye movements can disturb this fine balance[116]. Determining how normal fixation differs from pathological fixation might aid the differential and early diagnosis of neurological disease as well as the quantification of its progression and response to treatment.

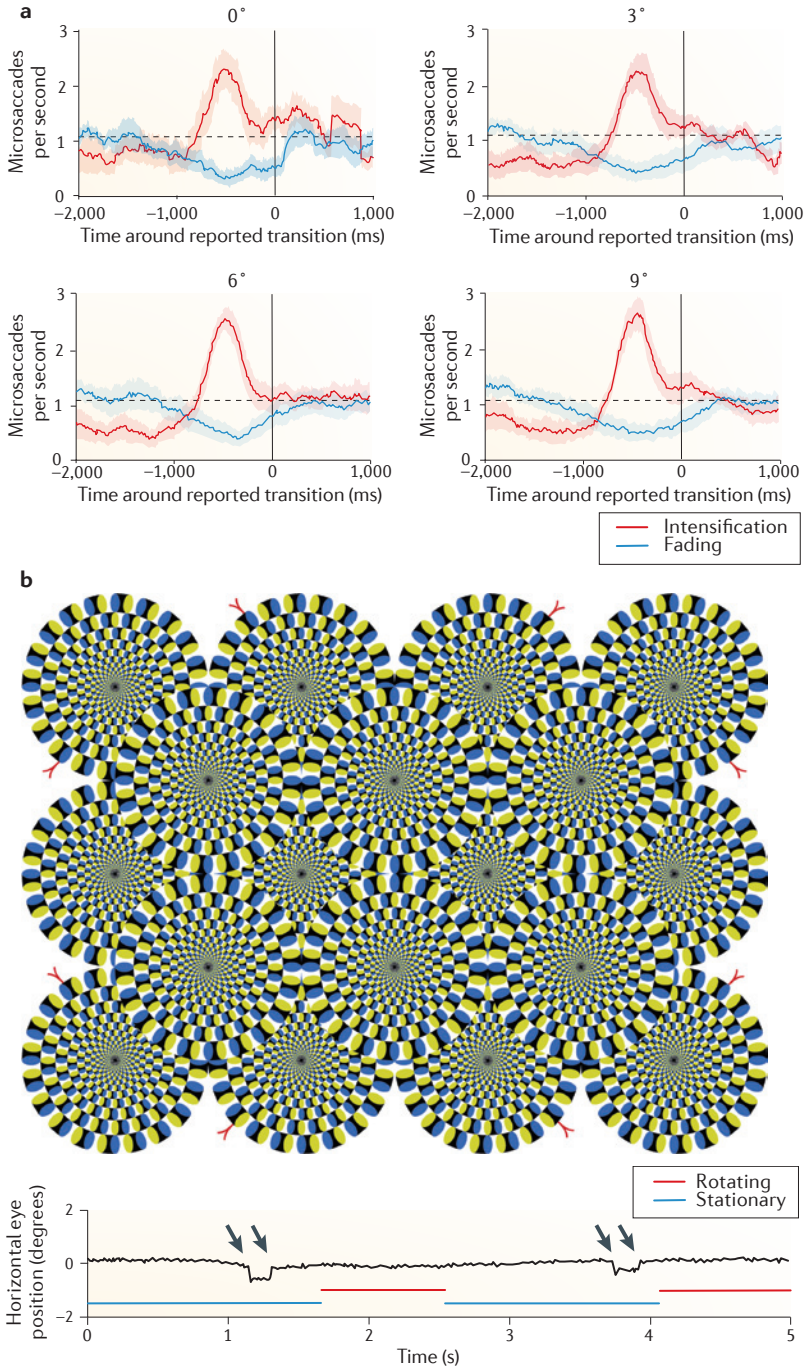

Figure 5 | **Perceptual effects of microsaccades.** **a** | Microsaccades counteract foveal and peripheral visual fading. Microsaccade rates increase before perceptual transitions towards target intensification (red) and decrease before transitions to target fading (blue) at foveal and peripheral eccentricities. Target eccentricity is indicated at the top of each panel. The horizontal lines show the average microsaccadic rate throughout the recording session. The shadows show standard error of the mean between subjects ($N = 7$). **b** | Microsaccades trigger illusory rotation. The top panel shows the 'rotating snakes' illusion. Fix your eyes on the centre of one of the 'snakes' and the motion will decelerate or even stop. Relax your fixation and the snakes will spin again. The bottom panel shows an example of one subject's eye position in relation to perceptual reports (red lines indicate rotating snakes and blue lines indicate stationary snakes). Arrows identify microsaccades. Part **a** is modified, with permission, from REF. 14 © (2012) Society for Neuroscience. The top panel of part **b** is modified, with permission, from REF. 146 © (2005) Kanzen. The bottom panel of part **b** is modified, with permission, from REF. 13 © (2012) Society for Neuroscience.

Recently, the concept of a microsaccade–saccade continuum[16–21,41] has extended to saccadic intrusions[22]. It has been proposed that the apparently dissimilar features of microsaccades and SWJs (the most common type of saccadic intrusion) result from two complementary mechanisms: one to produce microsaccades and another to correct fixation errors (resulting in square-wave coupling) when a given microsaccade is too large (see 'Microsaccades and fixation correction')[17]. The correlation between microsaccadic size and SWJ-coupling applied both to healthy subjects and to patients with progressive supranuclear palsy (PSP), which is an atypical Parkinsonism in which SWJs are a prominent clinical feature[17]. Determining how microsaccade dynamics are altered in PSP[17] and in other neurological disorders[24,117] provides information about the pathogenesis of these diseases[23], and it additionally serves to guide and constrain the models of the oculomotor mechanisms underlying microsaccade generation.

A few other studies have started to make headway concerning the characteristics of microsaccades in ophthalmic and neurological pathologies. For example, the clinical evaluation of microsaccades in amblyopia might help to determine the optimal duration of a treatment[118]. Amblyopes show decreased microsaccade production in the amblyopic (non-dominant) eye during monocular fixation[119], which is frequently associated with rapid fading of large portions of the visual field[120,121]. Perceptual fading in amblyopia might be related to Troxler fading in normal vision[10] (FIG. 5a), and it supports the possibility that microsaccades might supply more optimal sampling than drift (see 'Microsaccades as an optimal sampling strategy'). It has been proposed[118] that amblyopic therapies should not stop upon centralization of fixation and normalization of visual acuity but should extend until the normalization or stabilization of fixational eye movements. More recently, a scarcity of microsaccades in amblyopic eyes during monocular fixation concurrent with increased microsaccade magnitudes has been reported[122], and the authors have suggested that microsaccadic parameters could be used in the objective evaluation of eye movement function in amblyopia.

Children with cerebral palsy can also show microsaccadic impairment, which could compound their learning difficulties in regard to reading skills[123]. A negative correlation between microsaccade magnitude and visual acuity has been reported in patients with diabetic macular oedema[124].

The future of microsaccade research

Once, microsaccade research was one of the most controversial fields in visual and oculomotor neuroscience[1]. Today, converging evidence has resolved many previously contentious issues, but several points of discord remain. In this Review, we have aimed to clarify some of them, such as the ongoing lack of agreement about what constitutes an appropriate definition, or even an acceptable size, of a microsaccade (FIG. 1), or the differences and — more importantly — the commonalities in the physiological responses to microsaccades in areas of the visual pathway (FIG. 4). Seeking consensus on these matters will facilitate

Amblyopia
Visual acuity loss that is not attributable to uncorrected refractive error or known pathology. It is generally linked to strabismus and/or with the two eyes having unequal refractive power (that is, anisometropia).

further progress in research on both the causes of microsaccade production and the effects of microsaccades on vision, cognition and oculomotor control.

A productive discussion of the perceptual effects of microsaccades must separately address the impact of microsaccades on counteracting (that is, reversing) fading and on preventing fading. First, it is important to emphasize that stimuli do sometimes fade in everyday vision[125–127] despite the concerted actions of the three types of fixational eye movements. The evidence suggests that once a stimulus has faded, microsaccades bring it back with higher success than the other fixational eye movements[14]. It seems possible that microsaccades might restore vision at any level of stimulus contrast, size, spatial frequency and eccentricity for which perceptual fading occurs. In other words, microsaccades might restore the visibility of any stimulus that has faded during fixation. Future research should investigate this hypothesis.

Further questions concerning the impact of microsaccades on visibility remain. Why do not all stationary stimuli fade in everyday vision? That is, what stimulus parameters, or a combination thereof, defy perceptual fading? And what fixational eye movements, or a combination thereof, are responsible for preventing such fading?

A related question is why does the world remain visible for several hundred milliseconds between microsaccades? One possible answer is that intersaccadic drift is sufficient to maintain overall visibility, even in the absence of microsaccades. However, this hypothesis goes counter to the finding that drift does not contribute considerably to reviving faded targets[14]. Another possibility is that drift sustains the visibility of targets brought to life by microsaccades, even if the retinal motion produced by drift is not sufficient, by itself, to counteract fading once a target has vanished (this idea has never been tested). Finally, temporal filling-in processes could bridge perceptual gaps between saccades or microsaccades, so that perception appears continuous rather than intermittent. Observers can determine the gist of a briefly flashed scene in 150 ms[128], a time interval that cannot be reduced even with training. Thus, there might be a limit to the neural stages and speed involved in visual information processing[129]. Saccades and/or microsaccades, which occur every 200–300 s[18], may provide multiple single high-acuity snapshots of a scene[106]. Owing to the limitations in processing speed mentioned above, more frequent production of saccades and microsaccades might not improve vision significantly.

The picture of the brainstem circuitry underlying microsaccade generation is close to complete (FIG. 3b), but it is not known whether higher cortical areas show equivalent activity for saccades and microsaccades. No study has yet investigated the activity of the 'fixation' zones in the frontal eye fields or the basal ganglia during microsaccades[16], or correlated it with rostral SC activity. Such research could help to elucidate the interactions between the allocation of attention and microsaccade production.

Computational and mathematical modelling has become an integral part of research on microsaccades[21,57,81,91,130–132], serving as an indicator of the maturity of the field. Future studies are expected to include and rely more heavily on quantified models of microsaccade generation and microsaccadic function.

Importantly, there has been little research on the characteristics of microsaccades in neurological and ophthalmic disease, and how these might affect visual stability and perception. A recent study has found normal microsaccades to be rare in PSP[17], but the potentially distinctive features of microsaccades — including their relationship to saccadic intrusions — in most neurological disorders remain unexplored. This is likely to become an area of active inquiry, with valuable implications for both clinical and basic research.

1. Martinez-Conde, S., Macknik, S. L. & Hubel, D. H. The role of fixational eye movements in visual perception. *Nature Rev. Neurosci.* **5**, 229–240 (2004).
2. Yarbus, A. L. The perception of an image fixed with respect to the retina. *Biophysics* **2**, 683–690 (1957).
3. Ditchburn, R. W. & Ginsborg, B. L. Vision with a stabilized retinal image. *Nature* **170**, 36–37 (1952).
4. Riggs, L. A. & Ratliff, F. The effects of counteracting the normal movements of the eye. *J. Opt. Soc. Am.* **42**, 872–873 (1952).
5. Ditchburn, R. W. The function of small saccades. *Vision Res.* **20**, 271–272 (1980).
6. Kowler, E. & Steinman, R. M. Small saccades serve no useful purpose: reply to a letter by R. W. Ditchburn. *Vision Res.* **20**, 273–276 (1980).
7. Martinez-Conde, S. & Macknik, S. L. Windows on the mind. *Sci. Am.* **297**, 56–63 (2007).
8. Martinez-Conde, S. & Macknik, S. L. Shifting focus. *Sci. Am. Mind* **22**, 48–55 (2011).
9. Engbert, R. & Kliegl, R. Microsaccades uncover the orientation of covert attention. *Vision Res.* **43**, 1035–1045 (2003).
This study, together with reference 15, comprised the first systematic attempts to characterize the influence of attention on microsaccadic metrics. It also provided a widely used automatic and objective algorithm for microsaccade detection.
10. Martinez-Conde, S., Macknik, S. L., Troncoso, X. & Dyar, T. A. Microsaccades counteract visual fading during fixation. *Neuron* **49**, 297–305 (2006).
This study provided the first direct link between microsaccade production and enhanced visibility during fixation and demonstrated that microsaccades have perceptual value.
11. Troncoso, X., Macknik, S. L. & Martinez-Conde, S. Microsaccades counteract perceptual filling-in. *J. Vis.* **8**, 15 (2008).
12. Laubrock, J., Engbert, K. & Kliegl, R. Fixational eye movements predict the perceived direction of ambiguous apparent motion. *J. Vis.* **8**, 13 (2008).
13. Otero-Millan, J., Macknik, S. L. & Martinez-Conde, S. Microsaccades and blinks trigger illusory rotation in the "rotating snakes" illusion. *J. Neurosci.* **32**, 6043–6051 (2012).
This research indicated that transient oculomotor events such as microsaccades, saccades and blinks, rather than continuous drift, act to trigger the illusory motion in certain repetitive arrangements of luminance gradients (which is known as the 'rotating snakes' illusion).
14. McCamy, M. B. *et al.* Microsaccadic efficacy and contribution to foveal and peripheral vision. *J. Neurosci.* **32**, 9194–9204 (2012).
This study found that microsaccades are the most important eye movement contributor to restoring faded vision during fixation. It also demonstrated that microsaccades counteract both foveal and peripheral visual fading.
15. Hafed, Z. M. & Clark, J. J. Microsaccades as an overt measure of covert attention shifts. *Vision Res.* **42**, 2533–2545 (2002).
This study, together with reference 9, comprised the first systematic attempts to characterize the influence of attention on microsaccadic metrics.
16. Otero-Millan, J., Macknik, S. L., Serra, A., Leigh, R. J. & Martinez-Conde, S. Triggering mechanisms in microsaccade and saccade generation: a novel proposal. *Ann. NY Acad. Sci.* **1233**, 107–116 (2011).
17. Otero-Millan, J. *et al.* Distinctive features of saccadic intrusions and microsaccades in progressive supranuclear palsy. *J. Neurosci.* **31**, 4379–4387 (2011).
This study found normal microsaccades to be rare in PSP. It also proposed that microsaccades and SWJs are generated by the same circuit and that SWJs result from a coupling mechanism that generates a second corrective saccade shortly after a large fixation saccade, both in patients with PSP and in healthy individuals.
18. Otero-Millan, J., Troncoso, X., Macknik, S. L., Serrano-Pedraza, I. & Martinez-Conde, S. Saccades and microsaccades during visual fixation, exploration and search: foundations for a common saccadic generator. *J. Vis.* **8**, 21 (2008).
This study showed that microsaccades occur not only during prolonged fixation but also during exploration and search. A microsaccade–saccade continuum of spatiotemporal characteristics moreover supported the hypothesis of a common oculomotor generator for microsaccades and saccades.
19. Rolfs, M., Laubrock, J. & Kliegl, R. Shortening and prolongation of saccade latencies following microsaccades. *Exp. Brain Res.* **169**, 369–376 (2006).

20. Rolfs, M., Laubrock, J. & Kliegl, R. Microsaccade-induced prolongation of saccadic latencies depends on microsaccade amplitude. *J. Eye Movement Res.* **1**, 3 (2008).
21. Hafed, Z. M., Goffart, L. & Krauzlis, R. A neural mechanism for microsaccade generation in the primate superior colliculus. *Science* **323**, 940–943 (2009).
This research established a causal role of the SC in microsaccade production.
22. Gowen, E., Abadi, R. V., Poliakoff, E., Hansen, P. C. & Miall, R. C. Modulation of saccadic intrusions by exogenous and endogenous attention. *Brain Res.* **1141**, 154–167 (2007).
This article proposed that microsaccades and saccadic intrusions may lie on a continuum.
23. Chen, A. L. *et al.* The disturbance of gaze in progressive supranuclear palsy: implications for pathogenesis. *Front. Neurol.* **1**, 147 (2010).
24. Martinez-Conde, S. Fixational eye movements in normal and pathological vision. *Prog. Brain Res.* **154**, 151–176 (2006).
25. Martinez-Conde, S., Macknik, S. L., Troncoso, X. G. & Hubel, D. H. Microsaccades: a neurophysiological analysis. *Trends Neurosci.* **32**, 463–475 (2009).
26. Collewijn, H. & Kowler, E. The significance of microsaccades for vision and oculomotor control. *J. Vis.* **8**, 20 (2008).
27. Rolfs, M. Microsaccades: small steps on a long way. *Vision Res.* **49**, 2415–2441 (2009).
28. Mergenthaler, K. & Engbert, R. Microsaccades are different from saccades in scene perception. *Exp. Brain Res.* **203**, 753–757 (2010).
29. McCamy, M. B., Macknik, S. L. & Martinez-Conde, S. in *The New Visual Neurosciences* (eds Werner, J. S. & Chalupa, L. M.) (MIT Press, in the press).
30. Ko, H. K., Poletti, M. & Rucci, M. Microsaccades precisely relocate gaze in a high visual acuity task. *Nature Neurosci.* **13**, 1549–1553 (2010).
31. Boyce, P. R. Monocular fixation in human eye movement. *Proc. R. Soc. Lond. B* **167**, 293–315 (1967).
32. Young, L. R. & Sheena, D. Eye-movement measurement techniques. *Am. Psychol.* **30**, 315–330 (1975).
33. Schulz, E. Binocular micromovements in normal persons. *Graefes Arch. Clin. Exp. Ophthalmol.* **222**, 95–100 (1984).
34. Simon, F., Schulz, E., Rassow, B. & Haase, W. Binocular micromovement recording of human eyes: — methods. *Graefes Arch. Clin. Exp. Ophthalmol.* **221**, 293–298 (1984).
35. McCamy, M. B. *et al.* Simultaneous recordings of ocular microtremor and microsaccades with a piezoelectric sensor and a video-oculography system. *PressJ* (in the press).
36. Benedetto, S., Pedrotti, M. & Bridgeman, B. Microsaccades and exploratory saccdes in a naturalistic environment. *J. Eye Movement Res.* **4**, 1–10 (2011).
37. Ditchburn, R. W. & Ginsborg, B. L. Involuntary eye movements during fixation. *J. Physiol.* **119**, 1–17 (1953).
38. Krauskopf, J., Cornsweet, T. N. & Riggs, L. A. Analysis of eye movements during monocular and binocular fixation. *J. Opt. Soc. Am.* **50**, 572–578 (1960).
39. Lord, M. P. Measurement of binocular eye movements of subjects in the sitting position. *Br. J. Ophthal.* **35**, 21–30 (1951).
40. Van Horn, M. R. & Cullen, K. E. Coding of microsaccades in three-dimensional space by premotor saccadic neurons. *J. Neurosci.* **32**, 1974–1980 (2012).
This study found that premotor saccadic neurons control microsaccades in three-dimensional space, during both near and far viewing, by preferentially encoding the dynamic movement of an individual eye. The results indicated that microsaccades are not strictly conjugate.
41. Zuber, B. L., Stark, L. & Cook, G. Microsaccades and the velocity-amplitude relationship for saccadic eye movements. *Science* **150**, 1459–1460 (1965).
42. Reingold, E. M. & Stampe, D. in *Reading as a Perceptual Process* (eds Kennedy, A., Heller, D., Pynte, J. & Radach, R.) 119–145 (Elsevier, 2000).
43. Rolfs, M., Kliegl, R. & Engbert, K. Toward a model of microsaccade generation: the case of microsaccadic inhibition. *J. Vis.* **8**, 5 (2008).
This study provided behavioural evidence supporting the hypothesis that the SC may trigger both saccades and microsaccades.
44. Walker, R., Deubel, H., Schneider, W. X. & Findlay, J. M. Effect of remote distractors on saccade programming: evidence for an extended fixation zone. *J. Neurophysiol.* **78**, 1108–1119 (1997).
45. Yarbus, A. L. *Eye Movements and Vision* (Plenum Press, 1967).
46. Ratliff, F. & Riggs, L. A. Involuntary motions of the eye during monocular fixation. *J. Exp. Psychol.* **40**, 687–701 (1950).
47. Steinman, R. M., Cunitz, R. J., Timberlake, G. T. & Herman, M. Voluntary control of microsaccades during maintained monocular fixation. *Science* **155**, 1577–1579 (1967).
48. Steinman, R. M., Haddad, G. M., Skavenski, A. A. & Wyman, D. Miniature eye movement. *Science* **181**, 810–819 (1973).
49. Van Gisbergen, J. A., Robinson, D. A. & Gielen, S. A quantitative analysis of generation of saccadic eye movements by burst neurons. *J. Neurophysiol.* **45**, 417–442 (1981).
This study, together with reference 50, was the first examination of the neural bases of microsaccade generation.
50. Van Gisbergen, J. A. M. & Robinson, D. A. in *Control of Gaze by Brain Stem Neurons* (eds Baker, R. & Berthoz, A.) 301–308 (Elsevier/North-Holland, 1977).
51. Munoz, D. P. & Wurtz, R. H. Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. *J. Neurophysiol.* **70**, 559–575 (1993).
52. Brien, D. C., Corneil, J. H. & Fecteau, J. H. The behavioural and neurophysiological modulation of microsaccades in monkeys. *J. Eye Movement Res.* **3**, 1–12 (2009).
53. Goffart, L., Chen, L. L. & Sparks, D. L. Deficits in saccades and fixation during muscimol inactivation of the caudal fastigial nucleus in the rhesus monkey. *J. Neurophysiol.* **92**, 3351–3367 (2004).
54. Robinson, F. R., Straube, A. & Fuchs, A. F. Role of the caudal fastigial nucleus in saccade generation. II. Effects of muscimol inactivation. *J. Neurophysiol.* **70**, 1741–1758 (1993).
55. Guerrasio, L., Quinet, J., Buttner, U. & Goffart, L. Fastigial oculomotor region and the control of foveation during fixation. *J. Neurophysiol.* **103**, 1988–2001 (2010).
56. Cornsweet, T. N. Determination of the stimuli for involuntary drifts and saccadic eye movements. *J. Opt. Soc. Am.* **46**, 987–993 (1956).
57. Engbert, R. & Kliegl, R. Microsaccades keep the eyes' balance during fixation. *Psychol. Sci.* **15**, 431–436 (2004).
58. Costela, F. *et al.* Microsaccades correct fixation errors due to blinks. *Soc. Neurosci. Abstr.* 372.11 (New Orleans, 13–17 Oct 2012).
59. Corbetta, M. *et al.* A common network of functional areas for attention and eye movements. *Neuron* **21**, 761–773 (1998).
60. Goldberg, M. E. & Wurtz, R. H. Activity of superior colliculus in behaving monkey. II. Effect of attention on neuronal responses. *J. Neurophysiol.* **35**, 560–574 (1972).
61. Turatto, M., Valsecchi, M., Tame, L. & Betta, E. Microsaccades distinguish between global and local visual processing. *Neuroreport* **18**, 1015–1018 (2007).
62. Galfano, G., Betta, E. & Turatto, M. Inhibition of return in microsaccades. *Exp. Brain Res.* **159**, 400–404 (2004).
This research found that microsaccade direction can be biased away from a salient stimulus if the stimulus is irrelevant to the task.
63. Rolfs, M., Engbert, R. & Kliegl, R. Microsaccade orientation supports attentional enhancement opposite a peripheral cue: commentary on Tse, Sheinberg, and Logothetis. *Psychol. Sci.* **15**, 431–436 (2004) (2003).
64. Laubrock, J., Engbert, R. & Kliegl, R. Microsaccade dynamics during covert attention. *Vision Res.* **45**, 721–730 (2005).
65. Rolfs, M., Engbert, R. & Kliegl, R. Crossmodal coupling of oculomotor control and spatial attention in vision and audition. *Exp. Brain Res.* **166**, 427–439 (2005).
66. Gowen, E., Abadi, R. V. & Poliakoff, E. Paying attention to saccadic intrusions. *Brain Res. Cogn. Brain Res.* **25**, 810–825 (2005).
67. Horowitz, T. S., Fine, E. M., Fencsik, D. E., Yurgenson, S. & Wolfe, J. M. Fixational eye movements are not an index of covert attention. *Psychol. Sci.* **18**, 356–363 (2007).
68. Betta, E., Galfano, G. & Turatto, M. Microsaccadic response during inhibition of return in a target–target paradigm. *Vision Res.* **47**, 428–436 (2007).
69. Laubrock, J., Kliegl, R., Rolfs, M. & Engbert, R. When do microsaccades follow spatial attention? *Atten. Percept. Psychophys.* **72**, 683–694 (2010).
70. Valsecchi, M., Betta, E. & Turatto, M. Visual oddballs induce prolonged microsaccadic inhibition. *Exp. Brain Res.* **177**, 196–208 (2007).
71. Pastukhov, A. & Braun, J. Rare but precious: microsaccades are highly informative about attentional allocation. *Vision Res.* **50**, 1173–1184 (2010).
This study found that microsaccade direction is most informative about the location of spatial attention when microsaccade production is lowest.
72. Kliegl, R., Rolfs, M., Laubrock, J. & Engbert, R. Microsaccadic modulation of response times in spatial attention tasks. *Psychol. Res.* **73**, 136–146 (2009).
73. Tse, P. U., Sheinberg, D. S. & Logothetis, N. K. The distribution of microsaccade directions need not reveal the location of attention. *Psychol. Sci.* **15**, 708–710 (2004).
74. Horowitz, T. S., Fine, E. M., Fencsik, D. E., Yurgenson, S. & Wolfe, J. M. Microsaccades and attention: does a weak correlation make an index? Reply to Laubrock, Engbert, Rolfs, and Kliegl. *Psychol. Sci.* **18**, 367–368 (2007) (2007).
75. Laubrock, J., Engbert, R., Rolfs, M. & Kliegl, R. Microsaccades are an index of covert attention: commentary on Horowitz, Fine, Fencsik, Yurgenson, and Wolfe (2007). *Psychol. Sci.* **18**, 364–366; discussion 367–368 (2007).
76. Troncoso, X., Macknik, S. L., Otero-Millan, J. & Martinez-Conde, S. Microsaccades drive illusory motion in the Enigma illusion. *Proc. Natl Acad. Sci. USA.* **105**, 16033–16038 (2008).
77. Cui, J., Wilke, M., Logothetis, N. K., Leopold, D. A. & Liang, H. Visibility states modulate microsaccade rate and direction. *Vision Res.* **49**, 228–236 (2009).
78. Valsecchi, M. & Turatto, M. Microsaccadic responses in a bimodal oddball task. *Psychol. Res.* **73**, 23–33 (2009).
79. Valsecchi, M. & Turatto, M. Microsaccadic response to visual events that are invisible to the superior colliculus. *Behav. Neurosci.* **121**, 786–793 (2007).
80. Sinn, P. & Engbert, R. Saccadic facilitation by modulation of microsaccades in natural backgrounds. *Atten. Percept. Psychophys.* **73**, 1029–1033 (2011).
81. Engbert, R. Computational modeling of collicular integration of perceptual responses and attention in microsaccades. *J. Neurosci.* **32**, 8035–8039 (2012).
Computational modelling found that the integration of perceptual responses and attention at the level of the SC can explain modulation of microsaccade rates and directions in various visual tasks.
82. Martinez-Conde, S., Macknik, S. L. & Hubel, D. H. Microsaccadic eye movements and firing of single cells in the striate cortex of macaque monkeys. *Nature Neurosci.* **3**, 251–258 (2000).
83. Martinez-Conde, S., Macknik, S. L. & Hubel, D. H. The function of bursts of spikes during visual fixation in the awake primate lateral geniculate nucleus and primary visual cortex. *Proc. Natl Acad. Sci. USA* **99**, 13920–13925 (2002).
The parameters of microsaccade-triggered bursts of spikes in the lateral geniculate nucleus and area V1 varied depending on whether the stationary stimuli presented were optimal or non-optimal.
84. Tse, P. U., Baumgartner, F. J. & Greenlee, M. W. Event-related functional MRI of cortical activity evoked by microsaccades, small visually-guided saccades, and eyeblinks in human visual cortex. *Neuroimage* **49**, 805–816 (2010).
85. Meirovithz, E., Ayzenshtat, I., Werner-Reiss, U., Shamir, I. & Slovin, H. Spatiotemporal effects of microsaccades on population activity in the visual cortex of monkeys during fixation. *Cereb. Cortex* **22**, 294–307 (2011).
86. Bosman, C. A., Womelsdorf, T., Desimone, R. & Fries, P. A microsaccadic rhythm modulates gamma-band synchronization and behavior. *J. Neurosci.* **29**, 9471–9480 (2009).
87. Dimigen, O., Valsecchi, M., Sommer, W. & Kliegl, R. Human microsaccade-related visual brain responses. *J. Neurosci.* **29**, 12321–12331 (2009).
Electroencephalography recordings found that microsaccades are a source of sizable activity in the human visual cortex.
88. Martinez-Conde, S., Troncoso, X. G., Najafian Jazi, A., Otero-Millan, J. & Macknik, S. L. The contribution of retinal and non-retinal sources to area V1's responses to microsaccades: implications for visual stability and microsaccadic suppression. *Soc. Neurosci. Abstr.* 370.04 (New Orleans, 13–17 Oct 2012).
89. Albrecht, D. G. & Hamilton, D. B. Striate cortex of monkey and cat: contrast response function. *J. Neurophysiol.* **48**, 217–237 (1982).

90. Gawne, T. J., Kjaer, T. W. & Richmond, B. J. Latency: another potential code for feature binding in striate cortex. *J. Neurophysiol.* **76**, 1356–1360 (1996).
91. Donner, K. & Hemila, S. Modelling the effect of microsaccades on retinal responses to stationary contrast patterns. *Vision Res.* **47**, 1166–1177 (2007). **Modelling the effect of microsaccades on primate retinal responses indicated that microsaccades may enhance sensitivity to edges and improve spatial resolution.**
92. Hsieh, P. J. & Tse, P. U. Microsaccade rate varies with subjective visibility during motion-induced blindness. *PLoS ONE* **4**, e5163 (2009).
93. van Dam, L. C. & van Ee, R. Retinal image shifts, but not eye movements per se, cause alternations in awareness during binocular rivalry. *J. Vis.* **6**, 1172–1179 (2006).
94. Simoncelli, E. P. & Olshausen, B. A. Natural image statistics and neural representation. *Annu. Rev. Neurosci.* **24**, 1193–1216 (2001).
95. Bridgeman, B. & Palca, J. The role of microsaccades in high acuity observational tasks. *Vision Res.* **20**, 813–817 (1980).
96. Winterson, B. J. & Collewijn, H. Microsaccades during finely guided visuomotor tasks. *Vision Res.* **16**, 1387–1390 (1976).
97. Kuang, X., Poletti, M., Victor, J. D. & Rucci, M. Temporal encoding of spatial information during active visual fixation. *Curr. Biol.* **22**, 510–514 (2012).
98. Martinez-Conde, S. & Macknik, S. L. Fixational eye movements across vertebrates: comparative dynamics, physiology, and perception. *J. Vis.* **8**, 28 (2008).
99. Gilchrist, I. D., Brown, V. & Findlay, J. M. Saccades without eye movements. *Nature* **390**, 130–131 (1997).
100. Gilchrist, I. D., Brown, V., Findlay, J. M. & Clarke, M. P. Using the eye-movement system to control the head. *Proc. R. Soc. Lond. B* **265**, 1831–1836 (1998).
101. Gawne, T. J. & Martin, J. M. Activity of primate V1 cortical neurons during blinks. *J. Neurophysiol.* **84**, 2691–2694 (2000).
102. Macknik, S. L. & Martinez-Conde, S. The spatial and temporal effects of lateral inhibitory networks and their relevance to the visibility of spatiotemporal edges. *Neurocomputing* **58–60**, 775–782 (2004).
103. Macknik, S. L. & Livingstone, M. S. Neuronal correlates of visibility and invisibility in the primate visual system. *Nature Neurosci.* **1**, 144–149 (1998).
104. Shelley, M., McLaughlin, D., Shapley, R. & Wielaard, J. States of high conductance in a large-scale model of the visual cortex. *J. Comput. Neurosci.* **13**, 93–109 (2002).
105. Williams, P. E. & Shapley, R. M. A dynamic nonlinearity and spatial phase specificity in macaque V1 neurons. *J. Neurosci.* **27**, 5706–5718 (2007).
106. Uchida, N., Kepecs, A. & Mainen, Z. F. Seeing at a glance, smelling in a whiff: rapid forms of perceptual decision making. *Nature Rev. Neurosci.* **7**, 485–491 (2006).
107. Beeler, G. W. Visual threshold changes resulting from spontaneous saccadic eye movements. *Vision Res.* **7**, 769–775 (1967).
108. Zuber, B. L. & Stark, L. Saccadic suppression: elevation of visual threshold associated with saccadic eye movements. *Exp. Neurol.* **16**, 65–79 (1966).
109. Ditchburn, R. W. Eye-movements in relation to retinal action. *Opt. Acta (Lond.)* **1**, 171–176 (1955).
110. Krauskopf, J. Lack of inhibition during involuntary saccades. *Am. J. Psychol.* **79**, 73–81 (1966).
111. Sperling, G. in *Eye Movements and their Role in Visual and Cognitive Processes* (ed. Kowler, E.) 307–351 (Elsevier, 1990).
112. Herrington, T. M. *et al.* The effect of microsaccades on the correlation between neural activity and behavior in middle temporal, ventral intraparietal, and lateral intraparietal areas. *J. Neurosci.* **29**, 5793–5805 (2009).
113. Hafed, Z. M. & Krauzlis, R. J. Microsaccadic suppression of visual bursts in the primate superior colliculus. *J. Neurosci.* **30**, 9542–9547 (2010).
114. Nachmias, J. Determiners of the drift of the eye during monocular fixation. *J. Opt. Soc. Am.* **51**, 761–766 (1961).
115. Poletti, M. & Rucci, M. Eye movements under various conditions of image fading. *J. Vis.* **10**, 6 (2010).
116. Ciuffreda, K. J. & Tannen, B. *Eye Movement Basics for the Clinician* (Mosby-Year Book, 1995).
117. Serra, A., Liao, K., Martinez-Conde, S., Optican, L. M. & Leigh, R. J. Suppression of saccadic intrusions in hereditary ataxia by memantine. *Neurology* **70**, 810–812 (2008).
118. Ciuffreda, K. J., Kenyon, R. V. & Stark, L. Different rates of functional recovery of eye movements during orthoptics treatment in an adult amblyope. *Invest. Ophthalmol. Vis. Sci.* **18**, 213–219 (1979).
119. Ciuffreda, K. J., Kenyon, R. V. & Stark, L. Increased drift in amblyopic eyes. *Br. J. Ophthalmol.* **64**, 7–14 (1980).
120. Ciuffreda, K. J., Kenyon, R. V. & Stark, L. Fixational eye movements in amblyopia and strabismus. *J. Am. Optom. Assoc.* **50**, 1251–1258 (1979).
121. Ciuffreda, K. J., Kenyon, R. V. & Stark, L. Saccadic intrusions in strabismus. *Arch. Ophthalmol.* **97**, 1673–1679 (1979).
122. Shi, X. F. *et al.* Fixational saccadic eye movements are altered in anisometropic amblyopia. *Restor. Neurol. Neurosci.* **30**, 445–462 (2012).
123. Kozeis, N. *et al.* Visual function and execution of microsaccades related to reading skills, in cerebral palsied children. *Int. J. Neurosci.* **116**, 1347–1358 (2006).
124. Moller, F., Laursen, M. L. & Sjolie, A. K. Binocular fixation topography in patients with diabetic macular oedema: possible implications for photocoagulation therapy (3rd revision). *Graefes Arch. Clin. Exp. Ophthalmol.* **243**, 903–910 (2005).
125. Darwin, E. *Zoonomia; Or the Laws of Organic Life* Vol. 1 (Johnson, 1794).
126. Troxler, D. in *Ophthalmologische Bibliothek* (ed. Himly, K. & Schmidt, J. A.) 1–53 (Springer, 1804).
127. Coppola, D. & Purves, D. The extraordinarily rapid disappearance of entoptic images. *Proc. Natl Acad. Sci. USA* **93**, 8001–8004 (1996).
128. Thorpe, S., Fize, D. & Marlot, C. Speed of processing in the human visual system. *Nature* **381**, 520–522 (1996).
129. Fabre-Thorpe, M., Delorme, A., Marlot, C. & Thorpe, S. A limit to the speed of processing in ultra-rapid visual categorization of novel natural scenes. *J. Cogn. Neurosci.* **13**, 171–180 (2001).
130. Mergenthaler, K. & Engbert, R. Modeling the control of fixational eye movements with neurophysiological delays. *Phys. Rev. Lett.* **98**, 138104 (2007).
131. Engbert, R., Mergenthaler, K., Sinn, P. & Pikovsky, A. An integrated model of fixational eye movements and microsaccades. *Proc. Natl Acad. Sci. USA* **108**, E765–E770 (2011).
132. Inagaki, K., Hirata, Y. & Usui, S. A model-based theory on the signal transformation for microsaccade generation. *Neural Netw.* **24**, 990–997 (2011).
133. Brewster, D. On a singular affection of the eye in the healthy state, in consequence of which it loses the power of seeing objects within the sphere of distinct vision. *Ann. Philos.* **11**, 151 (1818).
134. Wade, N. J. & Tatler, B. W. *The Moving Tablet of the Eye: The Origins of Modern Eye Movement Research* (Oxford Univ. Press, 2005).
135. Kowler, E. Eye movements: the past 25 years. *Vision Res.* **51**, 1457–1483 (2011).
136. Krauskopf, J. Effect of retinal image stabilization on the appearance of heterochromatic targets. *J. Opt. Soc. Am.* **53**, 741–744 (1963).
137. Pessoa, L. & De Weerd, P. (eds) *Filling-in: From Perceptual Completion to Cortical Reorganization* (Oxford Univ. Press, 2003).
138. Simons, D. *et al.* Induced visual fading of complex images. *J. Vis.* **6**, 1093–1101 (2006).
139. Reppas, J. B., Usrey, W. M. & Reid, R. C. Saccadic eye movements modulate visual responses in the lateral geniculate nucleus. *Neuron* **35**, 961–974 (2002).
140. Saul, A. B. Effects of fixational saccades on response timing in macaque lateral geniculate nucleus. *Vis. Neurosci.* **27**, 171–181 (2010).
141. Snodderly, D. M., Kagan, I. & Gur, M. Selective activation of visual cortex neurons by fixational eye movements: implications for neural coding. *Vis. Neurosci.* **18**, 259–277 (2001).
142. Kagan, I., Gur, M. & Snodderly, D. M. Saccades and drifts differentially modulate neuronal activity in V1: effects of retinal image motion, position, and extraretinal influences. *J. Vis.* **8**, 19 (2008).
143. Leopold, D. A. & Logothetis, N. K. Microsaccades differentially modulate neural activity in the striate and extrastriate visual cortex. *Exp. Brain Res.* **123**, 341–345 (1998).
144. Hass, C. A. & Horwitz, G. D. Effects of microsaccades on contrast detection and V1 responses in macaques. *J. Vis.* **11**, 3 (2011).
145. Bair, W. & O'Keefe, L. P. The influence of fixational eye movements on the response of neurons in area MT of the macaque. *Vis. Neurosci.* **15**, 779–786 (1998).
146. Kitaoka, A. *Trick Eyes Graphics* (Kanzen, 2005).

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Competing interests statement
The authors declare no competing financial interests.

FURTHER INFORMATION
Susana Martinez-Conde's homepage: http://smc.neuralcorrelate.com

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