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Saccadic Eye Movements Modulate Visual Responses in the Lateral Geniculate Nucleus

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Summary

We studied the effects of saccadic eye movements on visual signaling in the primate lateral geniculate nucleus (LGN), the earliest stage of central visual processing. Visual responses were probed with spatially uniform flickering stimuli, so that retinal processing was uninfluenced by eye movements. Nonetheless, saccades had diverse effects, altering not only response strength but also the temporal and chromatic properties of the receptive field. Of these changes, the most prominent was a biphasic modulation of response strength, weak suppression followed by strong enhancement. Saccadic modulation was widespread, and affected both of the major processing streams in the LGN. Our results demonstrate that during natural viewing, thalamic response properties can vary dramatically, even over the course of a single fixation.

Introduction

Saccades are the rapid eye movements that are used to inspect the environment. They have an important perceptual function because they direct the central retina to salient regions of the visual scene and allow examination of these areas with high acuity. However, eye movements also pose a significant challenge to the visual system; with every saccade, an image of the world moves abruptly over the retina, stimulating all of its ganglion cells in concert. If neurons in the retina and central visual structures respond as they do during constant fixation, the resulting barrage of action potentials could disrupt the information that enters the brain soon after each eye movement.

Many mammals make fast eye movements, but saccades reach higher velocities and are more frequent in primates than in any other species (Carpenter, 1988). Despite this, our visual world remains subjectively stable. Strategies for dealing with the visual effects of saccades are therefore likely to be particularly well developed in humans and monkeys, although perhaps not unique to them (Lee and Malpeli, 1998; Lo, 1988).

While much is known about the basic response properties of neurons early in the primate visual system, relatively little is understood of how these cells behave during and soon after saccades. Because eye movements shift the retinal image, they are expected to influence the activity of visually responsive neurons (Bair and O'Keefe, 1998; Gallant et al., 1998; Gur and Snodderly, 1997; Leopold and Logothetis, 1998; Martinez-Conde et al., 2000). However, it is not yet generally established whether eye movements have an additional effect on the organization of visual receptive fields. Experiments that have carefully controlled the spatial properties of the retinal stimulus present during saccades have argued both for (Tolias et al., 2001) and against (DiCarlo and Maunsell, 2000; Wurtz, 1969) such an influence on cortical responses to briefly presented stimuli.

Defining the impact of eye movements on neural responses is also a requirement for understanding the well-known effects of saccades on human perception. Eye movements influence many aspects of low-level vision, including saccadic suppression of overall sensitivity (reviewed in Volkmann, 1986), as well as spatial (Cai et al., 1997; Lappe et al., 2000; Ross et al., 1997), temporal (Burr and Morrone, 1996), and chromatic (Burr et al., 1994) perception.

Recent experiments on the stimulus specificity of saccadic suppression make a number of testable predictions about its biological substrate. Eye movements have little effect on the detection of fine spatial detail and color, whereas they severely compromise the detection of stimulus motion and displacement (reviewed in Ross et al., 2001). The largely separate handling of color and motion information distinguishes the parvocellular and magnocellular pathways, two of the parallel processing channels of the primate visual system (Hendry and Reid, 2000; Merigan and Maunsell, 1993; Schiller and Logothetis, 1990). Accordingly, it has been proposed that eye movements selectively influence the activity of magnocellular neurons. However, previous studies have not revealed a consistent effect of saccades on magnocellular function (Bair and O'Keefe, 1998; Buttner and Fuchs, 1973; Ramcharan et al., 2001; Thiele et al., 2002).

Here we studied how saccades affect the response properties of relay neurons in the primate LGN. We probed saccadic responses with rich visual stimuli that revealed a consistent response change in virtually all magnocellular neurons: weak suppression, followed by strong enhancement. Furthermore, whereas saccadic modulation of parvocellular responses has never been reported, we find that when appropriate colored stimuli are used, saccadic enhancement is often seen. This approach has allowed us to extend the description of the receptive field, classically defined with respect to stimulus attributes such as space, color, and stimulus time, to a behavioral dimension: time before and after an eye movement.

Results

The visual stimulus used in these experiments had to fulfill two criteria. The first was that eye movements alone should not stimulate the receptive field. A full-field stimulus clearly meets this requirement. Because it lacks a spatial structure, the retinal stimulus remains

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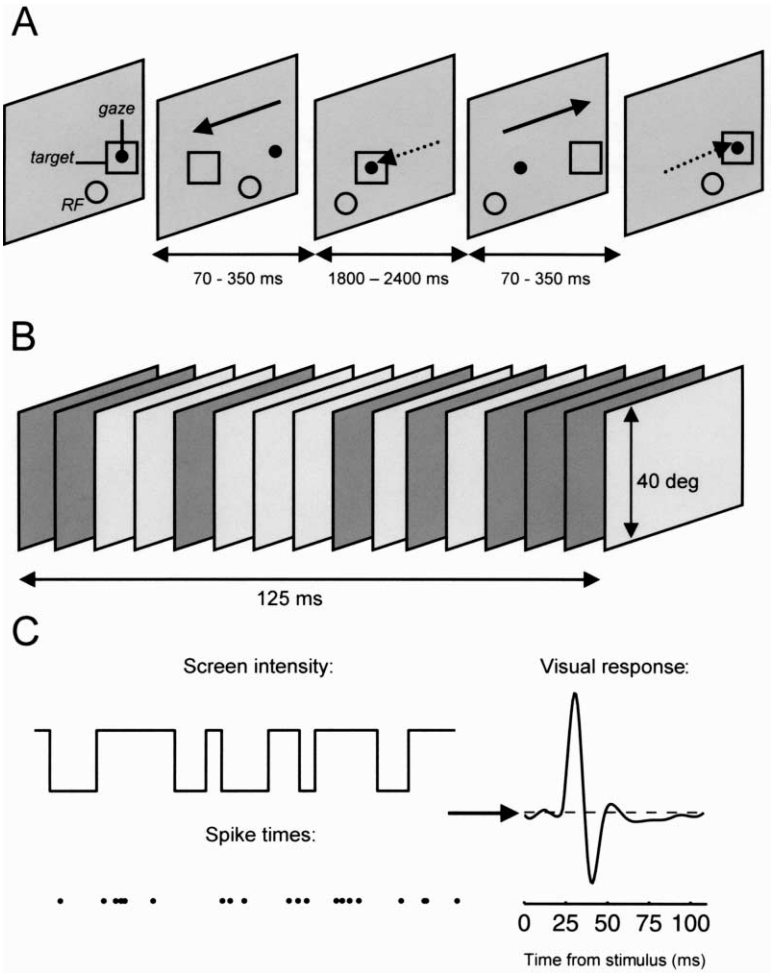


Figure 1. Experimental Design

(A) Schematic of the stimulus monitor, showing the position of the target (square), center of gaze (dot), and receptive field position (circle). Solid arrows indicate target displacement, and dashed arrows indicate saccades. The animal was rewarded for making an eye movement 70–350 ms after each target step. The screen schematic is not drawn to scale. (B) The screen intensity or chromaticity varied pseudorandomly between two values every ~7.7 ms. (C) Spike arrival times and stimulus values were cross-correlated to produce the impulse response function (here referred to as the visual response), shown at the right (Reid et al., 1997; see Experimental Procedures). The abscissa of the impulse response corresponds to time from the onset of the stimulus, and the ordinate has units of spikes/s.

identical before, during, and after the eye movement. In these experiments, the stimulus subtended approximately 45° by 45° of visual angle (Figure 1B), and saccade trajectories were always chosen so that the receptive field of the cell under study remained at least 10° from the edge of the stimulus screen. We also ensured that the saccade targets were located far from the receptive fields at all times during the experiment.

The second consideration was that the peri-saccadic visual response should be probed efficiently. The effects of eye movements on both perceptual (Diamond et al., 2000; Lappe et al., 2000) and physiological (Tolias et al., 2001) responses are known to evolve rapidly. Here we have used a complex time-varying stimulus that allows visual responses to be measured more efficiently over short time periods (Reid et al., 1997). This technique yields a better signal-to-noise (see Figure 3B) than previous approaches in which a stimulus is presented at either a single peri-saccadic time (Buttner and Fuchs, 1973; Lee and Malpeli, 1998; Robinson et al., 1986) or repetitively at a fixed rate (Ramcharan et al., 2001).

The experimental design is illustrated in Figure 1. Three animals were trained to fixate a small target that jumped between two positions approximately every 2 s (Figure 1A). Each target jump elicited a visually guided saccade. Throughout the experiment, the intensity of the entire screen flickered randomly between two values (Figure 1B). The rapidly modulated stimulus produced an ongoing, visually driven activity in LGN neurons. The onset of each saccade was used as a temporal reference point for the analysis of visual responses. Brief segments of the spike train were analyzed relative to the onset of each eye movement. Data from each of these time intervals were used to measure a series of visual responses, parametric in time from the saccade (Figure 1C; see Experimental Procedures).

We measured visually driven responses by correlating spike times with the stimulus, thereby generating full-field impulse response functions (Reid et al., 1997; Figures 3B, 6A, and 7A–7C). These functions can be thought of as the average firing rate of the neuron, above or below the mean, following the bright phase of the stimulus. The shape of the impulse response is similar for all neurons in the LGN. First, there is a flat portion, which corresponds to the response latency, followed by a sharp peak (positive for *on* cells and negative for *off* cells). After the peak, the response returns to zero and there is an overshoot, or rebound. At long delays, the visual stimulus no longer affects the activity of the neuron and the curve is flat. We will refer to the full-field impulse response function simply as the *visual response*.

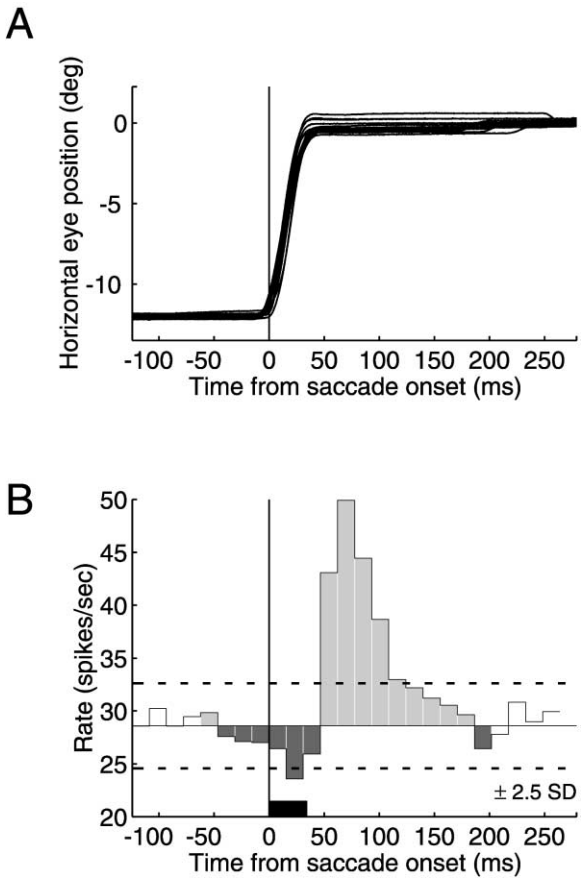


Figure 2. LGN Spike Rate Is Modulated around the Time of a Saccade

The animal made saccades between horizontal target locations 12° apart. (A) The horizontal component of the eye position for a subset of these trials. (B) The *peri-saccadic spike rate* from a single magnocellular neuron. The solid horizontal line is the mean spike rate produced by the flickering stimulus, measured during periods of fixation; the heavy dotted lines are ±2.5 SD of this value. The average saccade duration was 33.5 ms and is indicated by the horizontal black bar. For the period −75 ms to 200 ms, rate decrements are shaded dark gray, and increments are shaded light gray. The light and dark gray areas correspond, respectively, to the enhancement and suppression indices described in the Experimental Procedures (see also Figure 4B).

The Visual Response of LGN Neurons Is Modulated by Saccades

We illustrate our main result with a magnocellular cell that showed a change in response properties typical of our data set (Figures 2 and 3). In this experiment, we measured the visual response for different time intervals before, during, and after 12° horizontal saccades (Figure 2A). The mean spike rate over 329 trials is shown, aligned by the time of each saccade (Figure 2B). The eye movement had a significant effect on the firing rate, despite the fact that the visual stimulus was otherwise unchanged. The effect was biphasic: the mean rate dipped to ~15% below baseline soon after the onset of the saccade, and then peaked at approximately 60% above baseline around 75 ms after the eye movement.

In Figure 3, we show that the strength of the visual response also varied over the same peri-saccadic interval. Figure 3A shows the raster plot that generated the rate histogram shown in Figure 2B. We calculated a series of visual response functions from the spikes that arrived at different times relative to the eye movement. Four of these are shown in Figure 3B; the visual response functions plotted in different colors were generated from the correspondingly colored spikes in the raster plot. The visual responses plotted in gray are the same in all four panels and represent the control visual response obtained during fixation (see Experimental Procedures). Well before and well after the saccade, the visual response was a close approximation to the control (red and blue traces in Figure 3B). Just after the saccade, however, the amplitude of the visual response decreased (magenta trace in Figure 3B), and then increased (green trace in Figure 3B). Figure 3C plots the strength of the visual response as a function of time from the onset of the saccade. We will refer to this as the *peri-saccadic response function*.

Origin of the Effect

This saccade-related variation of the gain of the visual response is not predicted by our current understanding of geniculate processing. It reflects an effect of saccades on either retinal activity or retinogeniculate transmission. The stimulus was designed so that saccadic modulation of retinal activity was unlikely, but it cannot be excluded entirely. Because some global features of the display, such as the edges of the flickering stimulus, are not spatially invariant with saccades, they could in principle produce saccade-locked modulations of retinal activity.

We first asked whether a visual signal from remote regions of the retina might cause peri-saccadic effects (as in the "shift effect," see Derrington and Felisberti, 1998). With every saccade, the rapid motion of the screen edges stimulates the peripheral retina, albeit at least 10° from the receptive fields we studied. We therefore replicated the retinal consequences of the saccades by shifting the edges of the visual stimulus rapidly across the monitor as the animal fixated (see Experimental Procedures). In no case did we observe a significant modulation of visual responses in neurons that showed significant peri-saccadic response modulation ($n = 10$ cells; integral from 0–200 ms: $p < 0.005$, two-tailed paired t test).

Another feature of our display, the fixation target, might also have confounded our results. First, there might have been a visual response when the target disappeared at one position and appeared at another. When LGN responses were analyzed relative to this transition, however, no modulation of firing was seen until ~270 ms, when there was a monophasic enhancement. This latency is much too long to be visually driven (average visual response latency: 24.6 ms; $n = 16$ cells), but can be explained as the sum of the delays imposed by the average saccade latency (167 ms) and the time-to-peak of post-saccadic enhancement (~90 ms). Second, like the screen edges, the fixation point is a stationary feature that traces an arc across the retina with each eye movement, generating a potential shift effect. Because the trajectory of the saccade determines the shift of the fixation spot with respect to the receptive field,

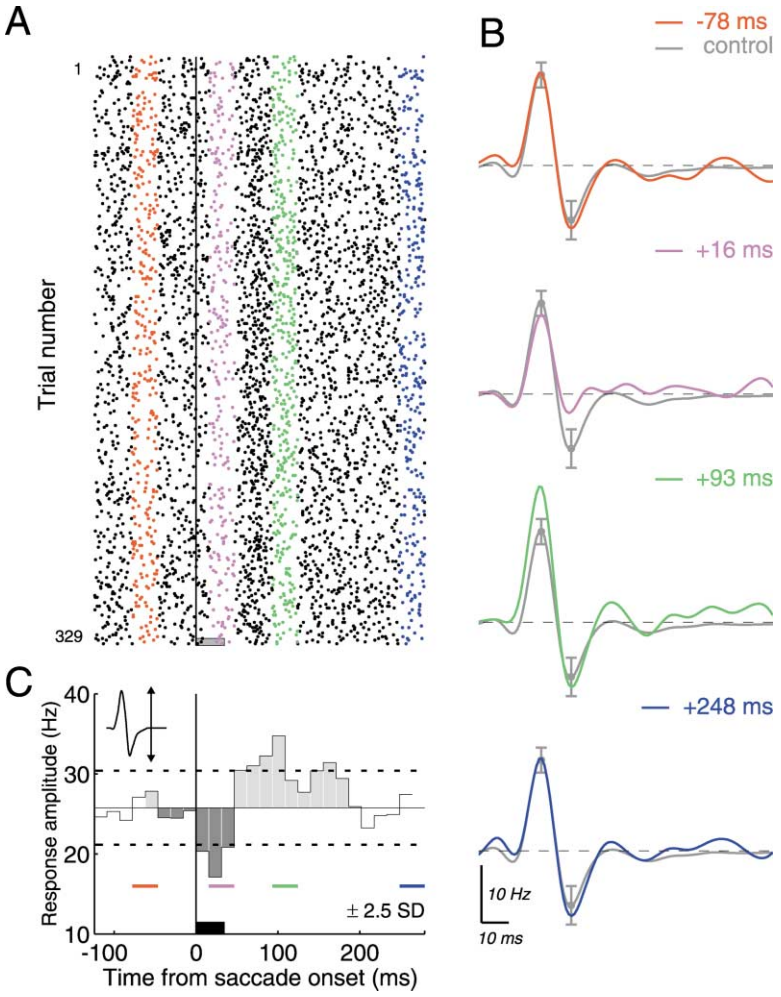


Figure 3. Visual Responsiveness Is also Modulated around the Time of a Saccade

(A) Raster plot of action potentials from the neuron in Figure 2, aligned to the onset of each saccade. Spikes are colored according to their timing relative to the start of each eye movement: red spikes occurred 78–47 ms before the saccade; magenta spikes: 16–47 ms after the saccade; green spikes: 93–124 ms after the saccade; blue spikes: 248–279 ms after the saccade. Intervals correspond to four stimulus frames (31 ms). The vertical sum of this raster plot yields the PSTH shown in Figure 2B. (B) The visual response functions for a subset of peri-saccadic times. The red, magenta, green, and blue visual responses were generated from the four correspondingly colored spike trains shown in (A), as described in the Experimental Procedures. The gray trace represents the control visual response, measured during periods of fixation; error bars: ±2.5 SD. (C) The peak-to-peak value of the visual response is plotted against time from the saccade: the *peri-saccadic response function* (format as in Figure 2B).

we compared saccadic modulation for saccades of different trajectories. We observed no significant differences in the area under the peri-saccadic response function for centrifugal versus centripetal saccades ($n = 51$ cells; integral from 0–200 ms: $p = 0.55$, two-tailed paired t test), nor for vertical versus horizontal saccades ($n = 4$ cells; integral from 0–200 ms: $p = 0.71$, two-tailed paired t test).

Finally, we controlled for the possibility that the sensitivity of retinal or LGN neurons might vary with the direction of gaze (e.g., Lal and Friedlander, 1989), an effect that would be confounded with saccadic modulation. We compared the visual response as the animal fixated at five positions at the mid- and endpoints of a saccade. We did not find a significant effect of eye position on the visual response of any LGN neuron that showed a significant peri-saccadic modulation ($n = 9$ cells). Moreover, across the entire data set ($n = 78$), visual response during straight-ahead fixation was statistically indistinguishable from the visual response measured during fixation of the eccentric target. Both findings argue against a gaze-dependent variation of response strength that could account for the peri-saccadic changes we observe.

Saccadic Effects Depend on Cell Type

With a black-and-white stimulus, we observed diverse effects of saccades on the visual responses of LGN neurons. Some cells were not affected by eye movements, while others showed dramatic changes just after eye movements. We first asked whether this tendency was related to cell type. The LGN contains at least two processing streams: the parvocellular system, whose neurons have small receptive fields and are color selective, and the magnocellular system, whose neurons have larger receptive fields, are not color selective but instead are highly sensitive to achromatic contrast (Kaplan and Shapley, 1986; Merigan and Maunsell, 1993; Wiesel and Hubel, 1966). A clear prediction from human psychophysical studies is that magnocellular neurons should be more susceptible to saccadic modulation than parvocellular neurons (Burr and Morrone, 1996).

For each neuron in our sample ($n = 78$), we calculated the visual response strength as a function of time (as shown in Figure 3C). If this peri-saccadic response function exceeded either an upper or lower significance limit (±2.5 SD; see Experimental Procedures), or both in sequence for at least two consecutive time points, the effect was deemed significant (see Experimental Procedures). The peri-saccadic visual responses were examined over an interval that started 75 ms before the saccade onset, allowing for possible pre-saccadic effects (see Lee and Malpeli, 1998; Tolias et al., 2001), and that ended 200 ms after the saccade onset, corresponding approximately to the refractory period of the saccadic system.

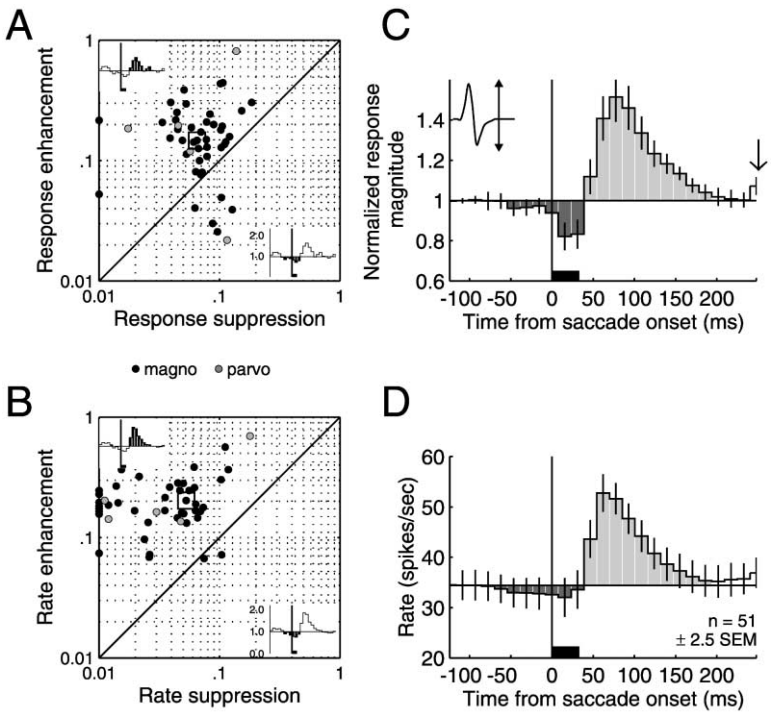


Figure 4. Population Data Showing the Prevalence of Peri-Saccadic Enhancement

(A) Normalized enhancement versus normalized suppression for peri-saccadic visual response strength. Each point represents data from a single physiologically identified cell (magnocellular or parvocellular), and only significantly modulated cells appear (n = 47). Insets in the upper left and lower right corners illustrate the time course of saccade-related modulation (as in Figures 2B and 3C) for the cell marked by a square. The normalized sum of the positive and negative values in these curves (shaded areas) yields the ordinate and abcissa of each data point in the scatter plot, as described in the text. The line of unit slope indicates balanced peri-saccadic enhancement and suppression. Most data points fall above the line, indicating a predominance of peri-saccadic enhancement. (B) As in (A), except for indices derived from the peri-saccadic spike rate. (C) The averaged peri-saccadic response function for the 47 neurons shown in (A), as well as 4 LGN neurons that were not classified definitively. The time course represents visual response strength relative to fixation, as a function of time from an eye movement (error bars: ±2.5 SEM). The format is otherwise as in Figures 2 and 3. (D) Peri-saccadic rate modulation for the neurons shown in (C).

Using this criterion, saccades were found to modulate the responses of 21% of the parvocellular neurons (5/24 cells; 3 *on*-center and 2 *off*-center) and 90% of magnocellular neurons (42/47 cells; 24 *on*-center and 18 *off*-center) in our sample. The greater effect of saccades on magnocellular responses is consistent with the finding that eye movements have the greatest effect on visibility when a target is most likely to be detected by the magnocellular pathway, but much less influence on targets thought to be detected by the parvocellular system (Burr and Morrone, 1996).

Response Enhancements Predominate

Given that saccades can have significant effects on the visual response properties of many LGN neurons, we asked whether the effects were predominantly response enhancements, response reductions, or some combination of the two. We computed two measures for each neuron that summarize changes in response strength as compared to conditions of fixation; we refer to these as the *normalized response suppression* and *enhancement* (see Experimental Procedures and Figures 4A and 4B, insets).

We examined the relative importance of the two effects for the population of parvo- and magnocellular neurons by plotting the normalized response enhancement versus suppression (for significantly modulated neurons, n = 47; Figure 4A). Data points that lie below the line of unit slope represent situations where there is a net suppression in response amplitude around the saccade, while points above the line indicate a net enhancement. Figure 4B has the identical format, except that it plots the indices derived from the spike rate rather than the visually evoked response functions (Figure 3C). In both plots, the center-of-mass lies above the line of unit slope. At the population level therefore, saccades have a predominantly enhancing effect on both the strength of the visual response and the firing rate in the LGN.

In an early study, Buttner and Fuchs found only a minimal effect of saccades on the firing rate of LGN neurons (Buttner and Fuchs, 1973). Some of the discrepancy with the present results may be attributed to different behavioral conditions: the duration of saccades in Buttner and Fuch's study varied from 50 to 180 ms, which is significantly longer than the 30–35 ms saccades in the present study. Further, in the earlier study, no distinction was made between parvo- and magnocellular neurons, so the separate effect of eye movements on these functional streams was not addressed.

A more recent study found that saccades had exclusively facilitatory effects on some magnocellular neurons (5/10 cells in Ramcharan et al., 2001). We report a more widespread (42/47 neurons), and more complex, type of magnocellular modulation: while response amplification predominates, some degree of response suppression is seen for most neurons. The visual stimulus and the design of the previous experiments made it difficult to distinguish peri-saccadic changes on the timescale that we report (Ramcharan et al., 2001). The higher signal-to-noise of our measurements may explain why we observed these peri-saccadic effects in a larger proportion of magnocellular neurons, as well as in 20% of parvocellular neurons when a black-and-white stimulus was used.

Time Course of the Saccadic Effect

We next examined the time course of saccadic modulation. To maximize the signal-to-noise of the estimate, we averaged the peri-saccadic response functions—

normalized by the response strength during fixation—of all neurons that showed significant saccadic modulation (n = 51 of 78, including those not definitively classified as either magnocellular or parvocellular). The modulation of visual response strength was biphasic (Figure 4C). Just after the onset of the saccade, the overall sensitivity dipped to 20% below its value during fixation. It then increased, peaking at an enhancement of approximately 50% greater than during fixation. The saccade-dependent modulation is complete by ~175 ms after the start of the saccade. The averaged peri-saccadic modulation of spike rate has a similar form (Figure 4D) as the visual response strength (Figure 4C).

A similar analysis of peri-saccadic modulation was performed for all cells, not just those for which a significant modulation was observed. When the visual responses of all parvocellular neurons were averaged, the peri-saccadic enhancement peaked at 9.3% above baseline; the averaged magnocellular responses peaked at 42.6% above baseline (data not shown).

An interesting feature of the averaged data shown in Figure 4C is that the early reduction in visual sensitivity appears to start *before* the onset of the saccade. In common with previous studies of the effects of saccades on both the LGN and extrastriate cortex, this effect was only seen in the aggregate data (Lee and Malpeli, 1998; Tolias et al., 2001); it was not a consistent or statistically significant effect in individual neurons. Alterations of visual response properties that precede the retinal image displacement caused by a saccade are further evidence for an extraretinal origin of the saccadic modulation we observe.

The biphasic modulation of LGN response strength we observed is similar to that reported by Lee and Malpeli for cats making saccades in complete darkness (Lee and Malpeli, 1998). Previous reports of post-saccadic enhancement of visually driven responses in both cats (Lee and Malpeli, 1998) and primates (Ramcharan et al., 2001), however, did not reveal the initial response suppression that we observed.

There is also an additional smaller peak in post-saccadic sensitivity that occurs at approximately 240 ms following the eye movement, well after the curve returns to the baseline (indicated by the arrow in Figure 4C). This represents the modulation of response strength by secondary saccades that sometimes followed the targeting saccades (see Figure 2A for examples of these). Secondary saccades occur when a targeting saccade fails to bring the eye exactly on target (Kapoula and Robinson, 1986; Kapoula et al., 1986). These eye movements were typically much smaller than the primary saccade, and occurred at least 150 ms after the primary saccade. A separate analysis of these eye movements is presented below.

Response Modulation Is Invariant with Saccade Size

The 12° saccades used in these experiments are larger than the eye movements typically made during natural viewing. If saccadic modulation scales with the size of the eye movement, the conditions of the present experiments may cause us to overestimate the extent of the modulation that the LGN ordinarily experiences. Since small eye movements also have shorter durations, it is possible that their effects on LGN activity would also be briefer than those summarized in Figure 4C.

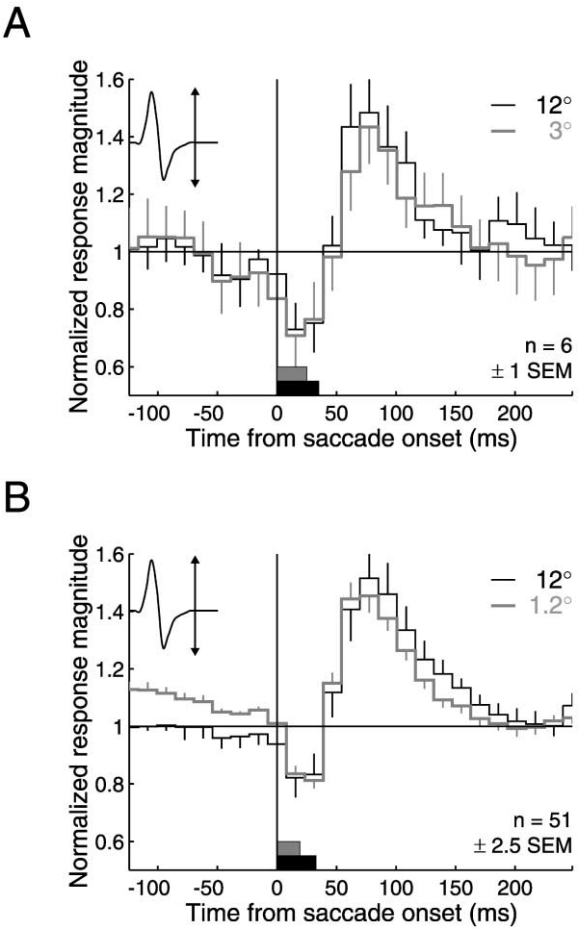


Figure 5. Saccade Amplitude Has Little Effect on Peri-Saccadic Modulation

(A) Six neurons were studied with both 12° (black) and 3° (gray) target separations. The format is otherwise as in Figure 5. The mean saccade durations were: 35.1 ms (12°) and 24.9 ms (3°). The two curves are statistically indistinguishable. (B) Averaged population curves for 12° targeting saccades (black lines; see Figure 5) and the smaller non-targeting saccades described in the text (gray lines; average amplitude = 1.24°; n = 51 neurons). The mean saccade durations were 32.8 ms (12°) and 19.1 ms (1.24°). Note that the pre-saccadic baseline for the small saccades is elevated. This is because the modulation due to these small saccades occurs on a baseline that is itself modulated by the previous targeting saccades.

We therefore explored the effects of saccade size on the peri-saccadic response function. In a subset of six cells, we repeated the standard experiment with 3° target steps. All of these neurons were magnocellular units in which a significant peri-saccadic effect was identified during 12° saccades. The peri-saccadic response functions for the 3° and 12° saccades were normalized by the response strength during fixation, separately averaged, and compared (Figure 5A).

Despite the 4-fold difference in saccade amplitude, the resulting peri-saccadic response functions appear practically indistinguishable. To quantify the statistical similarity between the 3° and 12° saccade conditions, we compared the integrated area beneath the peri-saccadic response function for each of the six neurons

shown in Figure 5A. There was no significant difference in the integral from 0 to 200 ms after the saccade ($p = 0.751$, two-tailed paired t test).

We next performed an analysis in which we compared the effects of large saccades, elicited by target steps, to the smaller saccades made at other points during the trial. These latter eye movements were of two types: (1) secondary saccades, made when targeting saccades fell short of the visual target (Kapoula and Robinson, 1986; Kapoula et al., 1986), and (2) small saccades made during nominal fixation (Leopold and Logothetis, 1998; Martinez-Conde et al., 2000; Skavenski et al., 1975). Because reflexive saccades and the "microsaccades" of fixation all generate comparable perceptual effects (Beeler, 1967), we combined data from these saccades in a single analysis.

Response modulation by small saccades (mean amplitude: 1.24°) was only slightly weaker than that evoked by 12° targeting saccades (Figure 5B; integral from 0–200 ms: $p = 0.021$, two-tailed paired t test). Because these peri-saccadic changes largely persist even as the amplitude of the eye movements varies by an order of magnitude, they are likely to be brought into play every time the eye moves.

Saccades Alter the Timing of Magnocellular Visual Responses

In addition to modulating the overall size of the visual response, saccades could also have striking effects on its time course. Impulse responses in the LGN are biphasic, with an initial peak (positive for *on* cells, negative for *off* cells) followed by a rebound of opposite sign (Usrey et al., 1999; Wolfe and Palmer, 1998). We found that the timing of both the peak and the rebound of the visual response accelerated soon after the eye movement. There was usually a more significant impact on the time at which the rebound occurred (Figure 6A). We assessed the extent of these changes across the population of LGN neurons, using the statistical tests described previously (changes >2.5 SD from the response during fixation; see Experimental Procedures).

We only observed significant timing changes in neurons in which there were also significant changes in the response amplitude ($n = 34/51$ significantly modulated neurons). Of these, all were magnocellular units. For each peri-saccadic interval, we averaged the peak (or rebound) times for all affected cells. The control (i.e., fixational) values of the peak (or rebound) were then subtracted; negative numbers therefore correspond to an acceleration of the visual response. Both the peak (Figure 6B) and the rebound (Figure 6C) accelerated soon after saccades. Responses were fastest ~60 ms after saccade onset and returned to baseline by 150 ms. This finding reiterates that peri-saccadic visual responses are not simply scaled versions of the response obtained under conditions of steady fixation (see also Figure 3B), and that eye movements must therefore influence both the timing as well as the strength of LGN responses.

A reduction of response latency by saccades has been described for neurons in the cat LGN (Fischer et al., 1996; Lee and Malpeli, 1998). However, our data indicate that saccades affect the entire temporal profile of the visual response, not just its latency. Indeed, eye movements have the greatest effect on the later phases of the visual response, such as the zero crossing. In other words, visual responses become slightly faster but yet more transient following a saccade. This finding closely parallels the effects of eye movements on the perceptual impulse response (Ikeda, 1986); the later phases accelerate significantly soon after saccades, while the early parts show only minimal changes (Burr and Morrone, 1996).

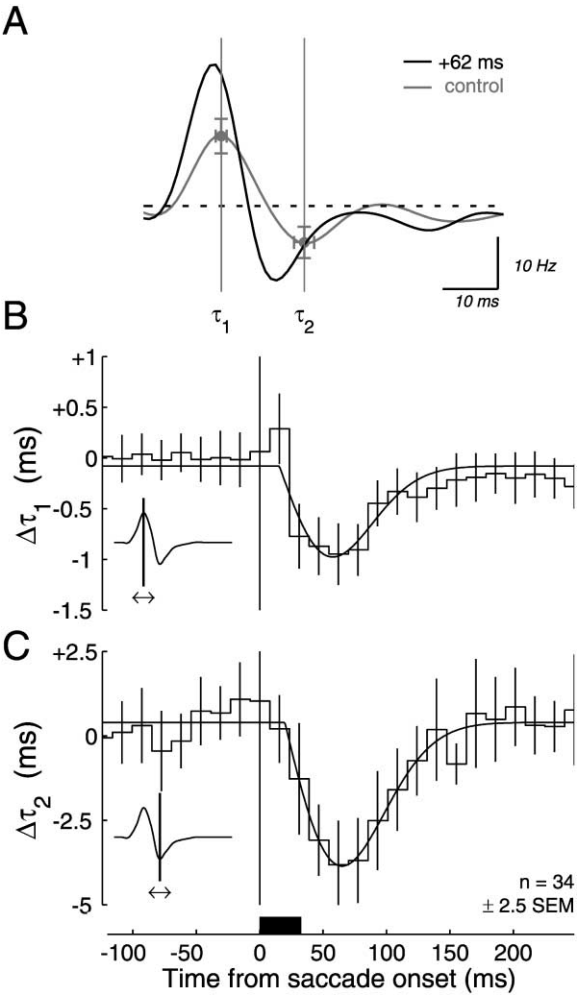


Figure 6. Magnocellular Responses Accelerate after Saccades

(A) Time courses of visual responses measured for an *on*-center magnocellular neuron during conditions of steady fixation (gray) and 62–92 ms after the start of the saccade (black). The peak time (τ_1) and rebound time (τ_2) occur earlier following saccades (error bars: ±2.5 SD). (B and C) Averaged peri-saccadic change in the timing of the visual response for 34 magnocellular neurons. (B) The difference between the peri-saccadic peak time (τ_1), and the peak time measured during conditions of fixation. Negative values indicate response acceleration. (C) Peri-saccadic changes in the rebound time (τ_2).

Parvocellular Responses to Colored Stimuli Are Modulated by Saccades

Eye movements are known to have effects on the perceptual processing of color information that are distinct from their impact on luminance-based vision (Burr and Morrone, 1996; Burr et al., 1994; Uchikawa and Sato,

1995). Color sensitivity is also an important feature of visual receptive fields, especially for parvocellular neurons, which receive antagonistic inputs from different cone classes (Wiesel and Hubel, 1966). One of the consequences of color opponency is that the black-and-white flicker used in these experiments is a much less effective visual stimulus for parvocellular neurons than for magnocellular neurons, in which cone signals reinforce each other.

We therefore addressed the possibility that eye movements might have different effects on color-selective neurons when a colored stimulus was substituted for the achromatic stimulus of the previous experiments. For 25 parvocellular neurons, we adapted our experimental protocol to use cone-isolating colored stimuli. These stimuli flickered between two colors that were chosen to modulate the cone class that provided the dominant input to each neuron, leaving the other two cone classes unmodulated (Estevez and Spekreijse, 1982; Reid and Shapley, 1992). We measured the peri-saccadic modulation of responses to these colored stimuli in exactly the same way as for the luminance-flicker experiments.

The overall effect of saccades on color-selective responses was qualitatively similar to the saccadic modulation of most magnocellular responses to the luminance stimulus: a predominant amplification of the response. Figure 7 shows individual examples of this phenomenon from three *on*-center parvocellular neurons, representing the three center cone types. The red-*on*, green-*on*, and blue-*on* center cells (Figures 7A–7C) all exhibited clear, statistically significant response enhancements soon after saccades. Unlike the case with magnocellular neurons (see Figure 6), the timing of parvocellular visual responses to cone-isolating stimuli was never altered significantly.

Of the 25 color-selective neurons tested with cone-isolating colored stimuli, significant modulation was only detected in *on*-center neurons (n = 12/16), while *off*-center neurons were unaffected by saccades under the same conditions (n = 0/9). Although we cannot currently offer an explanation for this difference, it is important to note that the *on*- and *off*-pathways of the primate visual system differ in a number of ways, both at the physiological (Benardete and Kaplan, 1999; Chander and Chichilnisky, 2001; Lankheet et al., 1998), and at the perceptual level (Chichilnisky and Wandell, 1996; Vassilev et al., 2000). Given these differences, the distinct effect of saccades on the *on*- and *off* pathways is not unprecedented.

The effect of eye movements is summarized for the population of significantly modulated neurons (all *on*-center) in Figure 7D, using the same conventions as previously (see Figure 4). All data points but one fall above the line of unit slope, indicating that peri-saccadic response enhancements predominate. The prevalence of post-saccadic response amplification echoes the psychophysical finding that some colored patterns actually become more visible soon after a saccade (Burr et al., 1994). The time course of the peri-saccadic response and rate modulation are shown in Figure 7E.

Saccades therefore have a fundamentally different effect on *on*-center parvocellular LGN neurons when an appropriately colored stimulus is used: 75% were modulated by saccades when presented with a colored stimulus, in contrast to the approximately 20% modulated when an achromatic stimulus was used. We conclude that the nature of saccadic modulation for parvocellular neurons is not fixed and invariable (Ramcharan et al., 2001), but depends fundamentally on the properties of the visual stimulus. Similarly, the effects of saccades on human perceptual sensitivity are markedly stimulus selective (Burr et al., 1994; Shioiri and Cavanagh, 1989; Uchikawa and Sato, 1995). The current result sheds light on why this should be so: different visual stimuli not only target different populations of cells with different susceptibilities to saccadic modulation (parvo- versus magnocellular), but they also determine the way in which eye movements influence parvocellular responses.

Discussion

In this study, we measured the response properties of neurons in the LGN at points before, during, and after saccades. Although saccades did not affect the visual stimulus, they produced a change in both the firing rate and the overall visual sensitivity of LGN neurons. These effects were widespread, and were observed in both parvo- and magnocellular neurons, provided that an appropriate visual stimulus was used. We show that saccadic modulation is not a fixed physiological property, and that the visual stimulus is the key to understanding the diversity of saccadic effects. Our results establish that a complete description of the receptive field, even at an early point in the visual pathway, must incorporate the effects of eye movements.

Eye Movements and Receptive Fields

The saccade-dependent receptive field provides a starting point for understanding the response changes that result from eye movements. Not only do our data successfully account for many previous findings (Lee and Malpeli, 1998; Ramcharan et al., 2001), but they also predict how LGN neurons should respond to an arbitrary visual stimulus (Benardete and Kaplan, 1999; Dan et al., 1996; Keat et al., 2001), presented at an arbitrary time relative to an eye movement. The current approach is generic, and is easily adapted to study the modulatory effect of other behaviors, such as spatial attention, or the modulation of other response properties, such as the spatial organization of receptive fields (Tolias et al., 2001).

It is well known that receptive fields are able to adapt to changing sensory requirements; for example, the strength and timing of early visual responses are altered when the properties of the retinal stimulus change abruptly (Brown and Masland, 2001; Carandini and Ferster, 1997; Chander and Chichilnisky, 2001; Muller et al., 1999; Rieke, 2001; Sanchez-Vives et al., 2000; Shapley and Victor, 1981; Smirnakis et al., 1997). Here we show that saccades also cause modulations of response strength, timing, and color processing. Significantly: (1) saccades have a stronger and more transient effect on visual responses than any previously described stimulus-dependent modulation, and (2) saccadic modulation is driven by changes in behavior, not the visual stimulus.

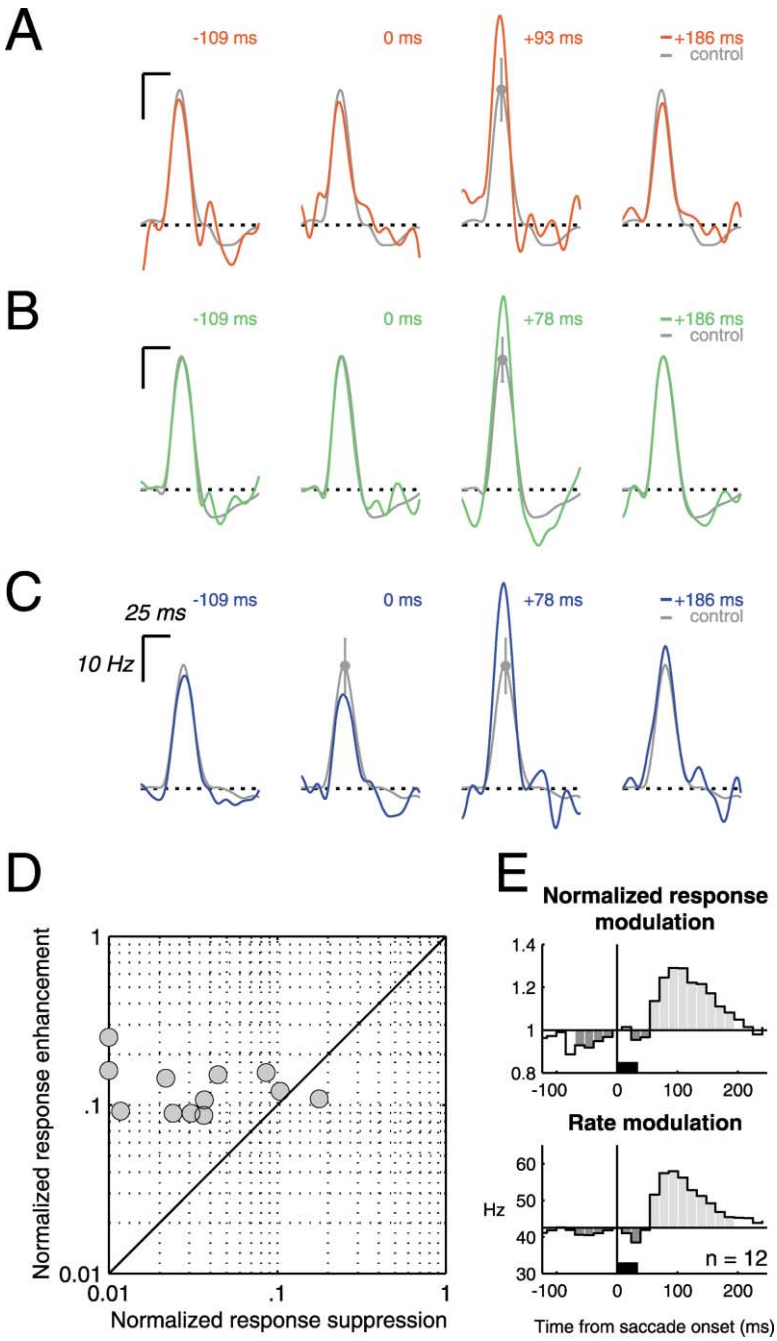


Figure 7. The Responses of Color-Opponent LGN Cells Are Modulated by Saccades When a Colored Stimulus Is Used

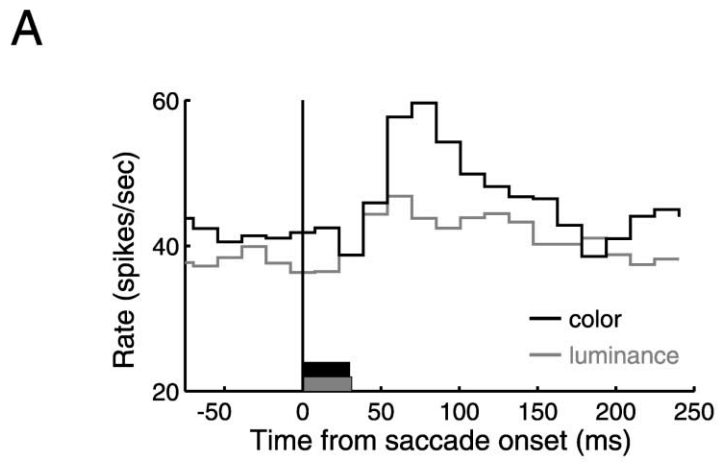
(A–C) Modulation of the visual response of the dominant cone type for 3 different color-opponent cells. (A) A red-*on* parvocellular neuron (dominated by the L cone) stimulated with an L cone isolating stimulus. L cone contrast: 21%. (B) A green-*on* neuron, stimulated with an M cone isolating stimulus. M cone contrast: 32%. (C) A blue-*on* cell, stimulated with an S cone isolating stimulus. S cone contrast: 89%. The visual responses shown in color are from different time intervals surrounding the saccade, indicated on the right of each panel. The visual response plotted in gray is the control response, generated from data collected during periods of fixation (see Figure 3B; error bars are ±2.5 SD). (D) Scatter plot of normalized enhancement versus normalized suppression of the visual response for color-opponent neurons stimulated through their dominant-cone mechanism. Only data from significantly modulated neurons, all *on*-center cells, are shown. The format is otherwise as in Figure 4. (E) Averaged time course of peri-saccadic response and rate modulation for neurons shown in (D). The format is as in Figure 4.

Nevertheless, both effects are likely to be brought into play during natural viewing, subjecting receptive fields at the earliest stages of visual processing to oculomotor and stimulus-driven adaptation. Since these changes happen over the timescale of the fixations that separate saccades, receptive fields are probably much more dynamic than they appear under standard experimental conditions.

Proposed Mechanism for Saccadic Modulation

Although we cannot completely eliminate a retinal origin of the effects presented here (e.g., Richards, 1969), we consider it unlikely for two reasons. By experimental design, the stimulus delivered to the classical receptive field during our experiments was unaffected by eye movements. Further, changes in the global stimulus configuration, such as shifting the screen edges or altering the saccade trajectory, failed to account for the saccade-related modulation we observed. Assuming that saccades produce no change in retinal activity, they must influence the way in which retinal information is processed by the LGN.

We show that eye movements do not impose an identical modulation for all retinal spike trains, but rather one that is specific for the retinal activity produced by certain visual stimuli. This distinction was most obvious for the



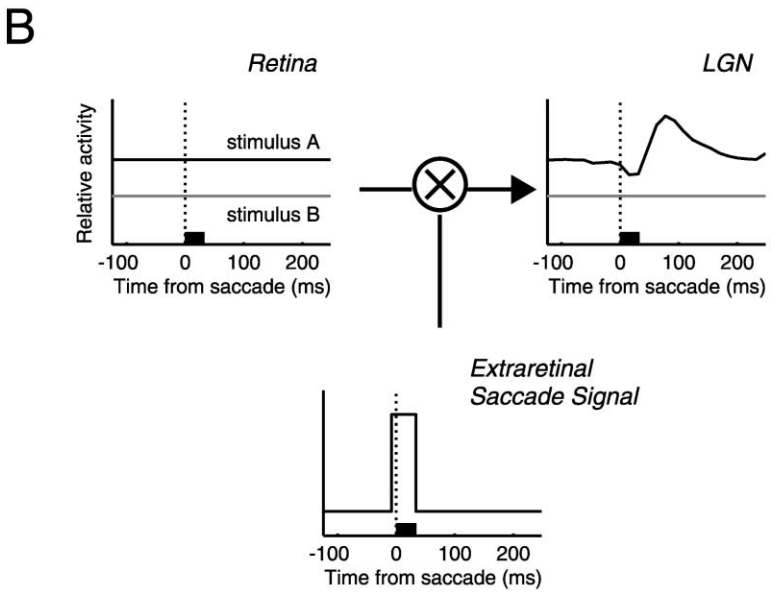


Figure 8. Stimulus-Dependent Effect of Saccades on Early Visual Processing

(A) Peri-saccadic spike rate modulation for a green-*on* parvocellular neuron, during interleaved presentation of an achromatic (gray trace) and an M cone isolating stimulus (black trace). The rate modulation produced by the achromatic stimulus was not significant, whereas there was a significant peri-saccadic enhancement for the colored stimulus. (B) Model in which the steady rate of visually driven activity is subjected to a saccade-dependent modulation by processing within the LGN. The extent of this modulation depends on the type of retinal activity evoked by the stimulus; some retinal patterns (black) are more susceptible to modulation than others (gray). Note that "relative retinal activity" refers to an arbitrary spiking statistic, not the mean rate.

population of *on*-center parvocellular neurons, which were more saccadically modulated when a colored stimulus was substituted for an achromatic one. Figure 8A shows an example of this stimulus-specific effect in a single color-opponent neuron: changing the appearance of the stimulus causes eye movements to have a profoundly different effect on the spike rate. Given that the temporal pattern of retinal activity determines the efficiency of retinogeniculate transmission during constant gaze (Mastronarde, 1987; Rowe and Fischer, 2001; Usrey et al., 1998), it is not surprising that different patterns of retinal input are more or less susceptible to the modulation that is activated by eye movements.

In Figure 8B, we propose how all of these factors may interact during saccades. The key feature, common to some previous models (e.g., Lal and Friedlander, 1989; Lee and Malpeli, 1998), is that saccades trigger a change in retinogeniculate transmission. The novel idea is that that the consequences of this extraretinal input depend critically on the statistics of the retinal spike train: as with the data shown in Figure 8A, the identical saccade signal may have quite different effects on the way the LGN responds to different retinal inputs. In our scheme, the saccade-related signal is permissive for the modulation of LGN responses, but the retinal signals specify what form that modulation takes.

Our experiments do not establish the physiological identity of the eye-movement signal depicted in Figure 8B, but a clear candidate is the modulatory input that projects from the brainstem to the thalamus. First, this projection is activated when primates make saccades (Bedworth and Singer, 1974; Cohen and Feldman, 1968). Second, stimulation of this ascending pathway alters the properties of the retinogeniculate synapse in a way that is consistent with the saccade-dependent response modulation we have described here. There is an enhancement of synaptic transmission from the retina to relay cells and overall amplification of relay cell responses (Eysel et al., 1986; Francesconi et al., 1988; Lu et al., 1993; McCormick and Pape, 1988), including a biphasic change in response amplitude that is strikingly similar to the one we measure (Doty et al., 1973; their

Figure 1). Signals from the brainstem can also modify the temporal properties of LGN relay neurons, causing effects that are similar to the timing changes that follow saccades (Hartveit and Heggelund, 1993; Humphrey and Saul, 1992; Wolfe and Palmer, 1998).

Implications for Post-Saccadic Behavior

There are parallels between the elevated spike rate that we observe in the magnocellular layers of the LGN soon after eye movements and the post-saccadic behavior of the primate oculomotor system. The gain of both the smooth pursuit system and the ocular following reflex—two systems that stabilize gaze—is enhanced in the wake of an eye movement (Busettini et al., 1996; Lisberger, 1998). The magnitude and the duration of this post-saccadic potentiation mirror the response enhancement we describe for the LGN. Both smooth pursuit and ocular following depend on visual cortical areas MT and MST, which receive strong projections from the magnocellular pathway (Maunsell et al., 1990). The enhanced magnocellular responses we observe may therefore help to prevent the post-saccadic retinal slip that potentially degrades high-acuity vision during natural viewing.

Implications for Saccadic Perception

These results address an unresolved question concerning saccadic suppression: where and how do eye-movement signals first interact with the visual signals that are suppressed? We show that saccade-dependent changes are consistently present at the level of the LGN, in almost all relay cells. Moreover, these physiological changes follow the same time course (Figure 4; Diamond et al., 2000; Lappe et al., 2000), and have the same invariance to saccade amplitude (Figure 5; Beeler, 1967; Stevenson et al., 1986), as peri-saccadic perceptual changes. Thus the physiological signature of eye movements is embedded in the information that reaches the visual cortex, arguing that saccades influence the very earliest stages of perceptual processing.

Our data permit a more directed examination of the hypothesis that the visual system makes special efforts to blunt the activity of the magnocellular visual pathway during saccades (Burr et al., 1994). This mechanism appears to act at an early point in the visual system, prior to the site of visual masking (Burr et al., 1994), and may rely on gain-control mechanisms that are present in the retina, LGN, and primary visual cortex (Burr and Morrone, 1996). This theory makes explicit predictions about the physiological effects of saccades, which have not yet been extensively tested.

We have examined parvo- and magnocellular responses to a stimulus with many of the features that lead to saccadic suppression in psychophysical experiments. Many of the predictions of the magnocellular hypothesis are confirmed by our findings: (1) eye movements do indeed have large effects on the amplitude of first-order responses to a canonical "magnocellular" stimulus, (2) these effects are much more prominent for neurons in the magnocellular than the parvocellular layers, (3) the effects are observed at the level of the LGN, clearly an early point in the visual system, (4) the effect appears to be mediated by an extra-retinal mechanism (Diamond et al., 2000), and (5) the physiological impulse response accelerates after eye movements, just as the perceptual impulse response does (Burr and Morrone, 1996; Ikeda, 1986). Furthermore, the amplification of color-selective parvocellular responses (Figure 7) echoes the enhanced sensitivity of the human visual system to colored patterns soon after a saccade (Burr et al., 1994).

It remains to be understood, however, why perceptual sensitivity to black-and-white stimuli decreases (Burr et al., 1994) whereas the biological sensitivity measured in these experiments predominantly increases soon after eye movements. One possibility is that saccades affect the biological noise that limits visual detection (Barlow, 1957). If saccades amplify the neural noise that limits perceptual decision-making to a greater extent than the visual signal we have measured here, they should lead to an overall suppression of perceptual sensitivity that is mediated by the magnocellular system.

Another possibility is that magnocellular but not the parvocellular system plays a significant role in masking the visibility of certain stimuli, during eye movements as well as during fixation. In this case, enhanced magnocellular activity would result in a relatively increased inhibition of a more central stage of visual processing. This theory would make the magnocellular neurons in the LGN the agent, rather than the target, of saccadic suppression.

Experimental Procedures

Data were collected from three monkeys: one adult female *Macaca fascicularis* (3.5 kg) and two juvenile male *Macaca mulatta* (4.3 and 4.6 kg). The experimental protocol conformed to National Institutes of Health and U.S. Department of Agriculture guidelines, and was approved by the Harvard Medical Area Standing Committee on Animals.

Visual Stimuli

Stimuli were presented at a refresh rate of 128 Hz on a 21 inch monitor. A software-implemented look-up table linearized the luminance of the monitor. We used a spatially uniform stimulus, modulated by a temporal white-noise stimulus (m sequence) to characterize the first-order response of LGN neurons, as described elsewhere (Reid et al., 1997).

All stimuli modulated the intensity of the monitor about a white point with CIE coordinates (x: 0.30, y: 0.33) and a mean luminance of 15–20 cd/m^2. The screen luminance and chromaticity were calibrated with a spectroradiometer (Photo Research PR-650, Chatsworth, CA). Parvocellular neurons were stimulated with a flicker of 50% or 100% contrast; magnocellular neurons were studied with 25% or 50% contrast, and occasionally 100% contrast. Cone-isolating stimuli were generated as described previously (Estevez and Spekreijse, 1982; Reid and Shapley, 1992).

Data Collection

Horizontal and vertical eye positions were measured with a search coil system (David Northmore, Inc., Bethesda, MD), and were digitized at 2.2 kHz per channel. Signals from tungsten-in-glass electrodes (Alan Ainsworth, Norwich, UK) were amplified, filtered, and digitized using the Discovery data-acquisition package (DataWave, Broomfield, CO), as described elsewhere (Usrey et al., 1998). For the majority of recording sites, the ocular dominance, receptive field location, achromatic contrast sensitivity, and chromatic opponency were measured during constant fixation.

The LGN is known to contain at least three processing streams: the parvo-, the magno-, and the koniocellular divisions. For the purposes of classification, all cells were tested with full-field stimuli at a number of different achromatic contrasts, to quantify contrast

sensitivity. Next, responses were defined as broadband or color-opponent by examining the polarity (*on* or *off*) of the responses to cone-isolating stimuli. We considered red-green and blue-yellow opponent cells to be parvocellular, and broadband cells to be magnocellular (although see Hendry and Reid, 2000). Neurons classified as magnocellular by this criterion also had faster visual latencies and higher contrast sensitivity (Kaplan and Shapley, 1986). Some LGN neurons were not identified definitively (for instance, broadband cells that had low contrast sensitivity). We recovered histological data from 2 of the 3 animals and verified that electrode penetrations entered all layers of the LGN.

Behavior

We trained each animal to track a small target (0.25° in diameter) that jumped between two positions every ~2 s (see Figure 1). A saccade was registered when the eye velocity exceeded 40°/s. The animal had to initiate a saccade within an interval of 70–350 ms after the target transition, and then hold fixation at the new target position for 900–1500 ms. Fixation was defined to be any eye position within a 1° to 2° square centered on the target position. Although we conditioned the animals to fixate the target before and after eye movements, the refractory period of the saccadic system did the most to ensure a saccade-free period during the peri-saccadic time window we analyzed. The experiments were blocked into segments of 80–100 trials. During a given block, the target appeared at one of only two positions: straight-ahead fixation and a position on either the horizontal or vertical meridian. The distance between the two targets was either 3° or 12°.

Data Analysis

Only data from neurons that were studied over 125 trials or longer were included in the current analysis. We present data from 78 neurons that were studied with an achromatic stimulus: 24 parvocellular neurons, 47 magnocellular neurons, and 7 cells that were not classified definitively. An additional 25 parvocellular cells were studied with a colored stimulus that modulated their dominant-cone mechanism in isolation. The eccentricity of the receptive fields studied ranged from 3.8° to 42°. The saccade target was located 4.6°–55° from the receptive field.

For each rewarded trial, the eye position data were smoothed (filter decay constant <2 ms), and differentiated to produce a record of eye velocity. The onset of the saccade was defined as the time when eye velocity first exceeded 40°/s; we often used a more variable threshold (30–60°/s) to define the offset of the eye movement. For every saccade included in the analysis, the experimenter verified the start and stop times. Saccades with an associated blink-related eye movement were excluded from the analysis (Riggs et al., 1987; Rottach et al., 1998). Main sequences for saccade velocity and duration did not depend on the background stimulus (achromatic flicker; colored flicker; or mean-luminance; data not shown), confirming that saccade metrics were not affected by the stimuli we used to characterize LGN responses.

To examine peri-saccadic modulation of LGN responses, we extracted the spike times that occurred in the range −124 ms to +279 ms relative to the time of saccade onset (i.e., from 16 stimulus frames before to 32 stimulus frames after the start of the eye movement). This period was subdivided into smaller intervals, with a temporal bin width of 30.8 ms, which corresponds to 4 stimulus frames. In all the analyses we show, the bins were spaced by 15.4 ms and overlapped each other by half their width (see Figure 3C).

Spikes from each interval were binned at the frame rate of the visual stimulus and then correlated with the intensity waveform of the flickering stimulus to yield the impulse response, as described elsewhere (Reid et al., 1997). This process created a series of impulse responses (or *visual responses*), indexed by time relative to the saccade. The visual responses were sampled in 7.7 ms steps, the stimulus refresh rate. These values were zero-padded for negative (non-causal) stimulus times and then interpolated to a 1 ms time resolution using a cubic spline. Visual response functions typically have two components: (1) an initial response that is positive for *on*-center neurons and negative for *off*-center neurons, followed by (2) a rebound of opposite polarity. We refer to these respectively as the *peak* and *rebound* phases of the response (Usrey et al., 1999). The strength of the visual response was defined to be the difference between the peak and the rebound (Smirnakis et al., 1997).

We determined the statistical significance of the various peri-saccadic time courses under the null hypothesis that the visual response at all times before and after the saccade was identical to that measured during periods of prolonged fixation. A period of fixation was defined to start at least 200 ms after and end at least 50 ms before a saccade of any magnitude. We generated confidence limits on the estimate of the baseline visual response with a bootstrap analysis in which we sampled spike data only from periods of fixation, using the same total number of time intervals that were used to generate the peri-saccadic visual response. We estimated the mean and variance of the visual response amplitude from 100–500 such bootstraps. This process generated an estimate of the range of visual response strength expected, given the number of trials obtained, assuming no effect of eye movements.

We adopted a significance criterion of 2.5 SD (see Figure 3C). Assuming a normal distribution of response amplitudes, the probability that any single bin in a 17 bin sequence exceeds this threshold is ~1.3%. Indeed, in approximately 2% of the bootstrapped data sets (synthesized from conditions of fixation), we observed a single bin that crossed the 2.5 SD threshold. Invariably, these threshold crossings reflected noise, rather than a prolonged response modulation. We therefore imposed the additional requirement that the 2.5 STD limit be exceeded in two consecutive time bins. Although it is arbitrary, this criterion never generated a false positive classification of any bootstrapped data set (0 instances of ~8500 bootstraps from 72 cells).

Peri-saccadic modulation of each response measure (response amplitude and spike rate) was summarized with two indices: the normalized enhancement and the normalized suppression. Normalized enhancement was calculated from the peri-saccadic spike rate functions (Figure 2B) and the peri-saccadic response functions (Figure 3C) by integrating the area that fell above the baseline (shaded light gray). Suppression was similarly calculated from all values that fell below baseline (shaded dark gray). These areas were normalized by the integral of the baseline, so that a doubling of the response strength for the entire interval would yield a value of 1.0; a doubling of the response in just one time bin therefore contributed 0.0625 to the index.

Control for Possible Retinal Effects

A set of control experiments addressed possible "shift" effects during saccades (Derrington and Felisberti, 1998; see Results). In these, the animal fixated a straight-ahead visual target as the far edge of the flickering display moved toward and away from the fixation point, simulating the visual stimulation of the peripheral retina that resulted from each eye movement. The distance and direction of the edge displacement corresponded to the peripheral retinal motion generated by saccades. For example, a vertical edge was displaced 12° into and out of the flickering field to replicate the retinal motion associated with 12° horizontal saccades. The edge motion occurred over five stimulus frames (39 ms), which approximately corresponded to the average duration of 12° saccades in the eye-movement experiments.

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