Neural discharge coupled to saccade offset in the cat visual cortex

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The increase in neural activity in cat visual cortex associated with eye movements has been thought to reflect a replica of the motor command signal. We examined the timing of the saccade-related increase in neural activity in cat areas 17 and 18 in relation to saccade onset and offset. The increase in activity was temporally coupled to saccade offset rather than onset both for visually guided saccades and for spontaneous saccades in the dark. Overall, it occurred 63 ms after saccade offset, and the peak was higher and sharper for data aligned at saccade offset than for onset. These results are inconsistent with the idea that saccade-related activity in cat visual cortex reflects a copy of the motor command signal. *NeuroReport* 11:1661–1664 © 2000 Lippincott Williams & Wilkins.

Key words: Cat; Efference copy; Proprioceptive; Saccadic eye movement; Visual cortex

INTRODUCTION

Increased neural activity in visual cortex coupled to saccadic eye movements has been reported in the cat [1–3] and monkey [4]. In the cat, this increase is observed for spontaneous eye movements in complete darkness, suggesting that the origin is extraretinal. Toyama *et al.* [3] supported the idea of efference copy (or corollary discharge) of the motor command as an extraretinal source of the increased activity by showing that the saccade-related excitation in cat striate cortex occurred in synchrony with activity in the oculomotor nuclei in darkness, even after retrobulbar paralysis of eye movements. However, the idea of corollary discharge is inconsistent with other findings. Saccade-related activity is coarsely, if at all, related to saccade parameters [3], and the latency of saccade-related activity from the onset of the saccade is variable [1,2]. Recently, Lee and Malpeli [5] reported a biphasic activity modulation in the cat lateral geniculate nucleus (LGN) in relation to saccades, consisting of presaccadic suppression and postsaccadic facilitation, that appeared to be coupled to saccade offset. They suggested that this modulation facilitates central registration of visual images by enhancing contrast between geniculate activity evoked by images before and after a saccade. If saccade-related activity reflects a neural replica of the motor command signal, one would predict that either its onset or peak is coupled to saccade onset, rather than offset. To explore this issue in the visual cortex, we examined the temporal relationship between neural activity and saccades, for both spontaneous and visually guided saccades, in cat areas 17 and 18.

MATERIALS AND METHODS

Six adult cats were prepared for chronic unit-recording, and for recording eye movements [6]. All surgery was performed under barbiturate anesthesia (2–10 mg/kg/h). After recovery, animals were trained to make saccadic eye movements toward briefly presented light-emitting diode (LED) targets in a darkened room for a water reward. The protocol for care and use of animals was approved by the Seoul National University Laboratory Animal Care Advisory Committee, and was in accordance with the NIH guide for the care and use of laboratory animals. The measures taken to avoid animals suffering at each stage of the experiment are described elsewhere in detail [7].

Tungsten-in-glass microelectrodes were used for extracellular recording of single cells and multiple-unit activity. Electrode penetrations were made vertically between Horsley-Clarke anterior -1 and $+1$, and lateral 1 and 3 mm, near the border region between areas 17 and 18. Data were collected for a visually guided saccade task (single cells, three cats) and during spontaneous saccades (multiple units, three cats). In the visually guided condition, targets were chosen from a 16×16 array of LEDs spanning $\pm 30°$ in horizontal and vertical directions, positioned 72.6 cm from the eyes. In complete darkness, a tone signaled the start of a trial, and 500 ms later, the center LED went on. If the animal successfully fixated the center LED within a $4 \times 4°$ window, this LED went off after a variable (300–900 ms) delay, and another, randomly chosen LED, to which the cat had to shift fixation, went on for 50 ms. Typically, saccadic latency was >150 ms, so there was no visual stimulus during the saccade. Trials with discrete visual response were excluded from analysis to prevent visual responses from confounding saccade-related activity.

For spontaneous saccades, no visual target was presented and the animals had no task. They were encouraged

to make eye movements by water rewards and an alarm buzzer. To compare motor-related activity with saccade-induced visual reafferent signals, in half the spontaneous saccade trials the recording room was illuminated, and in the other half the room was dark.

Saccade onset and offset times were defined with a velocity criterion (15 deg/s). To determine the onset time of single-cell activity, spike–density functions were derived by convolving the sequence of action potentials with a Gaussian kernel with a 15 ms s.d. For multiple unit activity, which showed more variable spontaneous activity, the interval to the third nearest spike, a variable kernel width depending on the level of neural activity, was taken as one sigma of the Gaussian kernel function [8]. The onset time of neural activity associated with visually-guided saccades was taken as the time when spike density rose above 150% of peak density during the 200 ms immediately before the saccade target appeared. For spontaneous saccades in the dark, the onset criterion was 300% of the peak density during the 200 ms period preceding the saccade.

RESULTS

Sixty-five single neurons recorded during visually guided saccade tasks increased their activity in relation to saccades. For the majority of these cells (61.5%), the peak of the cumulative spike–density function aligned at saccade offset was higher and sharper than that aligned at saccade onset. Figure 1(a,b) illustrates one such cell. The distribution of the time of peak spike density aligned at saccade onset was centered at 172 ms, and that aligned at saccade offset at 31 ms (not shown). To examine the time course of population activity, cumulative spike–density functions were derived by averaging the spike–density functions of all 65 cells aligned at saccade onset and offset (Fig. 1c,d). Saccade-related activity started before movement onset (Fig. 1c), increased abruptly near the time of movement offset, and persisted for >200 ms after saccade offset (Fig. 1d). The peak for alignment at saccade offset occurred 63 ms after saccade offset. This peak was sharper and larger than that for alignment at saccade onset. Overall, there was no indication that the activity was suppressed during saccades.

Determination of the nature of saccade-related activity critically depends on the timing of the earliest indication of neural activity. If initial activity is coupled to saccade onset, the interval from saccade onset to activity onset, or latency of activity (interval *b* in Fig. 2a) will remain the same regardless of saccade duration (interval *a* in Fig. 2a). Thus, the slope of the relationship between saccade duration and latency of activity would be zero. Alternatively, a slope near one would indicate that onset of neural activity is coupled to saccade offset (Fig. 2b).

For each of 33 single cells with a sufficient number of saccade trials for the following analysis (10–36 trials, mean 17), the latency of activity for each trial was plotted against saccade duration, and a linear regression line derived. Figure 2c shows these data for a representative cell, and Fig. 2d shows the distribution of slopes for all 33 cells. Although there are a few cells with slope near zero, the modal slope is much closer to one. Statistical tests (one-sample *t*-tests) indicate that the increase in activity is coupled to saccade offset rather than onset: the hypothesis

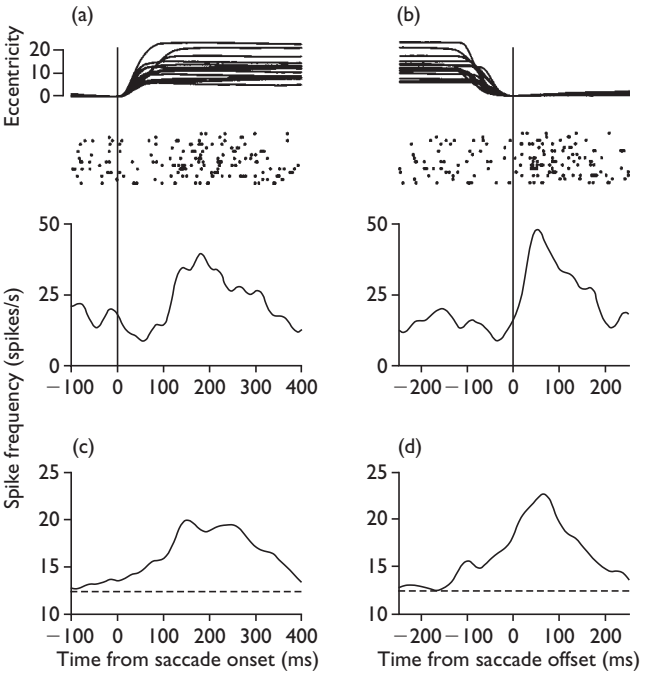

Fig. 1. Activity of a representative single cell during saccades toward a briefly presented visual target for data from 15 trials aligned at saccade onset (**a**) and offset (**b**). Eye position is expressed as eccentricity along the movement direction. Each dot represents a single action potential. The cumulative spike–density function peaks at 39.3 spikes/s at 183 ms in (a) and at 47.7 spikes/s at 53 ms in (b). Note that the peak activity is higher and sharper in (b) than in (a). Cumulative spike–density function of all 65 single cells aligned at saccade onset (**c**; peak = 20.1 spikes/s at 154 ms) and offset (**d**, peak = 23.6 spikes/s at 63 ms). Broken lines in (c) and (d) indicate baseline activity (average spike density during 200 ms immediately preceding target onset).

that the population slope is zero is rejected ($t_{32} = 6.28$, $p < 0.001$), but the hypothesis that the population slope is one is not ($t_{32} = -1.23$, $p > 0.23$).

Coupling between latency of activity and saccade offset also characterized spontaneous saccades. Figure 2 (e,f) shows plots similar to Fig. 2c for 59 multiple unit sites. For spontaneous saccades in the dark, the latency of activity increased with saccade duration (Fig. 2e) with a slope of 1.01 ($R^2 = 0.49$, $p < 0.0001$). For the same neuronal pool in the light, the data appear to consist of two clusters with different regression slopes. We attribute these to sensory and motor components of activity (see below), and fitted separate linear regression lines, which were optimized by minimizing the sum of residual error of individual data points from either of two regression lines that were updated with each iteration (Fig. 2f).

DISCUSSION

This study reveals two consistent temporal relationships between parameters of eye movements and neural activity. First, the peak of the cumulative spike–density function aligned at saccade offset was higher than that aligned at saccade onset. Second, the onset of increase in activity was temporally coupled to saccade offset rather than onset, both for controlled visually guided saccades and for spon-

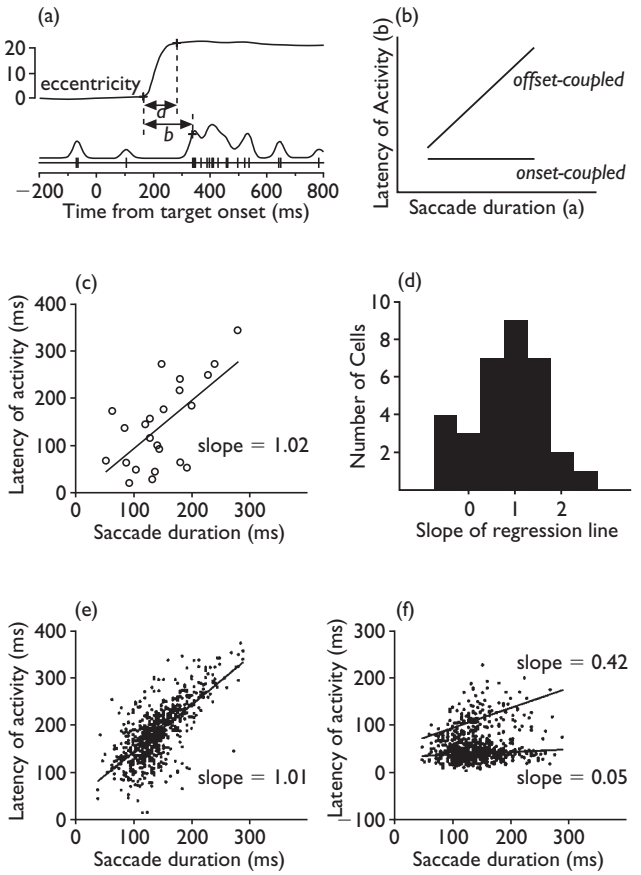

Fig. 2. Temporal relationships between saccade and neural activity. (**a**) Representative trial from the visually guided condition. Eye eccentricity, saccade duration (a), latency of activity (b), spike–density function, and the sequence of action potentials are illustrated. The LED target was turned on at time 0 for 50 ms. (**b**) Predicted relationships between saccade duration and latency of neural activity, under the assumption that the neural activity is coupled to offset (slope = 1), or to onset (slope = 0). (**c**) Scatter plot of saccade duration versus latency of neural activity for 23 visually guided saccade trials for a representative single cell. The slope of the linear regression line is 1.02. (**d**) Distribution of the slope of linear regression line illustrated in (c) for 33 single cells with more than 10 rewarded trials (mean = 0.84, s.d. = 0.77). (**e**) Scatter plot for saccade duration *vs* latency of neural activity for 662 trials from 59 multiple-unit sites for spontaneous saccades in the dark. (**f**) Scatter plot for 685 trials from the same 59 sites of (e) in the light. Two linear regression lines are fitted to the data, with slopes of 0.42 (y-intercept of 55.08) and 0.05 (y-intercept of 35.54).

taneous saccades in the dark. Thus saccade-related activity is unlikely to result from an efference copy signal, as previously proposed [3].

As reported previously [3], in the light, saccade-related excitation consists of two components reflecting visual reafference (i.e. sensory activation as the eye movements sweeps images across the retina) and saccade-related activity. Visual reafferent activity has a shorter latency [3,9], so it determines activity onset in the light, and undoubtedly accounts for the activity associated with the regression line whose slope is near zero in Fig. 2f. When activity reflecting the visual reafference was not strong enough to meet the threshold criterion, saccade-related activity was likely to determine the latency of activity, thus forming the cluster with a slope of 0.42. The fact that this slope is <1 (unlike that in Fig. 2e) is probably due to interaction between (or addition of) activity reflecting the visual reafference and that coupled to saccade offset, shortening the latency and thus reducing the slope.

Lee and Malpeli [5] reported that in the cat, LGN cells undergo presaccadic inhibition, followed by an activity enhancement coupled to saccade offset. The inhibition was much weaker and more irregular than the enhancement, and the source of both is unknown. The saccade-related change in cortical activity observed in the current study also appears coupled to saccade offset, but it differs from the LGN phenomenon in two ways. First, the peak of the postsaccadic increase in activity occurs earlier than in the LGN. Second, the cortical increase is not preceded by a period of inhibition. Thus, the cortical saccade-related activity does not appear to simply follow the LGN saccade-relate activity, although it is still possible that some of it has a geniculate origin.

The saccade offset-coupled activity observed in the current study is unlikely to be a rebound from inhibition by an efference copy signal, because our data provide no evidence of a period of suppression preceding the increase in activity (Fig. 1c,d). Its ultimate source and function remain uncertain, but possible candidates for the source include a proprioceptive signal related to muscle length or tension or a resettable integrator signal. A muscle proprioceptive signal reaches cat striate cortex [10], and its peak is likely coupled to the offset of centrifugal saccades. However, since the saccade-related cortical activity starts as early as 100 ms before saccade onset, decays about 200 ms after saccade offset even when the eye position remains stationary, a proprioceptive signal is not likely to be a major source of the saccade-related activity dealt with in the current study. The resettable integrator neuron and/or circuitry that has been postulated for several models for generation of saccadic eye movement [11,12] is thought to reach its peak activity at saccade offset. However, neurons showing this property have yet to be found. The time of peak of saccade-related activity roughly corresponds to a temporal window when the visual input at a newly fixated spatial locus arrives in the visual cortex. It is possible that high-level processes meticulously keep track of oculomotor performance, and thereby synchronize the arrival of visual input with them. Saccade-related activity in structures associated with mnemonic processes such as the hippocampus [13] may be a part of this operation.

CONCLUSION

The increase in neural activity in cat areas 17 and 18 in relation to saccadic eye movements was temporally coupled to saccade offset rather than onset both for visually guided saccades and for spontaneous saccades in the dark. Overall, it occurred 63 ms after saccade offset, which is earlier than a similar activity enhancement coupled to saccade offset in the cat LGN [5]. Because the increase in cortical activity was coupled to saccade offset, it was unlikely to be a neural replica of efference copy signal for saccadic eye movement. It was also unlikely to be a rebound from inhibition by an efference copy signal,

because of no evidence of a period of suppression preceding the increase. Thus, these results are inconsistent with the idea that saccade-related activity in cat visual cortex reflects a copy of the motor command signal.

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