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RESEARCH ARTICLE | *Sensory Processing*

Activity of primate V1 neurons during the gap saccade task

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Kim K, Lee C. Activity of primate V1 neurons during the gap saccade task. *J Neurophysiol* 118: 1361–1375, 2017. First published June 14, 2017; doi:10.1152/jn.00758.2016.—When a saccadic eye movement is made toward a visual stimulus, the variability in accompanying primary visual cortex (V1) activity is related to saccade latency in both humans and simians. To understand the nature of this relationship, we examined the functional link between V1 activity and the initiation of visually guided saccades during the gap saccade task, in which a brief temporal gap is inserted between the turning off of a fixation stimulus and the appearance of a saccadic target. The insertion of such a gap robustly reduces saccade latency and facilitates the occurrence of extremely short-latency (express) saccades. Here we recorded single-cell activity from macaque V1 while monkeys performed the gap saccade task. In parallel with the gap effect on saccade latency the neural latency (time of first spike) of V1 response elicited by the saccade target became shorter, and the firing rate increased as the gap duration increased. Similarly, neural latency was shorter and firing rate was higher before express saccades relative to regular-latency saccades. In addition to these posttarget changes, the level of spontaneous spike activity during the pretarget period was negatively correlated with both neural and saccade latencies. These results demonstrate that V1 activity correlates with the gap effect and indicate that trial-to-trial variability in the state of V1 accompanies the variability of neural and behavioral latencies.

NEW & NOTEWORTHY The link between neural activity in monkey primary visual cortex (V1) and visually guided behavioral response is confirmed with the gap saccade paradigm. Results indicated that the variability in neural latency of V1 spike activity correlates with the gap effect on saccade latency and that the trial-to-trial variability in the state of V1 before the onset of saccade target correlates with the variability in neural and behavioral latencies.

primary visual cortex; response time; saccadic eye movement; sensorimotor transformation; single-cell recording

THE PRIMARY VISUAL CORTEX (V1) is likely to mediate visually guided behavioral responses. Electrophysiological studies on monkeys performing visually guided saccade tasks have revealed the involvement of V1 in various functions beyond pure sensory processing, such as perception, memory, and decision making. These include, for example, saccade-related activity during the figure-ground task (Supèr 2006), trial-to-trial covariation between V1 activity and behavioral choice (Palmer et al. 2007), and the correlation of V1 activity with decision in an orientation-discrimination task (Nienborg and Cumming 2014). Because most animals with a fovea have a highly developed eye movement system, most visual functions are thought to be coordinated with saccades, and this is likely to be reflected in V1 activity. Understanding how neural activity in V1 is related to the initiation of visually guided saccades is the subject of the present study.

When monkeys make saccades toward visual stimuli that suddenly appear peripherally, the time of the first spike, or neural latency, of V1 activity elicited by the visual stimulus is correlated with saccade latency on a trial-to-trial basis (Lee et al. 2010). Ideally, the nature of the link between the time of the first spike and saccade latency would be evaluated by controlling spike timing, but this is difficult to do in awake monkeys. On the other hand, experimental manipulations are available that can robustly influence saccade latency. In the present study, we further examined the link between V1 activity and the latency of visually guided saccade during one such manipulation, the gap saccade paradigm.

In the gap saccade paradigm, in which a temporal gap is inserted between an observer's fixation point and the onset of a saccade target, saccade latency is reduced and express saccades occur more frequently—the gap effect (Dick et al. 2005; Dorris and Munoz 1995; Fischer and Boch 1983; Fischer and Ramsperger 1984; Jin and Reeves 2009; Kingstone and Klein 1993; Pratt et al. 1999, 2006; Reuter-Lorenz et al. 1991; Saslow 1967; Sparks et al. 2000). Previously, correlations of single-unit activity with the gap effect have been examined outside V1, in saccade-related areas such as the superior colliculus (Dorris et al. 1997) and the frontal eye fields (Dias and Bruce 1994; Everling and Munoz 2000). The main goal of the present study was to identify changes in V1 activity associated with the gap effect. Specifically, we determined whether the first spike of V1 activity, which has been shown to be correlated with the latency of visually guided saccade on a trial-to-trial basis (Lee et al. 2010), occurs earlier in the gap condition. We also determined whether changes in V1 activity correlate with the occurrence of express saccades, which we anticipated would be the case, given that express saccades are visually triggered (Fischer and Weber 1993) and that they cannot be generated without V1 (Boch 1989).

Rhesus monkeys were trained to make saccadic eye movements toward Gabor stimuli (sinusoidal luminance gratings spatially restricted within 2-dimensional Gaussian envelopes) that appeared either at the receptive field (RF) of the V1 cell under study or in the opposite hemifield. When a stimulus appeared at the RF, it matched the cell's preference in terms of size and orientation. As saccade latency decreased with increases in gap duration, the neural latency of V1 spike activity

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also decreased and the firing rate increased. The variability of neural latency was correlated with saccade latency on a trial-to-trial basis for identical gap conditions, and the variabilities of both neural and saccade latencies were correlated with the level of spontaneous activity of V1 before saccade target onset.

MATERIALS AND METHODS

Animal preparation. Two adult male monkeys (*monkeys DC* and *NB*; *Macaca mulatta*, 8–9 yr old) were used in the present study. The experimental procedures, including animal surgery and care, were approved by the Seoul National University Animal Care and Use Committee and, unless otherwise stated, were identical to those employed in a previous study (Lee et al. 2010).

Experimental procedures. During recording sessions, the animal was seated in a monkey chair with its head restrained. Extracellular potentials were recorded from V1 with platinum-iridium microelectrodes (Thomas Recording). For each recording session, the electrode and guide tube assembly was positioned at the dural surface and the electrode advanced with a five-channel minidrive (Thomas Recording), penetrating the dura. If an electrode broke during penetration or failed to record a single cell, the next electrode was advanced. The electrode impedance was 1–4 MΩ at 1 kHz. The neural signal from the electrode was amplified with a preamplifier at a gain of 20 and bifurcated to the main amplifiers for spike and local field potential signals, which were amplified with bandwidths of 0.5–9 kHz and 0.1–140 Hz, respectively (Thomas Recording). Eye position was monitored with a camera (ET-49, 230 Hz; Thomas Recording). Spike, local field potential, and eye position-related signals were digitized at a rate of 25 kHz with 16-bit resolution (PCI-6052E; National Instruments) and stored. The eye position signal was additionally digitized at a rate of 1 kHz by another computer that controlled the experimental sequence. We focus on the spike data in the present report.

The online determination that activity was from a single cell was based on the joint distribution of peak-to-peak duration and amplitude of action potentials. Once a single neuron was isolated, its RF position was roughly estimated with stimuli guided by a hand-operated computer mouse while the animal fixated on a spot. Then an optimal Gabor stimulus for the cell was quantitatively determined. For isolated single cells, we sequentially estimated the orientation, position (vertical and horizontal), and size of the Gabor stimulus that evoked the maximal activity while the monkey participated in a simple fixation task. Each of these parameters was estimated by plotting the mean spike count during a poststimulus period of 50–200 ms against the parameter dimension and by fitting the plot with a difference-of-Gaussians model with the least root mean squared error (Sceniak et al. 1999), using the following form:

$$s(x) = k_1 \exp\left[\frac{-(x-c)^2}{2\sigma_1^2}\right] - k_2 \exp\left[\frac{-(x-c)^2}{2\sigma_2^2}\right] + d$$

where s(x) is spike count for x of parameter dimension and k_1, k_2, c, and d are constants.

To determine the optimal stimulus size, circular Gabor stimuli ranging in diameter (defined as 5.5× the σ of Gaussian envelope function) from 0.2° to 2.0° in steps of 0.2° were presented at the center of the RF in randomly interspersed trials and the responses averaged over 5–10 trials for each size. The Gabor stimulus producing the maximal activity in a spatial summation test was taken as the optimal stimulus size. The mean (±SD throughout this report, unless otherwise specified) optimal stimulus size was 1.53 ± 0.13°, and the mean eccentricity of the optimal Gabor (and thus the RF) was 3.59 ± 0.29° in *monkey DC* and 4.17 ± 1.55° in *monkey NB*. Data were obtained from the left V1 in both monkeys. The spatial frequency of the Gabor stimulus was fixed at 2 cycles/°, and its contrast was 16% throughout the experiment for all cells, both of which were empirically chosen for eliciting vigorous neural responses and are within the range of known contrast sensitivity and spatial frequency selectivity (Albrecht and Hamilton 1982; De Valois et al. 1982). Although a constant spatial frequency may result in a delay in neural latency for some cells (Frazor et al. 2004), we opted for it because of time constraints resulting from testing multiple combinations of spatial frequency and contrast.

After the optimal stimulus was determined, the animal performed the gap saccade task (Fig. 1), under the control of computer programs written in MATLAB (The MathWorks) with the Psychophysics Toolbox (Brainard 1997; Pelli 1997). The task began with a 100-ms tone followed by the onset of a fixation target (0.3° × 0.3°, red dot) at the center of a gamma-corrected 24-in. flat CRT monitor (Sony GDM-FW900, 800 × 600, 100 Hz). The entry of gaze into a circular window of 1.5° diameter centered on the fixation target was taken as the time of fixation, and after a variable fixation duration a Gabor stimulus with a contrast of 16% was presented for 50 ms at the RF or at the location symmetrical to the RF in the opposite hemifield. The fixation duration was usually randomly varied between 400 and 600 ms, with steps of 50 or 100 ms, but on some occasions (<10%) the duration was varied between 250 and 800 ms. The animal's task was to make a saccade toward the Gabor stimulus within 600 ms of its onset, and maintain fixation for 300 ms, within a circular window of 2° diameter centered about the saccade target for a liquid reward. Eye positions were monitored with a camera (ET-49, 230 Hz; Thomas Recording) during the experiment and were corrected for delay in postprocessing.

Eye stability during fixation is obviously a concern when comparing neural activity across different conditions. Eye movements during fixation include microsaccades, drift, and tremor (Carpenter 1988). We derived an estimate of eye stability based on a metric,

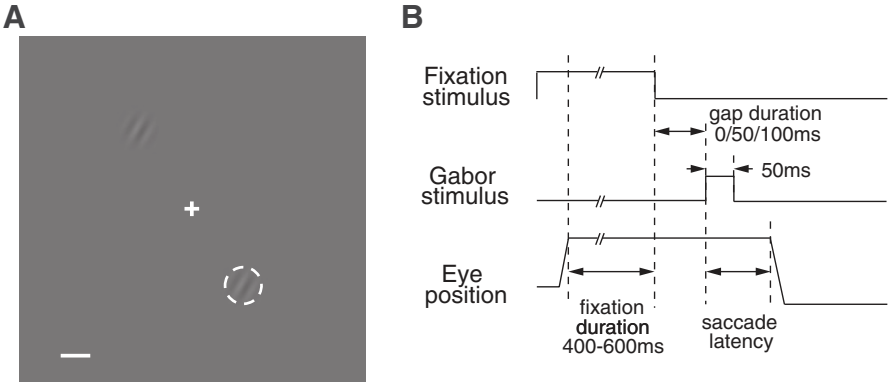

Fig. 1. Task paradigm. *A*: stimulus configuration. A white cross indicates the central fixation stimulus, and a dashed white circle (invisible to the animal) represents the boundary of the classical receptive field (for the example cell shown in Fig. 2). A Gabor stimulus in the RF or symmetrically across fixation served as a saccade target. The orientation matched for the cell's preference, whether presented in the RF or in the opposite hemifield. Scale bar, 1°. *B*: trial sequence of the gap saccade task. See text for details.

$$\mathrm{CV}(t) = \sum_{i=1}^{t} \sqrt{h_i^2 + v_i^2}$$

where CV(t) is the cumulative velocity of the eye from the start of an analysis window of interest to time t and h_i and v_i are instantaneous horizontal and vertical eye velocity at the ith bin of 1-ms width, respectively. We evaluated eye stability in behavioral data obtained from 20 sessions in the early phase of the study, during which various gap durations were employed. For this, we calculated CV(t), starting from 300 ms before saccade target onset, for each gap duration condition. It monotonically increased until ~150 ms after fixation target offset; then it started to increase rapidly. Thus with a gap duration of 200 ms eye fixation was already unstable at the time of saccade target presentation. This was not necessarily related to the occurrence of microsaccades, since the rate of monkey microsaccades is known to decrease as a trial progresses (Hafed et al. 2011). In any case, on the basis of these results, we limited the range of gap duration to 100 ms.

The trial conditions consisted of Gap0 (fixation offset and target onset occurring at the same time) and Gap50 and Gap100 (temporal gaps of 50 and 100 ms between fixation offset and saccade target onset, respectively) for both RF and RF-opposite sides. All trial conditions were pseudorandomized within a block. Because RF mapping lasted more than half an hour, in a given recording session data were obtained from only one cell. Once a monkey learned to hold the fixation target until its offset, it was successfully rewarded in >95% of the trials. If the animal failed a trial, which usually seemed to be caused by the animal's distraction, the failed trial condition was repeated at the end of the block.

Data analysis. The off-line procedures for sorting spikes and determining saccade latency, neural latency, and firing rate were identical to those employed in a previous study (Lee et al. 2010). In brief, saccade latency was defined with a velocity criterion of 15°/s. Spike density was derived by convolving the spike sequence with a kernel function of a total length of 150 ms:

$$R(t) = \left(1 - e^{-t/\tau_g}\right) \times \left(e^{-t/\tau_d}\right)$$

where τ_g and τ_d are time constants for the growth (1 ms) and decay (20 ms) phases, respectively (Thompson et al. 1996). Neural latency was defined as the time of the first spike after spike density crossed 1 SD above the mean density of the pretarget period of 200 ms and remained above the crossing level for at least 5 ms. The crossing point was searched backward from the peak density to avoid false discovery. Spike timing was downsampled to 1 kHz for subsequent analyses. Thus all temporal parameters of neural activity in this report have a 1-ms resolution.

Invalid trials were discarded during off-line analysis in three steps, based on behavioral, neural, and outlier criteria. The first step discarded trials in which the eye position overstepped the circular window of 2° diameter around the saccade target, eye velocity exceeded 50°/s during the saccade target presence for 50 ms, incorrect saccades were made, or saccade latency was <40 ms or >500 ms. These trials correspond to 12.6% of total trials. Additionally, for trials in which a saccade was made toward the RF, the second step discarded 12.9% of total trials: 8.3% of trials in which no neural discharge was discernible and 4.6% of trials in which neural latency could not be determined within a reasonable time window. The third step discarded the outlying trials corresponding to 4.7% of total trials in which saccade latency, firing rate during the posttarget period of 50–150 ms, or neural latency deviated >3 SDs from the mean of each trial condition.

Separation of express and regular-latency saccades. The distribution of saccade latency was often bimodal, with peaks for express and regular-latency saccade groups, particularly for rightward saccades (see below). We divided saccades into the two latency groups by fitting the frequency distribution of saccade latency with a six-parameter Gaussian model, $F(x) = A \times \mathrm{G}(\mu_1,\sigma_1) + B \times \mathrm{G}(\mu_2,\sigma_2)$, where $F(x)$ is the estimated frequency distribution of latency, x, in milliseconds, and A and B are the amplitude terms of two Gaussians with position and shape terms, μ and σ, respectively. For this fitting, we used raw latency, rather than its reciprocal (Carpenter 1981; Hall and Colby 2016), because goodness of fit was no worse with raw latency than that with its reciprocal in our data; for example, adjusted R^2 values for raw latency and its reciprocal (using cftool.m of MATLAB) were 0.98 and 0.94 for Fig. 10*I* and 0.99 and 0.99 for Fig. 10*J*, respectively. A least-square fit allowed us to identify a dip dividing the two groups within an experimental session. When bimodality was not apparent, the division latency was determined from the population distribution summed over all sessions for each gap duration condition for each animal, with this same least-square fitting method. The within-session division latency varied across sessions, and the mean division latencies for Gap0 and Gap50 conditions were longer than those based on the population distribution by 9.53 and 5.31 ms, respectively, and that for the Gap100 condition was smaller by 2.62 ms.

Detection of microsaccades. We identified microsaccades to determine whether their occurrence was related to the level of spontaneous discharge during the pretarget period before regular or express saccades. Provisional candidates were detected with a velocity criterion (>15°/s), and the onset and offset of microsaccades were determined with an acceleration criterion (550°/s^2) and visual inspection (Hafed et al. 2011; Kim et al. 2015). The velocity criterion was set high to avoid false positives in noisy recordings, but at the cost of missing of smaller-amplitude movements. With these criteria, we identified 5,259 microsaccades occurring in the 300-ms period spanning from 400 to 100 ms before target onset in 7,864 trials (4,252 before express saccades and 3,612 before regular saccades). Figure 2 illustrates one such example. Their mean amplitude was 21.22 ± 17.45 min arc.

Statistical test of difference in spike density. We statistically evaluated the difference in spike density between express and regular-latency saccade groups with a bootstrap procedure. The difference in spike density averaged with nonoverlapping windows of 5 ms was evaluated against the probability distribution derived from 1,000 simulations under the hypothesis of no difference. The tested window ranged from −250 ms to 150 ms of target onset. P values were controlled for incorrect rejections of the null hypothesis due to multiple comparisons by comparing the unadjusted P values with $(j/m) \times \alpha$, where j is the rank of the unadjusted P value, m is the number of comparisons, and α is the significance level (0.05 in this test). Unadjusted P values smaller than this quantity were accepted as significant (Hochberg and Benjamini 1990).

RESULTS

Data summary. These results are based on 74 single cells recorded from 74 sites in the left opercular V1 of two monkeys (45 in *monkey DC*; 29 in *monkey NB*) during 74 recording sessions. The mean recording depth from the dura surface was 1.33 ± 0.44 mm for *monkey DC* and 1.77 ± 0.44 mm for *monkey NB*. Although the dura was thinned every week, tissue drag during penetration was inevitable, and, accordingly, these numbers are rough estimates of the true cortical depth of recording sites and potentially contain considerable errors.

Effect of gap on V1 activity. Figure 3 illustrates the activity of a representative cell from *monkey DC* while it performed the task. With a gap duration of 0 ms (Gap0) most saccade latencies were around 200 ms (Fig. 3*A*), whereas with a gap duration of 100 ms (Gap100) most were around 100 ms (Fig. 3*C*). With a gap duration of 50 ms (Gap50), there were two latency groups, express and regular saccades (Fig. 3*B*). Accompanying the decrease in overall saccade latency as gap duration increased was a change in spike activity (Fig. 3*D*). The quantitative aspect of this change is given in Fig. 3*E*; with increases in gap duration, saccade latency decreased, the firing rate during the poststimulus period of 50–150 ms increased, and the neural latency decreased. The difference between Gap0

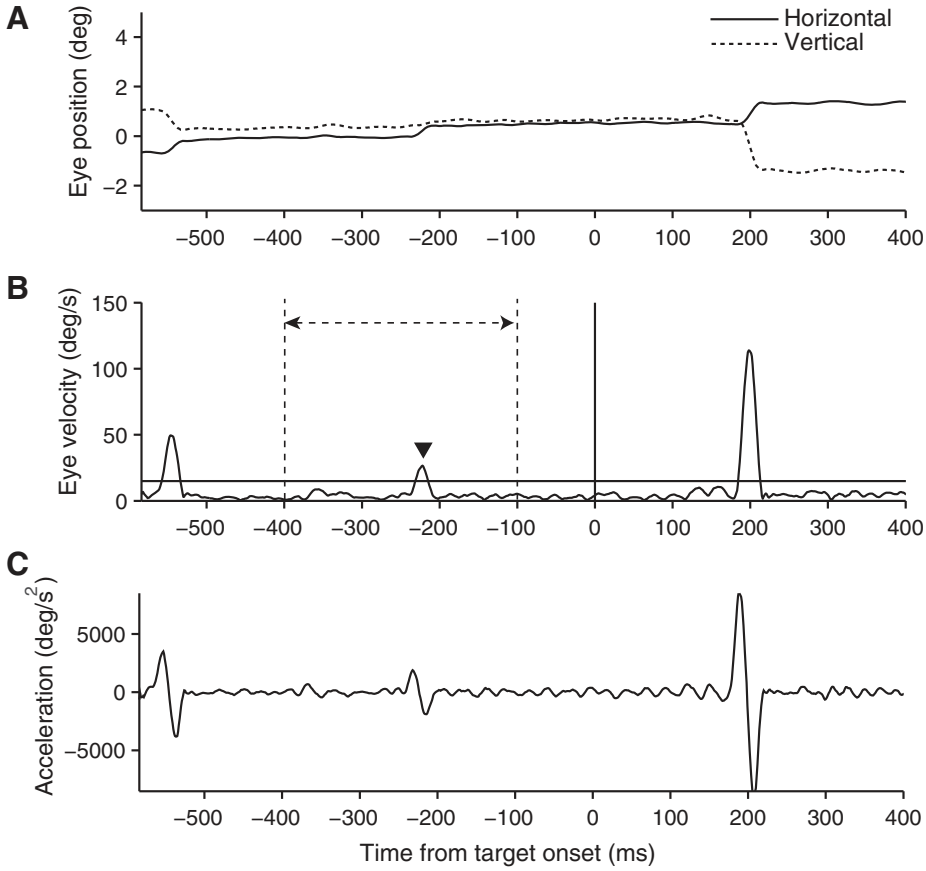

Fig. 2. Detection of microsaccades. *A*: horizontal and vertical eye position traces with respect to target onset. *B*: radial eye velocity trace of *A*, with the criterion of 15°/s (horizontal line) for detecting provisional microsaccades. Two dashed vertical lines represent the analysis period of 300 ms spanning from 400 to 100 ms before target onset (vertical solid line). Downward arrowhead indicates a detected microsaccade. *C*: eye acceleration trace of *B* with the criterion 550°/s^2.

and Gap100 was statistically significant for both firing rate and neural latency (Wilcoxon rank sum test, $P < 0.05$). Spike activity was similarly related to saccade type (express or regular latency) (Fig. 3, *F* and *G*): neural latency was shorter (Wilcoxon rank sum test, $P < 0.01$) and firing rate tended to be higher before express saccades than regular saccades, but the difference in firing rate was not statistically significant (Wilcoxon rank sum test, $P > 0.1$).

Figure 4 illustrates the overall gap effect, plotting the data for the entire sample separately for each monkey. In agreement with previous studies (Dorris and Munoz 1995; Fischer and Boch 1983; Sparks et al. 2000), mean saccade latency decreased as the gap duration increased; the mean saccade latencies combined from the two monkeys were 164.91, 123.26, and 99.87 ms for Gap0, Gap50, and Gap100 conditions, respectively. The overall mean latency for the two monkeys was comparable, 132.56 ± 16.01 ms in *monkey DC* and 128.4 ± 16.67 ms in *monkey NB*, and the difference was not significant (Wilcoxon rank sum test, $P = 0.23$). However, the two monkeys showed a noticeable difference in the pattern of saccade latency distribution. Although the proportion of express saccade increased with gap duration in both (Fig. 4, *A*–*F*), the separation between express and regular-latency saccade groups was larger and more distinctive in *monkey DC* (Fig. 4, *A* and *B*) than in *monkey NB* (Fig. 4*E*).

The difference between animals in neural activity evoked by the saccade target was also noticeable. The overall mean firing rate of *monkey DC* was 54.34 ± 23.57 spikes/s, which was higher than that of *monkey NB* (38.58 ± 22.01 spikes/s; Wilcoxon rank sum test, $P < 0.005$). The overall mean neural latency of *monkey DC* was 65.15 ± 9.77 ms, which was shorter than that of *monkey NB* (82.39 ± 17.30 ms; Wilcoxon rank sum test, $P < 10^{-4}$). These differences were possibly due to suboptimal RF mapping in *monkey NB*, which tended to be intolerant of the extended fixation task that was required before the main saccade task, which often lasted more than half an hour. Alternatively, *monkey NB*'s larger variability in neural activity during the pretarget period (see Fig. 11) might have resulted in a heightened threshold for determining neural latency, and thus a longer neural latency. Despite these differences, the mean neural latency decreased and mean firing rate increased for longer gap duration in both monkeys (Fig. 4, *G* and *H*); the *P* values from Kruskal-Wallis tests for the gap effect on firing rate and neural latency were 1.30×10^{-15} and 9.65×10^{-20}, respectively, for *monkey DC* and 0.014 and 1.48×10^{-3}, respectively, for *monkey NB*.

Trial-to-trial correlation. Figure 5 shows the general relationship between neural latency and saccade latency: a scatterplot for a representative cell (Fig. 5*A*) and histograms of Spearman's rank correlation coefficients for all 74 cells recorded from the two monkeys, regardless of gap duration and saccade type (express vs. regular) (Fig. 5*B*). Overall, the mean correlation coefficient between neural latency and saccade latency (Fig. 5*B*) was 0.10 (±0.12) and significantly different from zero (*t*-test, $P < 10^{-9}$). In 17 of 74 cells (22.9%) the correlation was significant ($P < 0.05$; Fig. 5*B*), and the mean coefficient of these cells was 0.23 (±0.06). This was consistent for both animals: for *monkeys DC* and *NB*, the mean Spearman correlation coefficient between neural latency and saccade latency was 0.11 ± 0.11 ($P < 10^{-7}$) and 0.08 ± 0.12 ($P <$

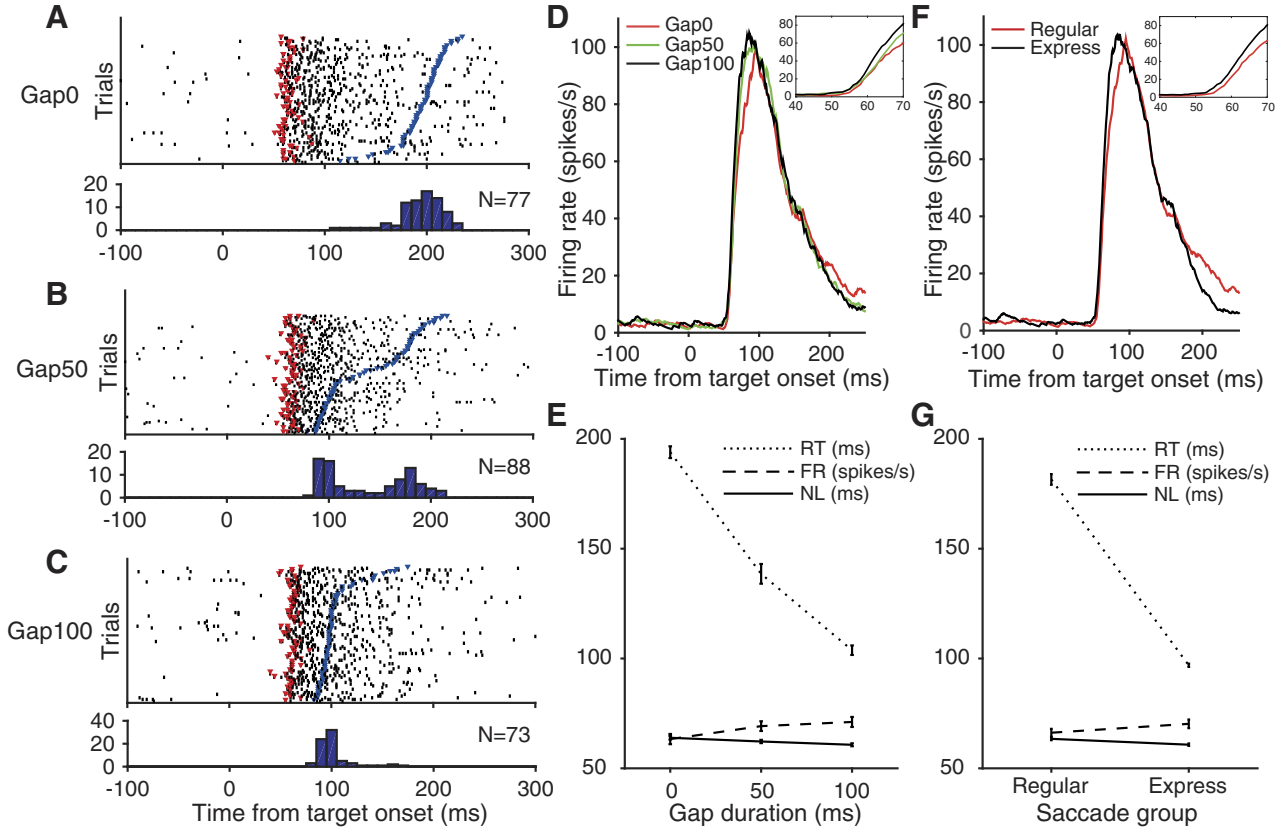

Fig. 3. Spike activity of a representative cell during the gap saccade task. *A–C*: raster plots (*top*) and saccade latency histograms (*bottom*) for gap durations of 0 (*A*), 50 (*B*), and 100 (*C*) ms. Raster plots are sorted according to saccade latency, as indicated with blue symbols. First spikes are marked with red symbols. Number of trials (*N*) is given for each panel. *D*: spike density plots of the same data. *E*: quantitative summary for the cell. Mean saccade latency (RT), firing rate (FR) during the poststimulus period of 50–150 ms, and neural latency (NL), with standard errors, as functions of gap duration. *F*: spike density plots for express and regular saccades. *Insets* in *D* and *F* show the activity increase in a finer timescale. *G*: same as *E* but for express and regular saccade groups.

0.005), respectively. The mean value of the Spearman partial correlation coefficient between neural latency and saccade latency controlling the gap duration for 74 cells was 0.05 ± 0.12 ($P < 10^{-3}$). Thus earlier neural latency was associated with shorter saccade latency.

A significant correlation between neural latency and saccade latency can introduce a "false" correlation between firing rate and saccade latency when firing rate is computed over a period defined with respect to target onset (Lee et al. 2010). Consistent with this, whereas the mean Spearman correlation between firing rate computed from 50 to 150 ms after target onset and saccade latency was -0.05 ± 0.10 ($P < 0.005$) and -0.08 ± 0.15 ($P < 0.005$) for *monkeys DC* and *NB*, respectively, the Spearman correlation between saccade latency and firing rate computed over a period of 100 ms starting from neural latency became less significant: -0.02 ± 0.10 ($P = 0.08$) for *monkey DC* and -0.06 ± 0.15 ($P = 0.02$) for *monkey NB*. Similarly, the correlation computed over a shorter period of 50 ms starting from neural latency became less significant: -0.03 ± 0.10 ($P = 0.05$) for *monkey DC* and -0.04 ± 0.18 ($P = 0.23$) for *monkey NB*. We also found a weak link between peak firing rate and saccade latency: the Spearman correlation coefficient between them was -0.03 ± 0.09 ($P < 0.05$) for *monkey DC* and -0.07 ± 0.16 ($P < 0.05$) for *monkey NB*.

Difference in V1 activity between express and regular saccades. A singular feature of the latency distribution during the gap saccade task is its occasional bimodality. The latency of the earlier mode, typically ~100 ms, characterizes express saccades, and that of the later mode characterizes regular-latency saccades. Since the generation of express saccade may not be simply a shortening of saccade latency, we document the neural activity related to gap duration regardless of the occurrence of express saccades and that related to express saccade occurrence regardless of gap duration.

Figure 6 illustrates the differences in neural latency between express and regular-latency saccades, averaged over all trials for 74 cells collected from the two monkeys. The neural latency was shorter before express saccades than before regular-latency saccades (Fig. 6*A*), by 4.40 ± 5.11 ms on average (*t*-test, $P < 10^{-9}$). When the above analysis was restricted to trials of the Gap50 condition, neural latency was similarly shorter by 3.97 ± 7.96 ms (*t*-test, $P < 10^{-4}$; Fig. 6*B*). The firing rate during the 50–150 ms after target onset for all trial conditions was higher for express with respect to regular-latency saccades by 2.94 ± 5.38 spikes/s on average (*t*-test, $P < 10^{-4}$) and similarly higher for the Gap50 condition, by 2.79 ± 7.44 spikes/s (*t*-test, $P < 0.005$) (not shown). The peak firing rate for express with respect to regular saccades on average for all three gap conditions and for Gap50 was higher by 2.90 ± 8.76 spikes/s (*t*-test, $P < 0.01$) and 1.56 ± 13.18 spikes/s ($P = 0.32$), respectively.

Note that the division of express and regular saccades shown in Fig. 6 was made within individual sessions. When the division was based on the population distribution of

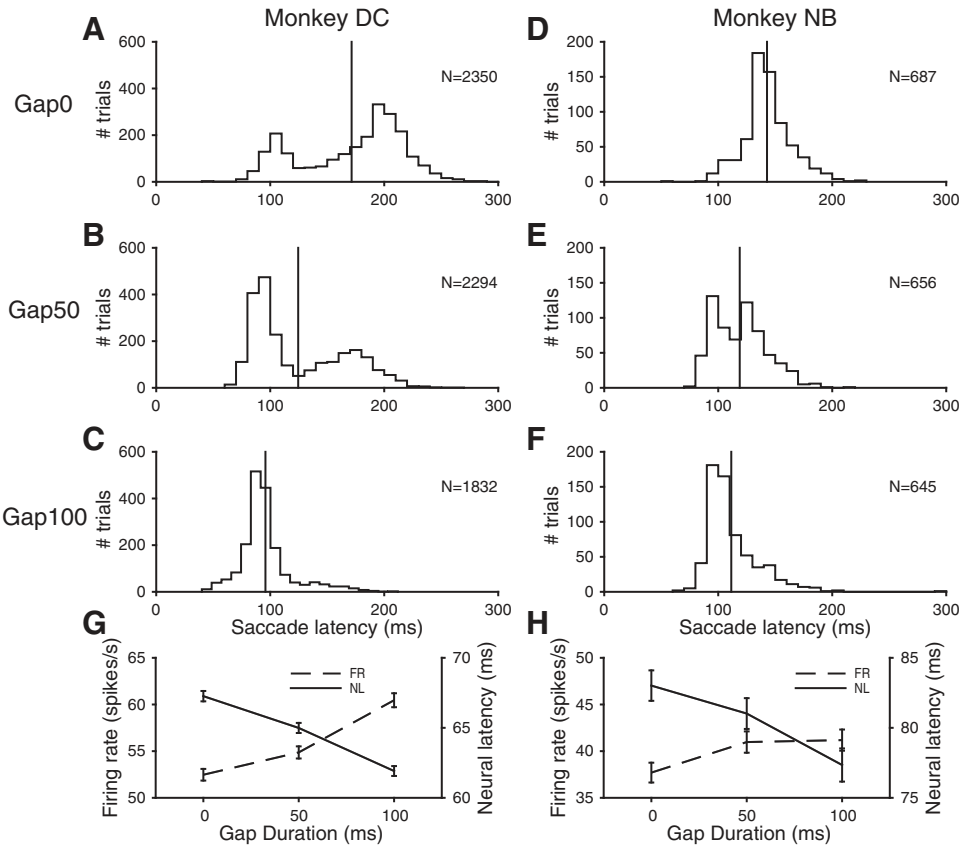

Fig. 4. Summary of the gap effects on saccade latency (*A–F*) and spike activity (*G* and *H*) for each monkey for all valid saccades made toward the RF that accompanied valid neural activity. *A–F*: mean saccade latency for each condition is indicated with a vertical line, showing a decrease as the gap duration increased from 0 (*A* and *D*), to 50 (*B* and *E*), to 100 (*C* and *F*) ms. Mean latency was 171.38, 124.53, 95.80 ms for *A–C*, respectively, and 142.79, 118.85, and 111.44 ms for *D–F*, respectively. Note that the distribution of saccade latency is bimodal in some conditions (*A*, *B*, and *E*). *G* and *H*: mean firing rate (FR) and neural latency (NL) vs. gap duration for *monkey DC* (*G*) and *monkey NB* (*H*).

saccade latency for each animal, the differences in neural latency and firing rate between express and regular-latency saccades were similarly significant (neural latency, $P < 10^{-6}$; firing rate, $P < 10^{-3}$).

Considering the possibility that the occurrence of express saccades and the gap effect are separate phenomena (Fischer and Weber 1993), we examined the changes in V1 activity due to an increased number of express saccades, or the gap effect. Figure 7 illustrates the saccade and neural latencies as a function of gap duration, divided into express and regular saccade groups for each animal. The mean latency of express as well as regular saccades varied with gap duration; the mean difference of express saccade latency between Gap0 and Gap100 conditions was significant (Wilcoxon rank sum test) in both animals: 28.09 ms ($P < 10^{-168}$) for *monkey DC* and 25.94 ms ($P < 10^{-53}$) for *monkey NB*. This indicates that the longer gap not only facilitated the occurrence of express saccades but also reduced their latency. This suggests that saccade latency can be predicted by two factors: saccade type (express or regular) and gap duration. This led us to estimate the independent contribution of these two factors to saccade latency. The mean Spearman partial correlation coefficient between saccade latency and gap duration after controlling saccade type was -0.53 (± 0.17, $P < 10^{-24}$) and -0.56 (± 0.23, $P < 10^{-12}$) across all sessions for *monkeys DC* and *NB*, respectively, suggesting that saccade latency is negatively correlated with gap duration regardless of saccade type. Similarly, the mean Spearman partial correlation coefficient between saccade latency and saccade type after controlling gap duration was 0.75 (± 0.08, $P < 10^{-42}$) and 0.68 (± 0.14, $P < 10^{-20}$) for *monkeys*

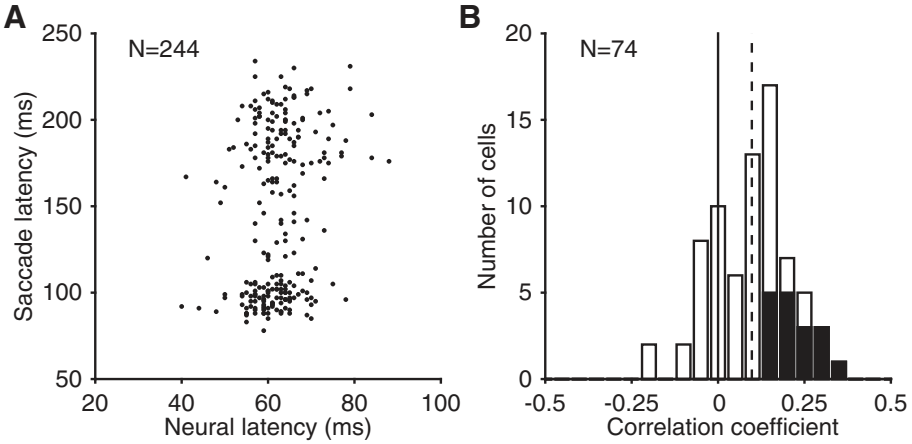

Fig. 5. Relationship between neural latency and saccade latency. *A*: scatterplot between neural latency and the latency of each saccade for a representative cell. The Spearman rank correlation coefficient between neural latency and saccade latency is 0.21 ($P < 10^{-3}$). *B*: histograms of Spearman rank correlation coefficient from 74 cells from 2 animals between neural latency and saccade latency. Dashed vertical line is the mean ($r = 0.10$). Filled bars indicate individual cells with significant correlations ($P < 0.05$).

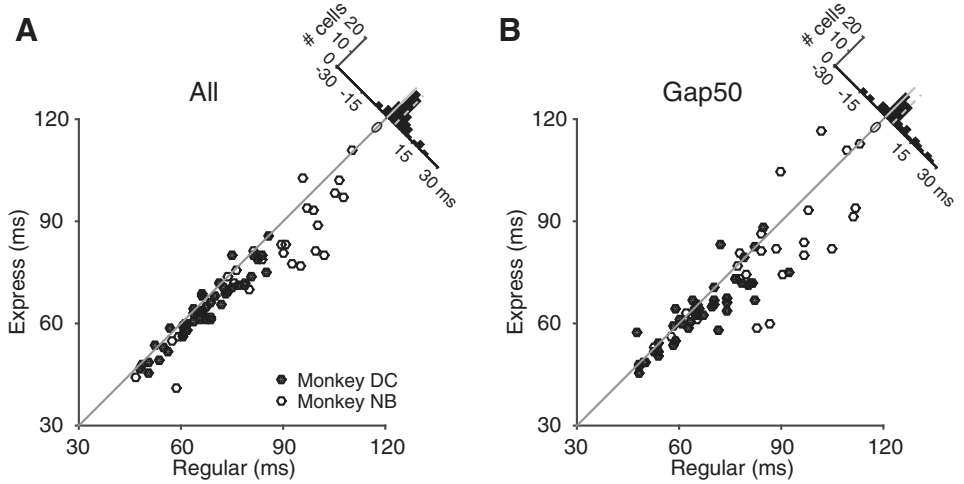

Fig. 6. Comparison of neural latency for all 74 cells from both monkeys between express and regular saccades for all conditions (*A*) and Gap50 (*B*). Each symbol represents the mean neural latency (ms) for each cell from *monkey DC* and *monkey NB*. Histograms at *top right* plot the difference, regular minus express, and its mean (dashed line) and zero (solid line).

DC and *NB*, respectively. This significant correlation suggests that the occurrence of express saccades is not fully explained by gap duration.

Similarly, we estimated independent contributions of saccade type and gap duration to neural latency. The mean Spearman partial correlation coefficient between neural latency and saccade type after controlling gap duration was 0.07 ($\pm$0.09, $P < 10^{-5}$) and 0.11 ($\pm$0.14, $P < 10^{-3}$) for *monkeys DC* and *NB*, respectively, suggesting that neural latency is weakly but significantly correlated with saccade type regardless of gap duration. The mean neural latency for express and regular saccades averaged across all gap conditions was 63.9 $\pm$ 9.7 ms and 65. 96 $\pm$ 10.37 ms, respectively, for *monkey DC* (the difference, 1.73 ms, is significant; *t*-test, $P < 0.01$) and 77.41 $\pm$ 19.27 ms and 83.91 $\pm$ 18.89 ms, respectively, for *monkey NB* (the difference, 5.62 ms, is significant; *t*-test, $P < 10^{-3}$). These results indicate that the occurrence of express saccades is mirrored in neural latency of V1 activity, supporting the idea that express saccades are visually triggered (Fischer and Weber 1993). The mean Spearman partial correlation coefficient between neural latency and gap duration after controlling for saccade type was -0.04 ($\pm$0.10, $P < 0.01$) and -0.04 ($\pm$0.12, $P = 0.08$) for *monkeys DC* and *NB*, respectively. Overall, the results from the above partial correlation analyses suggest that independent contributions of saccade type and gap duration to neural latency, while weak, are present. We note that although the mean Spearman partial correlation coefficient between neural latency and saccade type after controlling gap duration was significant (see above), the correlation between neural and saccade latencies within each saccade type for each animal was insignificant ($P > 0.07$), except for one condition of express saccade in *monkey DC*

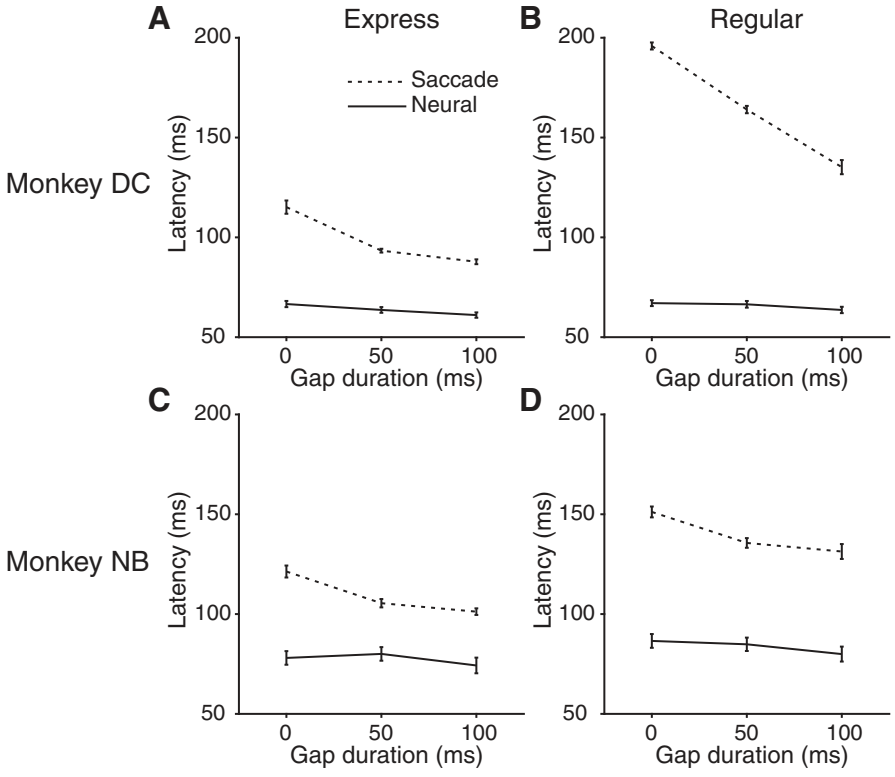

Fig. 7. Effects of gap duration on the saccadic and neural latencies of express (*A* and *C*) and regular (*B* and *D*) saccades for *monkey DC* (*A* and *B*) and *monkey NB* (*C* and *D*). Each symbol represents the mean (averaged across cell's mean) and its SE, also shown in Table 1.

(Fig. 7*A*; $r = 0.04$, $P < 0.05$). We also note that the Spearman correlation coefficient between peak firing rate and saccade latency within each saccade type was negative but insignificant ($P > 0.10$), except for one condition of regular saccade in *monkey NB* (Fig. 7*D*; $r = -0.08$, $P < 0.05$).

Effects of behavioral state on saccade latency and V1 activity. Changes in behavioral state may influence saccade latency as a recording session progresses. If V1 activity also gradually changes in the progress of a session, the activity and saccade latency may be spuriously correlated, as has been shown for EEG and behavioral measures (Schaworonkow et al. 2015). To examine this possibility, we first determined whether saccade latency and firing rate gradually changed as a function of trial number of the corresponding saccade, in chronological order within a session. The mean polynomial coefficients (the coefficient of linear trend with a least-square fit) for saccade latency as a function of trial number were 0.014 ± 0.04 (*t*-test for deviation from 0 slope, $P = 0.01$) and -0.02 ± 0.04 ($P = 0.02$) for *monkeys DC* (45 sessions) and *NB* (29 sessions), respectively. Similarly, the coefficients for firing rate (spike density during the poststimulus period of 50–150 ms of saccade target onset) as a function of trial number were -0.00 ± 0.05 ($P = 0.97$) and -0.01 ± 0.07 ($P = 0.38$) for *monkeys DC* and *NB*, respectively. Thus there was a weak linear trend for overall saccade latency to increase in *monkey DC* and decrease in *monkey NB* in the progress of a session, but firing rate did not change significantly for either monkey. The Spearman correlation coefficient between neural and saccade latencies and its statistical significance did not change after controlling trial number, indicating that there was no effect of trial number; Spearman correlation coefficient between neural and saccade latencies combining all sessions from two animals and its partial correlation after controlling trial number were both 0.10 (± 0.12, $P < 10^{-9}$). However, a series of questions arises beyond these simple relationships. For example, do the latencies of express and regular saccades change independently? If so, the overall change in saccade latency is meaningless. Does the proportion of express and regular saccades change in the progress of a session? If so, is the change in saccade latency concomitant with the change in V1 activity? We attempt to answer these questions next.

When a linear regression was fitted with least squares to saccade latency vs. trial number separately for express and regular-latency saccades, the slope of the regression line for express saccades (averaged over the 69 sessions that had >10 express saccades) was 0.003 ± 0.024 and that of regular-latency saccades (averaged over the 66 sessions that had >10 regular saccade trials) was -0.006 ± 0.036. The distributions were not significantly different from 0 (*t*-test, $P = 0.32$ and 0.16, respectively). There were significant coefficients for express saccades in 13 sessions and for regular-latency saccades in 9 sessions. Interestingly, these significant coefficients were all positive for express saccades and all negative for regular saccades. Thus overall saccade latency did not change over the course of a session, but in 13 of 69 sessions (18.8%) express latency increased and in 9 of 66 sessions (13.6%) the regular latency decreased as the session progressed. Figure 8*A* illustrates the data on saccade latency from one site in which both coefficients were significant; the slope of the regression line fitted to the latency of express saccades was 0.008 ($P = 0.03$), and that for regular saccades was -0.027 ($P < 0.01$). Thus the separation in latency between express and regular saccades decreased as the session progressed. The proportions of express and regular saccades did not obviously differ across the session, in this or other sessions.

If both saccade latency and V1 activity concomitantly change in the progress of a session, the slope of the regression line between saccade latency and trial number would be correlated with the slope of the regression line between V1 activity and trial number. Figure 8, *B* and *C*, show the change in V1 activity for the same session in Fig. 8*A*. The slope of the linear regression line between firing rate and trial number was 0.049 (*t*-test, $P = 0.005$) for express and 0.037 ($P < 10^{-3}$) for regular saccades (Fig. 8*B*) and that between neural latency and trial number was 0.000 ($P = 0.96$) for express and -0.006 ($P = 0.19$) for regular saccades (Fig. 8*C*). Thus, for both express and regular saccades, firing rate increased, but neural latency did not change, as the trial number increased, which is

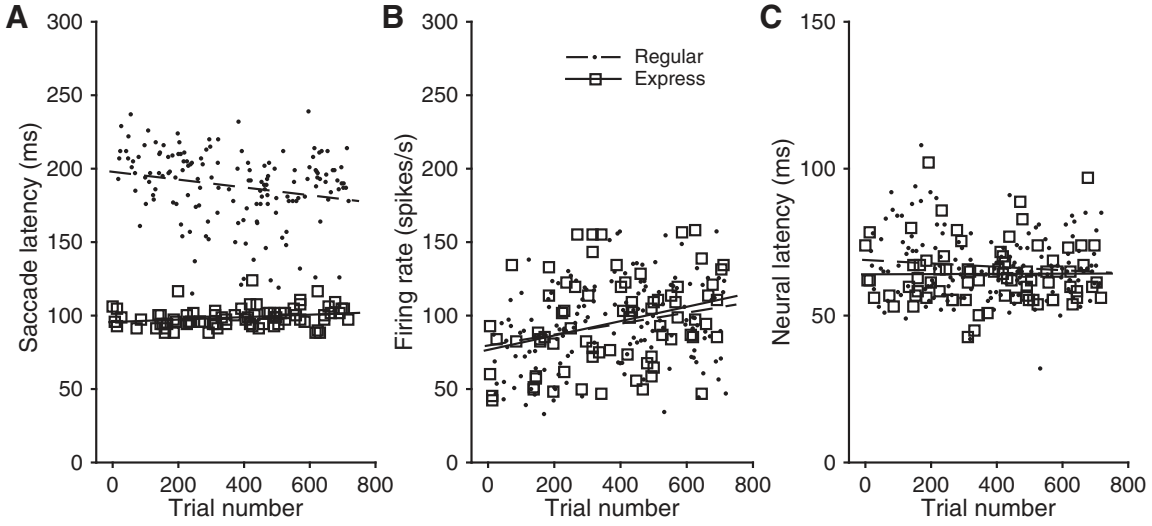

Fig. 8. Effects of behavioral state on saccade latency and firing rate: saccade latency (*A*), firing rate (*B*), and neural latency (*C*) as a function of trial number for an example session from *monkey DC*. Each symbol represents a regular or express saccade, and dashed and solid lines are linear regression lines for regular and express saccades, respectively.

not consistent with the pattern of change in saccade latency shown in Fig. 8*A*. We examined the relationship between these slopes for all 13 sessions in which the express latency increased in the progress of a session and for 9 sessions in which the regular latency decreased. The Pearson product-moment correlation coefficient between the two slopes, one between saccade latency and trial number and the other between neural latency and trial number, calculated from the 13 sessions in which the express latency increased, was −0.006, and this was not significant ($P = 0.99$). Similarly, the mean Pearson product-moment correlation coefficient between the two slopes, one between saccade latency and trial number and the other between firing rate and trial number, calculated from the same 13 sessions, was −0.28, and this was not significant ($P = 0.35$). These results indicate that in some sessions express latency increased over the course of a session, but this change did not accompany changes in V1 activity. Similar analysis for the nine sessions in which the regular latency decreased indicated no consistent relationship ($P > 0.1$). In summary, we found no evidence that saccade latency and neural latency of V1 concomitantly changed over the course of sessions and thereby produced a spurious correlation between them.

Pretarget activity correlated with neural and saccade latencies. In humans, the oscillatory cortical potential during the period preceding the onset of saccade target has been shown to correlate with saccade latency (Bompas et al. 2015; Drewes and VanRullen 2011; Everling et al. 1997; Hamm et al. 2010). This motivated us to determine whether the level of spike activity that immediately precedes the saccade target onset is correlated with saccade latency. For this purpose, we use the term "pretarget" instead of the "preparatory" discharge that has been used for describing the increasing activity of, among others, saccade-related neurons in the superior colliculus during the gap period (Dorris et al. 1997), for the following considerations. First, using the term "preparatory" for the V1 activity may be misleading, because it implicates a function that has not been proven. Second, the "preparatory" discharge in the superior colliculus was reported during the gap period (Dorris et al. 1997), whereas we did not examine this period, for the reasons outlined below. In previous studies on the gap effect, longer durations than those used in the present study were typical. For example, in Dorris et al. (1997) the gap duration could be up to 800 ms. In our study, we confined the gap duration within 100 ms because of the instability of the eye with longer gap durations (see below), because otherwise fixation-related eye movements such as microsaccades might have modulated V1 activity (Leopold and Logothetis 1998; Snodderly 2016). This limits the gap duration for studying V1. We calculated the mean pretarget spike density (PSD) from the temporal interval from 250 to 50 ms before saccade target onset. This interval covers most of the fixation duration but excludes the period in which spike activity is likely to be influenced by fixation stimulus onset or offset. Figure 9, *A* and *B*, show histograms of Spearman correlation between the PSD and saccade latency for each animal. The mean correlation coefficient was small but significantly negative (−0.08, $P < 10^{-7}$ in *monkey DC* and −0.07, $P < 0.05$ in *monkey NB*). The proportion of cells that showed a significant correlation was 13.3% (6 of 45) in *monkey DC* and 13.8% (4 of 29) in *monkey NB*, which is comparable to the proportion of buildup neurons in the superior colliculus for significant correlation between firing rate during fixation epoch and saccade latency (Table 1 of Dorris et al. 1997). Neural latency was negatively correlated with PSD (Fig. 9, *C* and *D*) in both animals (−0.05, $P < 10^{-3}$ in *monkey DC* and −0.12, $P < 10^{-3}$ in *monkey NB*). Thus a higher pretarget activity predicts a shorter neural latency and a shorter saccade latency.

We also examined the correlation between the PSD and the latency of saccades made toward targets presented in the hemifield opposite to the RF. Since all recordings were obtained from the left V1, these saccades were leftward. The distribution of saccade latency (Fig. 10, *A–F*) was mostly

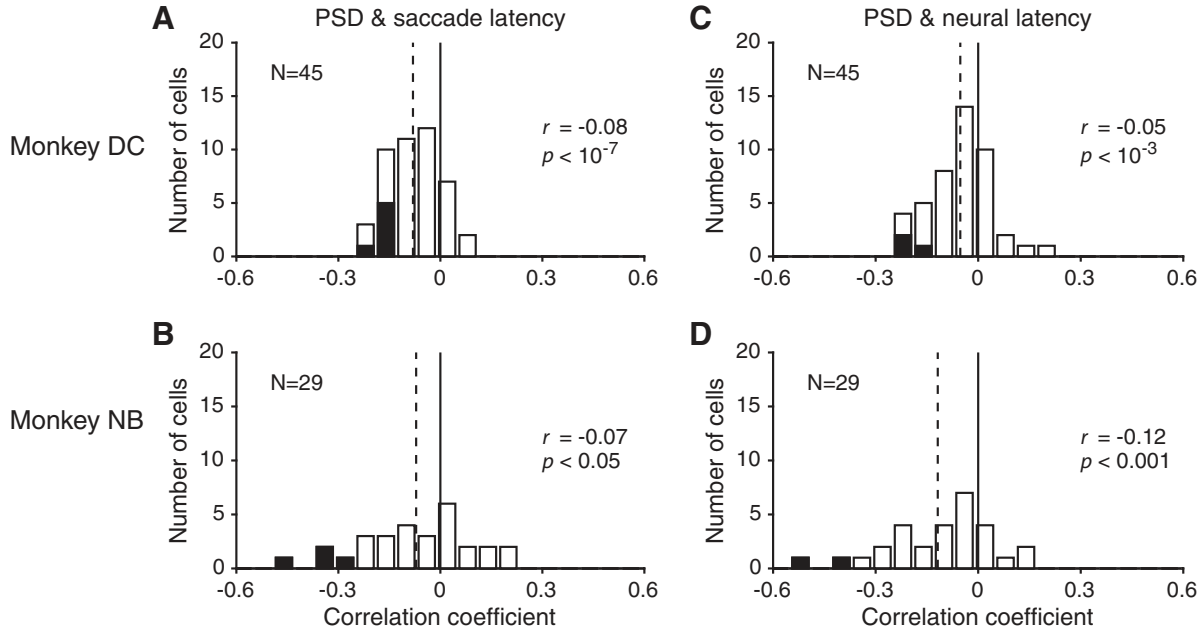

Fig. 9. Histograms of Spearman correlation coefficient between pretarget spike density (PSD) and saccade latency (*A* and *B*) and between PSD and neural latency (*C* and *D*). In each panel, filled and open bars indicate significant ($P < 0.05$) and nonsignificant coefficients, respectively, and the mean coefficient (dashed vertical line, *r*) and the *P* value from a *t*-test are given.

Table 1. *Saccade and neural latencies for Fig. 7*

Monkey	Saccade	Latency	Gap0	Gap50	Gap100
DC	Express	Saccade	115.15 (±3.32)	93.34 (±0.95)	87.78 (±1.21)
		Neural	66.66 (±1.55)	63.65 (±1.43)	61.08 (±1.34)
	Regular	Saccade	195.89 (±1.76)	164.03 (±1.83)	135.18 (±3.54)
		Neural	67.05 (±1.47)	66.47 (±1.67)	63.63 (±1.59)
NB	Express	Saccade	121.32 (±2.30)	105.44 (±2.09)	101.21 (±1.65)
		Neural	78.03 (±3.41)	80.04 (±3.41)	74.23 (±3.92)
	Regular	Saccade	151.16 (±2.72)	135.63 (±2.43)	131.34 (±3.73)
		Neural	86.55 (±3.45)	84.85 (±3.35)	79.96 (±3.74)

Values are means (±SE) of saccade and neural latencies in milliseconds for Fig. 7.

unimodal in both animals, unlike saccades made to the RF (Fig. 4). Nevertheless, the increase in gap duration systematically shortened saccade latency, as for saccades toward the RF: the mean latency for Gap0, Gap50, and Gap100 was 232.26, 206.51, and 190.74 ms, respectively, for *monkey DC* and 151.06, 143.69, and 136.58 ms, respectively, for *monkey NB*. Figure 10, *G–J*, show the combined latency histogram for each animal for saccades made to the target presented in the hemi-

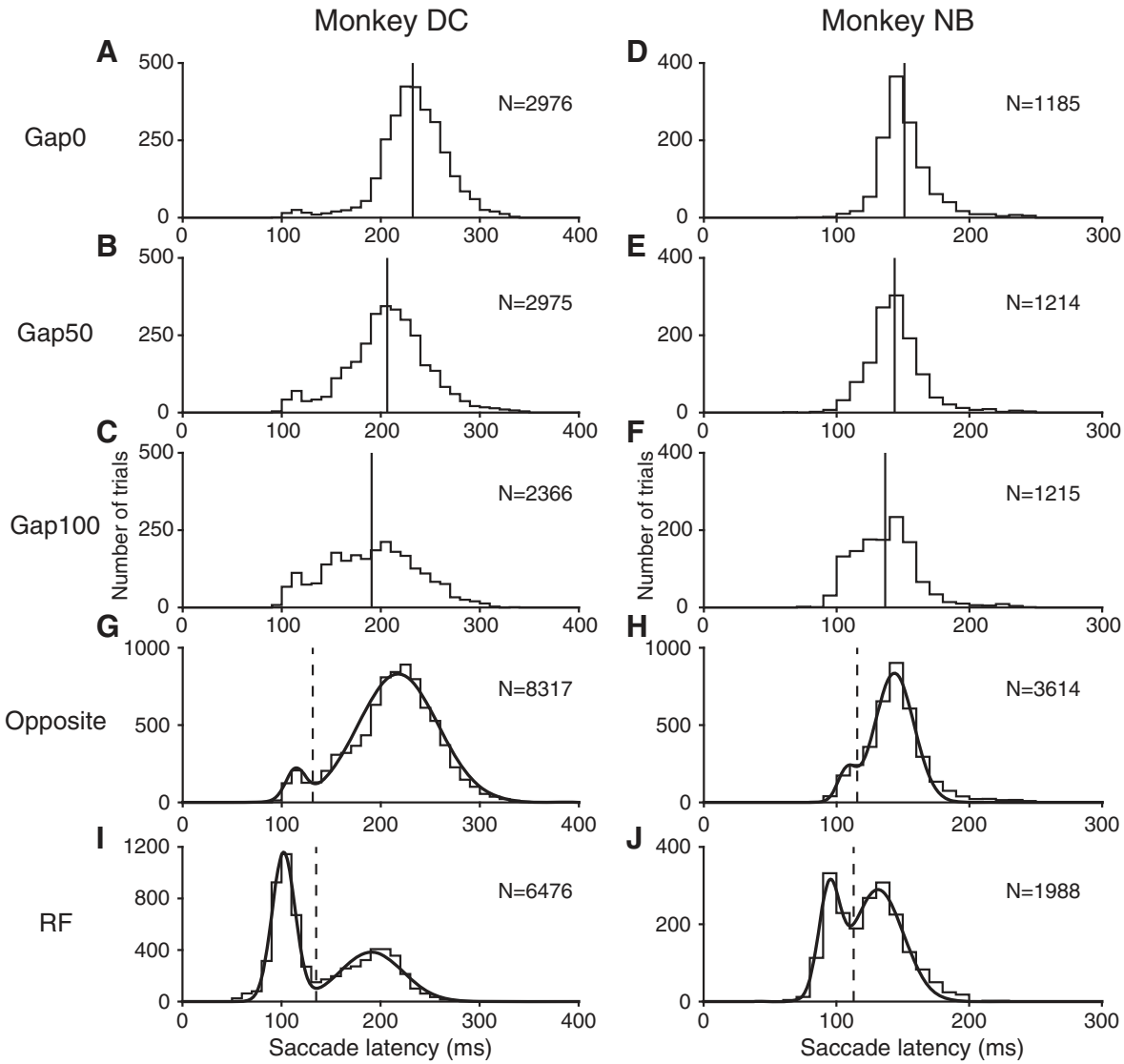

Fig. 10. Latency histograms of the saccades made toward targets presented in the hemifield opposite to the receptive field for Gap0, Gap50, and Gap100 for *monkey DC* (*A–C*) and *monkey NB* (*D–F*); vertical lines are the mean latency. *G* and *H*: histograms combined from *A–C* for *monkey DC* (*G*) and from *D–F* for *monkey NB* (*H*). *I* and *J*: latency histograms of the saccades made toward the target at the receptive field (RF), combined from Fig. 2, *A–C* (*I*) for *monkey DC* and from Fig. 2, *D–F* (*J*) for *monkey NB*. In *G–J*, thick curves are the fitted 2-Gaussian models. Dashed vertical lines are division latency between express and regular saccades; 131.3 (*G*), 115.5 (*H*), 135 (*I*), and 113 ms (*J*). Because of elimination of invalid trials for "RF" saccades based on spike activity, especially in *monkey NB*, the difference in the total number of trials between "Opposite" and "RF" saccades is pronounced.

field opposite to the RF (Fig. 10, *G* and *H*) and for saccades made to the target at the RF (Fig. 10, *I* and *J*). For saccades directed toward the RF, compared with those directed toward the opposite side ("Opposite"), express saccades were more frequent and the bimodal distribution was more distinct. RF mapping before the main saccade task possibly influenced this, because it is thought that although the gap reduces saccade latency regardless of training, express saccades depend on extensive exposure to targets (Dorris and Munoz 1995; Fischer and Ramsperger 1984; Rohrer and Sparks 1993). Intersubject variability in latency distribution (Gezeck et al. 1997; Gezeck and Timmer 1998; Nozawa et al. 1994) and asymmetry in latency distribution between rightward and leftward saccades (Gezeck and Timmer 1998; Sparks et al. 2000) have been noted previously. For Opposite saccades, the Spearman correlation coefficient between the mean PSD in the temporal interval 250 to 50 ms before target onset and saccade latency was 0.007 ± 0.096 ($P = 0.61$) for *monkey DC* and -0.05 ± 0.15 ($P = 0.09$) for *monkey NB*. Thus, in contrast to the "RF" saccades, we found no significant relationship between pretarget activity and saccade latency for Opposite saccades.

We have described above how the neural activity varied across cells in relation to saccade latency or occurrence of express saccades (Figs. 5, 6, and 9). We next consider the time course of the population spike density for express and regular saccades toward the target at the RF for each animal (Fig. 11). For this, for each animal the mean normalized spike density was first obtained for each cell and then averaged over all cells. The spike density pooled across cells was higher during the pretarget period before express saccades than that before regular saccades in both animals, but the difference tested for nonoverlapping windows of 5 ms was statistically insignificant in most analysis windows (Fig. 11, *C* and *D*). Overall, the mean difference in normalized firing rate during a 200-ms pretarget interval (250 to 50 ms before target onset) between express and regular-latency saccades was 0.007 ± 0.016 (*t*-test, $P = 0.007$) for *monkey DC* and 0.016 ± 0.08 (*t*-test, $P = 0.33$) for *monkey NB*.

In Fig. 11, *A*, *B*, *E*, and *F*, it also can be seen that the firing rate during the initial visual response after target onset was significantly higher for express than for regular saccades, consistent with the shorter neural latency and higher firing rate shown for individual cells in Fig. 6.

To determine whether a difference in eye stability between express and regular-latency saccade trials contributed to the difference in neural activity during the pretarget period, we compared estimates of eye stability between express and regular saccades with a metric described in MATERIALS AND METHODS, CV(*t*), the cumulative absolute radial velocity of the eye. When the overall cumulative velocity was averaged over all 74 cells, the cumulative velocity functions starting from 200 ms before target onset for express and regular-latency saccade trials closely overlapped within their individual standard errors until ~50 ms after target onset, which is about when saccades started (Fig. 12*A*). The mean absolute eye velocity over the pretarget period of 200 ms did not significantly differ between express and regular-latency saccade conditions (*t*-test, $P = 0.53$). Note that this metric is a crude estimate of fixational stability, and its accuracy is limited by our recording system, which only monitored one eye. Single-eye monitoring is inevitably insufficient for disconjugate fixational movements, such as drifts, leaving this outcome subject to confirmation by more refined studies. Furthermore, there was no difference in the occurrence of microsaccades between express and regular-latency saccade trials (Fig. 12*B*). The mean number of microsaccades during the 300-ms pretarget period from 400 to 100 ms before target onset in 7,864 trials was 0.67 (± 0.17) for

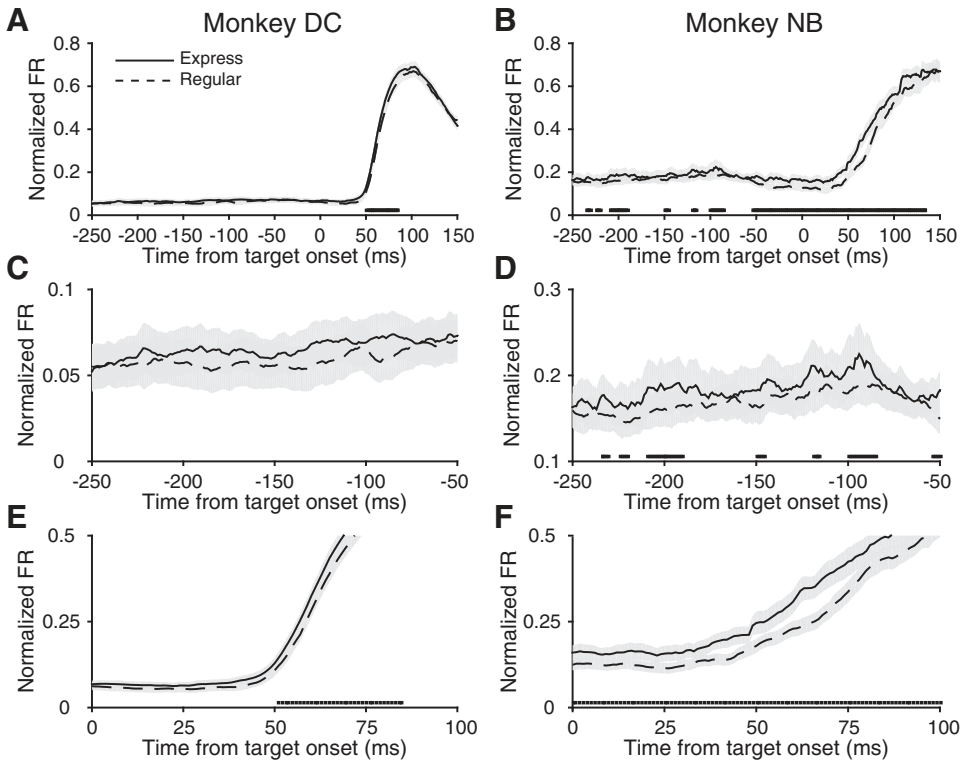

Fig. 11. *A* and *B*: comparison of spike density between express and regular saccade trials for *monkey DC* (*A*) and *monkey NB* (*B*). The numbers of express and regular saccades are 3,379 and 2,618 (*monkey DC*) and 873 and 994 (*monkey NB*), respectively. The spike density for each trial was first normalized to the maximum of each cell, averaged for express and regular saccades within each cell, and then averaged across all cells. *C* and *D*: blowup of pretarget spike density (PSD). *E* and *F*: blowup of posttarget spike density. One SE for the mean trace is indicated by shading. Marks above the *x*-axis represent the times of significant difference during 5-ms nonoverlapping windows, based on a bootstrap test ($P < 0.05$) and controlled for multiple comparisons.

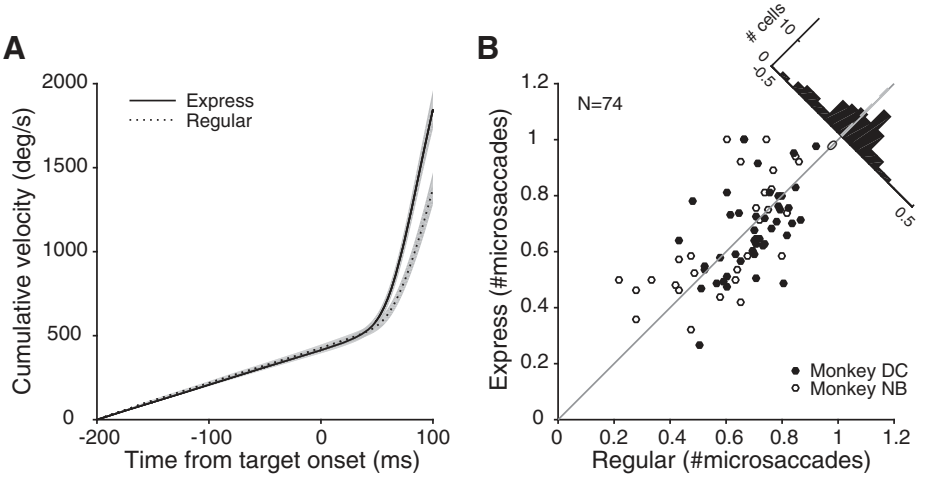

Fig. 12. Eye stability. *A*: mean CV(*t*), cumulative eye velocity functions for express and regular latency saccade conditions with 1 SE marked by shading. *B*: number of microsaccades that occurred during the 300-ms pretarget period from 400 to 100 ms before target onset. Each dot indicates the mean number of microsaccades in regular and express trials for each cell for each animal. Histogram at *top right* plots the difference in the number of microsaccades, regular minus express; its mean (dashed line) was −0.008 and nonsignificant (*t*-test, $P = 0.66$).

express saccade trials and 0.66 (±0.15) for regular-latency saccades, and this difference was not significant (*t*-test, $P = 0.66$). Similar results were obtained for each animal individually ($P = 0.22$ for *monkey DC* and $P = 0.07$ for *monkey NB*). During central fixation there was no visual contrast within the RF. Thus microsaccade-induced neural activity (Bosman et al. 2009; Kagan et al. 2008; Martinez-Conde et al. 2000) is not likely to explain this difference between express and regular saccades, even if there was a difference in occurrence of microsaccades, especially for small-amplitude microsaccades that we may have failed to detect. Thus we conclude that the difference in spike activity between express and regular saccades during the pretarget period was not related to differences in stability of eye fixation.

We next examined the possibility that the pretarget activity is related to performance in the preceding trial. It has been reported previously that monkey saccade latency (Dorris et al. 2000) and the occurrence of human express saccades (Carpenter 2001) are influenced by the preceding saccade direction (but see Bompas and Sumner 2008). We examined our data to determine whether the differential pretarget activity between express and regular saccade trials was related to the saccade order effect. When a saccade had been made in the preceding trial in the same direction as the current trial, saccade latency was nonsignificantly shorter by 1.69 ms, on average, than saccades in the opposite direction (*t*-test, $P = 0.09$). The differences between the same and opposite direction conditions in neural latency (0.07 ms) and firing rate (0.07 spikes/s) were not significantly different ($P = 0.89$ and 0.92, respectively). When two preceding saccades had been made in the same direction as the current trial, with respect to the opposite direction the difference in saccade latency increased to 2.21 ms, consistent with a previous report (Dorris et al. 1997), but this difference was also nonsignificant (*t*-test, $P = 0.11$). In this comparison, the difference in neural latency was 0.27 ms (*t*-test, $P = 0.68$), that for firing rate was 0.34 spikes/s (*t*-test, $P = 0.73$), and that for spike density during the 200-ms pretarget period was 0.25 spikes/s (*t*-test, $P = 0.59$). We conclude that the preceding saccade direction did not influence V1 activity during either pretarget or posttarget periods in our experimental paradigm. Note that the two potential saccade targets were diagonally symmetrical across fixation in our experiment, so that the return saccade from the target in the opposite hemifield in the previous trial is the same vector as that required if the target appears at the RF in the current trial, preserving order effects, if any.

Another type of saccade order effect has been reported, in which after express saccades were made in previous trials, regardless of gap duration, the percentage of express saccades increases, whereas after regular saccades the percentage of express saccades is significantly reduced (Paré and Munoz 1996). Consequently, we examined the possibility that pretarget activity reflects a manifestation of such effect. From the same data set used for Figs. 9 and 12, we isolated those trials in which saccades were made toward the RF with express latency after a saccade was made toward the RF in the immediately preceding trials: 765 trials from 45 sessions in *monkey DC* and 188 trials from 25 sessions in *monkey NB*. The percentage averaged across sessions for express saccade occurrence after an express saccade was made in the preceding trial was 55.52 ± 25.18% in *monkey DC* and 48.82 ± 33.4% in *monkey NB*, indicating that the proportion of express saccade occurrence was larger after an express saccade was made in preceding trials in *monkey DC* but not in *monkey NB* and both were statistically nonsignificant (*t*-test, $P = 0.15$, $P = 0.86$ for *monkeys DC* and *NB*, respectively). Our failure to confirm the order effect may be due to differences in experimental condition, such as the range of gap duration. The normalized firing rate during the pretarget period of −250 to −50 ms of target for the trials of express saccade tended to be higher after a express saccade, compared with a regular saccade, was made in the preceding trial in both monkeys: 0.07 ± 0.09 and 0.06 ± 0.09 *in monkey DC* and 0.19 ± 0.15 and 0.15 ± 0.15 in *monkey NB* for preceding express and regular saccades, respectively. These differences were not statistically significant (*t*-test, $P = 0.34$ and 0.22 for *monkeys DC* and *NB*, respectively). Thus we found no significant evidence that the pretarget activity reflected the influence from the saccade type or direction in the preceding trial.

DISCUSSION

Gap effects in V1. Changes in neural activity accompanying the behavioral gap effect have been previously described for the superior colliculus (Dorris and Munoz 1995; Edelman and Keller 1998; Sparks et al. 2000) and various extrastriate cortical regions, such as the lateral intraparietal area (Chen et al. 2013) and prefrontal cortex (Tinsley and Everling

2002). We found in the present study that changes in spike activity of V1 neurons also accompany the behavioral gap effect: saccade latency decreased with increases in gap duration, and, accompanying this change, the neural latency of V1 neurons decreased.

Are the changes in V1 activity during gap saccades compatible with the possibility that the superior colliculus confers gap-related effects on V1? The collicular visual-motor neuron activity is initially reduced ~60–70 ms after the offset of the fixation target (Sparks et al. 2000), and the buildup activity of superior colliculus changes ~100 ms after fixation offset in the gap saccade task (Dorris et al. 1997). Thus in the Gap100 condition, the times of first V1 spikes are within the window of potential influence from the collicular activity. In the Gap50 trials, however, first V1 spikes occur before the start of the activity reduction or buildup activity, and yet there were consistent gap effects on V1 activity (Fig. 4), suggesting that it is unlikely that the superior colliculus confers the gap effects on V1. Thus we conclude that the partial correlation between neural latency of V1 and saccade latency controlling for gap duration observed in the present study is not expected from the collicular contribution.

Turning off a fixation stimulus influences the latency of pursuit (Krauzlis and Miles 1996) and vergence (Takagi et al. 1995) eye movements, as well as saccades, suggesting a sensory origin for the gap effect. We suggest that V1 constitutes one such source. For most V1 neurons that respond to the visual saccade target, fixation offset is an event in the RF surround. In the gap paradigm, this would result in a surround interaction in which neural response to the RF stimulus is modulated by a focal stimulus in the RF surround (i.e., the fixation target), with a temporal gap between the offset of a surround stimulus and the onset of a RF stimulus. A focal stimulus presented in the distant surround zone of the RF, even in the hemifield opposite to the RF, can modulate the spike activity of V1 neurons evoked by a subsequently presented RF stimulus in a manner that depends on the temporal interval between the two stimuli (Kim et al. 2012, 2015). Thus the fixation target offset, a critical visual event for the gap effect, possibly interacts with ensuing spike generation evoked by the saccade target.

Potential link between neural latency of V1 and saccade latency. The significant correlation between V1 activity and saccade latency may indicate a link involving a functional role of V1, or alternatively a spurious relationship originating in a common source, such as attentional modulation of both V1 activity and saccade generation. In some sessions, saccade latency and/or V1 activity changed over the progression of the session, but the lack of correlation between these changes in latency and activity (Fig. 8) suggests that the trial-to-trial covariation between V1 activity and saccade latency is not a spurious relationship produced by long-term temporal structures of the influence of a common source.

Given the assumption that the V1 output provides stimulus information, such as its onset, to downstream stages, it appears that the trial-to-trial variability of neural latency of V1 in identical stimulus conditions is not noise that is rejected by pooling over a V1 population at downstream stages. Were this the case, the correlation between the neural latency of V1 and saccade latency should decrease as the pooled population increases in size. However, this prediction is not supported by the available data (Lee et al. 2010), suggesting that neurons downstream to V1 preserve, at least partly, the trial-to-trial variability of V1 spike activity through the stage of saccade generation. Nor is variation of V1 latency directly related to the variations in saccade latency. For example, neural latency is 4.37 ms shorter, on average, for express than for regular-latency saccades (Fig. 6*A*), which is far too small to account for the latency difference between express and regular saccades (79.9 ms for the saccades of Fig. 4*A*). This situation is comparable to that of the superior colliculus, where onset times of visual activity before express saccades precede those of regular-latency saccades for buildup and burst neurons by 3.1 and 2.4 ms, respectively (Dorris et al. 1997).

In addition to the small variability of neural latency compared with the variability of saccade latency, the magnitude of correlation between the neural latency of single V1 neurons and saccade latency may appear small (0.96; Fig. 5). However, we believe that the correlation increases with the size of the neural population from which the signals related to the response time are read (Lee et al. 2010). Furthermore, the variability in neural activity that is coupled to the variability in behavioral response must evolve along the visual-motor pathways through intervening stages between retinal and motor neurons whose activities are tightly coupled to stimulus and response timing, respectively—thus, from zero to perfect correlation with saccade latency (DiCarlo and Maunsell 2005). Therefore, one can expect that the magnitude of correlation between the neural latency of single V1 neurons and saccade latency increases as signals progress to the final motor stages, as has been shown for the latency of pursuit eye movements; the mean correlation coefficient between the latency of middle temporal visual area single neurons and pursuit latency is 0.15 (Lee et al. 2016), which is comparable to that found in the present study. Thus in explaining the origin of correlation between neural and saccade latencies, a gradual increase in the variability of saccade-related signals along the visual-motor pathway appears to be more parsimonious than a sudden appearance of full-range variability at the final motor system. Under gradual evolution of the signals related to behavioral response, a correlation that is close to zero would manifest an initial functional link. In terms of behavioral correlation, neural latency shows a stronger functional link than firing rate (Lee et al. 2010, 2016), and the larger correlation found between firing rate and behavioral responses does not necessarily mean a stronger functional link (Katz et al. 2016).

Functional significance of pretarget activity. Our analysis of the pretarget state of V1 was motivated by previous reports that cortical activity during the pretarget period is related to saccade latency (Bompas et al. 2015; Drewes and VanRullen 2011; Everling et al. 1997) and initiation of express saccades (Hamm et al. 2010). We found that although the pretarget spike density of V1 was low, it was significantly correlated with saccade latency and neural latency (Fig. 9). Overall, pretarget activity tended to be higher before express saccades than before regular-latency saccades (Fig. 11, *C* and *D*). Furthermore, when the pretarget activity was higher V1 neurons discharged earlier and saccadic latency was shorter. We emphasize that this difference should be distinguished from the difference in activity between express and regular saccades seen after saccade target onset, such as the buildup or previsual response of visual-motor neurons in the superior colliculus (Marino et al. 2015).

Thus it appears that the state of V1 is not fixed at the time of target presentation and that trial-to-trial variability in the state of V1 accompanies the variability in neural latency and the variability in saccade latency. These results represent, to our knowledge, the first cortical single-unit evidence consistent with reports that the oscillatory EEG potential during the pretarget period is correlated with initiation of human express saccades (Hamm et al. 2010) and that the spectral power of magnetoencephalography during the pretarget period obtained from wide cortical areas, including V1, is lower for fast than for slow saccades (Bompas et al. 2015).

The variability in pretarget spike activity may reflect a spontaneous change in global cortical state (Goris et al. 2014; Schölvinck et al. 2015), and thus the higher spike activity in V1 before express saccades relative to regular saccades may be a local manifestation of a more global regime for modulating visuo-saccadic signal processing. This may include the cholinergic activation that is thought to be related to generation of fast responses (Yu and Dayan 2005) and, in particular, express saccades (Aizawa et al. 1999). Other influences, such as dynamic alterations of cortical state (Arieli et al. 1996; Steriade et al. 1993) originating within the visual cortex (Sanchez-Vives and McCormick 2000) or outside the cortex (Park et al. 2014; Sirota and Buzsáki 2005), can be considered. However, our finding that, in contrast to the RF saccades (Fig. 9), the Opposite saccades showed no significant correlation between the pretarget activity and saccade latency in our experimental condition suggests that the mechanism can be confined to within one hemisphere.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

K.K. and C.L. conceived and designed research; K.K. performed experiments; K.K. and C.L. analyzed data; K.K. and C.L. interpreted results of experiments; K.K. and C.L. prepared figures; K.K. and C.L. drafted manuscript; K.K. and C.L. edited and revised manuscript; K.K. and C.L. approved final version of manuscript.

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