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# Temporal Interactions of Air-Puff–Evoked Blinks and Saccadic Eye Movements: Insights Into Motor Preparation

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**Gandhi, Neeraj J. and Desiree K. Bonadonna.** Temporal interactions of air-puff–evoked blinks and saccadic eye movements: Insights into motor preparation. *J Neurophysiol* 93: 1718–1729, 2005. First published October 6, 2004; doi:10.1152/jn.00854.2004. Following the initial, sensory response to stimulus presentation, activity in many saccade-related burst neurons along the oculomotor neuraxis is observed as a gradually increasing low-frequency discharge hypothesized to encode both timing and metrics of the impending eye movement. When the activity reaches an activation threshold level, these cells discharge a high-frequency burst, inhibit the pontine omnipause neurons (OPNs) and trigger a high-velocity eye movement known as saccade. We tested whether early cessation of OPN activity, prior to when it ordinarily pauses, acts to effectively lower the threshold and prematurely trigger a movement of modified metrics and/or dynamics. Relying on the observation that OPN discharge ceases during not only saccades but also blinks, air-puffs were delivered to one eye to evoke blinks as monkeys performed standard oculomotor tasks. We observed a linear relationship between blink and saccade onsets when the blink occurred shortly after the cue to initiate the movement but before the average reaction time. Blinks that preceded and overlapped with the cue increased saccade latency. Blinks evoked during the overlap period of the delayed saccade task, when target location is known but a saccade cannot be initiated for correct performance, failed to trigger saccades prematurely. Furthermore, when saccade and blink execution coincided temporally, the peak velocity of the eye movement was attenuated, and its initial velocity was correlated with its latency. Despite the perturbations, saccade accuracy was maintained across all blink times and task types. Collectively, these results support the notion that temporal features of the low-frequency activity encode aspects of a premotor command and imply that inhibition of OPNs alone is not sufficient to trigger saccades.

## INTRODUCTION

The conduction time required for neural signals to travel from the retina to the extraocular muscles is significantly shorter than the typical reaction time (~200 ms) of saccadic eye movements (Carpenter 1981). Sensory activation in neurons is observed ~60 ms after target onset, and the premotor burst precedes movement onset by ~20 ms, leaving >100 ms for sensorimotor integration. During this period, activity in saccade-related burst neurons across the oculomotor neuraxis is represented as a gradually increasing low-frequency discharge (reviewed by Munoz and Schall 2004). As shown for a subset of neurons in the frontal eye fields and superior colliculus (Hanes and Schall 1996; Paré and Hanes 2003), when the firing rate reaches a threshold activation level, they discharge a high-frequency volley of action potentials, leading to an inhibition of the pontine omnipause neurons (OPNs) that gate the saccadic system and an initiation of the desired movement. It has been suggested that the low-frequency activity, particularly in collicular neurons, represents a motor preparation signal (Dorris and Munoz 1998) that encodes both timing (Dorris et al. 1997; but also see Sparks et al. 2000) and metrics (Basso and Wurtz 1997; Glimcher and Sparks 1992, 1993; Gold and Shadlen 2000) of the planned movement.

The OPNs discharge at a tonic rate during fixation and abruptly cease their discharge during saccades (Cohen and Henn 1972; Keller 1974; Luschei and Fuchs 1972). We wondered whether transiently inhibiting the OPNs in advance of when they ordinarily pause effectively lowers the activation threshold level, permitting the oculomotor pathway to prematurely trigger a saccade of modified metrics and/or dynamics. Testing this hypothesis requires an experimental technique to quench OPN activity on a trial-by-trial basis. A few investigators have briefly noted that OPNs cease discharge during not only saccades but also blinks (Cohen and Henn 1972; Fuchs et al. 1991; Mays and Morrisse 1994). Since saccades and blinks are often temporally coupled (Evinger et al. 1994; Goossens and Van Opstal 2000a; Zee et al. 1983), it becomes difficult to determine whether the pause in activity is associated with the blink or the saccade. A blink evoked during visual *fixation*, however, is accompanied with only a small eye movement and the duration of the blink far outlasts the duration of the eye movement (Mays and Morrisse 1994). The duration of pause in OPNs is positively correlated with the duration of the blink, it is longer than the duration of the small eye movement associated with the blink, and the onset of the pause is tightly linked with the onset of the eyelid movement (Mays and Morrisse 1994). For saccades accompanied by blinks, saccade duration is typically shorter than the blink duration (Rambold et al. 2002; Rottach et al. 1998). The corresponding pause in OPN discharge outlasts saccade end, and pause duration is better correlated with blink duration (L. E. Mays, personal communication). In addition, microstimulation of the OPN region inhibits eye blinks (Mays and Morrisse 1995). Collectively, these results make a compelling argument that the pause in OPN discharge is related to blinks, not just eye movements.

Thus to indirectly test whether premature OPN inhibition effectively lowers the activation threshold level, we evoked blinks in monkeys (by delivering an air-puff to one eye) during various epochs of standard oculomotor tasks and recorded the

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resulting eye movement. We predicted that if the low-frequency activity contains a premotor component, the blink would trigger an eye movement. Most studies of saccade–blink interactions have reported a reduction in saccade latency, but blinks were evoked only near the average saccade reaction time (Evinger et al. 1994; Goossens and Van Opstal 2000a). We tested this hypothesis formally by delineating the interval during which blink-induced perturbations alter saccade latency, metrics, and kinematics.

## METHODS

### *Animal preparation*

Two rhesus monkeys (*Macaca mulatta*) weighing 5–8 kg were used for the study. All experimental protocols were approved by the Institute Animal Care and Use Committee at the University of Pittsburgh and complied with the guidelines of the Public Health Service policy on Humane Care and Use of Laboratory Animals. Each monkey underwent surgery in a sterile environment and under isoflurane or halothane anesthesia. A Teflon-coated stainless steel wire was implanted under the conjunctiva of one eye to measure eye position signals using the magnetic search coil technique (Robinson 1963). In one monkey, a stainless steel post, secured by stainless steel screws and bone cement, was placed on the skull for immobilizing the head (Gandhi and Sparks 2001). In the second monkey, head restraint was implemented using three lugs built from dental acrylic layers about stainless steel screws attached to the skull. One lug was positioned at the top front center of the skull and two at the back sides behind the ears (Balaban et al. 2002).

### *Behavioral tasks and experimental procedures*

Each monkey, seated in a primate chair, was placed in a dimly lit room, ~70 cm away from a visual display consisting of tri-state light emitting diodes (LEDs). The LEDs were spaced at 2° intervals on a cut cylindrical screen that spanned 96 and 80° in the horizontal and vertical dimensions, respectively. A PC operating on a Pentium-4 processor and running an in-house program written in LabView RT controlled all aspects of data acquisition (Bryant and Gandhi 2005). Real-time control and collection of eye and eyelid movement data were performed at 1 KHz.

The monkeys were trained to perform visually guided step, gap, and delayed saccade tasks. To generate sufficient data, each experimental session, referred to as a dataset, typically consisted of only one behavioral condition. Each trial began with the onset of a fixation point at straight-ahead location, and the monkey was required to fixate it within a 2° window for a randomly selected interval (300–600 ms, in increments of 100 ms). In the step task, the fixation point was extinguished, and simultaneously, a saccade target was illuminated. In the gap task, a 200-ms constant duration elapsed between fixation offset and target onset. In the delayed saccade task, both targets were simultaneously illuminated for a randomly selected duration (200–800 ms, in increments of 100 ms), and the monkey had to maintain central fixation during this overlap period. The cue to initiate a saccade was target onset in the step and gap tasks and fixation offset in the delayed saccade task. The animal was allowed 500 ms after the cue to reach within 6° of the target location, at which point the stimulus was relit and a liquid reward was delivered if fixation was maintained for 300–500 ms (increments of 100 ms).

As clarified in RESULTS, two target configurations were used. For the majority of datasets, the saccade target appeared with equal probability at either 20° to the right or 20° to the left. For several sessions of the gap task, the target appeared with equal likelihood at 1 of 24 different locations. The horizontal and vertical components of the target ranged from –20° to 20° in increments of 10°; no target was displayed at the straight-ahead location. In every behavioral task, the target could remain illuminated for ≤500 ms after the cue to initiate the saccade. If the eye position deviated outside the fixation window within this period, the saccade target was extinguished. Thus visual feedback did not contribute to saccade accuracy.

On 20–33% of the trials, the trigeminal blink reflex was induced by delivering a puff of air at random times to the eye implanted with the eye coil. The puff was generated by an air reservoir (output pressure: ~20 psi) and solenoid system located outside of the experimental room; we verified that solenoid clicks without air puff delivery did not evoke a conditioned response. The air flowed through a narrow Tygon tubing and released the puff ~2 cm from the eye. A flow meter (model 41211, TSI) was placed ~10 cm away from the eye to monitor the timing of the air puff delivery.

Eyelid movements were also recorded using the magnetic search coil technique. A small Teflon-coated stainless steel wire (~5 mm diam, 5 turns) was taped to the eyelid of the eye not implanted with the scleral coil. The eyelid coil signal, maintained in arbitrary units, was amplified in software to clearly identify eye closure as deflections in the vertical channel. Blinks were measured from the eyelid coil signal.

Based on pilot experiments using a freely hanging coil, we determined that the air-puff reached the eye 54.0 ± 4.3 (SD) ms ($n$ = 55) after the TTL pulse was triggered. Using the same air pressure, but with the coil now taped to the monkey's eyelid, eyelid deflection was observed in 78.3 ± 7.4 ms ($n$ = 119). Thus blink onset occurred 24.3 ± 7.4 ms after the air-puff reached the eye, comparable with that observed by Goossens and Van Opstal (2000a).

### *Data analysis*

Data were analyzed off-line using a combination of Matlab (The Mathworks) and in-house software. To detect saccade onset, the peak velocity was marked, and the algorithm marched "backward" in time until the velocity dropped below threshold (50°/s, unless noted otherwise) for ≥5 ms; the time at which velocity was greater than threshold was noted as saccade onset. This criterion was chosen because it was typically greater than the peak velocity of the eye movement that accompanied blinks during fixation, as determined by visual inspection. To mark saccade end, the detection routine marched "forward" to identify the first time-point after peak velocity for which velocity dropped below threshold (30°/s). An experimenter verified these measurements to ensure accuracy. We cite two reasons for choosing a static, threshold detection routine over a dynamical approach, such as subtraction of an averaged, blink-induced eye movement not accompanied by a saccade from blink-evoked saccades: *1*) a blink-associated saccade cannot be modeled as a linear superposition of blink-perturbed eye movement generated without a saccade and a saccade not accompanied by a blink (Goossens and Van Opstal 2000a); and *2*) the profile of the blink-induced eye movement without a saccade has dynamics that depend on the timing of the blink, i.e., whether the blink was induced in the presence of fixation point or during the gap interval (unpublished observations).

Saccade amplitude was computed as the eye displacement between saccade onset and offset. Saccade reaction time (latency) and blink time refer to the times of saccade and blink onset, respectively, relative to the cue to initiate the saccade. The analyses compare parameters of individual blink trials with corresponding, average measures from control movements in the same target condition. Since variables such as fatigue and motivation can induce transient changes in these parameters across the 2,000+ trials on a given day, we used the median values of the 20 preceding and 20 ensuing control movements for the average measures.

Statistical trends in linear regression analyses were evaluated with the $t$-test to determine whether the correlation coefficient, or equivalently, the slope, is significantly different from zero (Glantz 2002).

Statistical significance was evaluated at $P < 0.01$ level, unless noted otherwise.

## RESULTS

The combination of control and blink trials collected during an individual session is referred to as a dataset. A session lasted several hours, generally consisting of 1 day's worth of experiments, and the monkeys typically performed only one oculomotor task in a given session. For the condition when saccade target was presented at a 20° eccentricity, either to the right or to the left (Figs. 1–8), we collected 10, 12, and 11 datasets during step, gap, and delayed saccade tasks, respectively. The number of blink-perturbed movements per dataset averaged 280 ± 143 (SD) trials (range, 66–594 trials).

### *Latency interactions*

The effects of blinks on saccade reaction times during the different behavioral tasks can be assessed from the traces shown in Fig. 1, which plots eye amplitude and velocity as well as eyelid amplitude for control (*top*) and air-puff trials (*bottom*). First consider data from the step task (Fig. 1*A*). The blink that occurred well before target onset did not modify saccade latency (red traces), whereas for the blink evoked soon after target onset (blue traces), saccade latency was noticeably prolonged. When a blink was evoked late in a trial (yellow traces), it followed the eye movement, and the saccade reaction time was comparable with control trials. For intermediate eyelid closures (black, green, magenta, and cyan traces), blink and saccade onsets were correlated. Saccade-blink interactions in the gap task (Fig. 1*B*) were qualitatively similar to those observed for the step task. The blink induced well before target onset—for instance, early in the gap period (red traces)—had negligible effect on saccade execution, whereas the blink evoked closer to target onset—e.g., late in the gap period (yellow traces)—typically increased saccade latency compared with control trials. When a blink was triggered late in the trial (green traces), it followed saccade onset and therefore did not influence the reaction time. However, blinks induced toward the end of the gap period and around target onset (cyan and blue traces) occasionally triggered saccades with reduced reaction time, but some of these saccades were directed to the wrong target location (not represented in the figure, but discussed in *Saccade metrics*). Blinks evoked shortly after target presentation but before the average reaction time (black and magenta traces) also facilitated eye movement onset. In the delayed saccade task (Fig. 1*C*), blinks evoked after the saccade initiation cue modulated saccade latency similarly to step and gap tasks. The key exception noted from the delayed saccade task is that a blink evoked during the overlap period, after target presentation but before fixation offset, did *not* trigger a saccade until after the cue (black and blue traces).

A comprehensive picture of the latency interactions within individual sessions is presented in Fig. 2. The columns depict individual datasets for the three different oculomotor tasks, and the rows correspond to data from each of the two monkeys.

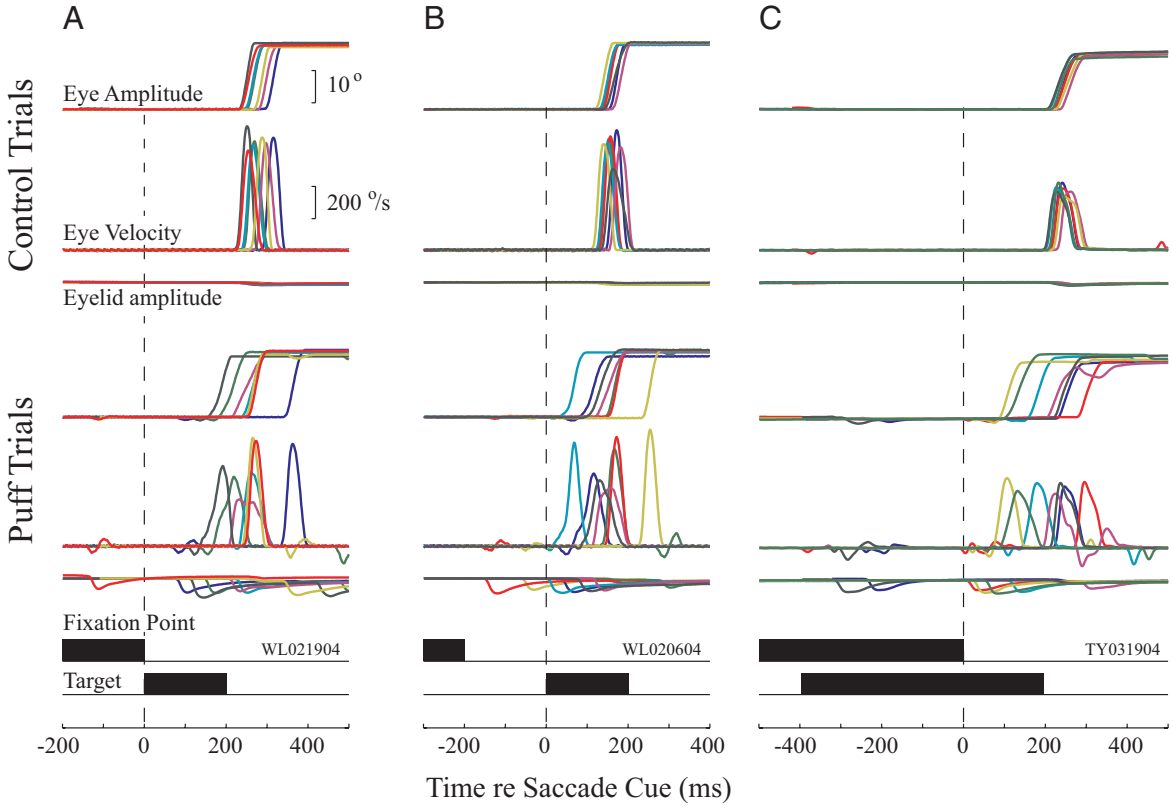


FIG. 1. Temporal traces of eye amplitude, eye velocity, and eyelid channel during control and air-puff trials for (*A*) step, (*B*) gap, and (*C*) delayed saccade tasks. Waveforms of eye and eyelid movements of each trial are color-coordinated. Eyelid signals are drawn in arbitrary units. Schematics of temporal evolution of behavioral tasks are shown at *bottom*. All traces are aligned on cue to initiate saccade, which is target onset for step and gap tasks and fixation point offset for delayed saccade task. Duration of saccade target and overlap period are arbitrarily schematized. See METHODS for details.

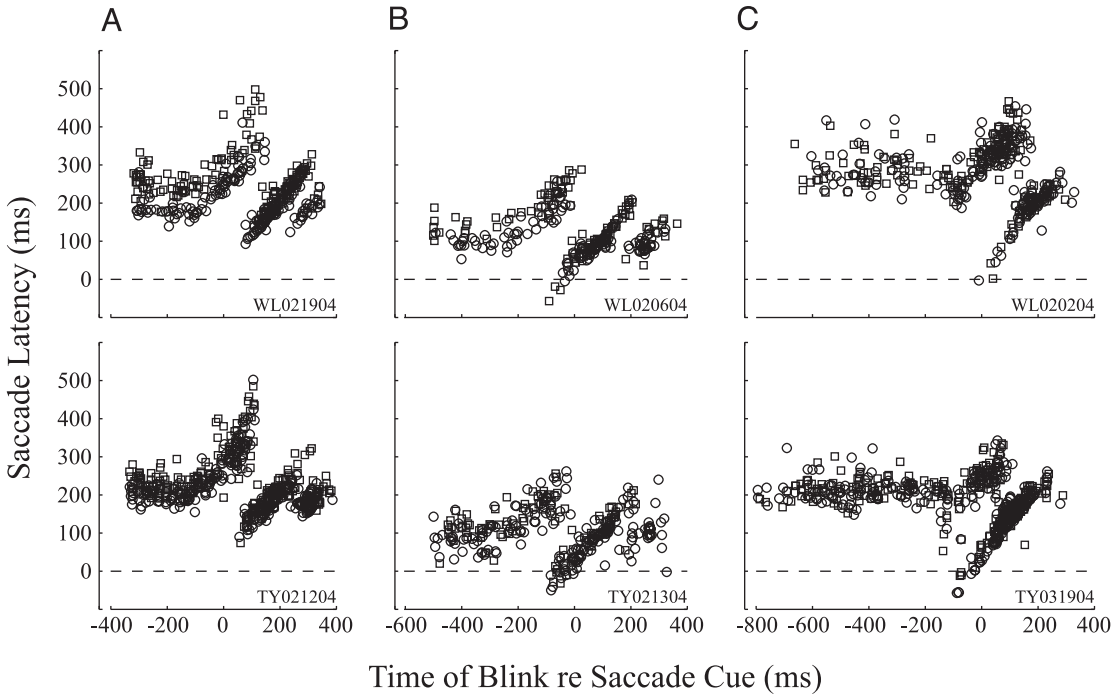


FIG. 2. Lawful variation in saccade latency as a function of blink time. Both measures are computed relative to time of saccade cue. *Columns*: data from individual datasets collected during (*A*) step, (*B*) gap, and (*C*) delayed saccade tasks. *Rows*: data from the 2 monkeys. Circles, rightward target; squares, leftward target. Dashed horizontal line drawn at saccade latency equal to 0.

The abscissa represents the time of blink relative to the time of saccade cue. Negative *x*-axis values refer to blinks evoked before target onset (gap and step tasks) or before fixation offset (delayed task). The ordinate is saccade latency, measured as the time from saccade cue to movement onset. A qualitative assessment indicates that each latency distribution can be separated into four clusters (also see Fig. 3*A*). *1*) Saccade latency remained relatively constant when blinks occurred more than ~200 ms before saccade cue (leftmost points). *2*) For blinks initiated <200 ms before the saccade cue, saccade latency typically increased. *3*) For blinks initiated shortly after illumination of the saccade initiation cue, the eye movement was generally triggered with the blink, as indicated by a drastic reduction in reaction time. The latency could be reduced to the express saccade latency range. In some cases, particularly for gap saccades (Fig. 2*B*), saccade latencies were even further reduced and were too short to be visually evoked. In such instances, the air-puff–triggered saccade likely revealed a bias

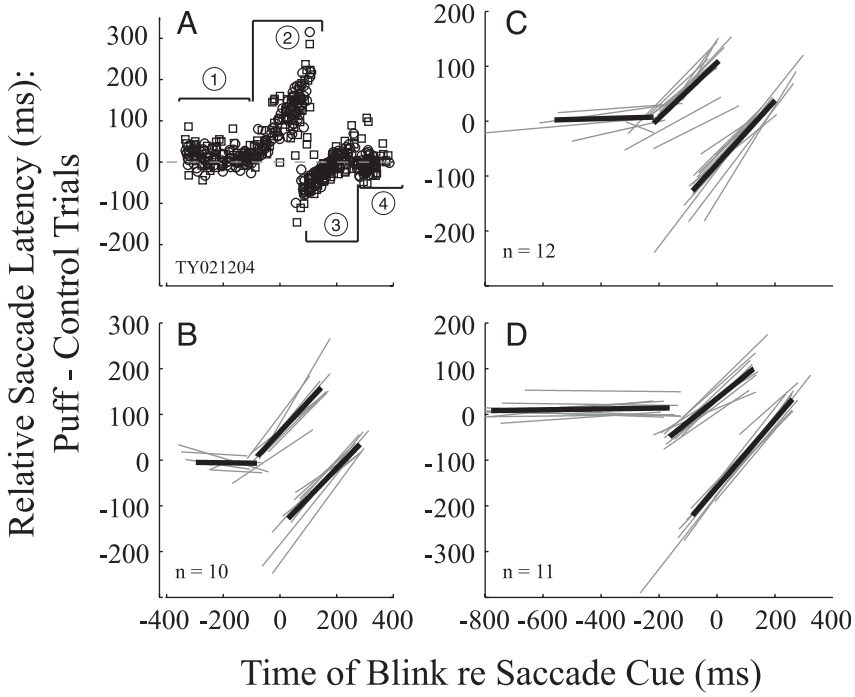


FIG. 3. Change in saccade latency relative to control trials of matched target conditions plotted as a function of blink time. *A*: same dataset as shown in *bottom left panel* of Fig. 2. Dashed horizontal line drawn at 0 to distinguish trials for which saccade reaction time relative to control trials was reduced (negative) or prolonged (positive). The 4 visually identified clusters indicate the differential effects of blink time on saccade latency. *B–D*: linear regressions analysis applied to all datasets in both monkeys. Gray lines show best fits for individual datasets of (*B*) step, (*C*) gap, and (*D*) delayed saccade tasks. Thick black traces are means of individual fits. Details and statistics are provided in text and Table 1.

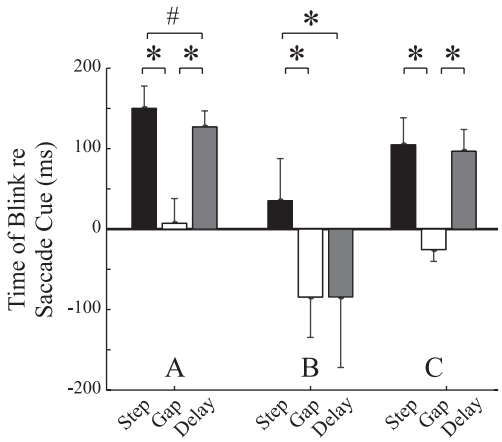


FIG. 4. Histogram comparing the transitional blink onset times for the step (black bars), gap (white bars), and delayed (gray bars) saccade tasks. Each bar represents an average value across datasets collected for each behavioral condition; error bars denote SD. *A*: latest blink time to increase saccade latency (*rightmost points* of cluster 2, Fig. 3*A*). Saccade onset was delayed for blink times as late as 150 ± 28, 7 ± 31, and 127 ± 20 ms after the initiation cue for step, gap, and delayed saccade tasks, respectively. *B*: earliest blink time to reduce saccade latency (*leftmost points* of cluster 3, Fig. 3*A*). Saccade onset was facilitated for blink times as early as 35 ± 53, −84 ± 50, and −84 ± 88 ms relative to the initiation cue for the step, gap, and delayed saccade tasks, respectively. *C*: Transition blink time after which blink onset reduces saccade latency in >50% of trials. Mean ± SD transition blink times were 105 ± 34, −25 ± 15, and 97 ± 27 ms across datasets of the step, gap, and delayed saccade tasks, respectively. $^{*}P < 0.01$, $^{\#}P < 0.05$; 2-tailed *t*-test.

or anticipatory plan for one of the two potential target locations. (These data were included in the analysis to show the range over which blinks triggered saccades.) Further delaying blink onset time also postponed saccade onset, until reaction time approached latency of control movements. *4*) Blinks evoked even later usually followed saccade onset (rightmost points). [To determine that saccade latency was indeed modulated by blinks, in one experiment, we delivered the air-puff to the back of the ear instead of the eye. The air-puff did not evoke blinks, and no trends in saccade latency were observed as a function of puff time relative to saccade initiation cue (data not shown).]

While Fig. 2 indicates the effects of blink time on saccade latency, it does not reveal how the reaction time distribution compares with control trials. To achieve this comparison, the moving median latency of control movements for matched target conditions (see METHODS) was subtracted from the absolute latency of individual blink trials. The distribution of relative saccade latency for one dataset (step task) is shown in Fig. 3*A*, which shows whether saccade latency was reduced (negative ordinate values) or prolonged (positive values) relative to control behavior.

The trends within the relative latency distributions across the four clusters, identified visually in Fig. 3*A*, were quantified using least-squares linear regression. The analyses were applied on each dataset of the three behavioral conditions. The data from clusters 1 and 2 were fitted with a piece-wise linear regression, and the fit that produced the lowest root-mean-square error was used to determine the transition from one cluster to another. Clusters 2 and 3 were visually distinguished from each other: cluster 2 included saccades with increased reaction time, whereas cluster 3 consisted of saccades with reduced latency. Cluster 4 trials were classified as movements for which blink onset occurred >10 ms after saccade onset, a value based on the observation that OPNs pause ~10 ms before blink onset (Mays and Morrisse 1994). In general, data in cluster 4 did not span a large range of blink times; thus a linear regression fit was not applied to these data.

Data from 10 datasets were available for the step task (Fig. 3*B*; Table 1), but only 6 datasets contained data over an interval sufficient to distinguish between the first two clusters. Only one of the six datasets exhibited a statistically significant trend in the first cluster (*t*-test, $P < 0.01$). For the gap task (Fig. 3*C*; Table 1), sufficient data to distinguish between the first and second clusters were available for 5 of 12 datasets. Only two of the five regressions were statistically significant for the first cluster (*t*-test, $P < 0.01$). Data from 11 datasets were available for the delayed saccade task (Fig. 3*D*; Table 1), and 0 of the 11 datasets showed a statistically significant trend in the first cluster. In contrast to the lack of an overall trend for the first cluster, the regressions in the second and third clusters were significant for all datasets and all behavioral tasks (*t*-test, $P < 0.01$).

It could be argued that the criterion of 50°/s used for the detection of saccade onset is on the high end. We intentionally chose this value because it was higher than the peak velocity of a typical blink-perturbed eye movement during fixation and therefore minimized false detection of saccades. We recognize that because saccade-blink interactions typically result in a slower movement (Goossens and Van Opstal 2000a; Rambold et al. 2002; Rottach et al. 1998), our estimate of saccade onset is likely a conservative measure. The most noticeable effects of a smaller threshold criterion would have been a change in the regression slope of the fit in cluster 3 (Table 1). The slope could hypothetically approach unity, which would only further validate our results. Thus we argue that, although the more realistic onset may actually occur earlier, our conclusions are not sensitive to the choice of threshold.

Figures 2 and 3 show considerable overlap between the data points in the second and third clusters, indicating a blink onset in this range can either increase or decrease saccade latency. We attribute this finding to the stochastic properties of the gradually increasing low-frequency discharge of saccade-related burst neurons in the oculomotor pathway (Hanes and Schall 1996; Munoz and Schall 2004) and to visual suppression associated with blinks (Volkmann et al. 1980). The ranges of overlap were quantified for each dataset of each task (Fig. 4).

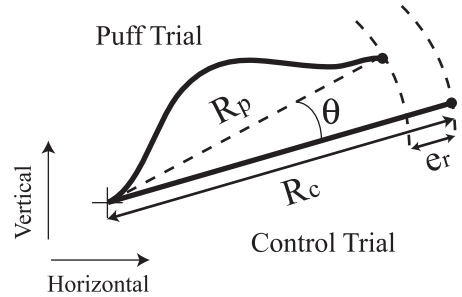


FIG. 5. Schematic representation of spatial profiles of control and blink-perturbed saccades. Saccade metrics were analyzed by 1st determining radial amplitude of each blink ($R_p$) and a median radial amplitude of selected control trials ($R_c$) to matched target conditions (see METHODS). Next, a radial error measure ($e_r$) was defined as $R_p - R_c$. A direction deviation ($\theta$) parameter, defined as the difference in directions of puff and control trials, was also computed.

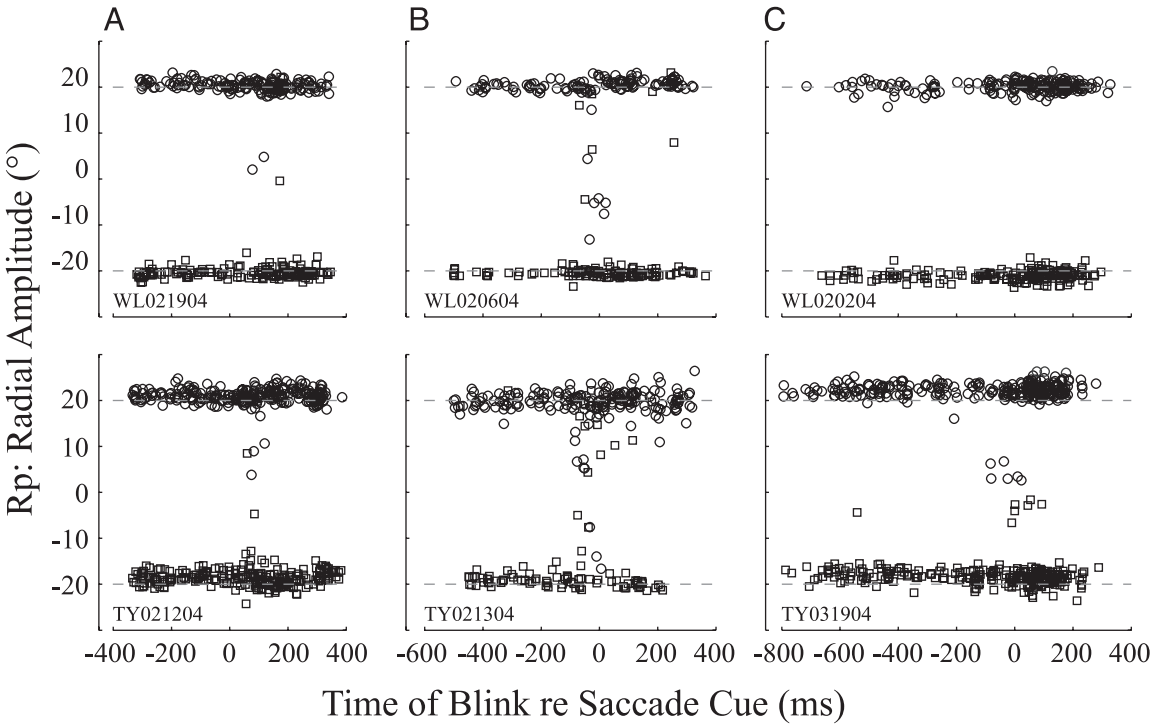


FIG. 6. Saccade amplitude plotted as a function of blink time for (*A*) step, (*B*) gap, and (*C*) delayed saccades. Same datasets and format as shown in Fig. 2.

The latest blink time that resulted in an increase in saccade latency, i.e., the rightmost points of cluster 2, was significantly different in the gap condition than in the step and delay tasks (2-tailed *t*-test, $P < 0.01$; Fig. 4*A*). There was also a small statistical difference between the mean values of step and delay trials (2-tailed *t*-test, $P < 0.05$). On the other hand, the earliest blink time that facilitated saccade onset, i.e., the leftmost points of cluster 3, was significantly different for step trials compared with gap and delayed saccade tasks (2-tailed *t*-test, $P < 0.01$; Fig. 4*B*). There was no statistical difference in the mean blink times of gap and delay trials (2-tailed *t*-test, $P > 0.1$).

To obtain an objective estimate of the transition blink time from prolonged (cluster 2) to reduced (cluster 3) reaction time, we binned the data according to blink onset time and computed the proportion of trials for which relative saccade latency was greater than zero. The center of the bin that dropped below 0.5 was chosen as the transition time (Fig. 4*C*). [Various binwidths (5- to 35-ms bins in increments of 5 ms) were tested and the results were comparable.] The mean transition time for gap trials was significantly different from step and delay tasks (2-tailed *t*-test, $P < 0.01$), but there was no statistical difference in the mean transition times of step and delay trials ($P > 0.1$).

### *Saccade metrics*

As shown by previous studies on saccade–blink interactions (Goossens and Van Opstal 2000a; Rambold et al. 2002; Rottach et al. 1998), the traces in Fig. 1 give the impression that saccade amplitude remains comparable with control trials across all blink times. We quantified this assessment by converting the final eye position relative to fixation point (straight ahead) into radial amplitude and direction for all puff and control trials (Fig. 5). The endpoint accuracy of the blink-perturbed movements was analyzed with respect to the control trials instead of the target location because *1*) behavioral parameters can vary across a session lasting several hours and *2*) visual feedback was absent since the target was extinguished before the animal reached it. Two parameters, radial error ($e_r$) and direction deviation ($\theta$)—defined as the difference between the radial amplitude and direction, respectively, of an individual blink-perturbed saccade and corresponding median parameters computed from selected control movement to the same target (see METHODS)—were computed. These parameters are similar to those used in other perturbation experiments (e.g., Gandhi and Keller 1999; Goossens and Van Opstal 2000a; Keller et al. 1996). Negative values of $e_r$ and $\theta$ denote that, relative to control saccades, blink-perturbed movements were hypometric and exhibited a larger counterclockwise rotation in final eye position, respectively.

Figure 6 plots the radial saccade amplitude ($R_p$) of all puff trials as a function of blink time (relative to saccade cue) for individual datasets of the three behavioral tasks. Figure 7 shows the radial error (*A–C*) and direction deviation (*D–F*) distributions as a function of blink time for a subset of these datasets. For the condition in which saccade target could appear at one of two known locations, the data showed no indication of a gradual buildup of saccade amplitude across any range of blink times, and in general, the radial error and direction deviation were invariant across blink time. The infrequent exceptions were movements triggered around the time of cue; these saccades were typically hypometric and/or were directed in the wrong, typically opposite, direction. This occurrence most likely reflects a bias or anticipatory signals that are executed before successful processing of the sensory target.

Regression analyses were applied to the radial error and direction deviation measures as a function of blink time. The fits were performed on the data distributed across the clusters

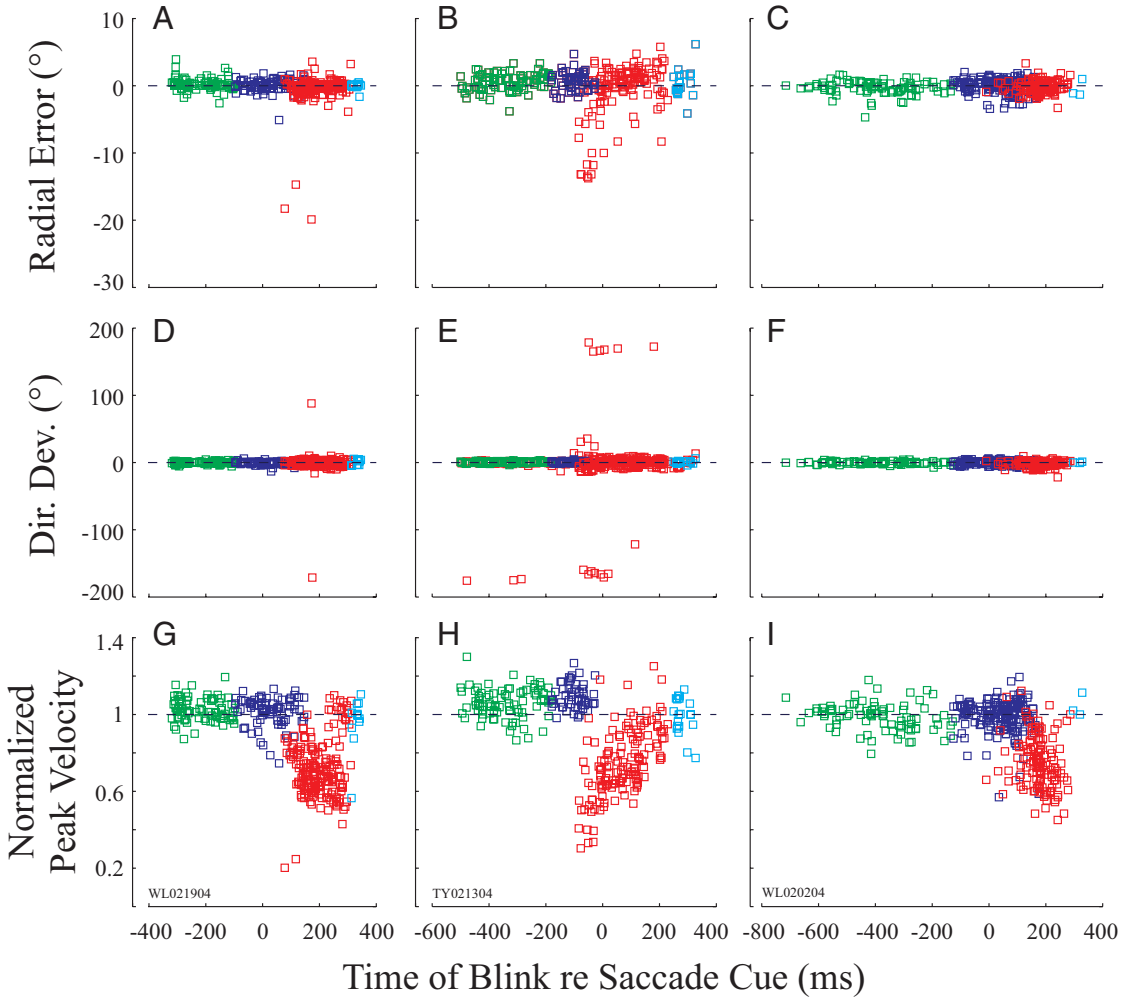


FIG. 7. Quantitative comparison of blink-perturbed trials with control movements to the same target location. Radial error (*A–C*), direction deviation (*D–F*), and normalized peak velocity (*G–I*) are plotted as a function of blink time for step (*left*), gap (*middle*), and delayed saccades (*right*). Different colors represent the 4 clusters, as determined from latency analysis (see Fig. 3*A*). Saccades to rightward and leftward targets are not differentiated. Only 3 datasets, 1 of each behavioral task, are shown. Data from other datasets were similar (see Table 1).

identified from the latency analyses. For direction deviation regressions, the mean slope and intercepts for all three clusters were not significantly different from zero (*t*-test, $P > 0.01$). For the radial error measure (Table 1), the mean slope and intercept across the datasets in the step, gap, and delayed saccade tasks were not significantly different from zero for clusters 1 and 2 (*t*-test, $P > 0.01$). For regressions applied to the third cluster, radial error was significantly correlated with

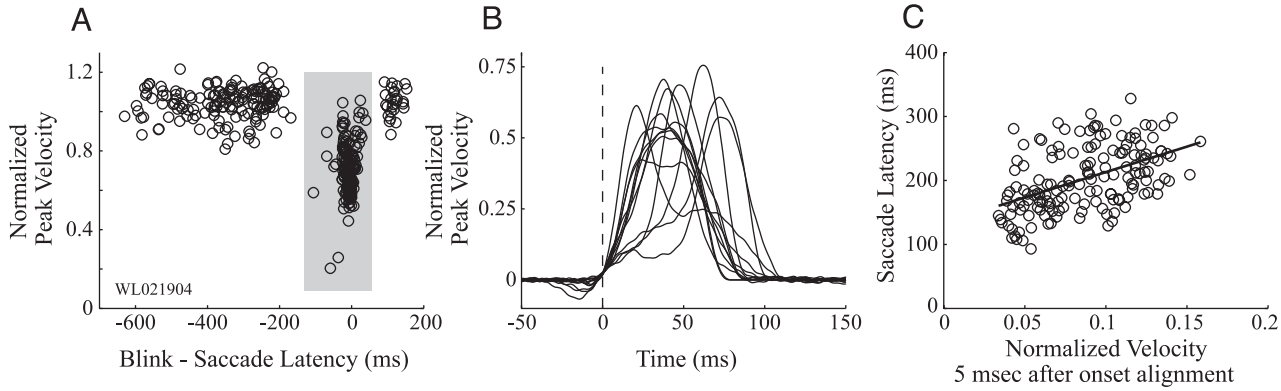


FIG. 8. Interactions of velocity and latency of saccades. *A*: normalized peak velocity is plotted as a function of the difference between blink and saccade onset times. Panel shows that normalized peak velocity is significantly attenuated only when blinks and saccades coincide temporally (shaded region). *B*: velocity profiles of a subset of attenuated trials, aligned on onset (20°/s velocity criterion). Vertical dashed line denotes alignment time. Note that several traces exhibit a negative velocity profile prior to onset; it represents the eye movement component due to the blink that precedes saccade. *C*: reaction time of saccades in shaded region of *A* plotted against instantaneous velocity 5 ms after onset alignment in *B*.

TABLE 1. *Summary of regression analyses*

| | Slope | Intercept | $r$ | No. of significant Datasets |
|---|---|---|---|---|
| | | *Saccade Latency (Puff–Control Trials) vs. Blink Time* | | |
| | ( ) | (ms) | | |
| Step task | | | | |
| Cluster 1 ($n$ = 6) | −0.010 ± 0.16 | −7.46 ± 29.54 | −0.062 ± 0.28 | 1 |
| Cluster 2 ($n$ = 10) | 0.68 ± 0.19 | 56.63 ± 20.30 | 0.67 ± 0.12* | 10 |
| Cluster 3 ($n$ = 10) | 0.65 ± 0.15 | −150.78 ± 39.43 | 0.82 ± 0.10* | 10 |
| Gap task | | | | |
| Cluster 1 ($n$ = 5) | 0.015 ± 0.13 | 10.55 ± 44.03 | 0.12 ± 0.27 | 2 |
| Cluster 2 ($n$ = 12) | 0.50 ± 0.19 | 106.54 ± 42.85 | 0.69 ± 0.13* | 12 |
| Cluster 3 ($n$ = 12) | 0.57 ± 0.14 | −78.04 ± 28.26 | 0.80 ± 0.10* | 12 |
| Delay task | | | | |
| Cluster 1 ($n$ = 11) | 0.009 ± 0.03 | 15.65 ± 20.20 | 0.035 ± 0.11 | 0 |
| Cluster 2 ($n$ = 11) | 0.51 ± 0.11 | 34.74 ± 18.55 | 0.68 ± 0.09* | 11 |
| Cluster 3 ($n$ = 11) | 0.74 ± 0.09 | −158.79 ± 26.62 | 0.82 ± 0.12* | 11 |
| | | *Radial Error vs. Blink Time* | | |
| | (°/ms) | (°) | | |
| Step task | | | | |
| Cluster 1 ($n$ = 6) | −0.001 ± 0.002 | 0.23 ± 0.44 | −0.053 ± 0.12 | 0 |
| Cluster 2 ($n$ = 10) | 0.001 ± 0.003 | 0.11 ± 0.26 | −0.026 ± 0.13 | 0 |
| Cluster 3 ($n$ = 10) | 0.015 ± 0.017 | −2.73 ± 3.67 | 0.22 ± 0.19† | 5 |
| Gap task | | | | |
| Cluster 1 ($n$ = 5) | 0.001 ± 0.002 | 0.48 ± 0.78 | 0.08 ± 0.20 | 0 |
| Cluster 2 ($n$ = 12) | 0.002 ± 0.005 | 0.23 ± 0.51 | 0.06 ± 0.20 | 0 |
| Cluster 3 ($n$ = 12) | 0.015 ± 0.010 | −1.41 ± 1.15 | 0.30 ± 0.15* | 6 |
| Delay task | | | | |
| Cluster 1 ($n$ = 11) | 0.0003 ± 0.001 | 0.34 ± 0.54 | 0.035 ± 0.13 | 1 |
| Cluster 2 ($n$ = 11) | 0.0001 ± 0.002 | 0.23 ± 0.30 | −0.007 ± 0.13 | 0 |
| Cluster 3 ($n$ = 11) | 0.011 ± 0.011 | −1.47 ± 1.64 | 0.23 ± 0.17* | 6 |
| | | *Normalized Peak Velocity vs. Blink Time* | | |
| | (1/ms) | ( ) | | |
| Step task | | | | |
| Cluster 1 ($n$ = 6) | −7.4E-05 ± 2.1E-04 | 1.03 ± 0.74 | −0.020 ± 0.17 | 0 |
| Cluster 2 ($n$ = 10) | −1.4E-04 ± 3.2E-04 | 1.00 ± 0.08 | −0.055 ± 0.13 | 0 |
| Cluster 3 ($n$ = 10) | 4.9E-04 ± 8.6E-04 | 0.69 ± 0.16* | 0.18 ± 0.27 | 3 |
| Gap task | | | | |
| Cluster 1 ($n$ = 5) | −3.9E-04 ± 7.9E-04 | 0.90 ± 0.25 | −0.08 ± 0.11 | 0 |
| Cluster 2 ($n$ = 12) | 3.5E-04 ± 4.8E-04 | 1.06 ± 0.04 | 0.15 ± 0.17 | 3 |
| Cluster 3 ($n$ = 12) | 2.5E-04 ± 7.7E-04 | 0.71 ± 0.06* | 0.15 ± 0.30 | 7 |
| Delay task | | | | |
| Cluster 1 ($n$ = 11) | 1.2E-04 ± 2.0E-04 | 1.06 ± 0.10 | 0.11 ± 0.18 | 4 |
| Cluster 2 ($n$ = 11) | 6.5E-07 ± 2.5E-04 | 1.03 ± 0.06 | −0.001 ± 0.08 | 0 |
| Cluster 3 ($n$ = 11) | −2.1E-04 ± 1.1E-03 | 0.81 ± 0.15* | −0.002 ± 0.33 | 6 |
| | | *Saccade Latency vs. Normalized Velocity 5 ms After Onset* | | |
| | (ms) | (ms) | | |
| Step task ($n$ = 10) | 615 ± 275 | 143 ± 29 | 0.39 ± 0.10* | 10 |
| Gap task ($n$ = 12) | 577 ± 231 | 50 ± 32 | 0.42 ± 0.14* | 11 |
| Delay task ($n$ = 11) | 445 ± 145 | 132 ± 24 | 0.29 ± 0.11* | 8 |

Values are mean ± SD. *$P < 0.01$ (or †$P < 0.05$) denotes whether mean correlation coefficient was significantly different from 0 (all regressions), or mean intercept was significantly different from 1 (normalized peak velocity regressions). No. of significant datasets was determined at $P < 0.01$ level for all regression analyses except saccade latency vs. normalized velocity, for which $P < 0.05$ was used. Regression summary of direction deviation is not shown because there were no instances of significant correlations. The mean slope and intercept were not significantly different from 0 for any clusters. Regression units are listed in parentheses below each heading. Dimensionless units are shown as empty parentheses.

blink time for all three behavioral tasks (step: $P < 0.05$; gap: $P < 0.01$; delay: $P < 0.01$). However, these "significant" trends must be interpreted with caution. Figure 7, *A–C* clearly shows that there are only a limited number of points that deviate from the overall distribution of data. These movements were associated with blinks evoked around the time of cue onset, most likely before the visual target could be processed. Thus these blink-triggered saccades most likely do not reflect a plan to initiate a target-directed saccade. Removal of these "outlier" points yielded correlation coefficients that were not significantly different from zero in all three behavioral tasks ($P > 0.01$).

### *Saccade kinematics*

Figure 7, *G–I* also shows the distribution of peak velocity, normalized to a moving median peak velocity of control saccades to the same target (see METHODS), as a function of blink time for a dataset from each of the three behavioral conditions. Linear regressions were applied to the three

clusters (Table 1), as determined from the latency analyses. The main effect, observed mainly in cluster 3, was a significant reduction in the intercept of linear fits. The slope of the regressions was significantly different from zero for several individual datasets of each behavioral task but not when averaged across all datasets within each condition (Table 1). [We also analyzed the time of peak velocity as a function of blink time (data not shown). The relationship was essentially a mirror image of the peak velocity distribution. It remained relatively constant except for trials belonging to cluster 3, for which the time of peak velocity increased.]

Attenuation of peak velocity in cluster 3 suggests that the effects on peak velocity are most pronounced when saccade and blink onsets occur close together. Thus we plotted normalized peak velocity as a function of the relative timing of each saccade-blink pair. Figure 8*A* shows data for one session of the step task. Trials for which blinks reduced velocity (shaded region) can be easily distinguished from movements not attenuated by blinks. [Recall from the latency analysis (Fig. 2) that for blink times spanning clusters 2 and 3, the distribution of saccade latency was bimodal and essentially nonoverlapping. As a result, there were very few trials when blink onset led saccade onset by 100–200 ms. Hence, it was rare to observe points just to the left of the shaded region in Fig. 8*A*.] The velocity profiles of the movements represented within the shaded box were realigned on saccade onset using a lower threshold (20°/s) and then normalized to peak velocity of control movements. A subset of these normalized waveforms is shown in Fig. 8*B*. Next, we correlated the instantaneous normalized velocity 5 ms after the alignment point with saccade latency (Fig. 8*C*). Saccade onset was significantly correlated with initial velocity of the eye movement: the slower the initial component of the movement, the shorter the latency. This trend was observed in nearly all datasets, independent of the behavioral task (Table 1). This is a critical finding because it suggests that the low-frequency activity observed during sensorimotor integration encodes saccade dynamics.

### *Increase in potential target locations*

To address the argument that the relative lack of target uncertainty may have contributed to the latency reduction and saccade accuracy, the two monkeys performed the gap task when the target could appear at 1 of 24 possible locations. The horizontal and vertical component of the target ranged from –20 to 20° in increments of 10°; the straight-ahead target location was omitted. All other parameters of the task were the same as in the two potential locations condition. Data were collected from seven datasets. The number of blink-perturbed movements per dataset averaged 472 ± 170 (SD) trials (range, 186–730 trials).

Figure 9 shows distributions of absolute saccade latency, normalized peak velocity, radial error, and direction deviation as a function of blink time for one dataset. The data were pooled across all target locations. The distributions of all four parameters were comparable in the 2 and 24 target locations conditions: the latency distribution revealed four clusters; peak velocity was reduced for data in the third cluster; and, after removal of the outlier points corresponding to blinks occurring around saccade cue, no trends were observed in either direction deviation or radial error. A comparison of the final eye positions in the control and puff conditions, parsed by target location, confirms this observation (Fig. 9*E*). Results from other sessions were comparable (data not shown).

## DISCUSSION

This study evaluated the stimulus-response time course over which reflexive blinks modify characteristics of saccadic eye movements. The trigeminal blink reflex was evoked by delivery of an air-puff to the eye as monkeys performed various oculomotor tasks. We found that the effect on latency was dependent on the blink time. Blinks that overlapped with onset of the saccade initiation cue (cluster 2 points, Fig. 3*A*) increased saccade latency relative to control trials, whereas blinks initiated shortly after the cue was presented (cluster 3 points, Fig. 3*A*) generally triggered the saccade during the eyelid depression. The reaction time could be reduced to the express saccade latency range and, in some cases, a movement,

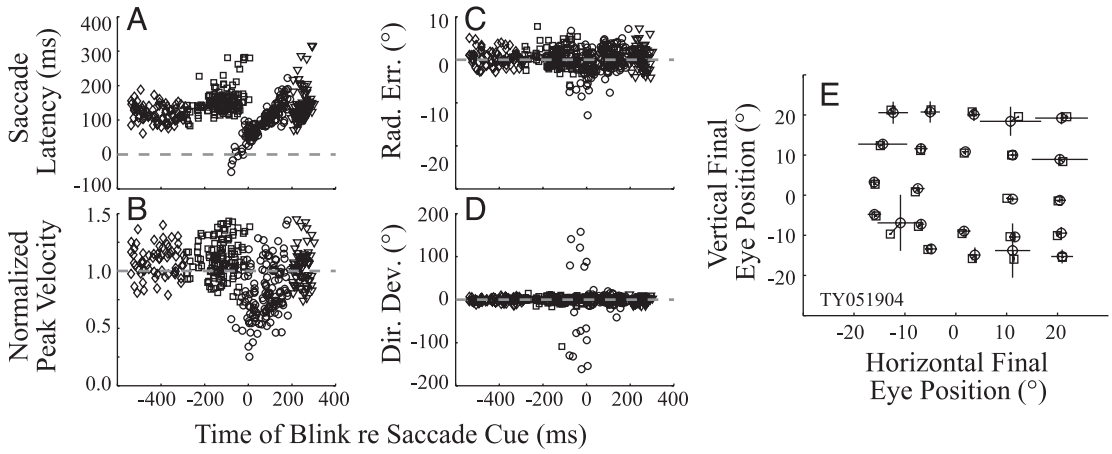


FIG. 9. Minimal perturbation of saccade metrics as a function of blink time when saccade target can appear at 1 of 24 potential locations. Distribution of latency (*A*), normalized peak velocity (*B*), radial error (*C*), and direction deviation (*D*) are plotted as a function of blink time. Different symbols represent the 4 clusters, as determined from latency analysis (diamonds, cluster 1; squares, cluster 2; circles, cluster 3; triangles, cluster 4). Data across all target locations are pooled together. *E*: accuracy of blink-perturbed movements. Mean horizontal component of control (squares) and blink-perturbed (circles) trials are plotted against mean vertical component for each of 24 target locations. Bars in both directions denote SD. Data are pooled across all blink times.

not necessarily directed to the upcoming target location, was triggered before the stimulus target was presented. Unlike the latency distribution, the peak velocity did not change systematically with blink time, although there was a significant reduction in this parameter when saccades temporally coincided with blinks (Figs. 7, *G–I,* and 8). Saccade accuracy was preserved across all blink times, but the variability in the distribution increased around the time of cue (Figs. 6 and 7).

In most previous studies of saccade–blink interactions (Evinger et al. 1994; Goossens and Van Opstal 2000a; Guitton et al. 1991; Rambold et al. 2002, 2004; Rottach et al. 1998; Watanabe et al. 1980; Zee et al. 1983), blinks were evoked (reflexive) or generated (voluntary) around the average saccade reaction time, producing a temporal overlap of eye closure and the rapid eye movement. The blink-induced perturbation facilitated saccade initiation (Evinger et al. 1994; Goossens and Van Opstal 2000a; Zee et al. 1983), altered the kinematics of the movement (peak velocity, acceleration and deceleration decrease, and eye movement duration increases), but preserved accuracy (Goossens and Van Opstal 2000a; Rambold et al. 2002; Rottach et al. 1998). Two recent studies, however, have considered the effects of blinks that occurred at other intervals. Rambold et al. (2002) asked humans to make self-paced saccades between two targets and, furthermore, to generate voluntary blinks during half of the saccades. This method yielded data in which blink onset relative to saccade onset ranged from approximately −200 to 200 ms. While an evaluation of the temporal effects of blink on saccade kinematics was permissible (and we obtained similar results), their experimental design (self-paced saccade generation) precluded an analysis of blink time on reaction time. In another study, Rambold et al. (2004) evoked reflexive blinks timed to occur before target onset as humans performed the step task. In their database, blink onset occurred 441 ± 48 ms before saccade onset, corresponding to ~240 ms before target onset. The distributions of saccade latency in the blink and control conditions were not significantly different (Rambold et al. 2004). In our datasets, comparable data correspond to saccades evoked when blinks were induced around −240 ms on the abscissa of Fig. 3*A*. Note that the distribution of saccade latency relative to control trials hovers around zero. Thus our observation in monkeys is in agreement with the finding in humans across this limited range of blink times (Rambold et al. 2004).

### *Transition in saccade latency*

The uniform sampling of blink times in our experiments also revealed an epoch in which blink onset either reduced or prolonged saccade latency. This is visualized as two distinct distributions of reaction times for blinks triggered around the saccade initiation cue (Figs. 2 and 3). What determines whether the movement observed on a puff-trial will exhibit an increase or a decrease in reaction time? Hanes and Schall (1996) proposed that the rate of increase in the low-frequency activity in saccade-related burst neurons in the frontal eye fields is a stochastic property. Thus at the time of blink onset, if the instantaneous firing rate of the low-frequency discharge is high enough to surpass the threshold activation level, which is also reduced due to the presumed inhibition of the OPNs, a saccade will accompany the blink. If the instantaneous rate is at a subthreshold level, visual suppression (Volkmann et al. 1980) and attenuation of activity in saccade-related burst neurons (Goossens and Van Opstal 2000b) due to the blink will delay saccade onset until after the eyes reopen and reprocess the initiation cue, resulting in an increase in saccade latency. Our analyses (Fig. 4*C*) indicated that, for step and delayed saccade tasks, the transition from an increase to a decrease in latency occurred for blinks triggered ~100 ms after the saccade cue. For the gap task, on the other hand, the transition occurred ~25 ms *before* the saccade target was presented. We attribute this effect to the elevated low-frequency discharge observed in the gap period when the target is presented at one of two locations (e.g., Dorris et al. 1997).

### *Insights into trigger mechanisms*

While the neural mechanisms shared by the saccadic and blinks systems have not been delineated, it is believed that OPNs, which discharge at a tonic rate during fixation and pause during saccades, are inhibited during blinks also (see INTRODUCTION). Thus we assume that during every blink observed in our study, an ensemble of OPNs sufficient to permit saccade initiation ceased its discharge. Within the bounds of this assumption, several inferences emerge regarding the role of the low-frequency activity as a motor preparation signal and of the OPNs as a saccadic trigger mechanism.

Interestingly, saccade facilitation was linked to the cue to initiate the movement, not to the onset of the visual target, a conclusion based on data collected during the delayed saccade task. The saccade target location was identified well before the cue to initiate the movement, yet blinks evoked during the overlap period did not facilitate saccade onset in trained animals. Even blinks timed to overlap with the visual response, observed 60–80 ms after target onset as a transient increase in firing rate in neurons in various oculomotor and visual structures, were not capable of triggering the saccade; data from these trials are included in the plots shown in Figs. 2*C* and 3*D*.

The temporal overlap of fixation and saccade targets in the delayed task separates the visual and premotor commands and introduces a prolonged sensorimotor integration period (Hikosaka and Wurtz 1983a), during which low-frequency discharge activity can be recorded in the superior colliculus, frontal eye fields, parietal eye fields, and other cortical and subcortical regions (for reviews, see Andersen 1995; Munoz et al. 2000; Wurtz et al. 2001). What function does this activity encode? One potential explanation is that the early component of the prolonged sensorimotor period activity may represent cognitive mechanisms such as spatial attention, target selection, memory, or perceptual decision (reviewed by Fecteau and Munoz 2003; Sparks 1999; Zhang and Barash 2004). However, reflexive blinks frequently triggered saccades throughout the overlap period in one monkey tested while being trained on the delayed saccade task (data not shown). Thus we cannot discount the possibility that motor preparation or intention related activity (also reviewed by Fecteau and Munoz 2003; Sparks 1999; Zhang and Barash 2004) may be present during the overlap period, although the discharge may encode other parameters also.

If a premotor command is indeed present in the activity recorded during the overlap period and, as discussed above, OPNs cease discharge during the blink, why doesn't a blink

induced during the overlap period elicit a saccade? At least two nonexclusive explanations are possible. *1*) Activity of saccade-related burst neurons, such as those reported in the superior colliculus (Goossens and Van Opstal 2000b), is attenuated during saccades perturbed by blinks as well as following chemical inactivation of the OPNs (Soetedjo et al. 2002). This reduced activity may not be sufficient to drive the burst generator. For this reason to be valid, the low-frequency discharge rate after accounting for the blink-induced attenuation must be greater for the gap and step tasks than for the delayed task because saccades were triggered in the two former behavioral conditions. *2*) The OPNs may not be the sole trigger mechanism that initiates saccades. The burst generator may be under control of an inhibitory influence that is more powerful than that of the OPNs and that persists during the overlap period. Two viable candidates are fixation-related neurons in the substantia nigra pars reticulata (Basso and Wurtz 2002; Handel and Glimcher 1999; Hikosaka and Wurtz 1983a,b) and in the superior colliculus (Munoz and Wurtz 1993). Descending projections from the substantia nigra to the pontomedullary reticular formation, analogous to those reported in rodents (Von Krosigk and Smith 1991), or projections from the neurons in the rostral colliculus to the OPN region, reported in the cat and monkey (Büttner-Ennever et al. 1999; Gandhi and Keller 1997; Paré and Guitton 1994), could directly or indirectly mediate the inhibition during the overlap period of delayed saccades. Toward the end of the gap period as well as after the cue to initiate the saccade, the baseline activity of nigra (Gore et al. 2002; Hikosaka and Wurtz 1983b; Munoz and Schall 2004) and rostral colliculus neurons (Munoz and Wurtz 1993) decreases, permitting the inhibition of OPNs to trigger the movement. This proposal requires that rostral colliculus neurons (Munoz and Wurtz 1993) and nigra cells that suppress activity prior to saccades (Basso and Wurtz 2002; Handel and Glimcher 1999; Hikosaka and Wurtz 1983a,b) should not reduce their discharge in association with blinks generated during the overlap period. Further studies are required to test this hypothesis.

### *Movement parameters encoded in the low-frequency discharge*

The dual-coding hypothesis of the role of the superior colliculus in saccade generation proposes that the spatial locus of activity dictates the metrics of the movement and the firing rate encodes its kinematics/dynamics (Sparks and Mays 1990). Based on the notion that the low-frequency discharge activity increases gradually, one would expect the initial velocity of the blink-perturbed eye movement to correlate with the instantaneous firing rate of the low-level activity: the shorter the saccade latency, the lower the firing rate and the slower the initial phase of the eye movement. The significant correlation between initial velocity, measured 5 ms after aligning the movements on a velocity threshold of 20°/s, and saccade latency (Fig. 8*C*; Table 1) supports this hypothesis. [Our results do not require the colliculus to solely encode saccade dynamics. Cortical (e.g., Bruce and Goldberg 1985; Dias and Bruce 1994; Hanes and Schall 1996; Mazzoni et al. 1996; Tinsley and Everling 2002) and other subcortical regions (Munoz and Schall 2004; Scudder 1988) also exhibit low-frequency discharge during sensorimotor integration, and it is possible that all or some of these structures encode aspects of the premotor command.]

It also has been suggested that the low-frequency discharge observed in superior colliculus neurons may represent target and/or movement selection (Basso and Wurtz 1997; Glimcher and Sparks 1992, 1993; Horwitz and Newsome 1999) and that the metrics of the movement develop gradually (Glimcher and Sparks 1992; 1993; Gold and Shadlen 2000). While Glimcher and Sparks (1992, 1993) provided indirect evidence, Gold and Shadlen (2000) used behavioral measures to argue for gradual changes in preparation of the metrics. In our experiments, in contrast, saccade accuracy was preserved across all blink times, and although the variability in the amplitude distribution was generally greater for blinks evoked around the cue to initiate saccades, the amplitude did not increase gradually. This observation held for datasets in which a target could appear in 1 of either 2 or 24 locations. Thus it is unlikely that the accuracy of saccades was a consequence of a predictive strategy.

Several nonexclusive interpretations can explain the discrepancies of metrics results, and further experiments are required to distinguish among the possible explanations. *1*) The difficulty of the perceptual decision task (Gold and Shadlen 2000) may have served as a bottleneck for specifying the metrics of the movement. Since our experimental design did not employ any difficulty or uncertainty regarding target selection, saccade accuracy was generally preserved. *2*) Perhaps the low-frequency discharge does encode information about saccade metrics but the goal of the movement may not be completely specified at the time when the perturbation triggers the saccade. The goal of the movement could develop during the ongoing movement, and the local feedback mechanism of the saccadic system may compensate for the initial indetermination, allowing the eyes to reach the desired position in the orbits and maintain the observed accuracy. *3*) As proposed for the dual-coding hypothesis (Sparks and Mays 1990), the spatial locus of activity in the superior colliculus and cortical regions specifies the movement metrics, whereas the temporal discharge patterns of the collicular neurons mediate saccade kinematics/dynamics. However, a sufficient number of spikes must be discharged to allow the dynamic motor error in the local feedback loop to reach zero (Goossens and Van Opstal 2000b); a reduced number of spikes could produce hypometric saccades (Stanford et al. 1996).

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## REFERENCES

**Andersen RA.** Encoding of intention and spatial location in the posterior parietal cortex. *Cereb Cortex* 5: 457–469, 1995.

**Balaban CD, McGee DM, Zhou J, and Scudder CA.** Responses of primate caudal parabrachial nucleus and Kolliker-fuse nucleus neurons to whole body rotation. *J Neurophysiol* 88: 3175–3193, 2002.

**Basso MA and Wurtz RH.** Modulation of neuronal activity by target uncertainty. *Nature* 389: 66–69, 1997.

**Basso MA and Wurtz RH.** Neuronal activity in substantia nigra pars reticulata during target selection. *J Neurosci* 22: 1883–1894, 2002.

**Bruce CJ and Goldberg ME.** Primate frontal eye fields. I. Single neurons discharging before saccades. *J Neurophysiol* 53: 603–635, 1985.

**Bryant CL and Gandhi NJ.** Real-time data acquisition and control system for the measurement of motor and neural data. *J Neurosci Methods* In press.

**Büttner-Ennever JA, Horn AK, Henn V, and Cohen B.** Projections from the superior colliculus motor map to omnipause neurons in monkey. *J Comp Neurol* 413: 55–67, 1999.

**Carpenter RHS.** Oculomotor procrastination. In: *Eye Movements: Cognition and Visual Perception*, edited by Fischer DF and Monty RA. Hillsdale, NJ: Erlbaum, 1981, p. 237–246.

**Cohen B and Henn V.** Unit activity in the pontine reticular formation associated with eye movements. *Brain Res* 46: 403–410, 1972.

**Dias EC and Bruce CJ.** Physiological correlate of fixation disengagement in the primate's frontal eye field. *J Neurophysiol* 72: 2532–2537, 1994.

**Dorris MC and Munoz DP.** Saccadic probability influences motor preparation signals and time to saccadic initiation. *J Neurosci* 18: 7015–7026, 1998.

**Dorris MC, Paré M, and Munoz DP.** Neuronal activity in monkey superior colliculus related to the initiation of saccadic eye movements. *J Neurosci* 17: 8566–8579, 1997.

**Evinger C, Manning KA, Pellegrini JJ, Basso MA, Powers AS, and Sibony PA.** Not looking while leaping: the linkage of blinking and saccadic gaze shifts. *Exp Brain Res* 100: 337–344, 1994.

**Fecteau JH and Munoz DP.** Exploring the consequences of the previous trial. *Nat Rev Neurosci* 4: 435–443, 2003.

**Fuchs AF, Ling L, Kaneko CRS, King WM, and Usher SD.** The timing of the response of brainstem omni-pause neurons relative to saccadic eye movements in rhesus monkeys. *Soc Neurosci Abstr* 17: 462, 1991.

**Gandhi NJ and Keller EL.** Spatial distribution and discharge characteristics of superior colliculus neurons antidromically activated from the omnipause region in monkey. *J Neurophysiol* 78: 2221–2225, 1997.

**Gandhi NJ and Keller EL.** Comparison of saccades perturbed by stimulation of the rostral superior colliculus, the caudal superior colliculus, and the omnipause neuron region. *J Neurophysiol* 82: 3236–3253, 1999.

**Gandhi NJ and Sparks DL.** Experimental control of eye and head positions prior to head-unrestrained gaze shifts in monkey. *Vision Res* 41: 3243–3254, 2001.

**Glantz SA.** *Primer of Biostatistics.* New York: McGraw Hill, 2002.

**Glimcher PW and Sparks DL.** Movement selection in advance of action in the superior colliculus. *Nature* 355: 542–545, 1992.

**Glimcher PW and Sparks DL.** Effects of low-frequency stimulation of the superior colliculus on spontaneous and visually guided saccades. *J Neurophysiol* 69: 953–964, 1993.

**Gold JI and Shadlen MN.** Representation of a perceptual decision in developing oculomotor commands. *Nature* 404: 390–394, 2000.

**Goossens HH and Van Opstal AJ.** Blink-perturbed saccades in monkey. I. Behavioral analysis. *J Neurophysiol* 83: 3411–3429, 2000a.

**Goossens HH and Van Opstal AJ.** Blink-perturbed saccades in monkey. II. Superior colliculus activity. *J Neurophysiol* 83: 3430–3452, 2000b.

**Gore JL, Everling S, Kobayashi Y, Dorris MC, and Munoz DP.** Saccadic preparatory signals in the FEF, SNr, and SC. *Soc Neurosci Abstr* 28: 464.462, 2002.

**Guitton D, Simard R, and Codere F.** Upper eyelid movements measured with a search coil during blinks and vertical saccades. *Invest Ophthalmol Vis Sci* 32: 3298–3305, 1991.

**Handel A and Glimcher PW.** Quantitative analysis of substantia nigra pars reticulata activity during a visually guided saccade task. *J Neurophysiol* 82: 3458–3475, 1999.

**Hanes DP and Schall JD.** Neural control of voluntary movement initiation. *Science* 274: 427–430, 1996.

**Hikosaka O and Wurtz RH.** Visual and oculomotor functions of monkey substantia nigra pars reticulata. III. Memory-contingent visual and saccade responses. *J Neurophysiol* 49: 1268–1284, 1983a.

**Hikosaka O and Wurtz RH.** Visual and oculomotor functions of monkey substantia nigra pars reticulata. IV. Relation of substantia nigra to superior colliculus. *J Neurophysiol* 49: 1285–1301, 1983b.

**Horwitz GD and Newsome WT.** Separate signals for target selection and movement specification in the superior colliculus. *Science* 284: 1158–1161, 1999.

**Keller EL.** Participation of medial pontine reticular formation in eye movement generation in monkey. *J Neurophysiol* 37: 316–332, 1974.

**Keller EL, Gandhi NJ, and Shieh JM.** Endpoint accuracy in saccades interrupted by stimulation in the omnipause region in monkey. *Vis Neurosci* 13: 1059–1067, 1996.

**Luschei ES and Fuchs AF.** Activity of brain stem neurons during eye movements of alert monkeys. *J Neurophysiol* 35: 445–461, 1972.

**Mays LE and Morrisse DW.** Activity of pontine omnipause neurons during eye blinks. *Soc Neurosci Abstr* 20: 1404, 1994.

**Mays LE and Morrisse DW.** Electrical stimulation of the pontine omnipause area inhibits eye blink. *J Am Optom Assoc* 66: 419–422, 1995.

**Mazzoni P, Bracewell RM, Barash S, and Andersen RA.** Motor intention activity in the macaque's lateral intraparietal area. I. Dissociation of motor plan from sensory memory. *J Neurophysiol* 76: 1439–1456, 1996.

**Munoz DP, Dorris MC, Pare M, and Everling S.** On your mark, get set: brainstem circuitry underlying saccadic initiation. *Can J Physiol Pharmacol* 78: 934–944, 2000.

**Munoz DP and Schall JD.** Concurrent, distributed control of saccade initiation in the frontal eye field and superior colliculus. In: *The Superior Colliculus: New Approaches for Studying Sensorimotor Integration*, edited by Hall WC and Moschovakis A. Boca Raton, FL: CRC Press, 2004, p. 55–82.

**Munoz DP and Wurtz RH.** Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. *J Neurophysiol* 70: 559–575, 1993.

**Paré M and Guitton D.** The fixation area of the cat superior colliculus: effects of electrical stimulation and direction connection with brainstem omnipause neurons. *Exp Brain Res* 101: 109–122, 1994.

**Paré M and Hanes DP.** Controlled movement processing: superior colliculus activity associated with countermanded saccades. *J Neurosci* 23: 6480–6489, 2003.

**Rambold H, El Baz I, and Helmchen C.** Differential effects of blinks on horizontal saccade and smooth pursuit initiation in humans. *Exp Brain Res* 156: 314–324, 2004.

**Rambold H, Sprenger A, and Helmchen C.** Effects of voluntary blinks on saccades, vergence eye movements, and saccade-vergence interactions in humans. *J Neurophysiol* 88: 1220–1233, 2002.

**Robinson DA.** A method for measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Bio-Med Eng BME* 10: 137–145, 1963.

**Rottach KG, Das VE, Wohlgemuth W, Zivotofsky AZ, and Leigh RJ.** Properties of horizontal saccades accompanied by blinks. *J Neurophysiol* 79: 2895–2902, 1998.

**Scudder CA.** A new local feedback model of the saccadic burst generator. *J Neurophysiol* 59: 1455–1475, 1988.

**Soetedjo R, Kaneko CR, and Fuchs AF.** Evidence that the superior colliculus participates in the feedback control of saccadic eye movements. *J Neurophysiol* 87: 679–695, 2002.

**Sparks DL.** Conceptual issues related to the role of the superior colliculus in the control of gaze. *Curr Opin Neurobiol* 9: 698–707, 1999.

**Sparks DL and Mays LE.** Signal transformations required for the generation of saccadic eye movements. *Annu Rev Neurosci* 13: 309–336, 1990.

**Sparks DL, Rohrer WH, and Zhang Y.** The role of the superior colliculus in saccade initiation: a study of express saccades and the gap effect. *Vision Res* 40: 2763–2777, 2000.

**Stanford TR, Freedman EG, and Sparks DL.** Site and parameters of microstimulation: evidence for independent effects on the properties of saccades evoked from the primate superior colliculus. *J Neurophysiol* 76: 3360–3381, 1996.

**Tinsley CJ and Everling S.** Contribution of the primate prefrontal cortex to the gap effect. *Prog Brain Res* 140: 61–72, 2002.

**Volkmann FC, Riggs LA, and Moore RK.** Eyeblinks and visual suppression. *Science* 207: 900–902, 1980.

**Von Krosigk M, and Smith AD.** Descending projections from the substantia nigra and retrorubral field to the medullary and pontomedullary reticular formation. *Eur J Neurosci* 3: 260–273, 1991.

**Watanabe Y, Fujita T, and Gyoba J.** Investigation of the blinking contingent upon saccadic eye movements. *Tohoku Psychol Folia* 39: 121–129, 1980.

**Wurtz RH, Sommer MA, Paré M, and Ferraina S.** Signal transformations from cerebral cortex to superior colliculus for the generation of saccades. *Vision Res* 41: 3399–3412, 2001.

**Zee DS, Chu FC, Leigh RJ, Savino PJ, Schatz NJ, Reingold DB, and Cogan DG.** Blink-saccade synkinesis. *Neurology* 33: 1233–1236, 1983.

**Zhang M and Barash S.** Persistent LIP activity in memory antisaccades: working memory for a sensorimotor transformation. *J Neurophysiol* 91: 1424–1441, 2004.