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RESEARCH ARTICLE

Interactions between gaze-evoked blinks and gaze shifts in monkeys

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Abstract Rapid eyelid closure, or a blink, often accompanies head-restrained and head-unrestrained gaze shifts. This study examines the interactions between such gaze-evoked blinks and gaze shifts in monkeys. Blink probability increases with gaze amplitude and at a faster rate for head-unrestrained movements. Across animals, blink likelihood is inversely correlated with the average gaze velocity of large-amplitude control movements. Gaze-evoked blinks induce robust perturbations in eye velocity. Peak and average velocities are reduced, duration is increased, but accuracy is preserved. The temporal features of the perturbation depend on factors such as the time of blink relative to gaze onset, inherent velocity kinematics of control movements, and perhaps initial eye-in-head position. Although variable across animals, the initial effect is a reduction in eye velocity, followed by a reacceleration that yields two or more peaks in its waveform. Interestingly, head velocity is not attenuated; instead, it peaks slightly later and with a larger magnitude. Gaze latency is slightly reduced on trials with gaze-evoked blinks, although the effect was more variable during head-unrestrained movements; no reduction in head latency is observed. Preliminary data also demonstrate a similar perturbation of gaze-evoked blinks during vertical saccades. The results are compared with previously reported effects of reflexive blinks (evoked by air-puff delivered to one eye or supraorbital nerve stimulation) and discussed in terms of effects of blinks on saccadic suppression, neural correlates of the altered eye velocity signals, and implications on the hypothesis that the attenuation in eye velocity is produced by a head movement command.

Keywords Blink · Saccade · Saccadic suppression · Gaze shift · Superior colliculus · Orbicularis oculi · Eyelid · Levator palpebrae

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Introduction

It is readily accepted that large changes in gaze are produced by coordination of movements across multiple segments that include the eyes, head, body, and even feet (Anastasopoulos et al. 2009). It is not as well appreciated, however, that blinks—rapid and transient depression of the eyelid—can also voluntarily accompany large redirections of the line of sight. In general, the frequency of producing a "gaze-evoked blink" increases with gaze amplitude, and the likelihood is greater for amplitude-matched movements produced when the head is unrestrained (von Cranach et al. 1969; Evinger et al. 1994). Engaging in a behaviorally relevant task reduces the probability of gaze-evoked blinks, compared to their prevalence during "refixational" saccades observed at the end of a laboratory-specified trial (Williamson et al. 2005). Furthermore, neuromuscular contractions that produce a blink are also observed during large gaze shifts generated with the eyes closed (Evinger et al. 1994), and patients with certain ocular motility disorders can only initiate a saccade by triggering it with a blink (Leuzzi et al. 1993). These results indicate that the gaze-evoked blink is not a reflexive behavior induced by stimulation of the cornea and eye lashes by wind but is most likely mediated by the same neural

commands that control multi-segmental movements (Evinger et al. 1994). Thus, investigations of the neural mechanisms of saccadic eye movements, either in isolation or in coordination with other effectors, must factor in the potential contributions of blinks.

The limited knowledge base concerning gaze-evoked blinks and their effects on gaze shifts stems primarily from behavioral studies on humans (von Cranach et al. 1969; Watanabe et al. 1980; Evinger et al. 1994; Rottach et al. 1998; Rambold et al. 2002; Williamson et al. 2005). The objective of the present study is to characterize their interactions during both head-restrained and head-unrestrained gaze shifts in nonhuman primates. Using this animal model permits the collection of an extensive database, and it also motivates electrophysiological studies of blink interactions with gaze shifts, provided that their effects are similar on humans and monkeys. Overall, the analyses verify previous observations that the main sequence of the saccadic eye component is altered such that the peak velocity is reduced and duration is prolonged; despite the blink-induced perturbation, the endpoint accuracy of gaze is preserved. In terms of new contributions, the likelihood of observing gaze-evoked blinks was found to be related to not only gaze amplitude but also subject-specific velocity kinematics of movements without blinks, and the implication of this result on the linkage between blinks and saccadic suppression (Volkmann et al. 1980; Watanabe et al. 1980) is considered; the effect of a gaze-evoked blink on the temporal profile of the eye velocity was evaluated, and its potential relevance to the attenuation in eye velocity linked to the accompanying head movement during head-unrestrained gaze shifts (Freedman and Sparks 2000) is discussed; the relationship between gaze amplitude and the relative timing of blink and gaze onsets was analyzed; the effect of blink on vertical eye velocity waveform was assessed briefly; and whether the reaction time of movements associated with gaze-evoked blinks is reduced was also tested.

Preliminary versions of this study have been published previously (Gandhi 2007; Gandhi and Katnani 2011).

Materials and methods

Four rhesus monkeys (*Macaca mulatta*) weighing 6–12 kg served as subjects. All experimental protocols were approved by the Institutional 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. Under aseptic conditions and isoflurane anesthesia, each animal underwent an initial surgery to implant a Teflon-coated stainless steel coil beneath the conjunctiva of one eye. A head-restraint post was also secured to the skull with titanium or stainless steel screws and bone cement. Another coil that would permit head movement measurements was also placed in bone cement. As all animals participated in other studies, a second surgery was performed to fix a stainless steel chamber over a craniotomy that provided access to either the superior colliculus or the pontomedullary reticular formation. Additionally, it should be noted that, as part of previous studies, monkeys WL and BN were often exposed to air-puff stimulus to induce the trigeminal blink reflex, although such puffs were not delivered when collecting data for the experiments described here. Monkeys BL and WY were rarely, if ever, tested with the air-puff stimulus.

Oculomotor performance was measured using the magnetic search coil technique. Gaze (eye-in-space) and head positions were measured from surgically implanted coils on the eyeball and in the head explant, respectively. Vertical deflections in the eyelid signal, measured in arbitrary units, were obtained from a small coil (5 mm diameter, 5 turns) that was taped to the upper lid on each experimental day (Gandhi and Bonadonna 2005). Eye (eye-re-head) position was computed as the difference between gaze and head signals. When the head was restrained, it was clamped in the straight-ahead position, so gaze and eye positions were identical. Gaze, head, and eyelid position data were sampled at 1 kHz.

Control of the experimental setup and data collection were accomplished by custom software written using the LabView real-time module (Bryant and Gandhi 2005). Visual targets were presented on a cylindrical board fitted with tri-state light-emitting diodes (LEDs) that spanned 96° horizontally and 80° vertically in 2° increments. A miniature laser module was also mounted on the head-restraint post. When turned on, the laser emitted a red beam and served to provide visual feedback regarding head position (Gandhi and Sparks 2001).

The animals performed visually guided "step" gaze shifts in either the head-restrained or head-unrestrained condition. Each trial initiated with the presentation of a fixation target, and the animal was required to bring its line of sight onto the target. If the head was unrestrained, the laser module was turned on and the animal also had to align the beam (i.e., the head) with the stimulus. Following a fixation period of 500–1,000 ms, the initial target was extinguished and another stimulus was simultaneously illuminated at another location. The animal was permitted 500 ms to bring its visual axis within 5° (radius) of the new target location and maintain fixation for 500–1,000 ms to obtain a liquid reward. The initial and final desired gaze positions varied between ±35°. Initial eye-in-head positions varied across this range when the head was immobilized, but the eyes were roughly centered in the orbits when the head was free to move. The discrepancy in

Table 1 Distributions of trials for horizontal movements with and without gaze-evoked blinks

Monkey	Head-unrestrained		Head-restrained	
	Blink	Nonblink	Blink	Nonblink
WL	1,176	3,704	1,230	7,394
WY	1,296	984	688	1,223
BN	2,083	2,548	977	3,974
BL	282	1,940	40	1,744

distributions of initial eye-in-head position for head-restrained and head-unrestrained conditions is due to a design constraint imposed in other studies (Gandhi and Sparks 2007; Bechara and Gandhi 2010b). Head-restrained and head-unrestrained conditions were usually performed on different days. The majority of data collection utilized horizontal target displacements, although a limited number of gaze shifts to vertical target displacements were collected in separate sessions. Table 1 provides a breakdown of the 31,283 horizontal, head-restrained, and head-unrestrained gaze shifts produced with and without gaze-evoked blinks by the four animals.

Data were analyzed offline using Matlab and custom software. For behavioral data, the onset and offset of gaze and eye-in-head components were identified using a velocity threshold criterion of 50°/s and 30°/s, respectively. Because head movements tend to be more variable than gaze shifts, a slightly more complex velocity threshold algorithm was used, as described previously (Chen and Walton 2005; Walton et al. 2007). Briefly, onset and offset were determined when a certain percentage of A/D points within a sliding window, as opposed to all of them, were found to be above (onset) or below (offset) a 6°/s velocity threshold. To determine the optimal blink onset and offset thresholds, lid "velocity" (i.e., change in arbitrary units/time) was computed. Because eye blinks are characterized by an extremely high eyelid velocity (Gruart et al. 1995; VanderWerf et al. 2003), the measured times of blink onset and offset were relatively insensitive to changes in threshold. Thus, the threshold could easily be set to a high-enough value to exclude most gaze-related eyelid movements that were not blinks. The experimenter verified these measurements to ensure accuracy.

Results

Probability of gaze-evoked blinks

To assess the likelihood of observing a gaze-evoked blink, rightward and leftward gaze shifts were pooled and grouped in 10° bins, and the fraction of blink trials in each bin was determined. This computation was performed separately for each animal and for head-restrained and head-unrestrained conditions. Figure 1a illustrates blink probability as a function of gaze amplitude. The individual traces highlight the two head mobility conditions (head-restrained: dashed lines, open symbols; head-unrestrained: solid lines, filled symbols) and the four animals (different colors). Statistical significances of these three factors were determined using a three-way ANOVA. In each animal, the probability of a gaze-evoked blink increased with gaze amplitude [$F(5,15) = 43.06$, $P \rightarrow 0$], a result in agreement with previous studies in humans (von Cranach et al. 1969; Watanabe et al. 1980; Evinger et al. 1994; Williamson et al. 2005). For each animal, the blink probability curve increased more rapidly for the head-unrestrained condition (solid lines) compared to the head-restrained case (dashed lines) [$F(1,15) = 26.75$, $P < 0.0001$]. This result verifies a previous report in humans (von Cranach et al. 1969). The statistical analysis also revealed a significant difference among animals [$F(2,15) = 30.81$, $P \rightarrow 0$]. This result is supported by the observation that the likelihood of a blink increased at different rates across animals. Monkey WY was likely to blink with every horizontal head-unrestrained gaze shift larger than 30°, while monkey BL produced blinks with less than 50% frequency for gaze shifts greater than 60°. Incidentally, these two animals had not participated in previous blink experiments. The other two animals (WL and BN), who were subject to air-puffs to induce the trigeminal blink reflex, exhibited intermediate gaze-evoked blink probabilities, suggesting that the trend in blink probability across animals is not a function of experimental history.

Figure 2a illustrates the average gaze velocity of head-restrained gaze shifts as a function of gaze amplitude. Average gaze velocity was computed as gaze amplitude divided by its duration. Each point represents the mean ± SD of the movements included in each 10° bin of gaze amplitude. Figure 2b shows the comparable plot for head-unrestrained gaze shifts. Importantly, the plot includes control or nonblink trials only, that is, a blink did not accompany the gaze shift. Hence, if all gaze shifts within a bin were accompanied with a blink—for example, the bin centered on 65° for monkey WL (blue circles, Fig. 2b)—then there is no corresponding data point for average velocity. In both head mobility conditions, the average gaze velocities for large-amplitude control

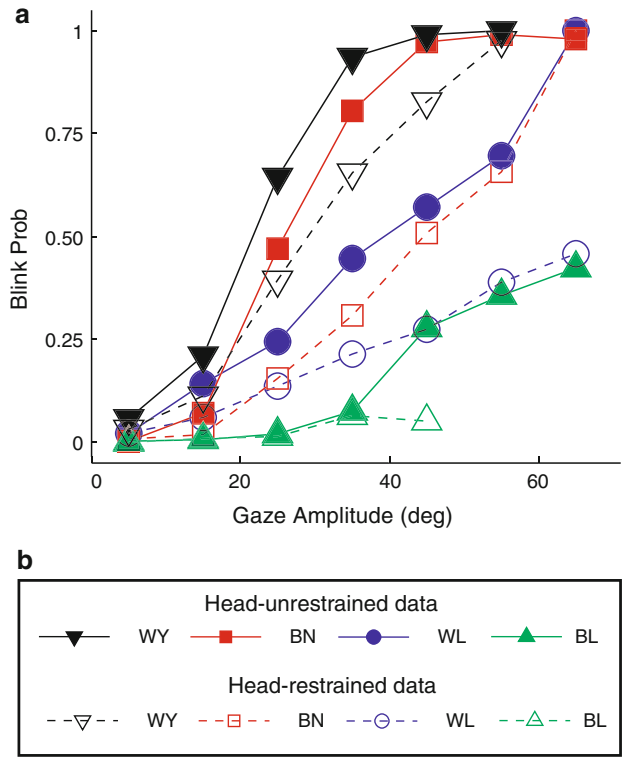

Fig. 1 Likelihood of observing gaze-evoked blinks with gaze shifts. **a** The probability of generating a gaze-evoked blink is plotted as a function of gaze amplitude during head-restrained saccades (*open symbols*, *dashed traces*) and coordinated eye–head movements (*filled symbols*, *solid traces*). Data were grouped into 10° bins according to the absolute value of gaze amplitude. The probability of trials with gaze-evoked blinks is indicated on the ordinate axis. **b** Legend identifies each *symbol*, *color* and *line-type* with an animal and head mobility condition. This convention is used in several figures that follow

movements were greater for monkeys BL (green) and WL (blue) than for monkeys WY (black) and BN (red). Interestingly, the likelihood of gaze-evoked blinks was also greater for the animals (WY, BN) with the slower average gaze velocities (Fig. 1a). This trend toward a negative correlation was further examined across animals by relating the control velocity kinematics for gaze amplitudes greater than 30° (because the eye velocity plateaus for large movements) with blink probability. For the head-restrained condition (Fig. 2c), the correlation coefficient (r) between average gaze velocity and blink probability was −0.5429, which approached statistical significance (t test, $P = 0.07$). Blink probability was even more strongly negatively correlated with peak gaze velocity ($r = -0.6582$, $P < 0.05$; data not shown). For head-unrestrained data (Fig. 2d), the correlation coefficient between average gaze velocity and blink probability was −0.883, which was statistically significant (t test, $P < 0.0001$). Blink probability was also negatively correlated with other velocity parameters (data not shown): average eye velocity ($r = -0.7848$, $P < 0.01$), peak gaze velocity ($r = -0.8656$, $P < 0.0001$) and peak eye velocity ($r = -0.8094$, $P < 0.001$). Collectively, these results suggest that animals that inherently produce high-velocity gaze shifts are less likely to show an accompanying gaze-evoked blink.

Effects of gaze-evoked blinks on eye velocity

Previous studies have reported that volitional blinks timed to overlap with gaze shifts grossly attenuate the eye velocity component (Rottach et al. 1998; Rambold et al. 2002). Figure 3 examines the temporal aspects of this phenomenon for head-restrained saccades accompanied by gaze-evoked blinks in monkeys. Eye velocity and eyelid position traces for individual trials are shown in the four rows, each corresponding to one animal. Each panel plots waveforms for amplitude-matched saccades with (blue traces) and without (red traces) gaze-evoked blinks. The data in the right column are for a larger-amplitude movement. Saccades without gaze-evoked blinks display a bell-shaped velocity profile with some skewness (longer deceleration phase) for large-amplitude movements. In contrast, the velocity traces of saccades with gaze-evoked blinks are grossly perturbed, and the pattern of perturbation differed across animals. For monkey WL (Fig. 3a), the magnitude of peak velocity was reduced and each velocity trace consistently displayed two peaks. The velocity profiles of monkey BN (Fig. 3c) also revealed two and often more peaks, but without the same repeatability as monkey WL. For monkeys WY and BL (Fig. 3b, d), the perturbation effect was less conspicuous, typically indicating a reduction in peak velocity and an increase in duration, although some trials did show a tendency for a second peak.

Examples of the various effects of gaze-evoked blinks on head-unrestrained gaze shifts are shown in Fig. 4. The presentation follows the same format as Fig. 3, but head velocity traces are also included in the illustration. In the absence of blinks (red traces), the eye velocity profiles exhibit only one peak with a prolonged deceleration phase. These results are qualitatively similar to those observed during the head-restrained condition. The presence of a blink (blue traces) consistently attenuated the ongoing eye velocity profile, which was followed by a reacceleration that resulted in one or more additional peaks. A two-peak profile was most common in monkey WL (Fig. 4a), but infrequent examples can be identified in the other animals also (e.g., Fig. 4b). The effects of gaze-evoked blinks in monkey BL (Fig. 4d) is most modest; the peak velocity is reduced and the duration increases, but the attenuation is not always as pronounced as in other animals. The trials illustrated for monkey BN (Fig. 4c) show that the velocity can remain attenuated without distinct, multiple peaks. For

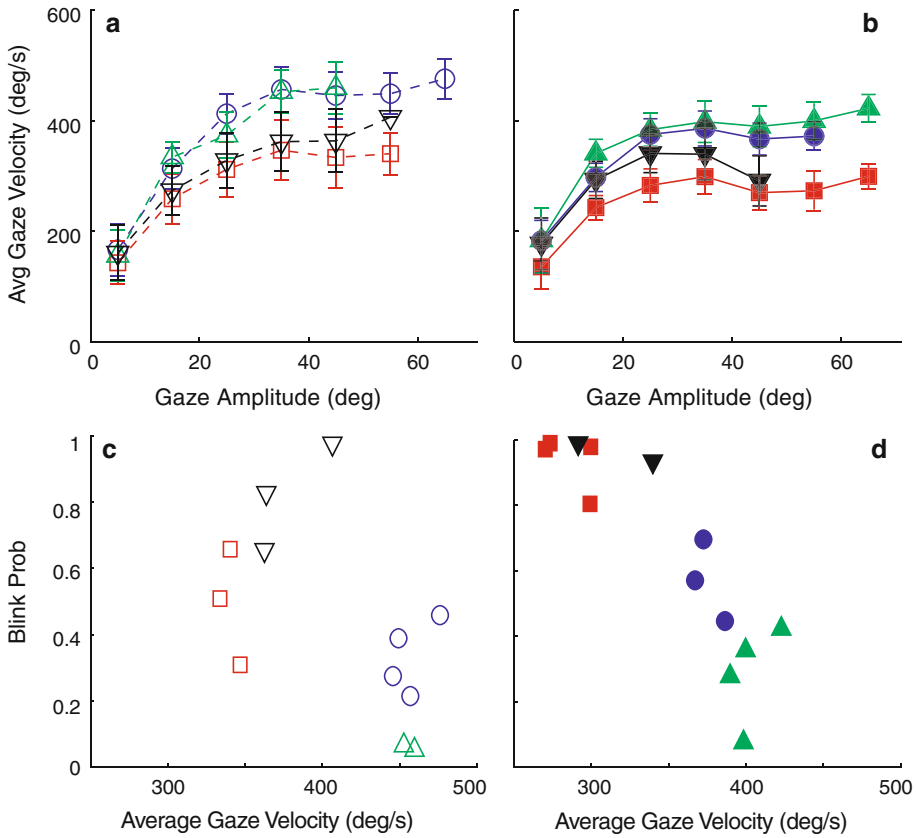

Fig. 2 Relationship between main sequence property and blink likelihood. **a**, **b** Average gaze velocity is plotted as a function of amplitude for head-restrained saccades (*left*) and head-unrestrained gaze shifts (*right*). Data were grouped into 10° bins according to gaze amplitude. Each point denotes the mean with one standard deviation *error bars* of the average velocity of trials *without* gaze-evoked blinks. **c**, **d** Blink probability is plotted as a function of average gaze velocity for large-amplitude gaze shifts, that is, for the range for which gaze velocity remains relatively constant for each animal. See Fig. 1b for assignment of *symbols*

some trials (right column), the velocity attenuation overlapped with or occurred prior to the onset of the gaze shift. The velocity attenuation persisted throughout the movement, which was generally longer in duration.

Two other features present in the temporal profile plots are noteworthy. One, gaze-evoked blinks do not attenuate head velocity. In fact, there is a hint of a slight increase in the magnitude and time of peak head velocity, and these data are considered in more detail later. Two, the eyelid profiles can appear quite different across monkeys, but they are fairly consistent for head-restrained and head-unrestrained conditions for an individual animal. No further analyses will be performed on the eyelid waveforms as it was outside the scope of the present study.

Main sequence

Generalization of the trends in kinematic features gleaned from the several examples of temporal traces can be better realized from the main sequence data of all 31,283 horizontal movements included in this study. Figure 5 displays peak gaze velocity as a function of gaze amplitude for head-restrained (left column) and head-unrestrained (middle column) movements. The right column plots peak eye velocity as a function of the saccadic ocular component of head-unrestrained gazes shifts. Blink and nonblink trials are shown as blue and red dots, respectively. Each row corresponds to a different animal.

Figure 5 shows that peak gaze and eye velocities were generally attenuated during gaze shifts accompanied by a blink. Despite the statistical differences across most gaze and eye amplitudes (see next paragraph), there is significant overlap between the distributions of peak velocity for amplitude-matched movements. This is partly caused by the simplistic method used to determine peak velocity: the maximum velocity reached across the entire duration of the movement. This method is potentially flawed because blink-attenuated velocity traces exhibit multiple peaks, and the maximum could be associated with one of the reaccelerated phases—for example, see blue traces in the top row, right column of Fig. 4. An alternative approach is to consider the average velocity for blink and control trials (Fig. 6). Although there is still some overlap, the separation between blink and nonblink trials is more pronounced. In agreement with the impression obtained from the temporal traces, the duration of movements accompanied by blinks were longer (Fig. 7).

To test for a statistically significant effect of blink, the data in each panel of Figs. 5, 6 and 7 were grouped into 10° increments of gaze amplitude (left and middle columns) or eye amplitude (right column). For each bin, the distributions of blink and nonblink trials were compared with a two-

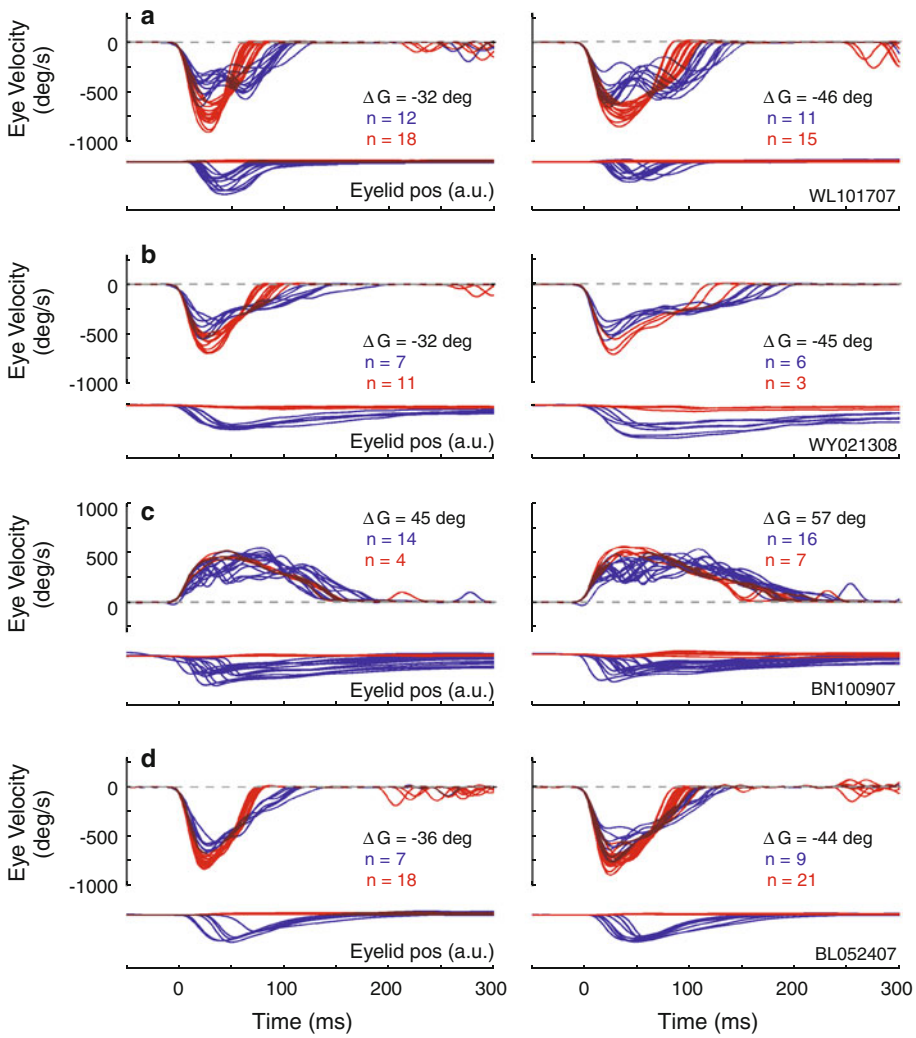

Fig. 3 Effects of gaze-evoked blinks on head-restrained saccades. Each panel illustrates individual trials of eye velocity (deg/s) and eyelid position (*au*: arbitrary units) traces as a function of time. Saccades produced with (*blue*) and without (*red*) accompanying gaze-evoked blinks are differentiated by *color*. The mean amplitude of saccades and the number of trials shown in each *panel* are indicated in the *inset* text. Note, however, that the ratio of displayed *red* and *blue* trials need not correspond to the probability of observing a gaze-evoked blink for the movement amplitude. All *plots* are aligned on movement onset. The data included in the *left column* correspond to a smaller-amplitude movement than the trials plotted in the *right column*. The *dashed*, *horizontal line* in *gray marks* zero deg/s. Data from the different animals are shown in the *different rows*: **a** monkey WL, **b** monkey WY, **c** monkey BN, **d** monkey BL

tailed *t* test, provided that at least 10 trials were present in each group. Bins for which the means of the two distributions are statistically different are denoted with an "×," and the symbol is placed at the center of each amplitude bin. For nearly all amplitudes larger than 10°, there was a statistically significant effect of gaze-evoked blinks on all three kinematic variables. The notable exceptions are the data for monkey BL. The limited number of significant bins is not because gaze-evoked blinks did not alter movement characteristics, but is instead due to the fact that this animal produced very few gaze-evoked blinks.

Relation to head amplitude

One interesting hypothesis associated with eye–head coordination states that the head movement command or its corollary discharge reduces the gain of the eye burst generator (Freedman and Sparks 2000; Freedman 2001). Attenuation in the output of the burst generator neurons reduces the velocity of the eye component of the gaze shift, and local feedback control of the saccadic system produces the reacceleration of the eye movement, which can appear as a second peak in the velocity waveform. The results above (Figs. 1, 4) show that the propensity of gaze-evoked blinks increases with large-amplitude gaze shifts, which typically incorporate a large-amplitude head component. Furthermore, the eye velocity often exhibits two or more peaks when accompanied by a gaze-evoked blink. Thus, it becomes necessary to evaluate eye velocity as a function of head amplitude for movements with and without gaze-evoked blinks.

Each panel in Fig. 8 plots several eye and head velocity waveforms as a function of time. Each trace is an average of numerous trials, and the color indicates the range of head amplitudes used to compute each mean trace. Averaged nonblink trials are plotted in the left column, while the mean of blink trials is shown in the right column. To make certain that the main sequence property of saccadic eye component does not influence the eye velocity, the analysis incorporated only movements with large eye

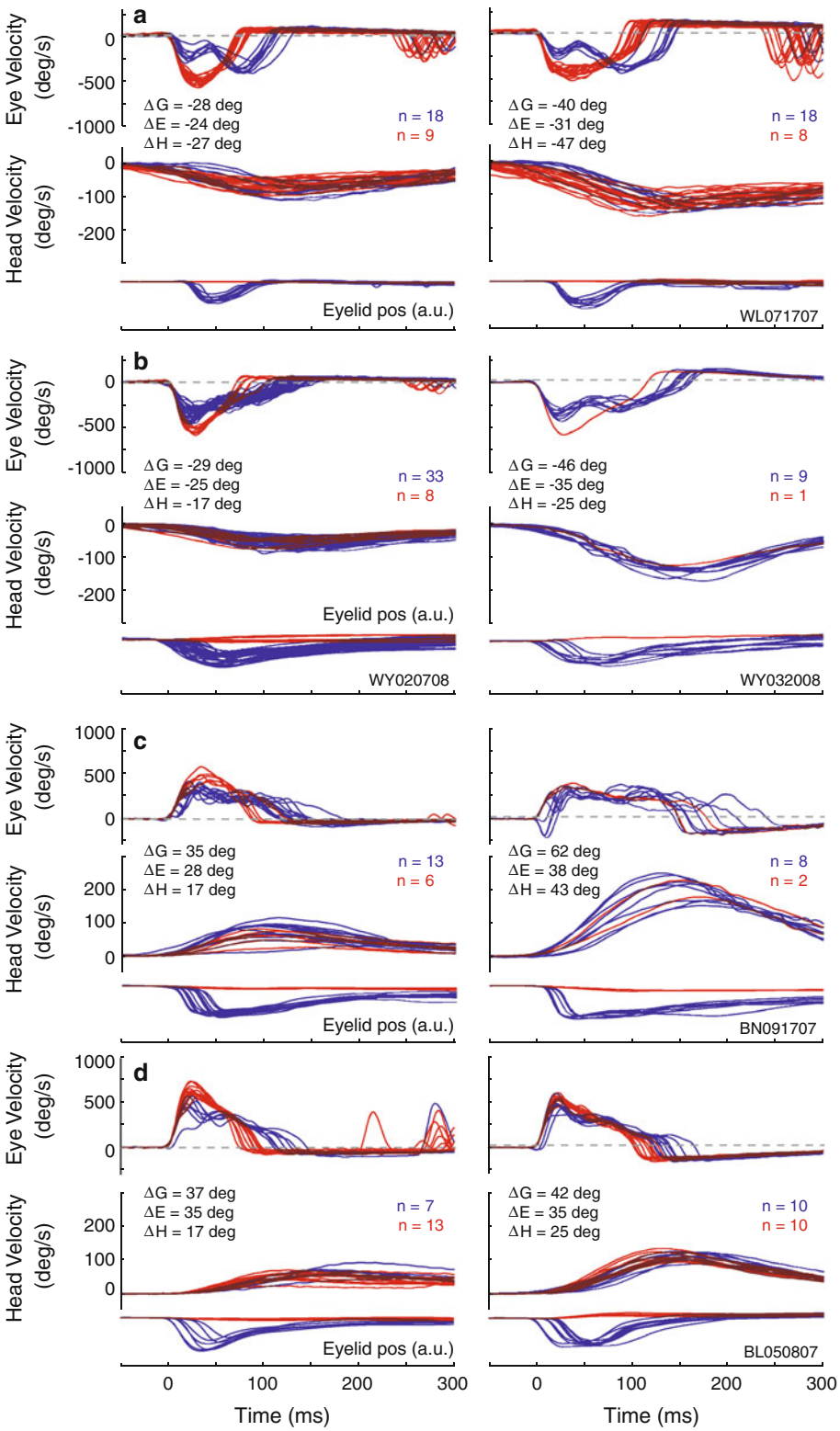

Fig. 4 Effects of gaze-evoked blinks on head-unrestrained gaze shifts. Data are in the same format as Fig. 3, except that head velocity profiles are also included in each *panel*

amplitudes (greater than 32°) for which the peak velocity is roughly saturated (Freedman and Sparks 2000). With these constraints, a comparison between blink and nonblink trials was possible only for monkeys WL and BL; not enough nonblink trials met these criteria to compute reliable averages for monkeys WY and BN.

The eye velocity of large-amplitude gaze shifts without a blink can best be described by a single-peaked, bell-

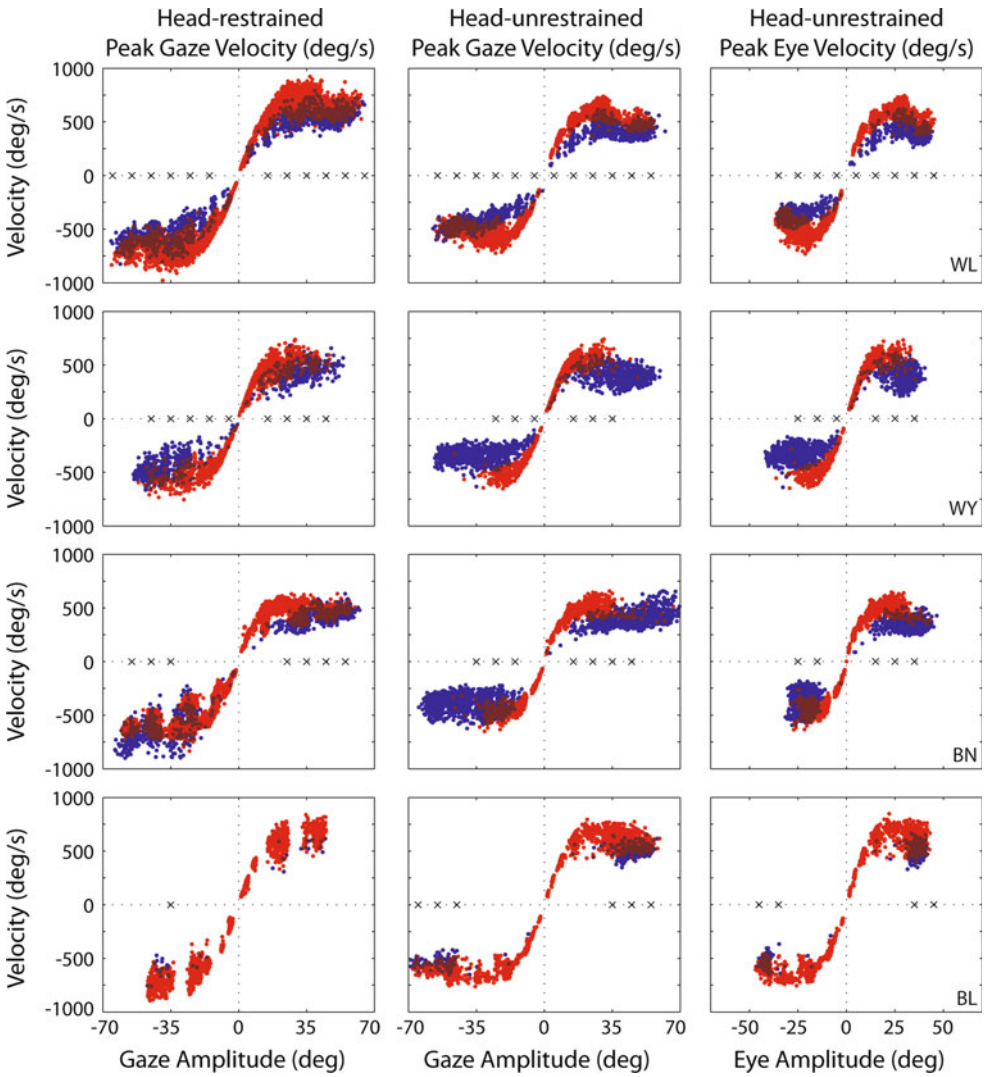

Fig. 5 Main sequence analysis for movements with (*blue*) and without (*red*) gaze-evoked blinks. *Left column* plots peak gaze velocity as a function of saccade amplitude for all head-restrained trials. Note that for head-restrained data, peak eye velocity equals peak gaze velocity. *Middle column* shows peak gaze velocity as a function of gaze amplitude for head-unrestrained data. *Right column* displays peak velocity of the eye component as a function of the saccadic eye component of head-unrestrained gaze shifts. Each *row* shows data from one animal, as identified by the *two letters* in the *bottom right* corner of the panels in the *right column*. Each point denotes one trial, and data from all horizontal movements (see Table 1) are illustrated. The "×" denotes the bin, tested in 10° increments, for which the main sequence parameter was significantly different between blink and nonblink trials (two-tailed *t* test, $P < 0.05$)

shaped profile that resembles the waveform associated with head-restrained saccades without blinks. This feature persists when data are sorted according to head amplitude (Fig. 8a, c), except that the deceleration phase is prolonged as the head amplitude increases. There is also a slight decrease in peak velocity. In contrast, gross attenuation and multiple peaks are pronounced in movements associated with gaze-evoked blinks. The strength of attenuation is much stronger in monkey WL, who generally produced slower saccades (see Fig. 2), than in monkey BL. These data look very similar to Fig. 5a, c of Freedman and Sparks (2000), in which the perturbed eye velocity waveform is attributed to head movement amplitude.

Blink timing

The waveforms in Figs. 3 and 4 show that blink onset relative to gaze onset can be variable. Figure 9 explores trends in this parameter as a function of gaze amplitude. Negative latency value means that blink onset lags gaze onset, and a positive metric indicates that blink onset leads gaze onset. The distributions of differences in blink and gaze latencies for all blink trials during head-restrained (Fig. 9a) and head-unrestrained (Fig. 9b) gaze shifts are shown for monkey WL. Each dot represents one trial, and its color indicates the initial gaze position according to the color axis in panel b. When the head was immobilized in the straight-ahead position, initial gaze position was equivalent to initial eye-in-head position. When the head was free to move, initial gaze position equaled head position in space because the eyes were roughly centered in the orbits, per the design of the behavioral task. The data were also grouped in 5° increments of gaze amplitude, combined across all initial gaze positions, and the mean and standard deviation of each bin were plotted as a function of gaze amplitude. Figure 9c, d plots these data for each of the four animals during head-restrained and head-unrestrained gaze shifts, respectively.

For the head-restrained condition, blink onset increasingly lagged gaze onset (and it became more variable) with

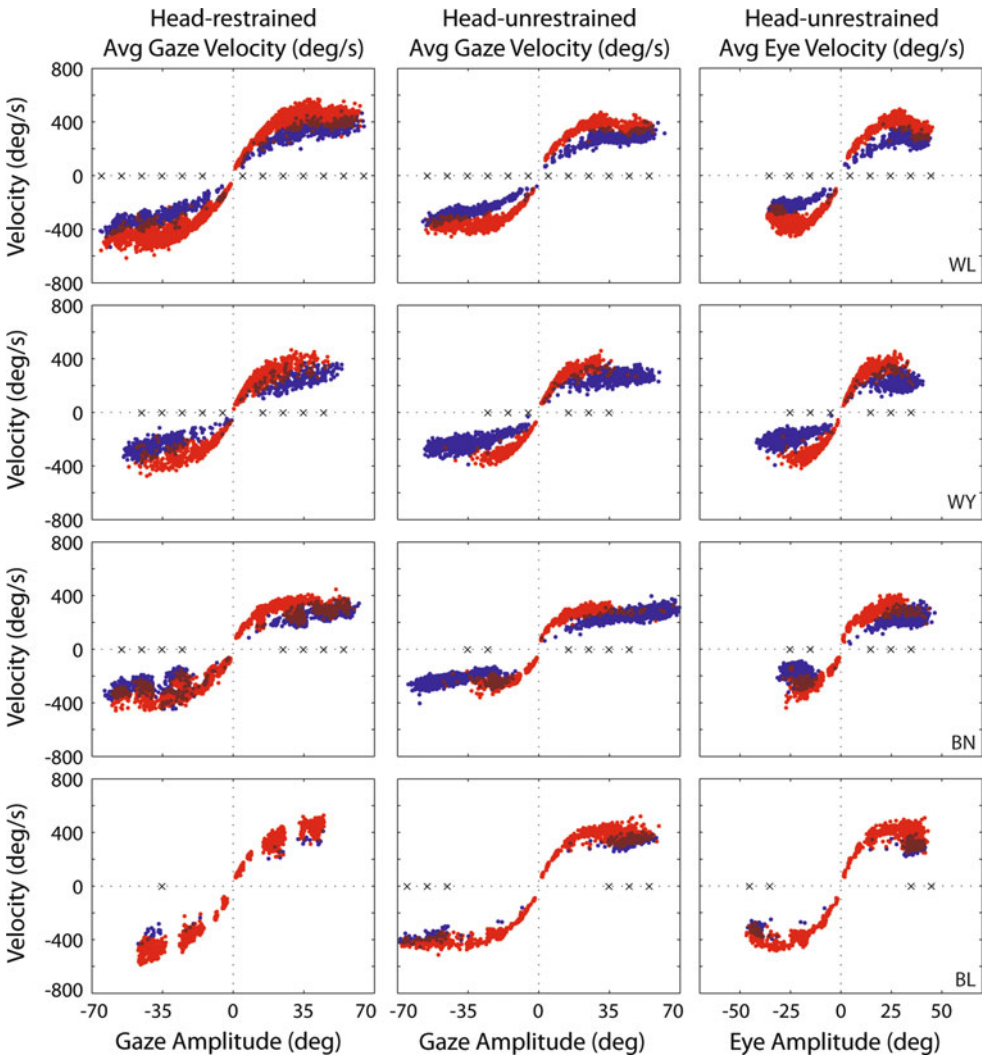

Fig. 6 A comparison of average velocity as a function of amplitude parameters for movements with (*blue*) and without (*red*) gaze-evoked blinks. Average velocity was computed as amplitude divided by duration. The illustration is in the same format at Fig. 5

larger-amplitude gaze shifts. A closer look at the distribution suggests that this pattern was dominated by saccades initiated when the initial eye position was contraversive to the direction of movement (blue dots, Fig. 9a) For the small subset of movements initiated with the eyes centered in the orbits (green dots) or directed ipsiversive to the direction of movement (red dots), the gaze-evoked blink often preceded the saccade. The trend in relative onset times as a function of gaze amplitude was less apparent when the head was allowed to move (Fig. 9b). Blink and gaze onset times were more likely to be aligned around movement onset even for large-amplitude movements. Consequently, there was more a chance for the blink to lead gaze onset. In such cases, the eyes could initially move in a direction different from that of the intended movement, and several examples of such trials are plotted in Fig. 4 (monkey BN). This pattern was observed across all animals (Fig. 9d).

Despite the variability in blink and gaze onset times for amplitude-matched movements, the attenuation in eye velocity varied systematically with the relative timing. Figure 10 plots eye amplitude, eye velocity, and eyelid velocity for an averaged nonblink movement (gray trace) and for several individual gaze shifts accompanied with a gaze-evoked blink. The eye and eyelid waveforms corresponding to the same movement are shown in the same color. The earliest blink (red traces) attenuated the eye velocity during the acceleration phase; the velocity data revealed a weak re-acceleration after the blink, but eye velocity increased gradually (nearly looking like a plateau) for the next 50–60 ms. For the other trials, in which blink onset followed the time of peak eye velocity, the blink accelerated the attenuation in eye velocity, and a larger reacceleration followed the blink. These traces exhibited clear dual peaks in their temporal profiles. Furthermore, the time at which a minimum was reached in the eye velocity

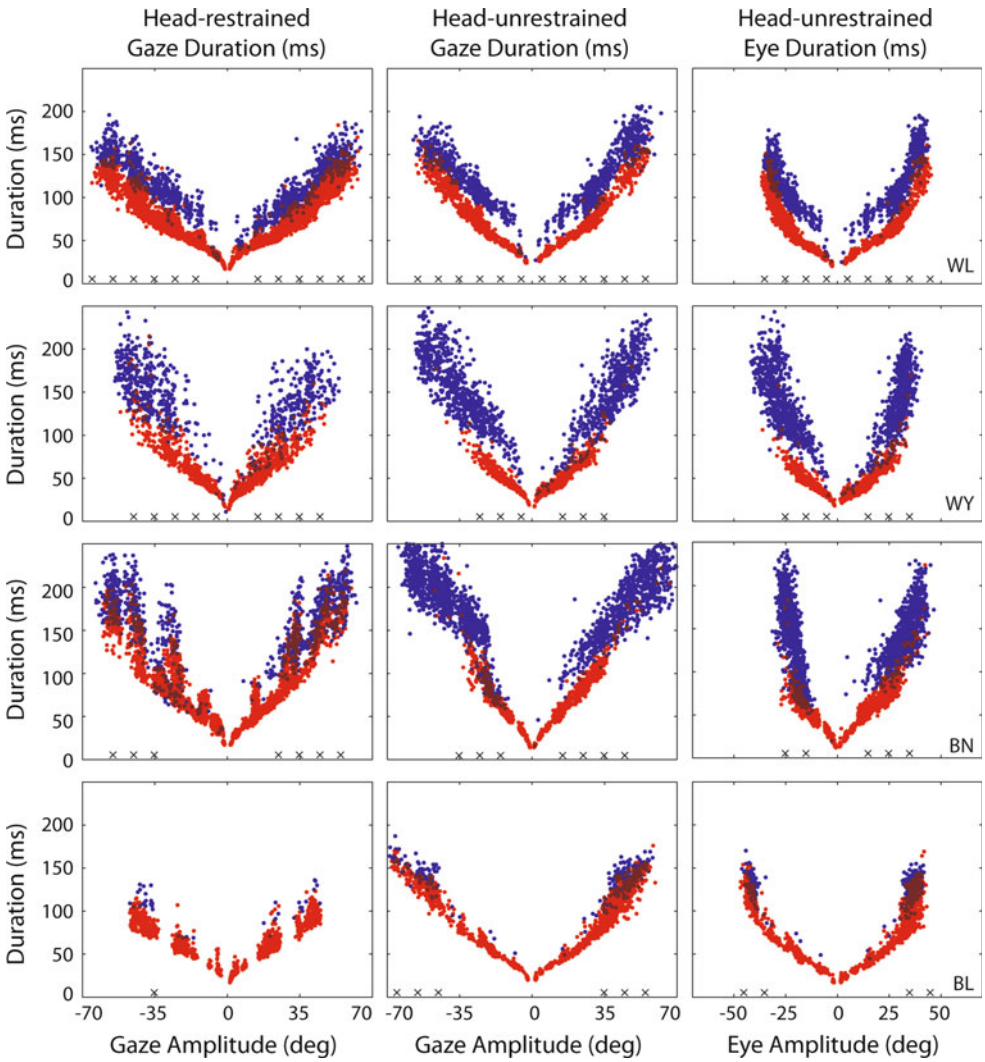

Fig. 7 A comparison of movement duration as a function of amplitude parameters for gaze shifts with (*blue*) and without (*red*) gaze-evoked blinks. The illustration is in the same format at Fig. 5

was a function of the blink time: in this example, the later the blink occurred, the more potent the attenuation in eye velocity.

Vertical saccades

Figure 11 illustrates examples for vertical head-restrained saccades. Temporal profiles of eye position, eye velocity, eyelid position, and eyelid velocity are shown for amplitude-matched saccades with and without gaze-evoked blinks. Consistent with the observations noted for horizontal movements, the eye velocity waveform is bell-shaped when not accompanied by a blink (red traces). The deflection in the eyelid channel on a nonblink trial is a lid saccade, which is commonly observed for vertical movements (Becker and Fuchs 1988). The presence of a blink (blue traces), as opposed to a lid saccade, produced a profound weakening in eye velocity, which then reaccelerated—hence, the dual peaks—to complete the movement. Therefore, the attenuation in eye velocity induced by gaze-evoked blinks is not limited to horizontal movements.

Other effects of gaze-evoked blinks

A comparative analysis of the effect of blink on reaction time and movement accuracy seems more appropriate when blink and nonblink trials are matched for initial and final target positions. Thus, head-restrained and head-unrestrained data were partitioned according to identical target configurations—in other words, the initial and final targets must be the same. With this approach, the desired gaze amplitude is equal, and the initial eye, head, and gaze positions are comparable. An additional criterion that a minimum of five blink and five nonblink trials be present for each target configuration was also imposed. This step was implemented to compute a reliable average metric.

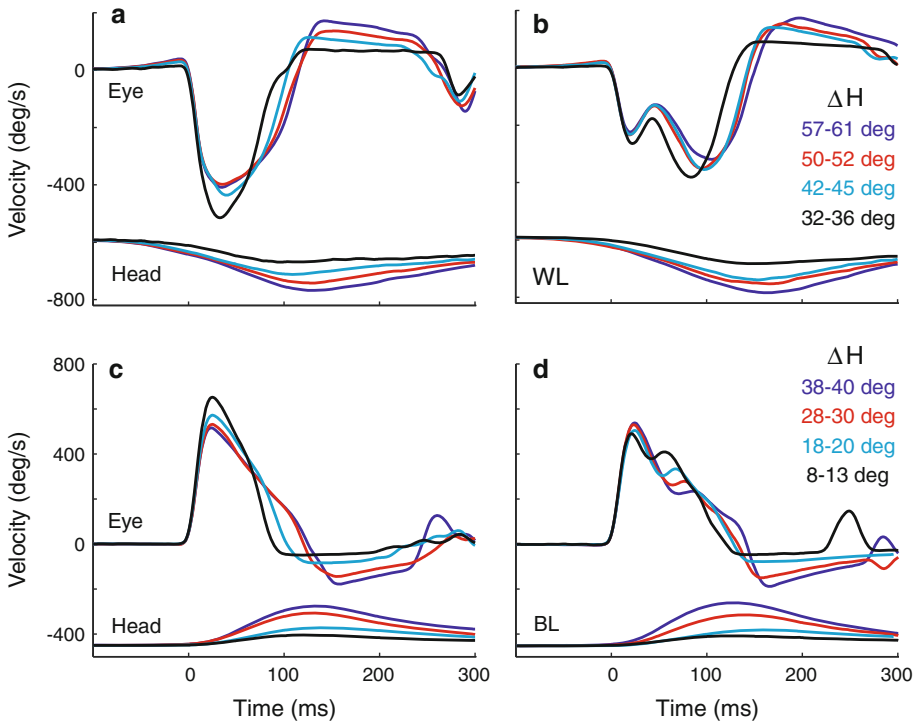

Fig. 8 Effects of gaze-evoked blinks on large-amplitude coordinated eye–head movements grouped according to head amplitude. All head-unrestrained gaze shifts with saccadic eye amplitude greater than 32° and in the same direction [*leftward* for monkey WL (**a**, **b**) and *rightward* for monkey BL (**c**, **d**)] were included in the analysis. Trials that met the inclusion criterion were grouped according to head amplitude, as identified by the *color* and *text* in *insets*, and sorted into trials with and without gaze-evoked blinks. The *panels* show temporal profiles of averaged eye-in-head and head-in-space velocities for these head-unrestrained gaze shifts without (**a**, **c**) and with (**b**, **d**) gaze-evoked blinks. Comparable *plots* for monkeys BN and WY are not illustrated because there were essentially no head-unrestrained trials without gaze-evoked blinks that met the inclusion criteria

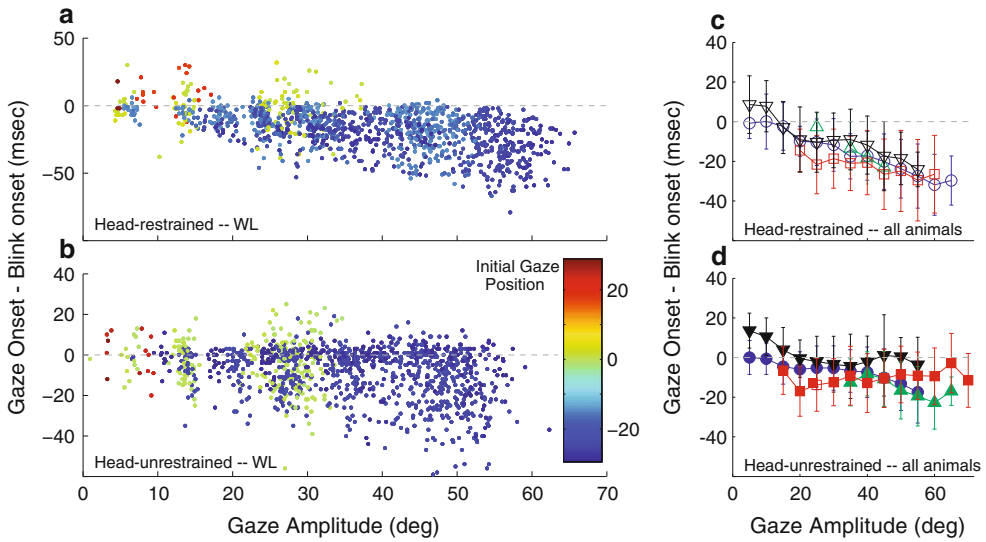

Fig. 9 Distribution of blink times. **a** For each head-restrained saccade accompanied by a gaze-evoked blink for monkey WL, the time of blink onset relative to gaze onset is plotted as a function of saccade amplitude. *Negative* latency value means that blink onset lags gaze onset, and positive metric indicates that blink onset leads gaze onset. The *color axis* in *panel b* defines the initial gaze position for each trial, which also equal initial eye-in-head position for head-restrained data. **b** Same display format for head-unrestrained data obtained in monkey WL. The *color* of each *dot* indicates initial gaze position, since the eyes were initially centered in the orbits prior to the onset of the gaze shift. **c**, **d** For each animal, the data were sorted into 5° bins of gaze amplitude. The mean ± one standard deviation of blink time relative to gaze onset is plotted as a function of gaze amplitude for head-restrained (**c**) and head-unrestrained (**d**) movements. The *color symbols* follow the convention established in Fig. 1b

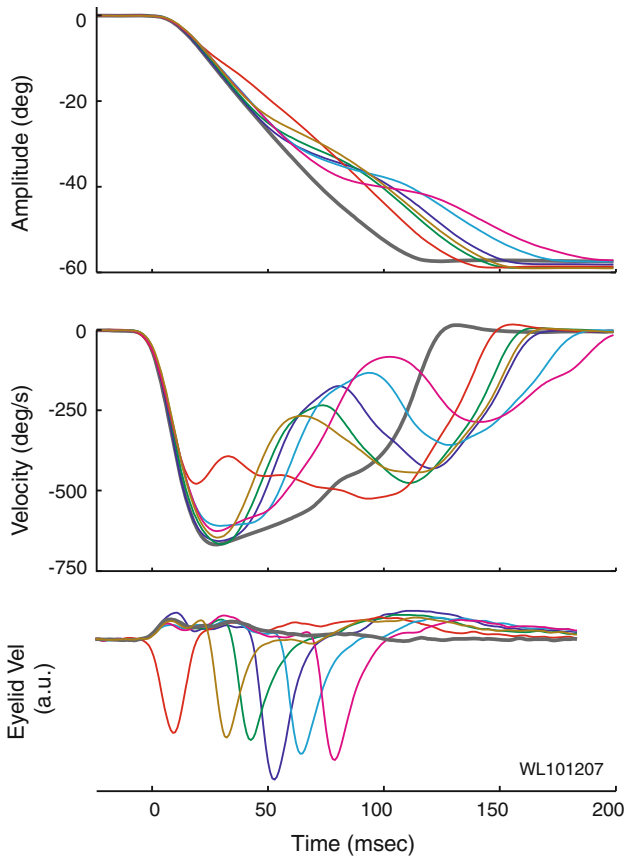

Fig. 10 Effect of blink timing on velocity waveform. Eye position (*top*), eye velocity (*middle*), and eyelid velocity (*bottom*) are plotted as a function of time. The *gray* trace is an average of several, same-amplitude head-restrained saccades produced without a gaze-evoked blink. Note that the eye velocity is a *bell-shaped* profile with a slightly prolonged deceleration phase, and the eyelid velocity trace remains relatively stable across the duration of the saccade. Individual, amplitude-matched, gaze-evoked saccade trials are shown in *color*. Corresponding traces of eye and eyelid movements are shown in the *same color*. The effect of a gaze-evoked blink is to induce a gross perturbation in the position and velocity traces. Furthermore, the timing of the blink contributes to the time at which the eye trajectory is compromised and also to the magnitude of attenuation in eye velocity

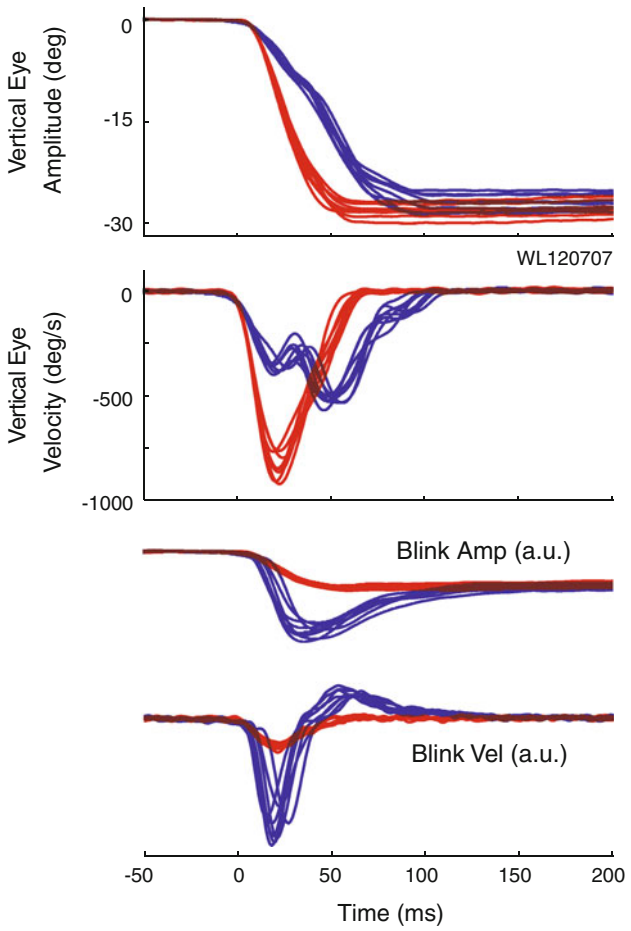

Fig. 11 Effects of gaze-evoked blinks on vertical head-restrained saccades. Eye position and velocity and eyelid position and velocity (*top* to *bottom*) waveforms are plotted as a function of time for individual amplitude-matched saccades. Saccades without blinks are shown in *red* and movements with gaze-evoked blinks are plotted in *blue*

Latency

Figure 12a compares the mean latency of saccades without blinks against the average latency for trials with gaze-evoked blinks. Each symbol represents mean behavior for one target configuration, and it is filled if the distributions of blink and nonblink latencies were significantly different based on a two-tailed t test ($P < 0.05$). The color denotes the animal. For better visualization, the difference in average latencies (blink–nonblink condition) is plotted as a function of gaze amplitude in Fig. 12b. Across all target configurations and all monkeys, the saccade reaction time was reduced by 11.7 ± 22.4 ms (median: 9.1 ms) when a gaze-evoked blink accompanied the eye movement. The effect was statistically significant for each of the four animals (paired t test, $P < 0.05$). There was no effect of desired gaze amplitude on the facilitation in latency in any of the four animals (one-way ANOVA, $P > 0.05$).

The results of the identical analysis on gaze latency of head-unrestrained movements are shown in Fig. 12c, d. Across all target configurations and all monkeys, the saccade reaction time was reduced by 10.7 ± 19.8 ms (median: 9.3 ms) when a blink accompanied the gaze shift. However, the effect was statistically significant for monkey WL only (paired t test, $P < 0.05$). There was also a significant effect of desired gaze amplitude on the facilitation in latency in the same animal (one-way ANOVA, $P < 0.05$) but not the other three. A separate analysis on the eye component was not performed because it equaled gaze latency in nearly every head-unrestrained trial. Figure 12e, f illustrates the (lack of) effect of gaze-evoked blinks on

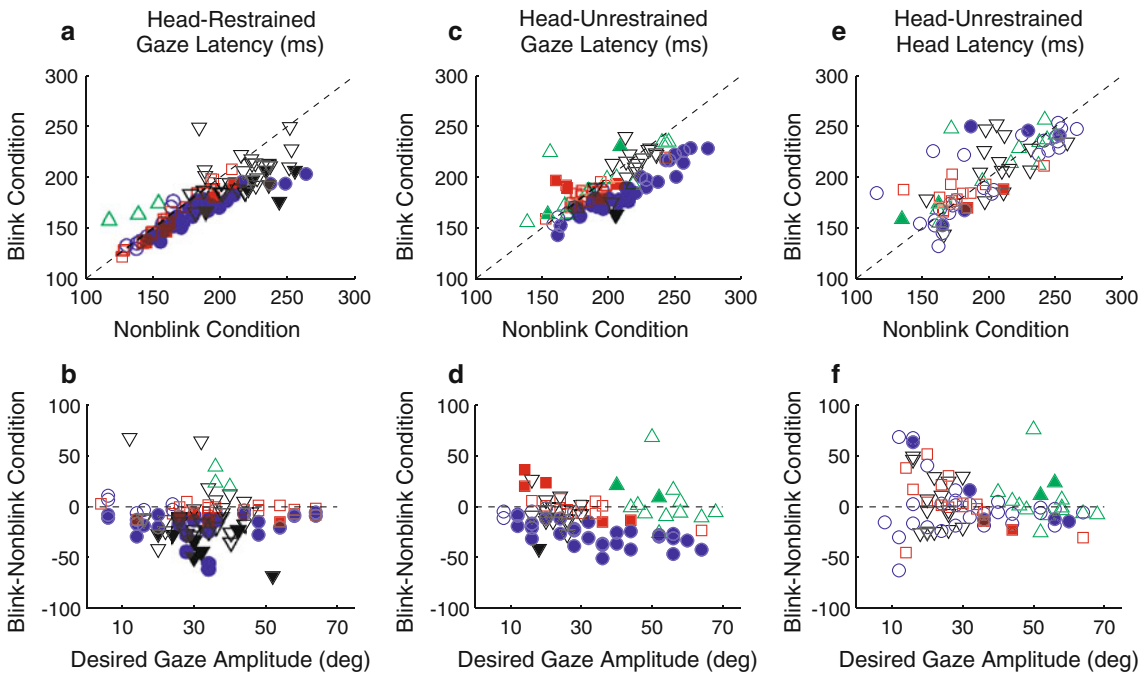

Fig. 12 Effects of gaze-evoked blinks on latency. The data were sorted according to target configuration, such that the initial and final target positions were identical for all trials in each dataset. **a** The average gaze latency for movements with gaze-evoked blinks is plotted against movements without accompanying blinks (nonblink condition) for head-restrained saccades. Each point represents the mean value obtained from each dataset. **b** The difference in latency values (blink–nonblink conditions) is plotted as a function of desired gaze amplitude. **c**, **d** Same format at (**a**, **b**) but for gaze latency of head-unrestrained movements. **e**, **f** Same format as (**a**, **b**) but for latency of head component of head-unrestrained gaze shifts. Comparable analysis for the eye component of gaze shifts is not provided as the results were nearly identical to the gaze latency data (**c**, **d**). The *color* of each *symbol* identifies the animal, following the notation introduced in Fig. 1b. The *open* and *filled symbol* convention, however, was not applied here. *Filled symbols* instead indicate statistically significant difference in latency between the blink and nonblink dataset (two-tailed t test, $P < 0.05$). *Diagonal dashed line* denotes unity *slope*, and *horizontal dashed line* marks zero difference in latency

head latency. On average, head onset was delayed by 5.3 ± 38.6 ms (median: −0.8 ms) when a gaze-evoked blink accompanied the movement, but this difference was not statistically different from zero (paired t test, $P > 0.2$). The difference in latency was also not influenced by the desired gaze amplitude (one-way ANOVA, $P > 0.05$).

Accuracy

The perturbations in eye movements can potentially serve as a useful test of internal feedback control of the oculomotor system. Thus, the accuracy of orienting responses was analyzed by comparing the difference (blink minus control trials) in mean horizontal amplitude of movements associated with the same target configuration; positive (negative) values indicate that the horizontal amplitude is larger (smaller) during movements associated with gaze-evoked blinks. In the head-restrained condition (Fig. 13a), saccades associated with blinks were generally larger than control movements. While the hypermetria was small (mean ± SD: 1.10 ± 0.98°; median: 0.98°), it was strongly statistically different from zero (t test, $P \rightarrow 0$). The difference in amplitude was not dependent on desired gaze amplitude, except for in monkey WL (one-way ANOVA, $P < 0.05$).

With the head-unrestrained, the same analysis was performed for gaze, eye-in-head, and head amplitudes. The mean gaze amplitude associated with gaze-evoked blinks was also greater than for matched movements without blinks (Fig. 13b). The overshoot was small (mean ± SD: 1.23 ± 1.30°; median: 0.79°) but strongly statistically different from zero (t test, $P \rightarrow 0$). The difference in amplitude was not dependent on desired gaze amplitude for any of the four animals (one-way ANOVA, $P > 0.05$). Furthermore, the distributions of difference in gaze amplitude for head-restrained and head-unrestrained conditions were not significantly different from each other (paired t test, $P = 0.4$). The saccadic eye component of gaze shifts was smaller during movements perturbed by gaze-evoked blinks (Fig. 13c). The reduction in amplitude was very small (mean ± SD: −0.38 ± 1.23°; median: −0.52°), but still statistically different from zero (t test, $P < 0.01$). There was no relation between amplitude difference and desired gaze amplitude (one-way ANOVA,

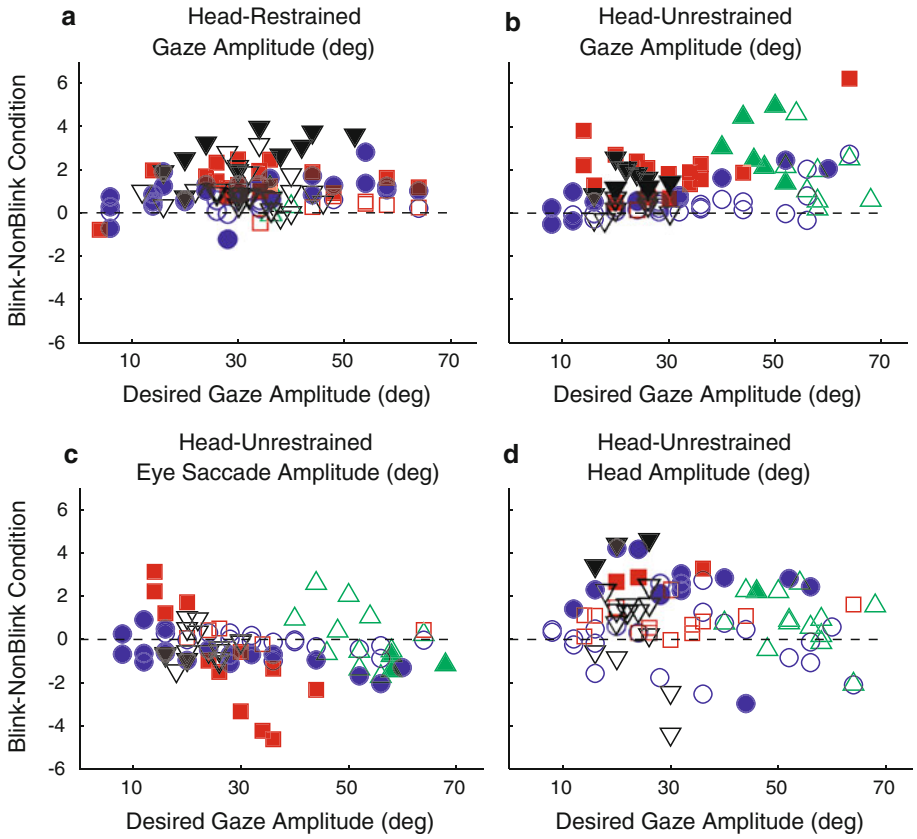

Fig. 13 Effects of gaze-evoked blinks on movement accuracy. **a** The difference in the average horizontal amplitude (blink–nonblink trials) is plotted as a function of desired gaze amplitude for head-restrained saccades. *Positive* value indicates larger amplitude during gaze shifts accompanied by gaze-evoked blinks. Each point represents the mean value obtained from each dataset parsed according to target configuration (see Fig. 12). Similar analyses performed on head-unrestrained data are shown for average difference in gaze amplitude (**b**), ocular saccade component (**c**) and head amplitude (**d**). The *color* and *open/filled symbol* convention is the same as that used in Fig. 12. The *horizontal dashed lines* mark zero difference in horizontal component amplitude

$P > 0.05$). However, the distributions of difference in gaze and eye-saccade amplitudes during head-unrestrained gaze shifts were significantly different from each other (paired t test, $P < 0.001$). Head amplitude was also slightly larger during gaze-evoked blink trials (mean ± SD: 1.02 ± 1.67°; median: 0.86°) (Fig. 13d), and this hypermetria was small but statistically significant (t test, $P < 0.001$). The distribution of difference in head amplitude was not dependent on desired gaze amplitude (one-way ANOVA, $P > 0.05$).

Head movement kinematics

The data sorted according to target configuration indicate that the onset times of head latency are not altered during movements associated with gaze-evoked blinks (Fig. 12e, f), but the accuracy analysis (Fig. 13d) suggests that head amplitude is slightly larger. Thus, the change in head movement kinematics must be implemented after its onset. Analyses suggest that the magnitude (Fig. 14a) and time (Fig. 14b) of peak head velocity increase during movements associated with gaze-evoked blinks. The magnitude of peak head velocity increased by 7.2 ± 6.8°/s (median: 6.9°/s), and the enhancement was significantly different from zero (t test, $P \rightarrow 0$). The change in peak head velocity was also dependent on desired gaze amplitude (one-way ANOVA, $P < 0.05$). Since head amplitude naturally increases with gaze amplitude, the change in peak velocity was also computed as a percentage increase (mean ± SD: 21.8 ± 41.6%; median: 12.4%), which also met the same statistical significance criterion. The time to reach peak velocity also increased modestly (mean ± SD: 5.5 ± 23.6 ms; median: 5.3 ms) but statistically significantly (t test, $P < 0.05$). The increase in time of peak head velocity was not dependent on desired gaze amplitude (one-way ANOVA, $P > 0.05$).

Discussion

The generation of a blink constitutes a rapid depression of the upper eyelid caused by cessation of activity in the levator palpebrae muscle and a burst of contractile activity in the orbicularis oculi muscle, followed by a gradual return of the lid to an elevated position as the activities in the two muscles return toward baseline levels (Björk and Kugelberg 1953; Evinger et al. 1984). This muscular innervation pattern occurs for blinks produced under a variety of conditions (Evinger et al. 1991; Gruart et al. 1995; Yeomans et al. 2002; VanderWerf et al. 2003). Most commonly, blinks occur spontaneously to wet and protect the cornea. They can also be volitional and often

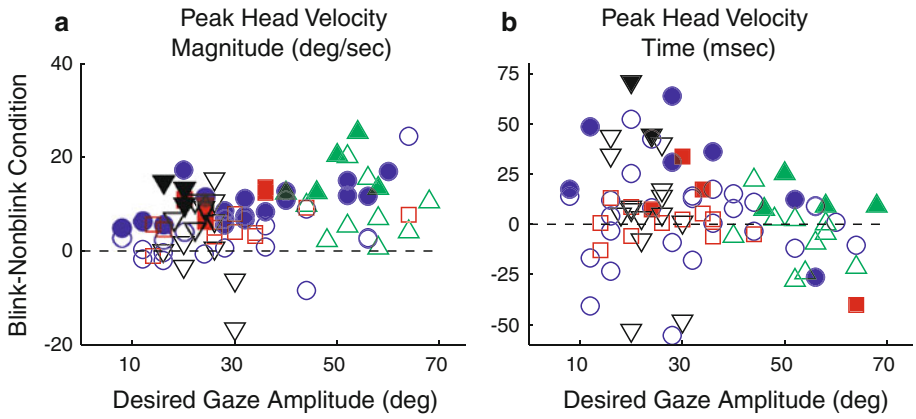

Fig. 14 Effects of gaze-evoked blinks on head movement kinematics. **a** The difference in the average *horizontal* peak head velocity (blink–nonblink trials) is plotted as a function of desired gaze amplitude. *Positive* value indicates bigger peak velocity during gaze shifts accompanied by gaze-evoked blinks. Each point represents the mean value obtained from each dataset parsed according to target configuration (see Fig. 12). **b** Same analysis for the time of peak head velocity. *Positive* value indicates that the head velocity peaks later when the gaze shift is accompanied by a gaze-evoked blink. The *color* and *open/filled symbol* convention is the same as that used in Fig. 12. The *horizontal dashed lines* mark zero difference in head kinematic

accompany facial movements such as winking or grimacing. Blinks can be obtained as a conditioned response. They can be evoked as a reflexive response triggered by mechanical (air-puff) stimulation of the cornea or the periorbital skin, electrical stimulation of the appropriate regions of the ophthalmic and infraorbital branches of the trigeminal nerve, and presentation of startling stimuli such as light flashes and tones. Gaze-evoked blinks accompany eye movements that redirect the line of sight. They are best thought of as being part of a volitional eye–head movement, although the subject may not be specifically aware of producing the blink. Importantly, these blinks are not reflexive movements evoked by wind rushing across the eye because the muscular innervation is observed even during gaze shifts produced with the eyes closed (Evinger et al. 1994).

Blink-induced perturbations on eye and head velocities

When a blink and a head-restrained saccade overlap temporally, the eye velocity waveform is grossly perturbed, an observation that holds for reflexive (Goossens and Van Opstal 2000a; Gandhi and Bonadonna 2005; Goossens and Van Opstal 2010), voluntary (Rottach et al. 1998, 2002) and gaze-evoked blinks (current manuscript). Similar patterns in eye velocity as well as gaze velocity, since it is the sum of eye and head components, are also observed during head-unrestrained gaze shifts accompanied by gaze-evoked blinks. To the best of my knowledge, comparable data on the effects of reflexive blinks on the eye and gaze components of head-unrestrained gaze shifts are not available. In general, the peak velocity is typically reduced, although it is not uncommon to observe attenuation in the velocity profile after it has reached the peak magnitude associated with amplitude-matched control trials (Fig. 10). Regardless of the exact timing of the perturbation, the average velocity is reduced and the duration of the movement is prolonged.

Interestingly, no reduction is observed in the kinematics of head movements accompanied by gaze-evoked blinks. In fact, both the magnitude and the time of peak head velocity increase modestly but significantly (Fig. 14). This is consistent with the notion that the head movement continues to accelerate and its velocity peaks at the end of the gaze shift (Chen and Tehovnik 2007), which is now delayed because of the longer movement duration. A lack of a perturbation effect on the head movement does not necessarily imply that the neural drive to the head movement is unmodified. It is possible that changes in the neural drive to the neck muscles are too small to overcome the biomechanical inertia of the ongoing head movement (e.g., Corneil et al. 2010). A comparison of the electromyographic activity of neck muscles during control and blink-accompanied gaze shifts perhaps might reveal modifications in the neural drive.

Figures 3 and 4 demonstrate that the blink-induced perturbations in eye velocity are variable across animals. What factors can account for the spectrum of blink-associated perturbations in eye velocity? One possible factor is the speed of eye movements. Monkey BL, who produced the fastest control movements (Fig. 2), expressed the weakest attenuation in eye velocity, while monkey BN, who had the slowest speed, exhibited the strongest perturbation effect. The animals with the intermediate speeds were most likely to produce dual peaks in their blink-accompanied velocity profiles. Another, not mutually exclusive, factor relies on the kinematics of the eyelid movement. For example, the blink duration of monkey WY is significantly longer than that of the other animals, and the perturbation on eye velocity is most pronounced.

Within an animal, the overall temporal features remained consistent, but some differences in the time and magnitude of attenuation can be observed. Factors that likely contribute to within-animal variability include gaze amplitude, the relative timing of the gaze and blink onsets, initial eye-in-head position, and blink metrics and kinematics. While the timing was considered here (Figs. 9, 10), the other parameters have yet to be tested systematically.

Neural signatures

The blink-induced perturbation in eye movement is not due to mechanical interference from rotation of the eyelid over the globe. Neural signals that correlate with the perturbed eye movement were observed at various nodes of the oculomotor neuraxis. For example, saccade-related burst neurons in the superior colliculus grossly modify their discharge patterns during head-restrained saccades perturbed by reflexive blinks (Goossens and Van Opstal 2000b). The characteristic high-frequency burst is dampened, but the duration of activity prolonged so that an approximately equal number of spikes is emitted as during an amplitude-matched control saccade. In addition to the focus on reflexive blinks, this same study also provided illustrations of neural activity during head-restrained saccades combined with gaze-evoked blinks. Interestingly, the burst was minimally altered, and so was the accompanying eye velocity. The spectrum of perturbations observed here (Figs. 3, 4) were not present in the figures provided by Goossens and Van Opstal (2000b). Thus, a more quantitative analysis is required to determine whether saccades with reflexive and gaze-evoked blinks are encoded differently by superior colliculus neurons. Also, preliminary data exist for the burst neurons located in the pontomedullary reticular formation (Bechara and Gandhi 2010a; Gandhi and Katnani 2011). The burst profile, which is thought to encode the eye velocity command, alters its discharge to reflect the perturbation induced by gaze-evoked blinks during both head-restrained and head-unrestrained gaze shifts. Thus, it seems reasonable to assume that the neural activity of downstream structures, such as the abducens motoneurons, also reflects the altered velocity waveforms. Recordings from abducens motoneurons show that the firing rate pattern is modified during eyelid movements associated with blinks (Evinger and Manning 1993; Trigo et al. 1999), although the eye movement waveform itself was not reported.

Interactions between eye and head pathways

Behavioral data published from several laboratories show that the eye velocity profiles of gaze shifts with large-amplitude head movements are attenuated in mid-flight, often producing velocity waveforms with multiple—usually two—peaks (Tomlinson and Bahra 1986; Munoz et al. 1991; Phillips et al. 1995; Tweed et al. 1995; Freedman and Sparks 1997b; Roy and Cullen 1998; Freedman and Sparks 2000). Freedman and Sparks (2000) proposed that as the head movement command accumulates during a trial, it increasingly decreases the gain of the eye burst generator, which attenuates the eye velocity command and in turn reduces the eye velocity. However, a local feedback circuit recognizes that the eye movement is not progressing quickly enough, which causes the burst generator output to increase. This reaccelerates the eye movement, producing a second peak in the velocity waveform. For small-amplitude gaze shifts, the head component is small and presumably so is the head movement command. In such cases, the effect of the head movement on the burst generator is negligible. In some cases, the attenuation induces an inflection in the velocity profile, usually during the deceleration phase. Simulations have demonstrated the feasibility of this hypothesis (Freedman 2001).

The data reported in Figs. 3, 4, 8, 10 and 11 demonstrate that comparable attenuation profiles in eye velocity can be attributed to the presence of gaze-evoked blinks during both head-restrained saccades and head-unrestrained gaze shifts. Thus, it is possible that the weakening in velocity profiles present in previous studies was caused by gaze-evoked blinks that went unnoticed. Perhaps, a corollary discharge of the blink motor command may be sufficient to induce the attenuation in the eye velocity, even if a smaller or negligible size blink is produced. Another possible option is that the nervous system issues a motor command for a coordinated movement of the eyes, head, and blink musculature, and the altered velocity waveform observed during such movements could be due to both eye–head coupling and eye–eyelid interactions (Gandhi and Katnani 2011). Finally, it should be recognized that the present study was not designed specifically to test the eye–head coupling theory. The data therefore do not explicitly support or refute this hypothesis. It is possible, for example, that eye movements just happen to be similarly influenced by both blinks and head movements.

Reduction of reaction time

A reflexive blink evoked after presentation of a target in the visual periphery, but before the typical reaction time of a head-restrained saccade, significantly reduces the latency of the eye movement (Goossens and Van Opstal 2000a; Gandhi and Bonadonna 2005; Castellote et al. 2006). The decrease in onset time could be as much as $\sim$100 ms, resembling express saccade latency. The reaction times of head-restrained saccades combined with gaze-evoked blinks are shortened as well, but the average reduction is

only ~10 ms (Fig. 12). When the head is unrestrained, the latency of the head movement, and presumably of the gaze shift also, is reduced after reflexive blinks evoked by microstimulation of the supraorbital nerve (Evinger et al. 1994). The comparable results for gaze-evoked blinks and head-unrestrained gaze shifts were mixed: a statistically significant reduction of ~10 ms in gaze onset was observed in only one animal, and head latency was not significantly altered in any of the four monkeys.

The reduction in latency of saccades triggered by reflexive blinks has been attributed to the discharge properties of omnipause neurons (OPNs) in the paramedian pontine reticular formation. While these neurons gate saccadic eye movements by discharging at a tonic rate during fixation and ceasing activity during saccades (Keller 1974; Evinger et al. 1982), they also become quiescent during the loopy eye movement induced by a blink (Fuchs et al. 1991; Mays and Morrisse 1994; Schultz et al. 2010). The reflexive blink is usually induced before the typical reaction time, when the animal is preparing a saccade. The blink-induced, premature pause in OPNs disinhibits the brainstem burst generator, which is being driven by the less-than-optimal, low-frequency activity in the oculomotor neuraxis (Goossens and Van Opstal 2000b; Gandhi and Katnani 2011). The weaker activity yields a slower, but nonetheless accurate, eye movement to the target location (Goossens and Van Opstal 2000a; Gandhi and Bonadonna 2005; Goossens and Van Opstal 2010). Gaze-evoked blinks, in contrast to reflexive blinks, typically lag the onset of gaze shifts (Fig. 9). Hence, the initial cessation of OPN discharge is not triggered by the blink-induced eye movement. The small reduction in reaction time must be due to additional factors, such as preparatory blink generation signals that contribute to inhibiting the OPNs, or to the activation threshold for triggering a movement being reached earlier in burst neurons.

Accuracy of gaze shifts

Models that address the control of gaze shifts can be grouped into two general categories. One class proposes that the oculomotor system serves to maintain the accuracy of gaze amplitude, without regard to the individual eye and head components that formulate the gaze shift (Guitton et al. 1990; Galiana and Guitton 1992; Lefèvre and Galiana 1992; Phillips et al. 1995). The other suggests that desired gaze displacement is decomposed into desired eye and head components and that feedback control only operates on the eye pathway (Freedman 2001). Perturbation approaches have been routinely used to differentiate between the models. The majority of studies have supported the gaze feedback model (Laurutis and Robinson 1986; Guitton and Volle 1987; Cullen et al. 2004; Gandhi and Sparks 2007), but evidence for eye-only feedback also exists (Freedman and Quessy 2004). The blink perturbation approach used here and previously (Rottach et al. 1998; Goossens and Van Opstal 2000a; Rambold et al. 2002; Rambold et al. 2004; Gandhi and Bonadonna 2005; Goossens and Van Opstal 2010) also demonstrates that gaze accuracy is preserved in both head-restrained and head-unrestrained conditions, despite the gross attenuation in eye velocity profiles. On average, the final gaze position associated with blink-evoked saccades overshot that of control trials only by ~1°, for both head-restrained and head-unrestrained gaze shifts. Interestingly, the average difference in the amplitude of the saccadic eye component of head-unrestrained gaze shifts (blink and control trials) was even smaller (less than 0.4°). Given the very small difference in the accuracy in both eye and gaze components, it appears that the blink paradigm used within the context used here does not produce data that can differentiate between the two classes of feedback models.

Blinks facilitate saccadic suppression

At many nodes in the visual sensory system, neurons respond to the rapid motion of an object while the eyes are stationary, but the response is suppressed when similar image motion is produced by a saccadic eye movement with the stimulus stationary (e.g., Robinson and Wurtz 1976; Thiele et al. 2002). Invoking the concept of saccadic suppression, it is assumed that a corollary discharge of the eye movement command suppresses the visual response. This mechanism helps account for the visual stability that persists across eye movements (see Wurtz 2008 for a review). Saccade-related activity in the superior colliculus is one potential source of the corollary discharge (Crapse and Sommer 2008). Interestingly, the maximum firing rate of population response in the superior colliculus is most brisk in the rostral and intermediate colliculus, regions that encode for gaze shifts smaller than 20°. It is gradually weaker in more caudal regions of the colliculus, which encodes larger-amplitude movements (Anderson et al. 1998; Van Opstal and Goossens 2008). This trend implies that the strength of saccadic suppression may be a function of gaze amplitude, strongest for small gaze shifts and gradually weaker for larger movements. It can be speculated then that signals related to gaze-evoked blinks, whose probability of occurrence increases with gaze amplitude, could facilitate or preserve saccadic suppression by closing the eye in cases when the corollary discharge signal is weak and peak eye velocity is reduced. This perspective is consistent with the observation that animals that inherently produce slower movements (without blinks) are more likely to generate gaze-evoked blinks (Fig. 2).

Other signals, in addition to a corollary discharge of the gaze displacement command, can also contribute to

generating gaze-evoked blinks and thereby facilitate saccadic suppression. For instance, near-"identical" activity profiles of high-frequency burst neurons in the reticular formation produce a pronounced attenuation in eye velocity during coordinated eye–head movements compared to head-restrained saccades (Bechara and Gandhi 2010b). It is believed that the superior colliculus output is comparable for similar-amplitude head-restrained and head-unrestrained movements (Freedman et al. 1996; Freedman and Sparks 1997a). However, the likelihood of producing a gaze-evoked blink is significantly greater in the head-unrestrained condition. Hence, an efference copy of the head movement command may be another source that contributes to the generation of blinks.

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References

Anastasopoulos D, Ziavra N, Hollands M, Bronstein A (2009) Gaze displacement and inter-segmental coordination during large whole body voluntary rotations. Exp Brain Res 193:323–336

Anderson RW, Keller EL, Gandhi NJ, Das S (1998) Two dimensional saccade-related population activity in superior colliculus in monkey. J Neurophysiol 80:798–817

Bechara BP, Gandhi NJ (2010a) Effect of blinks on the relationship between eye velocity and high-frequency burst neurons in the pons. Society for Neuroscience Abstracts Program No. 894.4

Bechara BP, Gandhi NJ (2010b) Matching the oculomotor drive during head-restrained and head-unrestrained gaze shifts in monkey. J Neurophysiol 104:811–828

Becker W, Fuchs AF (1988) Lid-eye coordination during vertical gaze changes in man and monkey. J Neurophysiol 60:1227–1252

Björk A, Kugelberg E (1953) The electrical activity of the muscles of the eye and eyelids in various positions and during movement. Electroencephalogr Clin Neurophysiol 5:595–602

Bryant CL, Gandhi NJ (2005) Real-time data acquisition and control system for the measurement of motor and neural data. J Neurosci Methods 142:193–200

Castellote JM, Kumru H, Queralt A, Valls-Sole J (2006) A startle speeds up the execution of externally guided saccades. Exp Brain Res 177:129–136

Chen LL, Tehovnik EJ (2007) Cortical control of eye and head movements: integration of movements and percepts. Eur J Neurosci 25:1253–1264

Chen LL, Walton MM (2005) Head movement evoked by electrical stimulation in the supplementary eye field of the rhesus monkey. J Neurophysiol 94:4502–4519

Corneil BD, Elsley JK, Nagy B, Cushing SL (2010) Motor output evoked by subsaccadic stimulation of primate frontal eye fields. Proc Natl Acad Sci USA 107:6070–6075

Crapse TB, Sommer MA (2008) Corollary discharge across the animal kingdom. Nat Rev Neurosci 9:587–600

Cullen KE, Huterer M, Braidwood DA, Sylvestre PA (2004) Time course of vestibuloocular reflex suppression during gaze shifts. J Neurophysiol 92:3408–3422

Evinger C, Manning KA (1993) Pattern of extraocular muscle activation during reflex blinking. Exp Brain Res 92:502–506

Evinger CA, Kaneko CR, Fuchs AF (1982) Activity of omnipause neurons in alert cats during saccadic eye movements and visual stimuli. J Neurophysiol 47:827–844

Evinger C, Shaw MD, Peck CK, Manning KA, Baker R (1984) Blinking and associated eye movements in humans, guinea pigs, and rabbits. J Neurophysiol 52:323–339

Evinger C, Manning KA, Sibony PA (1991) Eyelid movements. Mechanisms and normal data. Invest Ophthalmol Vis Sci 32:387–400

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

Freedman EG (2001) Interactions between eye and head control signals can account for movement kinematics. Biol Cybern 84:453–462

Freedman EG, Quessy S (2004) Electrical stimulation of rhesus monkey nucleus reticularis gigantocellularis. II. Effects on metrics and kinematics of ongoing gaze shifts to visual targets. Exp Brain Res 156:357–376

Freedman EG, Sparks DL (1997a) Activity of cells in the deeper layers of the superior colliculus of the rhesus monkey: evidence for a gaze displacement command. J Neurophysiol 78:1669–1690

Freedman EG, Sparks DL (1997b) Eye-head coordination during head-unrestrained gaze shifts in rhesus monkeys. J Neurophysiol 77:2328–2348

Freedman EG, Sparks DL (2000) Coordination of the eyes and head: movement kinematics. Exp Brain Res 131:22–32

Freedman EG, Stanford TR, Sparks DL (1996) Combined eye-head gaze shifts produced by electrical stimulation of the superior colliculus in rhesus monkeys. J Neurophysiol 76:927–952

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

Galiana HL, Guitton D (1992) Central organization and modeling of eye-head coordination during orienting gaze shifts. Ann N Y Acad Sci 656:452–471

Gandhi NJ (2007) Consequence of blinks on interactions between the eye and head components of gaze shifts. Society for Neuroscience Abstracts Program No. 178.2

Gandhi NJ, Bonadonna DK (2005) Temporal interactions of air-puff evoked blinks and saccadic eye movements: Insights into motor preparation. J Neurophysiol 93:1718–1729

Gandhi NJ, Katnani HA (2011) Interactions of eye and eyelid movements. In: Liversedge SP, Gilchrist ID, Everling S (eds) Oxford handbook of eye movements (in press)

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

Gandhi NJ, Sparks DL (2007) Dissociation of eye and head components of gaze shifts by stimulation of the omnipause neuron region. J Neurophysiol 98:360–373

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

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

Goossens HH, Van Opstal AJ (2010) Differential effects of reflex blinks on saccade perturbations in humans. J Neurophysiol 103:1685–1695

Gruart A, Blazquez P, Delgado-Garcia JM (1995) Kinematics of spontaneous, reflex, and conditioned eyelid movements in the alert cat. J Neurophysiol 74:226–248

Guitton D, Volle M (1987) Gaze control in humans: eye-head coordination during orienting movements to targets within and beyond the oculomotor range. J Neurophysiol 58:427–459

Guitton D, Munoz DP, Galiana HL (1990) Gaze control in the cat: studies and modeling of the coupling between orienting eye and head movements in different behavioral tasks. J Neurophysiol 64:509–531

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

Laurutis VP, Robinson DA (1986) The vestibulo-ocular reflex during human saccadic eye movements. J Physiol (Lond) 373:209–233

Lefèvre P, Galiana HL (1992) Dynamic feedback of the superior colliculus in a neural network model of the gaze control system. Neural Networks 5:871–890

Leuzzi V, Elli R, Antonelli A, Chessa L, Cardona F, Marcucci L, Petrinelli P (1993) Neurological and cytogenetic study in early-onset ataxia-telangiectasia patients. Eur J Pediatr 152:609–612

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

Munoz DP, Guitton D, Pélisson D (1991) Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat. III. Spatiotemporal characteristics of phasic motor discharges. J Neurophysiol 66:1642–1666

Phillips JO, Ling L, Fuchs AF, Siebold C, Plorde JJ (1995) Rapid horizontal gaze movement in the monkey. J Neurophysiol 73:1632–1652

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

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

Robinson DL, Wurtz RH (1976) Use of an extraretinal signal by monkey superior colliculus neurons to distinguish real from self-induced stimulus movement. J Neurophysiol 39:852–870

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

Roy JE, Cullen KE (1998) A neural correlate for vestibulo-ocular reflex suppression during voluntary eye-head gaze shifts. Nat Neurosci 1:404–410

Schultz KP, Williams CR, Busettini C (2010) Macaque pontine omnipause neurons play no direct role in the generation of eye blinks. J Neurophysiol 103:2255–2274

Thiele A, Henning P, Kubischik M, Hoffmann KP (2002) Neural mechanisms of saccadic suppression. Science 295:2460–2462

Tomlinson RD, Bahra PS (1986) Combined eye-head gaze shifts in the primate. I. Metrics. J Neurophysiol 56:1542–1557

Trigo JA, Gruart A, Delgado-Garcia JM (1999) Discharge profiles of abducens, accessory abducens, and orbicularis oculi motoneurons during reflex and conditioned blinks in alert cats. J Neurophysiol 81:1666–1684

Tweed D, Glenn B, Vilis T (1995) Eye-head coordination during large gaze shifts. J Neurophysiol 73:766–779

Van Opstal A, Goossens H (2008) Linear ensemble-coding in midbrain superior colliculus specifies the saccade kinematics. Biol Cybern 98:561–577

VanderWerf F, Brassinga P, Reits D, Aramideh M, Ongerboer de Visser B (2003) Eyelid movements: behavioral studies of blinking in humans under different stimulus conditions. J Neurophysiol 89:2784–2796

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

Von Cranach M, Schmid R, Vogel MW (1969) The relationship between gaze movement and eye blink under various conditions. Psychol Forsch 33:68–78

Walton MMG, Bechara BP, Gandhi NJ (2007) Role of the primate superior colliculus in the control of head movements. J Neurophysiol 98:2022–2037

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

Williamson SS, Zivotofsky AZ, Basso MA (2005) Modulation of gaze-evoked blinks depends primarily on extraretinal factors. J Neurophysiol 93:627–632

Wurtz RH (2008) Neuronal mechanisms of visual stability. Vision Res 48:2070–2089

Yeomans JS, Li L, Scott BW, Frankland PW (2002) Tactile, acoustic and vestibular systems sum to elicit the startle reflex. Neurosci Biobehav Rev 26:1–11