Differential Effects of Reflex Blinks on Saccade Perturbations in Humans

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INTRODUCTION

Blinks can occur spontaneously, reflexively, or voluntarily (Guitton et al. 1991; Manning and Evinger 1986) and involve not only a transient closure of the eyelids but also movements of the eyes (Collewijn et al. 1985; Evinger et al. 1984; Takagi et al. 1992). Conversely, large saccades (Evinger et al. 1991; Zee et al. 1983) and combined eye-head movements (Evinger et al. 1994) tend to elicit so-called gaze-evoked blinks. There is also a direct correlation between eye and eyelid movements during vertical gaze changes (Becker and Fuchs 1988). Thus the oculomotor system and blinking evidently interact.

Previous studies with macaque monkeys have shown that reflex blinks evoked by puffs of air on the eye influence various aspects of saccade behavior (Gandhi and Bonadonna 2005; Goossens and Van Opstal 2000a). For example, the evoked blinks triggered impending saccades, reduced their velocity, and increased their duration. The two-dimensional (2D) trajectories of saccades, which are virtually straight under normal conditions (Van Gisbergen et al. 1985), were also strongly perturbed in the blinking condition. Nevertheless, the accuracy of horizontal, vertical, and oblique saccades was remarkably well preserved in the absence of visual feedback. Similar results were obtained for gaze-evoked blinks (Goossens and Van Opstal 2000a).

Studies with human subjects have thus far compared the metrics of saccades while subjects either deliberately made or withheld concurrent blinks (Rambold et al. 2002; Rottach et al. 1998). Only minimal differences were found in these studies despite altered saccade kinematics in the blinking condition. Unfortunately, the advance provided by these findings is somewhat limited by several factors: 1) the target locations were highly predictable in these studies because subjects made self-paced saccades between two stationary targets, 2) visual feedback could be used as targets remained visible, and 3) saccade metrics were evaluated in only one dimension (amplitude). The first objective of this study with human subjects is therefore to quantify the effect of blinking on saccades in two dimensions under unpredictable, open loop test conditions (i.e., when visual feedback is absent).

Blinks affect saccadic eye movements via changes in the central premotor commands to the oculomotor neurons rather than through mechanical interference between the eye and eyelid. For example, there is evidence that blinks influence the activity of saccadic burst neurons in the paramedian pontine reticular formation (PPRF) (Cohen and Henn 1972; Mays and Morrissé 1995), and several investigators have noted that the omnipause neurons (OPNs) in the pons stop firing during blinks and saccades (Cohen and Henn 1972; Fuchs et al. 1991; Hepp et al. 1989; Mays and Morrissé 1994). More recently, it has been shown that blinks also reduce the saccade-related burst activity of neurons in the midbrain superior colliculus (SC) (Goossens and Van Opstal 2000b). Interestingly, the changes in saccade kinematics associated with blinking can be understood almost entirely from these changes in SC burst activity (Goossens and Van Opstal 2006; Van Opstal and Goossens 2008). However, the discharge patterns of saccade-related SC neurons do not reflect the blink-induced curvature of the saccade trajectory. Behaviorally, the actual curved movements can be described as the resultant of two superimposed movements: 1) a slow but straight goal-directed saccade and 2) a pure blink-related eye movement (Goossens and Van Opstal 2000a). As shown in Fig. 1, we hypothesized that this superposition could occur at the level of the brain stem saccade generator because burst cells in the pontine reticular formation that fire for saccades are also active for blink-related eye movements (Cohen and Henn 1972; Mays and Morrissé 1995), whereas SC cells do not fire for the latter movements (Goossens and Van Opstal 2000b).

It is not clear to what extent blinking influences the 2D trajectories of saccades in humans. Thus far, the data have been sketchy. Becker (1993) showed some temporal traces of saccades to demonstrate that sensory stimuli, such as electrical
shocks delivered to the supraorbital nerve, can result in interrupted saccades that closely resemble those obtained with electrical microstimulation of OPNs in the monkey (Becker et al. 1981; Keller 1977; King and Fuchs 1977). In both types of experiments, the eye stops in midflight and resumes its original straight path toward the target. On the other hand, an example presented by Rottach et al. (1998) suggested that blinks not only attenuate the velocity of saccades but also result in curved saccades because pure blink-related eye movements are superimposed on the normally straight saccade trajectory. Although the latter observation is more in line with our observations in the monkey (Goossens and Van Opstal 2000a), it remains elusive whether this apparent discrepancy could perhaps reflect potential differences between different types of blinks (Domingo et al. 1997). The second objective of this study is to investigate this latter hypothesis by using different types of blink-evoking stimuli.

In the first set of experiments, we used air-puff stimuli, and in the second set, we applied electrical stimulation of the supraorbital nerve. We report that saccade accuracy and precision were well preserved in two dimensions, even though the evoked blinks produced robust decreases in saccade velocity for both stimulus types. However, we found a remarkable difference between the resulting trajectory perturbations. Where air puff stimuli produced strongly curved eye movements, electrical stimulation of the supraorbital nerve produced a transient interruption of the saccade without altering its 2D trajectory. We argue that these findings support the theory (Fig. 1) that there are at least two distinct sites at which the blinking system interacts with the saccadic system.

METHODS

Subjects

Four healthy participants (between 21 and 40 yr of age) volunteered and gave informed consent before participating in the experiments. None of the subjects suffered from known visual, vestibular, or oculomotor disorders, except for subject JO (one of the authors) who is ambyopic in his right eye. All procedures were approved by the Radboud University Medical Centre Nijmegen.

Experimental setup

EXPERIMENTAL CONDITIONS. Subjects were seated in a chair facing a spherical array (radius 85 cm) of light-emitting diodes (LEDs) in an otherwise completely dark, sound-attenuated room (3 x 3 x 3 m).

FIG. 1. Hypothesized influence of reflex blinks on saccade generation. Under normal conditions (black), vigorous burst activity at a given location in the superior colliculus (SC) motor map results in saccades that are virtually straight. In the blinking condition (gray), instantaneous firing rates in the SC are reduced as a result of trigeminal inhibition, which leads to reduced eye velocities. In addition, a blink-related eye movement is superimposed on the intended, straight saccade at the level of the burst generator in the brain stem, which leads to strongly curved eye movement trajectories. Diagram modified after Goossens and van Opstal (2006) and Scudder (1988). SC, superior colliculus; BG, saccade burst generator; OPN, omnipause neurons; NI, neural eye position integrator; MN, extraocular motoneurons; F, firing rate of recruited SC neurons; t, time; \( \dot{f}_{dt} \), temporal integration; me(t), instantaneous motor error; \( \ddot{e}(t) \), eye velocity, H.V, horizontal and vertical eye position.
low-pass filtered (150 Hz), sampled at 500 Hz per channel, and stored on disk for off-line analysis.

**Experimental protocol**

**CALIBRATION PROCEDURES.** Each session started with three calibration runs. The first run served to calibrate the position signals from the eye coil. The task of the subjects was to fixate a series of targets (n = 72) on the LED array while keeping their head aligned with the center LED. In each trial, subjects pushed a button to start 1,000 ms of data acquisition as soon as they looked at the target. The second run served to calibrate the position signals from the eyelid coil. Toward that end, the subjects were asked to orient their head toward the same set of LEDs while fixating a dim LED that was attached to a thin rod on their helmet (at ~40 cm in front of the eyes) with their eyes. The latter ensured that the eye and eyelid maintained a fixed position relative to the head in each trial. The third run served to determine the reference position of the eyelid. This run consisted of 10 trials in which the subjects directed their head toward the center LED of the array as they did in the rest of the experiment, while fixating the center LED with their eyes. A comparable calibration procedure has been developed previously for measuring coordinated eye-head movements (Goossens and Van Opstal 1997).

**BLINK PERTURBATION PARADIGMS.** After the calibration runs were completed, either one of two blink-perturbation experiments were performed. In the first series of experiments, we presented air puff stimuli to elicit blinks near the onset of visually evoked saccades. In the second series of experiments, blinks were evoked by electrical stimulation of the supraorbital nerve. Two trial types were randomly interleaved in each experiment:

**CONTROL TRIALS.** Each trial started with the presentation of a fixation LED. After a variable period of 800–1,200 ms, the fixation LED was extinguished, and at the same time, a peripheral target LED was flashed for 50 ms at a pseudorandomly chosen location. Subjects were asked to look at the remembered location of the target LED as quickly and accurately as possible without moving the head. Two thirds of the trials were control trials.

**PERTURBATION TRIALS.** Perturbation trials were identical to control trials except that a puff of air was presented to the left eye (air puff trials), or an electrical stimulus was applied to the left supraorbital nerve (electrical stimulation trials), to elicit a bilateral blink reflex (latency ~50 ms) near the onset of the visually evoked saccade. Air puffs or electrical stimuli were delivered in different experimental sessions. The intensity and timing of the air puffs/current pulses was adjusted according to the subjects’ behavior. This was done in such a way that the saccades could be perturbed without causing discomfort to the subject (see RESULTS). One third of the trials were perturbation trials.

**FIXATION PARADIGM.** In part of the experiments, we also used a fixation paradigm to separately measure the rotations of the eye that accompany blinks and the latency of the evoked blinks. In each trial, the subject had to fixate the center LED for 1.0–1.5 s. In one third of the trials, either a puff of air was presented on the eye or the supraorbital nerve was electrically stimulated. Stimulus onset was timed 500–1,000 ms (randomized) after the onset of the central LED. Trials with and without air puff/electrical stimulus were randomly interleaved.

**Data analysis**

**CALIBRATION OF EYE AND EYELID POSITION.** The raw eye fixation data from the first calibration run and the corresponding known LED positions were used to fit sine functions that mapped the raw eye position signals to calibrated horizontal/vertical angles of eye position (Hess et al. 1992).

Eyelid movements were also measured in angular degrees. Calibration of the raw lid-coil signals involved the following steps. First, the raw eye-coil data from the second calibration run were calibrated with the sine-function parameters determined for the eye coil. Because the position of the eyelid relative to the eye (and head) was always the same in this run (caused by fixation of the head-fixed rod LED), the eye position in space, G, measured with the eye coil, also provides an accurate measure of the eyelid position in space, L, when the head is kept in different orientations. There is only a fixed difference, D, between the position of the eye and the eyelid: L = G + D. It is not necessary, however, to know this fixed position difference between the eye and eyelid to determine the sensitivity and voltage offsets of the lid-coil signals. To find these latter parameters of the sine functions, we simply mapped the raw lid-coil signals to the corresponding eye-in-space positions. This procedure yielded ‘precalibrated’ eyelid position signals, Lref. Lid-coil data from the third calibration run, in which subjects fixated the center LED of the target array with the head in the straight-ahead position, were precalibrated and averaged to yield an average reference position of the eyelid, Lref. Calibrated eyelid-position signals were subsequently computed from L = Lpre − Lref.

Radial eye position (Er) and vectorial eye velocity (Æ) were computed from the calibrated horizontal and vertical eye position and eye velocity signals using Pythagoras’ theorem: \[ E_r = \sqrt{H^2 + V^2} \] and \[ \dot{E} = \sqrt{H^2 + \dot{V}^2} \]

**SACCADE AND BLINK DETECTION.** Saccadic eye movements were detected off-line on the basis of the calibrated eye position signals by a computer program that applied a fixed 20°/s velocity threshold criterion to determine the onsets and offsets of the movement. The experimenter verified all identifications made by the program and corrected any saccade recognition failures.

Blinks evoked in fixation trials were detected separately with the same interactive computer program using the calibrated vertical eyelid position signals. Blinks could be distinguished from saccade-associated eyelid movements by their biphasic asymmetric velocity shape (Becker and Fuchs 1988; Collewijn et al. 1985). The velocity threshold criterion to determine onsets and offsets of the eyelid movements was set at 20°/s.

**SELECTION CRITERIA.** Data from the blink-perturbation paradigms were sorted into control trials and perturbation trials toward the same target location. We excluded any control and perturbation trials in which the latency of the eye movement onset was <80 ms or >400 ms with respect to the onset of the peripheral target. Control trials in which spontaneous or gaze-evoked blinks occurred before or during the saccade were also discarded from further analysis. Additionally, we excluded all perturbation trials in which blinks were absent or very small at the time of the saccadic eye movement. Toward that end, data were aligned with eye movement onset and we subtracted from the vertical eyelid movement in each trial the mean vertical eyelid displacement during control trials. Perturbation trials were included in the analyses only if the resulting difference eyelid movement had a downward peak velocity >100°/s during the saccade epoch (as defined by the median duration of control saccades).

**BLINK PARAMETERS.** The analyses considered only vertical movements of the eyelid. Blink amplitude in fixation trials was computed as the vertical displacement of the eyelid between the onset and offset of the downward phase of the eyelid movement. Downward eyelid displacements were taken positive. To estimate the amplitude of blinks in perturbation trials, data from control and perturbation trials were first aligned with the onset of the eye movement. Subsequently, the vertical eyelid movements during control trials were averaged to yield an average eyelid saccade, L(t). This averaged control movement was subtracted from the vertical eyelid movements in the individual perturbation trials. From the resulting difference move-
ments, \( L(\phi) - \bar{L}(\phi) \), we finally determined the maximum downward deviation of the eyelid in each trial.

**EYE MOVEMENT PARAMETERS.** We compared parameters of individual perturbation trials with corresponding, average measures in control trials toward the same target. Saccade amplitude, \( R \), and direction, \( \phi \), were computed from the vectorial eye displacement between saccade onset and offset. Given the mean vectorial displacement of the eye in control trials (amplitude \( \bar{R} \), and direction \( \bar{\phi} \)), all movement endpoints were expressed in the coordinates of this vector. Toward that end, each saccade vector, \([H, V] \), was rotated over the angle \( \varphi = -\bar{\phi} \) (counterclockwise rotation taken positive):

\[
\begin{aligned}
X &= H \cdot \cos(\varphi) - V \cdot \sin(\varphi) \\
Y &= H \cdot \sin(\varphi) + V \cdot \cos(\varphi)
\end{aligned}
\]

The new horizontal coordinate, \( X \), aligns with the mean displacement vector of control saccades, whereas the new vertical coordinate, \( Y \), is perpendicular to this vector. Using these new coordinates, we computed the Cartesian endpoint errors \( e_x = X - \bar{X} \) and \( e_y = Y \). The so-called orthogonal error, \( e_o \), which we defined previously (Goossens and Van Opstal 2000a their Fig. 5), is identical to \( e_y \).

The peak velocity, \( V_p \), of a saccade was defined as the maximum vectorial velocity of the eye. The mean velocity, \( V_m \), of a saccade was calculated from the path length, \( P \), of the 2D saccade trajectory and the saccade duration, \( D : V_m = P/D \). Path length, \( P \), quantifies the traveling distance of the eye (in deg) during the saccade and was obtained by temporal integration of the vectorial eye velocity \( E \) from saccade onset to saccade offset. To further quantify the 2D trajectory perturbations we used a so-called path undulation index, \( U \), which we defined as the ratio between path length and saccade amplitude minus 1 : \( U = P/R - 1 \). In this way, a path undulation value of zero corresponds with straight saccades. Values >0 indicate deviations from a straight, goal-directed path, but note that no assumption is made about the shape of the trajectory. The path undulation index is equally sensitive, for example, to perturbations resulting in parallel back and forth moments (e.g., vertical movements in Fig. 3A) as it is to perturbations that result in hooked or curved movements. In this respect, our path undulation index differs from earlier curvature measures in the literature (e.g., Van Gisbergen et al. 1985).

To measure the initial eye excursion associated with blinks during fixation, we first calculated the duration, \( d \), of the downward motion phase of the eyelid. We then determined the maximum radial displacement of the eye during a time window that ranged from blink onset until \( 1.5 \times d \) milliseconds after blink onset.

**RESULTS**

**Blinks during straight-ahead fixation**

In the fixation paradigm, we applied electrical stimulation to the supraorbital nerve or brief puffs of air on the eye while the subject tried to maintain fixation on the central LED. As is shown in Fig. 2A for one of our subjects (JG), electrical stimulation of the supraorbital nerve elicited blinks and eye movements (gray). The air puff stimuli also evoked blinks that were accompanied by back and forth movements of the eye (black). For both types of stimuli, the eye started moving at about the same moment as the eyelid. Consistent with earlier studies (Bour et al. 2000; Collewijn et al. 1985), the displacement of the eye during closure of the eyelids was always downward and toward the nose. The latency of the blinks, as quantified from the onset moments of the eyelid, ranged from

![Fig. 2](http://jn.physiology.org/ by 10.220.33.5 on September 24, 2016)
Examples of reflex blinks produced by electrical stimulation of the supraorbital nerve (gray; $t$-test, $P < 0.001$). For these larger blinks, the return phase of the eye movement often carried the eye across its starting position, resulting in a biphasic eye movement (Fig. 2A). The relationship between the amplitudes of eye and eyelid movements evoked by electrical stimulation was quantified with linear regression (dashed line Fig. 2C). As one can see in Table 2, slopes of the regression lines were significantly larger than zero in all four subjects tested ($t$-test, $P \ll 0.0001$).

### Perturbation of saccades by reflex blinks

In the blink-perturbation paradigm, saccades were elicited toward briefly flashed targets at different locations, whereas reflex blinks were evoked near saccade onset. The evoked blinks produced robust changes in the saccadic eye movements of all subjects. Figure 3 shows the results that were obtained in one of our subjects (JG) when the blinks were evoked by air-puff stimuli (Fig. 3, A and C) and when the blinks were evoked by electrical stimulation of the supraorbital nerve (Fig. 3, B and D). There are several important points to note in these examples. 1) Blinking produced a strong, transient decrease in eye velocity under both test conditions. 2) Electrical stimulation of the supraorbital nerve produced an almost complete halting of the eye movement in midflight. 3) In contrast, the air-puff stimuli evoked downward deflections of the eye that

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### TABLE 2. Amplitudes of the initial eye excursions increased with blink amplitude

<table>
<thead>
<tr>
<th>Subject</th>
<th>Slope</th>
<th>Intercept</th>
<th>Correlation</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>JG</td>
<td>0.043 ± 0.003</td>
<td>0.47 ± 0.10</td>
<td>0.86*</td>
<td>59</td>
</tr>
<tr>
<td>JO</td>
<td>0.091 ± 0.012</td>
<td>0.43 ± 0.13</td>
<td>0.91*</td>
<td>15</td>
</tr>
<tr>
<td>PH</td>
<td>0.114 ± 0.008</td>
<td>0.04 ± 0.20</td>
<td>0.92*</td>
<td>37</td>
</tr>
<tr>
<td>MF</td>
<td>0.168 ± 0.018</td>
<td>0.20 ± 0.09</td>
<td>0.91*</td>
<td>20</td>
</tr>
<tr>
<td>Pooled</td>
<td>0.059 ± 0.005</td>
<td>0.54 ± 0.12</td>
<td>0.75*</td>
<td>131</td>
</tr>
</tbody>
</table>

Listed are the slopes (mean ± SE in deg eye rotation per deg eyelid displacement) and intercepts (mean ± SE in deg) of the linear regression lines (c.f., Fig. 2C), as well as Pearson’s correlation coefficients and numbers of trials. Results are from supraorbital nerve stimulation.

Student’s $t$-test: *$P \ll 0.0001$.

$~\text{to}~80$ ms, and co-varied with the amplitude of the evoked blinks (Fig. 2B). Large blinks typically had shorter latencies than small blinks. We used linear regression to quantify this relationship for blinks evoked by electrical stimulation (Fig. 2B, dashed line; Table 1). Note that the slopes of the regression lines were significantly less than zero in all four subjects tested ($t$-test, $P < 0.05$). Taking this relationship into account, the latencies of air-puff and shock-evoked blinks were not significantly different (Fig. 2B; $t$-test, $P > 0.05$). Larger blinks were also associated with larger movements of the eye (Fig. 2C).

Under both stimulus conditions, the radial amplitude of the initial eye displacement ranged between $~0.1$ and $6^\circ$. However, for blinks of similar magnitude, the amplitudes of eye movements evoked by air-puff stimuli (black) were typically larger than the amplitudes of eye movements evoked by electrical stimulation of the supraorbital nerve (gray; $t$-test, $P < 0.001$). For these larger blinks, the return phase of the eye movement often carried the eye across its starting position, resulting in a biphasic eye movement (Fig. 2A). The relationship between the amplitudes of eye and eyelid movements evoked by electrical stimulation was quantified with linear regression (dashed line Fig. 2C). As one can see in Table 2, slopes of the regression lines were significantly larger than zero in all four subjects tested ($t$-test, $P \ll 0.0001$).

### Perturbation of saccades by reflex blinks

In the blink-perturbation paradigm, saccades were elicited toward briefly flashed targets at different locations, whereas reflex blinks were evoked near saccade onset. The evoked blinks produced robust changes in the saccadic eye movements of all subjects. Figure 3 shows the results that were obtained in one of our subjects (JG) when the blinks were evoked by air-puff stimuli (Fig. 3, A and C) and when the blinks were evoked by electrical stimulation of the supraorbital nerve (Fig. 3, B and D). There are several important points to note in these examples. 1) Blinking produced a strong, transient decrease in eye velocity under both test conditions. 2) Electrical stimulation of the supraorbital nerve produced an almost complete halting of the eye movement in midflight. 3) In contrast, the air-puff stimuli evoked downward deflections of the eye that

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![Figure 3](http://jn.physiology.org)
are roughly in line with the direction of the blink-related eye movements (cf., Fig. 2A). 4) The 2D trajectories of saccades in air puff trials (Fig. 3A, colored) were typically hooked as a result of the downward deflections, and they were much more variable than the nearly straight trajectories of corresponding control saccades (Fig. 3A, black). 5) Compared with the strongly curved trajectories of saccades in air puff trials, the 2D trajectory perturbations of saccades in electrical stimulation trials (Fig. 3B, colored) were remarkably small. 6) Despite the robust perturbations, stimulated saccades reached the target position with the same accuracy as the control movements in complete absence of visual feedback. 7) The endpoint accuracy of perturbed saccades was well preserved whether the blinks occurred near saccade onset or in saccade midflight. 8) The trajectory deflections evoked by air puffs at the beginning of a saccade (Fig. 3A) are roughly in line with the direction of the blink-related eye movements (cf., Fig. 2A), but they are not identical for the responses toward the different targets. Rather, the initial direction of the eye movement depends systematically on the target location, indicating that this early phase of the movement is not related to blinking alone.

**Saccade metrics in two dimensions**

Figures 4 and 5 relate the endpoints of blink-perturbed saccades to the endpoints of control saccades toward the same target locations. The endpoint accuracy of perturbed saccades was analyzed with respect to the control responses instead of the target locations, because the metrics of primary saccades toward a single visual target may depend on factors such as target eccentricity and predictability, the presence/absence of visual feedback, and the subject’s behavioral state. The insets in Figs. 4A and 5A show the different parameters that were used to quantify the endpoint accuracy in two dimensions.

Figure 4A compares the mean amplitudes of control saccades and perturbed saccades when blinks were evoked by air puff stimuli (black) and by electrical stimulation of the supraorbital nerve (gray). Note that the data closely align with the diagonal line (dashed), indicating that the mean amplitudes of perturbed saccades were normometric under both test conditions. Only subject MF showed slightly hypermetric responses in the air puff condition (see below). To better illustrate the trial-to-trial variability of the responses, Fig. 4 also shows the amplitude error (Fig. 4B) and the amplitude gain (Fig. 4C) of saccades in all perturbation trials as a function of the concomitant eyelid deviation. Dashed horizontal lines in these plots represent the intervals that contained 95% of the control data. Note that the amplitude errors scatter around zero, with the vast majority of data points falling between the 2.5 and 97.5 percentiles of the control data (76.5% of the air-puff trials and 87.8% of the electrical stimulation trials), irrespective of the size of the blink. Accord-
ingly, the amplitude gains scatter around one under both test conditions (Fig. 4C). Thus the saccade amplitudes remain normometric regardless of the blink magnitude.

Similarly, Fig. 5A compares the mean direction of perturbed saccades to the mean direction of control saccades toward the same target. Figure 5, B and C, plot the direction error and the orthogonal error of all perturbed saccades as a function of the concomitant eyelid deviation. Note that the data in Fig. 5A closely align with the diagonal line (dashed) and that both the direction errors (Fig. 5B) and the orthogonal errors (Fig. 5C) scatter around zero regardless of the eyelid deviation. Of all data points, <14% fell outside the intervals that contained 95% of the control data (dashed horizontal lines). Together with the data from Fig. 4, these results thus demonstrate that blink-perturbed saccades remain accurate in 2D irrespective of the blink magnitude.

In Figs. 4 and 5, we pooled the endpoint data from the four subjects because they produced very similar results. The latter is further shown in Fig. 6, A and B, which compares the mean amplitude gain and the mean direction error of the stimulated saccades under the two test conditions for each subject. Error bars indicate the corresponding SD. Horizontal gray areas indicate the mean variability (±SD) of the saccade endpoints in the control condition. Statistical analysis (t-test) showed that the mean amplitude gains were not significantly different from 1 (P > 0.05), except in subject MF. As mentioned earlier, this subject showed slightly hypometric responses in the air puff condition (black). Direction errors were not significantly different from zero in any of our subjects (t-test, P > 0.05). Differences between the two perturbation paradigms were also not statistically significant (t-test, P > 0.05).

Apart from the fact that the mean endpoints of control versus perturbed saccades were virtually identical, one may note in Fig. 6 that the precision of the saccades, as quantified by the SD of the endpoints, was very similar too (compare also horizontal vs. vertical error bars in Figs. 4A and 5A). In fact, we found no significant differences in the precision of saccades in any of our subjects (t-test, P > 0.05).

Saccade kinematics and trajectory perturbations

Figure 7 quantifies the influence of blinking on the kinematics and 2D trajectories of saccades in the two perturbation paradigms. Figure 7A compares the peak velocity of individual saccades in the perturbation trials to the average peak velocity of control saccades toward the same target locations. Linear regression analysis applied to these data showed a significant (t-test, P < 0.001) reduction in the peak velocity of saccades when the blinks were evoked by air puff stimuli (black) and when the blinks were evoked by electrical stimulation of the supraorbital nerve (gray). Note, however, that there was considerable variability in the perturbed responses and that there were many saccades whose peak velocity actually exceeded the average peak velocity of corresponding control saccades. Accordingly, the average reduction in peak eye velocity was only 3.2 ± 0.6% (SE). As shown in Fig. 7B, an alternative velocity parameter, namely the mean eye velocity (see METHODS), reflected the attenuations in eye velocity such as those observed, e.g., in the perturbation trials of Fig. 3, much better. Note that the vast majority of data points in Fig. 7B fall below the diagonal line (dashed), indicating a systematic reduction in the mean eye velocity under both blinking conditions compared with the control condition. The average reduction in mean velocity produced by air-puff and shock-evoked blinks was 18.8 ± 1.0 and 10.0 ± 1.0%, (mean ± SE) respectively.

In line with the robust decreases in mean eye velocity, saccade duration was much longer in many perturbation trials. The latter can be seen in Fig. 7C, which compares the duration of perturbed saccades under the two test conditions to the average duration of corresponding control saccades. One may also observe in Fig. 7C that the increases in saccade duration are systematically larger in the air puff trials compared with the electrical stimulation trials. Mean (±SE) increases in saccade duration were 47 ± 1.9 versus 16 ± 1.5%, respectively. Note that this difference between the two blinking conditions cannot simply be explained by differences in the mean or peak eye velocity alone because the data from the two perturbation paradigms in Fig. 7, A and B, largely overlap. Interestingly, we found that this differential effect on saccade duration resulted from markedly different changes in 2D saccade trajectories. To show this, Fig. 7D compares the path lengths of perturbed saccades to the average path lengths of corresponding control saccades under the two test conditions. Because the 2D trajectories of saccades in electrical stimulation trials were practically straight, like the corresponding control saccades (cf., Fig. 3B), the path lengths of saccades in electrical stimulation trials and in control trials were very similar (mean difference, 2.0 ± 0.5%). In contrast, the 2D trajectories of saccades in the air puff trials were strongly curved and more variable (cf., Fig.

![Figure 6](image-url)

**Fig. 6.** Saccade metrics in the individual subjects. Average values of the mean amplitude gain (A) and the mean direction error (B) for saccades that were perturbed by air puff–evoked blinks (dark gray) and by blinks evoked with electrical stimulation of the supraorbital nerve (light gray). Error bars denote ±SD. Horizontal gray areas indicate ±SD in the control condition (averaged across subjects).
3A), which resulted in much longer and more variable path lengths compared with the corresponding control saccades (mean difference, 17.9 ± 0.8%).

Relation to blink magnitude

Previous studies have, to our knowledge, not related the effects of blinking on saccade parameters to the magnitude of the concurrent blink. To fill this gap, Fig. 8 quantifies the changes in saccade metrics, kinematics, and trajectories as a function of eyelid deviation for two blink-perturbation paradigms applied in this study. Figure 8A plots the Cartesian endpoint errors of the perturbed saccades (see Methods). Figure 8B shows the distribution of mean eye velocity, normalized with respect to the mean eye velocity of corresponding control saccades. Figure 8C quantifies the trajectory perturbations by means of the path undulation index, which is the path length of a saccade normalized with respect to its amplitude (see Methods). As one might expect from the analysis in Figs. 4 and 5, the Cartesian endpoint errors showed no systematic relation to the blink magnitude (Fig. 8A). More specifically, both the means and the SD calculated across 10° amplitude bins (5° overlap) were not significantly correlated with the amplitude of the eyelid deviation (t-test, P > 0.05). Thus in both perturbation paradigms, the endpoints of saccades associated with large blinks were as accurate and as precise as the endpoints of saccades associated with small blinks. More surprisingly, we also found that the changes in mean eye velocity were not systematically related to the magnitude of the eyelid deviation (Fig. 8B; Pearson’s correlation coefficient r = 0.03; t-test, P > 0.05). Under both experimental conditions, the stimulation produced marked decreases in the mean eye velocity (15.2 ± 0.6%) even when the evoked blinks were comparatively small. Only the path undulations of saccades in the air-puff trials showed a significant change as a function of the eyelid deviation (Fig. 8C, black). Saccades associated with large air puff–evoked blinks typically had a much larger path undulation than saccades associated with small blinks (Pearson’s correlation coefficient, r = 0.58; t-test, P = 0.0001). In contrast, the path undulations of saccades in electrical stimulation trials remained close to zero even when the shocks evoked large blinks (Fig. 8C, gray; Pearson’s correlation coefficient r = 0.11; t-test, P > 0.05).

Discussion

In this study, we compared the influence of two types of reflex blinks on the trajectories and kinematics of memory-guided saccades in human subjects. To summarize, we obtained slow, strongly curved saccades when blinks were evoked by an air puff, whereas straight, briefly interrupted saccades were obtained when blinks were evoked with electrical stimulation of the supraorbital nerve. Although both types of blinks produced considerable changes and variability in the kinematics of the saccades, their 2D endpoints remained as accurate and as precise as the ones in the control condition. To our knowledge, these results are the first to confirm the preliminary observation of Becker (1993) that electrical stimulation of the supraorbital nerve can elicit interrupted saccades in humans and substantiate his claim that the endpoints of the resumed movements are accurate. They are also the first to show that the quantitative effects of blinks on saccades depend on the magnitude of the evoked blinks as well as on the nature of the applied stimulus.
Previous studies in both humans and monkeys (Goossens and Van Opstal 2000a; Rottach et al. 1998) have indicated that the perturbations in saccade kinematics brought about by blinks cannot be simply accounted for by linear summation of horizontal and vertical gaze deviations produced by blinks during fixation and unperturbed saccadic eye movements made without blinks. It was concluded therefore that blinks influence the central programming of saccades. This study in humans provides direct evidence to support this conclusion, because we found that blinks evoked by electrical stimulation of the supraorbital nerve produced considerable changes in saccade kinematics (duration and mean velocity), whereas concurrent perturbations of the 2D eye movement trajectories (here quantified by changes in path length) were negligibly small (Figs. 3 and 7). Note that co-contraction of extraocular eye muscles (Evinger and Manning 1993; Evinger et al. 1984) cannot account for this behavior either. Even in the unlikely event that such a mechanism would not produce 2D trajectory perturbations, it would still require implausible amounts of co-contraction to increase the plant stiffness to such high levels that it can completely halt the saccade in midflight (see Goossens and Van Opstal 2000a for theoretical details).

Robust perturbations of the 2D saccade trajectories were observed only in the air-puff condition. One might speculate that this salient difference between air-puff and shock-evoked perturbations could perhaps be explained by dissimilar strengths of the two types of stimuli rather than by stimulus type per se. If true, however, one would predict that the 2D trajectory perturbations of the saccades are the same when the amplitudes of the air-puff and shock-evoked blinks are the same. The results of our analysis in Fig. 8C clearly show that this was not the case. In fact, path undulations produced by shock-evoked blinks were not only small; they were also unrelated to the amplitude of the concomitant blink. Conversely, air puff–evoked blinks within the same amplitude range produced significant path undulations that increased systematically with the amplitude of the evoked blink. Our data thus show a striking difference between the effects of air-puff and shock-evoked blinks that goes beyond simple differences in the strength of the blink-evoking stimuli. This latter conclusion is consistent with the notion that supraorbital nerve stimulation and air-puff stimuli may differ in activated afferent fibers and subsequent interneuronal pathways in the brain stem (Berardelli et al. 1985; Domingo et al. 1997).

Interestingly, the pattern of gaze perturbations for reflex blinks during fixation (Fig. 2) indicates that the differential effects of air-puff versus shock-evoked blinks can be explained by quantitative differences in blink-related eye movements, when it is assumed that these movements are added on to slow, but otherwise straight, saccades (Fig. 1). During fixation, both air-puff and shock-evoked blinks produced transient horizontal and vertical perturbations of gaze, but the amplitudes of the back and forth eye movements that were associated with shock-evoked blinks were comparatively small, especially when compared with the larger eye movements that accompanied air puff–evoked blinks of the same magnitude (Fig. 2C). Thus if the superposition principle holds true for saccade and blink-related eye movement commands, it is expected from these data that the 2D trajectory perturbations and the resulting increases in path length are indeed larger in the air-puff condition.

Hence, the overall picture that emerges from the response patterns under the two blinking conditions is that the influence of blinks on the central programming of saccades consists of (at least) two separate components: 1) inhibition of a central eye velocity command that specifies a straight, intended eye movement trajectory and 2) superposition of horizontal and vertical back and forth movements of the eye, the amplitude of which depends on the nature and magnitude of the evoked reflex blink. Although it cannot be ruled out that the mechanical consequences of extraocular muscle co-contraction have some residual effect on saccades, our observations are clearly in line with the hypothesis of Fig. 1, which proposes that behavior (1) trigeminal inputs influence the programming of saccades at the level of the midbrain SC in such a way that its output represents a slow but straight intended eye movement and that 2) pure blink-related eye movements are superimposed on this movement command downstream, giving rise to perturbations of the 2D saccade trajectory.

Earlier studies (Becker 1993; Rambold et al. 2002; Rottach et al. 1998) have speculated that the changes in saccade kinematics that are associated with blinks could be caused by (re-)activation of the OPNs. The response pattern that we obtained with electrical
stimulation of the supraorbital nerve during saccades is indeed very similar to the behavior that is observed in monkeys when intrasaccadic electrical stimulation is applied to the OPN region (Keller et al. 1996). However, despite this striking similarity at the behavioral level, it is unlikely that the blink-related decreases in saccade velocity are caused by (re-)activation of the OPNs. As mentioned in the Introduction, recording studies have shown that OPNs pause during blinking and saccades (Cohen and Henn 1972; Fuchs et al. 1991; Mays and Morрисse 1994), which strongly suggests that they cannot cause the observed braking of the eye movements. Moreover, evoked blinks often reduce the latencies of impeding saccades (Gandhi and Bonadonna 2005; Goossens and Van Opstal 2000b), which is opposite to the effect one would predict for activation of the OPNs. Instead, there is good quantitative evidence now that the blink-related changes in saccade kinematics are caused by changes in burst activity of saccade-related neurons in the midbrain SC (Goossens and Van Opstal 2000b, 2006).

Does this mean that different explanations are needed for the nearly identical behavior that is observed with electrical stimulation of the supraorbital nerve in humans and electrical stimulation of the OPN region in monkeys? We think maybe not. First, it should be noted that electrical stimulation of the OPN region does not only activate the OPNs; it also leads to inhibition of saccade-related activity in the SC (Keller and Edelman 1994). Thus it remains undecided what really causes the interruption of saccades in the OPN stimulation paradigm. It could be caused by the inhibition of burst activity of medium-lead burst neurons in the brain stem (as is generally assumed), or, alternatively, it could result from the inhibition of saccadic burst activity in the SC. The latter possibility can also account for the finding that the saccade trajectory remains virtually straight when the eye decelerates during the shock-evoked interruptions. The former, traditional explanation, however, cannot readily account for this behavior, because the inhibitory effects of the OPNs on the horizontal and vertical burst generators would have to be precisely scaled according to the direction of the saccade to maintain the same instantaneous direction of eye movement during deceleration. We thus speculate that saccade interruptions obtained with electrical stimulation of the OPNs and with electrical stimulation of the supraorbital nerve may both result from transient inhibition of SC activity.

It remains to be tested, however, whether SC neurons also change their discharge in response to electrical stimulation of the supraorbital nerve as they do for air-puff and gaze-evoked blinks.

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