

Blink-Perturbed Saccades in Monkey. I. Behavioral Analysis

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Goossens, H.H.L.M. and A. J. Van Opstal. Blink-perturbed saccades in monkey. I. Behavioral analysis. *J Neurophysiol* 83: 3411–3429, 2000. Saccadic eye movements are thought to be influenced by blinking through premotor interactions, but it is still unclear how. The present paper describes the properties of blink-associated eye movements and quantifies the effect of reflex blinks on the latencies, metrics, and kinematics of saccades in the monkey. In particular, it is examined to what extent the saccadic system accounts for blink-related perturbations of the saccade trajectory. Trigeminal reflex blinks were elicited near the onset of visually evoked saccades by means of air puffs directed on the eye. Reflex blinks were also evoked during a straight-ahead fixation task. Eye and eyelid movements were measured with the magnetic-induction technique. The data show that saccade latencies were reduced substantially when reflex blinks were evoked prior to the impending visual saccades as if these saccades were triggered by the blink. The evoked blinks also caused profound spatial-temporal perturbations of the saccades. Deflections of the saccade trajectory, usually upward, extended up to $\sim 15^\circ$. Saccade peak velocities were reduced, and a two- to threefold increase in saccade duration was typically observed. In general, these perturbations were largely compensated in saccade mid-flight, despite the absence of visual feedback, yielding near-normal endpoint accuracies. Further analysis revealed that blink-perturbed saccades could not be described as a linear superposition of a pure blink-associated eye movement and an unperturbed saccade. When evoked during straight-ahead fixation, blinks were accompanied by initially upward and slightly abducting eye rotations of $\sim 2\text{--}15^\circ$. Back and forth wiggles of the eye were frequently seen; but in many cases the return movement was incomplete. Rather than drifting back to its starting position, the eye then maintained its eccentric orbital position until a downward corrective saccade toward the fixation spot followed. Blink-associated eye movements were quite rapid, albeit slower than saccades, and the velocity-amplitude-duration characteristics of the initial excursions as well as the return movements were approximately linear. These data strongly support the idea that blinks interfere with the saccade premotor circuit, presumably upstream from the neural eye-position integrator. They also indicated that a neural mechanism, rather than passive elastic restoring forces within the oculomotor plant, underlies the compensatory behavior. The tight latency coupling between saccades and blinks is consistent with an inhibition of omnipause neurons by the blink system, suggesting that the observed changes in saccade kinematics arise elsewhere in the saccadic premotor system.

INTRODUCTION

The oculomotor system and blinking evidently interact. It is well known, for example, that blink-evoking stimuli elicit a complex of motor actions that involve not only a transient

closure of the eyelids but also movements of the eye (e.g., Collewijn et al. 1985; Evinger et al. 1984). Conversely, saccadic eye movements are frequently accompanied by saccade-like movements of the upper eyelid (Becker and Fuchs 1988; Evinger et al. 1991). Moreover, large saccades (Evinger et al. 1991; Zee et al. 1983) as well as combined eye-head movements (Evinger et al. 1994) tend to elicit concomitant blinks. It has been proposed that these so-called gaze-evoked blinks may result from a common premotor drive to the saccadic and blink system (Evinger et al. 1994). In addition, there is neurophysiological evidence that several saccade-related areas can modulate reflex blinks (see following text). In the present study, we investigate how blinking affects the generation of saccades in monkey. Although it is common knowledge that blinking modifies saccades, quantitative data are scarce, and the involved mechanisms are still unclear.

During a blink, a burst of activity occurs in the normally quiescent lid-closing orbicularis oculi muscle while the tonic activity of the lid-raising levator palpebrae muscle ceases in time-linked fashion (see Evinger 1995 for review). Data from cat and rabbit indicate that the eye rotations associated with blinks result from a transient cocontraction of the extraocular muscles (Delgado-García et al. 1990; Evinger and Manning 1993; Evinger et al. 1984). As proposed by Evinger and Manning (1993), this muscle-activation pattern might result from a separate blink input to the extraocular motoneurons (OMNs). If true also for primates, one may wonder how the saccadic system accounts for blinking since it is generally assumed that the programming and generation of spatially accurate saccades does not rely on proprioception from the extraocular muscles (Guthrie et al. 1983). Instead, several reports have proposed that the saccadic system combines retinotopic visual input with extraretinal eye-position information, derived from an efference copy of the oculomotor command, to accurately redirect the eyes (Guthrie et al. 1983; Hallett and Lightstone 1976; Sparks and Mays 1983).

So far, experiments with human subjects indicate that saccade endpoints remain quite accurate when goal-directed saccades are perturbed in mid-flight by various blink-evoking stimuli (Becker 1993; Goossens and Van Opstal, unpublished observations; Rottach et al. 1998). As illustrated by Becker (1993), supra-orbital nerve stimulation, for example, results in briefly interrupted saccades that closely resemble those obtained with electrical stimulation of the omnipause neuron (OPN) region in the monkey brain stem (see e.g., Becker et al. 1981; Keller 1977; King and Fuchs 1977). Although the actual trajectory of the eye remained undisturbed in these experiments (i.e., the eye only stops in mid-flight and then resumes its original straight path), the latter data are generally considered

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the best evidence that the saccade trajectory is controlled by error feedback from efferent sources rather than by preprogrammed neural signals that are computed prior to saccade initiation.

According to this so-called local feedback hypothesis, the brain stem saccadic burst generator is controlled by an internal feedback circuit that continuously compares a desired eye movement with an internal representation (efference copy) of the actual movement until its goal is attained (Jürgens et al. 1981; Robinson 1975; Scudder 1988; Van Gisbergen et al. 1981). This concept is also used to explain how the saccadic system can generate, in the absence of visual feedback, accurate saccades of diminished velocity either due to pathology (Zee et al. 1976, 1983) or to pharmacological manipulation (Jürgens et al. 1981). Thus local feedback is presumed to make saccades more reliable and robust against errors. Since saccadic gaze shifts tend to elicit blinks (Evinger et al. 1991, 1994; Zee et al. 1983), it is conceivable that the saccadic system may also adequately deal with the effect of blinks on its performance, possibly through local feedback.

Accumulating data indicate that the saccade and blink systems may indeed interact at various premotor stages. Clinical studies have shown, for example, that blinks can accelerate pathologically slowed saccades (Zee et al. 1983) or initiate certain types of saccadic oscillations (Ashe et al. 1991; Hain et al. 1986). Moreover patients with Huntington's disease often blink to initiate voluntary saccades (Leigh et al. 1983).

It is currently thought that the OPNs serve as a shared element of the saccade and blink systems (Ashe et al. 1991; Evinger et al. 1994; Hain et al. 1986; Yee et al. 1994; Zee et al. 1983). OPNs are located in the pontine nucleus raphe interpositus (Büttner-Ennever et al. 1988) and are known to inhibit a variety of target neurons, including saccadic burst neurons in the reticular formation of the pons. Consistent with the proposed sharing of OPNs by the two systems, electrical microstimulation of the OPNs yields interrupted saccades (Becker et al. 1981; Keller 1977; King and Fuchs 1977) and a suppression of reflex blinks (Mays and Morrisette 1995). Moreover the tonic activity of OPNs has been shown to pause during saccades as well as blinks (Cohen and Henn 1972; Fuchs et al. 1991; Mays and Morrisette 1994).

More recently, the midbrain superior colliculus (SC), which is known to be critically involved in the generation of normal saccades, has also been implicated in the interactions between blinks and saccadic gaze shifts. For example, experiments in monkey (Gnadt et al. 1997) have shown that electrical microstimulation of the SC, like in rats (Basso et al. 1996), results in a transient suppression of air-puff-evoked trigeminal reflex blinks. Since the SC is currently thought to inhibit OPN activity (Raybourn and Keller 1977), Gnadt et al. (1997) reasoned that this blink suppression is not directly mediated by the OPNs. Rather, as in rodents (Basso and Evinger 1996), the SC could indirectly inhibit trigeminal blinks by activating the pontomedullary nucleus raphe magnus, which tonically inhibits spinal trigeminal neurons of the reflex blink circuit.

The purpose of the present paper is to explore, in detail, the effects of blinking on the generation of saccades in monkey and to provide a quantitative description of these interactions at the behavioral level. We have focused on the influence of air-puff-evoked blinks on the latencies, spatial trajectories and kinematics of two-dimensional saccadic eye movements. We

also examined the metrics and kinematics of blink-associated eye movements to assess how these movements interfere with saccades. To our knowledge, such data are not available in the current literature. To further investigate interactions between the two motor systems at the premotor level, the companion paper (Goossens and Van Opstal 2000) describes the neural activity patterns in the SC during blink-related saccade perturbations. A preliminary account of part of these data has been presented previously in abstract form (Goossens et al. 1996).

METHODS

Subjects and surgical procedures

Three adult male rhesus monkeys (*Macaca mulatta*; referred to as SA, PJ, and ER), weighing 8–9 kg, participated in the experiments. The animals had been trained to follow a small visual target with saccadic eye movements to obtain a small liquid reward. Records were kept of the monkeys' weight and health status and supplemental fruit and water were provided as needed. All surgical and experimental procedures were conducted in accordance with the European Communities Council Directive of November 24, 1986 (86/609/EEC) and were approved by the local university ethics committee.

The animals underwent three separate surgical sessions. Surgery was performed under sterile conditions while the animal was under inhalant anesthesia with N_2O/O_2 and halothane. In the first session, a head holder was placed on the skull by embedding eight titanium bone screws and four stainless-steel bolts in dental cement. This head holder allowed for rigid and painless head restraint during the experiments. In a second session, a thin gold-plated copper ring (~18 mm diam) was implanted underneath the conjunctiva of the left eye, following a method described by Judge et al. (1980). This ring, which became firmly attached to the eye by connective tissue, allowed for an accurate and wireless recording of eye position (Bour et al. 1984; Ottes et al. 1986; see also following text). Finally, a recording chamber was placed over a trephine hole to allow for single cell recordings in the superior colliculus that are described in the companion paper (Goossens and Van Opstal 2000).

Setup and experimental procedures

EXPERIMENTAL CONDITIONS. All experiments were performed in a completely dark, sound-attenuated room (dimensions, $3 \times 3 \times 3$ m). The head-restrained monkeys were seated in a primate chair facing an array of 85 light-emitting diodes (LEDs) at polar coordinates $R \in [0, 2, 5, 9, 14, 20, 27, 35]$ deg and $\Phi \in [0, 30, 60 \dots 330]$ deg. R is the eccentricity relative to the straight-ahead viewing direction, which was parallel to the stereotaxic anterior-posterior axis of the head. $\Phi = 0^\circ$ corresponds to a rightward position and $\Phi = 90^\circ$ is upward. The LEDs (diameter, 0.2°; intensity, $0.2 \text{ cd} \cdot \text{m}^{-2}$) were mounted on a spherical wire frame such that each LED was at a viewing distance of 85 cm.

AIR PUFFS. Trigeminal reflex blinks were evoked by brief air puffs on the left, recorded eye. These stimuli were generated by a pressure unit that was located outside the experimental room. In this way, the sound clicks produced by the air valve could not elicit an acoustic reflex blink. The air pulses (duration, 20 ms; intensity, 1.4–1.8 Bar at the source) were fed through a plastic tube (length, 4 m; diameter, 4 mm) that ended 1–2 cm in front of the eye. The fixed delay between triggering the pressure unit and the actual air puff on the eye was 43 ms. This was measured in vitro with a freely suspended search coil in front of the tube. The air-puff intensity was always well above threshold and, if necessary, adjusted during the course of an experiment (see *Perturbation paradigm*).

EYE AND EYELID POSITION RECORDING. The two-dimensional (2-D) orientation (referred to as "position") of the left eye was

recorded with the double-magnetic induction technique developed in our laboratory (Bour et al. 1984; Ottes et al. 1986). The horizontal (40 kHz) and vertical (30 kHz) oscillating magnetic fields that are required for this method were generated by two orthogonal pairs of 3×3 m square coils that were attached to the side walls, ceiling, and floor of the room. The eye-position-dependent currents that are induced in the implanted eye ring (see preceding text), were measured with a sensitive pick-up coil that was placed directly in front of the eye before the experiment. This coil signal was preamplified and demodulated into horizontal and vertical DC eye-position components by two lock-in amplifiers (PAR 128A). The resolution of this recording technique was $\sim 0.2^\circ$ in all directions.

Eyelid movements were measured with the magnetic search-coil induction technique (Collewijn et al. 1975) to detect the occurrence and onset moments of blinks. To that end, a small custom-made coil (~ 4 mm diam) was taped to the center of the lower margin of the upper-right eyelid. Signals from the lid coil were preamplified and demodulated into horizontal and vertical DC position components by a second set of lock-in amplifiers (PAR 120). It was verified, on the basis of the eye-position and eye-velocity profiles, that the presence of a small coil on the eyelid did not affect the metrics and kinematics of normal visually guided saccades.

Movements of the right eyelid (contralateral to the side of air-puff stimulation) were measured to avoid cross-talk between the lid-coil signals and the eye-ring signals. Although attempts were made to measure the delay of crossed blinks with respect to the ipsilateral responses in a fourth monkey (*GI*), the interference of the eye ring with the lid coil proved to be too strong to obtain reliable bilateral measurements of the eyelid movements. However, it is known for humans that the unilateral, short-latency electromyographic activity of the orbicularis oculi muscle (uncrossed R1 component) is quite small in the case of electrical stimulation of the supra-orbital nerve and absent after corneal stimulation (Berardelli et al. 1985). The small R1 response to supra-orbital nerve stimulation can also hardly be associated with a noticeable movement of the eyelid (Bour et al. 2000). Furthermore no significant latency difference between movements of the ipsilateral and contralateral eyelid was obtained for air-puff-evoked blinks in cynomolgus monkeys (Porter et al. 1993) and in a control experiment with two human subjects in our own setup (2 ms, unpublished observations). We assumed therefore that the latency difference in rhesus monkeys is also very small.

DATA ACQUISITION AND STIMULUS PRESENTATION. Timing of the stimulus events as well as data acquisition were controlled by a PC-80486, equipped with a data-acquisition board (Metrabyte DAS16) and a digital I/O card (Data Translation 2817). Horizontal and vertical eye and eyelid position signals were amplified, low-pass filtered (150 Hz) and sampled with 12-bit resolution at a rate of 500 Hz per channel. Data acquisition started 400 ms prior to the offset of the initial fixation point and continued for 1.5 s. The raw data were stored on disk for off-line analysis (see *Data analysis*).

Behavioral paradigms

STANDARD PROTOCOL. At the beginning and end of each experiment, the monkey fixated 85 targets throughout the oculomotor range up to eccentricities of 35° . To that end, saccades were evoked from the straight-ahead LED to all peripheral LEDs (see **EXPERIMENTAL CONDITIONS**). In each trial, one of the LEDs was pseudo-randomly selected and presented for 900 ms immediately after the central fixation spot (800–1,600 ms presentation time) disappeared. The animal was rewarded after fixating the peripheral target for 300 ms. A trial was aborted when initial fixation was not maintained for the required period. The data obtained in these trial blocks were used for calibration of on-line and off-line eye-position signals (see *Data analysis*).

PERTURBATION PARADIGM. This paradigm was used to study the influence of blinking on visually evoked saccades. Three different trial types were randomly interleaved.

Control trials. The animal had to look at an initial fixation point that was presented for a variable period of 600–1,200 ms. As soon as the fixation point disappeared, either one of five peripheral targets (randomized) was flashed for 50 ms, and the monkey was required to refixate the remembered position of that target by making a saccade in complete darkness (see Fig. 1B). To receive a reward, the animal had to maintain initial fixation until 80 ms after the offset of the fixation spot, and the target position had to be acquired within $\pm 4^\circ$ and fixated for ≥ 300 ms; 30% of the trials in each block were control trials.

Perturbation trials. An equal number of trials were exactly like the control trials except that an air puff was presented on the left eye to elicit a binocular blink reflex (latency ~ 20 ms; see **RESULTS**) near the onset of the visually evoked saccade (see Fig. 1C). The pressure unit was triggered at a fixed moment after the onset of the peripheral target, ~ 70 ms before the expected saccade onset to account for delays of both the air-puff and the blink reflex. To that end, the exact timing of the air puff was adjusted according to the mean saccade latency in control trials. The animal was rewarded at the end of each perturbation trial regardless of its performance. If necessary, the air-puff intensity was adjusted to the monkey's behavior during the course of an experiment. This was done in such a way that the saccades could be disturbed considerably without causing discomfort to the animal or completely disrupting its responses (see **RESULTS**).

Catch trials. In the remaining 40% of the trials, saccades were evoked toward targets that were presented for 900 ms at pseudo-randomly selected locations. Data obtained in these trials are not included in the present paper.

FIXATION PARADIGM. This paradigm was used to separately measure the rotations of the eye that accompany blinks as well as the latency of air-puff-evoked blinks. In each trial, the monkey had to fixate a straight-ahead LED for 1.5–2.0 s. The animal was rewarded for maintaining its gaze within a $\pm 4^\circ$ window throughout the demanded period. In 30% of the trials, referred to as *fixation-blink trials*, an air puff elicited a blink response (see Fig. 1A), and the monkey was always rewarded afterward. Trials with and without air puffs were randomly interleaved.

Data analysis

CALIBRATION OF EYE POSITION. Eye-position signals were calibrated off-line on the basis of 85 target fixations throughout the oculomotor range ($\pm 35^\circ$, see preceding text). Since we did not study the metrics and kinematics of the eyelid movements quantitatively, no attempts were made to calibrate these signals. Eyelid position signals are therefore presented in arbitrary units (au).

Because the double-magnetic induction method is characterized by smooth direction-dependent nonlinearities (Bour et al. 1984), two neural networks, one for each eye-position component, were trained to map the raw eye-position signals to the known associated target locations (see also Frens and Van Opstal 1997; Goossens and Van Opstal 1997; Melis and Van Gisbergen 1996). Each network consisted of three layers: two input units (representing the raw horizontal and vertical signal), five hidden units, and one output unit (representing either the horizontal or vertical component of the calibrated eye-position signal).

To train these networks, a training set was constructed that contained all reliable target fixations (typically, $n > 80$). The connectivity weights in each network were then optimized using a back-propagation algorithm based on the gradient descent method of Levenberg-Marquardt (Matlab 4.2, 5.0, The Mathworks). To that end, the raw fixation data from the training set were presented as inputs while clamping the corresponding target coordinates on the output. After 500 training epochs (taking about 1–2 min on a SUN-3/140 workstation), each network was always able to transform the raw eye-position data to a linear, calibrated eye-position signal with an accuracy better than 5% over the entire recording range ($\pm 40^\circ$).

Raw eye-position signals were subsequently calibrated by applying

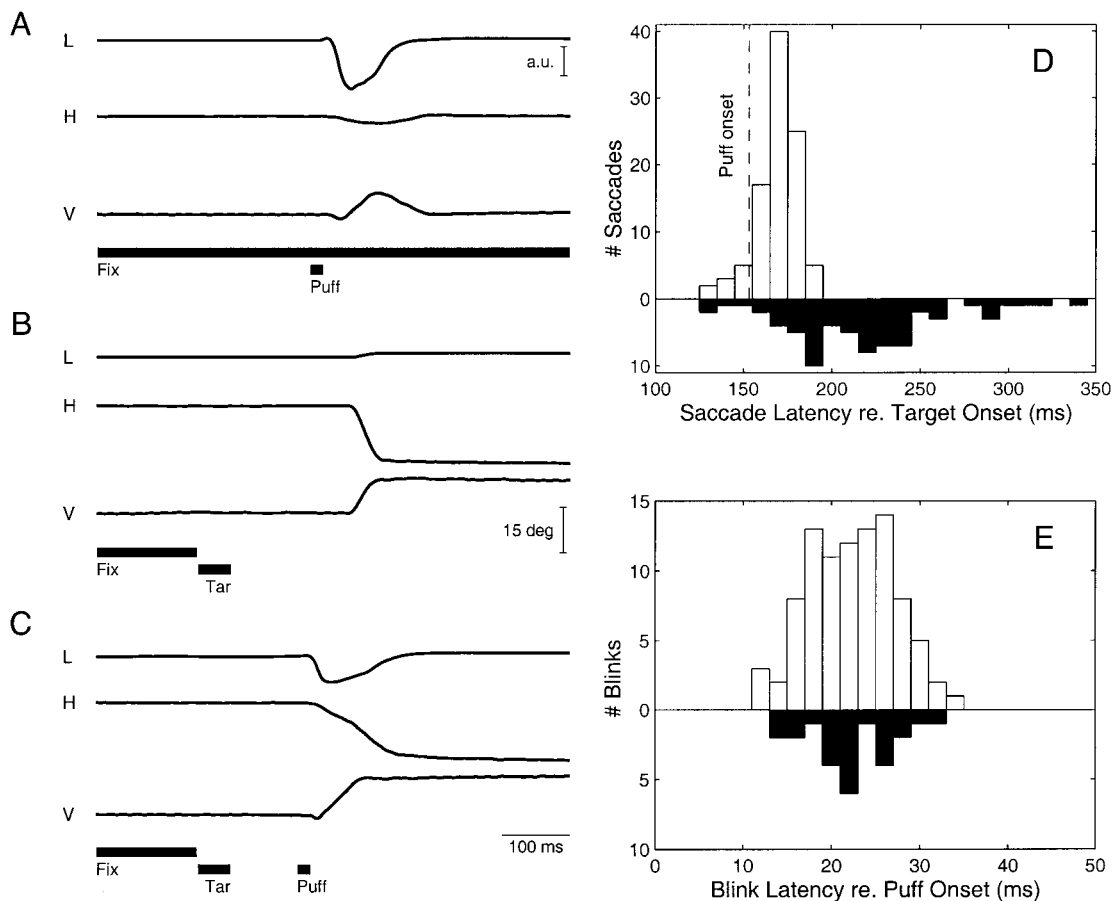


FIG. 1. Latency coupling between saccades and blinks. Example of responses obtained in 3 different trial types (left) together with the latency distributions of saccades and blinks for each of these trial types (right). Data from *monkey ER*. A: reflex blink evoked by an air puff during straight-ahead fixation. B: control saccade toward a briefly flashed visual target. C: blink-perturbed saccade toward the same target. Note that the saccade starts shortly (within 10 ms) after the air-puff-evoked blink. As in all subsequent figures, eye movements were measured at the left, stimulated eye, whereas lid movements were measured at the contralateral side (see METHODS). Traces show vertical eyelid position (L; in arbitrary units, au) and 2-dimensional (2-D) eye position (H, horizontal; V, vertical; in deg) as function of time. Presentation intervals of fixation (Fix), target (Tar) and air-puff (Puff) stimuli are indicated underneath. Puff intervals are corrected for the 43-ms transport time of the air puff to reach the eye. D: latency distribution of control saccades (■) and blink-perturbed saccades (□). Bin width 10 ms. Note the narrow latency peak, ~20 ms after the onset of the air puff (---). Mean saccade latencies (means ± SD) relative to target onset in control and perturbation trials were 216 ± 51 ms (n = 71) and 168 ± 14 ms (n = 95), respectively. E: latency distribution of reflex blinks in fixation-blink trials (■) and perturbation trials (□) relative to the air-puff onset at the contralateral eye. Bin width 2 ms. Note similar latencies in both conditions. Mean blink latencies were 23.4 ± 6.2 (n = 26) and 22.4 ± 4.9 (n = 95), respectively.

the trained feedforward networks and then low-pass filtered at 80 Hz (FIR-filter, Matlab). To ensure that the networks provided an accurate calibration throughout an experiment, the calibration procedure was repeated at least twice in each session, and calibrated eye-position signals were displayed on-line during data capture.

Radial eye-position (E) and vectorial eye velocity ($\dot{E}$) were computed from the recorded horizontal and vertical eye position and velocity by the use of Pythagoras' theorem

$$E = \sqrt{H^2 + V^2} \quad \text{and} \quad \dot{E} = \sqrt{\dot{H}^2 + \dot{V}^2}$$

SACCADE AND BLINK DETECTION. Saccades were detected off-line on the basis of the calibrated eye-position signals by a computer program which applied separate velocity criteria for saccade onset (40°/s threshold) and offset (30°/s threshold). Any saccade recognition failures were corrected by the experimenter after visual inspection of the identifications made by the marking program. This was especially important in the case of perturbed saccades. Onsets and offsets of perturbed saccades were judged on the basis of position and velocity traces as well as on their two-dimensional trajectories that could be redisplayed as a real-time movement (see also RESULTS). To

ensure unbiased detection criteria, no stimulus information was provided to the experimenter during saccade detection.

Blinks were detected separately with the same interactive computer program by using the raw vertical eyelid signals. Blink onsets could be readily detected on the basis of velocity and acceleration criteria since the initial eyelid movement during blinks is a very rapid downward movement (see RESULTS). Blink offsets were often poorly defined due to the low end velocity of the eyelid and were not used in the analysis. Blinks were easily dissociated from saccade-related eyelid movements because the former are characterized by a typical double-peaked velocity profile, whereas the latter are endowed with a roughly bell-shaped velocity profile (see e.g., Becker and Fuchs 1988; Evinger et al. 1991; Porter et al. 1993).

SELECTION CRITERIA. Saccades with latencies <80 ms or >400 ms with respect to the onset of the peripheral target were excluded from the analysis. Successful *control trials* were those in which no spontaneous or gaze-evoked blinks occurred. Successful *perturbation trials* were those in which the air puff evoked a reflex blink in a time window that ranged from 50 ms before the onset of the saccade until

50 ms after its expected offset. The latter was derived from the mean duration of control saccades toward the same target. No time window was used to analyze latency interactions between saccades and blinks. Successful *fixation-blink trials* were those in which the air puff did not elicit a saccade or saccade-like eye movement. Apart from these three trial types, we also identified trials in which spontaneous blinks occurred, either during straight-ahead fixation or after a goal-directed response. Trials that were rejected as control trials because the saccade was accompanied by a gaze-evoked blink were also marked for separate inspection.

RESULTS

The data presented in this paper were collected from three monkeys during 32 experimental sessions (15, 12, and 5 sessions with monkeys *PJ*, *ER*, and *SA*, respectively). In these experiments, air-puff stimuli were used to elicit reflex blinks while the animals were engaged in a saccade or a fixation task. In both cases, the air puffs reliably evoked binocular reflex blinks with latencies of 17.6 ± 4.5 ms (mean $\pm$ SD) (*SA*), 23.4 ± 6.2 ms (*ER*) and 20.2 ± 4.8 ms (*PJ*), as derived from the onset of the contralateral lid movement. Similar latencies were reported by Gnadt et al. (1997) for their rhesus monkeys. When evoked during straight-ahead fixation (Fig. 1A), blinks were accompanied by a transient, upward, and slightly abducting, rotation of the recording eye (see also following text for further details). Conversely, when the air puff was presented prior to the onset of an impending visual saccade (Fig. 1C), the saccade and the blink were initiated almost simultaneously as if the air puff triggered both motor responses. One might argue that the eye-movement onset reflects the blink-associated eye movement rather than the actual saccade onset. Note, however, that early in the movement, size, and shape of the horizontal eye-movement component are already different from that in Fig. 1A, indicating that the eye-movement onset and the actual saccade onset virtually coincide. As will be shown in the following text by a model-based analysis (see Figs. 11 and 12), the putative delay between the eye-movement onset and actual saccade onset was estimated to be ≤ 6 ms.

To further illustrate this tight latency coupling, Fig. 1D depicts the latency distribution of control saccades (■) and perturbed saccades (□). The histograms clearly show that the latency of saccades could be reduced by eliciting blinks. As may be observed, saccade latencies in control trials without air puffs (■) varied between 120 and 350 ms, which is typical for visually evoked saccades. By contrast, when air-puff stimuli were presented at a fixed moment near the expected saccade onset, the latencies of the eye movements were typically between 160 and 180 ms with respect to target onset (□), and occurred very shortly after the air puff arrived on the eye (---). In this example, the mean saccade latency was 168 ± 14 ms as opposed to 216 ± 51 ms in the control condition (*t*-test, $P < 0.0001$). A quantitatively similar tight latency coupling between saccades and blinks was reproducibly obtained with each monkey. Figure 1E depicts the latency distribution of reflex blinks, during fixation-blink trials (■) and during saccade perturbation trials (□), respectively. As one may observe, there were no significant latency differences between these two conditions.

Perturbation of saccades by blinks

As outlined in the INTRODUCTION, blinks are thought to interfere with saccade generation at several premotor levels. To gain further quantitative insight in the underlying interactions, we also examined the spatial trajectories and kinematics of blink-perturbed eye movements.

Figure 2 illustrates the results of a typical perturbation experiment with monkey *PJ*. Figure 2, A and B, compares a series of control saccades to a series of representative perturbed saccades with concomitant air-puff-evoked blinks. In the control condition (Fig. 2A), the monkey made approximately straight saccades to the target, and the bell-shaped velocity profiles ($\dot{E}$) were typical for 20° saccades (see e.g., Van Opstal and Van Gisbergen 1987). In Fig. 2B, an air-puff stimulus on the recording eye evoked a blink reflex near the onset of the saccade. In this condition, the 2-D saccade trajectories were substantially curved, typically upward, and they were much more variable than in the control condition. The kinematics of the eye movements were also strongly affected: the peak velocity was substantially reduced, and the duration exceeded that of control responses by almost 150 ms. These effects can be readily inferred from both the eye-position traces and the multi-peaked velocity profiles. Despite these profound spatial-temporal perturbations, the saccades still ended close to the position of the target even though all movements were made in complete darkness. Note that it made no difference whether blinks were evoked near saccade onset or in saccade mid-flight. One may also observe that the eye often showed a clear reacceleration toward the target position. This is most evident from the highlighted example (thick traces), in which the initial change in eye position is immediately compensated by a horizontal movement of the eye.

Very similar features were consistently observed when the saccades in control trials were accompanied by gaze-evoked blinks. As mentioned in the INTRODUCTION, such blinks are saccade-related events that tend to accompany large saccades (Evinger et al. 1991, 1994; Zee et al. 1983). To illustrate qualitatively that the effects of blinking were not specific to the applied perturbation paradigm, Fig. 3, A and B, shows a series of saccades that were perturbed by air-puff-evoked blinks and gaze-evoked blinks, respectively (thin traces). The mean unperturbed control saccade ($R = 32^\circ$) is superimposed in both panels (thick traces). Note that both types of blinks induced curved trajectories, increased durations, and reduced peak velocities. In both cases, there was also a clear goal-directed reacceleration of the eye after the initial perturbation. In many sessions, however, the number of gaze-evoked blinks was limited, depending on the amplitude of the evoked saccades. Gaze-evoked blinks were virtually absent for saccades $\leq 20^\circ$ or even $\leq 35^\circ$ when the animal was well motivated. Larger saccades (evoked from eccentric fixation points) were more frequently accompanied by gaze-evoked blinks, but the resulting perturbations, in general, were subtler than could be obtained with air-puff-evoked blinks. We have not analyzed these differences in quantitative detail.

Although blink-related perturbations were usually accounted for by the oculomotor system, we noticed that a limited fraction of the perturbed responses were not goal-directed. This bistable behavior is illustrated in Fig. 4 for a session with monkey *PJ* in which a relatively large number of such re-

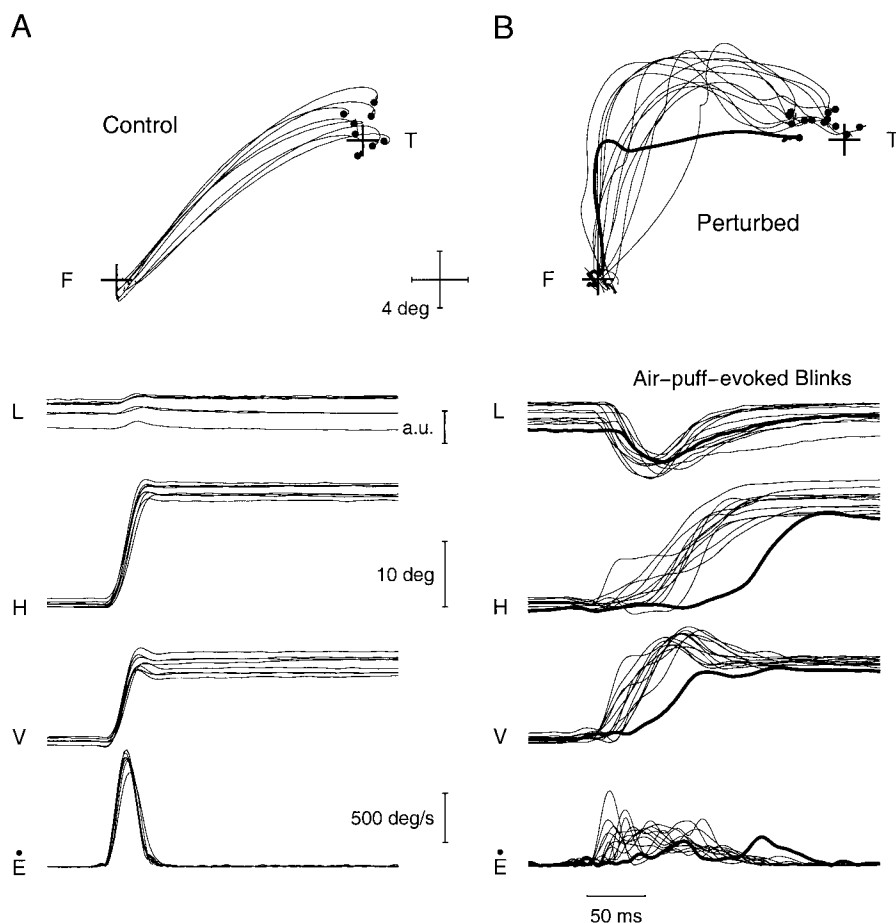


FIG. 2. Typical blink-perturbed saccades in the perturbation paradigm. Data from *monkey PJ*. Saccades were made in complete darkness to a target (T) that was briefly flashed at $[R, \Phi] = [20, 30]$ deg re. to the straight-ahead fixation point (F). Air puffs were presented in 30% of the trials to elicit a reflex blink at the time of the saccade. Trials are sorted into control (A) and perturbed (B) examples. The 2-D saccade trajectories are shown at the top. Subsequent traces show vertical eyelid position (L), horizontal (H), and vertical (V) eye position and vectorial eye velocity ($\dot{E}$; see METHODS) as function of time. All movements are aligned with saccade onset. Note comparable endpoint accuracies in A and B, despite the severe spatial-temporal perturbations of the saccade trajectory in B. Note also reaccelerations of the eye during compensation, particularly in the high-lighted example (thick traces).

sponses were obtained. Figure 4A shows the 2-D trajectories of all responses toward a target briefly presented at $[R, \Phi] = [60, 27]$ deg. Note that the perturbation was very poorly or not at all compensated (—; $\times$, endpoints) in six responses, while eight responses did show considerable compensation ($\cdot \cdot \cdot$; $\bullet$ endpoints). The scatter plot in Fig. 4B shows the Cartesian endpoint errors relative to the target of all control ($\circ$) and perturbed ($\bullet$ and $\times$) saccades evoked in this particular experiment (pooled data of responses to 5 nearby targets). One may notice that the endpoint errors were small in the far majority of perturbed responses ($\bullet$), while atypically large errors were obtained in 10 perturbation trials ($\times$; 24%).

The overall impression gained from the data in Figs. 2–4 was that blink-perturbed eye movements remained fairly accurate despite severe perturbations in both the trajectory and the kinematics. To quantify this property further, we analyzed the endpoint accuracy of saccades that were perturbed by air-puff-evoked blinks in comparison with unperturbed control saccades. To that end, we measured the difference between the endpoints of perturbed saccades and the mean endpoint of control saccades toward the same target in two dimensions. The difference between these two response types, rather than the absolute accuracy, was analyzed because absolute accuracy may depend on many variables such as target duration and location as well as the subject's motivation.

Figure 5 illustrates the measures that were used to quantify the 2-D accuracy of perturbed saccades as well as the magnitude of the spatial trajectory perturbations. As de-

picted in Fig. 5A, we measured the radial amplitude of each perturbed saccade, R_p , and computed the amplitude error, e_r , with respect to the mean amplitude of corresponding control saccades, $\bar{R}_c$. Positive values of e_r indicate that the perturbed saccade was hypermetric with respect to the average control response. We adopted this measure from Keller et al. (1996), who recently used it to quantify the accuracy of OPN-interrupted saccades. We also computed the difference between the endpoint of each perturbed saccade and the mean endpoint of control movements in the direction perpendicular to the mean control vector. Note that this “orthogonal” error, indicated as e_d in Fig. 5B, provides a measure of how well the oculomotor system compensated for the changes in eye position with respect to the normal saccade trajectory. These trajectory perturbations, indicated as d in Fig. 5B, were quantified by measuring the maximum deviation from the averaged trajectory of control saccades in the direction perpendicular to the mean control vector. Note that this measure is independent from the saccade kinematics. The latter were quantified by measuring duration and peak velocity of each saccade.

Perturbed responses that were clearly not goal-directed (see Fig. 4) are not considered in this analysis because we believe they resulted from a different, atypical response mode (see DISCUSSION). To identify these responses, a computer algorithm detected the outliers in the endpoint distribution of perturbed saccades. In this way, eye movements with amplitudes and directions that differed by more than

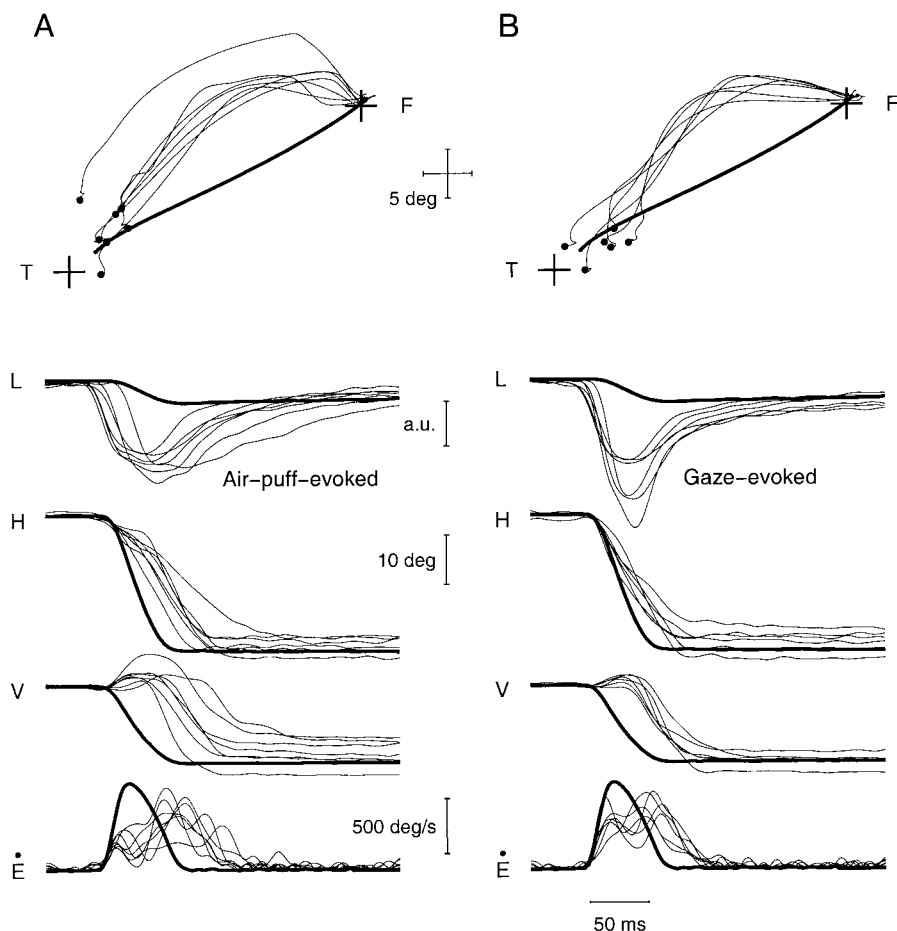


FIG. 3. Comparison of perturbed saccades that were accompanied by air-puff-evoked blinks (A) and gaze-evoked blinks (B). Data from *monkey SA*. Same format as Fig. 2. Mean control saccades are superimposed (thick traces). Targets were flashed at $[R, \Phi] = [34, 211]$ deg re to the shifted fixation point at $[R, \Phi] = [14, 30]$ deg from the center. Note qualitatively similar spatial-temporal perturbations of the saccades by both types of blinks.

four standard deviations from the mean were excluded (e.g., the $\times$ data points in Fig. 4B). The fraction of nongoal directed responses ranged between 0 and 30% but was typically restricted to 10–15%. Corrective saccades that sometimes followed the initial perturbed response were also not included in this analysis.

Saccade metrics and kinematics

Figure 6, A and B, compares the amplitudes of control and perturbed saccades obtained in a series of experiments in all three monkeys. Saccades were evoked by target displacement

ments ranging between 9 and 60° in *monkeys PJ* and *ER* and between 20 and 40° in *monkey SA*. For each target eccentricity, data were selected from representative sessions in which the largest number of responses were obtained ($n > 10$, in both conditions). Figure 6A depicts the mean amplitudes and the standard deviations of control saccades as a function of target eccentricity. The data show that the monkeys typically made slightly hypometric saccades, which is characteristic of visually evoked saccades. Figure 6B shows similar data for perturbed saccades except that the amplitude is expressed as an amplitude error relative to the mean

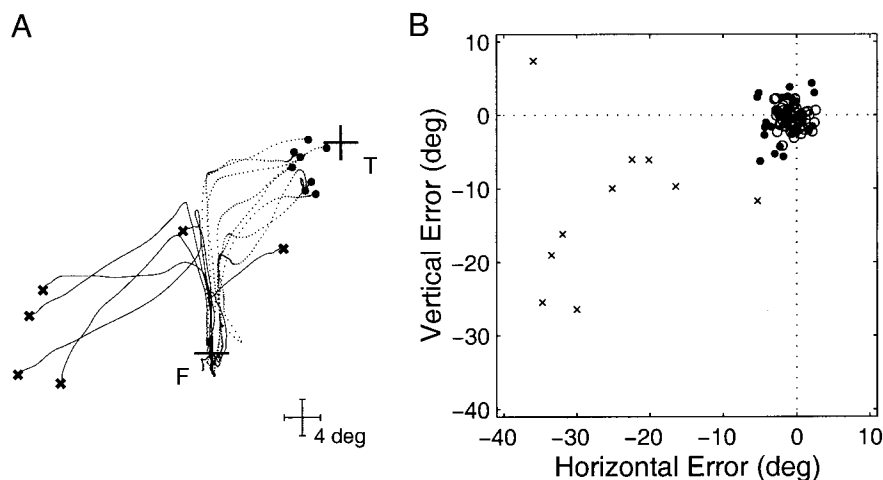


FIG. 4. Illustration of compensatory behavior vs. noncompensatory behavior. Data from *monkey PJ*. A: examples of blink-perturbed responses that showed little or no compensation (—) together with a series of movements in which the perturbation was accounted for ($\cdots$; 2 ms between each $\cdot$). Targets were flashed at $[R, \Phi] = [60, 27]$ deg re to the straight-ahead fixation point. B: endpoint scatter of all control ($\circ$; $n = 53$) and perturbed ($\bullet$, $n = 31$ and $\times$, $n = 10$) saccades obtained in this session. Endpoints are expressed as horizontal/vertical errors relative to the target. Data pooled for 5 different target displacements (up and to the right). Although a subset of responses was quite inaccurate ($\times$), the endpoint errors were small for the majority of perturbed saccades ($\bullet$).

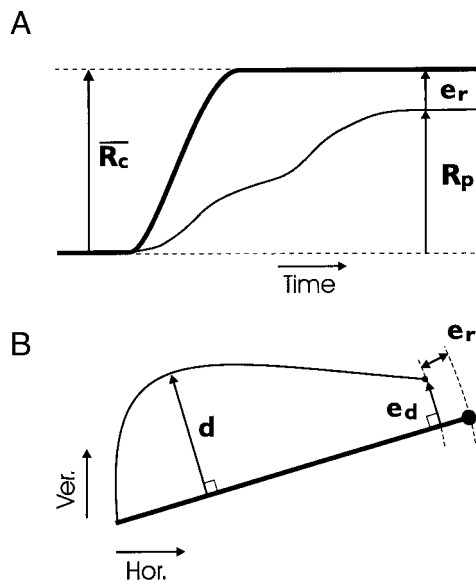


FIG. 5. Illustration of the various measurements made on each blink-perturbed saccade to quantify their metrics. A: schematic plot of radial eye position (E ; see METHODS) as function of time of a perturbed saccade (thin trace) and the average of a series of unperturbed control saccades (thick trace). $\bar{R}_c$ is the mean amplitude of the unperturbed control saccades, and R_p the amplitude of individual perturbed saccades. The amplitude error, e_r , is the difference in final amplitude between the averaged control saccades and the individual perturbed saccades, for the same target configuration. B: schematic plot of the 2-D trajectory of a perturbed saccade (thin trajectory) and the average of a series of unperturbed control saccades (thick trajectory). The orthogonal error, e_d , is the difference between the mean endpoint of control saccades and the endpoint of each individual perturbed saccade in the direction orthogonal to the mean control saccade. The maximum difference, d , between the mean control trajectory and the trajectory of each individual perturbed saccade, in the same orthogonal direction, was used to quantify the magnitude of the trajectory perturbation.

amplitude of the control saccades (e_r). Significant differences between control and perturbed responses are indicated (*, t -test, $P < 0.025$; otherwise $P > 0.1$). It can be seen that the amplitude errors were small ($< 3.0^\circ$) for target eccentricities $\leq 20^\circ$, while hypometric responses were obtained for larger eccentricities (mean errors up to -4.8°). Note, however, that the undershoots were usually small compared with the saccade amplitude (up to $\sim 10\%$), particularly in *monkey PJ*. Moreover in all cases both the trajectory and the kinematics of the eye movements were strongly modified by the blink reflex (see e.g., Fig. 2). The effects on saccade kinematics are quantified in Fig. 6, C and D (same data sets as in A and B). One may observe that the mean peak velocities of perturbed saccades (Fig. 6C; $\blacklozenge$, $\blacksquare$, $\bullet$, $—$) were reduced (t -test, $P < 0.0001$) compared with those of control saccades ($\diamond$, $\square$, $\circ$, $- - -$), often quite dramatically. One may further note that there were two- to threefold increases in the mean saccade duration (Fig. 6D; t -test, $P < 0.0001$). The standard deviations (error bars) also were much larger, indicating a large variability in the duration of perturbed saccades.

Further examination of the raw data suggested that the extent of compensation for the 2-D trajectory perturbations depended on the direction of the target jump. This directional dependence is illustrated in Fig. 7 by a worst-case example (*monkey SA*). Figure 7, A and B, compares large, perturbed saccades (thin trajectories) made to eccentric targets in two different direc-

tions. The mean control responses are also shown (thick trajectories). As may be observed, the change in movement direction was reasonably well accounted for when the saccades were made toward a target that was flashed near the horizontal meridian (Fig. 7A). By contrast, perturbed movements toward a target further down from the fixation point (Fig. 7B) not only fell short of the mean control response (and target) but also ended clearly above its endpoint. Note, however, that the eye movements were still directed toward the target location even though they started in a completely wrong direction (up and to the left).

This property is further quantified in Fig. 7, C and D, where the spatial trajectory perturbations as well as the orthogonal endpoint errors of perturbed saccades are shown as a function of target direction. Saccades were evoked to eccentric targets in various directions $\Phi \in [0, 30, \dots, 360]$ deg at either $R = 14^\circ$ or $R = 20^\circ$ in *monkeys ER* and *PJ* and at either $R = 20^\circ$ or $R = 27^\circ$ in *monkey SA*. Since we noticed no differences between leftward and rightward responses, target directions are presented as angles relative to the horizontal meridian, where $+90^\circ$ is upward and 0° is to the left/right. Figure 7C depicts the mean and standard deviations of the trajectory perturbations, d , for a series of representative sessions in which the largest number of responses were obtained ($n > 10$, in both conditions). The data show that the largest perturbations were obtained in oblique and horizontal directions. Note that these perturbations could be quite large (up to $\sim 15^\circ$) and that they were endowed with a substantial variability (large standard deviations). Although the trajectory perturbations were small for vertical saccades, these findings do not imply that vertical saccades were unaffected by blinks. Like horizontal and oblique saccades, their kinematics were severely disturbed.

Figure 7D presents the mean and standard deviations of the orthogonal endpoint errors, e_d , measured for the same perturbed saccades. Positive values indicate that the endpoints deviated in the same direction as the perturbation. The data show that the smallest errors were obtained for vertical target displacements, whereas systematically larger errors were found for horizontal and oblique-downward responses. Typically, these errors were much smaller than the amplitude of the trajectory perturbations (Fig. 7C; $e_d < d$, t -test, $P < 0.001$). Yet the errors were typically positive, which indicates that there were systematic deviations of the saccade endpoints in the direction of the perturbation (*, t -test, $P < 0.025$; otherwise $P > 0.1$). Hence it appeared that the movements compensated for deviations from the normal trajectory, albeit not equally well for all target directions tested. No significant compensation ($P > 0.1$) was obtained in only one experiment with *monkey ER* for target displacements in the 30° downward direction.

Blink-associated eye movements

The data presented in the preceding text indicate that the oculomotor system compensates, at least partly, for large blink-related perturbations in both direction and velocity. These results are consistent with the idea that a dynamic feedback circuit may control the saccade trajectory (see INTRODUCTION), but they do not exclude alternative possibilities. For example, a transient blink-related signal, in principal, could be added to the saccadic command at the level of the OMNs, and the resulting perturbation could be restored entirely by passive

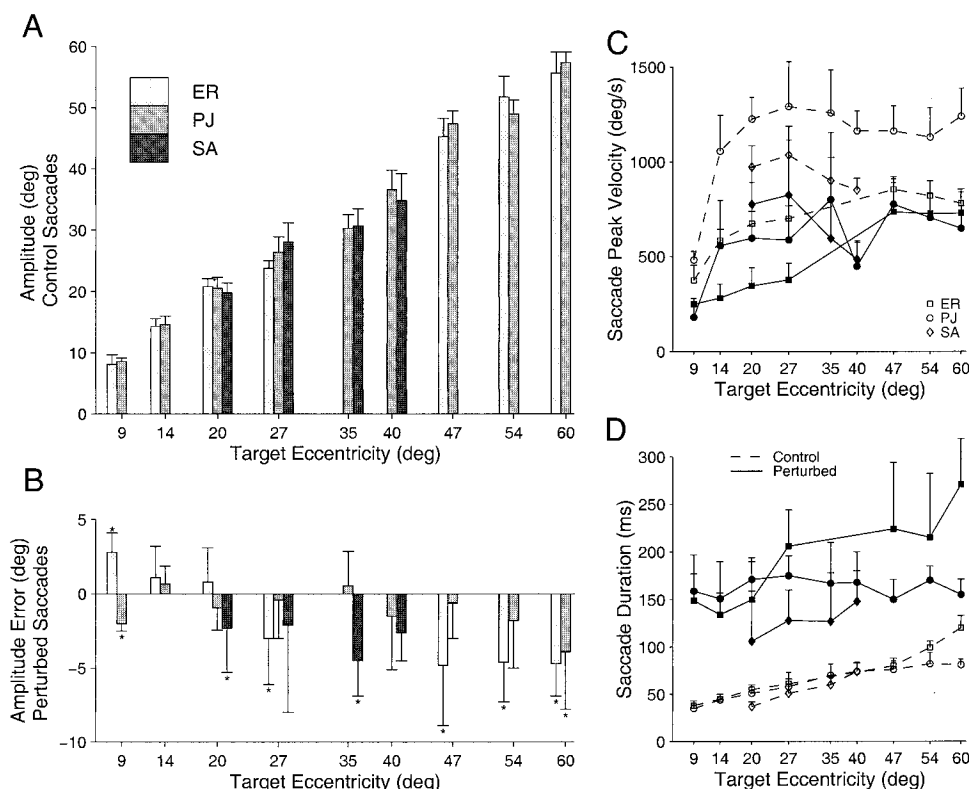


FIG. 6. Amplitude, peak velocity, and duration of blink-perturbed saccades compared with control saccades for all 3 monkeys. **A:** mean amplitude of unperturbed control saccades as function of target eccentricity. The fixation point was shifted from the straight-ahead position for target eccentricities beyond 35°. **B:** mean amplitude error of perturbed saccades relative to the mean amplitude of control saccades as function of target eccentricity (error measure e_r ; see Fig. 5). Note the differences in scale. **C:** mean peak velocity of control saccades ($\diamond$, $\square$, $\circ$, —) and perturbed saccades ($\blacklozenge$, $\blacksquare$, $\bullet$, ---) as function of target eccentricity. **D:** mean duration of control and perturbed saccades as function of target eccentricity. Note small amplitude errors despite severe perturbations of the saccade kinematics by air-puff-evoked blinks. Error bars indicate standard deviations. *, $e_r \neq 0$, $P < 0.025$.

elastic forces within the oculomotor plant. To obtain more insight into the possible mechanisms underlying the observed perturbations, we examined the eye movements accompanying blinks in more detail.

Figure 8 depicts a series of eye movements associated with air-puff-evoked reflex blinks in the fixation paradigm while the monkey (ER) attempted to fixate a straight-ahead fixation spot. The examples in Fig. 8, A and B, illustrate the two types of blink-associated eye movements that were reproducibly obtained in all three animals. As shown in Fig. 8A, the 2-D trajectories of blink-associated eye movement often described approximately closed loops, meaning that the eye returned to its initial position in a single movement. Note that there was considerable variability in these movements. Yet the largest excursions of the eye were consistently upward and slightly abducting. By examining also the eye movements during spontaneous blinks, we noticed that the direction and size of the loops depended on the initial eye position. This feature is illustrated in Fig. 9, which shows the 2-D trajectories of a series of eye movements that accompanied spontaneous blinks. Note, for example, that when the animal (PJ) was looking to the left, blinks resulted in a rightward initial eye rotation, while downward movements were obtained when the animal was looking upward. During straight-ahead viewing, spontaneous blinks were accompanied by eye movements that were initially upward and slightly abducting as was obtained also for air-puff-evoked responses.

This behavior, together with the increase in endpoint errors (Figs. 6 and 7), raised the question whether the observed compensation could have resulted entirely from passive restoring forces within the oculomotor plant. This would occur, for example, if a blink was associated with a transient activation of

the OMNs through a pathway that bypasses the local feedback circuit.

Interestingly, however, it appeared that the end position of the eye after a blink-associated eye movement was often clearly different from its initial position. This is illustrated in Fig. 8B, which depicts blink-associated eye movements evoked by air-puff stimuli in the same trial block as those shown in Fig. 8A. After such "truncated" eye movements, a downward corrective saccade toward the fixation spot frequently followed. The latencies of these corrective saccades (measured relative to the offset of the blink-associated eye movement) typically fell within the normal range of visually guided saccades, although strikingly short latencies (down to 20 ms) were observed as well. In Fig. 8B, for example, the shortest latency was 64 ms. One may also note that during this latency period, the eye remained stationary at its eccentric orbital position. Since the latter requires a tonic activation of extraocular muscles to prevent low-velocity drift (Robinson 1975), these data hint at an involvement of the neural eye-position integrator (see also DISCUSSION). In this respect, it is also of interest to note that the downward return movements of the eye in Fig. 8A were fairly rapid (i.e., peak velocities $\sim 200^\circ/\text{s}$) and did not follow a slow exponential time course. The latter feature is typical for the passive return movements of the eye that follow electrical microstimulation of the trochlear nerve or abducens nucleus (Sparks and Mays 1983; Sparks et al. 1987).

To further quantify the nature of blink-associated eye movements, we also analyzed their kinematics by dividing the movements into two subsequent phases: the (upward) eye excursion phase and the (downward) eye return phase (see Collewyn et al. 1985, for a similar analysis on blink-associated eye movements in humans). Figure 10, A–D, illustrates the

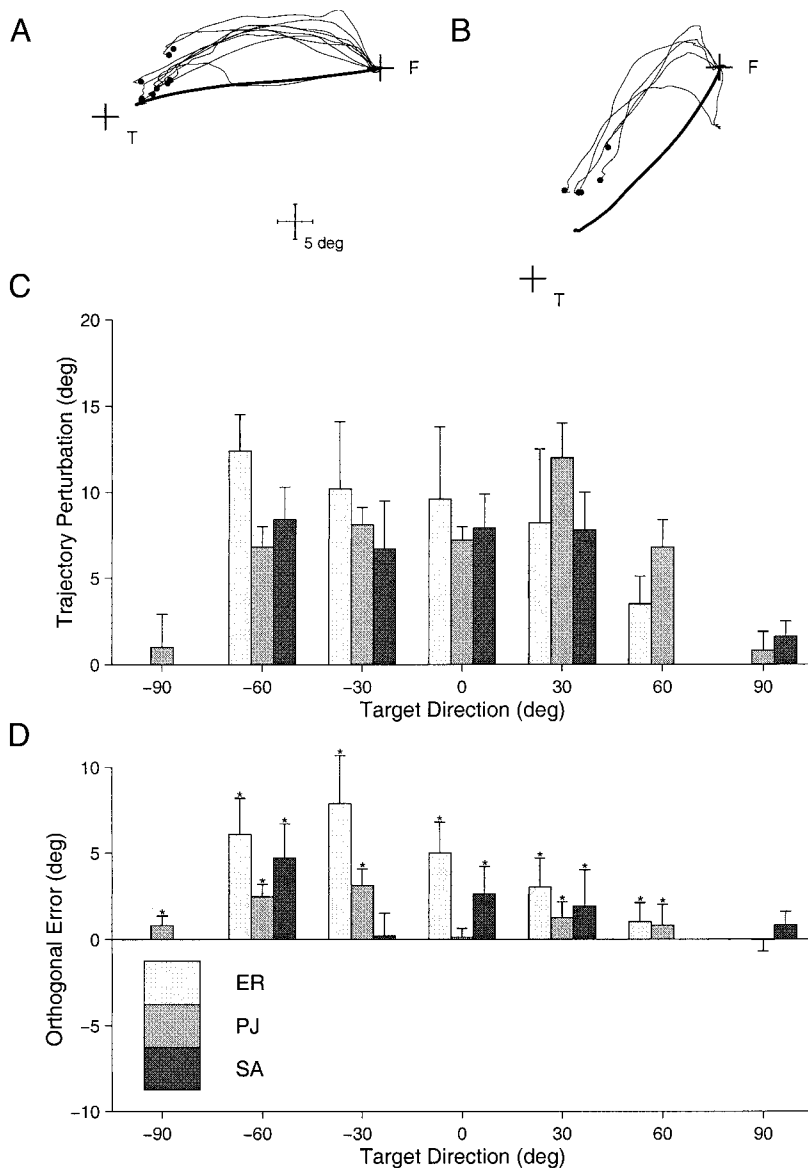


FIG. 7. Perturbations of the 2-D saccade trajectory induced by reflex blinks and saccade endpoint accuracy for the 3 monkeys (*ER*, *PJ*, and *SA*) tested. *A* and *B*: examples of perturbed responses in 2 different directions (*monkey SA*). Targets were flashed at $[R, \Phi] = [40, 191]$ and $[R, \Phi] = [40, 232]$ deg, in *A* and *B*, respectively. The perturbed saccades in *A* remain quite accurate, whereas the perturbations shown in *B* were only partially compensated. *C*: mean trajectory perturbation of blink-perturbed saccades as function of target direction (perturbation measure d ; see Fig. 5). Note large perturbations in all directions, except for purely vertical saccades (-90 and $+90^\circ$). *D*: mean orthogonal error of the same blink-perturbed saccades as function of target direction (error measure e_d ; see Fig. 5). Note directional dependence. Error bars denote standard deviations. *, $e_d \neq 0$, $P < 0.025$.

results of this analysis which included eye movements associated with air-puff-evoked blinks (○) and spontaneous blinks (●). All responses were obtained in the straight-ahead fixation task (pooled data from 8 sessions with *monkey PJ*). Figure 10, *A* and *B*, shows the velocity-amplitude-duration relations for the eye excursion movements. Figure 10, *C* and *D*, shows these relations for the eye return movements. Note that peak velocity as well as duration were approximately proportional to the amplitude of the movement. Table 1 lists the regression results of two monkeys (*ER* and *PJ*). Note also that the data obtained under spontaneous and air-puff-evoked blinking conditions overlap considerably. The average peak velocity for a $9-10^\circ$ excursion movement was $\sim 250^\circ/\text{s}$ and $\sim 200^\circ/\text{s}$ for a return movement of similar amplitude. Thus the peak velocity of return movements was only $\sim 20\%$ lower than for excursion movements, whereas one would have expected a considerable difference if the return movements were passive. For example, assuming a plant time constant of $T = 250$ ms, an entirely passive 10° return movement would have had a peak velocity of only $40^\circ/\text{s}$. For comparison, Fig. 10, *E* and *F*, shows the

velocity-amplitude-duration relations for (downward) corrective saccades that followed blink-associated eye movements (note the factor 2 scale difference with Fig. 10, *A-D*). One may readily observe that saccades have higher peak velocities and shorter durations and that they are more stereotyped.

Taken together, these findings suggest that the rapid return phase of blink-associated eye movements is under neural control rather than the mere result of elastic restoring forces within the oculomotor plant (see also DISCUSSION).

Superposition of two eye movements?

When electrical microstimulation was applied to the OMNs just before the onset of a visually evoked saccade, no active compensation for the stimulation-induced eye displacement was observed (Sparks and Mays 1983; Sparks et al. 1987). Rather, the eye movements could be well described by a linear superposition of the passive movements that occur after stimulation and the control saccade. Although the data in Figs. 8 and 10 suggest that the observed compensatory behavior in the

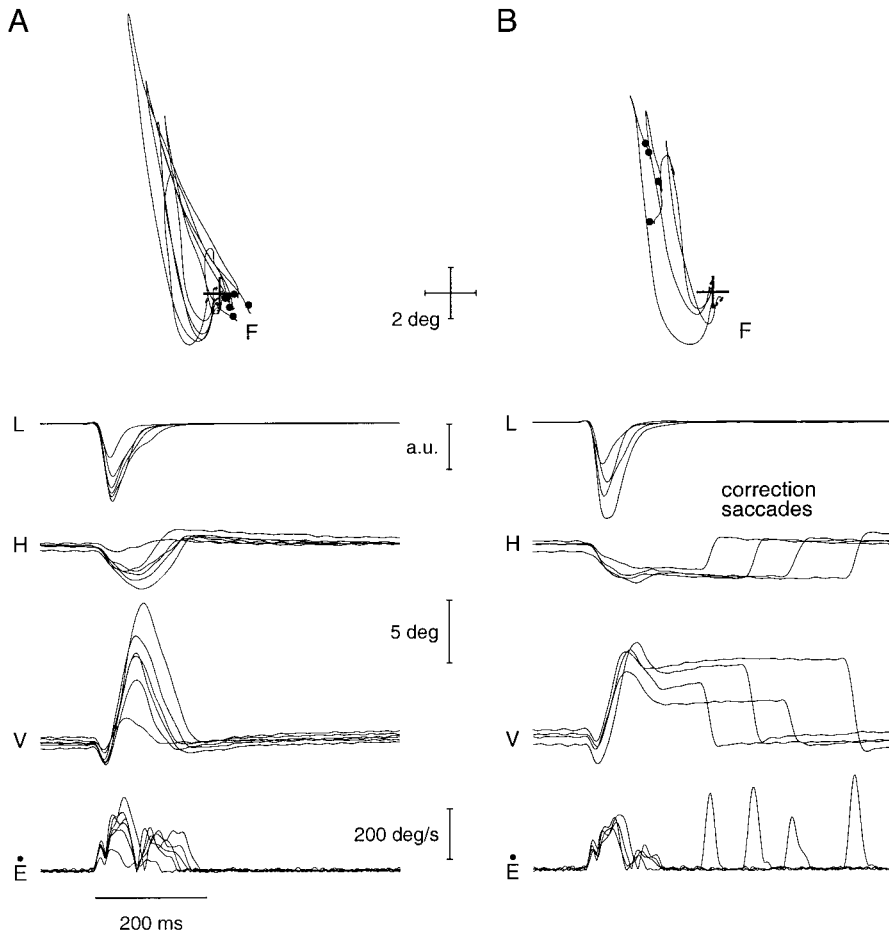


FIG. 8. Two types of blink-associated eye movements in the fixation paradigm. Data from *monkey ER*. Fixation was straight-ahead and blinks were evoked by air puffs. Depicted are 2-D eye-movement trajectories (top), eyelid (L) and eye-position (H and V) traces, as well as eye-velocity profiles ($\dot{E}$). In both response types, the maximum excursions of the left, recording eye were upward. A: the eye often returned to its initial position in a single movement, following a characteristic clockwise trajectory. B: in many cases, the eye instead ended at eccentric orbital positions. Those movements were typically followed by a downward correction saccade that brought the eye back to its starting position. Note the absence of drift prior to the corrective saccades.

case of blink-perturbed saccades does not result from passive restoring forces, the results so far do not exclude the possibility that blink-associated and saccadic eye-movement commands are independent and executed entirely in parallel. That is, compensation could be an intrinsic property of the blink system rather than the saccadic system.

This possibility was further examined in two ways. First, the average unperturbed control saccade was subtracted from perturbed saccades toward the same target to reconstruct the putative independent perturbation signal. In the case of a linear superposition of two separate commands at the motoneuron level, the reconstructed eye movements should be very similar

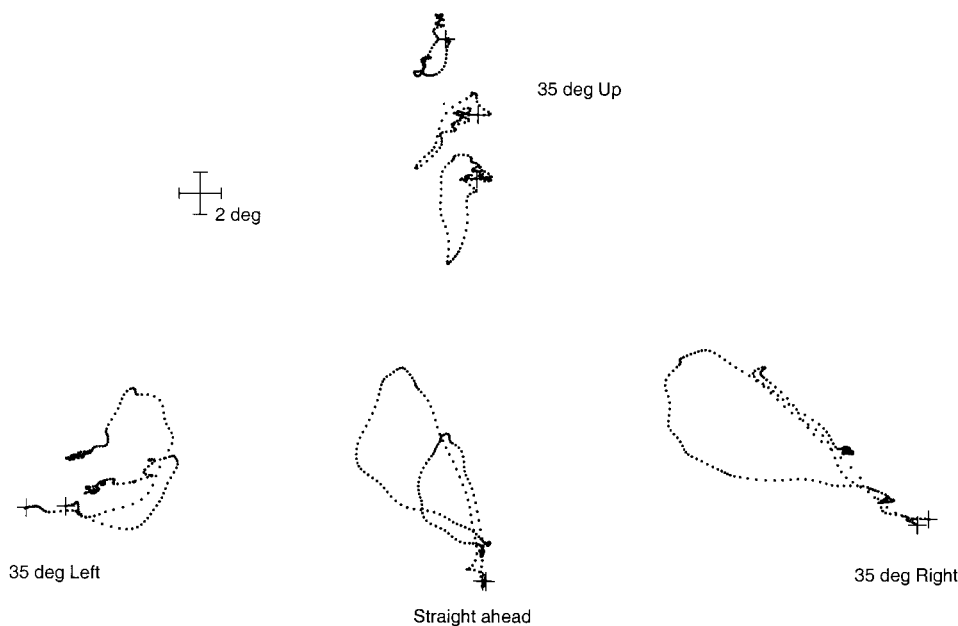


FIG. 9. Eye-position dependence of blink-associated eye movements. Data from *monkey PJ*. Shown are 2-D eye-movement trajectories associated with spontaneous blinks made when the animal was looking in different directions. For clarity, all eye movements starting at eccentric orbital positions have been shifted 10° toward the center. Starting positions are indicated by crosses (+), and there are 2 ms between each sample (•).

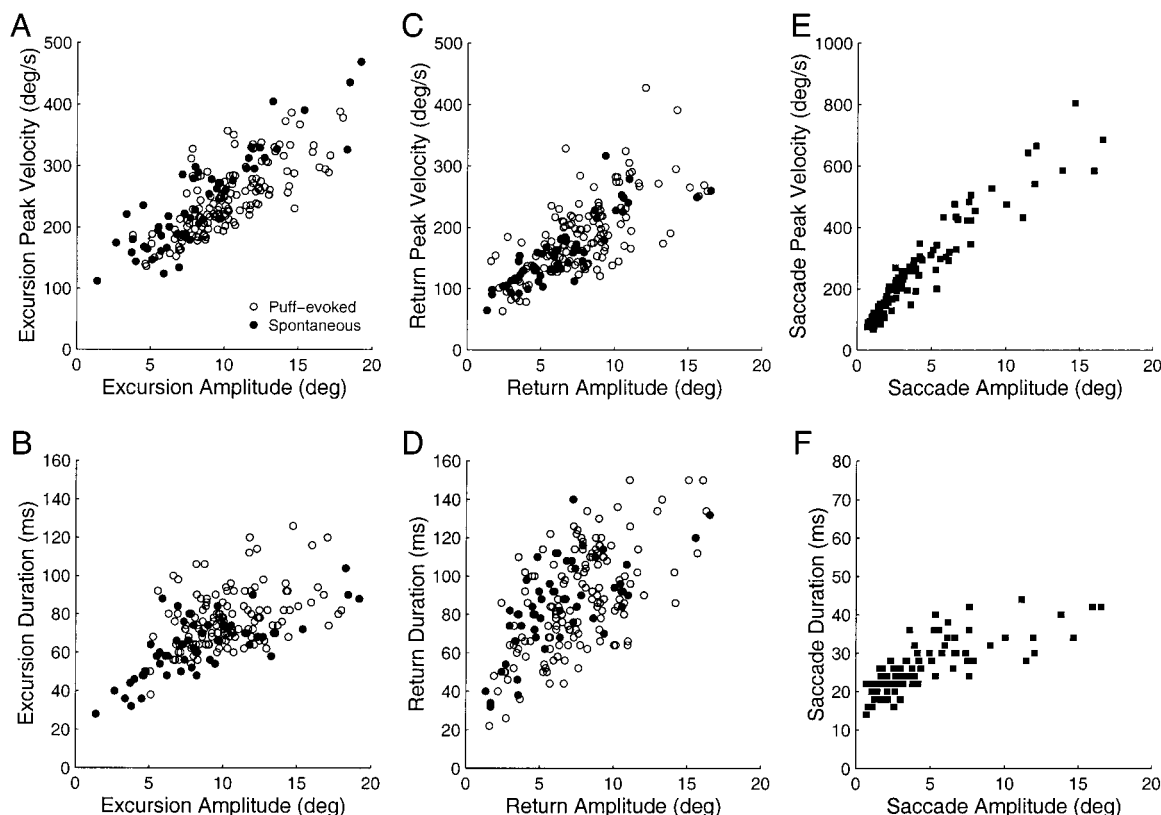


FIG. 10. Velocity-amplitude-duration relations of eye movements associated with spontaneous blinks (●), air-puff-evoked reflex blinks (○) and saccades (■). Pooled data from 8 sessions with *monkey PJ*. The animal was required to fixate straight-ahead. A and B: peak velocity and duration of (upward) blink-associated eye excursion movements as function of excursion amplitude. C and D: peak velocity and duration of (downward) blink-associated eye return movements as a function of return amplitude. E and F: peak velocity and duration of (downward) corrective saccades toward the central fixation spot after blink-associated eye movements. Note the differences in scale. Peak velocities and amplitudes were derived from $\dot{E}$ and E , respectively. Note that the data obtained under spontaneous and air-puff-evoked blinking conditions overlap considerably, the differences between excursion and return movements are relatively small, and saccades are much faster and shorter than blink-associated eye movements.

for saccades of different amplitude and closely resemble those of pure blink-associated eye movements measured in isolation. Alternatively, to reconstruct the putative independent saccade signal, the average blink-associated eye movement in response to air-puff stimulation alone was subtracted from perturbed saccades. In the case of linear superposition, the reconstructed eye movements should closely resemble the unperturbed control saccades, both in their trajectories and kinematics. Note

TABLE 1. Velocity-amplitude-duration relations of blink-associated eye movements

Subject	Excursion Phase	Return Phase	<i>n</i>
<i>ER</i>	$V_p = 14.7 \cdot R + 110$ (0.84)	$V_p = 14.4 \cdot R + 61$ (0.89)	111
	$D = 3.6 \cdot R + 50$ (0.70)	$D = 5.1 \cdot R + 38$ (0.86)	
<i>PJ</i>	$V_p = 15.1 \cdot R + 96$ (0.79)	$V_p = 14.4 \cdot R + 72$ (0.73)	198
	$D = 3.3 \cdot R + 41$ (0.60)	$D = 5.2 \cdot R + 49$ (0.61)	

Peak velocity (V_p ; in %s) and duration (D ; in ms) of blink-associated eye movements were described as a linear function of eye movement amplitude (R ; in deg), where separate equations were used for the excursion and return phase. Listed are the regression line equations, the corresponding correlation coefficients (r , between parentheses), and total number of responses (n) obtained from two monkeys (*ER* and *PJ*). The limited number of responses obtained from *monkey SA*, often lacking a clear return phase, did not allow for a reliable regression analysis. Data obtained under spontaneous and air-puff-evoked blinking conditions were pooled.

that the requirements should be met in both reconstructions if linear superposition is to be upheld.

Figure 11 shows illustrative examples of both analysis procedures. Figure 11, A and D, depicts a series of perturbed saccades toward two targets at different eccentricities (thin traces; $R = 20^\circ$ and $R = 9^\circ$, respectively). The mean control responses to these targets are also indicated (thick traces). Figure 11, B and E, shows the reconstructed movements (thin traces) that were obtained by subtracting control from perturbed saccades (data aligned with eye-movement onset). Shown are the 2-D difference trajectories as well as the eye-position (ΔH and ΔV) and eye-velocity ($\Delta \dot{E}$) difference signals as function of time (thin traces). For comparison, the average blink-associated eye movement (returning type; see Fig. 8A) in response to air-puff stimulation alone is superimposed (thick traces). Note that the reconstructed perturbations are not only different from the average blink-associated eye movement but also different for the two data sets (obtained in the same trial block). The latter is most evident from the 2-D trajectories. In both cases, the reconstructed trajectories formed approximately closed loops, which is indicative for full compensation, but the shape and orientation of these loops is clearly different. These features persisted when the perturbed and unperturbed responses were delayed with respect to each other rather than aligned to their onsets. Hence it appeared that blink-perturbed

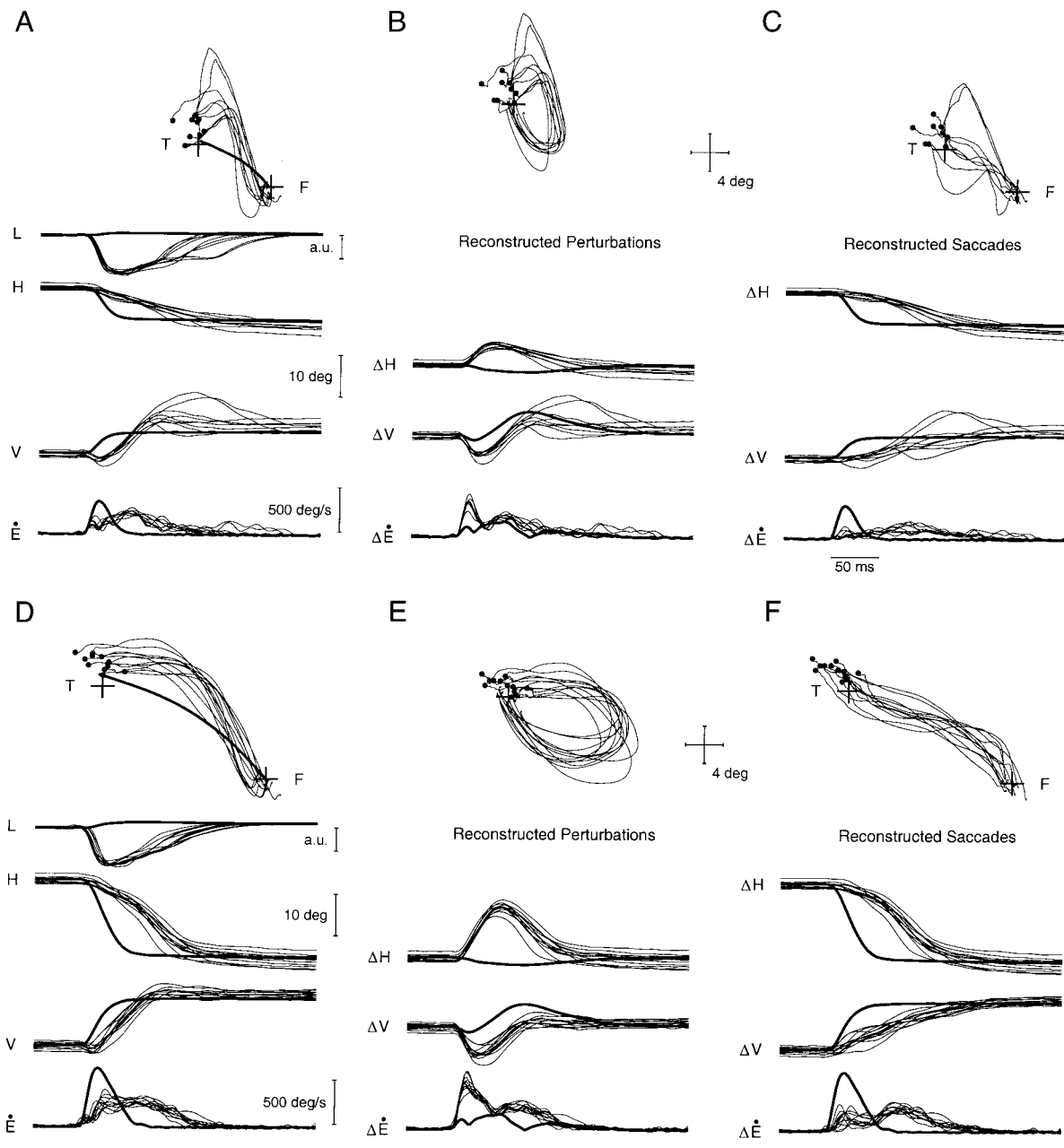


FIG. 11. Model-based analysis of blink-perturbed saccades. Data from *monkey ER*. **A**: individual perturbed responses (thin traces) toward a target flashed at $[R, \Phi] = [9, 150]$ deg with the mean control response (thick traces) superimposed. The 2-D saccade trajectories are shown at the *top*. Subsequent traces show eyelid (L) and eye position (H and V), as well as eye velocity ($\dot{E}$) as function of time. **B**: reconstructed perturbations obtained by subtracting the mean control saccade from each individual perturbed saccade. Thin traces show the resulting 2-D difference trajectories, the horizontal (ΔH) and vertical (ΔV) eye-position difference, and the eye-velocity difference ($\Delta \dot{E} = \sqrt{\Delta H^2 + \Delta V^2}$). Thick traces show the average eye movement associated with air-puff-evoked blinks (returning type; straight-ahead fixation). **C**: reconstructed saccades obtained by subtracting the average blink-associated eye movement from each individual perturbed response. Thin traces represent the resulting difference movements. Thick traces show the mean control saccade. **D–F**: similar data as in **A–C** but now for a series of saccades toward a target flashed at $[R, \Phi] = [20, 150]$ deg. Reconstructed perturbations yield closed-loop trajectories, indicating mid-flight compensation, but the shape and orientation of these counter-clockwise loops is different in **B** and **E**. Note also the discrepancy between the reconstructed perturbations and the measured blink-associated eye movements. Reconstructed saccades in **C** and **F** are quite different from the measured control saccades regarding their kinematics, but their 2-D trajectories are approximately straight, as is observed for measured control saccades.

eye movements could not be described by linear addition of an unperturbed saccade and a pure blink-associated eye movement. Figure 11, **C** and **F**, shows the alternative procedure, applied to the same data sets, in which the reconstructed

movements (thin traces) were obtained by subtracting the average blink-associated eye movement (returning type; see Fig. 8A) from the perturbed saccades (data aligned with eye-movement onset). For comparison, the mean unperturbed control

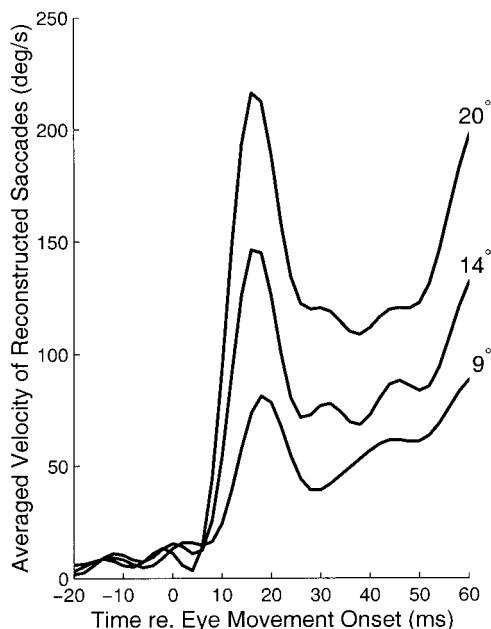


FIG. 12. Velocity profiles of reconstructed saccades derived from responses toward targets at 3 different eccentricities (9, 14, and 20°), averaged over a series of trials ($n > 20$). Data from *monkey ER*. Note that the delay between the eye-movement onset and the onset of the reconstructed saccades is ~ 6 ms. See Fig. 11 for the applied reconstruction procedure.

saccades are replotted in these panels (thick traces). As expected from the data in Fig. 11, *B* and *E*, the reconstructed saccades are clearly different from mean control saccade in that their position and velocity profiles are quite different for both data sets. Interestingly, however, it appeared that the reconstructed 2-D trajectories were more or less straight (albeit not for all responses toward the target at $[R, \Phi] = [9, 150]$ deg). Very similar results were obtained also for *monkey PJ*. For *monkey SA*, we obtained insufficient blink-associated eye movements of the returning type to compute a reliable average. Obviously, the reconstruction results in Fig. 11, *C* and *F*, were different when blink-associated eye movements of the truncated type (see Fig. 8*B*) were subtracted from the perturbed saccades.

Another feature that may be derived from the reconstruction data in Fig. 11, *C* and *F*, is that the delay between the eye-movement onset and the onset of the reconstructed saccades is very short. This is further detailed in Fig. 12, which shows the initial velocity profiles of reconstructed saccades that were derived from responses toward targets at three different eccentricities (9, 14, and 20°). To exclude mid-flight perturbed responses, data were averaged over a series of trials ($n > 20$) in which the onset of the contralateral blink lid movement preceded the eye-movement onset. Note that there is a rapid increase in velocity starting within the first 10 ms after eye-movement onset. Note also that the three traces already diverge after ~ 6 ms, indicating that even the early movements are part of the goal-directed response.

DISCUSSION

The data presented in this paper show, for the first time, various aspects of monkey saccadic behavior that are affected by trigeminal reflex blinks. In summary, air-puff-evoked blinks

had a strong influence on the latency as well as on the kinematics and spatial trajectories of visually evoked saccades. Near the onset of a blink, the ongoing movement direction of the eye was considerably modified, resulting in substantial deviations from the normal, approximately straight, saccade trajectory. These perturbed saccades often had a diminished peak velocity, and a two- to threefold increase in their duration was typically observed. Despite the strong disruptive nature of blinks, the animals could still generate quite accurate eye movements, as the perturbations were largely compensated. These compensations occurred in mid-flight, i.e., well before the eye movement ended, and did not rely on visual feedback since they were completed in total darkness.

In what follows, an attempt is made to identify the mechanisms that could underlie this complex oculomotor behavior. To that end, we will discuss the following issues: are the eye movements induced by blinks partly passive in nature (i.e., does the return phase of the blink-associated eye movements result from plant mechanics) or are they entirely due to a neural control signal and where in the neural circuitry do blink-related signals interfere with saccade generation? The latter point touches on the central concept in saccade models that a local feedback loop controls the saccade trajectory. It is also related to the question about the existence of a separate neural pathway generating blink-associated eye movements.

Direction of blink-associated eye rotations

There is some controversy in the literature about the direction of eye movements associated with blinks (see Evinger et al. 1984, for review). Measurements with search coils in human subjects (e.g., Collewyn 1985; Evinger et al. 1984; Goossens and Van Opstal, unpublished observations), and recently also in monkeys (Gnadt et al. 1997), have indicated that a transient downward and adductive rotation of the eye often accompanies blinks. In the experiments reported in the present paper, the largest eye excursions were typically upward and slightly abducting (Fig. 8). These results cannot be ascribed to an artifact of the double-magnetic induction technique (see METHODS) for the following reasons: first, this method allows for a wireless recording of eye orientation, preventing a potential obstruction of natural eye movements by wire leads in the orbit. Second, when blink-associated eye movements ended at an eccentric orbital position that was above the horizontal meridian, it was consistently observed that this eye position was maintained for a prolonged period of time until the animal generated a voluntary downward corrective saccade toward the fixation spot (Fig. 8*B*). Both features readily indicate that the preceding blink-associated eye movements were truly upward.

Note, however, that the actual eye-movement direction during blinks has been mentioned to depend on the initial eye position (e.g., Evinger 1995). Indeed, an eye-position dependence was also noticed (but not illustrated) by Gnadt et al. (1997) for their monkeys. Although not systematically investigated in the present study, we have qualitatively confirmed and illustrated such an eye-position effect on blink-associated eye movements in monkey (Fig. 9). Similar findings have been previously reported in cats (Gruart et al. 1993) and, more recently, also in humans (Bour et al. 1999). We therefore believe that differences in the actual "straight-ahead" eye position relative to the head (poorly specified in previous studies)

may better account for the apparent discrepancy in movement directions, than differences in recording techniques.

Latency coupling

The present experiments show that saccades and blinks are initiated almost simultaneously when an air-puff stimulus arrives just prior to an impending visual saccade (Fig. 1). A similar facilitation of saccade initiation by blinks has been previously observed in several clinical studies (Leigh et al. 1983; Zee et al. 1983), and also a reduction of head-movement latencies has been reported for healthy subjects (Evinger et al. 1994).

Although a short latency difference of ~ 6 ms between eye-movement onset and (putative) saccade onset emerged from our model-based analysis (Fig. 12), this apparent latency difference could be artificial. This may be understood by realizing that when saccade- and blink-related eye movements are superimposed (not necessarily linear), the net eye velocity will exceed the onset detection threshold (see METHODS) earlier for perturbed eye movements than for pure blink-associated eye movements. As a result, the subtraction method tends to overestimate the delay between eye-movement onset and saccade onset. The exact delay, however, is not readily deduced from the data. Presumably, it is < 6 ms, if not zero. Given these uncertainties, we believe it is parsimonious to consider the eye-movement onsets as the most reliable, model-free estimate of the actual saccade onsets (Fig. 1).

The tight latency coupling reported in this paper readily supports the idea also that the neural pathways that are involved in the initiation of saccades and blinks are tightly coupled. As reviewed in the INTRODUCTION, the OPNs are thought to embody this linkage. Several investigators have reported, for example, that the tonic activity of OPNs pauses during saccades as well as during blinks (Cohen and Henn 1972; Fuchs et al. 1991; Mays and Morrissey 1994). Thus when a blink is evoked just prior to a saccade, one would expect that the concomitant pause in OPN discharge results in the immediate initiation of the impending saccade due to the disinhibition of the saccadic burst generator.

Peripheral mechanisms?

Besides the clear modification of saccade latencies, blinking also had a substantial influence on the kinematics and on the spatial trajectories of visually evoked saccades (Fig. 2). A near-complete compensation for these saccade perturbations ensured, however, that the eye still landed close to the extinguished target (Figs. 2 and 4). Evinger and Manning (1993) reported that, except for the superior oblique, all extraocular muscles of the rabbit are coactivated during blinks. Since such activation pattern is not observed during other types of oculomotor behavior, they proposed that rabbit OMNs receive a blink-related input that is independent of their eye-movement inputs. Thus one could suspect that the eye-movement responses obtained in the present study resulted merely from a addition of independent blink-related and saccade-related motor commands at the motoneuron level.

To test for this simple hypothesis, we have performed the analysis outlined in Fig. 11. Under the implicit assumptions that the blink-associated eye movement and the saccade start

approximately simultaneously and that the mechanical properties of the oculomotor plant remain unaltered during saccade-blink responses, the conclusion of this analysis is that a simple linear addition of two independent motor commands cannot account for the observed behavior. Similar findings were recently reported for horizontal saccades in humans (Rottach et al. 1998). The first assumption is readily supported by the data in Fig. 12 that indicate a latency difference of ~ 6 ms, or less, between the eye-movement onset and the saccade onset.

The second assumption, however, merits some additional comments. In the event of extraocular muscle cocontraction, a concomitant change in the mechanical properties of the plant (as an increase of the overall plant stiffness) is also expected. It is interesting to consider the consequences of such a change. It is generally accepted that the brain stem saccade generator is organized in such a way that, under normal conditions, the pulse and step signals on the oculomotoneurons exactly cancel the plant dynamics. In other words, the overall transfer function of the brain stem-plant system equals unity. As a result, a burst signal proportional to eye velocity will yield a normometric saccade (i.e., neither undershoots nor overshoots; see Fig. 13, *bottom right*).

Suppose that the plant stiffness transiently increases because of a blink-related cocontraction, say from k to k' . The plant time constant is then consequently lowered to $T' = r/k'$ (with r the plant viscosity). The overall transfer function of the brain stem-plant system is then given by

$$H'(s) = \frac{k \cdot (1 + s \cdot T)}{k' \cdot (1 + s \cdot T')}$$

(with s the complex Laplace frequency, $s = j\omega$). Note that the gain of the brain stem-plant transfer would then always be lower than one. Only for very high frequencies does the gain approach unity. As a result, the saccadic system, when unaware of the new condition of the plant, will generate a movement that initially approaches the normometric amplitude of the control situation but then rapidly drifts back (with time constant T') to an eye position away from the target (Fig. 13, *top right*). The final amplitude, determined by the DC gain of the transfer function is given by $k/k' < 1$.

Clearly, this effect cannot be “repaired” by a simple gain modulation at the level of the brain stem burst generator. Thus under the increased stiffness condition, the eye is expected to systematically *undershoot* the target by a relative fraction that is given by $T'/T = k/k'$. The data indicate, however, that the actually observed undershoots were typically small (see e.g., Figs. 2 and 4) and hardly dependent on the saccade amplitude (Fig. 6). We conclude therefore that the increase in plant stiffness, if present, is probably limited to a few percent. Consequently, the saccadic system may assume that under blinking conditions the plant has not changed and that the internal brainstem model of the plant need not be updated dynamically.

Separate blink-related oculomotor signals?

One may then wonder about the nature of the signals that underlie the complex eye-movement trajectories. An important first question is whether the eye movements associated with blinks actually result from *separate* blink-related inputs to the OMNs.

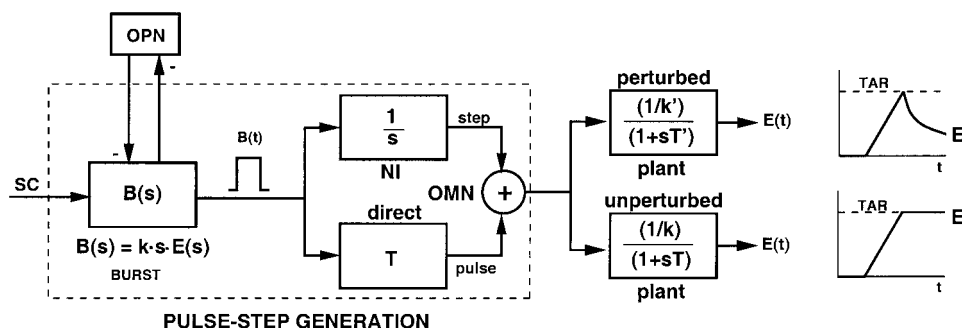


FIG. 13. Brain stem pulse-step saccade generator. Two simple plant models are incorporated (indicated by first-order low-pass filters in Laplace notation). The unperturbed plant (*bottom right*) is driven by neural control signals that are exactly matched to its properties and produces normometric saccades. The plant with increased stiffness, K' , represents the plant properties under the condition of extraocular muscle cocontraction (*top right*). If such cocontraction results from an independent blink pathway acting on the extraocular motoneurons (OMN), the pulse-step saccade controller remains unaware of this mechanical change. The resulting saccades then initially reach the target (TAR) but rapidly drift back to a position away from the target (see DISCUSSION, for further explanation). SC, superior colliculus; OPN, omnipause neurons; $B(s)$, Laplace notation of burst-cell activity; $B(t)$, simplified velocity pulse from the burst cells (BURST); "direct," scaled velocity signal from burst cells; NI, neural eye-position integrator. T and T' , time constant of unperturbed and perturbed plant, respectively; k and k' , stiffness of unperturbed and perturbed plant; $E(t)$, eye position as a function of time.

In cats and rabbits, trigeminal terminals on abducens motoneurons have been described (Baker et al. 1980; Cegavske et al. 1997). Similar findings have been reported regarding visual inputs involved in flash-evoked reflex blinks (Holstege et al. 1986). It appears, however, that only a limited percentage (10–15%) of cat abducens motoneurons exhibit a burst discharge after air-puff, supraorbital nerve, and flash stimulation and that this fairly weak burst of activity lags the onset of orbicularis oculi motoneuron activity 10 ms (Delgado-García et al. 1990; Trigo et al. 1999). In rabbits, the activation of extraocular muscles also lagged the onset of orbicularis oculi muscle activity, leading Evinger and Manning (1993) to suggest that extraocular motoneurons and facial motoneurons receive different afferent inputs. According to these investigators, the most likely source of blink-related input to rabbit OMNs could be the supraoculomotor region.

To our knowledge, it is still unknown whether such blink-related inputs to the OMNs exist in monkey. Unlike many other animals, primates do not have a retractor bulbi muscle, which, for example, in cat and rabbit, pulls the eye back into the orbit during blinks. Instead monkeys only have a small accessory lateral rectus muscle, which presumably evolved from the retractor bulbi system (Spencer et al. 1981). Because of these species-specific differences, the existence of separate blink-related inputs in primates is not clear.

In cat, it has been found that *lid* movements during spontaneous, flash-, tone-, and air-puff-evoked blinks exhibit different kinematics, suggesting a distinct elaboration in their respective sensory pathways (Domingo et al. 1997). Our present data, on the other hand, show that the kinematics of eye movements associated with spontaneous and air-puff-evoked blinks overlapped considerably (Fig. 10). This suggests that in monkey, these two types of eye movements are generated by a common pathway, rather than by blink-related signals of different origin converging onto the OMNs. We also noticed that blink-associated eye movements were often "truncated," yielding a substantial net eye rotation. Such responses were not followed by eye-position drift but rather by a corrective saccade (Fig. 8B). Similar results have been reported also by Takagi et al. (1992) for human subjects. These features are

difficult to reconcile with the idea that separate blink-related signals would act directly on the OMNs. In that case, one would expect that the return phase of blink-associated eye movements are merely a secondary, passive effect of cocontraction of the extraocular muscles. Yet the kinematics of the return movements further demonstrate that they too are under neural control (Fig. 10).

Whether or not separate blink-related signals act directly on the OMNs remains difficult to decide on the basis of behavioral data only. Yet the present results clearly show that such a signal does not simply add to a normal saccade. Moreover, subtraction of pure blink-associated eye movements from perturbed saccades yielded saccade reconstructions with altered kinematics compared with control saccades (Fig. 11, C and F). We conclude therefore that the blink system interferes to a considerable degree with the process of saccade generation at a premotor level that is upstream from the extraocular motoneurons.

Premotor interactions

Several findings in the present study support the idea that the eye movements associated with blinks could result from interactions within the oculomotor system itself:

First, we noticed that the initial change in eye position during blink-perturbed saccades was immediately followed by a reacceleration of the eye toward the target location. This reacceleration usually occurred in a direction quite different from the overall direction of the control saccade (see Figs. 2, thick trace, and 3 for illustrative examples). This adequate adjustment of the movement direction strongly suggests that the compensatory responses were based on accurate information about the actual changes in eye position. When it is assumed that these changes in eye position were due to a transient blink-related signal acting downstream from the local feedback loop of the saccadic system (e.g., at the OMNs), such compensatory behavior is not readily expected.

Second, both the metrics and kinematics of blink-associated eye movements (Figs. 8 and 10) indicate that these movements are entirely under neural control rather than that the return

phase results merely from passive elastic restoring forces within the oculomotor plant. In particular, the absence of an eye-position dependent drift after a truncated blink-associated eye movement (Fig. 8B) strongly suggests that the neural eye-position integrator, which subserves the generation of the step component of saccades (see e.g., Fig. 13), is involved. The latter would occur, for instance, when blink-associated eye movements would result from direct activation of the saccadic burst cells (since these cells provide direct input to the integrator) rather than from independent excitation of OMNs by a separate blink-related signal. Cohen and Henn (1972) indeed reported that a subset of saccadic burst neurons in the monkey paramedian pontine reticular formation (PPRF), which are recruited for rapid horizontal eye movements, also discharge during spontaneous blinks, irrespective of whether the associated eye movements are horizontal. Interestingly, a blink-related excitation of saccadic burst cells, in combination with OPN inhibition, would also provide an explanation for the occurrence of blink-induced saccadic oscillations (Hain et al. 1986).

Finally, blinks induced considerable changes in the saccade kinematics (Fig. 6), even after subtraction of pure blink-associated eye movements (Fig. 11, C and F). Several investigators (e.g., Becker 1993; Zee et al. 1983) have suggested that such changes might arise from an indirect influence of blinking on the saccadic burst generator through a modulation of the OPN discharge. The present results are indeed consistent with the idea that blinking affects the OPNs but, as discussed in the preceding text, the observed latency coupling between saccades and blinks can best be explained by an *inhibition* of the tonic OPN discharge. By contrast, to account for the measured reduction in saccade velocity (Fig. 6) by means of an OPN mechanism, one would have to assume an *excitation* of the OPNs. Since recording studies also indicate that the OPNs pause during blinks (Cohen and Henn 1972; Fuchs et al. 1991; Mays and Morrisette 1994), we propose that a change in OPN discharge does not underlie the changes in saccade kinematics observed in the present experiments. Possible effects due to cocontraction of the extraocular muscles cannot readily account for the changes in the saccade kinematics either (see preceding discussion).

Apart from the OPNs, the intermediate and deep layers of the SC also provide major input to the brain stem saccade generator (see e.g., Moschovakis and Highstein 1994; Sparks and Hartwich-Young 1989 for review). As was outlined in the INTRODUCTION, recent studies indicate that the midbrain SC is involved in the interactions between saccades and blinks (Basso and Evinger 1996; Basso et al. 1996; Gnadt et al. 1997). It is therefore conceivable that the observed changes in saccade kinematics may originate, at least partly, from changes in SC activity. Experimental support for this possibility will be provided in detail in the companion paper (Goossens and Van Opstal 2000), which describes the activity patterns of saccade-related neurons in the SC during blink-perturbed saccades.

Accuracy of error compensation

In a minority of trials, typically no more than 15%, no compensation for the disturbance occurred (Fig. 4). It is difficult to provide a convincing explanation for these cases only on the basis of behavioral data. Possibly, the response was pre-

maturely aborted in these trials (e.g., like blinks in the fixation paradigm; see Fig. 8B) due to processes that also abolished the initial saccade program. Neurophysiological evidence for this hypothesis will be provided in the companion paper (Goossens and Van Opstal 2000). In the majority of severely perturbed responses, however, a near-complete compensation for the saccade disturbance ensured that the eye landed close to the extinguished target (Figs. 2–4). The accuracy of the error corrections did not depend much on saccade amplitude (Fig. 6), although a slight dependence of final accuracy on saccade direction was observed (Fig. 7). We have no simple explanation for the latter phenomenon.

It is important to realize that all movements were executed under entirely open-loop conditions, i.e., in the absence of any visual feedback. In the previous sections, we have argued that the full sequence of movement events in the perturbation trials may be due to neural control rather than to plant mechanics and that the neural signals interact at premotor stages within the saccadic system. If true, the present compensation data provide strong additional support for the existence of a local feedback loop that is thought to control the instantaneous saccade trajectory.

Previous saccade-interruption paradigms [intrasaccadic stimulation of either the OPNs (Keller and Edelman 1994) or of the rostral SC (Munoz et al. 1996)] have so far only *halted* the saccade in mid-flight without disrupting the movement *direction*. In addition, electrical microstimulation may inadvertently excite adjacent oculomotor pathways (running both upstream and downstream), which makes the interpretation of stimulation data less obvious than at first glance. Indeed, OPN stimulation also transiently stops the saccade-related burst in the intermediate layers of the SC, possibly through a retrograde activation of rostral SC cells (Keller and Edelman 1994).

In contrast to electrical microstimulation, the blink-perturbation paradigm leads to a natural, noninvasive disturbance of the 2-D saccade trajectory as well as to considerable changes in both saccade kinematics and timing. The paradigm consistently affects all three major stages believed to underlie the saccade: the programming of the movement vector, the initiation of the saccade, and its actual execution. Although the interpretation of the results in terms of local feedback mechanisms is far from trivial and still not settled (see discussion in previous sections), we believe that this paradigm may provide a valuable tool to further investigate this issue.

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