

Effects of Voluntary Blinks on Saccades, Vergence Eye Movements, and Saccade-Vergence Interactions in Humans

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Rambold, H., A. Sprenger, and C. Helmchen. Effects of voluntary blinks on saccades, vergence eye movements and saccade-vergence interactions in humans. *J Neurophysiol* 88: 1220–1233, 2002; 10.1152/jn.00937.2001. Blinks are known to change the kinematic properties of horizontal saccades, probably by influencing the saccadic premotor circuit. The neuronal basis of this effect could be explained by changes in the activity of omnipause neurons in the nucleus raphe interpositus or in the saccade-related burst neurons of the superior colliculus. Omnipause neurons cease discharge during both saccades and vergence movements. Because eyelid blinks can influence both sets of neurons, we hypothesized that blinks would influence the kinematic parameters of saccades in all directions, vergence, and saccade-vergence interactions. To test this hypothesis, we investigated binocular eye and lid movements in five normal healthy subjects with the magnetic search coil technique. The subjects performed conjugate horizontal and vertical saccades from gaze straight ahead to targets at 20° up, down, right, or left while either attempting not to blink or voluntarily blinking. While following the same blink instruction, subjects made horizontal vergence eye movements of 7° and combined saccade-vergence movements with a version amplitude of 20°. The movements were performed back and forth from two targets simultaneously presented nearby (38 cm) and more distant (145 cm). Small vertical saccades accompanied most vergence movements. These results show that blinks change the kinematics (saccade duration, peak velocity, peak acceleration, peak deceleration) of not only horizontal but also of vertical saccades, of horizontal vergence eye movements, and of combined saccade-vergence eye movements. Peak velocity, acceleration, and deceleration of eye movements were decreased on the average by 30%, and their duration increased by 43% on the average when they were accompanied by blinks. The blink effect was time dependent with respect to saccade and vergence onset: the greatest effect occurred 100 ms prior to saccade onset, whereas there was no effect when the blink started after saccade onset. The effects of blinks on saccades and vergence, which are tightly coupled to latency, support the hypothesis that blinks cause profound spatiotemporal perturbations of the eye movements by interfering with the normal saccade/vergence premotor circuits. However, the measured effect may to a certain degree but not exclusively be explained by mechanical interference.

INTRODUCTION

Eye movements can be associated with eyelid blinks. Blinks can occur spontaneously, reflexively, or voluntarily (Guitton et al. 1991; Manning and Evinger 1986). Little is known about their influence on the neural control of conjugate saccades,

vergence, and combined saccade-vergence eye movements in humans.

A few lines of evidence indicate that blinks influence horizontal saccades in humans (Rottach et al. 1998) and vertical and horizontal saccades in monkeys (Goossens and van Opstal 2000a). For example, blinks reduce horizontal saccade velocity and increase their duration (Rottach et al. 1998). There is some evidence that vergence movements are facilitated by blinks (Peli and McCormack 1986). This blink influence has been explained by blink-induced changes in the neuronal oculomotor circuits in the brain stem (Goossens and van Opstal 2000a,b; Rottach et al. 1998).

Medium-lead burst neurons of the paramedian pontine reticular formation (PPRF) and rostral interstitial nucleus of the medial longitudinal fascicle (riMLF) provide the premotor saccadic command to the ocular motoneurons (Hepp et al. 1989). Vergence burst neurons in the midbrain provide the premotor vergence signals to the ocular motor command (Mays and Gamlin 1995). Several lines of evidence indicate that omnipause neurons (OPNs) in the nucleus raphe interpositus (rip) (Büttner-Ennever and Büttner 1988) control both saccadic and vergence burst neurons (Mays and Gamlin 1995; Zee et al. 1992). OPNs discharge spontaneously and cease firing during saccades and fast vergence eye movements (Hepp et al. 1989; Mays and Gamlin 1995). The OPNs in turn may be influenced by the neurons of the intermediate layers of the superior colliculus (SC). The intermediate layer of the SC projects to the raphe complex where OPNs have been reported (Büttner-Ennever and Horn 1995; Büttner-Ennever et al. 1997). Antidromic stimulation experiments have shown that fixation and build up cells of the SC project to or through the OPN region (Ghandi and Keller 1997).

Blinks decrease the neuronal activity during saccades in medium-lead burst neurons of the PPRF (Mays and Morisse 1995a), in OPNs (Hepp et al. 1989; Mays and Morisse 1993) and in saccade-related long-lead burst neurons in the intermediate layer of the SC (Goossens and van Opstal 2000b).

Thus because both OPN activity and SC long-lead burst neuron activity are decreased by blinks, it is possible that blinks influence the central premotor circuit of not only saccades (Rottach et al. 1998), but also vergence, and saccade-vergence interaction. In contrast, the eye-movement kinematics may be changed by mechanical interference of blink-induced

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eye movements on the one hand and saccadic, vergence, or combined saccade-vergence eye movements on the other hand.

Therefore we tested the hypotheses that blink-induced changes of horizontal saccades in humans (Rottach et al. 1998) also apply to vertical saccades, to vergence, and to saccade vergence interactions and that the effect is mainly caused by interference on the neuronal premotor level and not mechanically.

We used voluntarily elicited blinks because of their larger amplitude when compared with reflexive blinks (Manning and Evinger 1986) and to compare our data with a previous related study (Rottach et al. 1998). Preliminary data have previously been published in abstract form (Rambold et al. 2001).

METHODS

Subjects

Recordings were obtained from both eyes of five healthy subjects (4 males, 1 female), aged 28–40 yr. None of the subjects had manifest or latent strabismus and all had normal vision. One subject had a myopia of -1 diopter (dpt) and -1.5 dpt (HR), the others normal vision. The oculomotor tasks were performed without corrective spectacles or contact lens.

Recording technique

Binocular eye and lid movements were recorded with the Rempel search-coil system (Rempel Labs), which has three orthogonal magnetic fields and a frame size of 180-cm cube.

After the subjects had given their informed consent, scleral search coils (standard annulus, Skalar, Delft, The Netherlands) were placed in each eye under topical anesthesia. The two eyes and the right eyelid were calibrated using a combined off-line in vitro and in vivo calibration based on previous studies (Eggert et al. 1999; Tweed and Vilis 1987). The in vitro calibration was used to calculate the gain ratios and the offsets of the three magnetic fields for each coil independently. In vivo calibration was used to adjust the measured data to gaze straight ahead. Lid movements of the right eye were recorded with a modified technique as described elsewhere (Guitton et al. 1991; Rottach et al. 1998). A 3-mm-diam coil of 0.3-mm isolated copper wire (14 loops) was attached to the eyelid close to the upper eyelash, in the center near the lid margin by means of a double adhesive tape. The coil weighted less than 1 mg, and thus its weight was negligible (Guitton et al. 1991). Lid coil calibration was performed in the same way as the eye coils.

Experimental setup

The subject's head was comfortably stabilized in a natural upright position with a chin rest and the forehead was kept stationary by a firm head support. Eye and lid movements were recorded unfiltered with a 12-bit AD converter (NI PCI 6071E) at a sampling rate of 500 Hz. The noise on the eye position was 3 ArcMin, on the lid position 2% of the maximal amplitude. After calibration all position data were filtered by using a 100 Hz (3-dB value) Gaussian filter (MATLAB, The MathWorks, Natick MA).

For visual stimulation a red laser spot (spot diameter: 0.1° , 635 nm, LISA laser products OHG, Katlenberg, Germany) was front projected onto a flat white tangent screen that was 145 cm from the subject's eyes in dimly lit surroundings. The laser was moved with mirror-galvanometers (GSI Lumonics, Unterschleissheim, Germany), and precise timing was controlled by a PC. In addition, a red light-emitting diode (LED) was mounted 35–38 cm in front of the subject and exactly in between the eyes during gaze straight ahead.

Experimental paradigms

FOUR DIFFERENT PARADIGMS WERE PERFORMED BY THE SUBJECTS. *Paradigm 1*: blinks at stationary eye positions. To analyze blink-induced eye movements at stationary eye positions, voluntary blinks were performed during gaze straight ahead for 10 s.

Paradigm 2: blinks and saccades. To elicit conjugate saccadic eye movements, a laser target with 20° horizontal or vertical (right, left, up, down) eccentricity was presented on the tangent screen simultaneously with the target during gaze straight ahead (Collewijn et al. 1995; Rottach et al. 1998). The subjects were instructed to perform self paced saccades between these two targets at ~ 1 Hz. Subjects were asked to make voluntary blinks in $\sim 50\%$ of all saccades. Target pairs were presented for 10 s, and the task was repeated three times. We did not use an isovergence screen. The induced change in vergence was $\sim 0.2^\circ$ in a 20° saccade.

Paradigm 3: blinks and vergence. To elicit vergence movements, we used a paradigm described by Collewijn et al. (1995). A LED centered between the eyes at a distance of 35–38 cm and a laser target during gaze straight ahead at a distance of 145 cm distance were horizontally and vertically aligned so that the laser target was slightly elevated ($\sim 1^\circ$) over the LED. This elevated position was used to avoid ambiguous vergence eye movements (Collewijn et al. 1995). The LED distance between the subjects was variable (35–38 cm) to achieve a change in vergence amplitude of $\sim 7^\circ$. Both the LED and the laser target at a distance of 145 cm were presented simultaneously for 30 s, and the subjects performed vergence eye movements between the laser target and the LED at a frequency of approximately 1 Hz. The subject's task was to make voluntary blinks in about half of all vergence eye movements. The paradigm was repeated three times with short intervals of 1 min. This paradigm was performed at the beginning of the session. The total number of vergence movements was restricted to 80 to avoid the effects of repetitive stimulation on vergence performance (Yuan and Semmlow 2000).

Paradigm 4: blinks and saccade/vergence. Combined saccade-vergence movements were elicited by presenting eccentric laser targets at a distance of 145 cm as described in *paradigm 1* and the centered LED at a distance of 35–38 cm from the subject as in *paradigm 2*. The laser targets at different eccentricities (20° horizontally and vertically) and the LED as a target for gaze straight ahead were presented simultaneously. Subjects performed eye movements between the LED and the eccentric targets at ~ 1 Hz. Voluntary blinks were introduced in $\sim 50\%$ of the eye movements. The target pairs were presented for 10 s, and the task was repeated three times.

Analysis

Data were transformed into two-dimensional gaze vectors in degrees. Positive values were defined as upward and rightward directions. Eye movements were separated in horizontal and vertical conjugate (version) and horizontal disjunctive (vergence) components. The horizontal vergence component was calculated as left minus right horizontal eye position, the version components as the average of right and left eye positions (Collewijn et al. 1995). Data were not corrected for infinity. A vergence angle of 0° was equal to a distance of 145 cm from the subject's eyes.

Saccades were detected by a semiautomatic detection program (MATLAB, The MathWorks) that measured velocity and acceleration criteria. The saccade begin and end of the version component was detected at the level of 5% of the saccade peak velocity.

Vergence begin and end were detected semiautomatically by using a velocity cutoff level of $10^\circ/\text{s}$. The saccade detection criteria were not used because they failed due to additional superimposed blink-induced convergence-divergence in the blink condition (see Fig. 5). All horizontal asymmetric, incomplete, or ambiguous vergence responses (right vs. left eye) were excluded from the analysis.

Lid movements were normalized for calculation (1: complete lid

closure, 0: lid open at gaze straight ahead). Blinks were detected semiautomatically. Blink begin was detected at the cutoff level of 2 SD above baseline (Rottach et al. 1998). Blinks could be distinguished from eye-movement-associated lid movements by the biphasic asymmetric velocity shape (Guitton et al. 1991). Spontaneous blinks were in general slower than voluntary blinks (Evinger et al. 1991), and they often showed an interruption in velocity between lid opening and closing (Guitton et al. 1991). To exclude most of the spontaneous and reflexive blinks, all slow ($<60\%$ of the mean peak velocity) or extremely long blinks (>500 ms) were excluded. Despite this filter, spontaneous blinks could not be completely excluded. In addition, all double blinks (2nd blink before the end of the 1st blinks) or blinks in rapid sequence (interval of <50 ms between the blinks) were excluded. Only blinks with an amplitude of $\geq 50\%$ of total lid closure were further analyzed.

Eye movements were sorted according to their direction, vergence components (convergence, divergence), and blink occurrence (200 ms before eye movement to end of the eye movement). The following parameters were extracted from the eye movements for the version component separately: eye movement duration, amplitude, peak velocity, peak acceleration, and peak deceleration. The latency of blink onset to saccade (vergence) onset was calculated by blink onset minus saccade onset. Positive values indicate occurrence of the blink after, negative before saccade onset.

Vergence peak velocity was analyzed in two intervals: from blink begin until 70% of blink duration and from the time after 70% of total blink duration for 200 ms. These intervals were used to analyze the effect of blink-induced eye movements, which lasted about 60% of the blink duration. This was independent of the late blink effect on vergence (see RESULTS and Fig. 5).

Saccade-vergence interaction was analyzed for the version and vergence components separately. Begin and end of the eye movement was determined by the saccadic component. The vergence component of saccade-vergence interaction was not divided into a phases 1 and 2 as in vergence because the eye movement sequence was not that clear defined. Hence the mean vergence velocity over the time of the version component was calculated as change in position to change in time.

Statistics of all parameters were calculate with the Mann-Whitney *U* test and ANOVA-test (STATISTICA, StatSoft); *P* values of <0.05 were considered statistically significant.

RESULTS

All five subjects were examined for each of the four paradigms (methods): three subjects were recorded twice to acquire sufficient data. For *paradigms* 2 and 4 ≥ 100 saccades were required, for *paradigm* 3, a minimum of 40 to a maximum of 80 vergence eye movements.

Data are presented in the following sequence according to the paradigms (1–4): effect of blinks on fixations at stationary eye positions (1), conjugate saccades (2), vergence (3), and saccade-vergence interaction (4).

Properties of blink-induced eye movements during fixation

Blinks at stationary eye positions induced horizontal and vertical eye movements. Both eyes moved downward and toward the nose in all five subjects. Vertical eye movement amplitudes during blinks were on the average $2.1 \pm 1.0^\circ$. Horizontal version components were significantly smaller ($0.6 \pm 0.4^\circ$). The vergence amplitudes (on the average $2.7 \pm 1.1^\circ$) in the subjects ranged from 0.8 to 3.4° . There was a considerable variability in the blink-induced eye movements in all individuals (Fig. 1).

Blink duration generally outlasted the blink-induced eye movements. The duration of the blink-induced eye movements (190 ± 35 ms) was always shorter than the blinks (339 ± 100 ms). Thus blink duration exceeded the blink-induced eye movements by 140 ± 84 ms. Blink-induced eye movements started shortly before or with the blink onset. On the average, blink-induced eye movements ceased after $61 \pm 2\%$ of the blink duration.

Properties of conjugate horizontal and vertical saccades during blinks

We found similar blink effects on vertical saccades as has been described for horizontal saccades (Rottach et al. 1998). No significant change was observed in the mean amplitude of saccades in all subjects, when saccades in the blink (horizontal:

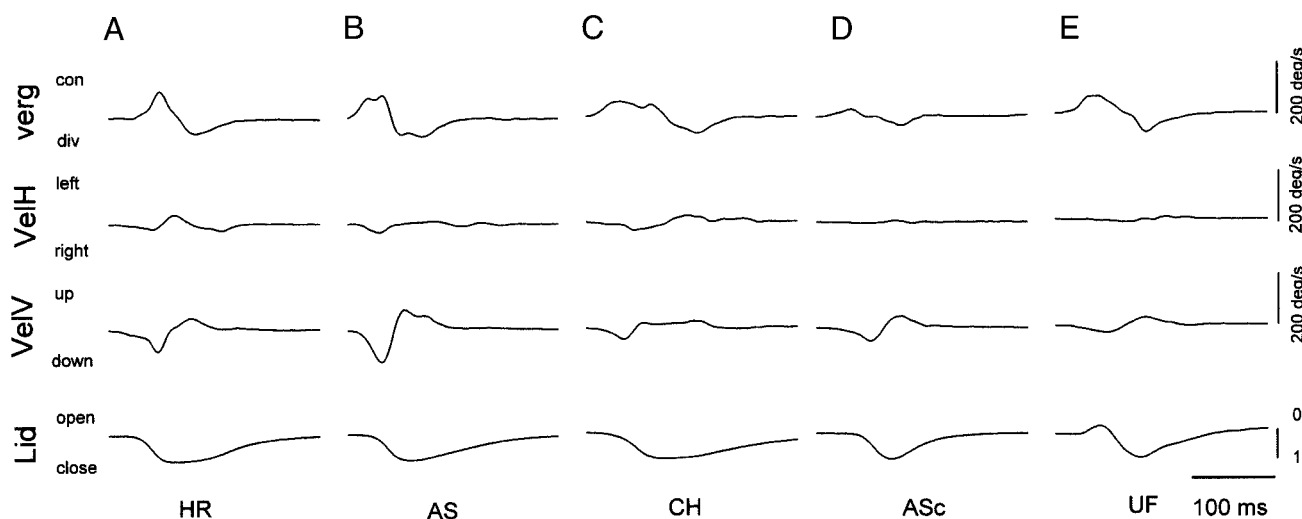


FIG. 1. Effect of blinks on the eyes at gaze straight ahead. Mean eye vergence (1st line), horizontal (2nd line), and vertical (3rd line) version velocity as well as eye lid position (4th line) are aligned to blink onset and averaged (5 blinks) for all subjects separately (A–E). Note that the blink duration exceeds the eye movement duration (verg: vergence velocity; VelH: horizontal version velocity; VelV: vertical version velocity; Lid: relative lid position). The initials of the subjects are shown below the figure.

18.3 \pm 0.9°, vertical: 19.2 \pm 1.3°) and no-blink conditions (horizontal: 18.6 \pm 1.8°, vertical: 18.8 \pm 1.3°) were compared. Blink-associated saccades showed a significant reduction in peak eye velocity (horizontal: from 418.3 \pm 43.9 to 271.0 \pm 63.4°/s, vertical: from 393.8 \pm 47.8 to 256.7 \pm 39.0°/s) and a prolonged duration (horizontal: from 66.0 \pm 5.8 to 116.8 \pm 20.8 ms, vertical: from 82.2 \pm 11.3 to 140.6 \pm 26.2 ms), for the blink (—, Fig. 2) compared with the no-blink condition (\cdots , Fig. 2, A3 and B3). The blink duration (350 \pm 97 ms) in all subjects was longer than saccade duration (horizontal: 116.8 \pm 20.8 ms, vertical: 140.6 \pm 26.2 ms). The detailed analysis of various dynamic parameters (saccade duration, peak velocity, peak acceleration, peak deceleration) is shown in Fig. 3, A–D, for each subject separately.

Four of five subjects showed with horizontal saccades a dynamic saccadic overshoot under the blink condition, which was $<0.5^\circ$. These overshoots occurred in only 10–30% of the saccades per subject. In the case of dynamic overshoot under the blink condition, there was minor or even no reduction in peak velocity. These were preferably induced by blinks starting at the saccade end. The vertical eye movement component during horizontal saccades showed an up-down movement and a convergence-divergence eye movement as during blinks while fixating a stationary target. During vertical saccades, there was a horizontal convergence-divergence eye movement during the initial phase of the blink.

As a new finding, the blink-associated effects on the saccade parameters depended on the temporal relation between blink

onset and saccade onset (latency; Fig. 4). This effect of latency was seen in all saccade parameters in all five subjects (Fig. 4 B), and the effect did not depend on saccade direction. Hence the data for all directions were analyzed together. Figure 4A shows this latency effect for one parameter (peak saccade acceleration; *subject HR*). Blink onset ≤ 150 ms before saccade onset decreased saccade acceleration $\leq 50\%$. The maximum of the effect was ~ 120 ms before saccade onset in this example. The range over all subjects was 150–90 ms (Fig. 4B). Generally, the shorter the latency, the smaller the blink effect on saccade acceleration, deceleration, peak velocity, and saccade duration. The blink effect on the saccade decreased and then disappeared at saccade onset. In three subjects, blinks had no influence on the saccade if they occurred during or after the saccade onset. Only in two subjects there was a small but not significant effect found on peak acceleration and peak velocity when the blink occurred ≤ 20 ms after the saccade onset. It is important to note that the mean blink duration was 339 \pm 66 ms for the example in Fig. 4A, i.e., the end of the blink occurred after the saccade.

Properties of horizontal vergence without blinks

The amplitude of vergence response was on the average 6.8 \pm 0.5°. All subjects performed symmetric vergence responses on both eyes. Generally, all subjects tended to make more small horizontal saccades during divergence than during convergence eye movements. Only one of five subjects showed

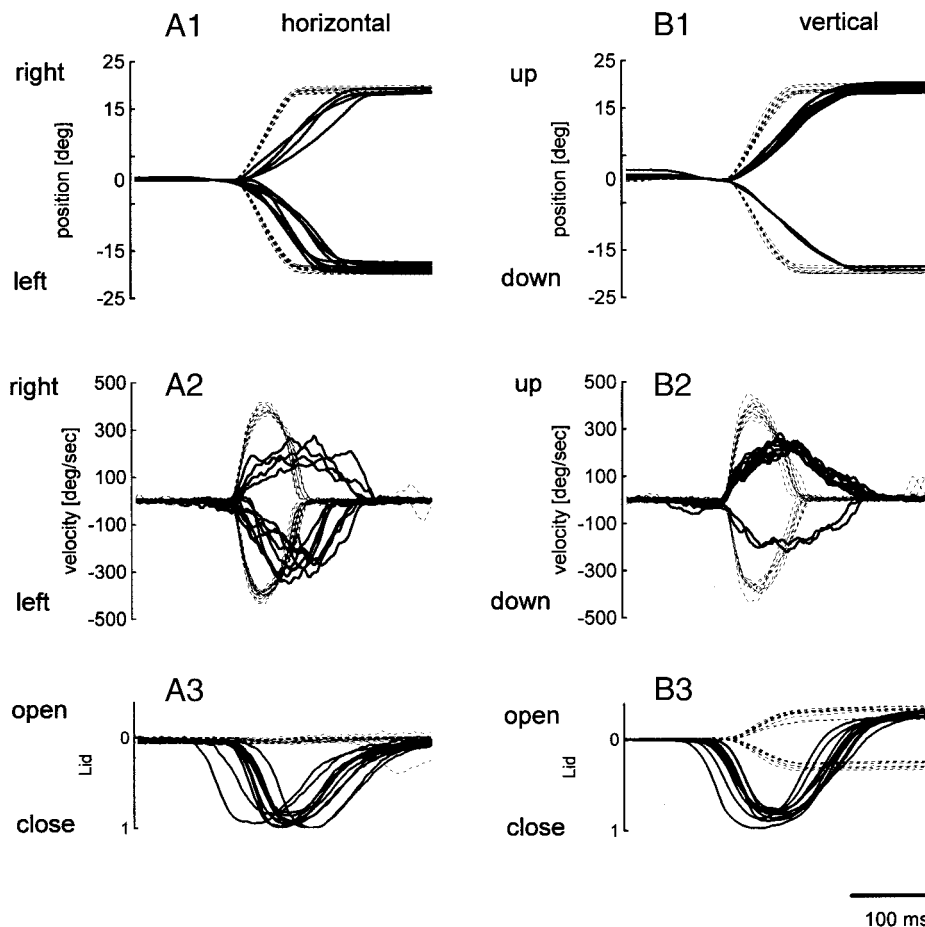


FIG. 2. Effects of blinks on conjugate saccades: original recordings. Traces for *subject AS* are aligned with respect to saccade begin. Horizontal (A) and vertical (B) saccades are displayed separately as eye position (A1 and B1), eye velocity (A2 and B2), and lid position (A3 and B3). Under the blink condition (—) in contrast to the control condition (\cdots), the saccade duration is increased and the peak velocity decreased for both horizontal (A, 1 and 2) and vertical (B, 1 and 2) saccades. The shift of the \cdots (B3) is the normal lid movement with vertical eye movements.

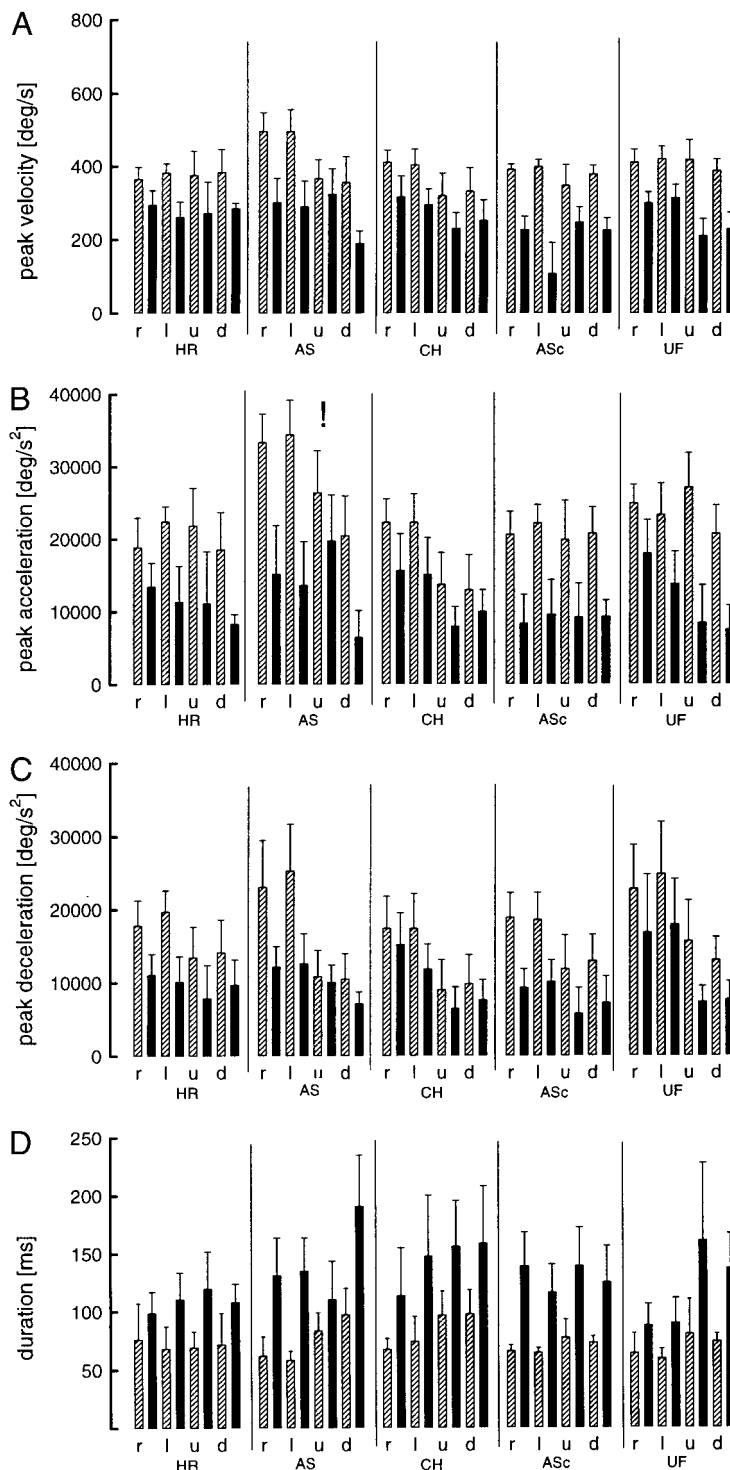


FIG. 3. Effect of blinks on conjugate saccades: quantitative analysis. Peak velocity (A), peak acceleration (B), peak deceleration (C), and saccade duration (D) are compared for the no-blink (▨) and the blink condition (■) and for each saccade direction (r: right, l: left, u: up, d: down) separately. The plots are given for each subject as indicated at the bottom of the figures. Bars give the mean values, the error bars the SD. All pairs (no-blink, blink) are statistically significant (Mann-Whitney-*U* test, $P < 0.05$) except those indicated (!). Peak velocity (A), peak acceleration (B) and peak deceleration (C) decrease under the blink condition compared with the control condition for all subjects and in all directions, while saccade duration (D) increases.

small horizontal saccades during convergence. However, all subjects made small vertical saccades with an amplitude $< 3^\circ$ in $\sim 70\%$ of the vergence movements. Hence, our term “vergence” eye movements were not pure vergence but instead vergence with small saccades. The mean peak vergence velocity differed for convergence and divergence (Collewijn et al. 1995): convergence eye movements in all subjects had higher peak velocities ($69.2 \pm 19.2^\circ/\text{s}$) than divergence ($51.7 \pm 9.8^\circ/\text{s}$). The velocity trajectories showed a slower decline in divergence than in convergence (Fig. 5, *B1* and *D1*, \cdots). The

duration of convergence was on the average shorter (225 ± 45 ms) than that of divergence (275 ± 31 ms). These data will subsequently be referred to as control vergence responses.

Properties of horizontal vergence during blinks

The influence on blinks on vergence eye movements has not been reported before.

Generally, some of the subjects always blinked at about the same time during a vergence movement, whereas others

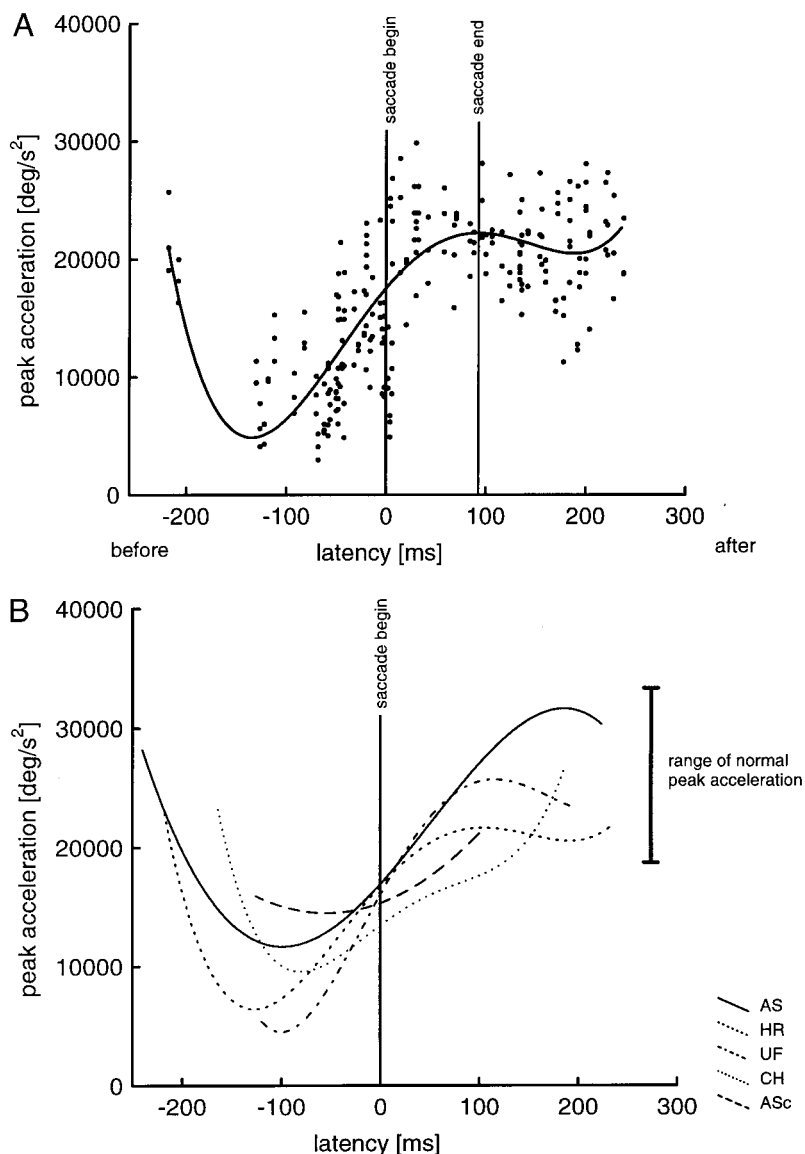


FIG. 4. Temporal effect of the timing of blink onset with respect to saccades onset. The effect of blinks on the peak acceleration of conjugate saccades for *subject HR* (A) and all subjects (B) are shown. The saccadic peak acceleration for saccades (version component) in all directions (right, left, up, down) is plotted versus the latency (blink onset relative to the saccade onset). Negative latencies indicate that a blink begins before and positive latencies refer to blink onset after saccade onset. Saccade begin (1st vertical line) is set to zero. The mean saccade end (2nd vertical line) is indicated. Data are fitted with a polynomial (4th grade). Blink onset ≤ 200 ms before saccade begin reduces the peak acceleration $\leq 50\%$ at ~ 120 ms before saccade begin. Blink onset during the saccade did not change peak acceleration. In B, the 4th-grade polynomials of the latency vs. peak acceleration for all subjects are presented as in A. Subjects names are indicated at the right margin.

showed some variability of the blink onset with respect to vergence onset. In contrast to the saccade-paradigm (2) where blinks often began before saccade onset (Fig. 2), blinks usually occurred at vergence onset or during the vergence eye movement, seldom before (Figs. 5 and 6). All subjects reported the divergence paradigm to be more difficult than the convergence paradigm with blinks. During the blink condition, there were less version saccades in the con- and divergence paradigm but slow horizontal ($<1^\circ$) and larger vertical eye movements (Fig. 5B, 1 and 2) were found when compared with the fixation paradigm (1; Fig. 1). There was no difference in the vergence amplitude for the convergence (no-blink: $6.8 \pm 0.5^\circ$; blink condition: $6.5 \pm 0.6^\circ$) or divergence (no-blink: $6.8 \pm 0.6^\circ$; blink condition: $6.45 \pm 0.6^\circ$). The total duration of the eye movements in the convergence-blink paradigm was increased over all subjects (convergence: in the no-blink condition, 225 ± 45 ms vs. 475 ± 65 ms in the blink condition; divergence: in the no-blink, 275 ± 31 ms vs. 511 ± 68 ms in the blink condition). However, vergence duration did not exceed blink duration (326 ± 117 ms) in all subjects.

PHASE 1: In the convergence- and divergence-blink paradigm (Fig. 5), there was a convergence-divergence eye-movement sequence in *phase 1* (70% of the blink time). The convergence-divergence eye-movement sequence during blinks was similar in the vergence (Fig. 5) and fixation paradigms (compare Fig. 5, A1 and B1, vs. Fig. 1, 1st trace).

In the convergence-blink paradigm, the mean peak velocities for convergence ($98.6 \pm 47.9^\circ/\text{s}$) and divergence ($55.3 \pm 28.7^\circ/\text{s}$) in *phase 1* did not differ from those with blinks at stationary eye positions (*paradigm 1*: convergence: $90.8 \pm 42.8^\circ/\text{s}$, divergence: $58.6 \pm 15.7^\circ/\text{s}$). In contrast, in the divergence-blink paradigm, the peak velocities of convergence components of *phase 1* ($78.0 \pm 43.9^\circ/\text{s}$) were smaller than those during blinks at stationary eye positions (*fixation paradigm 1*: $90.8 \pm 42.8^\circ/\text{s}$).

PHASE 2: In the convergence-blink paradigm, eye movements during *phase 2* (slow convergence) were variable and depended on the blink onset. The earlier the blink onset occurred with respect to vergence onset, the slower and longer the convergence in *phase 2* (Fig. 6). A comparison of convergence

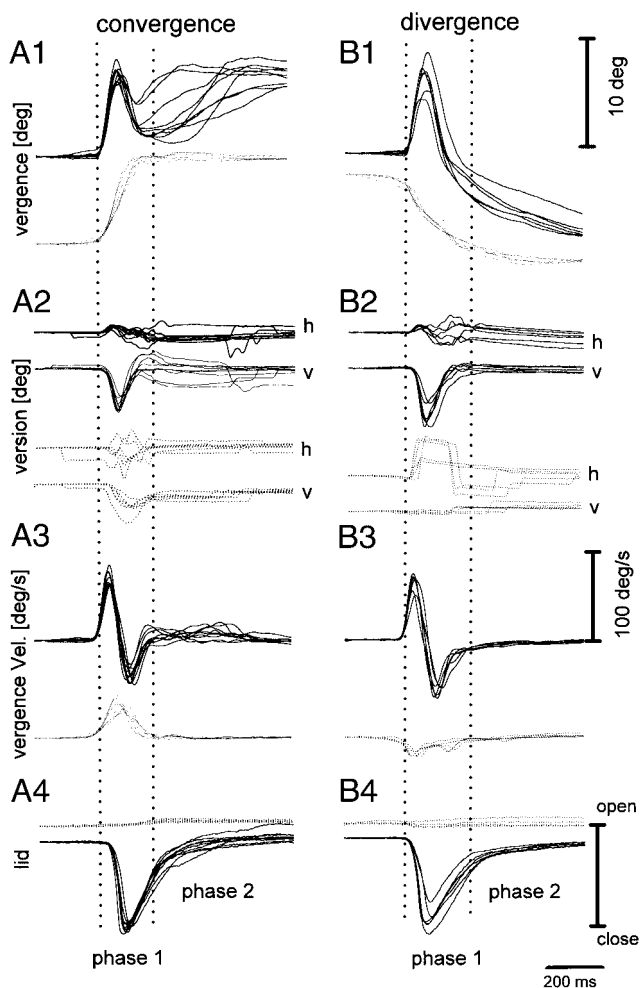


FIG. 5. Effect of blinks on horizontal vergence eye movements: original recordings. The vergence eye movements subjects (AS) are displayed separately for the convergence (A) and divergence (B) components of the vergence position (A1 and B1), version position (A2 and B2), vergence velocity (A3 and B3), and the relative lid position (A4 and B4). Eye movements under the blink condition (black solid traces) are compared with those under the no-blink condition (dotted trace). All traces are aligned to vergence onset. For better illustration the onset of the 2 phases of the vergence components are indicated by vertical dotted lines in Fig. 5 (see METHODS). In phase 1, a convergence-divergence movement is found in the convergence (A1) and in the divergence (B1) paradigms (for details see RESULTS). During control vergence, there are some small vertical saccades (A2, dotted line, indicated by v) and some small horizontal saccades (indicated by h). In contrast, more horizontal saccades are observed during divergence (B2, dotted line, h). In comparison, during the blink condition there are slow vertical and horizontal eye movements, but no saccades (A2 and B2, solid lines). h: horizontal; v: vertical version eye position. Note that vergence duration exceeds blink duration.

peak velocity in *phase 2* with the control vergence movement showed a significant reduction in all subjects (Fig. 7).

Phase 2 of the divergence-blink paradigm showed a slow drift to the final vergence position. The peak velocity of divergence in *phase 2* was on the average slower ($20.3 \pm 15.3^\circ/\text{s}$) than the control mean divergence velocity in the no-blink condition ($55.3 \pm 28.7^\circ/\text{s}$). In four of five subjects, these differences were significant (Fig. 7). *Subject UF* had blinks late in the time course of the vergence movement; this may indicate that the effect was not significant. The earlier the blink occurred with respect to vergence onset, the larger was the reduction in peak divergence velocity.

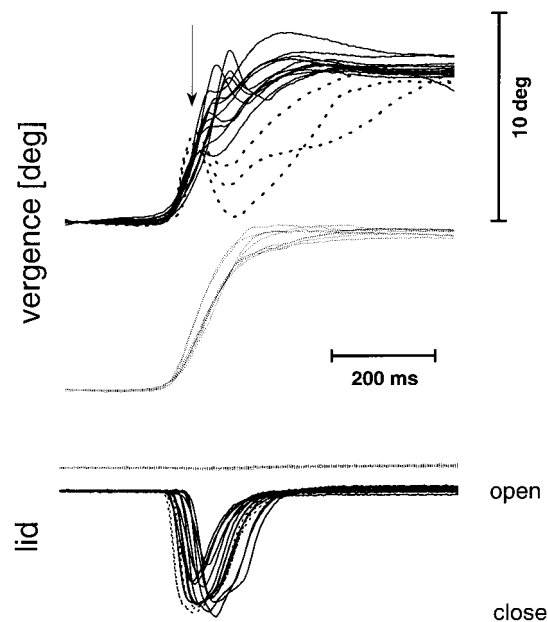


FIG. 6. The temporal effect of blink onset with respect to convergence onset is shown for *subject HR*. Vergence eye and lid position for the control (···) and blink condition (— and ---) are presented. Blinks early in the vergence (---; ↓) show a decrease of vergence velocity in *phase 2*, whereas blinks performed later during vergence eye movements (—) have either a small or no effect. ↓, the peak effect on vergence in the early eye lid blinks.

Combined vergence-saccade eye movements without blinks

When subjects were asked to perform combined saccade-vergence eye movements (*paradigm 4*), vergence eye movements were accelerated by accompanying saccades (Collewyn et al. 1995; Erkelens et al. 1989; van Leeuwen et al. 1998; Zee et al. 1992). The horizontal convergence peak velocities during horizontal ($137.4 \pm 19.4^\circ/\text{s}$) and vertical ($88.1 \pm 9.90^\circ/\text{s}$) saccades were increased in comparison with the mean peak velocities in the vergence task with small saccades ($69.2 \pm 19.2^\circ/\text{s}$; compare Fig. 5 with Figs. 8 and 10). Saccades with a divergence component showed increased peak velocities of the horizontal divergence compared with the divergence response

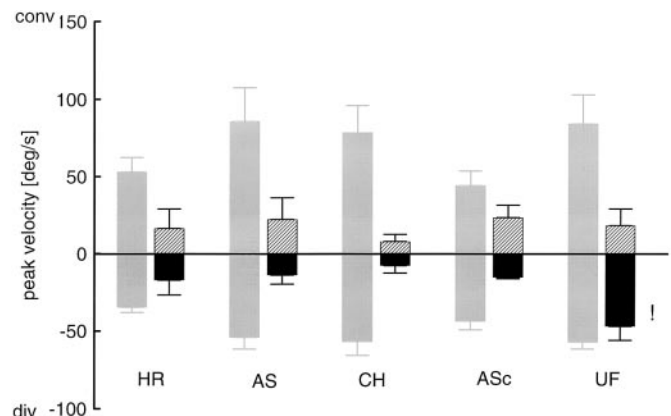


FIG. 7. Blink effect on peak velocity of vergence in *phase 2*. Vergence peak velocity components are shown during the blink condition for the convergence (positive, ■) and divergence (negative, ■) of *phase 2* and compared with vergence components during the no-blink condition (□) for all subjects (indicated at the bottom of the figure). Peak velocity is significantly reduced in all subjects, except for *subject UF* as indicated (!). (conv, convergence; div, divergence)

($51.7 \pm 9.8^\circ/\text{s}$) of *paradigm 3*. The divergence peak velocity was $85.2 \pm 9.5^\circ/\text{s}$ during horizontal and $64.9 \pm 15.3^\circ/\text{s}$ during vertical saccades.

Combined vergence-saccade eye movements with blinks

The blink effect on combined vergence-saccade eye movements has not been reported so far. We first present data of the blink effect on the version followed by the vergence component.

VERSION. Saccades with a vergence component were compared under the blink versus no-blink conditions. The effects on the version components were similar to those with conjugate saccades (*paradigm 2*, compare Fig. 2 vs. Figs. 8 and 10). There was no difference between the convergence and the divergence condition. Generally, the duration of version components increased whereas peak velocity decreased in all saccade directions and in all subjects in comparison with the control (no-blink condition; Fig. 8 *2nd trace*). The amplitude in the blink and no-blink conditions did not change. The saccade parameters for horizontal saccades were averaged because there was no significant difference between right and left saccades. The blink duration exceeded saccade duration in the blink-condition in both vergence directions of *paradigm 4* (convergence condition: eye duration: 126 ± 21 ms; blink duration: 334 ± 82 ms; divergence condition: eye duration: 123 ± 17 ms; blink duration: 361 ± 111 ms). Blink effects are presented for convergence and divergence components separately.

Saccades with convergence components. The saccade duration increased for horizontal saccades from 67.5 ± 5.7 ms (no-blink) to 121.5 ± 23.4 ms (blink), while the peak saccade velocity decreased from 412.8 ± 33.4 to $296.4 \pm 55.3^\circ/\text{s}$ as did the acceleration ($24,940 \pm 4,727$ to $16,786 \pm 5,562^\circ/\text{s}^2$) and deceleration ($19,097 \pm 3,119$ to $11,913 \pm 3,128^\circ/\text{s}^2$).

Under the blink condition, vertical saccade duration (76.12 ± 10.8 ms) increased on the average to 137.4 ± 22.4 ms. Vertical peak version velocity decreased from on the average 382.9 ± 43.6 to $254.1 \pm 33.8^\circ/\text{s}$ (Fig. 9A). There was no significant difference found between upward and downward peak velocity. Peak acceleration during blinks decreased from $21,444 \pm 4,840^\circ/\text{s}^2$ in the no-blink to $12,375 \pm 4,835^\circ/\text{s}^2$ in the blink condition and peak deceleration from $14,273 \pm 3,586^\circ/\text{s}^2$ in the no-blink to $8,123 \pm 1,986^\circ/\text{s}^2$ in the blink condition. Peak acceleration and peak deceleration did not show significant differences between saccades in the upward and downward directions.

Saccades with divergence components. As with saccades and convergence components, the divergence duration was increased while peak velocity and acceleration were decreased during accompanying blinks. Saccade duration was increased for horizontal saccades from 69.0 ± 6.6 to 116.6 ± 21.4 ms, while version peak velocity (406 ± 32.7 to $313.2 \pm 25.6^\circ/\text{s}$; Fig. 11A) and acceleration ($25,497 \pm 4,458$ to $16,080 \pm 3,014^\circ/\text{s}^2$) decreased. Deceleration was not significantly different in two subjects.

The saccade duration of vertical saccades increased from 91.6 ± 21.6 ms under the no-blink to 149.7 ± 24.1 ms under the blink condition. Vertical mean version peak velocity decreased on the average from $347.2 \pm 51.5^\circ/\text{s}$ (no-blink) to $234.9 \pm 29.4^\circ/\text{s}$ (blink condition). Peak acceleration was de-

creased from $19,859 \pm 4,115$ to $10,693 \pm 3,190^\circ/\text{s}^2$ and peak deceleration from $10,773 \pm 3,514$ to $7038 \pm 887^\circ/\text{s}^2$ during blinks. All subjects showed significant differences between the blink versus the no-blink condition for nearly all parameters, i.e., for peak velocity (Fig. 11A), peak acceleration and saccade duration. Some subjects did not show any significant effect for deceleration; however, the trend was the same.

VERGENCE. The accompanying horizontal vergence component was also changed during blinks in the combined saccade-vergence paradigm with divergence and convergence components (Figs. 8 and 10) as in the vergence paradigm. However, in the blink condition, the effect was limited to an increase in the total duration and a decrease in peak vergence velocity (Figs. 8 and 10) of *phase 1*.

Similar to the vergence paradigm (3, Fig. 5) there was a convergence-divergence-convergence eye movement for the convergence (Fig. 8, *4th line*) or a convergence-divergence eye movement for the divergence condition (Fig. 10, *4th line*) of *paradigm 4*. However, the vergence sequence, which always began with convergence, was not as clearly defined as that with pure vergence. It often showed more changes in the vergence direction (Figs. 8 and 10, *4th line*).

In *paradigm 4* with convergence, there was a decrease in mean velocity of convergence for nearly all directions in all subjects (Fig. 9B). On the average, a decrease in mean convergence velocity was found during horizontal saccades from 75.1 ± 20.0 to $30.4 \pm 53.1^\circ/\text{s}$, and in vertical saccades from 43.3 ± 22.3 to $25.0 \pm 10.1^\circ/\text{s}$.

In *paradigm 4* with divergence, the mean divergence velocity was decreased in three of five subjects in three directions (Fig. 11B). No significant effect was observed in one subject (CH). In one subject (AS), the blink effect was significant only for downward eye movements (Fig. 11B). The blink effects were additionally not significant for rightward saccades in one subject (ASc), and for upward saccades in two others (HR and UF).

The *timing* of the blink in this paradigm (4) with respect to the saccade onset had effects on the saccade. Blink onset before saccade onset decreased the peak acceleration during the saccade by a factor of two, while blinks during the saccade have only a marginal or no effect on the saccade. The maximal blink effect on saccade parameters occurs when blinks start ~ 100 ms before the saccade.

DISCUSSION

To test the hypothesis that blinks can influence certain types of eye movements in humans via brain stem neuronal circuits, we investigated the effect of voluntary blinks on saccades, vergence, and saccade-vergence interaction.

As a major finding the kinematic parameters of eye movements (velocity, acceleration, deceleration, eye-movement duration) were substantially changed by blinks in all three paradigms (2–4: saccades, vergence, and saccade-vergence interaction) when compared with amplitude-matched controls. For the first time, we could show that blinks not only effect horizontal saccades (Rottach et al. 1998) but also vergence (with small saccades) and saccade-vergence interaction in humans in a similar way. Furthermore, this effect depended on the latency of the blinks (blink onset with respect to eye movement onset). The maximum effect on saccades, vergence,

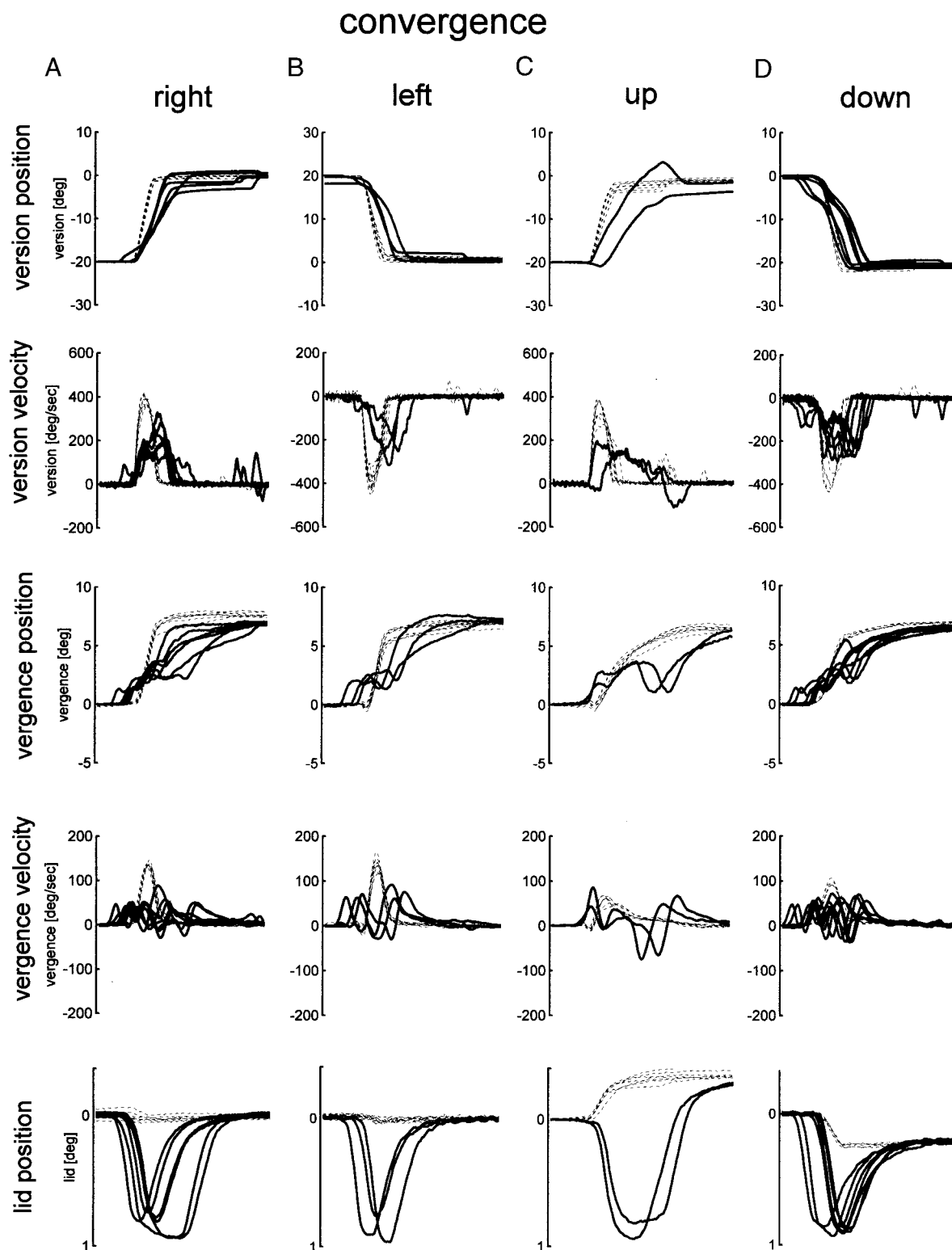


FIG. 8. Effect of blinks on saccade-vergence interaction during convergence: original recordings. From *top to bottom* the horizontal version (position, velocity), horizontal vergence components (position, velocity), and lid position are shown in all directions separately (vertical columns right, left, up, down, A–D). The no-blink condition (---) and blink condition (—) are compared. All data are aligned to version onset. *Version* components (1st and 2nd traces) in all directions show an increase in duration and a decrease in peak velocity during the blink condition. The *vergence* component (3rd and 4th trace) for most directions starts with a transient convergence (positive values), followed by some divergence-convergence oscillations, and a subsequent slow convergence movement to the desired eye position. In comparison with the no-blink condition (· · ·), there was an increase in duration during the blink condition. Saccade vergence movements are completed before the end of the blink.

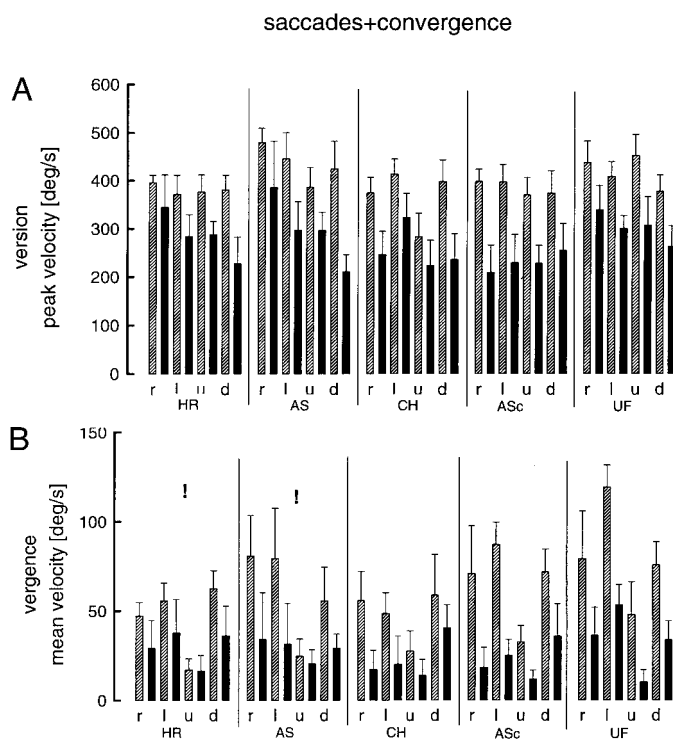


FIG. 9. Effect of blinks on saccade-vergence interaction during convergence: quantitative analysis. Peak version velocity (A) and mean vergence velocity (B) are compared for the no-blink condition (▨) with the blink condition (■) for each saccade direction (r: right, l: left, u: up, d: down) separately. The plots are given for the individual subjects (indicated at the bottom of the figures). Bars give the mean values, the error bars the SD. All pairs (no-blink, blink) are statistically significant (Mann-Whitney-U test, $P < 0.05$) except those indicated (!). Peak version velocity (A) and mean vergence velocity (B) are decreased during blinks for nearly all subjects.

and saccade-vergence interaction occurred when blink onset was before or during the early phase of the eye movement. In contrast, the eye-movement amplitude was not changed during blinks. Altogether these data provide several lines of evidence supporting the hypothesis that the blink effect may be mainly of central origin.

We investigated voluntary blinks, which differ from reflexive and spontaneous blinks (Evinger et al. 1991; Guitton et al. 1991, 1995). Spontaneous and reflexive blinks were mostly excluded (METHODS). Because blinks tend to suppress further blinks (Powers et al. 1997), we estimate that our analysis included >90% of voluntary blinks.

Effect of blinks on gaze during fixation

Our finding for the effect of blinks on gaze straight ahead during fixation are in accordance with those of previous studies (Bour et al. 2000; Collewyn et al. 1985, Evinger et al. 1991; Riggs et al. 1987). Blinks during gaze straight ahead elicited an eye movement toward the nose and downward.

All blink-elicited eye movements started with the blink onset (Collewyn et al. 1985) but were completed before the end of the blink. Blink-elicited eye movements were completed on the average after 60–70% of the blink duration (Collewyn et al. 1985; Rottach et al. 1998). Slower than saccades (Collewyn et al. 1985), they are thought to be caused by co-contraction of all eye muscles except the superior oblique muscle (Evinger et al.

1994; Evinger et al. 1984) but not by mechanical eye-lid interaction (Collewyn et al. 1985).

Effects of blinks on saccades

For the first time, we could show that voluntary blinks not only change the kinematics of horizontal saccades (Rottach et al. 1998) but also those of vertical saccades in humans. Blinks decreased saccade velocity, acceleration, and deceleration but increased saccade duration (Goossens and van Opstal 2000a; Rottach et al. 1998); however, the amplitudes were not changed.

This effect of blinks on saccades cannot be explained by visual feedback due to the short saccadic duration (horizontal: 66 ms and vertical: 82 ms) and ballistic nature of saccades (Rottach et al. 1998). In contrast, the blink effect could be caused by a superposition of two simultaneous eye-movement commands: visually guided saccades and blink-induced eye movements (at static eye positions). This could lead to a subsequent decrease of the saccadic velocity due to changes in the eye muscle tone. However, at least four aspects argue against this hypothesis: the blink effect on saccades is not a simple additive effect of saccades and the blink-induced eye movements (Goossens and van Opstal 2000a); the orbital transfer function predicts a normometric saccade with a subsequent drift, which we and others did not find (Goossens and van Opstal 2000a); a superposition should cause an increase in the expected centripetal/centrifugal difference in blink-perturbed saccades that was not observed in horizontal saccades (Rottach et al. 1998); finally, the blink effect should have different effects on upward than on downward eye movements because the superior oblique muscle is not activated during a blink (Evinger and Manning 1994). We and other investigators did not observe this finding (Goossens and van Opstal 2000a).

Our generalized finding for saccades in humans supports the hypothesis that the effect of blinks on saccades is mainly exerted centrally in the premotor circuit (Goossens and van Opstal 2000b; Rottach et al. 1998).

In contrast, during a blink the eye retracts due to extraocular eye muscle co-contraction (Evinger and Manning 1994; Evinger et al. 1984). Hence, the peripheral hypothesis cannot be dismissed. The degree, however, by which blink-induced eyes movements can additionally influence saccades remains unclear.

Effect of blinks on vergence

Blinks not only affected saccades but also vergence eye movements. The vergence eye movements had associated small vertical and infrequently horizontal saccades especially in the control condition but less in the blink condition. Hence our term vergence may mean that vergence eye movements are associated with small saccades (amplitude $<3^\circ$).

In the vergence-blink condition, a superposition effect of blink-induced eye movements and vergence eye movements were found in *phase 1* (time-locked with blink-induced eye movements). This might be an argument that the changes in *phase 1* are caused by a peripheral interaction. Some evidence comes from the same eye-movement sequence during *phase 1* as with blink-induced eye movements at fixation (*paradigm 1*). The convergence peak velocity did not change in the conver-

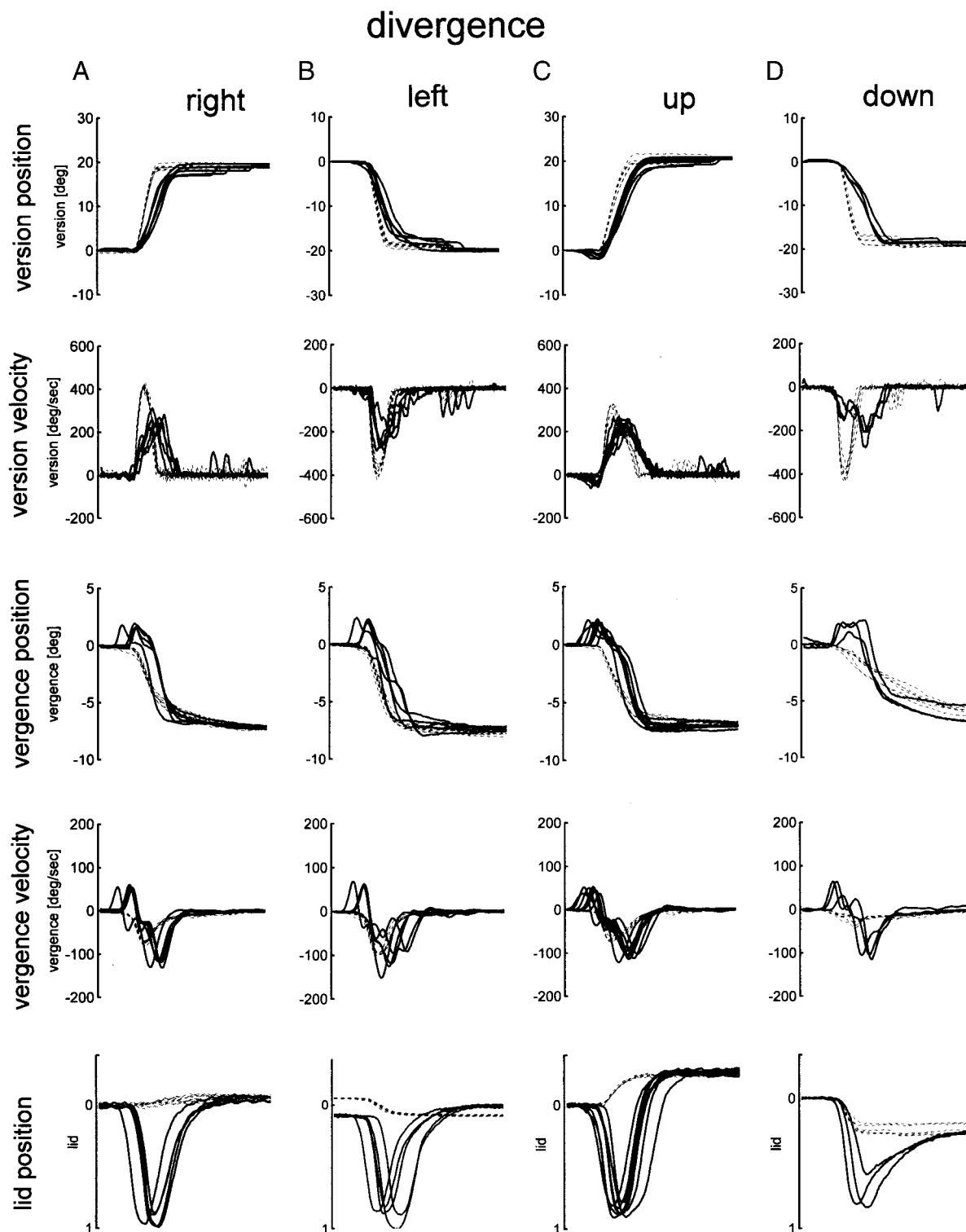


FIG. 10. The effect of blinks on saccade-vergence interaction during divergence: original recordings. Version (position 1st trace, velocity 2nd trace), horizontal vergence components (position 3rd trace, velocity 4th trace), and lid position (5th trace) are shown in all directions (vertical columns: right, left, up, down, A–D) separately. The no-blink condition (---) and blink condition (—) are compared. All data are aligned to version onset. Version components (1st and 2nd traces) in all directions show an increase in duration and a decrease in peak velocity during the blink condition. The vergence component for most directions starts with a transient convergence, followed by a fast divergence eye movement and subsequently a slow divergence movement to the desired eye position. In comparison to the no-blink condition (---), the blink condition has an increased duration. Note that the saccade vergence movements are completed before the blink end.

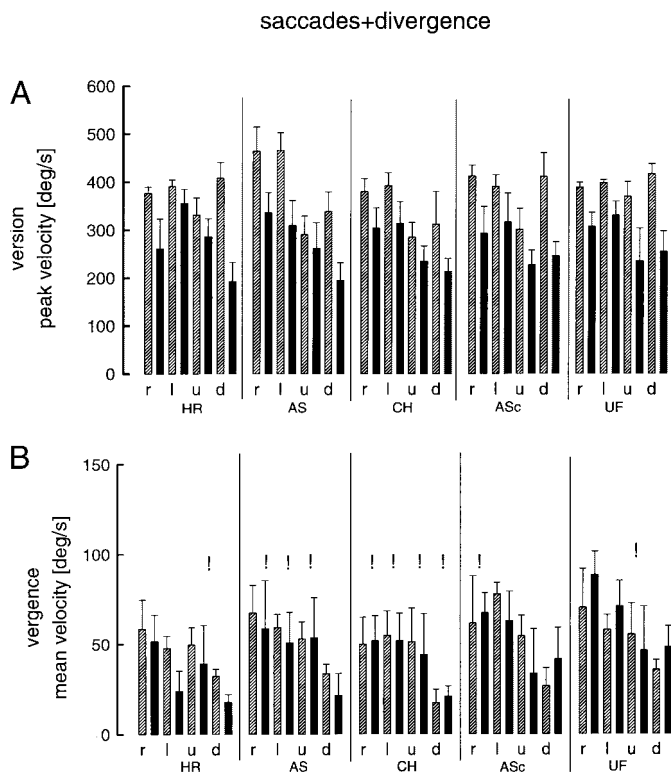


FIG. 11. The effect of blinks on saccade-vergence interaction during divergence: quantitative analysis. Peak version velocity (A) and mean vergence velocity (B) are compared for the no-blink (▨) and the blink condition (■) for each saccade direction (r: right, l: left, u: up, d: down) separately. The plots are given for the individual subjects (indicated at the bottom of the figures). Bars give the mean values, the error bars the SD. All pairs (no-blink, blink) are statistically significant (Mann-Whitney-U test, $P < 0.05$) except those indicated (!). Peak version velocity (A) is decreased during blinks, whereas mean vergence velocity (B) is not significantly decreased in all subjects.

gence-blink paradigm, but the divergence peak velocity increases in the divergence-blink paradigm compared with the fixation paradigm (I).

In *phase 2*, however, the effect of the blinks on vergence eye movements can be observed without the superimposed effect of blink-induced eye movements. Hence, eye movements in *phase 2* cannot be explained by a superposition of blink-induced and vergence eye movements.

The changes of the dynamic parameters of vergence eye movements with blinks in all subjects cannot be attributed to the decrease in the number of small saccades during the blink condition. There are more smaller saccades during our control vergence eye movements compared with the blink condition. Small saccades can enhance vergence eye movements (Collewyn et al. 1995). In the absence of saccades, vergence eye velocity decreases to values of “pure” vergence (Collewyn et al. 1995). Our measured peak vergence velocity of *phase 2* in the vergence-blink condition is slower than the values for “pure” vergence (Collewyn et al. 1995). Hence, the effect of blinks on vergence cannot be explained by a different number of saccades.

There is also no evidence that *phase 2* is driven by visual feedback. The initial, preprogrammed vergence component lasts for ~ 200 ms and is followed by the late visually driven component (Hung et al. 1986; Semmlow et al. 1986, 1993). In all our subjects, *phase 2* started within 200 ms after vergence

onset, i.e., before the visual feedback. There is no visual feedback during blinks; hence most of *phase 2* was probably caused by the initial preprogrammed vergence component, while the subsequent interval could be driven by the late visually controlled component.

Because blinks had an effect particularly on the vergence component of *phase 2*, a blink-induced change in the central programming of vergence is likely. A passive eye drift after the superposition is unlikely because the vergence peak velocity was lower (convergence: $17.6 \pm 6^\circ/\text{s}$ and divergence: $13.6 \pm 4.1^\circ/\text{s}$) than the expected peak velocity ($35^\circ/\text{s}$ for 7° amplitude) calculated by the orbital time constant of 200 ms (Cannon and Robinson 1987). Altogether, these findings indicate that the blink effect on the vergence eye movements can be explained by changes in the central programming of eye movements.

Effect of blinks on saccade-vergence interaction

The hypothesis that saccades and vergence can influence each other in their kinematic parameters (i.e., peak velocity, acceleration, duration) and that they are synchronized if executed together (Collewyn et al. 1995; Erkelens et al. 1989; Zee et al. 1992) led us to expect a specific blink-induced effect on saccade-vergence interaction. Our results show that blinks not only had an effect on the saccadic and vergence systems if tested separately but also when saccades and vergence eye movements were performed simultaneously.

There was a similar effect of blinks on the *version* component in the saccade-vergence interaction paradigm (4) and in the saccade paradigm (2). The kinematic parameters of the version components (saccades) were decreased, whereas the duration was increased.

There was a different effect on the *vergence* component in *paradigms 4* and *3*. While there was an increase in the duration of the eye movements and a decrease in the mean vergence velocity in the blink condition in *paradigms 3* and *4*, a long *phase 2* was missing in *paradigm 4*. *Phase 2* in the blink condition of *paradigm 4* was extremely short or did not exist compared with vergence (*paradigm 3*).

A second difference between the results of *paradigms 3* and *4* was that *paradigm 3* showed a clear convergence-divergence-(convergence) sequence that was not comparably found in *paradigm 4*. The convergence-divergence-(convergence) eye movement sequence makes some kind of superposition of the blink-induced and the saccade-vergence eye movements possible. Due to the short-duration of saccade-vergence interaction the blink effect is probably once again not caused by visual feedback.

Temporal effect of blinks on eye movements

The latency of blinks (blink onset with respect to eye movement onset) had a strong influence on the eye movements. Blinks starting ~ 100 ms before saccade onset had the strongest effect on the saccade kinematics in conjugate saccade and saccade-vergence interactions. Similarly, the blink effect on vergence movements showed a latency dependency with respect to vergence onset. Blinks changed vergence eye movements most when they were made before or in the first 20 ms of vergence movements. In contrast, two superimposed eye movements should have the largest impact on the eye movement onset; we did not find this result.

The maximal effect of blinks occurred 100 ms before saccade onset. If a small delay from the end of the levator palpebrae motoneuron activity to lid depression (10–59 ms) (Fuchs et al. 1992) is considered, the latency for the lid movement execution amounts to 100–160 ms. Because brain stem burst neurons of the SC (>20–100 ms) (Goossens and van Opstal 2000b), ponto-medullary burst neurons (2–120 ms) (Hepp et al. 1989), and OPNs (16 ms) (Raybourn and Keller 1977) have onset latencies of <120 ms, a direct effect of blinks on saccade preprogramming appears feasible.

Evidence for influence of blinks on central premotor programming

To show that blinks affect the neuronal circuit of saccade, vergence, and saccade-vergence interactions, one has to explain two blink effects on eye movements: increased duration and decreased peak velocity. Animal experiments have revealed three important locations in the brain stem, where blinks could interact with saccades and/or vergence movements: OPNs, saccade-related burst neurons in the intermediate layer of the superior colliculus, and medium-lead burst neurons of the paramedian pontine reticular formation. All structures will be discussed separately.

OPN and blinks

Several lines of evidence indicate that OPNs in the nucleus raphe interpositus (rip) (Büttner-Ennever and Büttner 1988) control both saccadic (Hepp et al. 1989) and vergence (Mays and Gamlin 1995) burst neurons. While OPNs are spontaneously active, they pause during saccades (Keller 1977). During pure vergence, there is no modulation of the OPN activity (Mays and Gamlin 1995), whereas stimulation of the OPN area slows vergence movements (Mays and Gamlin 1995). Saccade-vergence interaction is also triggered by the OPNs (Mays and Gamlin 1995; Zee et al. 1992).

Ibotenic acid injections in the OPN region located in the nucleus rip in monkey caused a decrease in saccadic peak velocity and an increase in saccade duration with amplitudes of equal size (Kaneko 1996). As in rip lesions blinks decrease OPN discharge even without eye movements (Cohen and Henn 1972; Fuchs et al. 1991; Mays and Morisse 1993).

Thus the blink-induced reduction of the OPN activity may lead to a prolonged eye movement duration and decreased peak velocity in not only horizontal (Rottach et al. 1998) but also vertical saccades and even vergence and saccade-vergence interaction.

Saccade generator

A subset of the MLBN of the PPRF, the horizontal saccade generator, are active during blinks (Cohen and Henn 1972). However, during blink-saccade interactions the discharge rate of medium-lead burst neurons in the PPRF is reduced (Mays and Morisse 1995a). This may explain the slowing of not only horizontal (Rottach et al. 1998) but of all saccades in our study. Burst neurons of the vertical saccade generator, the rostral interstitial nucleus of the medial longitudinal fascicle (riMLF), also discharge during blinks (unpublished observations). It is not yet known if their neuronal activity in saccade-blink interaction is decreased. If the burst neurons in riMLF behaved like

the PPRF during blinks, the slowing of our blink-associated vertical saccades might be explained.

SC

The SC is critically involved in the saccade generation of normal saccades. Stimulation of the SC changes not only conjugate but also disjunctive (vergence) eye movements (Chaturvedi and van Gisbergen 1999, 2000).

Blinks decrease the activity of saccade-related burst neurons (SRBN) in the deep and intermediate layer of the SC (Goossens and Van Opstal 2000b). During blink-perturbed saccades, SC burst neurons showed prolonged activity (Goossens and Van Opstal 2000b). This was not found during gaze-evoked blinks, and voluntary blinks were not tested. Blink-evoked prolongation of SRBN activity was found for all directions (Goossens and Van Opstal 2000b); this may explain why not only horizontal (Rottach et al. 1998) but also vertical saccades are prolonged in our study. The prolonged activity may also explain the increase in duration of vergence and saccade-vergence interaction. However, these paradigms were not yet specifically tested in these studies.

Our findings indicate that the conceptual model of blink influence on the premotor saccadic circuit (Goossens and van Opstal 2000b) may be extended to vergence and saccade-vergence interactions. Most of our blink-induced changes on the saccade and vergence kinematic parameters could be explained by blink effects on the premotor circuit involving the SC, the OPN area, or the PPRF. The uniform blink effect on saccades and vergence eye movements suggests that blinks might also influence vergence through the same neuronal circuits, i.e., OPN or SC. However, so far there are no related single-unit recordings with respect to vergence in these areas. In particular, the effect of blinks should be tested on the premotor vergence area in the midbrain and the nucleus reticularis tegmenti pontis (NRTP). Finally, we cannot exclude that some part of the blink effect on eye movements is caused by an additional peripheral component, e.g., due to the co-activation of eye muscles during the blinks. The blink effects on eye movements in *phase 2* and the temporal influence of blinks on the eye movements, however, argue against this assumption.

Conclusion

For the first time, we showed that blinks affect not only horizontal saccades but also vertical saccades, vergence eye movements, and saccade-vergence interaction in humans. While the saccade and vergence duration is increased during blinks, the peak velocity, acceleration and deceleration is decreased. In contrast, the amplitude of saccades and vergence was not changed during blinks. Blinks have a maximum effect when elicited ~100 ms before eye movements. This blink effect can probably not be explained by visual feedback or only by mechanical interaction but to a great extent by changes in the premotor programming of saccades and vergence eye movements.

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