Saccade–Vergence Interactions in Macaques. I. Test of the Omnipause Multiply Model

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Busettini, C. and L. E. Mays. Saccade–vergence interactions in macaques. I. Test of the omnipause multiply model. J Neurophysiol 94: 2295–2311, 2005. First published May 25, 2005; doi:10.1152/jn.01336.2004. Horizontal vergence eye movements are movements in opposite directions used to change fixation between far and near targets. The occurrence of a saccade during vergence causes vergence velocity to be transiently enhanced. The goal of this study was to test in the monkey the previously described Multiply Model (Zee et al. 1992) that holds that, in humans, the speeding of vergence during a saccade may be the result of the disinhibition of a subgroup of vergence-related neurons by the saccadic omnipause neurons (OPNs). In agreement with the Multiply Model: 1) the onset of the enhancement was closely related to saccadic onset, and thus linked to the onset of the OPN pause; 2) the magnitude of the vergence velocity enhancement was strongly dependent on saccade–vergence timing. Contrary to the Multiply Model: 1) the peak of the vergence velocity enhancement was dependent on saccadic peak velocity; 2) the dependency on saccadic peak velocity was not the indirect result of a dependency on saccadic duration and therefore on the duration of the OPN pause; 3) the decline of the vergence enhancement, identified by the time of the peak of the enhancement velocity, occurred too early to be linked to the end of the OPN pause; 4) vergence enhancement had a saccadic-like peak-velocity/size main sequence. Overall, the evidence is incompatible with the OPN Multiply hypothesis of vergence enhancement. Alternative models are described in an accompanying paper.

INTRODUCTION

Saccades are rapid movements of the eyes used to transfer fixation between visual targets. These movements are generally conjugate, which is to say that the two eyes move the same amount and direction. In contrast, saccade-free horizontal vergence eye movements (either convergence or divergence) are much slower movements of the two eyes in the opposite direction. These movements allow transfer of fixation between targets at different distances from the observer. Because saccade-free vergence movements and saccades differ considerably in latency and dynamics, it has often been assumed that they are generated by different, independent neural subsystems (Rashbass and Westheimer 1961a,b; Westheimer and Mitchell 1956). This view is supported by clinical and experimental neurophysiological studies (Judge and Cumming 1986; Mays 1984; Mays et al. 1986). A striking example is the syndrome of internuclear opthalmoplegia, in which adduction is impaired for conjugate eye movements, including saccades, while convergence may be spared (Cogan 1970; Gamlin et al. 1989b).

Under natural conditions, when gaze is shifted between objects at different distances and eccentricities from the observer, vergence movements are combined with saccades. Ono et al. (1978a,b) showed that when horizontal saccades were combined with horizontal vergence changes there was an increase in vergence velocity above the value predicted by the linear addition of a conjugate saccade to a saccade-free symmetrical vergence movement. Enright (1984, 1992) confirmed and extended Ono’s findings that when vergence was combined with horizontal saccades, the amplitudes of the horizontal saccades in the two eyes were often quite different. He concluded that this was the result of different neural pulse and step innervation patterns for the two eyes. This view is supported by reports by Zhou and King (1998) and Sylvestre and Cullen (2002) of left-eye and right-eye saccadic burst neurons in the pons.

Zee et al. (1992) evaluated four models of saccade–vergence interactions. Two of them do not involve independent saccadic eye control or nonlinear vergence–saccade interactions at the level of the oculomotor plant, but allow for vergence-related neural activity to be gated by saccade-related pontine omnipause neurons (OPNs). The gating by the OPNs has, as a behavioral consequence, a brisk intrasaccadic change in the open-loop gain of the vergence system, which can be seen as a multiplicative effect. In the literature they are therefore often referred to as “Multiply Models.” Both of these models are consistent with the following observations: 1) the enhancement of vergence velocity by vertical saccades (Enright 1984; Van Leeuwen et al. 1998; Zee et al. 1992), which would implicate OPNs in this interaction; 2) the existence of midbrain vergence burst neurons encoding vergence velocity signals (Mays et al. 1986); 3) evidence that some of these vergence burst neurons, which do not fire during conjugate saccades (Mays et al. 1986), are more active during saccades in combined saccade–vergence trials (Mays and Gamlin 1995); 4) stimulation of the omnipause area slows the vergence response (Mays and Gamlin 1995); 5) similar slowing effects are seen during stimulation of the rostral pole of monkey superior colliculus (Chaturvedi and van Gisbergen 2000), an area known to project to the OPNs (Büttner-Ennever and Horn 1994); and 6) stimulation of the caudal intermediate and deep layers of the superior colliculus during an ongoing vergence response generates saccade-related vergence enhancement (Chaturvedi and van Gisbergen 1999). This enhancement can be interpreted as the effect of the OPN pause associated with the stimulation-elicited saccade on the vergence response. Alternative interpretations of these results are illustrated in the accompanying paper (Busettini and Mays 2005).

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Our implementation of the Multiply Model is depicted in Fig. 1 for three different behavioral tasks. The main difference with respect to the two OPN models proposed by Zee et al. is in the signal encoded by the vergence-related cells gated by the OPNs. In their two models, the gating was on hypothetical cells coding vergence motor error. In our case the gated cells are a
subsection of midbrain vergence burst cells, which were previously described as carrying a vergence velocity signal (Mays et al. 1986). Descriptions of the elements are given in the figure caption. The inputs to this model are pure vergence and pure conjugate saccadic commands. In the case of slow (symmetrical) convergence without a saccade (top left), a vergence command causes a firing pattern in midbrain convergence burst neurons (CB1) that resembles the vergence velocity profile (Mays et al. 1986). Figure 1, bottom right shows a spline fit of the firing profile for one such convergence burst cell (trace FR), along with an associated (smooth) vergence velocity trace (trace SE), after Mays and Gamlin (2000). The same signal is encoded by another subgroup of convergence burst neurons (CB1*), which is inhibited, through the connection highlighted in red, by the tonic activity of OPNs (indicated in blue). The tonic OPN inhibition is strong enough that the CB1* cells are silent. The CB2 cells act as a summing junction of the CB1 and CB1* signals. Thus during saccade-free vergence, the CB1 and CB2 subgroups are indistinguishable. Convergence burst tonic (CBT) cells (Zhang et al. 1992) receive both a vergence velocity signal from the CB2 group and a vergence position signal that is obtained by integration (VNI) of the CB2 output. The vergence velocity + position command from the CBT cells is added linearly to existent (static) signals at the level of the left- and right-eye medial rectus motoneurons (LMR and RMR) and a slow symmetrical convergence is the result.

Figure 1, top right depicts a convergence–saccade combination with a horizontal (rightward) saccade. This condition, in which gaze is shifted from a far to a near target offset to one side, typically produces markedly unequal horizontal saccades (Enright 1992; Ono et al. 1978b). The vergence command is generated as in the previous panel, but the occurrence of a vergence is associated with the cessation of activity in the OPNs, which results in the release of the inhibition on the CB1* cells. The disinhibited CB1* cells produce a pulse of activity (in green) corresponding to the OPN pause that is added to the nonenhanced CB1 contribution at the level of the CB2 cells. This pulse of activity can be seen as a brief weighted unmasking of a CB1-like activity corresponding to the OPN pause (k × FR) and it is shown as trace EFR in the bottom right of Fig. 1. The panel shows the pulse associated with the same saccade (i.e., same OPN duration) occurring at five different times within the vergence response to illustrate the critical importance of vergence–vergence timing. The weighting factor k is related to the number of gated CB1* cells, their velocity gains, and their synaptic weights relative to the CB2 cells. Thus during the OPN pause the CB1* subgroup is active and the CB2 firing is equal to (1 + k) × FR, whereas the CB1* subgroup is silent and the firing of the CB2 cells is at nonenhanced levels (i.e., FR) when the OPNs are active.

The overall behavioral effect is a pure multiplicative modulation of the FR activity, even though each cell acts as a linear weighted summation junction of the excitatory FR and inhibitory OPN signals. The OPN behavior during combined saccade–vergence trials is largely unaffected by the ongoing vergence (Bussettin and Mays 2003), with a pause corresponding only to saccades and a robust tonic firing otherwise. As a consequence, we expect to see a close correspondence between the occurrence of saccades (and OPN pause) and vergence enhancement. The enhanced vergence signal from the CB2 cells, after integration by the VNI, is added to the saccadic horizontal pulse and step commands at the level of the LMR and RMR motoneurons. The (conjugate) saccadic command is communicated to the LMR and RMR motoneurons by the left and right abducens internuclear (LAI and RAI) neurons in the pons. For clarity the circuitry responsible for the reciprocal innervation of the lateral recti is not shown (Moschovakis et al. 1996). The vergence–related activities of AI neurons and lateral rectus motoneurons are identical, i.e., both decrease somewhat for convergence and increase for divergence (Gamlin et al. 1989a; Sylvestre and Cullen 2002). This observation has no bearing on the model other than the fact that the vergence signal to the medial rectus motoneurons must be large enough to overcome the inappropriate AI inputs. The simple addition of the (conjugate) saccadic and (disconjugate) enhanced vergence commands produces an accentuated pulse-step command for the left eye and a diminished pulse-step command for the right eye, resulting in a significantly unequal horizontal saccade in the two eyes. A similar situation exists for the speeding of divergence, using divergence burst cells (not shown, but see Mays et al. 1986).

Figure 1, bottom left depicts a convergence–saccade combination with a purely (upward) vertical saccade. The occurrence of a vertical saccade is similarly associated with a cessation of OPN activity, which, operating through the CB1*, CB2, VNI, and CBT cells, provides an extra horizontal vergence pulse of activity to both the LMR and RMR during the vertical saccade. If no horizontal conjugate movement is called for, then there is no significant activity change in the horizontal saccadic circuitry.

There are several important and directly testable predictions of this model.

1) Because OPNs pause for all saccades with similar timing characteristics (Bussetini and Mays 2003), horizontal and vertical saccades should be equally effective in speeding vergence.

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**Figure 1.** Multiply Model of saccade–vergence interactions. Top left: convergence without any saccade. Top right: convergence with a horizontal saccade. Bottom left: convergence with a vertical saccade. Diagonally shaded boxes denote elements concerned exclusively with vergence. Gray shading indicates active elements during the specific task. Some boxes identify types of neurons, with a schematic representation of their firing pattern for the indicated situation. Abbreviations for these boxes: LMR and RMR, left and right medial rectus motoneurons (midbrain); CBT, convergence burst-tonic cells (midbrain); CB1 and CB2, types of convergence burst neurons (midbrain); CB1*, types of convergence burst neurons inhibited by OPNs; OPN, omnipause neurons (pons); HEBN and HIBN, saccadic excitatory and inhibitory horizontal burst neurons (pons); VEBN, saccadic excitatory vertical burst neurons (midbrain); LAI and RAI, left and right abducens internuclear neurons (pons). Other boxes represent higher-level functions such as CNI, conjugate neural integrator (horizontal) and VNI, vergence neural integrator (horizontal). SACC GEN is the saccadic generator, responsible for the cyclopean saccadic burst and the saccadic triggering. Pluses (+) and minuses (−) indicate excitatory and inhibitory connections. Bottom right: firing profile of a CB1 convergence burst neuron (red trace labeled FR) from Mays and Gamlin (2000) after cubic spline filtering, together with the associated vergence velocity trace (blue trace labeled SE) for a convergence movement with no saccades. In absence of saccades, the firing profile (FR) of the CB1 and CB2 cells is indistinguishable. Top section: simulates the firing (green trace labeled EFR) of the CB1* cells predicted by the Multiply Model during saccade-related OPN cessation for the same saccade (i.e., same pause duration) occurring at 5 (A–E) locations during the vergence movement. The firing of the CB1 cell is not modified by the OPN pause. It is evident that the time at which the saccade (and the associated OPN pause) occurs within the vergence response plays a major role in the amplitude of the vergence enhancement.
movements and show a similar timing of enhancement onset with respect to saccadic onset.

2) The amount of vergence enhancement should be exclusively determined by the CB1 firing (FR) at the time of the OPN pause (Fig. 1). No direct dependency on saccadic parameters such as size or peak velocity is expected. Because even small saccades are associated with OPN pauses of some minimum duration (Busettini and Mays 2003), small saccades should be as effective as somewhat larger saccades in speeding vergence, assuming that the duration of the OPN pause is sufficient to allow vergence enhancement to develop fully.

3) Because the vergence burst profile FR is a positively skewed function, saccades that occur relatively soon after the onset of the vergence movement will be more effective in increasing vergence velocity than saccades occurring later. However, very early saccades may be relatively ineffective in speeding vergence if they occur before the vergence burst reaches its peak.

4) If vergence enhancement is initiated by the OPN pause, then the deceleration of enhancement should be associated with the end of the pause.

For the hypothesis that there is a linear transformation between the vergence motor error and the vergence velocity command (Zee et al. 1992; local feedback model of the vergence system), whether OPN gating acts at the vergence motor error level or at the vergence velocity level is irrelevant with respect to these four points. Thus the conclusions of this paper apply to the original OPN-related models of Zee et al. as well. The following experiments were conducted in trained rhesus monkeys, which Maxwell and King (1992) showed to have saccade–vergence interactions that are similar to those of humans.

METHODS

Eye movement recordings were made from four juvenile rhesus monkeys (Macaca mulatta) weighting 6–10 kg, identified as X01, 21, 71, and 941. The data for this study were acquired before craniotomies for attaching head restraints and ocular search coils are described in humane care and use of laboratory animals. The surgical procedures with FDA, AAALAC, and U.S. Public Health Service Policy on the humane protocols were approved by the UAB IACUC and complied for the subsequent single-unit experiments. All procedures and experimental protocols were approved by the UAB IACUC and complied with FDA, AAALAC, and U.S. Public Health Service Policy on the humane care and use of laboratory animals. The surgical procedures for attaching head restraints and ocular search coils are described in detail in Busettini and Mays (2003).

Behavioral task

Animals were trained to look at a visual target for a juice reward, which was delivered by a computer that compared eye position to target position. They were required to make transfers of fixation in depth and/or direction in response to target steps generated by a visual display, the details of which can be found in Walton and Mays (2003). The visual subtense for each monitor was +15° of horizontal and “Left” and “Right” if it was within ±15° of vertical and “near” or “far” distance depending on the trial, but in some sessions it was randomly offset to allow the introduction of saccades larger than one-half of the visual subtense of the monitors. Saccades were defined as “Up” and “Down” if their Pythagorean distance was within ±15° of vertical and “Left” and “Right” if it was within ±15° of horizontal. Only saccades inside those four orthogonal subsets were analyzed.

Additional requirements for their inclusion in the data sets, if not specified otherwise, were: 1) the associated stimulus step had to be in the same angular range of the direction of the saccade, to reduce the impact of random saccades, often seen during changes in depth; 2) they had to be primary saccades, i.e., the first saccade after the target step; 3) the saccadic latency following the target step was not <50 ms to eliminate anticipatory saccades; and 4) if present, the vergence response had a latency not <50 ms to eliminate anticipatory vergence movements. Using a cyclopean peak velocity of 40°/s as minimum threshold for our automatic saccadic search, all detected conjugate eye movements had a cyclopean amplitude–peak velocity relationship after a saccadic main sequence (Becker 1989). Saccades during vergence often had peak velocities lower than the conjugate main sequence but the deviations from the conjugate values were never large and were continuous with them, strongly suggesting that these movements were also saccades, albeit more or less slowed. Conjugate saccades were defined as those where the peak vergence velocity did not reach a 10°/s vergence threshold or, if the threshold was reached as the result of vergence transients, the saccade had an associated total vergence change (including the pre- and post-saccadic smooth vergence contributions, if present) between −0.5 and 0.5°. Saccades executed within total changes in depth >0.5° were considered disconjugate. Conjugate saccades were defined as “far” if the static vergence angle at saccadic onset was <2° and were defined as “near” if the static vergence angle was >7°. As previously reported (Collewijn et al. 1988a), an initial transient divergence was often seen during horizontal saccades, and sometimes during vertical saccades (Collewijn et al. 1988b) as well, even if no change in depth was required. On this issue see also Sylvestre et al. (2002).

Data acquisition and preprocessing

A computer controlled the presentation of stimuli, delivery of rewards, and acquisition of the eye signals (1-KHz acquisition rate; ~300-Hz hardware low-pass filtered). The search coil signals were linearized off-line using data acquired at the beginning of the session. Eye position traces were obtained from the linearized eye position signals using a cubic spline fit with weight of 1 × 10^8 (timescale in seconds). A lower spline weight (5 × 10^5), i.e., more filtering, was used for saccade-free smooth vergence traces because of their lower-frequency characteristics and for a fine adjustment of the vergence onset and offset of all trials. All other vergence measures for combined vergence–saccade movements and all saccadic measures were obtained from the traces with the higher spline weight. The spline weights were selected using a cross-validation technique so as to be the lowest weights (i.e., with the maximum local filtering effect) that required a wide range of conjugate and disconjugate steps, not readily obtainable with a set of real targets in space.

The selection of target steps induced the animals to make purely symmetrical vergence movements (i.e., slow saccade-free convergence and divergence), horizontal and vertical saccades between targets at optical infinity (i.e., conjugate saccades between two far targets), horizontal and vertical saccades with convergence (i.e., moving from a far to a near target), horizontal and vertical saccades while converged (i.e., between two near targets), and horizontal and vertical saccades during divergence (i.e., moving from a near to a far target). All trials were pseudorandomly intermixed to avoid anticipation by the animal. Horizontal and vertical cyclopean target steps from 0 to 25° were used, along with vergence demand changes from 0 to 13°. Usually the initial target was at the center of the screen, at a “near” or “far” distance depending on the trial, but in some sessions it was randomly offset to allow the introduction of saccades larger than one-half of the visual subtense of the monitors. Saccades were defined as “Up” and “Down” if their Pythagorean distance was within ±15° of vertical and “Left” and “Right” if it was within ±15° of horizontal.

Saccades inside those four orthogonal subsets were analyzed.
did not statistically affect the measure averages of the saccades and vergence responses when compared with unfiltered data (Eibak 1999). Horizontal version (H) was computed as average (HR + HL)/2 of the two horizontal eye positions. Horizontal vergence position (VG) was calculated as HL – HR. For the vertical eye movements, the vertical eye positions were used to compute an average vertical version signal (VR + VL)/2 and all vertical measures were made on the vertical version (V). Pythagorean, or vectorial (cyclopean) position (PY), was defined as $\sqrt{HL^2 + V^2}$. Velocity (HR, VR, HL, VL, H, V, PY) traces were computed using a two-point backward differentiation algorithm, defined as $y'_n = (y_n - y_{n-1})/(t_n - t_{n-1})$. Rightward, upward, and convergence movements are represented by positive values, whereas leftward, downward, and divergence movements are represented by negative values.

**Measurement of eye movement parameters**

The measurements used to characterize the vergence–saccade interactions are illustrated in Fig. 2. and were determined automatically by a computer. The target step that the animal followed occurred at time 0 (not shown). Vergence onset and offset were first determined using the vergence velocity trace with the higher spline weight with $10^\circ/s$ as threshold. Then, taking this as a starting point, a $3^\circ/s$ threshold value was used to determine vergence onset (vertical line marked VGONS in Fig. 2) and vergence offset (vertical line marked VGOFF) using the vergence velocity trace with the lower spline weight. Total vergence change was defined as the change in vergence between VGONS and VGOFF, thus including the contributions of the smooth vergence and, in some cases, the enhancement(s) associated with the saccade(s) executed during the change in depth. We observed that the animals occasionally reached the largest vergence changes imposed by our visual stimuli with more than one vergence movement, with clear plateaus in the vergence velocity between the segments. We identified the magnitude of the movement by the total vergence change achieved by the primary (initial) segment and not by the total disparity error presented to the animal. All our analyses considered only the primary segment of the vergence movements.

An automatic multistep process, described in the APPENDIX, determined saccadic onset ($S_{ONS}$) and end ($S_{OFF}$). All saccadic measures are with respect to the Pythagorean (i.e., conjugate) profile of the saccade for both conjugate saccades and saccades during vergence. The peak of the Pythagorean velocity is indicated by the vertical line at $P_Y^PK$. The vertical line at $V_{GPK}$ indicates the “saccade-related” peak vergence velocity (on trace VG) during the saccade–vergence trial. For very late saccades the smooth peak vergence velocity could be higher than the peak vergence velocity associated with the saccade. Consequently, for saccade–vergence trials the search for the peak vergence velocity was limited to the interval 20 ms before saccadic onset and 20 ms after saccadic offset and this peak was termed “saccade-related” to be distinguished from the absolute peak, which was, in some cases, not associated with a saccade. The interval between $V_{GONS}$ and $S_{ONS}$ indicates the time between the onset of vergence and the onset of the saccade (vergence lead). Smooth vergence movements without saccades tended to be highly stereotyped, and so it was possible to directly compare the velocity of vergence associated with a saccade (VG in Fig. 2) to that of a typical smooth vergence movement of the same amplitude (smooth estimate $SE$).

For primary saccades with a vergence lead interval of least 5 ms, a computer algorithm aligned a smooth vergence movement from the animal’s data set with the presaccadic period of the vergence (gray horizontal bar in the third left panel) for an estimate of the saccadic effect on the vergence response. Potential candidates for the match were all the smooth saccade-free traces in the animal’s data set that had total vergence amplitudes within $\pm 0.5^\circ$ of the total vergence amplitude of the saccade–vergence trial. The algorithm selected the best-fitting smooth vergence trace (least-square error criterion) in the presaccadic segment ($S_{ONS} - V_{GONS}$) after synchronization of the start of the smooth vergence under test with the start of the vergence of the combined movement. $SE_{V_{GPK}}$ is the value of the smooth vergence velocity estimate at the time of the peak of the saccade-related vergence velocity. The dotted trace (E) is the difference between the vergence velocity associated with the saccade and the matched smooth vergence velocity estimate, and so indicates the degree of enhancement of the vergence velocity by the saccade.

An automatic multistep process, described in the APPENDIX, determined the beginning of the enhancement ($E_{ONS}$). $E_{PK}$ is the peak of the vergence velocity enhancement, whereas $E_{V_{GPK}}$ is the value of the vergence velocity enhancement at the time of the peak of the saccade-related vergence velocity. Because of the much slower dynamics of the smooth vergence velocity, the two peak enhancement values usually occurred at the same measure time, as in the example in Fig. 2. Soon after the end of the saccade the enhancement velocity usually crossed zero (ZC), indicating that the postsaccadic vergence velocity decreased below the estimated smooth vergence velocity that would be observed if no saccade had occurred. This point was considered the end of the enhancement $E_{OFF}$. In the few cases that a zero crossing was not observed, the end of the enhancement was the end of the vergence response. Using a two-point backward trapezoidal integration $\int \frac{1}{2} \left[ f_{n} + f_{n-1} \right] \times (t_n - t_{n-1})$ on the enhancement velocity, we computed the enhancement area (EA), i.e., the area

![Fig. 2. Quantification of the oculomotor response. Figure shows an example of the temporal development of a convergence response combined with a rightward saccade and the points at which measurements were taken. Right: same data as those on left with a 4-fold expansion of the timescale for a better identification of the central events. Top (A): eye position records. Middle (B): eye velocity records. Bottom (C): vergence velocity records. Traces: HL, horizontal left eye position; HR, horizontal right eye position; H, horizontal version position; V, vertical version position; VG, vergence position; SE, smooth vergence estimate; E, enhancement estimate. Dots above the symbols indicate velocity. Same color pattern is used for both position and velocity traces. Events: $V_{GONS}$, onset of the vergence response; $V_{GOFF}$, offset of the vergence response; $S_{ONS}$, onset of the saccade; $S_{OFF}$, offset of the saccade; $P_{YPK}$, peak of the saccade Pythagorean velocity; $V_{GPK}$, peak of the saccade–vergence velocity. $E_{ONS}$, onset of the vergence enhancement; $E_{OFF}$, offset of the vergence enhancement, usually identified by the zero-crossing of the vergence velocity enhancement $ZC$; $E_{PK}$, peak velocity of the enhancement; $E_{V_{GPK}}$, value of the vergence velocity enhancement at the time of the peak of the saccade-related vergence velocity; $SE_{V_{GPK}}$, value of the smooth vergence velocity estimate at the time of the peak of the saccade-related vergence velocity; $E_{PKLAG}$, time of peak enhancement velocity relative to saccadic onset. Thick gray horizontal line (bottom left) indicates the presaccadic smooth vergence period ($S_{ONS} - V_{GONS}$), which duration was termed “vergence lead.” Area of the enhancement (with sign) between $E_{ONS}$ and $E_{OFF}$ is the enhancement area EA. Trial parameters: rightward saccade during vergence from animal 71 with total vergence change 11.5°, horizontal size 6.3°, and vertical size $-0.5^\circ$.](JNeurophysiol_Vol_94_October_2005_Fig_2.png)

(J Neurophysiol • Vol. 94 • October 2005 • www.jn.org)
covered by the enhancement velocity (E) within the interval \( E_{\text{OFF}} - E_{\text{ONS}} \).

**RESULTS**

**Saccade-related vergence transients and vergence enhancement**

Conjugate saccades—where no change in depth is required—are often characterized by intrasaccadic transient vergence changes, typically a transient divergence followed by a compensatory convergence (Collewijn et al. 1988a,b; Maxwell and King 1992; Sylvestre et al. 2002). Do such transients interact with vergence enhancement? Figure 3A, which shows a single saccade with convergence for animal X01 with a very short vergence lead (11 ms), suggests that this could indeed be the case when the vergence lead is too short to allow a sufficient development of the enhancement to overcome the divergence transient. With slightly longer vergence leads, as shown in Fig. 3B, the transient divergence quickly disappears. To analyze these effects, we compared the amplitude of the saccade-related negative vergence peak for saccades during convergence (npk, indicated by the arrows in Fig. 3) with those of conjugate saccades with similar directions, peak Pythagorean velocities and similar static vergence angles, i.e., “far” conjugate saccades. Transient divergence tended to be slightly larger when the animal was converged and so the two conjugate data sets were kept separate for these comparisons. For both conjugate and disconjugate saccades the saccade-related negative peak of vergence velocity (npk) was defined as the minimum value reached by the vergence velocity in the interval starting 20 ms before saccadic onset and ending 20 ms after saccadic offset and can therefore have positive values during saccades with convergence.

If there were no true saccade-related negative peak (i.e., the initial divergence was cancelled by the enhanced convergence), the algorithm would pick the lowest positive value in that interval, as in Fig. 3B. This is not the case for conjugate saccades, where nearly all saccades had a biphasic wave in the vergence velocity with a negative half-wave followed by a positive half-wave. Similarly, the saccade-related positive peak vergence velocity (ppk) was defined as the maximum value

![FIG. 3. Effects of saccade-related transient divergence on vergence enhancement. A: single trial from animal X01 with a short vergence lead (11 ms). B: similar trial with a slightly longer vergence lead (23 ms). Both trials are rightward saccades (~6° horizontal version with ~10° convergence). Format and abbreviations are the same as those in Fig. 2. Initial divergence transient in A is masked by the ongoing convergence in the trial with slightly longer vergence lead (B). Arrows indicate the saccade-related negative vergence peak (npk) of the trial, which is defined as the minimum value in the vergence velocity observed in the interval starting 20 ms before saccadic onset and 20 ms after saccadic offset.](http://jn.physiology.org/)

![FIG. 4. Saccade-related transient vergence as a function of vergence lead and peak saccadic velocity. A1 and B1: animal X01’s peak values of the initial divergence transient, i.e., npk, for rightward (A1) and downward (B1) saccades with convergence as a function of vergence lead. This is a quantitative demonstration of the effect described in Fig. 3. However, larger, faster saccades tended to have shorter vergence leads, so A2 and B2 plot the same data as a function of saccadic peak velocity. The two variables, vergence lead and saccadic peak velocity, have virtually the same relationship to the divergence transient. A3 and B3: peak values of the positive (gray dots labeled ppk) and negative (black dots labeled npk) vergence transients associated with the conjugate “far” rightward (A3) and downward (B3) saccades from the same animal. Reverse-contrast solid lines are second-order polynomial fits. Because a similar pattern is seen with both saccades with vergence and conjugate saccades (which have no vergence lead), this indicates that, in the general case, the magnitude of the saccadic transients is a function of saccadic peak velocity and, when not masked by the convergence enhancement, has a comparable amplitude. Npk is defined as the minimum value in the vergence velocity observed in the interval starting 20 ms before saccadic onset and 20 ms after saccadic offset, whereas ppk is defined as the maximum value in the vergence velocity observed in the interval starting 20 ms before saccadic onset and 20 ms after saccadic offset.](http://jn.physiology.org/)
reached by the vergence velocity in the interval starting 20 ms before saccadic onset and ending 20 ms after saccadic offset. For divergence–saccade trials ppk may be negative. Figure 4A1 shows the relationship between negative vergence peak and vergence lead for all rightward saccades with convergence in the range 9–13° for animal X01. This animal had the most pronounced negative vergence peaks during convergence as well as the largest conjugate vergence transients. Because we noted that saccades with short vergence leads tended to be the larger, faster saccades, we plotted the same data (Fig. 4A2) against saccadic peak velocity. The similarity between the two plots is quite striking. The negative vergence peak during convergence is larger for faster saccades, which systematically occurred at the shortest vergence leads, making the two variables almost interchangeable. Figure 4A3 shows the saccade-related negative (black dots labeled npk) and positive (gray dots labeled ppk) vergence peaks of the biphasic wave in the vergence velocity trace for all the “far” rightward conjugate saccades for this animal. The main result here is that faster saccades had larger transients, and this was seen for both conjugate saccades, consistent with the report by Sylvestre et al. (2002), and for saccades with convergence. For the rightward conjugate saccades of this animal, the half-waves were largely symmetric and the positive and negative vergence peaks had similar amplitudes.

Vertical saccades also generated (horizontal) vergence transients, as can be seen, for example, from the saccade-related vergence negative peaks for the downward saccades (total vergence changes 9–13°) from the same animal (Fig. 4, B1, B2, and B3). These panels follow the same format as the left panels. The saccade-related negative vergence peak during convergence for downward saccades (Fig. 4, B1 and B2) was smaller than that for the rightward saccades (Fig. 4, A1 and A2), but the downward “far” conjugate saccades also had comparable smaller transients (compare Fig. 4A3 with 4B3). The reversed-contrast lines in Fig. 4, A3 and B3 are second-order polynomial fits of the data. The similarities in the trends strongly suggest that the negative vergence transients that appear in the saccades during convergence at the shortest vergence leads are generated by the same mechanism that is responsible for the transient divergence in the conjugate saccades. The most important conclusion is that, at least qualitatively, the divergence transients observed during the saccades with convergence, when not masked by the convergence enhancement, are comparable to the transients observed during conjugate saccades. Therefore we considered it reasonable to use the conjugate negative and positive vergence transient measures (conjugate npk and ppk values) as estimates of the contribution of the vergence transients to the vergence enhancement for the saccades during vergence. Transients were highly idiosyncratic between animals and, within each animal, with direction, and often quite small. Nonetheless, as evident in Fig. 3A, these transients, when large, would have measurable effects in the estimation of the latency of vergence enhancement and its overall temporal development.

Latency of vergence velocity enhancement with respect to saccadic onset

Although some OPN cells are modulated by vergence velocity, there is very little overall change in the average timing between pause onset and cyclopean saccadic onset (Busettni and Mays 2003) for saccades during vergence with respect to conjugate saccades. If the vergence enhancement were caused by the release of an inhibition on the CB1* cells associated with the OPN pause, we would expect a strong link between cyclopean saccadic onset and enhancement onset. To have a sufficiently robust estimate of the latency of the enhancement, measures were made only on convergence–saccade trials with (positive) peak enhancement velocity >50°/s and on divergence–saccade trials with (negative) peak enhancement velocity <−50°/s. For convergence, as expected by the interaction between divergence transients and enhancement, there was a strong trend for faster, larger saccades to have delayed enhancement onsets. The increase in enhancement latency with saccadic peak velocity was significant (P < 0.01) in 13 of the 16 convergence data sets [slope range −0.001 ms/(°/s) to 0.023 ms/(°/s)], with no evident directional trend. For divergence, six data sets showed a significant reduction in enhancement latency with peak saccadic velocity, consistent with a synergy between the divergence transient and the divergence enhancement. Four data sets showed a significant increase, and six data sets showed no significant changes, with slope ranges from −0.011 to 0.014 ms/(°/s). Again, there was no evident directional trend.

For a direct comparison of the enhancement latencies for different animals and directions, we computed the mean value of the enhancement latency for each of the 32 restricted (in terms of peak enhancement) data sets after an additional restriction of the saccadic peak velocity to values between 200 and 400°/s. Saccades in this range of peak velocities show robust vergence enhancement but relatively small divergence transients (Fig. 4). Within each animal’s data set and each vergence direction, there were no consistent differences in enhancement latency for the four saccadic directions. Furthermore, there was no statistical difference between the convergence and divergence overall averages. The average value of the enhancement latency averages for the 16 convergence data sets was 3.5 ms (SD ± 4.2 ms; range from −2.5 to 10.3 ms) and for the 16 divergence data sets was 2.9 ms (SD ± 2.7 ms; range from −0.2 to 10.3 ms).

The latency data strongly suggest a tight linkage between the occurrence of the saccade, irrespective of saccadic direction, and the vergence enhancement, which is also consistent with a linkage to the OPN pause during the saccade.

Role of saccade–vergence timing in vergence enhancement

The Multiply Model predicts that the degree of enhancement should directly depend on the timing of the saccade with respect to the ongoing firing profile of the vergence burst cells (FR in Fig. 1). Figure 5 shows saccade-related peak vergence velocity VGpk as a function of vergence lead for vertical saccades. Because the firing of the vergence burst cells is linearly related to the total vergence change (Mays et al. 1986), the range of total vergence change (Fig. 5, A and B) was restricted to 9 to 13°, and the range of total divergence change (Fig. 5, C and D) was restricted to −9 to −13° to better illustrate the temporal development of the smooth response. Red points represent the saccade-related peak vergence velocity VGpk for saccades with peak Pythagorean velocity in the range 50–250°/s, green points are for saccades with range
250–500°/s, and blue points are for saccades with peak Pythagorean velocity >500°/s. Black points represent the values of the smooth vergence velocity estimates at the time of the occurrence of the saccade-related peak vergence velocity ($\mathbf{SE}_{\mathbf{VGPK}}$ in Fig. 2). The vertical distances between the black points and the red, green, and blue points are the degree of enhancement of peak vergence velocity associated with saccades at the time of the saccade-related peak vergence velocity ($\mathbf{VG}_{\mathbf{PK}}$). Red dots represent the saccade-related peak vergence velocity ($\mathbf{VG}_{\mathbf{PK}}$) for saccades with peak Pythagorean velocity ($\mathbf{PY}_{\mathbf{PK}}$) in the range 50–250°/s, green dots are for saccades with range 250–500°/s, and blue dots are for saccades with peak Pythagorean velocity above 500°/s. Vertical gray stripes identify the restricted vergence lead ranges used in the associated subplots of saccade-related peak vergence velocity ($\mathbf{VG}_{\mathbf{PK}}$) as a function of peak saccadic velocity ($\mathbf{PY}_{\mathbf{PK}}$) and saccadic duration. Continuous lines in the $\mathbf{VG}_{\mathbf{PK}}$ as a function of $\mathbf{PY}_{\mathbf{PK}}$ subplots are second-order polynomial fits of the amplitudes of same-direction vergence transients of the conjugate saccades in the same cyclopean direction and with similar static vergence. Gray bands were at 65–75 ms for $\text{A}$, 40–50 ms for $\text{B}$, 95–115 ms for $\text{C}$, and 65–75 ms for $\text{D}$. As expected from the Multiply Model, vergence enhancement has a dependency on vergence lead that mirrors the development of the smooth vergence estimate with vergence lead. Nonetheless, there is an evident additional dependency on saccadic dynamics which cannot be explained as an indirect dependency on saccadic duration or to the modulation with saccadic dynamics of the vergence transients. This is incompatible with the Multiply Model.

**Role of saccadic dynamics in vergence enhancement: vertical saccades**

Saccades follow what has been called the “main sequence” (Becker 1989) that refers to the observation that there is a monotonic relationship between saccadic size and saccadic peak velocity. There was a clear tendency, evident in Fig. 5, for faster, and thus larger, saccades to show a greater degree of vergence enhancement than smaller, slower saccades for the same vergence lead. To examine the role of saccadic dynamics without the effects of vergence lead, we restricted vergence lead to narrow (10 ms in Fig. 5, $\text{A}$, $\text{B}$, and $\text{D}$; 20 ms in $\text{C}$) movements (black points). This variability could arise if saccadic dynamics were to play a role in the saccade–vergence interaction.
ranges centered around the areas of maximum scatter, identified as vertical gray bands in the figure, and plotted the peak vergence velocity of these subsets against saccadic peak velocity and saccadic duration (Fig. 5, subplots). These subplots show that, for the same level of CB1 firing, peak vergence velocity was positively correlated with saccadic peak velocity but not with saccadic duration, as evident from the $R^2$ and $t$-values of the linear regressions of the data in the subplots. The often robust positive correlation between peak saccadic velocity and peak vergence velocity and the lack of—or even negative—correlation with saccadic duration, which is correlated with the pause duration of the OPNs (Busettini and Mays 2003), are not consistent with the Multiply Model. Because of the very limited scatter of the smooth vergence velocity estimates inside the bands with respect to the scatter of the saccade-related peak vergence velocity, it is clear that this dependency with saccadic dynamics is encoded in the enhancement peak velocity $E_{\text{PK}}$.

One potentially confounding variable is the saccade-related transient vergence. As illustrated in Fig. 4, both negative and positive transients increase with saccadic peak velocity. Is this dependency responsible for the modulation of vergence velocity with saccadic peak velocity illustrated in the subplots? The solid curves in the subplots of Fig. 5 are second-order polynomial fits of the peaks of the same-direction half-waves of the transient vergence of the downward conjugate saccades with similar peak velocity and initial static vergence, i.e., conjugate “far” ppk values for convergence sets and conjugate “near” npk values for divergence sets. These curves are calculated in the same way as the curves shown in Fig. 4, A3 and B3. They show that the transient vergence is far too small to be the source of the modulation of vergence velocity with saccadic peak velocity, even in the unlikely event that they sum in phase with the enhancement peak proper. The saccade-related transient vergence oscillations contribute very little to the overall vergence enhancement for vertical saccades and cannot account for the observed dependency with saccadic dynamics.

Role of saccadic dynamics in vergence enhancement: horizontal saccades

One of the primary reasons for studying the effects of vertical saccades on vergence movements is to minimize any mechanical and/or neuronal interactions (e.g., nonlinear saturation) between horizontal vergence and horizontal saccades. With the exception of these hypothetical interactions, the Multiply hypothesis predicts that horizontal saccades should have the same effects on vergence as vertical saccades. Figure 6 shows the relationship between vergence lead and saccade-related peak vergence velocity $V_{\text{PK}}$ for leftward saccades. The format of Fig. 6 and the ranges of total vergence changes are the same as those of Fig. 5. As with vertical saccades: 1) vergence lead was a major factor in determining vergence enhancement; 2) when vergence lead was restricted to narrow (10-ms) bands to examine the role of saccadic velocity and duration in the determination of the vergence enhancement for similar CB1 firing values, there was a positive correlation between peak saccadic velocity and saccade-related peak vergence velocity within each band, but peak vergence velocity was uncorrelated with saccadic duration; and 3) the increases in transient vergence with peak saccadic velocity did not appear to be large enough to account for the increase in peak vergence velocity associated with faster horizontal saccades. The similarities between Figs. 5 and 6 are quite remarkable, suggesting that the mechanism underlying vergence enhancement is the same for both horizontal and vertical saccades and both require the involvement of a saccadic signal encoding saccadic dynamics.

Systematic variation of vergence and saccadic latencies with saccadic size

Figures 4, 5, and 6 suggest that larger, higher-velocity saccades show a very strong tendency to have shorter vergence leads than smaller, slower saccades. This could be explained by a systematic decrease in saccadic latency and/or an increase in vergence latency with saccadic size, directly related to target eccentricity. To examine these possibilities, the latencies with respect to target onset of the conjugate saccades, (primary) saccades with vergence (including saccades with vergence lead <5 ms), and vergence were plotted with respect to the cyclopean saccade size as averages inside saccade size bins $3^\circ$ wide. The average latency of smooth saccade-free symmetrical vergence was also computed. The saccadic latency values with respect to target onset are shown in Fig. 7A (convergence trials in black and “far” conjugate trials in gray) and Fig. 7B (divergence trials in black and “near” conjugate trials in gray) for the downward saccades of animal X01 with total vergence change in the $9–13^\circ$ range. Smaller conjugate saccades (gray bars) tended to have longer latencies and more scatter than medium-size conjugate saccades, as previously observed by Bell et al. (2000). For both convergence (Fig. 7A) and divergence (Fig. 7B), saccadic latency was longer (black bars) than for similar size conjugate saccades, especially for small saccades and divergence. This is consistent with the report by Honda and Findlay (1992) that, in humans, saccades to targets in different depth planes have longer latencies. Where the latency effects were significant, a single exponential characterized the latency of the saccades with vergence as function of saccadic size (average space constant 6.3 ms/°; SD $\pm$3.1 ms/°; 25/32 sets). The shorter saccadic latencies appeared to be largely responsible for the shorter vergence lead times associated with larger, faster saccades. This effect was enhanced by a roughly linear increase in vergence latency with larger saccades, especially for convergence (Fig. 7C). 5 indicates the latency of the smooth symmetric vergence for the same $9–13^\circ$ range. For divergence, as in the case illustrated in Fig. 7D, the effects were often not significant.

The bottom four panels provide an overall view of the saccadic and vergence effects averaged across all animals for convergence and divergence in the $9–13^\circ$ range (5–9° range for animal 941). Figure 7E (convergence) and 7F (divergence) show the overall averages, for each saccadic size bin, of the 16 (four animals $\times$ four saccadic directions) average percentage variations in latency of the saccades with vergence with respect to the conjugate saccades of similar size. Figure 7G (convergence) and 7H (divergence) show the overall averages, for each saccadic size bin, of the 16 average percentage variations in latency of the vergence with saccades with respect to the smooth saccade-free symmetric vergence. With normalization, the exponential patterns of the conjugate and disconjugate sets compensated for each other, with the exponentials collapsing...
to a linear trend (convergence: intercept 34.6%, slope $-1.5\%$°, $P < 0.01$; divergence: intercept 52.5%, slope $-3.3\%$°, $P < 0.01$). The increase in vergence latency with saccadic size was linear over the entire range for convergence (Fig. 8G) and more robust than that for divergence (Fig. 8H), where it peaked at the 9–12° bin and was more variable (convergence: intercept 1.7%, slope 1.1%/°, $P < 0.01$; divergence: intercept 0.6%, slope 0.7%/°, $P < 0.01$). Some of the decrease of the vergence latency for larger saccades with divergence is likely the result of the divergence transient associated with the saccade masking the delayed onset of the vergence response proper. The vergence and saccadic variability in latency with saccadic size (linked to target eccentricity) was strong and very consistent, causing smaller, slower saccades to occur later in the vergence movement and larger, faster saccades to occur earlier, for all animals, saccadic directions, and vergence directions. Moreover, when the total vergence change was $<9–13$°, the smaller saccades tended to occur earlier, gradually overlapping the latencies of the conjugate data sets. Saccadic onset and vergence onset are not time locked with each other. Indeed, saccadic and vergence latencies tend to go in opposite directions as a function of saccadic size.

**Vergence enhancement and OPN timing**

If the OPN pause initiates vergence enhancement, then the end of the pause (PE in Fig. 8) should be associated with the start of the decline in enhancement velocity ($E_{PK}$). A recent examination of OPN activity for saccades with and without vergence (Busettini and Mays 2003) indicated that average OPN activity for conjugate and disconjugate saccades resumes
0.25 + 0.85 \times \text{saccadic duration (ms)} \text{ after saccadic onset } S_{\text{ONS}} \text{ (interval } P_{\text{ELAG}} \text{ in Fig. 8). The minimum average trigger lead for the OPN pause (the interval between the latest possible presaccadic spike, indicated as } P_{\text{TR}} \text{ in Fig. 8, and saccadic onset } S_{\text{ONS}} \text{) was also conservatively estimated to be 4.1 ms. If we therefore assume that no change in OPN activity can have any effect on eye movements in } \leq 4.1 \text{ ms, vergence enhancement declines (interval } E_{\text{PKLAG}} \text{ in Fig. 8) which begin before the time given by } 4.1 + 0.25 + 0.85 \times \text{saccadic duration (in ms)} \text{ cannot be linked to pause end (interval } P_{\text{ELAG}^*} \text{ in Fig. 8). As evident in Fig. 1, bottom right, if the OPN pause occurs during the decaying phase of the CB1 firing (examples } D \text{ and } E, \text{ it is possible that the peak of the enhancement may occur before the end of the OPN pause simply because the CB1 signal, per se, is higher at the beginning of the OPN pause than near its end. To eliminate this confounding possibility, in Fig. 8 are reported only trials in which the estimated end of the OPN pause (PE) occurred before the peak of the estimated smooth vergence velocity } SE, \text{ i.e., only when the OPN pause occurred during the acceleration phase of the CB1 firing. The vast majority of intervals } E_{\text{PKLAG}} \text{ (black dots) are shorter than the estimated } P_{\text{ELAG}^*} \text{ (dashed gray line), indicating that the peak enhancement velocity in these trials occurred before the estimated end of the OPN pause. Thus the evidence does not support a link between OPN firing profile and vergence enhancement profile, providing an additional argument against the Multiply Model.}

\text{Vergence enhancement has a saccadic-like main sequence}

The results illustrated so far, although often unsupportive of the Multiply hypothesis, are all compatible with the idea that vergence enhancement is an interaction between a smooth vergence-related signal and a saccadic burst. One property of saccades is the correlation between (cyclopean) size and peak velocity (Becker 1989), called the “main sequence.” If the vergence interaction with the saccadic burst is a linear scaling, we expect to find a strong relationship between enhancement peak velocity and enhancement area. The top half of Fig. 9 shows the enhancement main sequence (gray dots labeled E) for downward saccades during convergence in animal X01 (Fig. 9A), during convergence in animal 21 (Fig. 9B), during divergence in animal X01 (Fig. 9C), and during divergence in animal 21 (Fig. 9D). The black dots labeled SV are the smooth vergence main sequence of that animal for the corresponding data sets. Linear regressions of the means are reported as continuous lines.

\text{FIG. 7. Saccadic and vergence latency variability with (saccadic) eccentricity. A: average saccadic latencies from target onset for all downward primary saccades for animal X01 for convergence in the range 9 to 13° (black) and for all downward primary “far” conjugate saccades (gray). B: average saccadic latencies for all downward primary saccades for animal X01 for divergence in the range −9 to −13° (black) and for all downward primary “near” conjugate saccades (gray). Data are parsed into 3° saccadic size bins. Vertical lines indicate SDs. Continuous lines: single exponential fits of the means inside each saccadic bin. Smaller conjugate saccades tended to have longer latencies and more scatter than larger-size conjugate saccades. This effect was greater for saccades with vergence. C (convergence) and D (divergence): vergence latencies from target onset as a function of saccadic size for the same data sets. Bars labeled S indicate the average latency of the smooth vergence with no saccades (i.e., no eccentricity) for the same range and direction of total vergence change. There was a roughly linear increase in vergence onset latency associated with larger saccadic size, especially for convergence. This was not always true for divergence, as in the case in D, E, and F: average percentage change in saccadic latency among all animals and saccadic directions for convergence (E) and divergence (F) in the 9–13° range (5–9° range for animal 941). Bars represent the average percentage increase in latency of the saccades with vergence with respect to their corresponding conjugate data sets. Linear regressions of the means are reported as continuous lines. G (convergence) and H (divergence): average percentage increase in latency of the vergence with saccades with respect to the corresponding (smooth) vergence with no saccades (i.e., no eccentricity). Overall increase in vergence latency with saccadic size was linear in the entire range for convergence and more robust than for divergence, where it peaked at the 9–12° bin.
vergence direction, i.e., the dependency of smooth saccade-free peak vergence velocity with total vergence change. The black dots labeled CS define the saccadic main sequence of that animal for the conjugate saccades in the same direction and with similar static vergence: “far” for convergence and “near” for divergence. The presence of a main sequence for the enhancement was quite clear, but the scatter of the enhancement main sequence was often larger than that of either the smooth vergence or the conjugate saccadic main sequence. This scatter was often more pronounced for horizontal saccades, as evident in the bottom half of Fig. 9, which illustrates the data for rightward saccades in the same sequence of panels. Might this scatter be a reflection of the cyclopean metrics of the associated saccades not following the conjugate main sequence? It is known that horizontal saccades during vergence are often slower than conjugate saccades of similar amplitude (Collewijn et al. 1995). For vertical saccades this seems to be less evident (van Leeuwen et al. 1998).

Figure 10 suggests that this may be the case. The cyclopean main sequence of the rightward saccades during convergence for animal X01 (Fig. 10A1, black dots) shows a much larger scatter than the (cyclopean) conjugate main sequence (i.e., with no associated vergence changes; Fig. 10A2, gray dots). This affects the associated enhancement main sequence (Fig. 10A2) and a qualitative analysis of the scatter shows that the areas of largest variability are related to the same trials for both plots (arrows). The animal (21) showing the smallest scatter in the enhancement main sequence for rightward saccades during convergence (Fig. 10B2) had also the smallest variability in the saccadic main sequence with respect to the conjugate main sequence (Fig. 10B1). For divergence, all animals, including X01, showed less dynamical variability in the cyclopean main sequence during vergence but, when present, as in the case of the rightward saccades of animal X01, the largest deviations in saccadic dynamics (Fig. 10C1) also corresponded to the largest deviations in the enhancement main sequence (Fig. 10C2). Animal 21 had also the smallest dynamical variability of the rightward saccadic main sequence during divergence (Fig. 10D1) and of the enhancement main sequence (Fig. 10D2) as well.

If the scatter of the enhancement main sequence is functionally related to a dynamical dissociation between size and dynamics of the originating saccades, we expect the scatter to be related, at least in part, to the amount of the dissociation. In fact, for a given enhancement area, the scatter in the enhancement peak velocity $E_{PK}$ was found to be correlated with saccadic peak velocity, i.e., for enhancements of similar areas, faster saccades generated faster enhancements. We therefore quantified the enhancement main sequence as a double-linear correlation, with a constant, of $E_{PK}$ with the enhancement area and the cyclopean peak velocity of the associated saccade (Table 1). The constant $I$ was small and highly variable and simply represented a (small) rotation of the linear regression if the data presented some saturation for the largest enhancement areas, as in the cases in Fig. 9, D and H. This was a minor effect because the addition of a quadratic term in $EA$ did not significantly improve the overall $R^2$.

The most remarkable result was the constancy of $M$ between animals and saccadic directions. For convergence, its average value was $33.7 \, \text{s}^{-1}$ (SD $\pm 4.7 \, \text{s}^{-1}$; range 23.0 to 41.5 $\text{s}^{-1}$). For divergence, its average value was $25.0 \, \text{s}^{-1}$ (SD $\pm 4.0 \, \text{s}^{-1}$;...
al. 1997). Nonetheless, there was no significant correlation between the slope of the smooth vergence-related signal and the (cyclopean) saccadic burst. The interaction between a smooth vergence-related signal and the saccadic burst, vergence enhancement being the result of a linear interaction between a smooth vergence-related signal and the (cyclopean) saccadic burst.

**DISCUSSION**

**Saccadic parameters and vergence enhancement**

The primary goal of this study was to test several predictions of the Multiply Model under a wide range of saccadic and vergence conditions. The most critical prediction was that the peak of the vergence enhancement velocity should not be influenced by saccadic metrics, with the exclusion of a possible decrease for very short saccadic durations. This prediction was not confirmed. The effects of saccadic dynamics on vergence velocity can be readily seen in the subplots in Figs. 5 and 6. Maxwell and King (1992) showed a positive correlation between peak saccadic speed (velocity) and peak vergence speed for saccades of several sizes but these authors did not attempt to account for the effects of vergence lead. Given the potent range 16.7 to 31.3 s⁻¹). The values of M for divergence were significantly lower than the values for convergence (paired t-test, P < 0.01) and this might be consistent with the observation that smooth divergence is, in humans, dynamically slower than convergence (Hung et al. 1997). Nonetheless, there was no significant correlation between the slope of the smooth saccade-free vergence peak-velocity/size main sequence and the M value. The contribution of the term C, associated with peak saccadic velocity, was often important and significant (P < 0.01) in 29/31 cases. Faster saccades generate slightly faster enhancements than predicted by the enhancement area alone. With the saccadic dynamics correction, the predictive power of the modified enhancement main sequence was very high, with an average R² of 0.90 for convergence and 0.87 for divergence (columns E).

For comparison, in Table 1 are reported also the R² of a quadratic fit, with constant, of the cyclopean main sequence of the associated saccades, i.e., during vergence (columns S) and of the conjugate saccades with the same direction and static vergence level (columns Co). There was no direct correlation between the importance of the term C and the quality of the associated saccadic main sequence. Animal 941, for example, had the saccadic main sequences with the largest scatter in saccadic peak velocity among our animals for all saccades, but often showed narrow enhancement main sequences and with small values for C. Nonetheless, strong divergence transients during convergence–saccade trials, associated with a negative contribution to the enhancement area, would also increase the scatter in the enhancement main sequence, as in the trials indicated by the arrows in Fig. 9, A and E. Nevertheless, a narrow (scattered) enhancement main sequence was often associated with a narrow (scattered) saccadic main sequence. The R² values of the saccadic main sequences for disconjugate saccades (columns S), for both horizontal and vertical saccades, were usually worse than the R² values of the conjugate saccades (columns Co). The effects were smaller for divergence than for convergence but the increased scatter was statistically significant (paired t-test of the S and Co columns; P < 0.01) for both convergence and divergence, confirming that saccades during vergence have, in general, a higher variability in their main sequences. These results further reinforce the hypothesis that the vergence enhancement is a linear interaction between a smooth vergence-related signal and the cyclopean saccadic burst.
The only restrictions on the data sets are a verge lead of at least 5 ms and that the saccade be a primary saccade to estimate SE and thus by subtraction, the enhancement profile $E$, $I$, $M$, and $C$: parameter estimates of the double-linear correlation with constant of $E_{pk}$ in $EA$ and $PY_{pk}$ with (in parentheses) the associated 95% Wald confidence intervals (Systat). The $R^2$ labeled $P$ are the $R^2$ observed versus predicted measure for the enhancement main sequence. The $R^2$ labeled $S$ are the $R^2$ of the associated cyclopean saccadic main sequence and the $R^2$ labeled Co are the $R^2$ of the main sequence of the conjugate saccades with same direction and static verge. The saccadic main sequences were fitted using a quadratic function in saccadic size with a constant (Becker 1989). The last four rows report the averages, SD, and ranges of each parameter and $R^2$ for the 16 convergence and 16 divergence data sets, respectively. Vergence enhancement has a saccadic-like peak-velocity/size main sequence, which we interpret as evidence for the involvement of signals encoding saccadic dynamics in its generation. The presence of a significant term $C$ indicates that faster saccades generate faster verge enhancements for similar enhancement sizes. Number of trials in each of the 32 data sets is >170.

**Saccade–vergence timing**

As suggested by the Multiply Model, the timing of the saccade relative to verge onset (vergence lead) proved to be an important variable in determining the degree of verge enhancement. Honda and Findlay (1992) reported that saccades involved in changes in depth in humans had longer latencies. A surprising finding of our study was that when the

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<td>X01 u</td>
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<td>$36.7$ ($\pm 1.0$)</td>
<td>$29$ ($\pm 6$)</td>
</tr>
<tr>
<td>X01 l</td>
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<td>$78$ ($\pm 8$)</td>
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<tr>
<td>X01 r</td>
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<td>$158$ ($\pm 7$)</td>
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<tr>
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<td>$26$ ($\pm 8$)</td>
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<tr>
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<td>$41.5$ ($\pm 0.7$)</td>
<td>$38$ ($\pm 5$)</td>
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<tr>
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<td>$31.8$ ($\pm 0.6$)</td>
<td>$51$ ($\pm 6$)</td>
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<tr>
<td>71 d</td>
<td>$3.8$ ($\pm 2.1$)</td>
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<td>$27$ ($\pm 5$)</td>
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<tr>
<td>71 u</td>
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</tr>
<tr>
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<td>$101$ ($\pm 7$)</td>
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<tr>
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<tr>
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<td>941 u</td>
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</tr>
<tr>
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<tr>
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<tr>
<td>MAX</td>
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<td>$41.5$</td>
<td>$158$</td>
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FIG. 10. Saccadic and enhancement main sequence variability. A1: superposition of the cyclopean main sequence of the rightward saccades of animal X01 during convergence (black dots) and the (cyclopean) main sequence for “far” rightward conjugate saccades, i.e., with no associated verge changes (gray dots). A2: enhancement main sequence for the same rightward saccades of animal X01 during convergence trials in A1. B1 and B2: 21 rightward saccades and convergence. C1 and C2: X01 rightward saccades and divergence. D1 and D2: 21 rightward saccades and divergence. There appears to be a correlation between the scatter in the saccadic main sequence during vergence and the scatter in the associated enhancement main sequence. Arrows show areas of related variability between the saccadic main sequence and the enhancement main sequence.
timing of the target presentation and the location of the targets were unpredictable, larger saccades were associated with shorter vergence leads. This was attributed to the combined effects of two tendencies (Fig. 7): the larger the saccade (i.e., more eccentric the target), the shorter the saccadic latency and the longer the vergence latency. This indicates that the mechanisms responsible for triggering the onset of the saccade and the vergence movement are not directly linked to each other, responding to changes in saccade size, related to target eccentricity, with opposite polarities.

Despite its importance in determining the extent of the interaction between saccades and vergence, the timing of saccades relative to vergence has never been systematically studied. Several studies (Ono et al. 1978a,b; Oohira 1993) investigated only a limited range of saccadic and vergence sizes, a situation that would not generate a wide range of vergence leads. Zee et al. (1992) looked at a range of saccadic and vergence sizes in their study of these interactions in humans, but did not investigate the influence of saccade–vergence timing. In the most systematic study of saccade–vergence interactions to date, Collewijn et al. (1997) noted, in humans, that presaccadic vergence movements occurred mainly in the interval about 100 ms before saccadic onset, but did see presaccadic vergence ≤200 ms before the saccade. Their observations regarding presaccadic vergence are consistent with our findings. There was a major difference, however. In the Collewijn et al. (1997) study, targets were continuously visible to the human subjects, whereas in our study they were not and their presentation was randomized in time and space. Although Collewijn and colleagues did not investigate vergence lead as a variable per se, they noted that the amount of presaccadic vergence increased for larger vergence demands, and also increased for smaller version (i.e., saccadic) demands. These findings are consistent with our observations that larger saccades are associated with shorter vergence leads, if one assumes that shorter vergence leads provide less time for the buildup of presaccadic vergence.

Our study also provides the first quantitative measures relating the onset of vergence enhancement to the onset of the associated saccade. By carefully estimating the smooth vergence movement that likely would have occurred if there had been no saccade, we were able to estimate the onset of the enhanced vergence and its peak. We found that enhancement onset is tightly linked to saccadic onset.

The role of saccade-related vergence transients

Collewijn and colleagues observed a transient divergence–convergence movement of the eyes associated with conjugate horizontal saccades (Collewijn et al. 1988a) as well as with conjugate vertical saccades (Collewijn et al. 1988b) in humans. Later, these same authors (Collewijn et al. 1995) noted that the magnitude of the initial divergence velocity increased as a function of saccadic size, at least ≤40°. Maxwell and King (1992) observed the same phenomenon in monkeys and, more recently, Sylvestre et al. (2002), also in the monkey, found a linear relationship between transient vergence velocity and peak saccadic velocity. Our results are in general agreement, except that we saw a monotonic but curvilinear relationship between divergent and convergent peak velocity and peak saccadic velocity (Fig. 4, A3 and B3). The magnitude of the saccade-related vergence transient was consistently smaller for vertical saccades (Fig. 4B3) than for horizontal saccades (Fig. 4A3). We also found a very similar initial divergent velocity effect for saccades with convergence (Fig. 4, A2 and B2). The subplots in Figs. 5 and 6 compare the magnitude of the observed saccade-related peak vergence velocity with the magnitude of the same-direction transient vergence of the conjugate saccades in the same direction and with similar static vergence. Although the vergence transients might contribute to the overall peak vergence velocities, they appear to account for a very small fraction of the response. This conclusion is essentially the same as that reached by Maxwell and King (1992).

Rejection of the OPN Multiply hypothesis

Although some of our observations are consistent with the OPN Multiply hypothesis, the influence of saccadic velocity on enhancement and the existence of a saccadic-like enhancement main sequence are not. One possible way, consistent with the Multiply Model, in which saccadic parameters could influence the peak of the vergence enhancement is if very short duration saccades result in such brief OPN cessations that the vergence enhancement signal lacks the time to fully develop. If this were the case, we might expect to see a positive correlation between vergence enhancement and saccadic duration, especially when very small saccades are included. Instead, the subplots in Figs. 5 and 6 show that the effect of saccadic duration, when present, was in the wrong direction because the longest and slowest saccades had lower enhancement peaks. The modulation with saccadic peak velocity is therefore an independent effect and not a consequence of the covariability of saccadic size, peak velocity, and duration, known to exist for conjugate saccades. Although the acceleration of vergence enhancement was clearly associated with saccadic onset, which is causally linked with the onset of the OPN pause, enhancement deceleration was not. Indeed, the peak of the enhancement often occurred many milliseconds before the point at which OPN activity resumes, indicating that the end of the OPN pause is not responsible for turning off the vergence enhancement. The existence of an enhancement main sequence similar to the saccadic main sequence is the strongest evidence for the involvement of saccadic burst signals in the generation of the vergence enhancement. Based on these observations, we believe that the evidence warrants rejection of the OPN Multiply hypothesis.

APPENDIX: SACCADIC ONSET AND OFFSET ALGORITHM

In determining saccadic onset and offset we faced two major problems: 1) the very large range of saccadic dynamics in our data sets, from saccades with peak Pythagorean velocities as low as 40°/s to >1,000°/s; and 2) the presence, mainly in some saccades during divergence, of random cyclopean pre- and/or postcaccadic drifts. Three examples of saccades of different cyclopean dynamics presenting such drifts are illustrated in Fig. A1, A, B, and C, all from animal X01. The trials in Fig. A1, A, B and C are upward saccades whereas the trial in Fig. A1C is a rightward saccade, all executed inside a divergence movement of 11–12°. The resemblance of the dynamics of this postcaccadic drift to vergence velocity, its presence for both
A first pass of the trials searched for segments with a peak Pythagorean velocity (PY) >40°/s. From the peak point, we identified an “onset” search interval starting 3 ms before the peak Pythagorean velocity and extending 60 ms back in time. Similarly, we identified an “offset” interval starting 3 ms after the peak Pythagorean velocity and lasting 120 ms forward. In the case of another saccade occurring inside the search intervals, the durations of those intervals were reduced to half the distance between the two peaks. The search for the onset and offset was based on a two-segment linear interpolation inside each of the two intervals, identified by the vertical lines in Fig. A1. These interpolations were done on a combined version velocity trace (C) obtained as the sum (with sign) of the horizontal and vertical version velocity. To make the algorithm independent of saccadic direction, the polarities of the two version velocities were adjusted so that the horizontal and vertical main velocity profiles were always positive. One segment had a zero slope with variable y-offset, whereas the second was a linear function with variable slope and the same y-offset of the first segment. The pivot points of the two-segment linear interpolation giving the best square error fits were identified as saccadic onset and offset, respectively. A visual inspection of a large number of saccades showed that this algorithm was very reliable. The algorithm performed well on the few asymmetric saccades that occurred, as defined by Sylvestre et al. (2002), which are characterized by an acceleration plateau, as illustrated in Fig. A1D.

For the determination of enhancement onset, we applied the two-segment linear interpolation to an interval of the enhancement velocity starting 30 ms before a 10°/s velocity threshold time mark and ending 3 ms from enhancement peak. For very large saccades presenting small convergence enhancements and large divergence transients, the algorithm sometimes converged on the divergence transient. As described in RESULTS, the analysis of the latency of the enhancement was done on restricted (in terms of minimum peak enhancement velocity) data sets to minimize this problem.

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