

# Conjugate Ocular Oscillations during Shifts of the Direction and Depth of Visual Fixation

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**PURPOSE.** To characterize dynamic properties of combined saccade-vergence eye movements that occur as the point of visual fixation is shifted between objects lying in different directions and at different depths.

**METHODS.** Using the scleral search-coil technique, eye movements were measured in 10 normal subjects as they made voluntary, disjunctive gaze shifts comprising a range of saccades and vergence movements.

**RESULTS.** By analyzing eye acceleration records, the authors identified small-amplitude (0.2–0.7°), high-frequency (23–33 Hz), conjugate horizontal oscillations of the eyes during the vergence movement that followed the initial saccade. When the shift of the fixation point required a large vergence component (17°), every subject showed these oscillations; they were present in approximately a third of responses. Approximately 5% of responses showed oscillations that had horizontal and vertical components. Oscillations were less prominent with shifts that had smaller vergence components and were absent after saccades made between targets located at optical infinity.

**CONCLUSIONS.** These findings suggest that a common mechanism gates both the saccadic and vergence components of disjunctive gaze shifts, a likely candidate being the pontine omnipause neurons. When a saccade is immediately followed by a prolonged vergence movement, the omnipause neurons remain silent, leading to small-amplitude saccadic oscillations. Shifts in the point of visual fixation that require a large vergence movement may be a useful experimental strategy to induce saccadic oscillations. (*Invest Ophthalmol Vis Sci.* 1999;40:1681–1686)

Clear binocular vision requires that the foveal region of each eye, which contains the highest photoreceptor density, be pointed at the object of interest. Under natural conditions, we frequently shift our point of visual fixation between objects that lie in different directions and at different depths in the environment. The ability to change the line of sight (gaze angle) of each eye voluntarily from one object to another is achieved by two distinct types of eye movements: saccades and vergence.<sup>1</sup>

Voluntary shifts of gaze angle between different objects located at distance is achieved mainly by saccades—rapid movements that carry the eyes in the same direction (versional or conjugate movements). The premotor signals for saccades made in the horizontal plane are generated by burst cells in the reticular formation of the pons, so-called because these neurons give an intense burst of discharge preceding each rapid eye movement.<sup>2–4</sup> The activity of burst neurons is gated by so-called omnipause neurons, which lie in the adjacent nucleus

raphe interpositus and are tonically active except during saccades.<sup>5–7</sup> The high-gain properties of the saccadic system make it prone to development of high-frequency (10–35 Hz) conjugate oscillations of the eyes that become manifest in certain disease states.<sup>8,9</sup>

Voluntary shifts of the line of sight between objects lying at different depths in the environment require vergence movements, during which the eyes rotate in opposite directions (disjunctive rotations). When coupled with conjugate gaze shifts, vergence movements are initiated by midbrain vergence burst neurons,<sup>10</sup> and recent electrophysiological evidence suggests that these cells also are inhibited by omnipause neurons lying in nucleus raphe interpositus.<sup>11</sup> The vergence system is not as high-gain as the saccadic system (e.g., eye accelerations are lower), but vergence oscillations can be induced in certain experimental conditions at frequencies of up to 2.5 Hz.<sup>12</sup>

Most natural shifts of the fixation point are made between objects lying at different gaze angles and depth planes in the visual environment, requiring both saccadic and vergence components. During studies of such combined saccade-vergence movements, we fortuitously found that, during the vergence movement that followed the saccade, conjugate oscillations of the eyes occurred at frequencies indicating that they were saccadic in origin.

## METHODS

### Subjects and Recording Methods

We studied 10 normal subjects (age range 25–51 years; 9 male), all of whom gave informed consent. The study was conducted

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in accordance with the tenets of the Declaration of Helsinki and was approved by our institutional review board.

We measured horizontal and vertical eye movements using the magnetic search-coil technique, with 6-ft field coils (CNC Engineering, Seattle, WA) that used a rotating magnetic field in the horizontal plane and an alternating magnetic field in the vertical plane. Search coils were calibrated before each experimental session using a protractor device. The system was 98.5% linear over an operating range of  $\pm 20^\circ$ , the SD of system noise was less than  $0.02^\circ$  and cross talk between horizontal and vertical channels was less than 2.5%.

### Visual Stimuli

To elicit combined saccadic-vergence movements, we initially used a version of the classic Müller paradigm in which fixation is alternatively shifted between distant and near targets, both aligned on the visual axis of one eye.<sup>13</sup> Although this stimulus requires a movement of only the unaligned eye, both eyes make a combined saccadic-vergence gaze shift. The far visual stimulus was a bright laser spot projected onto a wall at 7.3 m (optical infinity). The near visual stimulus was a 2-mm LED positioned along the visual axis of one eye so that a convergence angle of approximately  $17^\circ$  was required to view it binocularly. Subjects' heads were restrained while they made self-paced shifts of the fixation point between the far and near targets.

To determine how different combinations of vergence and versional movements might influence the generation of conjugate oscillations, we performed four control experiments on four of the subjects. The first control (horizontal nonaligned) was with both stimuli separated in the horizontal plane so that a horizontal saccade of approximately  $8^\circ$  and a change in vergence angle of approximately  $8^\circ$  were required (i.e., both targets not aligned on one eye). A second control (midsagittal and vertical) was with both targets aligned on the subject's midsagittal plane but with the far target  $8^\circ$  higher, so that a symmetrical vergence movement of approximately  $8^\circ$  and vertical saccade of approximately  $8^\circ$  were required. A third control (oblique nonaligned) was with the stimuli separated in both horizontal and vertical planes, so that a horizontal saccade of approximately  $8^\circ$ , a vertical saccade of approximately  $8^\circ$ , and a change in vergence angle of approximately  $8^\circ$  were required. A fifth control was with two far targets separated horizontally by approximately  $16^\circ$  so that saccades without vergence were required.

Because transient saccadic oscillations are reported to occur during blinks,<sup>14,15</sup> we monitored eyelid movements using vertical electro-oculography electrodes in two subjects.

### Data Analysis

To avoid aliasing, coil signals were passed through Krohn-Hite Butterworth filters (bandwidth 0–150 Hz) before digitization at 500 Hz with 16-bit resolution. These digitized coil signals were filtered with an 80-point software filter (Remez FIR; bandwidth 0–100 Hz). We compared original and filtered signals of eye position, velocity, and acceleration and detected no attenuation or phase shift. Eye velocity and acceleration were obtained using a four-point differentiator based on a least-squares procedure that produced similar peak values to, but introduced less noise than, a simple two-point differentiation algorithm.<sup>16</sup> The equation used had the following structure:

$$f'(x_k) = \frac{1}{T_s} \cdot \left\{ \frac{8 \cdot [f(x_{k+1}) - f(x_{k-1})] - [f(x_{k+2}) - f(x_{k-2})]}{12} \right\}$$

where  $T_s$  is the sampling period,  $x_k$  is the current point in time,  $f(x_k)$  is eye position at time  $x_k$ , and  $f'(x_k)$  is eye velocity at time  $x_k$ . With this differentiator and a digitization frequency of 500 Hz, the bandwidth for the first derivative was 0 to 170 Hz and for the second derivative was 0 to 148 Hz. Recording from a search coil fixed to a stationary mounting, using this differentiator, the overall system noise had an SD of less than 1.0 deg/sec for velocity and less than 450 deg/sec per sec for acceleration. All responses were analyzed interactively. The saccadic component of gaze shift was defined as the movement that started when eye velocity exceeded 50 deg/sec and ended when eye velocity fell below 50 deg/sec. We made several estimates of the frequency of conjugate oscillations occurring during each experimental run, using Fourier transforms and interactive measurement of the period of oscillations.

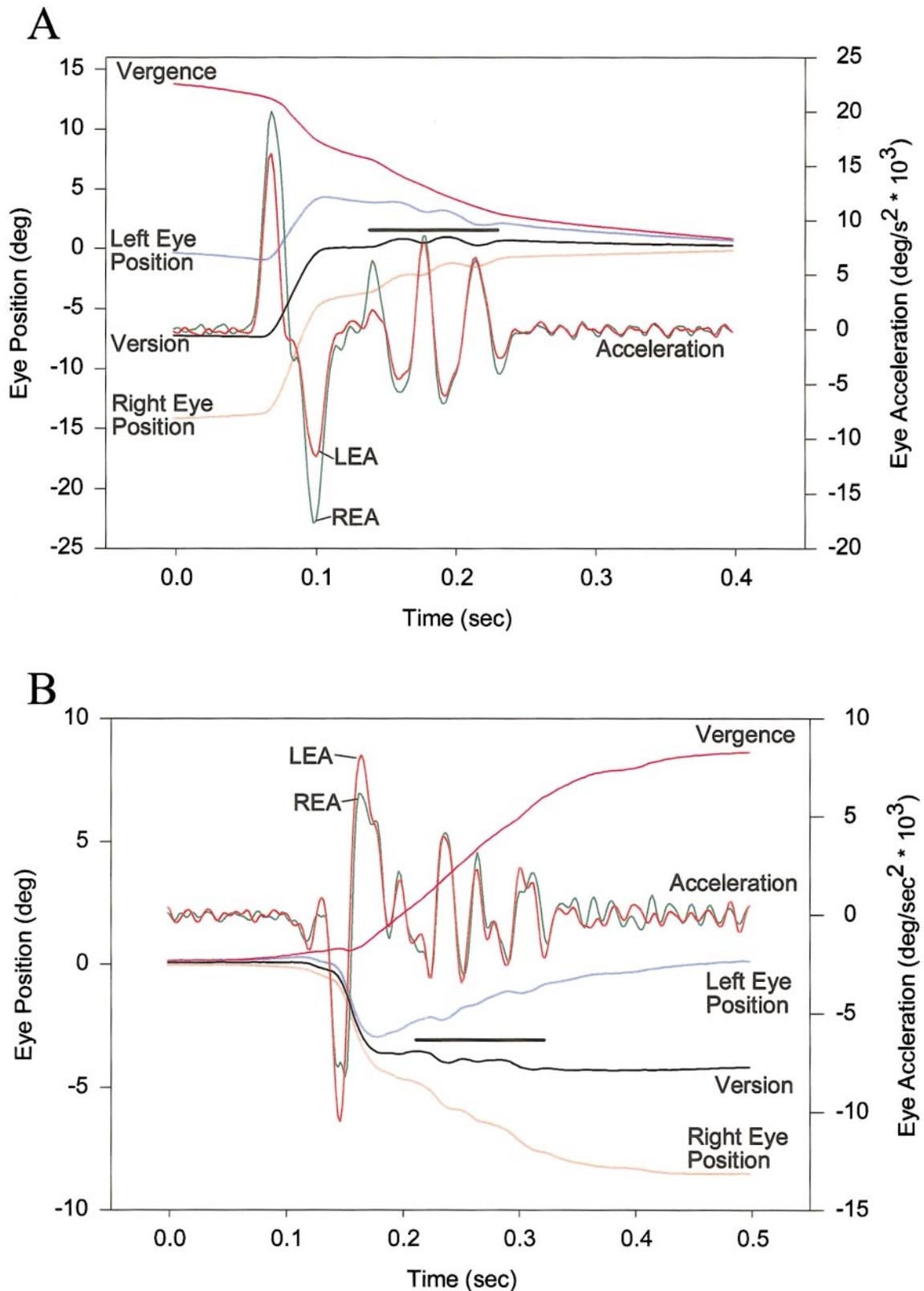
## RESULTS

Records of representative responses to the Müller paradigm are shown in Figure 1; the position and acceleration of each eye is displayed along with the vergence angle and version. After an initial vergence response, a saccade occurred and then the vergence movement completed the response. Note that the initial high-acceleration saccadic component was over within 60 msec, but that the vergence movement continued afterward for more than 200 msec. During this latter period, conjugate oscillations of the eyes were present at a frequency of approximately 30 Hz. These oscillations were small in amplitude but were apparent on the position trace. We confirmed that they were present during gaze shifts when subjects did not blink.

We found that all 10 subjects showed such oscillations during testing with the Müller paradigm. Table 1 summarizes representative values for the amplitudes and frequencies of these oscillations, for each subject. The median occurrence rate of these oscillations for all subjects was 33% of trials (range 16%–50%). During the initial vergence response, which preceded the saccade, conjugate oscillations were usually absent (Fig. 1A); an exception to this trend is shown in Figure 1B.

We used the  $\chi^2$  test to compare the proportion of responses showing oscillations occurring during the Müller paradigm with the other paradigms (Table 2). Some representative records are shown in Figure 2. We found that the proportion of responses showing oscillatory responses during the Müller paradigm was significantly greater than for all the control conditions ( $P < 0.01$ ). No oscillations were encountered during saccades between the distant targets, apart from occasional dynamic overshoots.<sup>9</sup>

We also looked for vertical oscillations during each of the experimental and control experiments. Five subjects showed occasional conjugate vertical oscillations, which were invariably associated with horizontal oscillations at a similar frequency; examples are shown in Figure 2. Considering all subjects and trials, vertical oscillations occurred in a median of 5% of trials (range, 0%–35%).



**FIGURE 1.** Representative records of individual responses when one subject shifted the fixation point from the near to the far target (A) and another subject shifted from far to near (B). The targets were aligned on the subjects' left eyes. Features common to both records are that vergence showed an initial smooth response, which was divergent in (A) and convergent in (B). Next, a saccade carried the right and left eyes in the same direction; this achieved an acceleration of more than  $5000 \text{ deg}/\text{sec}^2$ . After the saccade, the vergence movement continued, and conjugate oscillations at approximately 30 Hz were superimposed (*horizontal bars*); these are evident on both the position and acceleration records. When the vergence movement was almost complete, these conjugate oscillations ceased. Version is the average of right and left eye position. Note different scales for eye position and acceleration. Rightward movements are indicated by positive values. REA: right eye acceleration; LEA: left eye acceleration.

TABLE 1. Summary of Characteristics of Conjugate Oscillations in 10 Subjects

Subject	Peak-to-Peak Amplitude (deg)	Frequency of Horizontal Oscillations (Hz)	Vertical Oscillations Also Present
1	0.4	29	No
2	0.7	23	No
3	0.2	29	Yes
4	0.3	26	No
5	0.2	33	Yes
6	0.2	24	Yes
7	0.4	30	No
8	0.2	27	Yes
9	0.3	28	No
10	0.2	25	Yes

## DISCUSSION

Conjugate oscillations of the eyes at frequencies exceeding 10 Hz are generally thought to be saccadic in origin.<sup>8,9</sup> Their presence during vergence movements was an unexpected finding. Although records of eye acceleration are prone to noise, the magnitude of these oscillations in each subject was much greater than when the eyes were still, and they did not occur with conjugate saccades (Fig. 2D). Furthermore, the same oscillations were often detectable in our position records and appear on some published figures of combined saccadic-vergence movements from other laboratories.<sup>1,13,17</sup> In one such study, occasional horizontal, conjugate oscillations were noted when a vertical saccade was combined with a horizontal vergence movement<sup>17</sup>; this is similar to our midsagittal and vertical paradigm. Our observations indicate that horizontal conjugate oscillations occur whenever a shift in the fixation point requires a substantial vergence component in addition to a saccade. Thus, the highest incidence in our study occurred during the Müller paradigm, in which no saccade was required (although a disjunctive one invariably occurred) and most of the shift of the point of fixation was achieved by a vergence movement. Because almost all vergence movements are accompanied by a saccade,<sup>1</sup> any large change in the vergence angle might be expected to induce these conjugate oscillations. This is an issue deserving of further study.

The presence of these conjugate oscillations suggests that the saccadic system is still active (i.e., the omnipause neurons are silent) during the vergence movement that follows the saccade. Current models of saccade generation suggest that if the omnipause neurons are not inhibiting burst neurons and a motor command is no longer provided to the burst neurons,

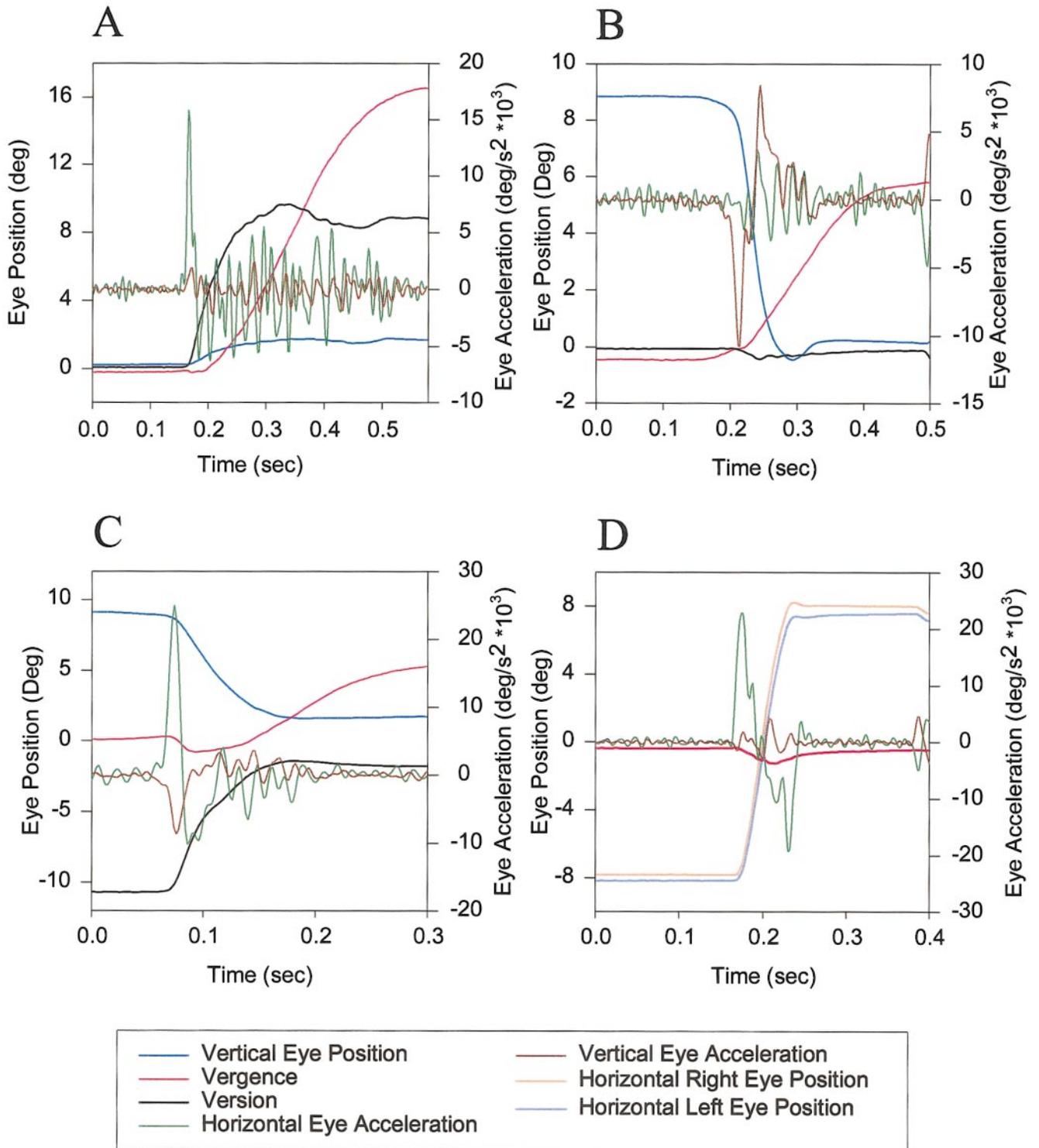
then small saccadic oscillations will occur.<sup>8</sup> This occurs, for example during oblique saccades if the vertical component is pathologically slow; horizontal oscillations occur during the completion of the vertical component.<sup>18</sup> The oscillations shown by our subjects also support the hypothesis that both saccades and vergence burst neurons are gated by omnipause neurons.<sup>18</sup> The latter idea has received electrophysiological support from the demonstration that microstimulation of omnipause neurons slows ongoing vergence movements.<sup>11</sup> Thus, one interpretation of the present findings is that omnipause neurons become silent whenever the motor error (difference between desired change in eye position and the current eye position) calls for a conjugate gaze shift above a minimum threshold. The inhibition of omnipause neurons allows for the generation of a saccadic eye movement, but the firing of these neurons does not resume until the global motor error (combined version and vergence errors) declines below a threshold level. If the version error is reduced below threshold before the vergence error, then the omnipause neurons are still silent, and saccadic oscillations may be produced by discharge of burst neurons.

Although our subjects showed conjugate oscillations during most of the vergence movements that followed saccades, oscillations were usually absent for the vergence movement made before the saccadic movement. Thus, it appears that the initial vergence movement that preceded the saccade did not require that the omnipause neurons cease discharge. Our subjects made self-paced gaze shifts, and it is possible that the initial vergence movements were anticipatory in nature, similar to the conjugate drifts of the eyes that precede saccades made in response to predictable target jumps.<sup>19</sup> The dynamic prop-

TABLE 2. Percentage Rate of Occurrence of Horizontal Conjugate Oscillations for Each Experimental Condition

Subject	Müller	Horizontal Nonaligned	Midsagittal and Vertical	Oblique Nonaligned
4	45	10	30	25
5	50	30	25	15
6	30	15	10	20
8	45	10	20	30
Mean	42	16	21	22

Based on analysis of 20 consecutive responses for each condition in four subjects.



**FIGURE 2.** Representative records from subject 5 in response to (A) the Müller paradigm (targets aligned on right eye), (B) midsagittal and vertical paradigm, (C) oblique nonaligned paradigm, and (D) two targets located at optical infinity. Note that oscillations followed the saccade in (A, B, and C), but not in (D), when no subsequent vergence movement took place. Oscillations in the vertical plane were most evident in (A), which had the best-developed horizontal component. Horizontal and vertical eye position and acceleration are from the right eye. Scales and polarities are as in Figure 1.

erties of these initial vergence movements suggests that they may not depend on vergence burst neurons.

Some normal subjects are able to induce a “voluntary” nystagmus, which consists of high-frequency saccadic oscilla-

tions.<sup>20,21</sup> Interestingly, such people commonly use a voluntary vergence effort as a strategy to induce their saccadic oscillations. Our observations suggest that most people unwittingly show development of saccadic oscillations during com-

bined saccadic-vergence movements—a marker of the common pontine switch that enables us to make such gaze shifts. The ability to induce saccadic oscillations experimentally provides a new tool to test current models for saccade generation.

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### References

1. Collewijn H, Erkelens CJ, Steinman RM. Voluntary binocular gaze shifts in the plane of regard: dynamics of version and vergence. *Vision Res.* 1995;35:3335-3358.
2. Horn AKE, Büttner-Ennever JA, Suzuki Y, Henn V. Histological identification of premotor neurons for horizontal saccades in monkey and man by parvalbumin immunostaining. *J Comp Neurol.* 1997;359:350-363.
3. van Gisbergen JAM, Robinson DA, Gielen S. A quantitative analysis of generation of saccadic eye movements by burst neurons. *J Neurophysiol.* 1981;45:417-442.
4. Zhou W, King WM. Premotor commands encode monocular eye movements. *Nature.* 1998;393:692-695.
5. Horn AKE, Büttner-Ennever JA, Wahle P, Reichenberger I. Neurotransmitter profile of saccadic omnipause neurons in nucleus raphe interpositus. *J Neuroscience.* 1994;14:2032-2046.
6. Keller EL. Participation of medial pontine reticular formation in eye movement generation in monkey. *J Neurophysiol.* 1974;37:316-332.
7. Keller EL, Edelman JA. Use of interrupted saccade paradigm to study spatial and temporal dynamics of saccadic burst cells in superior colliculus in monkey. *J Neurophysiol.* 1994;72:2754-2770.
8. Ashe J, Hain TC, Zee DS, Schatz NJ. Microsaccadic flutter. *Brain.* 1991;114:461-472.
9. Leigh RJ, Zee, DS. *The Neurology of Eye Movements*, Edition 3. New York: Oxford University Press, 1999.
10. Mays LE, Porter JD, Gamlin PDR, Tello C. Neural control of vergence eye movements: neurons encoding vergence velocity. *J Neurophysiol.* 1986;56:1007-1021.
11. Mays LE, Gamlin PDR. A neural mechanism subserving saccade-vergence interactions. In: Findlay JM, Walker R, Kentridge RW, eds. *Eye Movement Research: Mechanisms, Processes and Applications*. Amsterdam: Elsevier; 1995:215-223.
12. Zuber BL, Stark L. Dynamical characteristics of the fusional vergence eye-movement system. *IEEE Trans Sys Sci Cyber.* 1968;SSC-4:72-79.
13. Enright JT. The remarkable saccades of asymmetrical vergence. *Vision Res.* 1992;32:2261-2276.
14. Rottach KG, Das VE, Wohlgenuth W, Zivotofsky AZ. Properties of horizontal saccades accompanied by blinks. *J Neurophysiol.* 1998;79:2895-2902.
15. Hain TC, Zee DS, Mordas M. Blink-induced saccadic oscillations. *Ann Neurol.* 1986;19:299-301.
16. Savitzky A, Golay MJE. Smoothing and differentiation of data by simplified least squares procedures. *Anal Chem.* 1964;38:1627-1639.
17. Zee DS, FitzGibbon EJ, Optican LM. Saccade-vergence interactions in humans. *J Neurophysiol.* 1992;68:1624-1641.
18. Rottach KG, von Maydell RD, Das VE, Zivotofsky AZ, et al. Evidence for independent feedback control of horizontal and vertical saccades from Niemann-Pick type C disease. *Vision Res.* 1997;37:3627-38.
19. Kowler E, Steinman RM. The effect of expectations on slow oculomotor control, I: periodic target steps. *Vision Res.* 1979;19:619-632.
20. Hotson JR. Convergence-initiated voluntary flutter: a normal intrinsic capability in man. *Brain Res.* 1984;294:299-304.
21. Yee RD, Spiegel PH, Yamada T, Abel LA, Zee DS. Voluntary saccadic oscillations resembling ocular flutter and opsoclonus. *J Neuro-ophthalmol.* 1994;14:95-101.