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CROSS AXIS VOR INDUCED BY PURSUIT TRAINING IN MONKEYS: FURTHER PROPERTIES OF ADAPTIVE RESPONSES

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INTRODUCTION

The brain uses several eye movement subsystems to insure good visual acuity (see Ref. 22 for review). In every day life, these subsystems do not work independently but interact with each other to maintain the accuracy of eye movements. For example, the vestibulo-ocular reflex (VOR) interacts with the smooth pursuit system when a subject tracks a slowly moving object during head movement in order to maintain stable gaze. Moreover, when consistent conflicting information is provided to the subsystems, they reveal adaptive changes so that accurate eye movements may once again be produced (see Ref. 10 for review).

Recently, we have shown in trained monkeys that repeated interaction between the pursuit and vestibular systems in the orthogonal plane (cf. 26) induces cross axis VOR that appears only after the interaction training (6). When pursuit training was done at one sinusoidal frequency either in-phase or out-of-phase with chair rotation, the gains (eye/chair) of the cross axis VOR were largest at the training frequency and approximately in-phase or out-of-phase with the chair; phase advanced at lower frequencies and lagged at higher frequencies (6). This is similar to the change induced by whole field-slip stimuli during chair rotation in several animal species including humans (e.g. 2, 18, 21). Multi-frequency channels including vestibular integrators have been suggested to explain the frequency selective behavior of adaptive VOR gain changes induced by whole field-slip stimuli (18). The similarity in the response phase of the cross axis VOR induced by pursuit training (6) and whole field-slip stimuli (e.g. 18, 21) suggests that similar "integrators" may be involved in the cross axis VOR induced by pursuit training. To understand further nature of "integrators", we examined responses of the cross axis VOR after animals were trained to adapt phase-shift training (cf. 15) in the first series of this study.

We reported previously that adaptive changes were not induced when well-trained monkeys fixated a stationary spot that was projected onto a moving patterned visual background during chair rotation, suggesting that peripheral retinal slip *per se* does not seem to be effective in cross axis adaptation (6). However, it is well known that peripheral retinal slip inputs induce adaptive VOR gain changes (10). To understand this discrepancy, in the second series of this study we examined our monkeys with various combinations of pursuit, whole field-slip and vestibular stimuli, not only after the monkeys had been well trained the fixation

task but also during the initial training period in which monkeys were still unable to fixate the stationary spot against a moving patterned visual background during chair rotation.

Our adaptation paradigms require a dissociation of eye movement and gaze movement, since the monkeys were trained to track an orthogonally moving target spot by smooth pursuit eye movement during the VOR induced by chair rotation. Cells carrying signals related to gaze velocity are well known to exist in the brainstem and cerebellar floccular lobe (e.g. 17, 19, 24). However, it has also been reported that some caudal fastigial nucleus neurons respond both to smooth pursuit and saccades (3) and that some frontal pursuit-related neurons respond to eye position (28). These results suggest the possibility that gaze shift produced by saccades alone may induce adaptive cross axis VOR. This possibility was examined in the third series of this study.

It is well known that the cerebellar floccular lobe contains many gaze velocity Purkinje cells (GVPs) (17) and is necessary for VOR adaptation (10, 19). To examine how GVPs respond during our adaptation paradigms, we recorded from horizontal GVPs during the cross axis VOR induced by pitch rotation in the fourth series of this study.

METHODS

Four Japanese monkeys (*Macaca fuscata,* 4.5-6.0 kg) were prepared surgically under aseptic conditions with a pair of head holders, and a scleral search coil was implanted on the right eye to record horizontal and vertical eye movement. All procedures were evaluated and approved by the Animal Care and Use Committee of the Hokkaido University School of Medicine. Our methods for animal preparation, training, recording and data analysis are described in detail elsewhere (6, 7). The monkeys sat in a restraining chair with their heads held firmly in the stereotaxic plane. The chair was fixed to a turntable with two rotational degrees of freedom under computer control. A tangent screen was positioned 75 cm in front of the animals' eyes and subtended 60° by 80° of visual angle. A laser spot (0.2° in diameter) was back-projected onto the screen. A video-projector was used to present a random-dot pattern onto the screen when necessary.

Adaptation paradigms: the monkeys were rotated sinusoidally at a single frequency (0.5 Hz, ± 10°) either in the pitch or yaw plane while presenting a target spot that moved along the plane orthogonal to the rotation plane either in-phase or with 90° phase shift with respect to the chair signal (e.g. Fig. 1A, C). The monkeys were rewarded for tracking the laser spot for apple juice reward. To examine the interaction of pursuit, whole field-visual pattern and vestibular stimuli, a random-dot pattern was projected onto the screen using a video projector. The monkeys were rotated sinusoidally either in the pitch or yaw plane while both the target spot and pattern or either one of the two moved along the plane orthogonal to the rotation plane in-phase with the chair. In the latter condition, the other (spot or pattern) stimuli remained stationary on the screen during chair rotation. In all these paradigms, the monkeys were rewarded for tracking or fixating the spot for 1-2 hours, and eye movements induced by rotation alone were examined in complete darkness before and after training. To examine selectivity of eye movement responses to the training frequency, chair rotation was applied at 0.1-1.0 Hz (± 10°) before and after 1-2 hrs of training in complete darkness.

To examine whether a change in gaze shift alone in the orthogonal plane during chair rotation is sufficient to induce the cross axis VOR, the monkeys were rotated in the pitch plane at 0.3 Hz (± 10°) while the target spot was stepped, instead of moving sinusoidally, at 5 horizontal

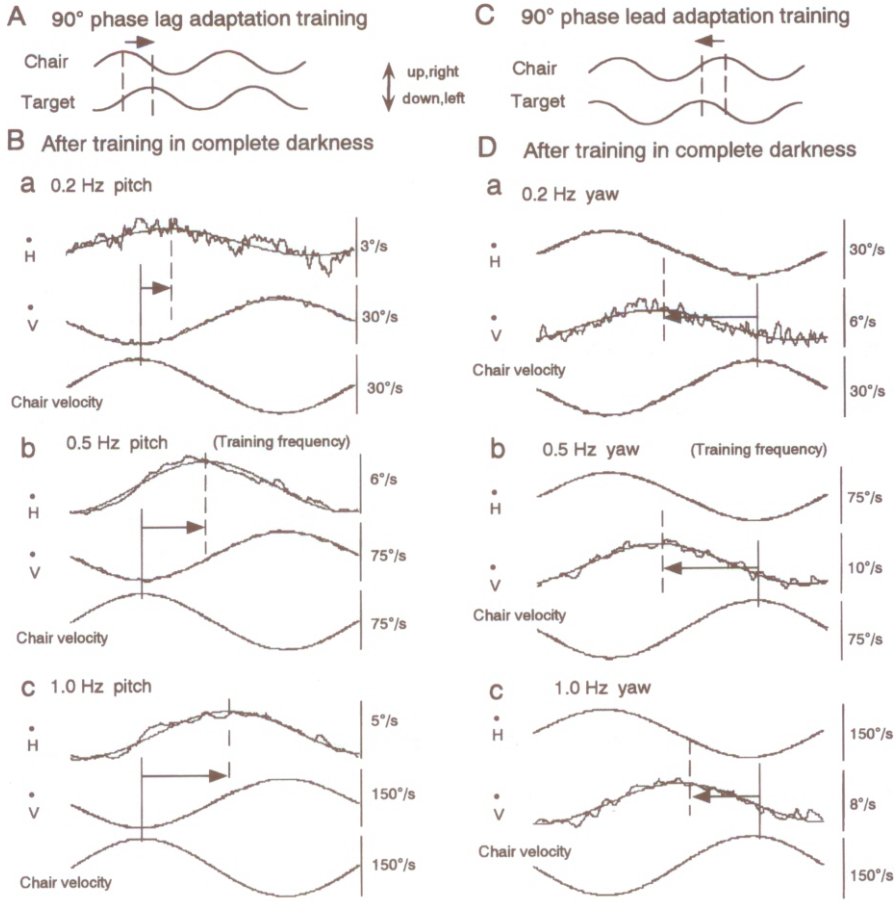

Fig. 1. - *Phase-shift training and appearance of cross axis VOR in complete darkness after training.*

A and C show training paradigms. B and D show eye movement responses evoked by pitch rotation (B) and yaw rotation (D) in complete darkness after 60 min of training. $\dot{H}$ and $\dot{V}$ indicate horizontal and vertical eye velocity, respectively. For further explanation, see text.

positions with equal time interval (straight ahead position, ± 5° and ± 10°, e.g. Figure 4A). Extracellular recordings were made in the floccular lobe as described previously (7).

Eye-, target-, chair-position signals and single cell discharges were digitized at 303Hz using a 16 bit A/D board (National Instruments) on a Macintosh Quadra computer. All digitized data were displayed off-line on a computer screen. Velocity signals of eye, target and chair were calculated by the computer as previously described (6, 7). Saccades were marked with a cursor on the eye-velocity traces and removed using our interactive computer program. Ten to thirty cycles were averaged to obtain means. Phase shift was calculated as the difference in phase between the fundamental component of eye-velocity and stimulus-velocity after deleting saccades. Eye gain was calculated as the peak amplitude of the fundamental component of eye-velocity divided by that of stimulus-velocity. Eye velocity plots in *x-y* coordinates was also used to visualize slow eye movement responses. To analyze Purkinje cell responses, cycle rasters and histograms were constructed for the discharge of each cell by averaging 10-30 cycles as previously described (6,7).

RESULTS

Cross axis VOR induced by phase-shift pursuit training

As reported previously, whole body rotation in complete darkness before cross axis pursuit training induced the VOR only in the rotation plane but not in the orthogonal plane. Figure 1 (B, D) shows examples of averaged eye velocity responses in complete darkness induced by vertical (pitch, B) and horizontal (yaw, D) rotation at 3 different frequencies after phase-shift training. After horizontal pursuit training with 90° phase lag to the chair during pitch rotation (Fig. 1A), horizontal eye movement responses were induced by pitch rotation alone in complete darkness with phase lag (re chair velocity) of about 90° (Fig. 1Bb). The magnitude of phase shift depended on rotation frequency (Fig. 1B indicated by arrows); less lag at lower frequency (Fig. 1Ba) and more lag at higher frequency (Fig. 1Bc) compared to the training frequency of 0.5 Hz (Fig. 1Bb). After vertical pursuit training with 90° phase lead to the chair during yaw rotation (Fig. 1C), vertical eye movement responses were induced by yaw rotation alone in complete darkness with considerable phase lead to the chair (Fig. 1D, indicated by arrows). Thus, these eye movement responses conform to the training paradigms.

Figure 2 (A, C) summarizes gains and phases of orthogonal eye movement responses plotted against the frequency of yaw (Fig. 2A) and pitch (Fig. 2C) rotation after 60 min pursuit training. Responses shown with filled triangles and filled squares are means (± SD) for 6-12 sessions for 3 monkeys for phase-lead and -lag adaptation paradigms, respectively. Responses shown with open squares are means for in-phase training for comparison. In the latter condition, gains were highest at the training frequency and lower at other stimulus frequencies, whereas the phases were most nearly in-phase with stimulus velocity at the training frequency (0.5 Hz) and tended to advance at lower frequencies (Fig. 2A, C), similar to our previous results (6).

After phase-shift training, the cross axis VOR was observed in complete darkness during yaw and pitch rotation with considerable phase shift towards the directions (either lead or lag) consistent with the training paradigms (Fig. 2A, C). However, gain behavior was different between yaw (Fig. 2A) and pitch rotation (Fig. 2C). Gains at 0.1 Hz induced by yaw rotation remained similar to the gains at the training frequency (0.5 Hz) after phase-shift training (Figure 2A, filled symbols), behavior different from in-phase training (Figure 2A, open squares), although pitch rotation after phase-shift training resulted in gain behavior similar to in-phase training (Fig. 2C). In contrast, neither the phase- shift training nor in-phase training produced any significant change in gain or phase of the collinear VOR. Therefore, all data were combined in Figure 2 (B, D). These results indicate that adaptive changes are specific to the parameters of pursuit training stimulus.

Interaction of pursuit, whole field- visual pattern and vestibular stimuli in inducing cross axis VOR adaptation

Figure 3A shows examples of eye-velocity plots in *x-y* coordinates (see inset) induced by pitch rotation. Horizontal spot movement was combined with or with-

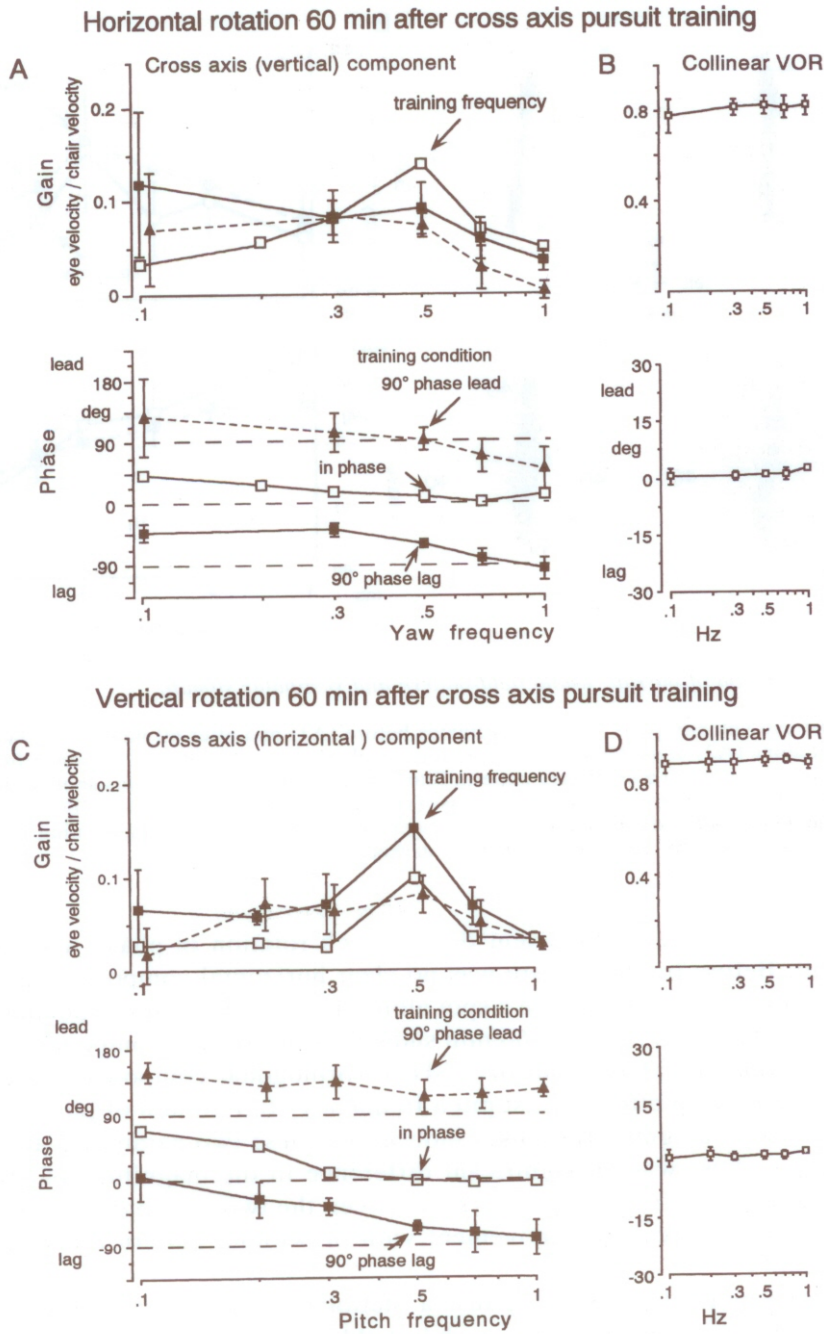

Fig. 2. - *Gain and phase of cross axis (A, C) and collinear (B, D) VOR plotted against stimulus frequency induced by yaw (A, B) or pitch (C, D) rotation in complete darkness after 60 min of training.*

For further explanation, see text.

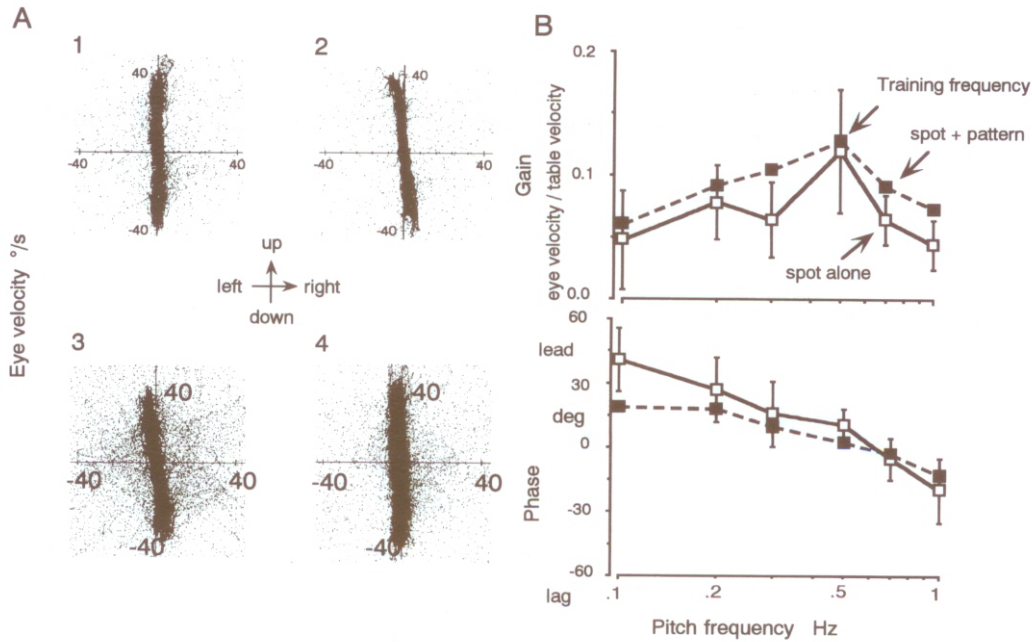

Fig. 3. - *Interaction of pursuit, whole field-pattern and vestibular stimuli.*

A shows eye velocity plots in x-y coordinates before (A1) and after 60 min of in-phase training with a spot alone (A2) or spot and pattern moving together (A3). A4 plots eye velocity after 120 min of pursuit training against a stationary pattern. Pitch rotation (0.5 Hz, ± 10°) was applied in complete darkness in A1-A4. B summarizes gain and phase (re chair velocity) of cross axis VOR with spot alone (open squares) or spot and the pattern moving together (filled squares) during training against pitch frequency. All data were recorded in complete darkness.

out random-dot pattern movement during pitch rotation in-phase with the chair movement. Before training, there was no clear horizontal component (Fig. 3A1). Plots after in-phase training with a spot alone (Fig. 3A2) or with a spot and pattern moving together (Fig. 3A3) for 60 min show clear horizontal components. Fig. 3B compares gains and phases (mean ± SD) of orthogonal components obtained in complete darkness plotted against pitch frequency after 90 min of pursuit training for these two paradigms. Responses induced by these two paradigms are similar. In particular, there was no significant difference in the magnitude of cross axis VOR at the training frequency (0.5 Hz) between the two paradigms. Yaw rotation combined with vertical spot movement with or without pattern movement gave similar results.

Cross axis pursuit training against a stationary pattern was performed in 4 monkeys with a total of 6 sessions, each lasted for 2 hours. As an example is shown in Figure 3A4, none of the sessions showed a clear orthogonal component in complete darkness after training.

We showed previously that visual input alone was insufficient in inducing cross axis VOR when well trained monkeys fixated a stationary spot projected onto a

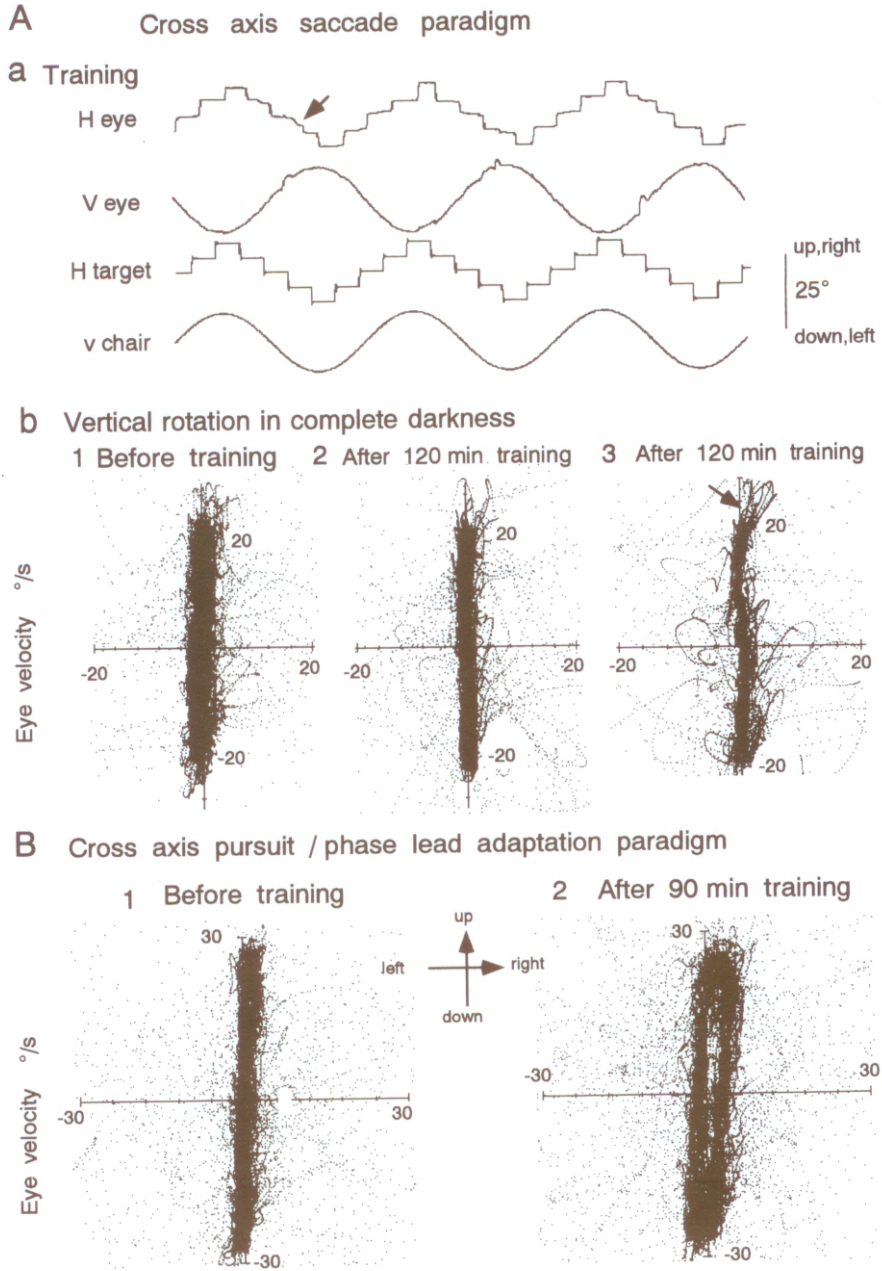

Fig. 4. - *Eye position records during cross axis saccade paradigm (Aa) and eye velocity plots in x-y coordinates before (Ab1) and after (Ab2, Ab3) 120 min of training.*

Pitch rotation was applied in complete darkness at 0.3 Hz (± 10°) in Ab1-3. B shows eye velocity plots in *x-y* coordinates before (B1) and 90 min after 90° phase-lead training (B2) at 0.5 Hz (± 10°). Pitch rotation was applied in complete darkness at 0.5 Hz (± 10°) in B1-2.

moving patterned visual background during yaw or pitch rotation (6). To confirm this observation, we asked 2 monkeys to fixate a stationary spot against moving pattern in the orthogonal direction during pitch rotation for 2 hours. Initially, both monkeys were unable to fixate the stationary spot during pattern movement, and they had to be trained this fixation task for 3 days. We recorded eye movement responses during these initial training periods. Cross axis VOR was indeed obtained after 2 hours of initial training. However, after 3 days when the monkeys were able to fixate the spot well during the training, none of the monkeys showed consistent orthogonal components in a total of 5 sessions even after 2 hours of training, similar to our previous results.

Cross axis saccade paradigm

A total of 10 sessions were tested in 3 monkeys. For each session, the training (e.g. Fig. 4Aa) continued for 2 hours. Fig. 4Ab shows examples of eye-velocity plotted in x-y coordinates (see inset) induced by pitch rotation in complete darkness before (Fig. 4Ab1) and after (Fig. 4Ab2) horizontal saccade training. No sinusoidal horizontal component was consistently induced by pitch rotation after training in any of the sessions, although fragmental horizontal components were induced occasionally during pitch rotation (Fig. 4Ab3, indicated by arrow). In the same monkeys, however, in-phase or phase-shift training clearly induced orthogonal eye movement responses (e.g. Fig. 4B1 vs B2).

Recordings of horizontal GVPs in the cerebellar floccular lobe

A total of 5 GVPs were recorded in the cerebellar floccular lobe during our adaptation paradigms. An example is shown in Figure 5. This cell increased activity during ipsiversive pursuit, but no modulation was observed during pitch rotation in the dark before training (Fig. 5B, C). While recording this cell, the monkey performed horizontal pursuit coupled with pitch rotation (Fig. 5A). After 60 min of training, the target spot was turned off (Fig. 5D). Modulation in cell activity was still observed. Cell response evoked by pitch rotation in complete darkness is summarized in Figure 5E. Clear response appeared after training together with horizontal eye movement responses. Figure 5F plots amplitudes of modulation of cell discharge against horizontal peak eye velocities during different behavioral conditions (indicated by keys). Eye velocity sensitivities are similar before and after training. Similar results were obtained in the remaining horizontal GVPs.

DISCUSSION

Cross axis VOR induced by phase-shift adaptation paradigms

Considerable phase shift was observed in the cross axis VOR in our phase-shift paradigms (Figg. 1, 2) (cf. 15). Our results indicate that although frequency tuning was maintained during pitch in the phase-shift paradigms, it was not maintained during yaw, resulting in higher gains at lower stimulus frequencies compared to the

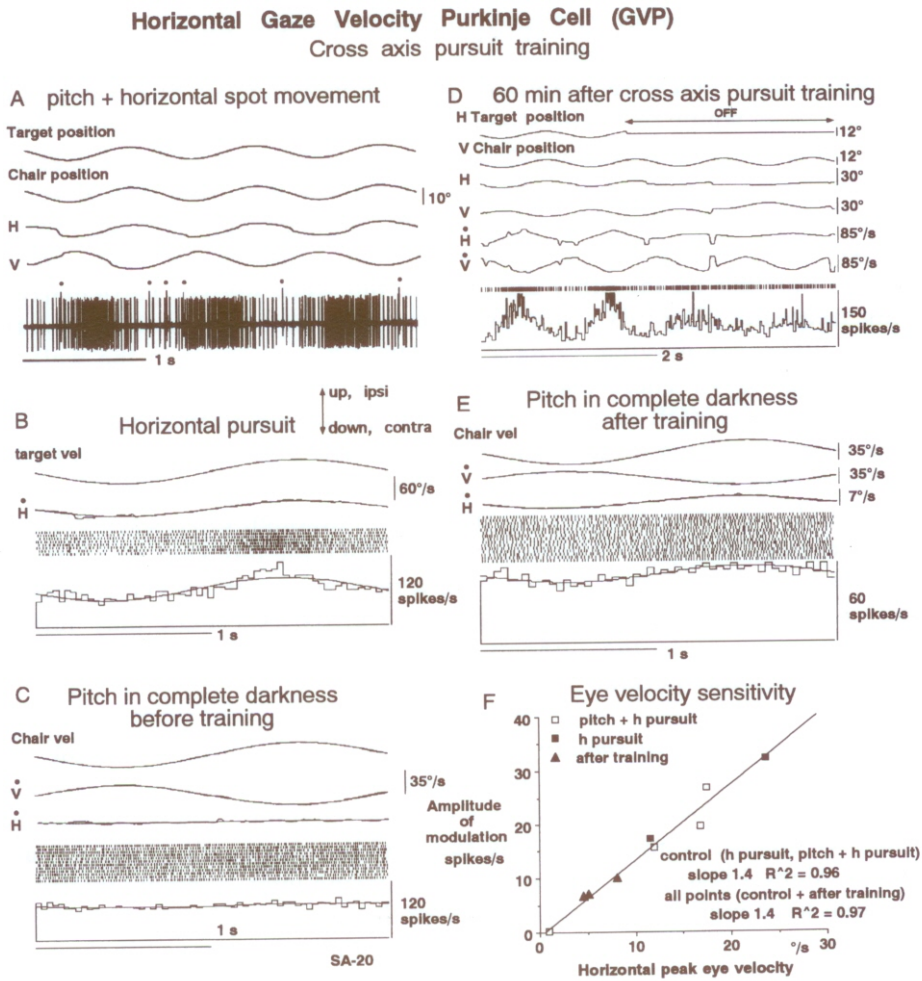

Fig. 5. - *Behavior of a horizontal GVP of the floccular lobe.*

Dots above cell discharge in the bottom trace in A indicate complex spikes. The third and fourth traces in A indicate horizontal (H) and vertical (V) eye position. Traces in B, C and E are target velocity, horizontal eye velocity ($\dot{H}$), vertical eye velocity ($\dot{V}$), chair velocity and cell raster and histograms. D shows cell behavior after 60 min of training and immediately after the target was turned off. The bottom two traces show cell discharges. F plots amplitude of cell modulation against horizontal peak eye velocity during pitch rotation combined with horizontal pursuit (open squares), during horizontal pursuit alone before training (filled squares) and during pitch rotation in complete darkness after training (filled triangles). For further explanation, see text.

gains during yaw (Fig. 2A and C) despite the fact that training without phase-shift resulted in similar gain curves between yaw and pitch rotation (6). Since pitch rotation activates not only vertical canals but also otolith organs (see Ref. 29 for review), the difference may well be induced by otolith inputs (1, 9). This interpretation suggests that the responses induced by yaw rotation (Fig. 2A) may reflect the activity induced by canal inputs alone.

Interaction of pursuit, whole field-visual pattern and vestibular stimuli in inducing cross axis VOR adaptation

It is well known that VOR adaptation is effectively induced by peripheral retinal slip produced by whole field-slip stimuli during chair rotation (10). In the collinear VOR, Scudder and Fuchs (25) reported in monkeys that whole-field slip and foveal slip are both effective in causing VOR gain changes and are quantitatively about equal (also 19). Our results, however, indicate that the response magnitudes of the cross axis VOR induced by spot alone on one hand and by spot and pattern movement together on the other did not add but were similar, particularly at the training frequency (Fig. 3B). Moreover, if one of the two stimuli was stationary while the other was moving, cross axis VOR did not appear in the well-trained monkeys (Fig. 3A4). These results indicate a difference between the cross axis VOR and collinear VOR and suggest that the cross axis VOR induced by pursuit training shares common mechanisms with the cross axis VOR induced by whole-field slip stimuli and that if conflicting information is given between these two visual stimuli, adaptive changes are inhibited. Although cross axis VOR indeed appeared during the initial training period in which the monkeys were still unable to fixate a stationary spot projected onto a moving patterned visual background during chair rotation, the appearance of the cross axis VOR may reflect eye movement responses in the orthogonal direction or lack of adequate fixation command during this period.

Specific involvement of smooth eye movements in the cross axis VOR

Our results showing that none of the 3 monkeys with a total of 10 sessions induced adaptive VOR by the cross axis saccade paradigm (Fig. 4Ab) suggest that the adaptive change is not induced by eye position change alone during saccades in our paradigm. Fixation of a stationary spot during inter- saccadic intervals (Fig. 4Aa) might have inhibited the appearance of the cross axis VOR. Although we do not exclude the possibility that adaptive changes may be induced if chair rotation is given more stepwise rather than sinusoidal, we think that it is unlikely since vestibular signals are interrupted during saccades by position-vestibular-pause cells in the vestibular nuclei (see Ref. 22 for review). These results suggest that the cross axis VOR is specifically induced by smooth eye movements during chair rotation.

Although the cross axis VOR was never induced by saccade training in this study, fragmental orthogonal components appeared after training (Fig. 4Ab3). Note that there was a change in saccade trajectories with the target during chair rotation. Slow fragmental eye movements clearly appeared in the plane orthogonal to the rotation during training (Fig. 4Aa, indicated by arrow). Although we do not know whether such slow eye movements during training are the result of a different strategy, such eye movements would be effective in maintaining the target continuously on the fovea during rotation. Appearance of such components might have been related to fragmental orthogonal components observed in complete darkness (Fig. 4Ab3, indicated by arrow).

To examine how well our results are explained by existing VOR models, we tested the VOR equalizer model of Miles et al. (20). The phase and gain curves without phase-shift training (Fig. 2A, C, open squares) are well explained by their model (Fig. 6B, labeled as no integrator through dashed pathways in A). However, the large phase shift produced by our phase-shift training was difficult to be simulated by their model. We, therefore, added another integrator (Fig. 6A, thick lines) in their model. When the time constant of this integrator was short (T = 0.15s), the gain and phase curves are similar to those without the integrator (Fig. 6B). By increasing its time constant, considerable phase shift in eye velocity was observed (Fig. 6B, T = + 20 or – 20s) comparable to our present results (Fig. 2A, C, filled symbols) with the gain curve similar to our cross axis VOR induced by yaw (Fig. 2A), but not pitch (Fig. 2C) rotation. We have shown recently using horizontal trapezoidal rotation that the latency of the cross axis VOR induced by our pursuit paradigms is much longer (mean ~ 42 ms) than the collinear VOR latency (~ 15 ms) (cf. 13). When the monkeys were trained using our in-phase training paradigm, the time constant of cross axis VOR measured by trapezoidal chair rotation in complete darkness is very short (mean ~ 80 ms) (23), comparable to our simulation results without the integrator (Fig. 6B, T = 0.15). These results suggest that the cross axis VOR may require another integrator in addition to the well-known vestibular integrator (5). However, the gain and phase behavior induced by pitch rotation after phase-shift training (Fig. 2C) was still difficult to be

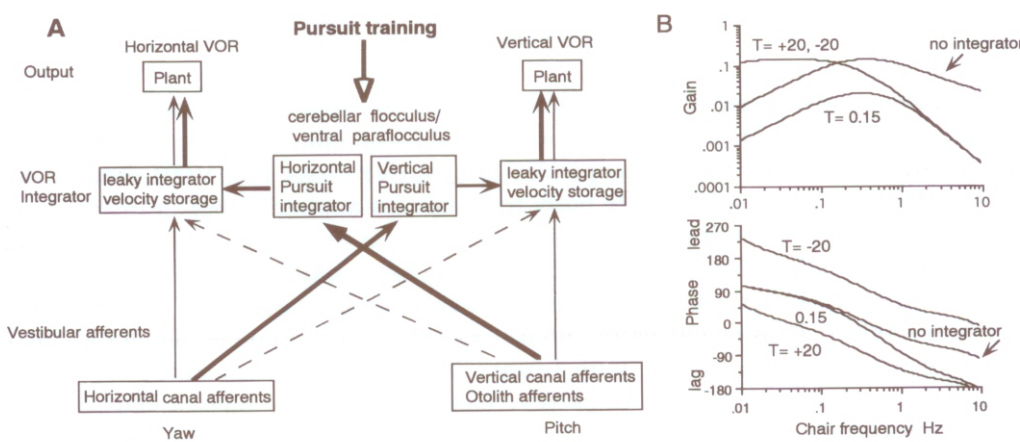

Fig. 6. - *A is a schematic diagram of the collinear VOR and hypothetical diagram of the cross axis VOR (dashed or think lines), while B represents gain and phase curves of the cross axis VOR. Traces labeled as* "no integrator" *in B were calculated using the VOR equalizer model of Miles et al.* (20) *through dashed pathway in A.*

For weights of the different channels of the model at 0.5 Hz (20), we used 0.1, 0.1, 0.1, 1.0, 0.5 and 0.1 for channel #1 through #6, respectively, to obtain best fit for the experimental data. All other parameters used were the same as described in Miles et al. (20). We also added a pursuit related-integrator in the cross axis pathways (thick lines in A) and changed the time constant of this integrator. Gain and phase curves of the cross axis VOR thus obtained are summarized in B against stimulus frequency.

simulated by adding this integrator, suggesting further elements (e.g. otolith input, Fig. 6A) are necessary. It is well known that floccular horizontal GVPs respond during smooth pursuit but do not respond during the normal collinear VOR (17, 19). The similar eye velocity sensitivity of GVPs before and after training (Fig. 5F) suggests that they respond during the cross axis VOR induced by chair rotation to maintain adaptive changes and that the above integrator may be related to smooth pursuit (Fig. 6A).

Smooth pursuit and direct optokinetic response (ocular following) share many brainstem and cerebellar pathways (16, 27). On the other hand, independent mechanisms are also used in higher structures for these two types of eye movements, since some neurons in the cortical visual and motor areas and dorsolateral pontine nucleus respond to either one of the two kinds of visual stimuli suitable to induce these two eye movement responses (4, 8, 11, 12, 14). Since the adaptive cross axis VOR is tuned to the parameters of the pursuit-training stimulus not only in the training frequency but also in the phase-shift paradigms, and since conflicting information between pursuit and whole field-slip inhibits appearance of the cross axis VOR, generation (not necessarily maintenance) of the cross axis VOR may require cortical mechanisms specific for smooth pursuit (Fig. 6A). Since many pursuit-related cortical neurons respond to vestibular input (see Ref 4 for review), such smooth pursuit pathways responding to vestibular input may become active by repeated interaction of pursuit-vestibular interactions.

SUMMARY

We have shown recently in alert monkeys that repeated interaction between the pursuit and vestibular systems in the orthogonal plane induces adaptive changes in the VOR. To examine further properties of adaptive cross axis VOR induced by pursuit training, sinusoidal whole body rotation was applied either in the pitch or yaw plane while presenting a target spot that moved orthogonally to the rotation plane with either 90° phase-lead or 90° phase-lag to the chair signal. After one hour of training at 0.5 Hz (± 10°), considerable phase-shift was observed in orthogonal eye movement responses consistent with the training paradigms by identical chair rotation in complete darkness, with further lead at lower frequencies and lag at higher frequencies. However, gains (eye/chair) induced by phase- shift pursuit training was different during pitch and yaw rotation. Although frequency tuning was maintained during pitch in the phase-shift paradigms, it was not maintained during yaw, resulting in higher gains at lower stimulus frequencies compared to the gains during yaw. This difference may reflect otolith contribution during pitch rotation. To understand further the nature of signals that induce adaptive cross axis VOR, we examined interaction of pursuit, whole field-visual pattern and vestibular stimuli. Magnitudes of the cross axis VOR with a spot alone on one hand and with a spot and pattern moving together in the same plane on the other during chair rotation were similar, and when one of the two visual stimuli was stationary during chair rotation, our well trained monkeys did not induce the cross axis VOR. These

results suggest that the cross axis VOR induced by pursuit training shares common mechanisms with the cross axis VOR induced by whole field-slip stimuli and that if conflicting information is given between the two visual stimuli, adaptive changes are inhibited. Horizontal GVPs were recorded in the cerebellar floccular lobe during pitch rotation coupled with horizontal pursuit stimuli. These GVPs did not respond to pitch in the dark before training, but responded after 60 min of pursuit training with eye velocity sensitivities similar to those before training. Adaptive change in the VOR was specific to smooth eye movements but not to saccades in our paradigms.

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REFERENCES

1. Baker, J., Harrison, R.E.W., Isu, N., Wickland, C. and Peterson, B. Dynamics of adaptive change in vestibulo-ocular reflex direction. II. Sagittal plane rotations. *Brain Res.*, **371**: 166-170, 1986.
2. Collewijn, H. and Grootendorst, A. Adaptation of optokinetic and vestibulo-ocular reflexes to modified visual input in the rabbit. *Prog. Brain Res.*, **50**: 771-781, 1979.
3. Fuchs, A.F., Robinson, F.R. and Straube, A. Role of the caudal fastigial nucleus in saccade generation. I. Neuronal discharge patterns. *J. Neurophysiol.*, **70**: 1723-1740, 1993.
4. Fukushima, K. Corticovestibular interactions: anatomy, electrophysiology, and functional considerations. *Exp. Brain Res.*, **117**: 1-16, 1997.
5. Fukushima, K. and Kaneko, C.R.S. Vestibular integrators in the oculomotor system. *Neurosci. Res.*, **22**: 249-258, 1995.
6. Fukushima, K., Fukushima, J., Chin, S., Tsunekawa, H. and Kaneko, C.R.S. Cross axis vestibulo-ocular reflex induced by pursuit training in alert monkeys. *Neurosci. Res.*, **25**: 255- 265, 1996.
7. Fukushima, K., Chin, S., Fukushima, J. and Tanaka, M. Simple-spike activity of floccular Purkinje cells responding to sinusoidal vertical rotation and optokinetic stimuli in alert cats. *Neurosci. Res.*, **24**: 275-289, 1996.
8. Fukushima, K., Fukushima, J. and Kaneko, C.R.S. Properties of neurons encoding vestibular related signals in and near the frontal eye fields of alert monkeys. *Soc. Neurosci., Abstr.*, **23**: 473, 1997.
9. Harrison, R.E.W., Baker, J.F., Isu, N., Wickland, C.R. and Peterson, B.W. Dynamics of adaptive change in vestibulo-ocular reflex direction. I. Rotations in the horizontal plane. *Brain Res.*, **371**: 162-165, 1986.
10. Ito, M. *The Cerebellum and Neural Control.* New York, Raven Press, pp. 133-374, 1984.
11. Kawano, K., Shidara, M. and Yamane, S. Neural activity in dorso-lateral pontine nucleus of alert monkeys during ocular following responses. *J. Neurophysiol.*, **67**: 680-703, 1992.
12. Kawano, K., Shidara, M., Watanabe, Y. and Yamane, S. Neural activity in cortical area MST of alert monkey during ocular following responses. *J. Neurophysiol.*, **71**: 2305-2324, 1994.

13. KHATER, T.T., QUINN K.J., BAKER, J.F. AND PETERSON, B.W. The latency of the cat vestibulo-ocular reflex before and after short- and long-term adaptation. *Exp. Brain. Res.*, **94**: 16-32, 1993.
14. KOMATSU, H. AND WURTZ, R.H. Relation of cortical areas MT and MST to pursuit eye movements. III. Interaction with full-field visual stimulation. *J. Neurophysiol.*, **60**: 621-644, 1988.
15. KRAMER, P.D., SHELHAMER, M. AND ZEE, D.S. Short-term adaptation of the phase of the vestibulo- ocular reflex (VOR) in normal human subjects. *Exp. Brain Res.*, **106**: 318-326, 1995.
16. LEIGH, R.J. AND ZEE, D.S. *The Neurology of Eye Movements.* 2nd ed. Philadelphia, F.A. Davis, pp. 15-264, 1991.
17. LISBERGER, S.G. AND FUCHS, A.F. Role of primate flocculus during rapid behavioral modification of vestibuloocular reflex. I. Purkinje cell activity during visually guided horizontal smooth- pursuit eye movements and passive head rotation. *J. Neurophysiol.*, **41**: 733-763, 1978.
18. LISBERGER, S.G., MILES, F.A. AND OPTICAN, L.M. Frequency-selective adaptation: evidence for channels in the vestibulo-ocular reflex? *J. Neurosci.*, **3**: 1234-1244, 1983.
19. MILES, F.A. AND LISBERGER, S.G. The "error" signals subserving adaptive gain control in the primate vestibulo-ocular reflex. *Ann. N.Y. Acad. Sci.*, **374**: 513-525, 1981.
20. MILES, F.A., OPTICAN, L.M. AND LISBERGER, S.G. An adaptive equalizer model of the primate vestibulo-ocular reflex. Vol. 1, In: BERTHOZ, A., MELVILL JONES, G. (Eds.) *Adaptive Mechanisms in Gaze Control*, Amsterdam, Elsevier, *Reviews in Oculomotor Research*, pp. 313-326, 1985.
21. PENG, G.C., BAKER, J.F. AND PETERSON, B.W. Dynamics of directional plasticity in the human vertical vestibulo-ocular reflex. *J. Vest. Res.*, **4**: 453-460, 1994.
22. ROBINSON, D.A. Control of eye movements. In: BROOKHART J.M. and MOUNTCASTLE J.M. (Eds.), *Handbook of Physiology*, Bethesda, American Physiological Society, pp. 1275-1320, 1981.
23. SATO, T., YOKOYAMA, R., FUKUSHIMA, J. AND FUKUSHIMA, K. Latency of cross axis vestibulo- ocular reflex induced by pursuit training in monkeys. *Neurosci Res.*, **33**: 65-70, 1999.
24. SCUDDER, C.A. AND FUCHS, A.F. Physiological and behavioral identification of vestibular nucleus neurons mediating the horizontal vestibuloocular reflex in trained rhesus monkeys. *J. Neurophysiol.*, **68**: 244-264, 1992a.
25. SCUDDER, C.A. AND FUCHS, A.F. The error signal for modification of vestibuloocular reflex gain. *Ann. N.Y. Acad. Sci.*, **656**: 884-885, 1992b.
26. SCHULTHEIS, L.W. AND ROBINSON, D.A. Directional plasticity of the vestibulo-ocular reflex in the cat. *Ann. N.Y. Acad. Sci.*, **374**: 504-512, 1981.
27. SHIDARA, M. AND KAWANO, K. Role of Purkinje cells in the ventral paraflocculus in short-latency ocular following responses. *Exp. Brain Res.*, **93**: 185-195, 1993.
28. TANAKA, M. AND FUKUSHIMA, K. Neuronal responses related to smooth pursuit eye movements in the periarcuate cortical area of monkeys. *J. Neurophysiol.*, **79**: 835-847, 1998.
29. WILSON, V.J. AND MELVILL JONES, G. *Mammalian Vestibular Physiology.* New York, Plenum Press. 1979.