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Gravity and the vertical vestibulo-ocular reflex

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Summary. We studied the vertical vestibulo-ocular reflex (VOR) and vertical visual-vestibular interaction induced by voluntary pitch in the upright and onside positions in eight normal human subjects. Subjects were trained to produce sinusoidal (0.4 to 1.6 Hz) pitch head movements guided by a frequency modulated sound signal. Eye and head movements were recorded with a magnetic search coil. There was no significant difference between the pooled average gain (eye velocity/head velocity) of the vertical VOR in the upright and onside positions. Vertical VOR gain in any position could be more or less than 1.0 for individual subjects. By contrast, gain with an earth-fixed visual target was always near 1.0. Asymmetries in the gain of upward and downward VOR, pursuit and fixation suppression of the VOR were found in individual subjects, but in the group of normal subjects there was no significant difference between gain of up and down eye movements induced by vestibular, visual or visual-vestibular stimulation in any position. We conclude that during voluntary pitch otolith signals are not critical for normal functioning of the vertical VOR.

Key words: Vestibulo-ocular reflex – Visual-vestibular interaction – Onside pitch – Fixation-suppression – Human

Introduction

In the cat, upright pitch elicits a vertical VOR which is more symmetric and has a more compensatory gain than the VOR induced by onside pitch (Tomko et al. 1988). The difference is presumably due to the fact that upright pitch stimulates both otoliths and vertical canals whereas onside pitch stimulates only the canals. In other words, the vertical VOR may require both otolith and canal signals for normal functioning. Since otolith signals are not generated with upright pitch in microgravity, an inadequate vertical VOR in space has been hypothesized to produce visual-vestibular mismatch and space motion sickness (Lackner and Graybiel 1981).

To our knowledge there have been no studies comparing the vertical VOR during upright and onside pitch in human subjects. Studies of low frequency onside pitch in humans (Benson and Guedry 1965; Baloh et al. 1983) did not find a consistent gain asymmetry in the vertical VOR although fixation suppression of the VOR was asymmetric (downward slow phases inhibited better than upward slow phases). Such asymmetries in visual-vestibular interaction could also have important implications in the mechanism of space motion sickness.

Methods

Subject selection

Eight normal subjects were interviewed to rule out ophthalmologic, neurologic or otologic disorders. They included two males and six females with an age range of 19 to 43 years.

Eye and head movement recordings

Vertical eye movements were recorded by the magnetic contact lens, search coil technique described by Collewijn and colleagues (1975). Several turns of a fine wire embedded in a soft contact lens was placed on the eye after topical anesthetic was applied. The lens stayed on the eye approximately thirty minutes. This system can record eye movements as small as 20 min of arc and has a vertical range of ± 30° (Yee et al. 1985). Head movements were recorded with a similar coil mounted on the forehead. Both coils were calibrated at the beginning of each recording session.

Test procedures

Subjects were seated or lying in the right lateral position (right ear down) with the head in the center of the field coils (four feet in diameter). After practicing sinusoidal head movements (amplitude ± 5–10 degrees) guided by a frequency modulated sound signal (0.4 to 1.6 Hz) each subject underwent the following test battery:

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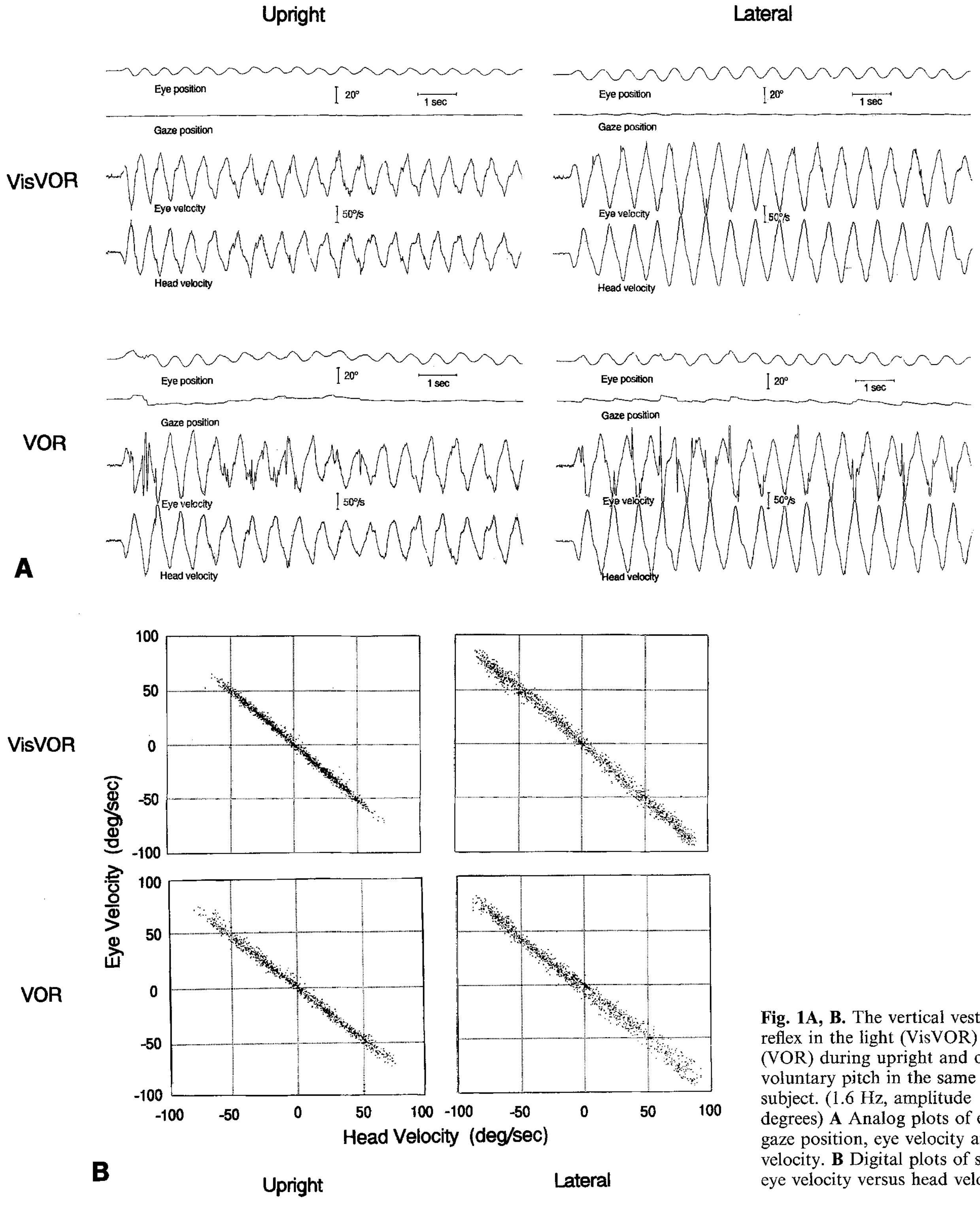

Fig. 1A, B. The vertical vestibulo-ocular reflex in the light (VisVOR) and dark (VOR) during upright and onside voluntary pitch in the same normal subject. (1.6 Hz, amplitude ±5–9 degrees) **A** Analog plots of eye position, gaze position, eye velocity and head velocity. **B** Digital plots of slow phase eye velocity versus head velocity

1) Vertical smooth pursuit – laser target back-projected on a featureless screen directly in front of the subject (0.2 Hz, peak velocity 22.5 deg/s; 0.4, 0.8, 1.6 Hz, peak velocity 45 deg/s). 2) Visual-vestibulo-ocular reflex (VisVOR) – pitch while fixating a target at 2 M. 3) Vestibulo-ocular reflex (VOR) – pitch in the dark imagining the fixation target from 2. 4) Fixation suppression of the VOR (VOR + Fix) – pitch while fixating on a target mounted on a bite-bar (target 15 cm from the bridge of the nose).

Data analysis

Vertical gaze position (relative to space) and head position were recorded from the eye and head coils, respectively. These two signals were subtracted to produce vertical eye position (relative to the orbit). Both position signals were differentiated with operational amplifiers to produce eye and head velocity traces (e.g., see Figs. 1A, 2A). In addition, the data were digitized at a rate of 200 samples/s

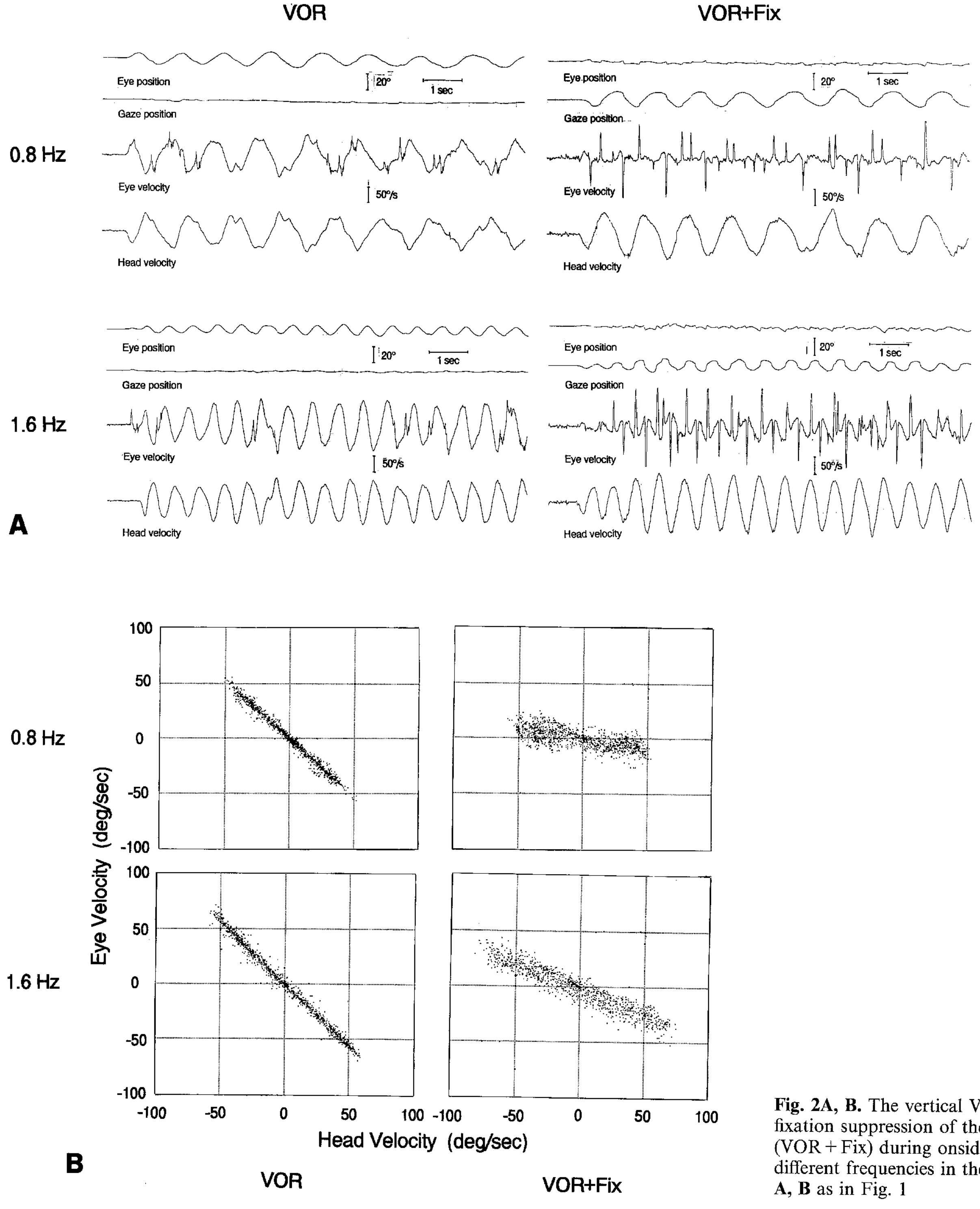

Fig. 2A, B. The vertical VOR and fixation suppression of the vertical VOR (VOR + Fix) during onside pitch at 2 different frequencies in the same subject. **A, B** as in Fig. 1

(Baloh et al. 1988). Fast components were identified and removed based on their direction and characteristic velocity profile. Fast components were replaced by connecting points on each side of the missing segment with a quadratic regression line. Plots of slow phase eye velocity vs. head velocity were generated for each test condition (e.g. see Figs. 1B and 2B) and the slope (gain) in each direction was calculated by fitting a least-square linear regression line to the data. Also, a fast Fourier transformation was performed giving the magnitude, phase and DC bias of the fundamental (A_1) and first 5 harmonics (A_2–A_6) of the eye and head velocity for cycles 2–7 (the first cycle was always discarded) (Baloh et al. 1988). Harmonic distortion (percent) was defined as:

$$\frac{\sqrt{A_2^2+A_3^2+A_4^2+A_5^2+A_6^2}}{A_1}\times 100.$$

All statistical comparisons used two-tailed Student's t test for paired observations.

Table 1. Mean gain (± standard deviation) for up and down slow components of the vertical vestibulo-ocular reflex under 3 different visual conditions (see text for definitions) in the erect and onside positions ($n=8$)

Frequency (Hz)	Erect		Onside	
	Up	Down	Up	Down
VisVOR				
0.4	1.00 ± 0.03	0.99 ± 0.05	1.01 ± 0.04	1.00 ± 0.03
0.8	1.02 ± 0.05	1.00 ± 0.04	1.00 ± 0.06	1.02 ± 0.05
1.6	0.98 ± 0.05	0.99 ± 0.04	0.99 ± 0.04	0.99 ± 0.03
VOR				
0.4	0.83 ± 0.24	0.78 ± 0.26	0.79 ± 0.23	0.74 ± 0.18
0.8	0.98 ± 0.12	0.95 ± 0.16	0.91 ± 0.16	0.92 ± 0.14
1.6	0.95 ± 0.12	0.96 ± 0.11	0.95 ± 0.21	0.92 ± 0.13
VOR–FIX				
0.4	0.12 ± 0.08	0.11 ± 0.09	0.15 ± 0.09	0.12 ± 0.11
0.8	0.25 ± 0.11	0.28 ± 0.13	0.26 ± 0.13	0.21 ± 0.13
1.6	0.45 ± 0.18	0.42 ± 0.21	0.43 ± 0.21	0.40 ± 0.23

Results

Vestibulo-ocular reflex

Representative recordings of eye position, gaze position, eye velocity and head velocity during voluntary pitch (1.6 Hz, amplitude 5–7 deg.) are shown in Fig. 1A for the same subject in the upright and onside position with the lights on (VisVOR) and in the dark (VOR). At this frequency and amplitude the VisVOR consisted of a smooth compensatory eye movement. Fast components (saccades) occasionally interrupted the smooth VOR eye movements. The gaze position trace was flat during the VisVOR, indicating ocular stability in space (eye velocity was equal and opposite to head velocity). The VOR gaze position trace was also stable except for intermittent saccades and for a static downward velocity bias in the lateral position (giving the appearance of upbeat nystagmus). This subject did not exhibit nystagmus in the lateral position with the head still. The eye velocity and head velocity traces were approximately equal and opposite under each test condition (i.e., the gain of the VOR and VisVOR was the same in both positions).

Although the head position signals appeared sinusoidal, the head velocity signals exhibited obvious distortion. From frequency analysis the harmonic distortion of the head velocity traces shown in Fig. 1A were as follows: VisVOR (upright), 5.9%; VisVOR (lateral), 5.4%; VOR (upright), 9.7%; VOR (lateral), 6.7%; Overall harmonic distortion of the head velocity ranged from 3.7 to 27.4% (mean ± standard deviation = 9.4 ± 5.6%). There was no significant difference ($p > 0.05$) in the mean harmonic distortion of the head velocity signal for the erect versus the onside position at any frequency. Furthermore, the plots of slow phase eye velocity vs. head velocity (Fig. 1B) were remarkably linear regardless of the amount of harmonic distortion (i.e., gain measurements were not affected by the harmonic distortion). The subject whose data is shown in Fig. 1 achieved higher peak head velocities in the lateral position compared to the erect position; others showed just the opposite. The mean DC bias of the eye velocity traces was not significantly different ($p > 0.05$) from zero for any test condition indicating that there was no consistent velocity bias in the vertical VOR for the erect or lateral position.

Table 2. Mean gain (± standard deviation) for up and down smooth pursuit in the erect and onside positions ($n=8$)

Freq – peak vel. [°/s]	Erect		Onside	
	Up	Down	Up	Down
0.2–22.5	0.90 ± 0.11	0.88 ± 0.13	0.91 ± 0.10	0.90 ± 0.12
0.4–45	0.64 ± 0.19	0.63 ± 0.22	0.62 ± 0.15	0.63 ± 0.23
0.8–45	0.51 ± 0.21	0.47 ± 0.23	0.49 ± 0.18	0.50 ± 0.24
1.6–45	0.29 ± 0.22	0.27 ± 0.16	0.29 ± 0.19	0.30 ± 0.22

There was no significant difference ($p > 0.05$) between the mean gain of up and down slow phases of either the VOR or VisVOR at any frequency or in any position (Table 1). We also calculated the average gain (up + down/2) for the VOR and VisVOR responses and found no significant difference ($p > 0.05$) between these values in the erect versus lateral position at any frequency of pitch. VOR gain measurements consistently showed greater scatter (i.e., larger standard deviations) than the VisVOR measurements. As expected, over the frequency range studied the eye and head velocity signals were almost exactly 180° out of phase.

Fixation suppression of the VOR

Fig. 2A illustrates representative recordings of eye position, gaze position, eye velocity and head velocity during onside voluntary pitch (0.8 and 1.6 Hz) in the dark (VOR) and in the light with a head-fixed target (VOR–FIX). As in Fig. 1 the VOR gaze position traces were nearly flat indicating that the eye and head velocity were approximately equal and opposite. The subject did not completely suppress the VOR at either frequency although suppression was much better at 0.8 Hz compared to 1.6 Hz. As suggested by the analog data the gain (slope) of the VOR was symmetrical and fixation suppression was approximately equal in both directions (Fig. 2B).

Mean VOR–FIX gain values from similar plots during voluntary pitch in the erect and onside positions in 8 subjects are given in Table 1. There was no significant difference ($p > 0.05$) between fixation suppression of up and down VOR slow phases at any frequency in either position. Furthermore, there was no difference ($p > 0.05$) between the average (up + down/2) VOR–FIX gain in the erect versus onside position at any frequency. Finally, the mean gain of up and down pursuit was not significantly different ($p > 0.05$) at any frequency in either position in the 8 subjects (Table 2).

The average gain (up + down/2) of vertical pursuit, VOR and VOR–FIX at different frequencies are shown

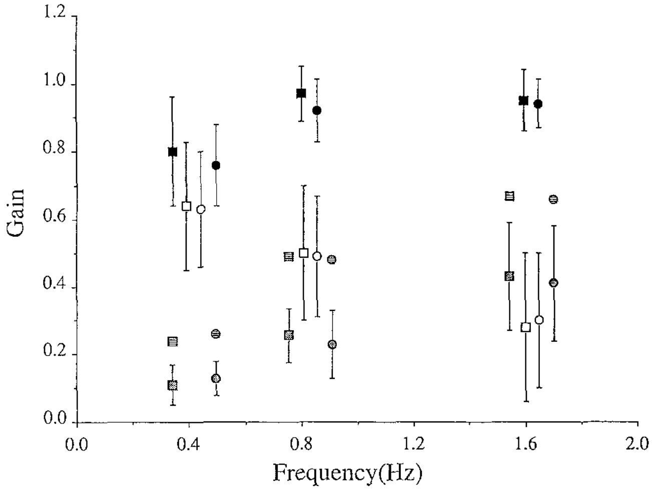

Fig. 3. Mean (± 1 standard deviation) vertical pursuit (open symbols), VOR (closed symbols) and VOR + Fix (hatched symbols) gain measurements (up + down/2) in the erect (squares) and onside (circles) position ($n = 8$). Predicted VOR–FIX gain values (symbols with horizontal lines) based on a linear interaction of smooth pursuit and the VOR (Lau et al. 1978) are given for comparison

in Fig. 3. Vertical pursuit gain rapidly fell with increasing frequency while vertical VOR–FIX gain gradually increased with increasing frequency. VOR gain was relatively fixed over this frequency range. Predicted VOR–FIX gain values assuming a simple linear interaction model of pursuit and the VOR (Lau et al. 1978) are also shown in Fig. 3. The observed fixation suppression gain values are lower than the predicted values (particularly at 0.8 and 1.6 Hz) indicating that additional mechanisms of suppression must be involved (see Discussion).

Discussion

Vertical VOR

Unlike prior studies in the cat (Tomko et al. 1988), we did not find that the human vertical VOR induced by onside pitch was any different from the vertical VOR induced by upright pitch. There was no consistent asymmetry between up and down VOR slow phases in either position and the average gain over the frequency range of 0.4 to 1.6 Hz was not significantly different in the two positions. In the cat, the asymmetry between up and down VOR slow phases induced by onside pitch was greatest at low frequencies (less than 0.1 Hz) and actually reversed at higher frequencies (1.0 Hz). The difference in gain between upright and onside pitch in the cat was greatest at low frequencies but was also present in frequency range of 0.1 to 1.0 Hz (overlapping the lower end of the frequency range studied in this report).

An important difference between the cat and human studies is the fact that the cat received passive pitch whereas the human subjects performed active pitch. Jell et al. (1988), and Collewijn et al. (1988), reported that the gain of both the horizontal and vertical VOR in the erect position was approximately 15% higher with active than with passive motion. Similarly, the vertical VOR gain measurements with active pitch in this study are about 20% higher than our previously reported measurements obtained with passive pitch in the erect position (Baloh et al. 1986). Consistent with these observations Robinson and Tomko (1987) found secondary vestibular neurons in the cat that responded at higher rates and for a larger part of the movement during active head movements compared to passive movements delivered with a turntable. Neck sensory input accounted qualitatively for the extra firing present during voluntary movement. Also, efferent "motor command" signals are available to improve performance during voluntary head movements. Deficiencies in the human vertical VOR with onside pitch that might be present with passive movements could thus be corrected during active movements.

Vieville et al. (1986), measured the vertical VOR gain to active head oscillations before, during and after a seven-day space flight in a single astronaut and found that vertical VOR gain dropped approximately 30% when measured on day 1 of the space flight compared to pre-flight measurement. The vertical VOR gain remained low for the first four days of space flight but then returned to normal by the sixth day of flight. Surprisingly, the horizontal VOR showed a similar drop in gain during the initial days of space flight with a return to normal by day 7. Since otolith input is not considered to be critical for the normal functioning of horizontal VOR, the observed decrease in both vertical and horizontal VOR gain in microgravity may be nonspecific, related to the presence or absence of otolith signals rather than dynamic changes in these signals. Consistent with this interpretation, Vesterhauge et al. (1982), found that the horizontal VOR gain decreased during the zero-g phase of parabolic flight and increased during the 2-g phase. Obviously voluntary onside pitch is different from voluntary pitch in microgravity.

Studies in monkey (Matsuo and Cohen 1984) and man (Baloh et al. 1983) have found a consistent asymmetry in velocity storage within the vertical VOR during onside pitch. The time constant of up slow phase velocity is greater than that of down slow phase velocity after step changes in angular velocity. Vertical optokinetic-after-nystagmus (OKAN) shows the same asymmetry when tested in the onside position. This asymmetry is clearly related to otolith input (at least in the monkey) since it disappears when the same subjects are tested in the erect position (Matsuo and Cohen 1984). An asymmetry in velocity storage would not affect the onside vertical VOR gain measurements over the frequency range used in this study, however.

Visual-vestibular interaction

Even though the VOR gain fluctuated from values as low as 0.6 at 0.4 Hz in one subject to as high as 1.2 at 1.6 Hz in another subject, the VisVOR gain (pitch in the light with an earth-fixed target) was consistently near 1.0 with a standard deviation less than 0.05. In other words, regardless of minor deficiencies in the vertical VOR the normal functioning visual vestibular reflex has a gain close to 1 over the frequencies of natural head movements in both the upright and lateral positions. Therefore, even if the vertical VOR gain were to decrease in microgravity the visual-vestibulo-ocular reflex should still work normally and the subject should not experience oscillopsia. The VisVOR can also quickly adjust to changes in visual signals. Collewijn and colleagues (1983) demonstrated that compensatory eye movements in the light during active head movements could be rapidly adapted by as much as 36% from baseline conditions when normal subjects were fitted with magnifying or reducing spectacles. Even greater immediate visual modulation of the VOR is observed during the wearing of telescopic spectacles (Demer et al. 1987).

Unlike prior studies (Benson and Guery 1965; Baloh et al. 1983) that found an asymmetry in fixation suppression of the vertical VOR during passive onside pitch at low frequencies of rotation (downward slow phases inhibited better than upward) we found no significant difference between fixation suppression of upward and downward VOR slow phases during active onside pitch in the frequency range of 0.4–1.6 Hz. There are several possible explanations for this discrepancy. First, prior studies may not have tested a representative sample of normal subjects. This is clearly not the case since we have tested more than 20 normal subjects with passive low-frequency onside pitch (unpublished data) and every one exhibited the predicted asymmetry. Secondly, the VOR–FIX asymmetry may be frequency dependent. Different frequencies were used with the passive and active onside pitch studies. The subject whose active pitch data is shown in Fig. 2 (with no asymmetry) was later tested with passive low frequency (0.05 Hz) onside pitch at comparable peak head velocities and showed the expected asymmetry. It is not physically possible to produce low frequency, high velocity active pitch and due to torque limitations of most rotational platforms (including ours) the peak velocities of high frequency passive onside pitch are limited. Since VOR–FIX gain markedly increases at higher frequencies asymmetries may be less apparent at these frequencies. Thirdly, and probably the most important explanation for the differences in vertical VOR–FIX data is the difference between active and passive head movements discussed earlier.

Fixation suppression of the VOR in man has generally been attributed to the smooth pursuit system (Dichgans et al. 1978; Barnes and Edge 1983). Pursuit in one direction is used to cancel VOR slow phases in the opposite direction. However, our finding of symmetrically poor vertical pursuit at high frequencies despite relatively good fixation suppression of the vertical VOR up to 1.6 Hz suggests that there must also be another mechanism for suppression. At lower frequencies and velocities where vertical pursuit is good the pursuit system cancels the VOR (probably following a simple linear interaction model) (Lau et al. 1978). At higher frequencies where pursuit deteriorates a second suppression system is required. This second system is not as effective as smooth pursuit since suppression is never complete (as it can be at lower frequencies) but it does help to stabilize gaze. Robinson (1982) proposed a model in which a signal proportional to the velocity of a planned head movement is used to cancel the VOR. This mechanism would only function during active head movements (such as in our study).

In conclusion, asymmetries previously observed in the vertical VOR and fixation suppression of the vertical VOR during passive pitch were not seen during active pitch in either the erect or onside positions. Presumably with active head movements efference and neck sensory information compensate for deficiencies in the vertical VOR and improve vertical ocular stability.

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