

## ORIGINAL PAPER

Mingjia Dai · Leigh McGarvie · Inessa Kozlovskaya  
Theodore Raphan · Bernard Cohen

## Effects of spaceflight on ocular counterrolling and the spatial orientation of the vestibular system

Received: 29 March 1994 / Accepted: 21 July 1994

**Abstract** We recorded the horizontal (yaw), vertical (pitch), and torsional (roll) eye movements of two rhesus monkeys with scleral search coils before and after the COSMOS Biosatellite 2229 Flight. The aim was to determine effects of adaptation to microgravity on the vestibulo-ocular reflex (VOR). The animals flew for 11 days. The first postflight tests were 22 h and 55 h after landing, and testing extended for 11 days after reentry. There were four significant effects of spaceflight on functions related to spatial orientation: (1) Compensatory ocular counterrolling (OCR) was reduced by about 70% for static and dynamic head tilts with regard to gravity. The reduction in OCR persisted in the two animals throughout postflight testing. (2) The gain of the torsional component of the angular VOR (roll VOR) was decreased by 15% and 50% in the two animals over the same period. (3) An up-down asymmetry of nystagmus, present in the two monkeys before flight was reduced after exposure to microgravity. (4) The spatial orientation of velocity storage was shifted in the one monkey that could be tested soon after flight. Before flight, the yaw axis eigenvector of optokinetic afternystagmus was close to gravity when the animal was upright or tilted. After flight, the yaw orientation vector was shifted toward the body yaw axis. By 7 days after

recovery, it had reverted to a gravitational orientation. We postulate that spaceflight causes changes in the vestibular system which reflect adaptation of spatial orientation from a gravitational to a body frame of reference. These changes are likely to play a role in the postural, locomotor, and gaze instability demonstrated on reentry after spaceflight.

**Key words** Spaceflight · Otoliths  
Ocular counterrolling · Velocity storage · Monkey

### Introduction

Adaptation to microgravity presents a unique set of challenges to the vestibular system. On earth, the otoliths are subject to a constant gravito-inertial acceleration (GIA) due to gravity. Tilting the head does not change the magnitude of the GIA, it only rotates it relative to the head. Translation induces an additional acceleration component which effectively rotates the GIA vector and increases its magnitude. In space, the GIA component due to gravity is absent, and the otoliths only sense the linear acceleration associated with translation. Consequently, the linear acceleration vector never rotates relative to the head in space, but only changes its magnitude along the direction of movement. The semicircular canals which respond to angular acceleration function in microgravity as they did on earth.

Since there is no otolith-induced compensatory torsion of the eyes (ocular counterrolling, OCR) in space, and since compensatory torsional eye movements due to head-on-body tilt are negligible in flight (Hofstetter-Degen et al. 1993), the demand for otolith-driven OCR is probably much reduced. It has been postulated that there is a reinterpretation of otolith input in microgravity so that linear acceleration, sensed by otolith organs, is now interpreted primarily as translation (Reschke et al. 1984; Parker et al. 1985; Arrott and Young 1986; Young et al. 1986). In support of this, interaural linear acceleration after spaceflight produces predominantly

---

M. Dai (✉) · L. McGarvie · B. Cohen  
Department of Neurology,  
Box 1135,  
Mount Sinai School of Medicine,  
1 East 100th Street, New York, NY 10029, USA;  
FAX no: 212-831-1610

B. Cohen  
Department of Physiology and Biophysics,  
Mount Sinai School of Medicine,  
New York, USA

I. Kozlovskaya  
Institute of Biomedical Problems, Moscow, Russia

T. Raphan  
Department of Computer and Information Science,  
Brooklyn College, CUNY, USA

horizontal compensatory eye movements (Arrott and Young 1986; Young et al. 1986).

The otolith-ocular reflex that produces OCR on earth has been studied in considerable detail (Fischer 1927; Camis and Creed 1930 for early review; Miller and Graybiel 1971; Diamond et al. 1979; Diamond and Markham 1983; Collewijn et al. 1985; Takemori et al. 1989), but less is known about OCR after spaceflight. There is evidence that OCR is reduced after exposure to microgravity, but the data are not conclusive. Differences in the results may reflect variations among individuals, in experimental procedures, and in techniques of measurement. Measured with afterimages (Fischer 1927), OCR was reduced in two cosmonauts for up to 14 days after landing (Yakovleva et al. 1982), recovering only at the next test point of 36 days. There was also anticompany torsion ("paradoxical counter-rolling") in the direction of head tilt in some subjects after long-duration missions (L.N. Kornilova, unpublished work). After the Spacelab-1 Mission, OCR, measured from photographs, was reduced on average by 28% and 56% to one side in two subjects 1 day after landing (Vogel and Kass 1986). Changes in gain to the other side were inconclusive. Using afterimages, OCR was reduced by 57% in one astronaut for 5 days after the 1992 Russian-German MIR Space Mission (Hofstetter-Degen et al. 1993). In the COSMOS 2044 Mission, we studied torsional eye movements of monkeys with implanted search coils using controlled dynamic tilts during off-vertical axis rotation (OVAR). The gain of OCR could not be measured due to technical problems, but the phase of OCR was unchanged, suggesting that the otoliths were still sensing gravity normally after flight (Cohen et al. 1992a). The first purpose of this study was to determine whether the gain of otolith-induced, compensatory ocular torsion against gravity (OCR) changed after spaceflight.

Yaw and pitch head angular movements are probably largely unchanged in space, although activation of the semicircular canals by pitch and roll head movements may be reduced at high frequencies in the absence of locomotion (Grossman et al. 1988). There was no change in the yaw axis vestibulo-ocular reflex (VOR) gain of humans during flight in Spacelab-1 (Benson and Vieville 1986) or of monkeys after the COSMOS 2044 Mission (Cohen et al. 1992a). There are conflicting reports as to whether the active yaw axis VOR gain, which involves intention, cervico-ocular reflexes, and pursuit is modified, however (Kozlovskaya et al. 1986; see Cohen et al. 1992a, for review). There is less information about changes in gain of the VOR for rotation about the pitch and roll axes (pitch and roll VOR, respectively). The roll or torsional VOR, induced by active sinusoidal head-on-body tilt and measured by video-oculography, was reduced in the first 4 days of flight in one subject (Clarke et al. 1993). The second purpose of these experiments was to determine whether spaceflight affected the pitch and roll VOR.

Velocity storage in the vestibular system of monkeys is spatially oriented on earth (Dai et al. 1991, 1992;

Raphan and Cohen 1988; Raphan et al. 1992). As a result, when horizontal optokinetic nystagmus (OKN) is elicited about an animal's yaw axis while it is in a tilted position, vertical and torsional components develop during the optokinetic afternystagmus (OKAN) that tend to bring the axis of rotation of the eyes toward the spatial vertical. A similar reorientation of eye velocity toward the axis of gravity, attributable to velocity storage, has been found in human OKN (Gizzi et al. 1994). There is reason to believe that there could be alterations in spatial orientation after adaptation to microgravity (Cohen et al. 1992a). The third purpose of these experiments was to test the hypothesis that adaptation to microgravity is associated with a shift in orientation of velocity storage from a gravitational to a body axis.

The current series of experiments was an extension of studies begun on the COSMOS 2044 flight. Steps of velocity and sinusoids were used to test the gain of the yaw, pitch, and roll VOR. OCR was evaluated by static tilts and dynamically by off-vertical axis rotation. Finally, OKAN, induced by yaw axis OKN in tilted conditions, was used to test the orientation of the velocity storage system. Preliminary results on OCR have been reported elsewhere (Dai et al. 1993).

---

## Materials and methods

### General overview

Twelve male rhesus monkeys of approximately 4 kg were used in these experiments. The experiments conformed to the *Principles of Laboratory Animal Care* (NIH publication 85-23, revised 1985) and were approved by the Institutional Animal Care and Use Committee (IACUC). The animals were also utilized in studies of cellular activity in the vestibular nerve (Correia 1993) and of the effects of high-frequency linear acceleration on ocular movements (Tomko et al. 1993). Other investigations were done on the musculoskeletal, immune, and regulatory systems of these animals, similar to those reported in association with a previous COSMOS flight (COSMOS 2044 Mission 1992). From this group of control animals, two were chosen (monkeys 26,151 and 27,906). They flew in space for 12 days on the COSMOS Biosatellite Flight 2229. In this paper we compare the preflight and postflight eye movements of these two animals and relate them to the eye movements of the control animals tested at the same times. For convenience, we will refer to the flight animals as 6151 and 7906.

General care and handling of the animals was the same as described in a previous paper (Cohen et al. 1992a). During pre- and postflight testing, the animals were housed in the vivarium at the Institute of Biomedical Problems in Moscow. Surgical implantation of head bolts that painlessly immobilized the head in stereotaxic coordinates during testing and of coils for eye movement recording was done approximately 4 months before flight; preflight testing took place 3 months before flight. Each animal was tested at least twice with 2 or more days between sessions. Testing was done in the daytime when the animals were fresh and alert, and food was withheld before testing. At the end of testing, we rated the animals according to their performance on the VOR tests. This, along with the ratings of performance on other tasks by other investigators formed the basis for selection of the flight monkeys.

The flight animals were launched on 29 December 1992, flew for 298 h (12.4 days) and were recovered on 10 January 1993. While in space, the monkeys' bodies were restrained, but their heads, arms and legs were free. They performed behavioral testing to obtain water, moving their head and eyes toward visual targets and pressing a lever to receive a reward. The status of the animals

was intermittently monitored by down-linked video. There were changes in the vacuum sensor in the food spout of 6151, and the food intake of this animal dropped several days before landing; its nutrition was maintained with fruit juice. In addition, from the 9th to the 11th flight day, the temperature in the capsule rose from 20 to 31°C before it stabilized and dropped. As a result, the flight was terminated 2 days earlier than planned. 6151 was dehydrated after flight, but its general activity level was normal at the landing site. On the return flight to Moscow, it had orthostatic hypotension and fainted. It was resuscitated, but it was not tested until 55 h after landing. At that time, its condition had returned to normal. 7906 was healthy on landing.

At the end of the flight, the capsule was parachuted to the earth. The animals were recovered by helicopter within 30 min after landing. They were kept in their chairs and held in darkness to the extent possible while they were flown back to the Institute in Moscow by jet. Testing of 7906 began 22 h after landing. Post-flight testing of 6151 was delayed until 55 h after landing. The postflight tests extended for 11 days.

### Surgery

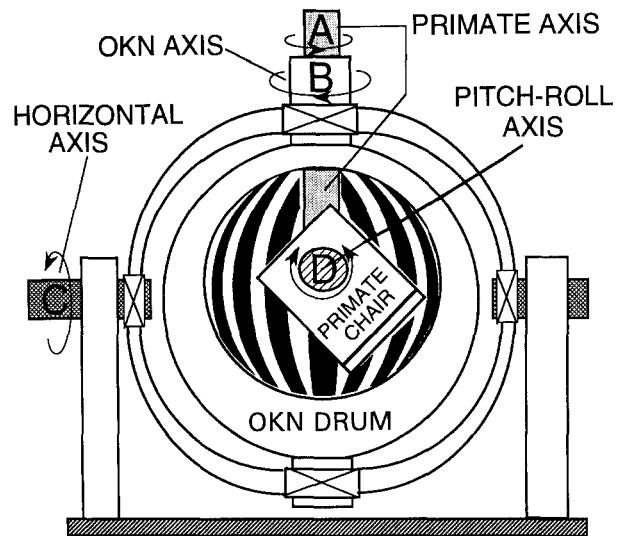
With the animals under anesthesia, using sterile surgical conditions, coils were implanted in the frontal plane of both eyes (frontal plane coils) under the conjunctiva to record horizontal and vertical eye position (Robinson 1963; Judge et al. 1980). A third coil was implanted on the top of the left eye (roll coil) to record torsional eye movement (Robinson 1963). To implant the roll coil, Tenon's capsule was opened about 2 mm below the tarsal plate, and the superior rectus muscle was identified and freed medially and laterally. A three-turn, 11-mm coil was fashioned by passing the wire under the superior rectus muscle. The leads were then twisted for 15–20 cm, and the coil diameter was measured with a sterile caliper. Anteriorly, the coil was sutured to the globe medial and lateral to the insertion of the superior rectus. Posteriorly, the coil lay under the superior rectus muscle on the top of the eye. A tension loop was pushed into a pocket lateral to the superior rectus. The coil wires were led out of the eye through the lateral portion of Tenon's capsule, passed subcutaneously to the top of the skull, and soldered to a head mount. Postoperatively, the animals were treated with antibiotics, steroids, and analgesics. Typical impedances were 67  $\Omega$  for the frontal plane coils and 56  $\Omega$  for the roll coils.

### Conventions

Rotational stimuli, eye position, and eye velocity were determined by a right-hand rule referenced to the head coordinate frame. Horizontal eye movement is described by a rotation of the eye whose vector is along the yaw or head-to-feet axis. Vertical eye movement is a rotation whose vector is along the pitch or interaural axis, and torsional eye movement is a rotation of the eye whose vector is along the roll or naso-occipital axis. Right, up, and clockwise (viewed from the back) eye movements and eye velocities are represented in the figures by upward deflections of the eye position and velocity traces. We define compensatory eye movements induced by head movement around the yaw, pitch, and roll axes as the horizontal or yaw, vertical or pitch, and torsional or roll VOR, respectively. Gain is eye velocity divided by stimulus (or head) velocity. OCR is the compensatory torsion of the eyes when the head is tilted with regard to gravity. We assume that the optic axis is close to the roll axis of the head coordinate frame.

### Experimental apparatus

A four-axis vestibular and optokinetic stimulator (Neurokinetics, Pittsburgh) was transported from New York to the Institute of Biomedical Problems in Moscow for these experiments. Each of the four axes went through the center of the head and was independently controlled by computer. The rotator consisted of a pri-



**Fig. 1** Four-axis vestibular and optokinetic stimulator used in this series of experiments. See Materials and methods for a description of the apparatus. (OKN optokinetic nystagmus)

mate axis (Fig. 1A), through the center of which was a pitch-roll axis (Fig. 1D) to which the primate chair was attached. The maximum acceleration and deceleration of the primate axis was 200°/s<sup>2</sup>. The pitch-roll axis was positionally controlled to provide  $\pm 90^\circ$  of excursion at a maximum acceleration of 600°/s<sup>2</sup>. It produced pitch or roll, depending on whether the animal was positioned so that its interaural or naso-occipital axis was aligned with the axis of rotation, respectively.

The primate and pitch-roll axes were enclosed in a light-tight, optokinetic sphere, 109 cm in diameter, with 10° vertical black and white stripes on the inside. When the OKN axis (Fig. 1B) rotated, the sphere produced full-field motion that induced OKN and OKAN. The optokinetic sphere and the primate axis were fixed to a spine that surrounded the sphere. The spine was attached to a horizontal axis (Fig. 1C) which was supported by A-frames. The spine was positionally controlled to pivot  $\pm 180^\circ$  about the horizontal axis. Thus, the primate, pitch-roll, and OKN axes could be tilted by positioning them about the horizontal axis (Fig. 1C).

By tilting the structure and putting the primate axis (Fig. 1A) in motion, the animal could be rotated about an off-vertical axis. Since the primate axis and the axis of the optokinetic sphere were coaxial and independent, the visual surround and monkey could be rotated at the same rate and in the same direction to produce a relative stationary surround. This was useful for suppressing the component of vestibular nystagmus attributable to velocity storage (Raphan et al. 1979; Waespe et al. 1983) during velocity steps at the onset of OVAR.

### Experimental control and data acquisition

The monkeys' heads were fixed to a plastic frame that held a square-field coil, 25.4 cm on a side. The frame was attached to the primate chair. Movements of the left eye were measured in three dimensions and of the right eye in two dimensions with the magnetic scleral search coils. Voltages associated with eye position and with the position and velocity of the various axes were recorded by analog amplifiers with a bandwidth of d.c.–40 Hz and fed to analog-digital (A/D) convertors. Voltages associated with eye positions were sampled at 600 Hz, and stimulus data were sampled at 150 Hz. Eye positions, analog-differentiated eye velocities, and stimulus data were also displayed on an eight-channel chart recorder (Astromed) and an oscilloscope.

We used preflight calibrations to compare the eye movements of the flight animals before and after flight. Our assumption was

that the eye-movement recording system had the same gain in the pre- and postflight testing. This was supported by the following: (1) the settings and gains of the instruments and the eye coil system were noted and maintained constant throughout the mission; (2) there was no change in the resistance of the eye coils, measured in each experiment, before and after flight; (3) Utilizing the same system for recording eye movements, there was no change in the pre- and postflight calibrations of the control monkeys.

### Experimental paradigms

A 486 PC was used to control the experiments. Each stimulus paradigm was called in by a computer program specifically designed for that experiment. To calibrate the horizontal and vertical output of the eye coils, the monkeys were placed upright and left ear 90° down, respectively, then rotated in light about a vertical axis at 30°/s to the right and left for 20 s while they viewed the earth-stationary OKN stripes. Under this condition, the velocity gain (slow-phase eye velocity/head velocity) of the combined visual-vestibulo-ocular reflex was assumed to be close to unity for the yaw and pitch eye velocities. Position calibrations for horizontal and vertical eye movements were derived from the velocity calibrations. Baseline or primary (zero) eye position was determined in a manner similar to that for the roll eye position calibration described below.

A position calibration of the roll coil for each monkey was determined by mounting a coil of the same size on a jig and rotating it  $\pm 15^\circ$  in the magnetic field. A value of A/D convertor counts was determined that corresponded to the 15° position change. The baseline or primary roll eye position was estimated by averaging 20 s of eye position with the monkey upright in the darkness. This position calibration was then used to obtain a calibration of roll eye velocity. Using this technique, the velocity gain of the torsional VOR, induced by a step rotation about a naso-occipital axis with the monkey prone, was about 0.6. This agrees with other studies of the gain of the roll VOR in rhesus monkeys using other calibration techniques (Crawford and Vilis 1991; Yue et al. 1994) and in humans (Collewijn et al. 1985; Furman and Baloh 1992). Preflight calibrations were used throughout.

To test static OCR, the monkey was positioned upright for 20 s in darkness. It was then tilted 90° at an angular velocity of 3°/s to its left and right. Spontaneous torsional eye positions were recorded for each of the three positions for 20 s. OCR was also studied dynamically during OVAR at an angular velocity of 60°/s. The advantages of OVAR are that it affords a measure of otolith response during tilt without canal activation, and that multiple cycles of recording of eye position can be averaged to obtain a robust measure of alteration in eye position with regard to head position relative to gravity.

To produce OVAR, the upright animal was rotated together with the illuminated optokinetic sphere at 60°/s. After the nystagmus had disappeared, the lights were turned off while the animal continued to rotate. The rotation axis was then tilted with a speed of 3°/s to angles of 15°, 30°, 45°, 60°, 75°, and 90° with respect to gravity. Each angle of tilt was held for 6 cycles of rotation. During OVAR, compensatory horizontal nystagmus developed and reached a steady state level. Since the animal's head was continuously reoriented with respect to gravity, roll eye position was altered continuously in direction and magnitude at a frequency of 0.17 Hz. We called this dynamic OCR. OVAR was done with animals rotating right and left.

Animals were tested in two different experimental paradigms to evaluate the gain of the roll VOR. First, the animal was rotated about a vertical naso-occipital axis in darkness at angular speeds of 30°/s, 45°/s, 60°/s, 75°/s, and 90°/s with short (5-s) velocity steps (acceleration 200°/s<sup>2</sup>) to the right and left. Clockwise and counterclockwise rotations were interleaved in an ascending order. Between rotations the animal was stationary in light for 5 s to discharge any postrotatory nystagmus. Second, with the animal upright, it was oscillated sinusoidally in darkness around a horizontal naso-occipital axis at frequencies of 0.025, 0.05, 0.077, 0.1, and 0.125 Hz over a peak-to-peak amplitude of 60°. Between testing at

each frequency, the monkey was stationary in light for 5 s. The duration of sinusoidal oscillation varied, ranging from 5–10 cycles/frequency.

The gain of the vertical VOR was investigated in the same way as the roll VOR. First, the monkey was rotated in left side down position for 5 s with steps of angular velocity of 30°/s, 45°/s, 60°/s, 75°/s, and 90°/s in both directions around a vertical interaural axis. The VOR gain is approximately constant at these velocities (Matsuo and Cohen 1984). Second, with the monkey upright, it was oscillated sinusoidally about a horizontal interaural axis over a peak-to-peak amplitude of 60° at frequencies of 0.017, 0.025, 0.05, 0.077, 0.1, and 0.125 Hz. Because the response to stimulation at frequencies lower than 0.025 Hz was too small to be analyzed, we only present gain data which were obtained at frequencies of 0.025 Hz and above. The velocity steps allowed us to evaluate the up and down gain of vertical nystagmus separately, whereas sinusoidal stimuli permitted evaluation of the offset level of the sinusoids from zero velocity, which reflected spontaneous vertical nystagmus.

The gain of the horizontal VOR was tested with the monkey rotating upright at angular speeds of 30°/s, 60°/s, 90°/s, and 120°/s to the right and left for 5 s about a spatially vertical axis that was coaxial with the body axis.

### Data analysis

The primary roll eye position was determined by averaging voltages associated with spontaneous roll eye positions over 20 s. With the animals upright, the variation in primary position was less than  $\pm 0.2^\circ$ . Roll eye positions for 90° tilts to the right and left were referenced to the upright measures. Most horizontal and vertical eye movements were not more than 20° from the baseline or primary position (Dai et al. 1991). Thus, any errors incurred in computing roll eye position or velocity when moving from secondary to tertiary positions were small. To insure this, the analysis was confined to roll components of horizontal and vertical eye positions of less than 10° from primary position. This constituted  $\approx 80\%$  of the data.

Dynamic OCR was measured from OVAR experiments. Five to six cycles of roll eye positions were averaged for each tilt angle. The trigger signal for averaging came from a potentiometer, which registered angular position about the yaw axis (Fig. 2, YAW POS). The mean roll eye position was fitted with a sine function at the dominant harmonic. The peak value of the fitted sine curve was taken as the amplitude of the OCR.

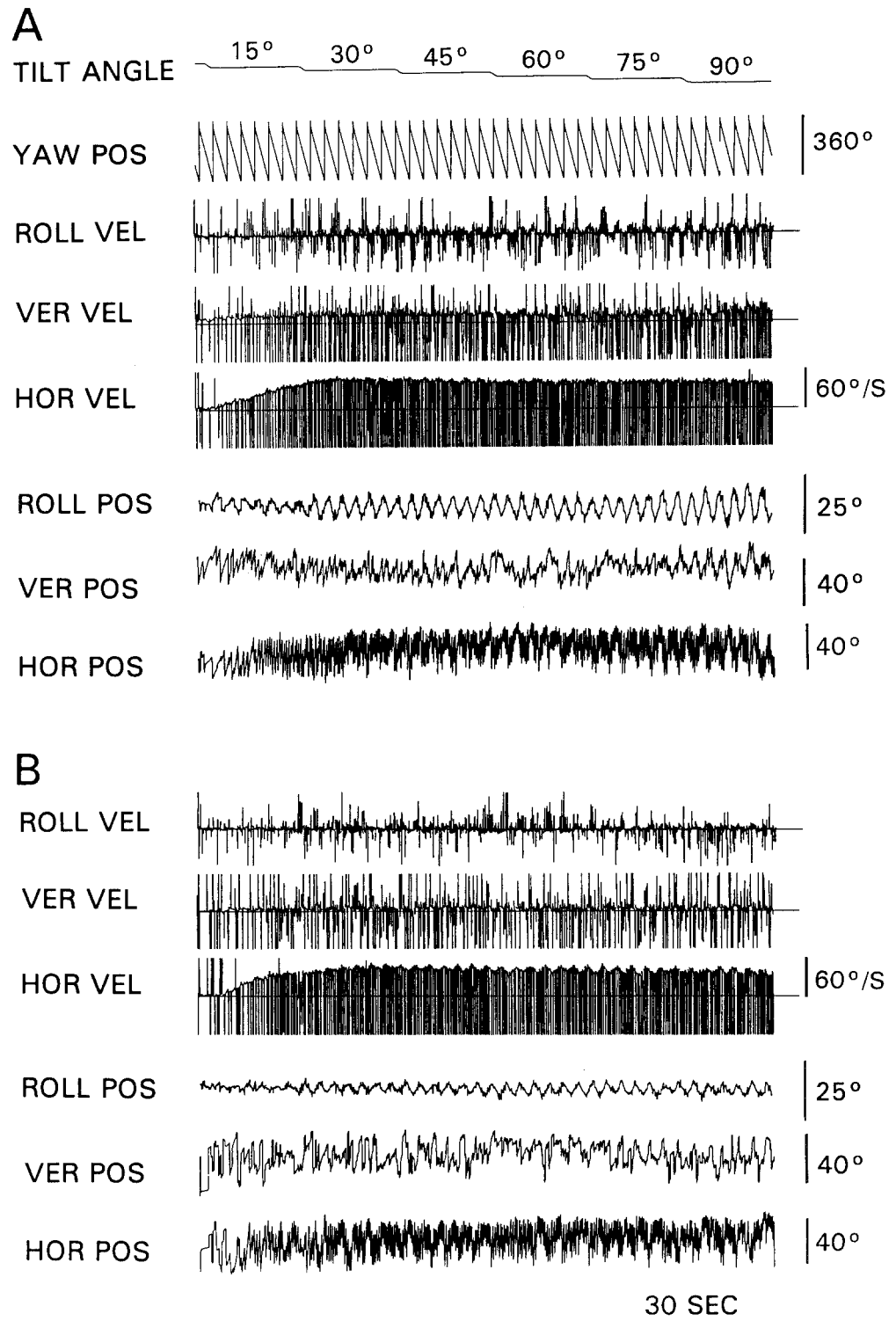
To determine the step gain of roll and vertical VOR, eye position data were digitally differentiated (Singh et al. 1981), and quick phases of nystagmus were removed by an algorithm based on order statistic filters (Engelkind and Stevens 1990). The data were smoothed by averaging each four points, reducing the effective sampling rate to 150 Hz. Slow-phase velocities associated with the first three beats of nystagmus were averaged, and the gain was determined by dividing the mean eye velocity by the stimulus velocity.

To calculate the gain of vertical and roll eye velocity from the oscillation experiments, the quick phases of eye velocity were first removed. Five to ten cycles of slow-phase eye velocity were averaged and fitted by a sinusoidal function. The peak vertical or roll eye velocity was taken from the amplitude of fitted curves. The gain was the ratio of peak eye velocity divided by the peak stimulus velocity.

The eigenvector angles with respect to gravity were computed from cross-coupling during OKAN using a methodology based on the model of velocity storage (Raphan and Sturm 1991; Dai et al. 1991). After obtaining the eigenvector angle derived from the system matrix of velocity storage, it was checked by computing a phase trajectory slope at the portion of the data that approached zero (Raphan et al. 1992; Dai et al. 1992). Errors between the computed angle and the angle of the slope were within  $\pm 2^\circ$ .

Significance levels were based on a two-tailed Student's *t*-test. The degrees of freedom (*df*) for unpaired data were calculated from the harmonic mean. Two standard deviations ( $\pm$  SD) were used to express the variance around the mean.

**Fig. 2A, B** Nystagmus induced by off-vertical axis rotation (OVAR) in darkness at 60°/s about tilted axes before (A) and 7 days after (B) spaceflight for monkey 6151. A The axis of rotation was tilted from 0 to 90° in the dark, inducing OVAR nystagmus (top trace, TILT ANGLE). A, B Roll, vertical, and horizontal eye velocities and positions are shown from top to bottom. A There was a weak modulation in slow-phase velocity before flight during OVAR nystagmus (HOR VEL, fifth trace), but prominent modulation in roll eye position (ROLL POS, sixth trace). B After flight, there was an increase in the modulation of horizontal slow-phase velocity (HOR VEL, third trace), and a decrease in the roll modulation (ROLL POS, fourth trace). Steady state horizontal eye velocity was the same before and after flight. Upward spontaneous nystagmus was reduced after flight (VER POS and VER VEL)



## Results

### Static and dynamic OCR

Static OCR was about  $\pm 6^\circ$  in the five monkeys tested before flight and in the three control monkeys tested in the postflight period (range 4.6–7.6°; Table 1). There was a small difference in static OCR between left and right 90° tilts across the five monkeys preflight and the three control monkeys postflight (Table 1; clockwise OCR:

$6.4 \pm 0.9^\circ$ ; counterclockwise OCR:  $5.7 \pm 1.0^\circ$ ), but the difference was not statistically significant ( $P = 0.069$ , paired,  $df = 7$ ). After spaceflight, the magnitude of OCR was reduced by about 70% in the two flight monkeys to a mean of  $1.8^\circ \pm 0.7^\circ$ . The difference in the preflight and postflight OCR, which remained over the 11 days of postflight testing, was statistically significant in the two flight animals ( $P < 0.001$ , unpaired,  $df = 18$ ; preflight  $n_1 = 10$ , postflight  $n_2 = 10$ ). In contrast, there was no change in OCR of the three control monkeys tested at

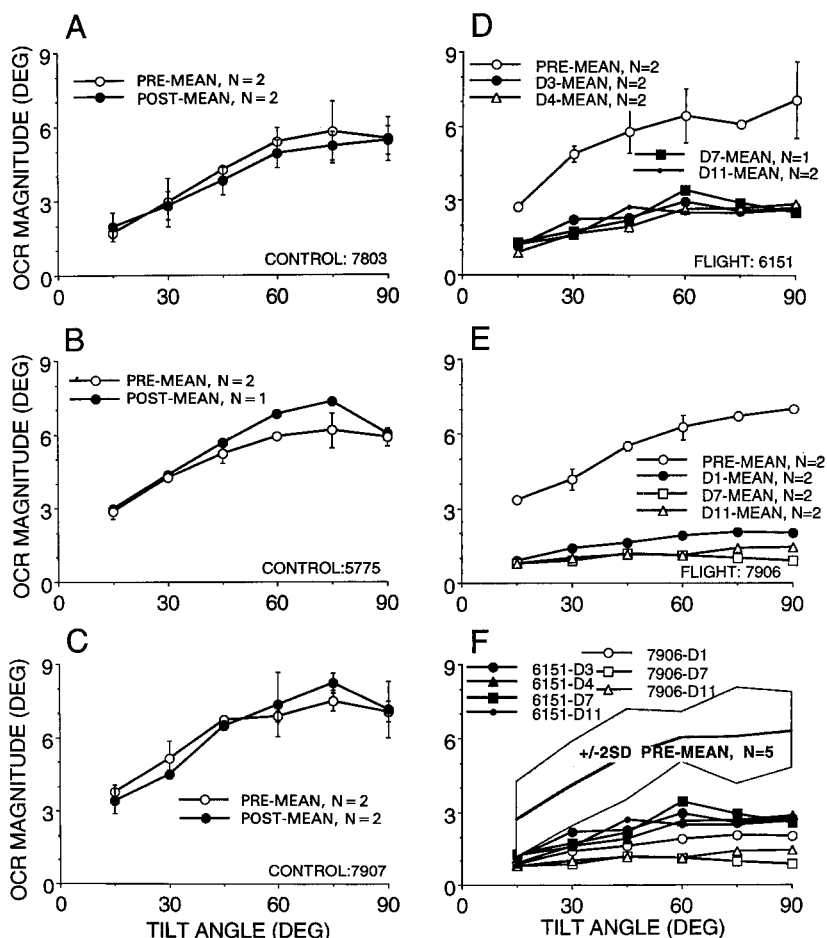
**Table 1** Compensatory ocular counterrolling (OCR) in two flight monkeys and three control monkeys in response to 90° of static tilt. Shown are the mean values of OCR before flight for each animal, the values in the postflight period for the two flight animals (7906 and 6151), and the postflight values for the three con-

trol animals. The means of static OCR for controls were  $6.4^\circ \pm 0.9^\circ$  and  $5.7^\circ \pm 1.0^\circ$  for clockwise and counterclockwise torsion, respectively. Analogous postflight values for two flight monkeys were  $1.6^\circ \pm 0.3^\circ$  and  $1.9^\circ \pm 1.0^\circ$

	OCR direction	Preflight magnitude (deg)	Postflight Magnitude (deg)				Timed controls
			Day 1	Day 3	Day 7	Day 11	
<b>Flight monkey</b>							
7906	Clockwise	$7.0 \pm 1.7$	$1.2 \pm 1.2$		$1.6 \pm 1.3$	$2.1 \pm 0.5$	
	Counter clockwise	$5.3 \pm 1.2$	$2.2 \pm 1.1$		$1.4 \pm 1.0$	$0.5 \pm 0.8$	
6151	Clockwise	$7.6 \pm 1.5$		$1.6 \pm 1.6$		$1.7 \pm 1.3$	
	Counter clockwise	$5.3 \pm 1.3$		$3.2 \pm 1.1$		$2.1 \pm 1.3$	
<b>Control monkey</b>							
7803	Clockwise	$5.8 \pm 0.2^a$				$5.8 \pm 0.9$	
	Counterclockwise	$4.6 \pm 1.2^a$				$6.9 \pm 2.7$	
7907	Clockwise	$7.5 \pm 2.2^a$				$6.9 \pm 1.9$	
	Counterclockwise	$7.2 \pm 2.0^a$				$6.5 \pm 2.3$	
5775	Clockwise	$5.3 \pm 2.9^a$				$5.7 \pm 2.4$	
	Counterclockwise	$4.8 \pm 1.3^a$				$4.8 \pm 2.0$	

<sup>a</sup> Timed controls

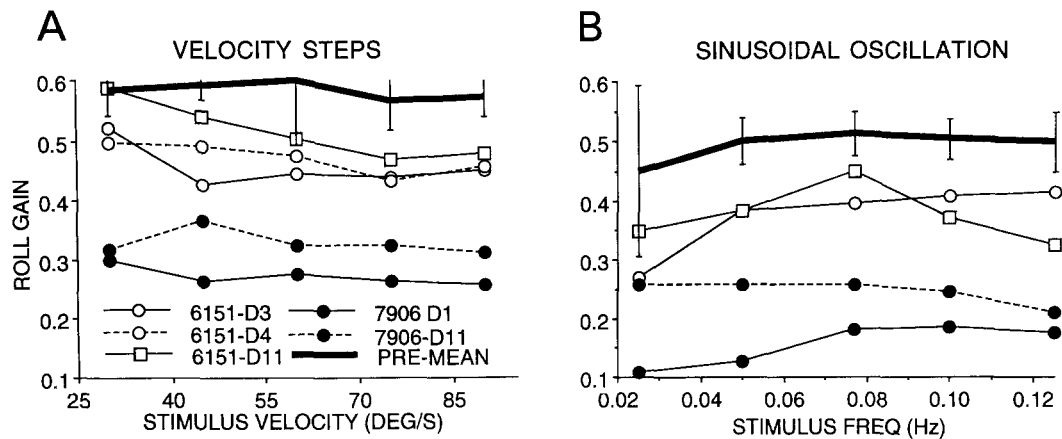
**Fig. 3** A–E Magnitude of preflight (*PRE*) and postflight (*POST*) dynamic ocular counterrolling (OCR) induced by OVAR in three control monkeys (A–C) and two flight monkeys (D,E). The mean values of 5–6 cycles were averaged for rotation to the right and to the left. The vertical error bars are  $\pm 1$  SD. Each animal was tested 60–90 days before flight and had several tests after flight from the 1st postflight day (*D1*) to the 11th day (*D11*). F The shaded area shows the mean  $\pm 2$  SD for the three control animals as well as preflight values for the flight animals. Note that the postflight data fell more than 2 SDs from the mean at all tilt angles



the same time before and after flight (Table 1;  $P=0.920$ , unpaired,  $df=14$ ; preflight  $n_1=10$ , postflight  $n_2=6$ ). There was no difference between the clockwise and counterclockwise OCR in the flight monkeys during the postflight period ( $P=0.624$ , paired,  $df=4$ ).

Dynamic OCR was assessed using OVAR. Typical trials for 6151 are shown in Fig. 2. The animal was first

rotated about a vertical axis until its yaw axis slow phase velocity declined to zero (not shown). Then, the axis of rotation was tilted 15–90° (Fig. 2A, TILT ANGLE, first trace) while the yaw axis rotation continued (YAW POS, second trace in Fig. 2A), inducing nystagmus. Before flight, the sinusoidal modulation in roll eye movement increased with increases in tilt angle of the



**Fig. 4** **A** Gains of the roll vestibulo-ocular reflex (VOR) induced by velocity steps between 30 and 90°/s. The mean for preflight testing is shown by a *heavy solid line* (PRE-MEAN). Error bars are  $\pm 2$  SD. There was a decrease in roll VOR gain for both 6151 (open symbols) and 7906 (filled symbols) after flight. **B** Gains of the roll VOR induced by sinusoidal oscillation around a horizontal naso-occipital axis. The *heavy line* shows the preflight mean  $\pm 2$  SD. After flight there was a decrease in the gain of the roll VOR. As with velocity steps (**A**), the gain decrease was greater for 7906 (50%; filled symbols) than for 6151 (15%; open symbols)

rotation axis (Fig. 2A, ROLL POS). After landing, the amplitude of dynamic OCR was substantially reduced (Fig. 2B, ROLL POS). Changes in 7906 were similar to those in 6151.

The maximum torsion induced by OVAR before and after flight for all angles of tilt is shown in Fig. 3D for 6151 and in Fig. 3E for 7906. The reduction of dynamic OCR was slightly greater in 7906 than in 6151, but neither monkey had recovery of OCR over the 11-day postflight period. The mean magnitude of OCR during preflight testing of 6151, 7906, and the control monkeys was  $6.3^\circ \pm 0.7^\circ$  when the axis of rotation was tilted 60–90°. In contrast, the mean OCR of 6151 and 7906 after flight was  $2.2^\circ \pm 0.7^\circ$  for the same angles of tilt.

These data are summarized in Fig. 3F. The postflight OCR of the two flight monkeys fell more than 2 SDs below the preflight mean of five monkeys, a highly significant difference. The mean reduction in dynamic OCR after flight was about 70%. This was the same as the reduction in static OCR.

We considered various artifacts that might account for the reduction in OCR in the flight monkeys. The same values were obtained for OCR of the control monkeys pre- and postflight (Fig. 3A–C), ruling out changes in the apparatus. It was postulated that there might be adhesions in the supraorbital area around the roll coil of the flight monkeys that had tethered the eye whose torsion had been measured. On day 5, monkey 7906 was anesthetized. Under sterile conditions, the conjunctiva of each eye was grasped with fine forceps at the lateral margins of the limbus and the eye was torted  $\pm 45^\circ$ . There was no difference in the apparent physical force needed to tort either eye. Since it was possible that adhesions around the left eye had been broken by physically torting the eye, we compared OCR before and after the procedure. There was no difference in the static and dy-

namic OCR before and after the mobility test (Table 1, Fig. 3E). These tests provide evidence that the coil-bearing eye was not tethered in roll after flight and that the findings were due to neural processing.

### Roll VOR

The roll VOR was measured in two experimental paradigms: the monkeys were rotated at constant velocities about a vertical naso-occipital axis while prone (velocity steps), and they were sinusoidally oscillated about a horizontal axis while upright. The means and SDs of the control and flight animals in preflight testing are shown by the heavy lines and error bars in Fig. 4. The gain of the roll VOR was reduced in both modes of stimulation on average about 50% in 7906 (Fig. 4, filled symbols) and about 15% in 6151 (Fig. 4, open symbols). With the exception of the step gain at 30°/s and the response to oscillation at 0.025 Hz in 6151 on day 11, the pre- and postflight roll gains of the two monkeys were significantly different, separated by more than 2 SDs. There was no reduction in the gain of the roll VOR in the control monkeys in the postflight period.

### Vertical VOR

There was upward spontaneous nystagmus of about 5°/s in the two monkeys before flight. This is a common finding in normal rhesus monkeys (personal observation). The spontaneous nystagmus in 6151 can be seen in the vertical position and velocity traces of Fig. 2A (fourth and seventh traces). The upward spontaneous nystagmus was reduced when 6151 was first tested, 3 days after reentry (Fig. 2B, second and fifth traces). The upward spontaneous nystagmus of 7906 was also reduced when tested 1 day after landing.

The two experimental monkeys, as well as the control monkeys, had an asymmetry of the step gain of the vertical VOR before flight. The mean upward gain of these two monkeys at all velocities was  $0.96 \pm 0.03$  before flight, and the downward gain was  $0.75 \pm 0.04$  (Table 2). In the first postflight test, there was a mean decrease in the gain of the upward VOR to  $0.90 \pm 0.03$ , and an increase in the gain of the downward VOR to

**Table 2** Gains of the vertical vestibulo-ocular reflex tested with velocity steps with the animals in a left ear 90° down position in the pre- and postflight periods for upward and downward slow-phase velocities. Before flight, the mean upward gain was  $0.96 \pm 0.04$  and the postflight values were 0.89 and  $0.90 \pm 0.03$ . Before flight, the mean downward gain was  $0.75 \pm 0.04$ ; it was  $0.80 \pm 0.02$  and  $0.85 \pm 0.03$ , respectively, on the first tests after flight

Direction of slow phase velocity	Velocity step %/s	Monkey	Preflight gain	Postflight gain			
				Day 1	Day 3	Day 7	
Up	30	7906	0.95	0.90	0.93	0.96	
		6151	0.97				
	45	7906	0.97	0.88	0.93	0.97	
		6151	0.97				
	60	7906	0.93	0.85	0.89	0.95	
		6151	0.97				
	75	7906	0.93	0.93	0.89	0.97	
		6151	1.00				
	90	7906	0.91	0.88	0.87	0.97	
		6151	1.00				
	Means			$0.96 \pm 0.03$	$0.89 \pm 0.03$	$0.90 \pm 0.03$	$0.97 \pm 0.01$
	Down	30	7906	0.66	0.83	0.87	0.80
6151			0.77				
45		7906	0.75	0.82	0.85	0.82	
		6151	0.78				
60		7906	0.72	0.78	0.87	0.81	
		6151	0.72				
75		7906	0.73	0.79	0.82	0.82	
		6151	0.81				
90		7906	0.77	0.78	0.82	0.77	
		6151	0.74				
Means				$0.75 \pm 0.04$	$0.80 \pm 0.02$	$0.85 \pm 0.03$	$0.78 \pm 0.03$

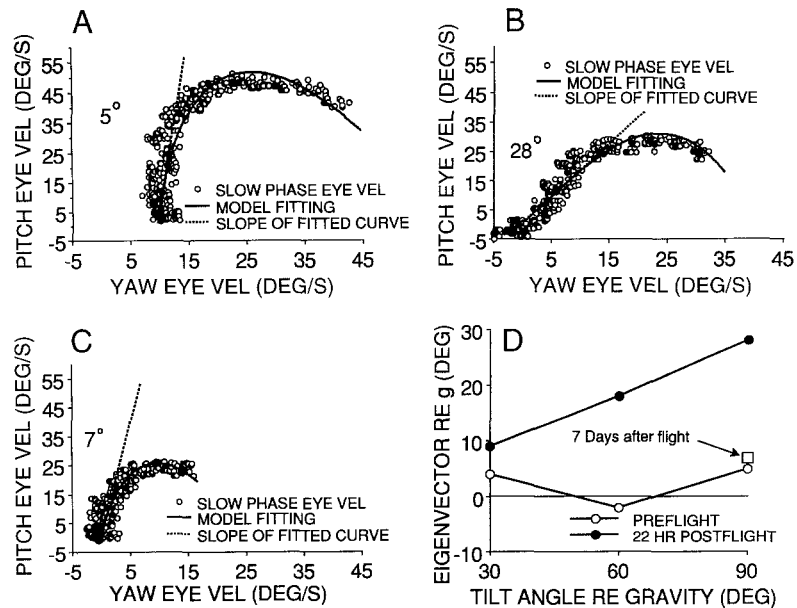
**Table 3** Gains of the vertical vestibulo-ocular reflex tested with sinusoidal rotation about a horizontal interaural axis during the pre- and postflight periods. There was a decrease in gain just after flight

Monkey	Frequency (Hz)	Preflight gain	Postflight gain		
			Day 1	Day 3	Day 11
7906	0.050	0.68	0.63		0.72
	0.077	0.72	0.62		0.77
	0.100	0.72	0.68		0.73
	0.125	0.71	0.68		0.74
Mean		$0.70 \pm 0.01$	$0.65 \pm 0.03$		$0.74 \pm 0.02$
6151	0.050	1.01		0.87	0.91
	0.077	1.0		0.91	0.95
	0.100	0.98		0.89	0.93
	0.125	0.93		0.89	0.91
Mean		$0.98 \pm 0.01$		$0.89 \pm 0.01$	$0.92 \pm 0.01$

**Table 4** Pre- and post-flight gains of the horizontal vestibulo-ocular reflex. There was no difference in the pre- and postflight gains

Monkey	Velocity Step %/s	Preflight gain	Postflight gain	
			Day 1	Day 3
7906	30	0.98	0.96	
	60	0.94	0.99	
	90	1.00	1.00	
	120	1.00	1.00	
	Mean		$0.98 \pm 0.03$	$0.99 \pm 0.02$
6151	30	0.98		0.98
	60	1.00		0.97
	90	1.00		0.99
	120	$0.99 \pm 0.01$		0.97
Mean		$0.99 \pm 0.01$		$0.98 \pm 0.01$





**Fig. 5 A–C** Phase plane plots of vertical (*ordinate*) and horizontal (*abscissa*) eye velocity during cross-coupling of horizontal optokinetic afternystagmus (OKAN). The animal (7906) was in a 90°-tilted, side-down position, and optokinetic nystagmus (OKN) was induced by rotation of the visual surround around its yaw axis at 60°/s. OKAN slow-phase velocities began in each graph on the *right*, and the velocities progressed toward zero to the *left* in a curved fashion. Each *circle* represents the velocity of one slow phase. Apparent *filled symbols* are due to overlap of data points. The *solid curved lines* represent the fit of the data using a modified Levenberg-Marquardt algorithm (Raphan and Sturm 1991; Dai et al. 1991). The *straight dotted lines* are the trajectories of the last part of the decaying OKAN, showing the slope of the fitted curve as the data approached zero. **A** Before flight, the yaw axis eigenvector had an angle of 5° from the vertical. **B** Twenty-two hours after flight, the yaw axis eigenvector had shifted 28° from the vertical toward the body axis. **C** Seven days later, the yaw axis eigenvector had returned to 7° from the vertical, close to its original position. **D** Summary of the shift in the orientation vector toward the body axis at tilt angles of 30°, 60°, and 90°

$0.82 \pm 0.03$  for both monkeys. These differences were small but statistically significant (decrease in upward gain for 7906:  $P=0.04$ , paired,  $df=4$ ; decrease for 6151:  $P=0.01$ , paired,  $df=4$ ; increase in downward gain for 7906:  $P=0.04$ , paired,  $df=4$ ; increase for 6151:  $P=0.02$ , paired,  $df=4$ ). If the gains of the up and down VORs were combined, there was no difference between them in the pre- and postflight tests (7906:  $P=0.78$ , paired,  $df=9$ , day 1; 6151:  $P=0.74$ , paired,  $df=9$ , day 3). Thus, the increase in the gain of the downward VOR was at the expense of a decrease in gain for the upward VOR.

By 7 days after landing, the upward VOR gains had begun to return to preflight levels, and there was no statistical difference between pre- and postflight values in the two monkeys (7906:  $P=0.07$ , paired,  $df=4$ ; 6151:  $P=0.12$ , paired,  $df=4$ ). The downward VOR gain dropped to its original level in 6151 ( $P=0.81$ , paired,  $df=4$ ), but not in 7906 ( $P=0.03$ , paired,  $df=4$ ).

Measured with sinusoids, the vertical VOR gain was slightly reduced after landing (Table 3; 6% for 7906,  $P=0.023$ , paired,  $df=3$ ; and 9% for 6151,  $P=0.004$ , paired,  $df=3$ ). By the 11th day, the gains of the vertical

VOR had returned to the same or slightly less than the preflight levels for both monkeys (Table 3; 7906,  $P=0.064$ , paired,  $df=3$ ; 6151,  $P=0.035$ , paired,  $df=3$ ). Thus, there was a slight reduction in the vertical VOR gains measured with sinusoids 1–3 days after landing which had largely returned to preflight level by 11 days.

One interesting aspect of the vertical nystagmus induced by sinusoidal oscillation was its asymmetry, measured by the shift of the mean vertical velocity from zero. This offset followed the same pattern as the spontaneous nystagmus and the change in vertical gains during step testing. Before flight, the offset for 7906 was  $4.9^\circ/\text{s} \pm 0.2^\circ/\text{s}$  in the upward direction. One day after flight, the offset was reduced to  $2.4^\circ/\text{s} \pm 0.4^\circ/\text{s}$ . By the 11th day, the offset was  $5.8^\circ/\text{s} \pm 0.2^\circ/\text{s}$  or slightly greater than the preflight level. Monkey 6151 had a similar change in offset of upward slow-phase velocity for the last test in which the offset was still smaller than the preflight level (preflight,  $6.3^\circ/\text{s} \pm 0.9^\circ/\text{s}$ ; postflight day 3,  $2.0^\circ/\text{s} \pm 0.7^\circ/\text{s}$ ; postflight day 11,  $4.0^\circ/\text{s} \pm 0.6^\circ/\text{s}$ ).

#### Horizontal VOR

The gains of the horizontal VOR were pooled for rotations to the right and left, since there was no difference between them. The preflight and postflight gains were the same (Table 4; 7906:  $P=0.65$ , paired,  $df=3$ ; 6151:  $P=0.10$ , paired,  $df=3$ ), similar to findings from the COSMOS 2044 flight (Cohen et al. 1992a). There was also no change in the gains of the steady state horizontal velocity during OVAR, which were the same before and after flight in both monkeys. In the example shown in Fig. 2, the mean velocity was 40°/s both pre- and postflight. The amplitude of the modulation in horizontal slow phase velocity during OVAR was increased postflight in 6151, as in the monkeys in the 1989 flight (Cohen et al. 1992a). There was no change in the amplitude of modulation in 7906.

## Spatial orientation of velocity storage (OKAN)

Orientation vectors were determined from OKAN by computing the eigenvectors associated with the feedback matrix of the velocity storage integrator (see Raphan and Sturm 1991 and Dai et al. 1991 for derivation). Before flight, the yaw axis eigenvector angle was  $5^\circ$  with respect to the spatial vertical for 7906 at  $90^\circ$  tilt (Fig. 5A), consistent with the yaw axis eigenvector of other normal monkeys (Dai et al. 1991). Twenty-two hours after landing, the yaw axis eigenvector was  $28^\circ$  for  $90^\circ$  of tilt, indicating that it had moved significantly away from spatial vertical (Fig. 5B). By 7 days after landing, the eigenvector angle was  $7^\circ$  (Fig. 5C), having returned to close to its preflight level (Fig. 5A).

Figure 5D shows the changes in eigenvector angle 22 h after flight for tilts of  $30^\circ$ ,  $60^\circ$ , and  $90^\circ$  (filled circles). The displacement of the orientation vector toward the body axis after flight was consistent at each of these angles. There were differences in the peak values of the horizontal and vertical eye velocities before and after flight (Fig. 5A–C) due to habituation of velocity storage (Cohen et al. 1992b). Despite the habituation, the spatial orientation of the yaw axis eigenvector returned to normal and was closely aligned with the spatial vertical (Fig. 5C,D). Thus, habituation, which affected the temporal characteristics of horizontal and vertical eye velocity, did not affect the spatial orientation of velocity storage. This suggests that spatial orientation of velocity storage may be independent of the state of vestibular habituation.

Testing of the orientation of velocity storage was limited in 6151 after flight because it could not be tested until the 3rd day (55 h). At that time, the animal was drowsy during optokinetic testing, and the spatial orientation of its OKAN could not be adequately evaluated. In later tests of 6151, on days 7 and 11, there was no alteration in the spatial orientation of velocity storage as compared to preflight values. Regardless, the data for 7906 are consistent with the hypothesis that the spatial orientation of OKAN tends to move toward a body axis as a result of adaptation to microgravity.

---

## Discussion

The major finding of these experiments is that compensatory eye movements, which are dependent on orientation of the head with regard to the spatial vertical, were altered after adaptation to microgravity. This included the torsional otolith-ocular reflex induced by head tilt, the up-down asymmetry of vertical nystagmus, and the spatial orientation of velocity storage. The reduction in the up-down asymmetry and the alteration in spatial orientation of velocity storage were short-lasting and disappeared by several days after landing. The alteration in OCR, on the other hand, lasted throughout the 11-day postflight period. There was also a reduction in the gain of the roll VOR, which is dependent on the vertical semicircular canals. This was less than the ef-

fects of microgravity on OCR. The gains of the horizontal and vertical VOR were not changed after spaceflight.

## Ocular counterrolling

The reduction in OCR was substantial (70%). It was about the same in the two experimental monkeys and was present in every postflight test. These results are in general agreement with previous results after spaceflight (Yakovleva et al. 1982; Arrott and Young 1986; Vogel and Kass 1986; Hofstetter-Degen et al. 1993). In some studies, the magnitude of the reduction was large, as in the monkeys, but the duration of the reduction was shorter. However, two cosmonauts subjected to long-duration flights also had reduced OCR for tilt to one side for up to 14 days after landing (Yakovleva et al. 1982).

On earth, torsional eye movements (OCR) are activated by lateral head tilt with regard to gravity and tend, although weakly, to maintain the orientation of the eyes relative to gravity. In space, the otoliths are not activated by lateral head tilt, neck receptors do not contribute to OCR (Hofstetter-Degen et al. 1993), and lateral translations, which are associated with OCR on earth, mainly induce a horizontal component of eye movement (Arrott and Young 1986). Thus, the torsional response to otolith input is reduced or absent for linear or translational movements in space, and maintenance of torsional eye movements is dependent mainly on roll angular acceleration sensed by the semicircular canals.

It seems reasonable that the central nervous system (CNS) would adapt the spatial response of the VOR in microgravity while maintaining body-oriented, compensatory mechanisms, i.e., those linked to the semicircular canals, which are in a head frame of reference. This would explain the lack of adaptation of the canal-oriented horizontal and vertical VOR. It does not explain the reduction in the roll VOR. Neither the distribution of the axes about which the head rotates nor the frequency or magnitude of translation while engaged in routine activities in space are known. One possibility is that there are relatively few low-frequency roll head movements in space, resulting in depression of the canal-ocular roll reflex over the course of spaceflight. Were this to be substantiated, a program of head movements which produced compensatory torsional ocular movements after the first 3 days might be a natural countermeasure.

How the adaptive changes in OCR are produced is speculative. Synaptic changes have been found in the otolith hair cells after spaceflight (Ross 1993), although it is not known whether afferent input from the otoliths is altered. The finding that the steady state levels of horizontal velocity induced by OVAR were unaffected by spaceflight in both the previous (2044) and the present (2229) COSMOS missions would imply that the otolith organs were sensing gravity correctly and that the otolith afferents were not adapted. Rather, it seems probable that the changes in OCR and roll VOR gain were due to central adaptation.

## Asymmetry of vertical slow-phase velocity

Another aspect of eye movement that depends on spatial information is the asymmetry of vertical eye movements. There are gain and time constant asymmetries in the vertical nystagmus of rhesus monkeys that are dependent on head orientation with regard to gravity (Matsuo et al. 1979, 1984; Dai et al. 1991). These asymmetries are abolished by ablation of the otoliths (Igarashi et al. 1978) or by reorienting the head toward the upside-down position (Raphan et al. 1989). The asymmetry in vertical slow-phase velocity had a tendency to be equalized by spaceflight. Shortly after flight the level of upward spontaneous nystagmus as well as the asymmetry in vertical slow-phase velocity were reduced.

Vertical gain asymmetry is also present in humans; upward OKN generally has a higher gain than downward OKN on earth (Clement et al. 1986; Murasugi and Howard 1989). In space, there was a downward drift of the eyes, signifying a downward rather than an upward directional bias (Clement and Berthoz 1990). The reorientation of the vertical slow-phase velocity of astronauts was in the same direction as the downward shift in the vertical nystagmus of the monkeys. The reduction of the vertical asymmetry implies that there is adaptation from a spatial to a body frame of reference in a situation where vertical asymmetries have no functional meaning.

There was a slight reduction in the gain of the pitch sinusoids when the monkeys oscillated around a horizontal interaural axis after flight. Since this stimulus activated the otoliths as well as the canals, the small reduction may also have been due to the adaptive change in the otolith system.

## Spatial orientation of velocity storage

On earth, optokinetic and vestibular nystagmus are oriented around the spatial vertical in animals and humans (Lansberg et al. 1965; Harris and Barnes 1987; Dai et al. 1991; Gizzi et al. 1994). The theoretical basis for this is the representation of velocity storage as an approximate linear system that can be characterized by eigenvalues and eigenvectors that represent its time constant and orientation vectors, respectively (Raphan and Sturm 1991). For stimuli along the subject's yaw axis, cross-coupling will occur when the yaw axis eigenvector is not along the subject's yaw axis (Dai et al. 1991). This cross-coupling brings the axis of eye rotation into approximate alignment with gravity. The yaw axis eigenvector of monkeys was similar to the perception of the spatial vertical of humans (Dai et al. 1991). Therefore, the yaw axis eigenvector of velocity storage in the monkey can be regarded as an internal representation of its spatial orientation.

Study of spatial orientation of velocity storage after flight was limited to one animal (7906), since the other monkey was initially sick. The large change in the orientation angle 22 h after landing ( $5^\circ$  to  $28^\circ$ ) suggests that space flight had altered the monkey's internal representation of the spatial vertical, moving the yaw axis eigen-

vector toward the body axis. The deviation of the yaw axis eigenvector toward the body axis may have been larger immediately after landing. Findings from monkey 7906 are consistent with those of a previous COSMOS mission. One of the two monkeys lost the ability to shorten the horizontal time constant of post-rotatory nystagmus after space flight following head tilt (Cohen et al. 1992a). This reduction in time constant during cross-coupling is part of the reorientation of velocity storage in a gravitational field (Dai et al. 1991; Angelaki and Hess 1994).

Thus, we have demonstrated changes in the vestibular system after space flight that can be related to an alteration of spatial orientation. On earth, there is a spatial reference of the vertical due to gravity as well as from the body axis and visual references. In microgravity, without the spatial reference, there appears to be adaptation toward a body centric frame, and reflexes that are spatially oriented on earth are suppressed. Normal spatial orientation is essential for the maintenance of gaze, posture, and locomotion. The changes in orientation noted after spaceflight may play an important role in the postural, locomotor, and gaze instability on reentry. By understanding the functional alterations in orientation after spaceflight, it may be possible to devise countermeasures for these alterations.

**Acknowledgements** This work was supported by NASA Grants NAG 2-573 and NAG 2-703. We thank Victor Rodriguez, Nicholas Pasquale, Mischa Sirota, and Philip Cook for technical assistance.

## References

- Angelaki D, Hess BJM (1994) Inertial representation of angular motion in the vestibular system of rhesus monkeys. I. Vestibulo-ocular reflex. *J Neurophysiol* 71:1222-1249
- Arrott AP, Young LR (1986) M.I.T./Canadian vestibular experiments on the Spacelab-1 mission. 4. Vestibular reactions to lateral acceleration following ten days of weightlessness. *Exp Brain Res* 64:347-357
- Benson AJ, Vieville TH (1986) European vestibular experiments on the Spacelab-1 mission. 6. Yaw axis vestibulo-ocular reflex. *Exp Brain Res* 64:279-283
- Camis M, Creed RS (1930) *The physiology of the vestibular apparatus*. Clarendon, Oxford
- Clarke AH, Teiwes W, Scherer H (1993) Vestibulo-oculomotor testing during the course of a spaceflight mission. *Clin Invest* 10:740-748
- Clement G, Vieville FL, Berthoz A (1986) Modifications of gain asymmetry and beating field of vertical optokinetic nystagmus in microgravity. *Neurosci Lett* 63:271-274
- Clement G, Berthoz A (1990) Cross-coupling between horizontal and vertical eye movements during optokinetic nystagmus and optokinetic afternystagmus elicited in microgravity. *Acta Otolaryngol (Stockh)* 109:179-187
- Collewijn H, Steen J van der, Ferman L, Jansen TC (1985) Human counterroll: assessment of static and dynamic properties from electromagnetic scleral coil recordings. *Exp Brain Res* 59:185-196
- Cohen B, Kozlovskaya I, Raphan T, Solomon D, Helwig D, Cohen N, Sirota M, Yakushin S (1992a) Vestibular reflex of rhesus monkeys after spaceflight. *J App Physiol [Suppl]* 73:121S-131S
- Cohen H, Cohen B, Raphan T, Waespe W (1992b) Habituation and adaptation of the vestibulo-ocular reflex; a model of dif-

- ferential control by the vestibulo-cerebellum. *Exp Brain Res* 90:526–538
- Correia MJ (1993) Studies of vestibular neurons in normal, hyper- and hypogravity. Final Science Report, NASA COSMOS 2044 Mission (1992) *J Appl Physiol [Suppl]* 73:(2)
- Crawford JD, Vilis T (1991) Axis of eye rotation and Listing's law during rotations of the head. *J Neurophysiol* 65:407–423
- Dai M, Raphan T, Cohen B (1991) Spatial orientation of the vestibular system: dependence of optokinetic after-nystagmus on gravity. *J Neurophysiol* 66:1422–1439
- Dai MJ, Raphan T, Cohen B (1992) Characterization of yaw to roll cross-coupling in the three-dimensional structure of the velocity storage integrator. *Ann NY Acad Sci* 656:829–831
- Dai M, Cohen B, Raphan T, McGarvie L, Kozlovskaya IB (1993) Reduction of ocular counter-rolling (OCR) after spaceflight. *Neurosci Abstr* 23:343
- Diamond SG, Markham CH (1983) Ocular counterrolling as an indicator of vestibular otolith function. *Neurology* 33:1460–1469
- Diamond SG, Markham CH, Simpson NE, Curthoys IS (1979) Binocular counterrolling in humans during dynamic rotation. *Acta Otolaryngol (Stockh)* 87:490–498
- Engelkind EJ, Stevens KW (1990) A new approach to the analysis of nystagmus: an application for order statistic filters. *Aviat Space Environ Med* 61:859–864
- Fischer MH (1927) Messende Untersuchungen über die Gegenrollung der Augen und die Lokalisation der scheinbaren Vertikalen bei seitlicher Neigung des Gesamtkörpers bis zu 360°. I. Mitteilung. Neigung bis zu 40° (Untersuchungen an Normalen). *Graefes Arch Clin Exp Ophthalmol* 118:633
- Furman JMR, Baloh RW (1992) Otolith-ocular testing in human subjects. *Ann NY Acad Sci* 656:431–451
- Gizzi M, Raphan T, Rudolph S, Cohen B (1994) Orientation of human optokinetic nystagmus to gravity: a model-based approach. *Exp Brain Res* 99:347–360
- Grossman GE, Leigh RJ, Abel LA, Lanska DJ, Thurston SE (1988) Frequency and velocity of rotational head perturbations during locomotion. *Exp Brain Res* 70:470–476
- Harris LR, Barnes GR (1987) Orientation of nystagmus is modified by head tilt. In: Graham MD, Kemink JL (eds) *The vestibular system: neurophysiologic and clinical research*. Raven, New York, pp 539–548
- Hofstetter-Degen K, Weizig J, Baumgarten R von (1993) Oculovestibular interactions under microgravity. *Clin Invest* 10:749–756
- Igarashi M, Takahashi T, Kubo T, Levy JK, Homick JL (1978) Effect of macular ablation on vertical optokinetic nystagmus in the squirrel monkey. *ORL J Otorhinolaryngol Relat Spec* 40:312–318
- Judge SJ, Richmond BJ, Chu FC (1980) Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 20:535–538
- Kozlovskaya IB, Barmin VA, Kreidich YV, Repin AA (1986) The effects of real and simulated microgravity on vestibulo-oculomotor interaction. *Physiologist* 28(6):S51–S56
- Lansberg MP, Guedry FE, Graybiel A (1965) Effect of changing resultant linear acceleration relative to the subject on nystagmus generated by angular acceleration. *Aerospace Med* 36:456–460
- Matsuo V, Cohen B (1984) Vertical optokinetic nystagmus and vestibular nystagmus in the monkeys: up-down asymmetry and effects of gravity. *Exp Brain Res* 53:197–216
- Matsuo V, Cohen B, Raphan T, DeJong V, Henn V (1979) Asymmetric velocity storage for upward and downward nystagmus. *Brain Res* 176:159–164
- Miller II EF, Graybiel A (1971) Effect of gravito-inertial force on ocular counterrolling. *J Appl Physiol* 31:697–700
- Murasugi CM, Howard IP (1989) Up-down asymmetry in vertical optokinetic nystagmus and after-nystagmus: contribution of the central and peripheral retinae. *Exp Brain Res* 77:183–192
- Parker DE, Reschke MF, Arrott AP, Homick JL, Lichtenberg BK (1985) Otolith tilt translation reinterpretation following prolonged weightlessness: implications for preflight training. *Aviat Space Environ Med* 56:601–607
- Raphan T, Cohen B (1988) Organizational principles of velocity storage in three dimensions: the effect of gravity on cross-coupling of optokinetic after-nystagmus. *Ann NY Acad Sci* 545:74–82
- Raphan T, Sturm D (1991) Modeling the spatiotemporal organization of velocity storage in the vestibuloocular reflex by optokinetic studies. *J Neurophysiol* 66:1410–1421
- Raphan T, Matsuo V, Cohen B (1979) Velocity storage in the vestibulo-ocular reflex arc (VOR). *Exp Brain Res* 35:229–248
- Raphan T, Cohen H, Dai M, Cohen B (1989) Effects of gravity on asymmetrical velocity storage. *Neurosci Abstr* 19:503
- Raphan T, Dai M, Cohen B (1992) Spatial orientation of the vestibular system. *Ann NY Acad Sci* 656:140–157
- Reschke MF, Anderson DJ, Homick JL (1984) Vestibulospinal reflexes as a function of microgravity. *Science* 225:212–213
- Robinson DA (1963) A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Eng* 10:137–145
- Ross MD (1993) Morphological changes in rat vestibular system following weightlessness. *J Vest Res* 3:241–251
- Singh A, Thau FE, Raphan T, Cohen B (1981) Detection of saccades by a maximum likelihood ratio criterion. *Proceedings of the 34th Annual Conference of Eng Biol, Houston, Tex.*, pp 136
- Takemori S, Tanaka M, Moriyama H (1989) An analysis of ocular counterrolling measured with search coils. *Acta Otolaryngol (Stockh) [Suppl]* 468:271–276
- Tomko DL, Kozlovskaya IB, Paige GD, Badakva AM (1993) Adaptation to micro-gravity of oculomotor reflexes (AMOR): otolith-ocular reflexes. Final Science Report, NASA
- Vogel H, Kass JR (1986) European vestibular experiments on the Spacelab-1 mission. 7. Ocular counterrolling measurements pre- and post-flight. *Exp Brain Res* 64:284–290
- Waespe W, Cohen B, Raphan T (1983) Role of the flocculus and paraflocculus in optokinetic nystagmus and visual-vestibular interactions: effects of lesions. *Exp Brain Res* 50:9–33
- Yakovleva IY, Kornilova LN, Serix GD, Tarasov IK, Alekseev VN (1982) Results of vestibular function and spatial perception of the cosmonauts for the 1st and 2nd exploitation on station of Salut 6. *Space Biol (Russia)* 1:19–22
- Yue Q, Straumann D, Henn V (1994) Three-dimensional characteristics of rhesus monkey vestibular nystagmus after velocity steps. *J Vest Res* 4:313–323
- Young LR, Oman CM, Watt DGD, Money KE, Lichtenberg BK, Kenyon RV (1986) M.I.T./Canadian vestibular experiments on the Spacelab-1 mission. 1. Sensory adaptation to weightlessness and readaptation to one-g: an overview. *Exp Brain Res* 64:291–298