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RESEARCH ARTICLE

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Ocular counterrolling induced by centrifugation during orbital space flight

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Abstract During the 1998 Neurolab mission (STS-90), four astronauts were exposed to interaural centripetal accelerations (Gy centrifugation) of 0.5*g* and 1*g* during rotation on a centrifuge, both on Earth and during orbital space flight. Subjects were oriented either left-ear out or right-ear out, facing or back to motion. Binocular eye movements were measured in three dimensions using a video technique. On Earth, tangential centrifugation that produces 1*g* of interaural linear acceleration combines with gravity to tilt the gravitoinertial acceleration (GIA) vector 45° in the roll plane relative to the head vertical, generating a summed vector of 1.4*g*. Before flight, this elicited mean ocular counterrolling (OCR) of 5.7°. Due to the relative absence of gravity during flight, there was no linear acceleration along the dorsoventral axis of the head. As a result, during in-flight centrifugation, gravitoinertial acceleration was strictly aligned with the centripetal acceleration along the interaural axis. There was a small but significant decrease (mean 10%) in the magnitude of OCR in space (5.1°). The magnitude of OCR during postflight 1*g* centrifugation was not significantly different from preflight OCR (5.9°). Findings were similar for 0.5*g* centrifugation, but the OCR magnitude was approximately 60% of that induced by centrifugation at 1*g*. OCR during pre- and postflight static tilt was not significantly different and was always less than OCR elicited by centrifugation on Earth for an equivalent interaural linear acceleration. In contrast, there was no difference between the OCR generated by in-flight centrifugation and by static tilt on Earth at equivalent interaural linear accelerations. These data support the following conclusions: (1) OCR is generated predominantly in response to interaural linear acceleration; (2) the increased OCR during centrifugation on Earth is a response to the head dorsoventral 1*g* linear acceleration component, which was absent in microgravity. The dorsoventral linear acceleration could have activated either the otoliths or body-tilt receptors that responded to the larger GIA magnitude (1.4*g*), to generate the increased OCR during centrifugation on Earth. A striking finding was that magnitude of OCR was maintained throughout and after flight. This is in contrast to most previous postflight OCR studies, which have generally registered decreases in OCR. We postulate that intermittent exposure to artificial gravity, in the form of the centripetal acceleration experienced during centrifugation, acted as a countermeasure to deconditioning of this otolith-ocular orienting reflex during the 16-day mission.

Keywords Vestibulo-ocular reflex · Microgravity · Otoliths · Artificial gravity · Countermeasure · Human

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Introduction

When the head is tilted laterally, the eyes rotate or tort around the line of sight (Fleisch 1922; Miller 1962; Diamond and Markham 1983; Collewijn et al. 1985). Termed "ocular counterrolling" (OCR), this torsion is an orienting reflex (Baarsma and Collewijn 1975; Raphan and Cohen 1996) that tends to align the yaw (*Z*) axis of the eyes with the spatial vertical. During tangential centrifugation (Woellner and Graybiel 1959; Miller and Graybiel 1970; MacDougall et al. 1999), head translation (Arrott and Young 1986), and while turning corners (Imai et al. 2001), the OCR reflex orients the eyes toward the gravitoinertial acceleration (GIA)[1], the vector

[1] In the absence of other linear accelerations, the GIA is equivalent to the acceleration of gravity, and is aligned with the spatial vertical.

sum of the imposed linear accelerations (including gravity) acting on the head. Recent work has shown that rolling the head and eyes into the direction of the GIA plays a role in maintaining balance and gaze when making sharp turns during locomotion (Imai et al. 2001).

The otolith organs, the utricle and saccule, are the primary graviceptors of the body, and sustained OCR is primarily a response of otolith activation by low-frequency linear acceleration. Although the semicircular canals also induce torsional eye movements during high-frequency (0.1–10 Hz) angular head roll, these responses are transient. In contrast, otolith-induced OCR responses are sustained during static tilts of the head or the GIA, with a gain of approximately 0.1 in the frequency range 0–0.3 Hz in humans (Miller 1962; Diamond and Markham 1983), with the gain falling at higher frequencies (Telford et al. 1997). OCR has a magnitude linearly related to the component of linear acceleration along the interaural axis, rather than to the angle of head tilt (Benjamins 1918; Woellner and Graybiel 1959; Miller and Graybiel 1970). This suggests that otolithic units with polarization vectors that have components along the interaural axis are primarily responsible for the generation of OCR. Recent studies have indicated, however, that the head vertical (dorsoventral) linear acceleration component may also contribute to the OCR response (De Graaf et al. 1996; Merfeld et al. 1996; MacDougall et al. 1999).

Deconditioning of otolith-spinal and otolith-ocular reflexes following adaptation to microgravity has been proposed as the basis of many of the postural, locomotor, and gaze control problems experienced by returning astronauts (Homick and Reschke 1977; Young et al. 1984; Parker et al. 1985; Anderson et al. 1986; Kenyon and Young 1986; Reschke et al. 1986; Young et al. 1986; Paloski et al. 1992; Dai et al. 1994; Clément and Reschke 1996; Merfeld 1996). Consequently, OCR has been used in many postflight studies to gauge the effect of microgravity exposure on otolith function. There is evidence that OCR is reduced postflight in about 75% of astronauts tested, but the data is relatively sparse, primarily due to the difficulty in recording torsional eye movements. A number of different experimental procedures have been employed, including flash afterimages and flash photography of the eyes. Afterimages are subject to perceptual reporting, and flash photography has a low temporal resolution, usually about 1–2 frames/s. OCR, measured using afterimages, was reduced in two cosmonauts for 14 days after landing (Yakovleva et al. 1982). Following the 10-day Spacelab-1 mission, OCR to leftward roll tilts, measured from single-frame photographs, was reduced by 28–56% in three subjects and unchanged in one subject (Vogel and Kass 1986). Asymmetries in the OCR response to left and right static roll tilts were also observed. Using afterimages, OCR was reduced by 57% in one astronaut for 5 days after the 1992 Russian-MIR mission (Hofstetter-Degen et al. 1993). OCR, measured from photographs, was also reduced in two subjects during postflight sinusoidal linear oscillations at 0.4 Hz and 0.8 Hz (Arrott and Young 1986). OCR gain, also measured from photographs, was depressed in four subjects following the 2-week SLS-2 mission. In addition, asymmetries in OCR to left/right roll tilt were observed in all subjects. (Young and Sinha 1998). The development of video-oculography (Clarke et al. 1991; Moore et al. 1991, 1996) has led to significant improvements in OCR measurements in humans at sampling rates of up to 60 Hz. OCR gain, measured using video-oculography following a 30-day MIR mission, decreased in one astronaut, but increased in two others who had been in space for 180 days (Diamond and Markham 1998).

Strong evidence for deficits in postflight otolith function has been obtained from two monkeys following a 14-day COSMOS mission (Dai et al. 1994, 1998). Torsional eye position was measured postflight using implanted scleral search coils, which provide a robust and accurate measure of ocular torsion. The eye movements were measured during off-vertical axis rotation (OVAR), which presents a sinusoidal linear acceleration stimulus to the otoliths suitable for averaging, and during static roll-tilt. There was a highly significant (70%) reduction (more than 2 SD) in OCR gain, which persisted for the 11 days in which the animals were tested postflight. In addition, vergence of the eyes, an otolith-mediated response to naso-occipital linear acceleration, was also reduced during this 11-day period (Dai et al. 1998).). Thus, although the data are not entirely consistent, the majority of subjects tested have exhibited a decrease in their OCR response following short-duration missions.

During the Neurolab STS-90 mission in 1998, a short-arm human centrifuge was flown that generated sustained linear accelerations of 0.5*g* and 1*g* along the interaural axis of the head, and eye movements were recorded in three dimensions with video-oculography. For the first time, it was possible to study otolith-ocular responses to sustained centripetal linear acceleration in space without the effects of a constant gravitational vector. This allowed us to determine the relative importance of interaural and head dorsoventral linear acceleration in the generation of OCR. We also had the first test of the effects of exposure to artificial gravity on postflight otolith-ocular reflexes. In this paper we present a direct comparison of the OCR responses during pre-, in-, and postflight centrifugation, as well as during pre- and postflight static tilt. The perceptual responses of the astronauts to centrifugation both in-flight and on Earth are reported elsewhere (Moore et al. 2000; Clément et al. 2001).

Materials and methods

Centrifugation

This experiment was carried out on the National Aeronautics and Space Administration (NASA) Neurolab STS-90 space shuttle mission, which took place from 17 April 1998 to 2 May 1998. The experiments were approved by the Institutional Review Board at Johnson Space Center in Houston and were performed in accor-

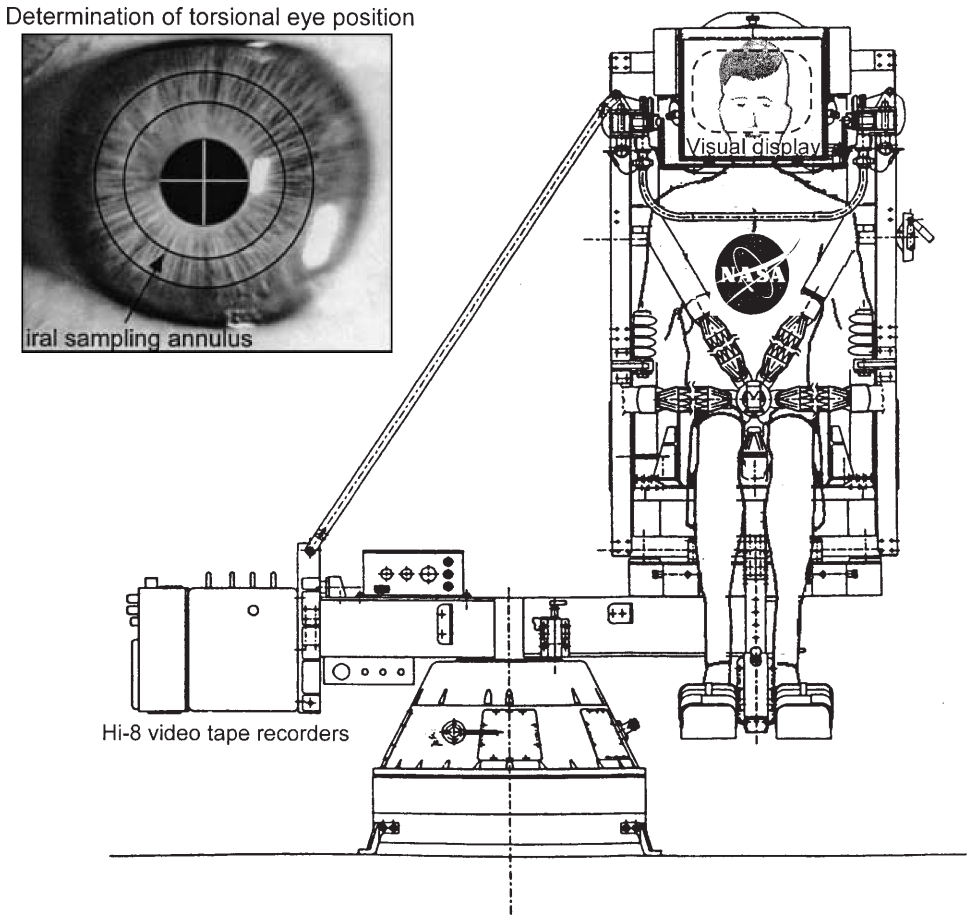

Fig. 1 Schematic of the Neurolab flight centrifuge, configured for the left-ear-out (LEO) orientation (adapted from European Space Agency documentation). The subject was firmly held in place by a five-point safety harness, foot rests, and Velcro handgrips. A visual display and miniature video cameras were mounted directly in front of the subject's face. Video images of the subject's eyes were recorded onto two Hi-8 video tape recorders mounted on the opposite end of the rotator beam. Torsional eye position was measured from video images of the eye (*inset*), using pattern-matching of iral gray-level information sampled from an annular region centered on the pupil

dance with the ethical standards laid down in the 1964 Declaration of Helsinki. Subjects gave their informed consent prior to their inclusion in the study. Each of four crewmembers (two Mission Specialists and two Payload Specialists) served as subjects and as in-flight operators for this experiment. They were designated as subjects A, B, C, and D. Astronauts were exposed to in-flight 1*g* centrifugation on flight days 2, 5, 10, 11, and 16. Baseline data were collected in Houston 90 days, 60 days, and 15 days prior to launch (L–90, L–60, and L–15) on a centrifuge that was a replicate of the flight centrifuge. The same tests were repeated in Houston 24 h after return (R+1) and on subsequent days (R+2 and R+9). Two crewmembers (A and B) were also exposed to 0.5*g* centrifugation on flight days 7 and 12, and baseline 0.5*g* data were obtained from all four subjects on L–30 and R+4.

In-flight and ground-based centrifuges

Two centrifuges were utilized in this experiment. The European Space Agency developed the flight model (Fig. 1), and Neurokinetics (Pittsburgh, Pa.) built a ground-based centrifuge located at Johnson Space Center. Both centrifuges were functionally identical, with the exception of the tilt capability of the ground centrifuge (see Static tilt, below). For the experiments in this paper, subjects sat upright, with the body vertical (*Z*) axis parallel to the axis of rotation at a radius of 0.5 m, and were oriented either left-ear out (LEO), as in Fig. 1, or right-ear out (REO). A restraint system, consisting of a five-point harness, thigh, shoulder and neck pads, and a knee strap, held the body firmly in place (Fig. 1). A custom-made facemask, consisting of a fiberglass front and back shell that were molded to the bony features of the skull, restrained the subject's head such that Reid's baseline, the line that joins the infraorbital point to the superior border of the external auditory meatus (World Federation of Neurology 1962), was parallel with gravitational horizontal (on Earth) and orthogonal to the axis of rotation. The subject held handgrips mounted either side of the chair, which incorporated a push-button used for calibration of the video system and an emergency rotation-abort switch.

Visual display

The visual display consisted of a 158×167 mm liquid-crystal display screen mounted in a box directly in front of the subject's face on the centrifuge chair (Fig. 1). The visual display had a field of view of ±44° horizontally and ±40° vertically. Black dots were presented on an amber background for calibration purposes prior to testing. In addition, a centering point was displayed both prior to and during rotation to obtain measures of OCR (see Data analysis, below).

Video eye-movement recording

Binocular eye movements were recorded by two miniature NTSC video cameras mounted either side of the visual display unit. The cameras provided video images at a frame rate of 30 Hz. Two rectangular banks of nine infrared light-emitting diodes (wavelength 950 nm) were attached to each camera to illuminate the subject's eyes. The diodes were not visible to the subject. Images of the subject's eyes were directed onto charge-coupled devices of the video cameras via an infrared beam-splitter that was transparent to light in the visible range. This allowed the subject a clear view of the visual display. The horizontal and vertical position of the cameras and their focus were adjusted manually by the operator, to obtain optimal images of the subject's eyes, using a small video monitor as a guide. Two custom-made Hi-8 video tape recorders, mounted on the opposite end of the rotator beam from the subject (Fig. 1), were used to record binocular eye movements. The European Space Agency developed both the visual display and eye-movement recording equipment.

Coordinate frames

A head-fixed right-handed coordinate frame $\{X_h, Y_h, Z_h\}$ was defined such that X_h was parallel to the naso-occipital axis (positive forward), Y_h parallel to the interaural axis (positive left), and Z_h normal to the X_h–Y_h plane (positive upward). The origin of the head coordinate frame was the intersection of these axes, located on the interaural axis at a point midway between the vestibular labyrinths. The head, held firmly by the facemask, was oriented such that when in the LEO or REO position the stereotaxic horizontal (X_h–Y_h) plane was orthogonal to both the gravitational vertical (on Earth) and the axis of rotation. The naso-occipital (X_h) axis was normal to the visual display screen. An eye-fixed coordinate frame $\{X_e, Y_e, Z_e\}$ was also defined with the origin at the center of the eye and X_e passing through the center of the pupil (positive forward) and normal to Y_e–Z_e plane. When the subject fixated on the center of the visual display, $\{X_e, Y_e, Z_e\}$ and $\{X_h, Y_h, Z_h\}$ were aligned.

Experimental protocol

In each run, subjects were accelerated at 26°/s^2 in darkness to a constant angular velocity of 254°/s or 179°/s, which generated a 1*g* or 0.5*g* centripetal acceleration along the interaural axis, respectively. Approximately 40 s into the profile, subjects were prompted for a verbal perception report (Moore et al. 2000; Clément et al. 2001). After 65 s at constant velocity in darkness, subjects were presented with a centering display dot for 9.5 s and instructed to fixate the dot. Eye-movement data recorded during this period were used to calculate OCR (see Data analysis, below). Subjects were then decelerated at 26°/s^2 to rest in darkness either immediately following the center display or after optokinetic and smooth pursuit stimuli were displayed (not considered in this paper). A typical trial consisted of clockwise (CW) LEO centrifugation (facing motion), counterclockwise (CCW) LEO (back to motion), CCW and CW REO (facing motion and back to motion), and CW rotation while lying supine along the rotator beam (lying on back or *G*z centrifugation). Only data from the LEO and REO orientations (*G*y centrifugation) are considered here. The video eye monitors were calibrated by having the subject fixate on 25 points at known gaze angles prior to the first LEO and REO runs.

Data analysis

Following the Neurolab mission, ground and in-flight Hi-8 videotapes were dubbed onto Betacam SP tapes for postprocessing. The tapes were analyzed with a Betacam video tape recorder (Sony UVW-1800) and an IBM-compatible computer fitted with custom-made video digitization and display hardware, developed by the European Space Agency. The digitized video images were processed field by field (where a single field consisted of either the odd or even lines from a complete video frame), providing a sampling rate of 60 Hz. The coordinates of the pupil center in the image field were calculated using a partial ellipse fit (Zhu et al. 1999a). The pupil center locations at 25 known gaze positions obtained during calibration formed the basis of a three-dimensional spherical model of the eye, which was used to determine horizontal and vertical eye position from the pupil center of subsequent images (Moore et al. 1996). Torsional eye position was obtained using polar cross-correlation of the gray-level intensity information of the iris sampled from a circular annulus (Fig. 1, inset) centered on the pupil (Moore et al. 1991). Improved accuracy of torsional computation was achieved using geometric algorithms that

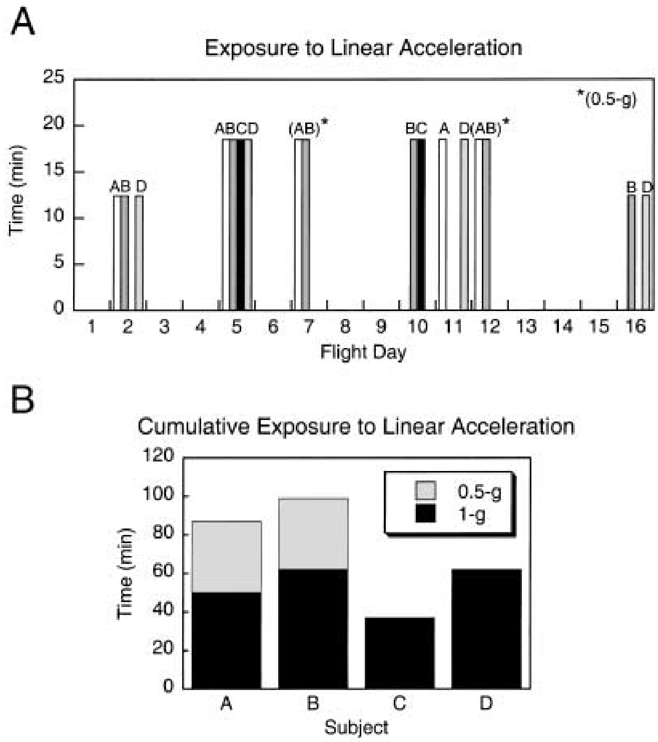

Fig. 2 **A** Exposure of the four payload crewmembers (subjects A, B, C, and D) to 1*g* linear acceleration during the Neurolab flight. Subjects A and B were also exposed to 0.5*g* linear acceleration on flight day (FD) 7 and FD 12 (denoted by *asterisks*). Subject C was not exposed to artificial gravity until FD 5, whereas the other three payload crew were centrifuged less than 24 h after orbital insertion (FD 2). In addition, subject C's total exposure time was limited to less than half the other payload crew. **B** Cumulative exposure to in-flight linear acceleration

compensated for the eccentricity of the iral sampling annulus according to eye orientation (Haslwanter and Moore 1995; Moore et al. 1996). Eye position in head coordinates was represented as Euler angles in a Fick (yaw, pitch, roll) rotation sequence (Fick 1854) and could be converted to an equivalent axis-angle representation in a head-fixed frame (Raphan 1998; Imai et al. 2001). According to the right-hand rule, eye movements to the left, down, and clockwise from the subject's point of view were positive. Video systems based on these algorithms have previously demonstrated accuracy and resolution of the order of 0.1° (Moore et al. 1991, 1996, 1999).

The measure of OCR during centrifugation was obtained from the mean of 3 s (180 samples) of torsional eye position data when subjects were fixating a center point after 65 s of rotation, as determined from the horizontal and vertical eye position traces. A baseline for OCR was calculated in a similar manner from 3 s of data prior to rotation. A final estimate for ocular torsion was calculated by subtracting this baseline from the OCR value measured during centrifugation.

In-flight exposure to sustained linear acceleration

All four payload crewmembers were exposed to sustained 1*g* linear acceleration during the course of the 16-day Neurolab mission (Fig. 2A). Approximately 80% of this exposure was in the form of centripetal acceleration directed along the subjects' interaural axis during *G*y centrifugation. In addition, subjects underwent –*G*z centrifugation, where the centripetal acceleration was directed along the head dorsoventral axis (Moore et al. 2000; Clément et al.

2001). Cumulative exposure times to all 1*g* centripetal accelerations were 50 min, 62 min, 37 min, and 62 min for subjects A, B, C, and D, respectively (Fig. 2B). In addition, subjects A and B were each exposed to a total of 38 min of 0.5*g* linear acceleration (Fig. 2B). Payload crewmembers A, B, and D had their first centrifugation session on flight day (FD) 2, less than 24 h into the mission (Fig. 2A). Subject C did not experience in-flight centrifugation until the 5th flight day (FD 5). In addition, due to mission operational constraints, subject C's exposure time was limited to approximately half that of the other payload crew (Fig. 2B).

Static tilt

Full-body static roll tilt was performed in Houston, using the tilt mode of the ground centrifuge, and at Kennedy Space Center in Cape Canaveral, using a static tilt chair developed at Mount Sinai Medical Center. Preflight baseline data collection was carried out 60 days and 30 days prior to launch (L–60 and L–30) in Houston. Postflight data were obtained on the day of return (R+0) 2–4 h after landing at Kennedy Space Center and in Houston on R+1, R+4, and R+9.

Tilt chairs

The ground centrifuge at Johnson Space Center was also used as a static tilt chair. With subjects in the REO orientation, the entire centrifuge chair assembly could be tilted about an axis located underneath the subjects' seat, and they could be placed at roll-tilt angles between 0° (upright) and 90° left-ear down. A digital inclinometer was used to set the angle of tilt. In the tilt chair at Kennedy Space Center, subjects were seated in an automobile racing seat and firmly held in place by a 5-point safety harness, adjustable padded shoulder and neck supports, and a fiberglass back shell to support the head. Subjects could be roll tilted from the upright (0°) in 15° steps to 90° left-ear down about an axis behind their head. A pin mechanism locked the chair in place at each angle. A 3-m-diameter white hemisphere, centered at the eye level, was positioned in front of the subjects to display points of light and optokinetic stimuli (not considered in this paper). A static 5-point display, consisting of a center point and four eccentric points at ±10° horizontal and vertical gaze angles, was used to calibrate eye movements.

Video eye-movement recording

Owing to operational constraints, it was not possible to utilize the European Space Agency's video equipment for data collection at Kennedy Space Center. Monocular video recordings of the right eye were obtained from a miniature video camera (Eyecam; Iscan, Cambridge, Mass.) attached to a lightweight headset (combined weight 114 g), which tightly fitted the head. Consequently, there was minimal camera movement during static tilt (Moore et al. 1999). The eye was illuminated by a single 940-nm infrared light-emitting diode. The image of the eye was reflected onto the charge-coupled device of the camera by an infrared-sensitive "hot" mirror, which was transparent to light in the visible frequency range and allowed the subject a clear field of view. Video output was recorded onto an S-VHS video tape recorder (JVC HR S10000U) for later processing.

Experimental protocol

An identical protocol was used for all test sessions. Following subject ingress and calibration of the video system, subjects were roll-tilted from the upright (0°) to 60° left-ear down in 15° increments. The chair was locked in place at each tilt angle, and after 40 s subjects were prompted for a verbal report of their tilt perception. Video images were then recorded for approximately 10 s while the subject viewed a centering dot on the visual display. This segment was used to measure OCR.

Data analysis

Postprocessing of the videotapes from the R+0 test session at Kennedy Space Center was carried out on an IBM-compatible computer, which controlled a S-VHS video tape recorder (JVC SRS 365U) via a RS 232 port. We have developed custom software to process three-dimensional eye movement data at a sampling rate of 60 Hz in close to real time. A robust partial ellipse fit was employed to obtain an accurate pupil center estimate (Zhu et al. 1999a). Eye movements were calibrated using pupil center coordinates obtained while the subject was fixating on a calibration grid of known horizontal and vertical targets. A simple three-dimensional model of the eye was used to obtain calibration coefficients from the raw pupil center coordinates (Moore et al. 1996). Torsional eye position was measured using template matching of iral gray-level data from two video images in the spatial domain and a "city-block" distance metric to determine relative torsional eye position (Zhu et al. 1999b). Eye position was represented as Euler angles using a Fick rotation convention (Fick 1854). According to the right-hand rule, eye movements to the left, down, and clockwise (from the subject's point of view) were positive. Videotapes from the test sessions at Johnson Space Center in Houston (L–60, L–30, R+1, R+4, and R+9) were processed using the European Space Agency's video eye position monitor (see Centrifugation, above).

Right eye position data from each test session were obtained in Fick coordinates as described above. A baseline for torsional eye position was calculated from the mean of 3 s of torsion data acquired while the subject fixated on the center point of the calibration display prior to being tilted. Torsional eye position was determined in a similar manner while the subject looked at a centering dot at each roll-tilt angle. A final estimate for ocular torsion was calculated by subtracting the baseline torsion value from that measured during static tilt.

Results

OCR during centrifugation

During constant angular velocity *G*y centrifugation, there is a radial inward linear (centripetal) acceleration, A_c, regardless of the direction of rotation (Fig. 3A), which is aligned with the interaural axis. On Earth, the equivalent acceleration of gravity, A_g, is aligned with the head vertical (dorsoventral) axis. The sum of A_g and A_c, the GIA vector, is tilted in the roll plane with respect to the head dorsoventral axis (Fig. 3A, B). Ground-based centrifugation with 1*g* of centripetal acceleration generated a GIA vector with a magnitude of 1.4*g* tilted 45° with respect to the head (Fig. 3A). *G*y centrifugation at 0.5*g* on Earth generated a GIA magnitude and tilt of 1.1*g* and 27°, respectively. In microgravity, however, the gravitational component was negligible and the GIA was equivalent to the centripetal acceleration. Subjects tended to perceive the GIA as the "spatial vertical" during centrifugation, both on Earth and in-flight (Moore et al. 2000; Clément et al. 2001), and had a strong sense of roll tilt in the opposite direction (Fig. 3A), termed the "somatogravic illusion" (Gillingham and Wolfe 1985).

In addition to this perceptual response, there were robust torsional movements of the eyes during *G*y centrifu-

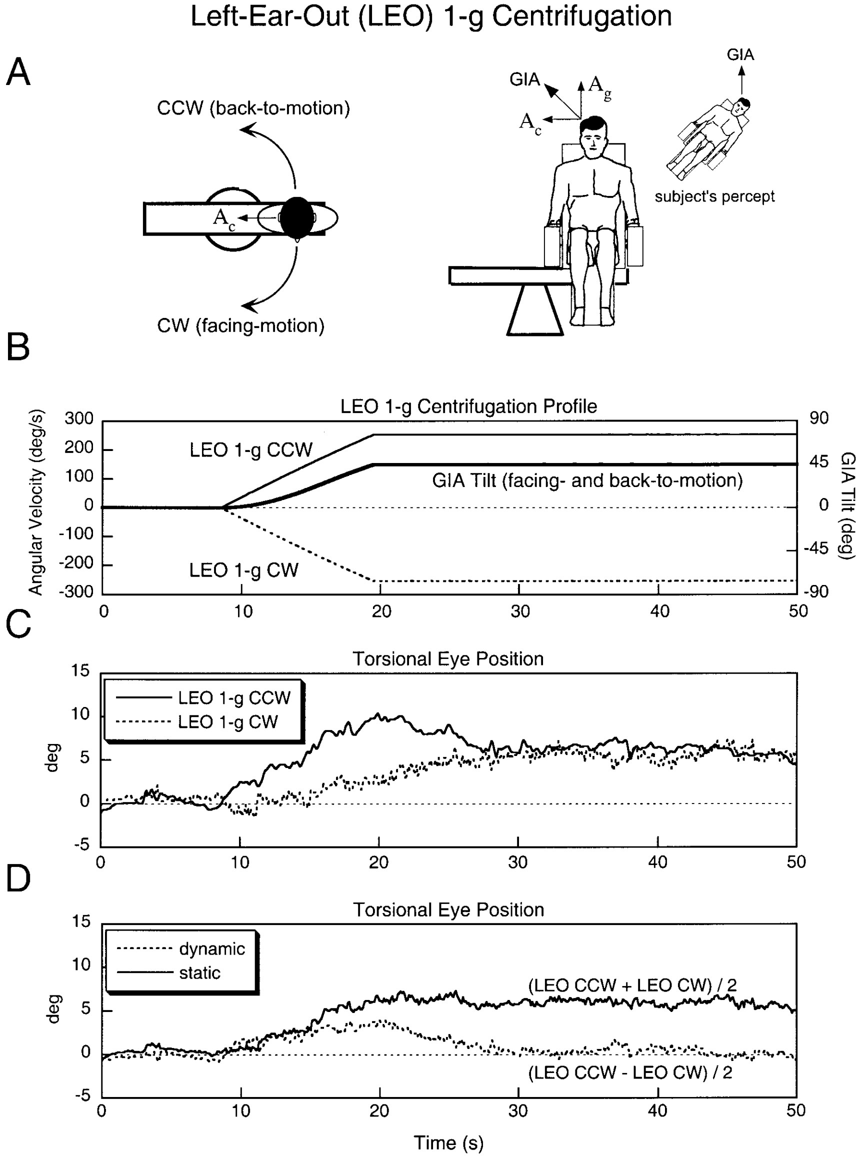

Fig. 3 **A** Left-ear-out (*LEO*) constant-velocity centrifugation generated a centripetal acceleration, A_c, which summed with the equivalent acceleration of gravity, A_g, to tilt the gravitoinertial acceleration (*GIA*) vector in the roll plane relative to the subject's head. All subjects perceived the tilted GIA as the "spatial vertical" and had a strong sense of roll-tilt in the opposite direction. **B** Rotation velocity profiles for LEO back-to-motion (counterclockwise, *CCW*) and facing-motion (clockwise, *CW*) centrifugation, which generated a 1*g* centripetal acceleration at steady state and a 45° roll-tilt of the GIA. The direction of GIA tilt was CW during LEO centrifugation (from the subject's point of view), regardless of the direction of rotation. During right-ear-out (REO) centrifugation (not shown), the roll-tilt of the GIA was CCW. **C** Torsional right eye position data from subject B during LEO 1*g* centrifugation on Earth. During angular acceleration, there was a dynamic ocular torsion component whose direction was dependent on the direction of rotation. Upon reaching constant angular velocity, this dynamic component decayed, and static ocular counterrolling (OCR) was generated by the otoliths in response to the tilted GIA. **D** The dynamic and static components of the ocular torsion response could be isolated by superposing the torsional eye position records during facing-motion and back-to-motion centrifugation. The dynamic torsional response to angular acceleration (*dashed trace*) reached a maximum at onset of steady state and decayed over the following 10 s. The static OCR component (*solid trace*) rose in a linear fashion with the GIA tilt, reaching a plateau of approximately 6° at onset of constant velocity

gation, characterized by dynamic and static components. The dynamic component decayed at onset of constant velocity and was dependent on the direction of rotation. For example, a LEO CCW angular acceleration (back to motion) generated positive (CW) torsional eye position, i.e., the upper pole of the eye rolled to the subject's right (Fig. 3C, solid trace). CW rotation (facing motion) initially generated negative (CCW) ocular torsion (Fig. 3C, dashed trace). Thus, the dynamic component added to the static component of OCR when moving back to motion and subtracted from it when facing motion. The directional dependence of the dynamic ocular torsion response has previously been observed during on-center rotation and is probably a semicircular canal response

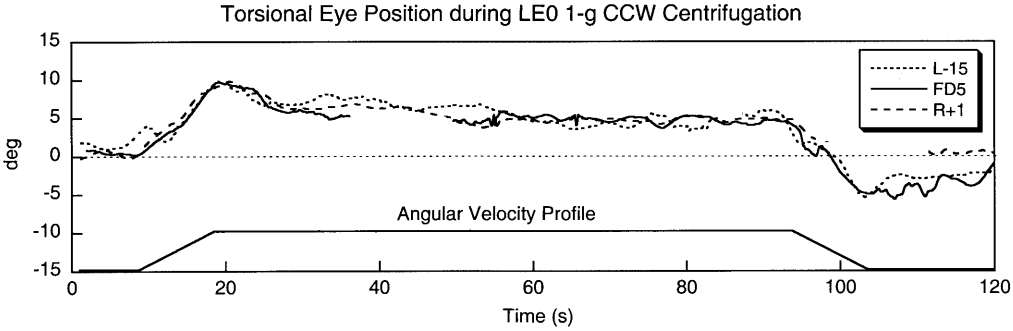

Fig. 4 Torsional right eye position data from subject B during LEO back-to-motion (CCW) 1*g* centrifugation. Preflight (*L–15*), in-flight (*FD5*), and postflight (*R+1*) torsion data are shown overlaid, and there was little variation in OCR magnitude in-flight or after landing. (Note that missing data indicates a period where the eye was closed)

(Smith et al. 1995). The static OCR component was generated by the otoliths in response to the GIA (Fig. 3C, D), reaching a plateau during constant-velocity centrifugation. In contrast to the dynamic component, static OCR was in the same direction (toward the GIA vector) for a given subject orientation (LEO or REO), regardless of the direction of rotation (Fig. 3C). This was due to the fact that the centripetal acceleration, and therefore the GIA tilt, were in the same direction during facing-motion and back-to-motion centrifugation (Fig. 3A, B).

The dynamic component can be seen in the torsional eye position data from subject B during LEO 1*g* centrifugation on Earth (Fig. 3C). When back to motion (Fig. 3C, solid trace), ocular torsion developed rapidly during angular acceleration, reaching a maximum of 10° at the onset of constant velocity rotation, before decaying to a steady state value of approximately 6° after 10 s at constant velocity. During facing-motion centrifugation (Fig. 3C, dashed trace), the eye initially torted in the negative direction, then rolled back in the positive (CW) direction, reaching a plateau of approximately 6° after 10 s of constant velocity, which was the same magnitude as for back-to-motion centrifugation. As the otolithic OCR component had the same polarity for facing motion and back to motion, the dynamic component could be isolated by subtracting the two torsional eye-position traces and halving the result. Dynamic torsional eye positionreached a peak of approximately 4° at onset of constant velocity centrifugation then decayed with a time constant of 6 s (Fig. 3D, dashed trace). The static OCR response was extracted by averaging the facing-motion and back-to-motion traces (Fig. 3D, solid trace), which cancelled the oppositely directed dynamic components. The static OCR response (Fig. 3D, solid trace) followed the tilt of the GIA (Fig. 3B, thick solid trace), reaching a maximum of approximately 6° where the GIA tilt reached a plateau of 45° at onset of constant velocity. We obtained our measures of OCR magnitude after approximately 1 min of constant-velocity rotation, when the dynamic contribution had ceased.

A comparison of torsional eye position data from subject B during a 1*g* LEO back-to-motion (CCW) rotation profile 15 days prior to launch (L–15), on flight day (FD) 5 and 1 day after landing (R+1) showed little difference between the eye-movement response in microgravity and on Earth (Fig. 4). This trend was consistent across the four payload crewmembers, with little variation in OCR magnitude throughout the mission (Fig. 5). Moreover, the OCR response was roughly proportional to the applied interaural linear acceleration, with OCR magnitude during 0.5*g* centrifugation (Fig. 5B) approximately 60% of that generated during 1*g* centrifugation (Fig. 5A).

ANOVA tests revealed no significant effect of test day, and no significant differences between right and left eye data, during *G*y centrifugation ($P>0.05$). Consequently, right and left eye data were grouped into pre-, in-, and postflight bins for each subject and centrifuge orientation (Fig. 6). There were small decreases in the mean value of in-flight OCR from preflight means during 1*g* *G*y centrifugation in all subjects (Fig. 6A). Payload crewmembers A, B, and D exhibited a symmetrical decrease in mean OCR magnitude in-flight of 6.6% (range 4.0–10.9%) compared with preflight mean OCR. This only achieved statistical significance for subject A (Fig. 6A). Postflight, OCR generally increased back to preflight levels for these three subjects in a symmetrical manner (Fig. 6A, B).

In contrast, subject C developed a marked OCR asymmetry in response to left/right tilts of the GIA during in-flight centrifugation. Subject C exhibited a significant ($P=0.0002$) 26% decrement in mean OCR in-flight during 1*g* REO centrifugation (Fig. 6A), but had only a 7.5% decrease during LEO centrifugation. This asymmetry was maintained after landing. In response to postflight 1*g* REO centrifugation, OCR magnitude returned to preflight values (2.5% decrease), but there was a highly significant 28.9% increase ($P=0.0001$) during 1*g* LEO centrifugation. The asymmetry for subject C was also apparent during postflight 0.5*g* centrifugation, where the OCR response in REO was not significantly different from preflight, but there was a large 65.2% increase ($P=0.003$) in OCR during LEO centrifugation (Fig. 6B). Thus, during both in-flight and postflight centrifugation, subject C always generated significantly larger OCR when in the LEO orientation.

The overall mean OCR response was determined by combining LEO and REO OCR data from the four payload crewmembers (Fig. 7). On Earth, 1*g* *G*y centrifugation elicited an OCR response of 5.7±1.1° (mean and SD). During in-flight 1*g* centrifugation, there was a

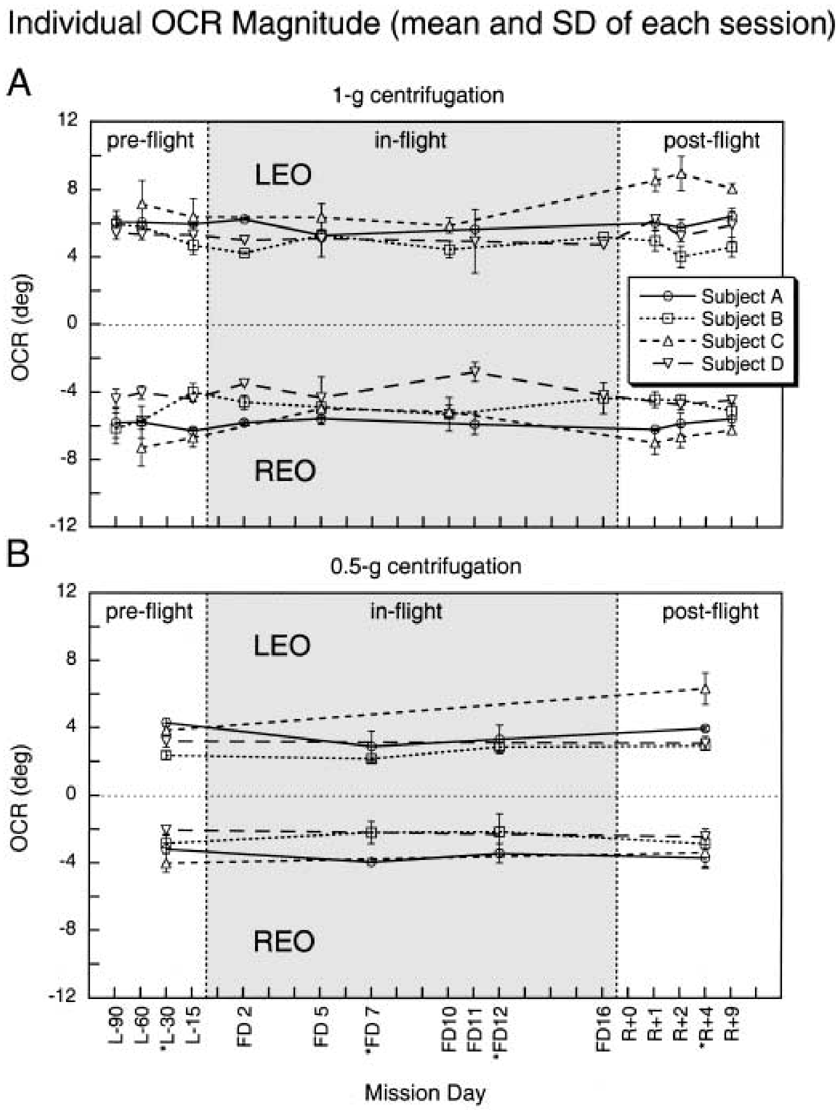

Fig. 5A, B Mean OCR magnitude from each test session (mean and SD of all right and left eye OCR data) for each subject during **A** 1*g* and **B** 0.5*g* centrifugation. OCR in response to LEO and REO centrifugation was essentially symmetrical and exhibited little variation throughout the mission. The magnitude of OCR generated in response to 0.5*g* centrifugation (*L-30*, *FD7*, *FD12*, *R+4*) was approximately 60% of that induced by 1*g* centrifugation

small but significant (P=0.0025) 10% decrease[2] in OCR magnitude to 5.1±0.9°. The magnitude of OCR during postflight 1*g* centrifugation was 5.9±1.4°, which was not significantly different from preflight values (Fig. 7). A similar trend was observed during 0.5*g* *G*y centrifugation. Preflight centrifugation generated 3.3±0.9° of OCR. There was an 11% decrease observed in OCR during inflight 0.5*g* centrifugation to 3.0±0.8° (mean and SD of subjects A and B only), but this was not statistically significant. Postflight 0.5*g* centrifugation generated a weak but significant (P=0.02) increase[3] in postflight OCR to 4.1±1.5° compared with preflight values (Fig. 7).

[2] This could not be attributed solely to the large in-flight decrease exhibited by subject C during REO centrifugation. An analysis of pooled pre- and in-flight OCR data from subjects A, B, D revealed a similar in-flight decrease in mean OCR magnitude with respect to preflight (0.5°), which was also statistically significant (P=0.02).

[3] In contrast to the in-flight decrease in OCR during 1*g* centrifugation, the significant increase in OCR during postflight 0.5*g* centrifugation was due to the large (65%) increase in subject C's R+4 REO data. The small number of postflight data points (from the single R+4 test session) was probably responsible for this effect.

OCR during static tilt

The OCR response was further investigated by statically tilting the body left-ear down in a chair during pre- and postflight testing. Consistent with the centrifugation results, there was no significant change (P>0.05) in OCR 2–4 h after landing (R+0) and on subsequent postflight test days, compared with preflight values (Fig. 8A). It is interesting to note that the magnitude of OCR generated by 45° left-ear-down static tilt (3–4°) was significantly less than that induced by a 45° tilt of the GIA during preflight 1*g* *G*y centrifugation (5.7°; Fig. 8A, filled square). Previous studies have suggested that OCR is linearly related to the magnitude of interaural linear acceleration (Woellner and Graybiel 1959; Miller and Graybiel 1970). Our OCR data exhibited a linear relationship with interaural linear acceleration during static tilt (mean of all pre- and postflight data), with a slope of 5.04°/g (R=0.995; Fig. 8B, filled circles, dashed line). The magnitude of OCR during preflight centrifugation followed this linear relationship (Fig. 8B, filled

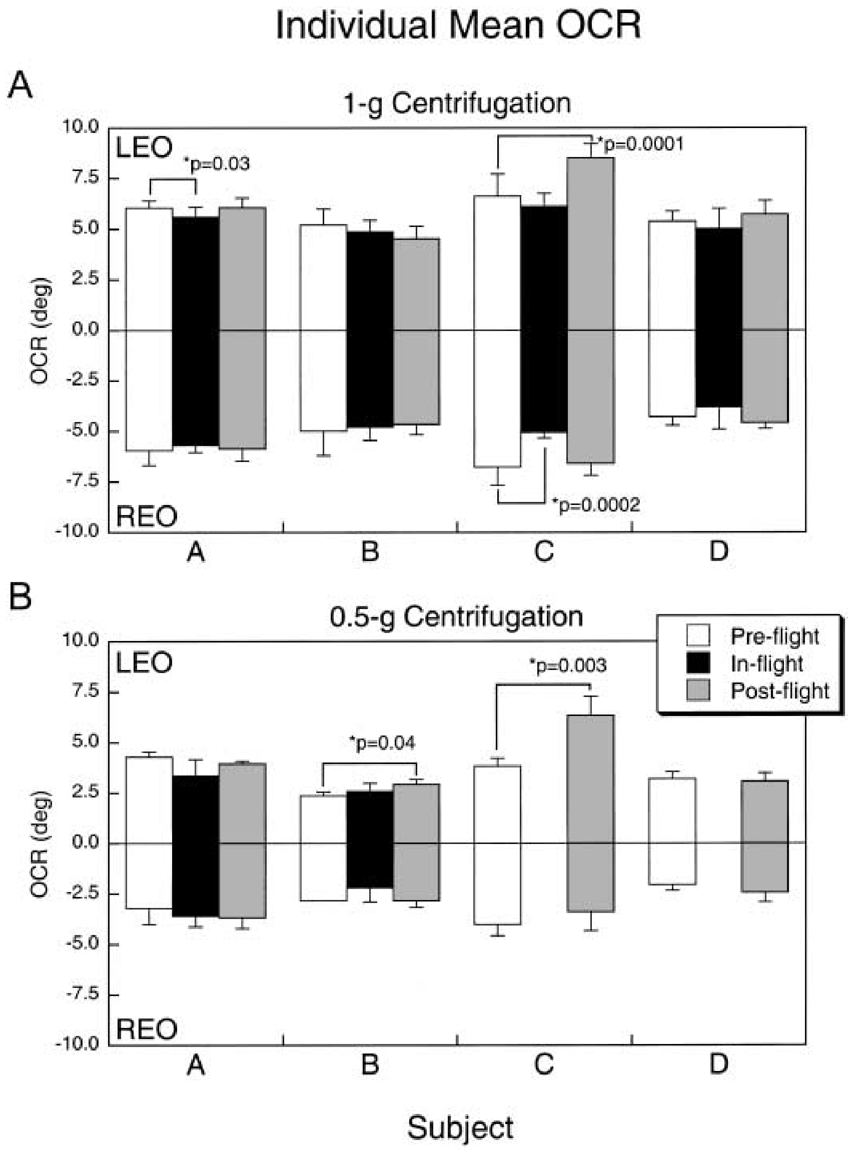

Fig. 6A, B OCR data were pooled into pre-, in-, and post-flight bins for each subject during **A** 1*g* and **B** 0.5*g* LEO and REO centrifugation (mean and SD). Subjects demonstrated a tendency toward a small symmetrical decrease in in-flight OCR of around 7%, and postflight OCR magnitudes close to preflight values. The exception was subject C, who exhibited a large 26% decrease in in-flight OCR during REO 1*g* centrifugation, and a large postflight increase in OCR during 1*g* (29%) and 0.5*g* (65%) LEO centrifugation, relative to preflight means

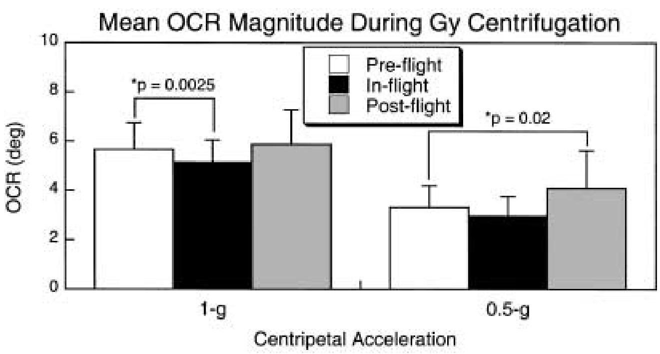

Fig. 7 Overall mean OCR response (mean and SD of all subjects combined LEO and REO data) revealed a significant 10% decrease in in-flight OCR during 1*g* *G*y centrifugation, and no significant postflight changes, relative to preflight. There was a similar in-flight decrease in mean OCR during 0.5*g* *G*y centrifugation, but this did not reach significance due to the small number of in-flight subjects (N=2). There was a weak but significant increase in mean postflight OCR from preflight values

squares), but still had a significantly larger magnitude than for static tilt at an equivalent interaural linear acceleration (0.5*g* centrifugation, P=0.03[4]; 1*g* centrifugation, P=0.01[5]). During both 0.5*g* and 1*g* centrifugation in microgravity, where the head dorsoventral gravitational component was absent, the OCR magnitude was not significantly different from that induced by static tilts on Earth with equivalent interaural linear acceleration (Fig. 8B, open squares).

[4] Comparison of all preflight 0.5*g* centrifugation data with all 30° (0.5*g* interaural linear acceleration) static tilt data.

[5] Note that there were no data for 90° (1*g* interaural linear acceleration) static tilt. The preflight 1*g* centrifugation data were compared with the extrapolated OCR value for 90° static tilt obtained from the linear fit to the static tilt data (5.04°). In order to use ANOVA, an assumption was made that the variance at this point was equivalent to that at the last available data point (i.e., 60° static tilt).

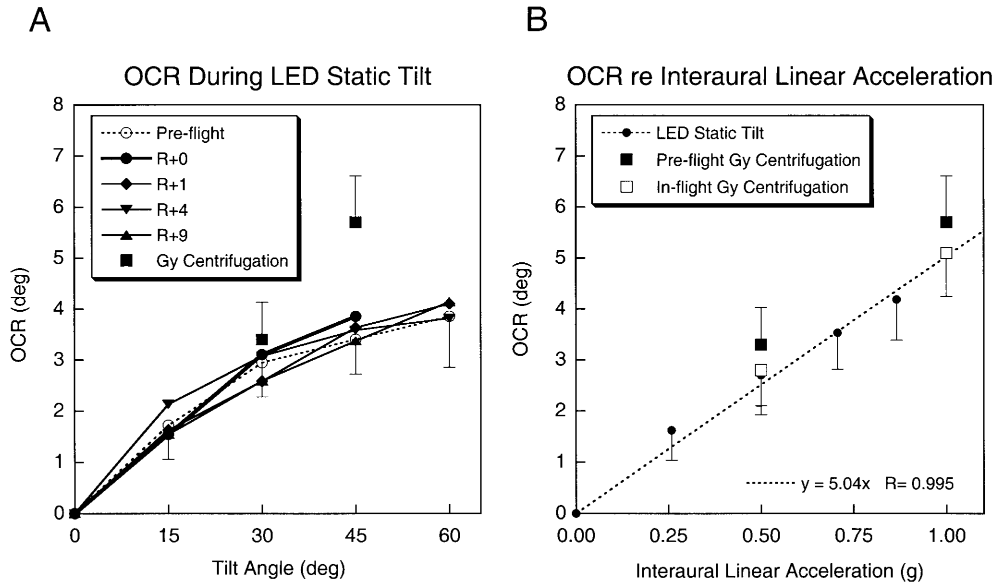

Fig. 8 A Mean OCR magnitudes (mean of four payload crew, right eye) during pre- and postflight left-ear-down (*LED*) static tilt. Consistent with the centrifugation results, there were no significant postflight changes in OCR on the day of landing (*R+0*) and on subsequent postflight test days (*R+1*, *R+4*, and *R+9*). (Note: For clarity, SD shown on preflight data only. Preflight data are the means of OCR measures obtained 60 days and 30 days prior to launch). Superimposed on the plot (*filled squares*) is OCR measured during preflight *G*y centrifugation (mean and SD). OCR measured at a 45° static tilt angle was significantly less than that generated by a 45° GIA tilt during centrifugation. **B** OCR during left-ear-down static tilt (mean and SD of all test sessions) exhibited a linear relationship with interaural linear acceleration (*filled circles, dashed line*). OCR generated by preflight *G*y centrifugation was significantly larger than that induced by a static tilt with equivalent interaural linear acceleration (*filled squares*). In contrast, there was no difference between OCR produced by in-flight *G*y centrifugation and by static tilt with equivalent interaural linear acceleration (*open squares*). This suggests that the larger dorsoventral linear acceleration component during centrifugation on Earth contributed to the OCR response

Discussion

The main findings of this study were that the OCR reflex in response to sustained interaural linear acceleration induced by *G*y centrifugation was essentially maintained in microgravity, and that OCR magnitude was proportional to the magnitude of applied interaural linear acceleration. Mean values of in-flight OCR were slightly lower (10%) than preflight values across all subjects. There was no significant difference in OCR generated during pre- and postflight centrifugation, suggesting that adaptation to microgravity and readaptation to gravity did not alter the gain of OCR. Consistent with this, there was no change in the OCR induced by static tilt before and after flight.

The ocular torsion response during *G*y centrifugation is comprised of a dynamic component at the onset of rotation superimposed on a static otolith-mediated component, which reached a plateau during constant-velocity centrifugation. Previous studies of this phenomenon utilizing *G*y centrifugation (S. Wearne, unpublished PhD thesis) and on-center rotation (Smith et al. 1995) have suggested that the dynamic torsion response is probably generated by the semicircular canals ("centered" torsion). Our findings are in agreement with this interpretation. In our subjects, the dynamic component increased in response to the angular acceleration and decayed over approximately 10 s upon reaching constant angular velocity. Furthermore, the polarity of the dynamic ocular torsion was dependent on the rotation direction (Fig. 3C, D), whereas the static OCR component was related to the orientation of the centripetal acceleration and therefore independent of the direction of angular acceleration. The torsional position response during facing-motion and back-to-motion centrifugation is consistent with the interpretation that a canal-dependent dynamic torsional component added to the otolith-generated static OCR response when subjects were oriented back to motion during LEO and REO centrifugation, and subtracted from it when facing motion. By sampling OCR after 65 s of rotation, we ensured that our measures reflected the static component only.

Our finding that preflight OCR during static tilts and *G*y centrifugation were approximately linear functions of interaural acceleration up to 1*g* (Fig. 8B) are in accord with previous studies (Woellner and Graybiel 1959; Miller and Graybiel 1970). Our data are also consistent with findings that *G*y centrifugation on Earth generates significantly greater OCR than during static roll tilt with an equivalent interaural acceleration, which has been attributed to the larger head dorsoventral linear acceleration (1*g*) during centrifugation (MacDougall et al. 1999). Centrifugation in space gave us a unique opportunity to test this hypothesis, in that it generated the same interaural linear acceleration as on Earth, but with no head dorsoventral gravitational component. During both 0.5*g* and 1*g* *G*y centrifugation in microgravity, OCR was generated with the same magnitude as that induced by static roll tilts on Earth with an equivalent interaural linear acceleration (Fig. 8B). The data are consistent with the hypothesis that OCR is primarily generated in response to interaural linear acceleration. The increased OCR during terrestrial centrifugation was probably due to the larger dorsoventral linear acceleration, which contributed approximately 10% of the total OCR magnitude.

The mechanism by which the dorsoventral component of linear acceleration contributes to OCR is not clear. One possibility is that OCR is generated in response to a weighted sum of interaural and head dorsoventral linear accelerations that activates both the utricles and saccules (De Graaf et al. 1996; Merfeld et al. 1996; MacDougall et al. 1999). An interesting observation from our data was that OCR magnitude during in-flight 0.5*g* centrifugation was not significantly different from OCR during 30° static roll tilt on Earth, where the interaural linear acceleration was also 0.5*g* (Fig. 8B). This is despite the fact that in space there was no dorsoventral linear acceleration, whereas the dorsoventral component during 30° static tilt was 0.87*g*. This suggests that if the dorsoventral linear acceleration contributes to OCR it is not a linear relationship. Alternatively, increased OCR during centrifugation on Earth may be due to activity arising in somesthetic and body-related graviceptors in response to the larger GIA magnitude[6]. Evidence for an extraotolithic contribution to OCR is found in both humans and animals. Significant static torsional eye position was generated (1.5°–2°) when labyrinthine-defective humans were statically tilted or centrifuged (Miller and Graybiel 1970), and similar OCR magnitudes were observed during static tilt in monkeys after bilateral labyrinthectomy (Krejcova et al. 1971). OCR in rabbits was substantially larger during head-on-body tilts than when the animals were tilted en bloc (Magnus 1924; Hughes 1971), demonstrating contributions of neck proprioceptors to OCR in rabbits. Moreover, it has recently been shown in the cat that tilts of the body are reflected in vestibular nuclei activity in the absence of the labyrinths (Yates et al. 2000). This may provide a mechanism for the integration of somesthetic and otolithic input for the generation of OCR.

Although there is some variability in results from previous studies, approximately 75% of subjects tested have exhibited a decrease in postflight OCR (Yakovleva et al. 1982; Arrott and Young 1986; Vogel and Kass 1986; Hofstetter-Degen et al. 1993; Dai et al. 1994, 1998; Diamond and Markham 1998; Young and Sinha 1998). Our finding that there was no reduction in postflight OCR magnitude compared with preflight values in all four payload crewmembers raises the possibility that in-flight exposure to artificial gravity, in the form of intermittent 1*g* and 0.5*g* centripetal acceleration, was a countermeasure to deconditioning of otolith-based orientation reflexes. The only subject to exhibit signs of otolith deconditioning, i.e., a substantial asymmetry in OCR to right and left tilts of the GIA, was exposed to significantly less centrifugation than the other payload crew. Subject C's OCR asymmetry developed in space and persisted throughout the 9 days of postflight testing. This subject also exhibited a corresponding asymmetry in perception during in- and postflight centrifugation, with a consistently larger perception of roll tilt when in the REO position (Moore et al. 2000; Clément et al. 2001). It is interesting to note that this perceptual bias was in the opposite direction to the bias in the OCR response, with significantly more OCR generated in the LEO orientation. Asymmetries in low-frequency otolith sensitivity to roll tilts of the GIA have previously been observed in astronauts postflight (Vogel and Kass 1986; Young and Sinha 1998) and may have a significant impact on postural control, especially when turning corners (Ito et al. 1995; Imai et al. 2001). Subject C was not exposed to artificial gravity until 5 days into the flight, and received less than half the exposure time (37 min) as the other 3 payload crewmembers, who were centrifuged less than 24 h after orbital insertion, and received an average exposure of 83 min over four to six in-flight sessions. If intermittent in-flight centrifugation did in fact act to prevent otolith-ocular deconditioning, the results suggest that any countermeasure effect may be reliant on early and/or cumulative exposure to artificial gravity.

Recent studies have suggested that the otoliths play a role in the activation of sympathetic outflow in response to changes in posture, triggering a vestibulosympathetic reflex, which produces changes in heart rate and vascular tone that contributes to maintain blood flow to the brain during orthostatic stress (Doba and Reis 1974; Essandoh et al. 1988; Ray et al. 1997; Yates and Miller 1998; Kaufmann et al. 1999). There were no symptoms of orthostatic intolerance (an inability to maintain blood flow to the brain when upright) during postflight tilt-tests in any of the four payload crewmembers exposed to in-flight centrifugation (I. Biaggioni, unpublished work; Levine 2000). If the finding that 64% of astronauts experience profound symptoms of postflight orthostatic intolerance is a general phenomenon (Buckey et al. 1996; Fritsch Yelle et al. 1996), it is unlikely that four crewmembers on the same flight would not exhibit symptoms of orthostatic intolerance by chance (0.36^4 or approximately 1 in 60). This raises the possibility that in-flight centrifugation may have acted to prevent deconditioning of otolith-sympathetic reflexes during exposure to microgravity to help maintain orthostatic tolerance into the postflight period.

The locomotor, gaze, and cardiovascular deficits commonly observed in astronauts following space flight are a source of major concern if there is necessity for immediate egress or for adequate postflight functioning in a gravitational environment. Artificial gravity has long been proposed as a potential countermeasure to these debilitating effects of space travel (see Young 1999 for review). The relative simplicity of short-arm centrifugation stands in contrast to other more complex artificial gravity scenarios such as rotating rooms or spacecraft. If in-

[6] *G*y centrifugation with centripetal accelerations of 1*g* and 0.5*g* generates a GIA magnitude of 1.4*g* and 1.1*g*, respectively.

termittent in-flight centrifugation were to prove to be a countermeasure to the deconditioning of otolith-based ocular, postural, and sympathetic reflexes in microgravity, it could facilitate future long-duration missions such as the International Space Station or interplanetary exploration.

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