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Spatial orientation of the angular vestibulo-ocular reflex (aVOR) after semicircular canal plugging and canal nerve section

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Abstract

We investigated spatial responses of the aVOR to small and large accelerations in six canal-plugged and lateral canal nerve-sectioned monkeys. The aim was to determine whether there was spatial adaptation after partial and complete loss of all inputs in a canal plane. Impulses of torques generated head thrusts of $\approx 3,000^\circ/\text{s}^2$. Smaller accelerations of $\approx 300^\circ/\text{s}^2$ initiated the steps of velocity ($60^\circ/\text{s}$). Animals were rotated about a spatial vertical axis while upright (0°) or statically tilted fore-aft up to $\pm 90^\circ$. Temporal aVOR yaw and roll gains were computed at every head orientation and were fit with a sinusoid to obtain the spatial gains and phases. Spatial gains peaked at $\approx 0^\circ$ for yaw and $\approx 90^\circ$ for roll in normal animals. After bilateral lateral canal nerve section, the spatial yaw and roll gains peaked when animals were tilted back $\approx 50^\circ$, to bring the intact vertical canals in the plane of rotation. Yaw and roll gains were identical in the lateral canal nerve-sectioned monkeys tested with both low- and high-acceleration stimuli. The responses were close to normal for high-acceleration thrusts in canal-plugged animals, but were significantly reduced when these animals were given step stimuli. Thus, high accelerations adequately activated the plugged canals, whereas yaw and roll spatial aVOR gains were produced only by the intact vertical canals after total loss of lateral canal input. We conclude that there is no spatial adaptation of the aVOR even after complete loss of specific semicircular canal input.

Keywords

Monkey; Vestibulo-ocular reflex; Semicircular canals; Vestibular nerve; Eye movements; Cervico-ocular reflex

Introduction

The orientation of the individual semicircular canals in head coordinates has been determined for various species (Curthoys et al. 1977; Blanks et al. 1985; Reisine et al. 1985, 1988; Dickman 1996; Della Santina et al. 2005; Ifediba et al. 2007; Bradshaw et al. 2009). In primates, the average plane of the vertical canals is not orthogonal to the lateral canal plane, but is tilted back by 10° (Reisine et al. 1985, 1988). Therefore, there is no head orientation in which one pair of canals can be exclusively activated by rotation (Yakushin et al. 1995, 1998), leaving open the possibility that central processes have the capability to adapt coding of the spatial planes to compensate for loss of spatial input following lesions. Such spatial adaptation following canal plugging has been posited to generate altered response characteristics when the individual canals are stimulated (Böhmer et al. 1982; Böhmer and Henn 1983; Böhmer et al. 1985; Angelaki and Hess 1996; Angelaki et al. 1996). Other studies have shown that plugging of a canal reduces the cupula/endolymph time constant from ≈ 4 to ≈ 0.07 s and alters the response characteristics in that plane (Yakushin et al. 1998). Each canal pair continues to contribute to the spatial aVOR according to its geometrical orientation, and other canals do not adapt to compensate for the response alteration in the plugged plane. This simple model explains the characteristics of the aVOR for low and mid-band frequency responses without the necessity for assuming spatial adaptation of remaining canals (Yakushin et al. 1998). The model also predicts that the gain and phase of the canal responses changed toward normal as the frequency of head rotation increases from 3 to 20 Hz. (Yakushin et al. 1998), a finding confirmed by others (Lasker et al. 1999; Rabbitt et al. 1999; Hess et al. 2000). Changes in the firing rates of canal afferents in the eight nerves observed at different frequencies are consistent with a reduced time constant of the plugged canal (Rabbitt et al. 1999, 2009; Sadeghi et al. 2009).

One reason that canal plugging might not induce a spatial reorientation of the response characteristics of central vestibular neurons is that plugging maintains the resting discharge of the afferents in the canal nerves and central neurons (Goldberg and Fernandes 1975; Rabbitt et al. 2009; Sadeghi et al. 2009) and maintains the high-frequency characteristics of the aVOR response (Yakushin et al. 1998), fostering an invariance of the spatial orientation in central processing. In contrast, a complete loss of neural input from a canal plane might have a different effect on both peripheral and central processing (Raphan et al. 1983). Canal nerve section causes a profound loss of all input from the affected canal, including its resting discharge, both in peripheral and central pathways. Moreover, bilateral lateral canal nerve ablation causes a complete loss of peripheral input for both low and high frequencies in a specific spatial plane. It is natural to consider, therefore, whether spatial adaptation might occur to account for the total loss of central processing of information about the lost plane.

Halmagyi, Curthoys, and coworkers have developed high-frequency, high-acceleration stimuli, i.e., head thrusts, that can be used to determine whether there is a loss of canal function over a wide range of frequencies following various peripheral vestibular lesions (Aw et al. 1994, 1995a, b, 1996, 2001; Curthoys and Halmagyi 1995; Halmagyi et al. 2001, 2008). In this study, we utilized both high-acceleration thrusts and steps of velocity with moderate accelerations to determine their differential effects on canal plugging and canal nerve section. The aim was to determine whether spatial adaptation could be demonstrated

after both lateral canal nerves were severed and to determine the differences of adaptation to canal nerve section from those of canal plugging.

Methods

Eye movements of two cynomolgus monkeys (*Macaca fascicularis*, M97050 and M98079) were studied before and after section of both lateral canal nerves. Data were compared to that obtained from two cynomolgus monkeys with all six semicircular canal plugged (M9357 and M98078). Data from five cynomolgus monkeys with various pairs of the semicircular canals plugged were used for comparison. The experiments conformed to the Guide for the Care and Use of Laboratory Animals (National Research Council 1996) and were approved by the Institutional Animal Care and Use Committee. Data obtained by sinusoidal oscillation at frequencies 0.2–4 Hz from animal M9357 and from five additional animals tested at 0.2 Hz were previously reported (Yakushin et al. 1995, 1998). After completion of data taking for the present study, spatial orientation of central vestibular neurons was tested in animals M97050 and M98079 at 0.2 Hz (Yakushin et al. 2005).

Surgical procedures

Animals were operated in three stages. In the first stage, a head mount was implanted to hold the animal's head painlessly during experiments (Sirota et al. 1988; Yakushin et al. 2000). About 2 weeks later, two scleral search coils were implanted on the left eye. One, placed around the iris, recorded horizontal and vertical components of eye movement (Robinson 1963; Judge et al. 1980). The other, placed on top of the eyeball, recorded torsional eye movement (Dai et al. 1994). After an adequate amount of pre-lesion data had been obtained, the canal nerves were sectioned. The techniques for canal plugging and lateral canal nerve section are described in detail elsewhere (Cohen et al. 1983; Yakushin et al. 1995). Briefly, the bony lateral canal was exposed through the middle ear using a posterior approach. After the ampullae of the lateral and anterior canals were identified, bone was cleared from an area behind the lateral canal ampulla to visualize the lateral canal nerve. The nerve was then cut in the area behind the lateral canal ampulla using a #11 scalpel blade. Although the lateral canal nerve was visualized, the depth of the cut could vary. Therefore, whether the lateral canal nerve had been completely sectioned and whether there was damage to the adjacent anterior canal nerve was not known definitely before histological analysis.

Experimental protocols and data analysis

Eye movement recording and calibration—Signals derived from the two scleral search coils implanted on the left eye were related to the yaw, pitch, and roll eye movements. These signals were calibrated for velocity by rotating animals in light at 30°/s about a spatial vertical axis while upright, side down, and prone (Raphan et al. 1979). A right-hand rule-based coordinate system was used in this study. The positive direction of eye movements was left for yaw, down for pitch, and clockwise for roll movements from the animal's point of view. It should be noted that yaw, pitch, and roll eye velocities were used interchangeably with horizontal, vertical, and torsional eye velocities, respectively.

Rotational stimulation protocol—Vestibular stimuli were delivered using a multi-axis rotator (Neurokinetics Inc., Pittsburgh) (Dai et al. 1991; Reisine and Raphan 1992; Yakushin et al. 1998). During experiments, animals sat in a primate chair with their heads fixed in the horizontal stereotaxic plane (upright). Animals were rotated in darkness about a vertical axis with the primate chair positioned either upright (0°) or tilted forward (nose down, +) or backward (nose up, −) over ±90° in 10° increments. Steps (ramps) of velocity and thrusts of acceleration (Halmagyi and Curthoys 1988; MacDougall et al. 2009; Weber et al. 2009) in

the clockwise (CW) and counterclockwise (CCW) directions were given in random order for at least 10 times. Step stimuli had constant accelerations of $270^\circ/\text{s}^2$, reaching a velocity of $60^\circ/\text{s}$ over 250 ms (Yakushin et al. 1997, 1998). To produce rapid head impulses, the axis was driven manually to a peak head velocity of $\approx 60\text{--}120^\circ/\text{s}$ within 70 ms from the onset of rotation with peak accelerations of $\approx 3,000^\circ/\text{s}$. Pitch eye velocities were negligible for this protocol and were not considered in the analysis.

To verify which canal function was affected by the surgery, animals were rotated about the axis that was normal to the lateral, right anterior–left posterior (RALP) and left anterior–right posterior (LARP) canal planes. Thus, to test lateral canal function, the animal was tilted 40° forward to align the vertical canal planes with the spatial vertical and then rotated with pulses of acceleration about a spatial vertical axis. To test the vertical semicircular canals, animals were positioned right ear down, and then the head was rotated about the yaw axis of the head 45° CCW and CW to bring the RALP or LARP canal planes, respectively, into the plane of rotation (Cremer et al. 1998; Aw et al. 2001).

Eye movement processing and analysis—Eye movement-related signals were differentiated using an 11-point digital filter, and saccades were identified using maximum likelihood detection criterion (Singh et al. 1981) and removed for further processing and analysis. In response to step rotation, eye velocities of the canal-plugged animals reached peak values within ≈ 70 ms and stayed at this level for ≈ 100 ms. We used this 100-ms interval (onset shown in Fig. 4a–d by gray vertical lines) to compute the aVOR gain by dividing it by the head velocity ($60^\circ/\text{s}$). For all canal-plugged animals, this type of eye velocity profile was observed in every head orientation (Yakushin et al. 1998). There were no eye velocities in lateral canal nerve-sectioned animals tested with their heads tilted 40° forward, but slow-phase eye velocities followed head velocity profiles in all other head orientations (not shown). To compute aVOR gains in response to step rotations in these animals, the first second of head rotation in the steady state was used to determine the aVOR gain.

We define two types of gains for thrusts of head acceleration and steps of velocity: (1) temporal gains and (2) spatial gains. Temporal gains were defined as the ratio of amplitude of yaw or roll eye velocities relative to the head velocity about a spatial vertical axis. Gains were computed for both CW and CCW rotation. The convention for positive and negative gains was consistent with the positive directions for the head coordinate frame and the right-hand rule, which we established in our earlier study (Yakushin et al. 1998). Positive yaw eye velocity is along an axis through the top of the head. Therefore, when tilted forward and rotated about a spatial vertical axis, the yaw eye velocity is always 180° out of phase with the head velocity. We referred to this as a positive gain. For roll, the positive direction is along the forward occipito-nasal axis, and positive rotations of the eyes are clockwise from the animal's point of view. The phase of the roll relative to the stimulus velocity is therefore dependent on the head position. When the head is tilted forward, the roll eye velocity is in phase with the stimulus velocity. When tilted back, the roll eye velocity is 180° out of phase with the stimulus velocity. We chose to have the gains for roll positive when the head is tilted forward as this is the direction for positive pitch of the head (Yakushin et al. 1998). In this head orientation, the roll eye velocity is in phase with stimulus velocity. The temporal gains were then plotted as a function of head tilt and fit with a sinusoid:

$$y = A \cdot \cos(\theta + \varphi) \quad (1)$$

where θ was the tilt angle of the head, and φ is the phase of the spatial response curve. The values A and φ are defined as the spatial gain and phase of the response.

Statistical analysis—A pairwise *t*-test was used to verify the asymmetry of the responses evoked from reciprocal canal pairs. An analysis of variance (ANOVA) (Keppel 1991; Yakushin et al. 1995) was used to evaluate whether there was a sinusoidal variation in the data distribution for the spatial gain curves or whether it was just noise. A second purpose was to evaluate whether the model given by Eq. 1 predicted the data. The null hypothesis (H_0) was that the sinusoidal fit of the data is not significantly different from the average value of the data distribution. To evaluate the null hypotheses, the variance of the bias value C was compared to the variance of difference between the data and the fit to the data, $y = A \cos(x + B) + C$, where B is the phase of the response. If the ratio of two errors, which follow an F distribution, was significant at $P < 0.05$, the null hypothesis was rejected.

We next tested the hypotheses that gains plotted as a function of head tilt were consistent with that predicted by the model based on the geometry and dynamics of the canals (Yakushin et al. 1998). The null hypothesis was that the sinusoidal fit to the data was not different from the model predictions. In this case, the variance of the difference between the data and model predictions was compared to the variance between the data and the best sinusoidal fit to the data. If the F statistic does not exceed a critical value, the null hypothesis cannot be rejected.

Model predictions of the aVOR responses for animals with interrupted canal function

We first fit data obtained from the normal animals using Eq. 1. To predict the aVOR gains after bilateral lateral canal nerve section, a previously described model was utilized (Yakushin et al. 1998). This model computes yaw, pitch, and roll components of the aVOR based on the contribution of the individual canals to the overall aVOR gain, based on the orientation of the canal with respect to the axis of head rotation. In this study, we utilized the same values of the canal gain, as well as the same canal orientation in head coordinates as before (Yakushin et al. 1998). We further assumed that the time constant of the normal canal is 4 s, while that of the plugged canals is 0.070 s to predict responses of the canal-plugged animals (Yakushin et al. 1998). This model was capable of accurately predicting the aVOR gains at frequencies from 0–20 Hz. To predict spatial responses of animals with sectioned canal nerves, the dominant time constant of the canal whose nerve had been sectioned was set to zero. From this, the maximal ‘spatial yaw gain’, which occurred when the animals were tilted 50° back, was 0.44, and the spatial torsional response was 0.45.

Results

Normal animals

Yaw gains of normal animals tested with thrusts of head accelerations were maximal when the animals were upright and the gains decreased as the animals were tilted forward or backward. In contrast, the roll gains were minimal with the animals in an upright position and increased as they were moved close to a prone or supine orientation (Fig. 1). Pitch aVOR gains in this paradigm were negligible in all fore-aft head orientations. The average spatial yaw aVOR gain tested with thrusts of acceleration for three normal animals was 0.87 ± 0.09 , and it occurred at $4 \pm 4^\circ$. The average spatial roll aVOR gain of these animals was 0.52 ± 0.04 , when they were positioned at $81 \pm 4^\circ$. Similarly, when the aVOR was tested with steps of velocity, the average spatial yaw gain was 0.92 ± 0.04 , occurring at $6 \pm 4^\circ$, and the average roll gain was 0.60 ± 0.02 at $93 \pm 10^\circ$. Thus, yaw and roll aVOR gains and phases from thrusts and steps of acceleration were similar in the normal animals.

Spatial responses after bilateral lateral canal nerve section

When M97050 was tested 10 days after the surgery with steps of velocity, there were only weak responses in yaw and roll (Fig. 2a, d). The spatial horizontal and torsional gains

gradually increased over the first month (Fig. 2b, e) reaching the values close to the gains and spatial phases predicted by the model for lateral canal-sectioned animals (Fig. 2, gray curves). It was previously reported that canal surgery could lead to the cupular detachment of the ampullar roof (Rabbitt et al. 1999, 2009). If this is the case, then operation near the lateral canal ampullae could affect the anterior canal, and therefore, responses obtained in the first week after surgery could be due to activation of the posterior canals only.

This animal (M97050) was also tested with head acceleration thrusts 2 months after surgery. Its spatial yaw gains were 0.32 and 0.25 for CW and CCW rotations, respectively (Fig. 3a, filled symbols). Roll aVOR gains were 0.37 and 0.31 for CW and CCW rotations, respectively (Fig. 3b, filled symbols). These values were close to those obtained 1 month earlier with steps of velocity.

Animal M98079 was tested from the 2 week after surgery. It had no response in any head orientation for the first 3 months. Then, small responses were evoked when the head was tilted about 50° backward. Spatial responses (gain as a function of head orientation), however, could not be established until 7 months. Spatial responses to the steps of velocities at 7 months were 0.15 in yaw (Fig. 2c, filled symbols) and 0.37 in roll (Fig. 2f, filled symbols) with the peak gain occurring when the head was tilted about 50° backward. The roll responses were closely predicted by the model in this animal.

This animal was also tested with thrusts of head acceleration 8.5 months after surgery. Yaw gains were 0.27 (Fig. 2b, filled symbols), and roll spatial gains were 0.32 (Fig. 3d, filled symbols). These responses were somewhat smaller than those predicted for an animal that had functioning anterior and posterior canals (Fig. 3b, d, gray curves). The findings suggest that there may have been damage to remaining canals or their nerves in addition to the lateral canal nerve sectioning. This was confirmed by histology (Fig. 5). Interestingly, the spatial responses obtained from M98079 long after surgery are similar to that obtained in M97050 1 week after nerve section. This may indicate that animal M98079 had only posterior canals intact.

Temporal and spatial responses after canal plugging

The dominant time constant of the plugged canals in animal M9357 was 0.070 s (Yakushin et al. 1998). Since head thrusts are short duration stimuli, they should be sufficient to activate the plugged canals. Examples of the head and yaw eye velocities that were induced with rotations about an upright position are shown in Fig. 4a, b. The eye velocities matched the stimulus velocity for either direction of head rotation up to the time of the peak head velocity (vertical gray lines). Following that, the stimulus and eye velocities decreased and reversed direction. The amplitude of the reversal was approximately equal to the initial response and could be followed by a slight overshoot in the initial direction of movement. The reversal and overshoot were probably secondary to the forces exerted to stop the head movement. In this paper, we will only consider the initial response.

The average spatial yaw and roll aVOR gains obtained in response to thrusts of acceleration 16 months after canal plugging are shown in Fig. 4e–h (red). The spatial yaw gain was 1.04 for the CW and 1.08 for the CCW directions, and these gains occurred at head tilts of -10° and -7° , respectively (Fig. 4e, f, black curves). The roll aVOR gains were 0.53 and 0.56, for the CW and CCW directions, respectively, with corresponding spatial phases of 70° and 75° . The model predictions of gain and spatial phase for both yaw (gain = 1.0, phase = 0°) and roll (gain = 0.6, phase = 90°) (Fig. 4g, h, black curves) were not significantly different from the data, given the variations in data from individual monkeys.

When the animal was tested with steps of velocity (acc. $270^\circ/\text{s}^2$) in the upright position, eye velocity matched stimulus velocity, before plugging (Fig. 4c, d, compare dark blue and black traces). After plugging, the induced eye velocities were substantially smaller, reaching peak velocities within ≈ 70 ms from the onset of head rotation (gray vertical lines; Fig. 4c, d, light blue). This was consistent with the finding that the dominant time constant of the plugged canals was ≈ 70 ms. The spatial yaw aVOR gain obtained with steps of head velocity was ≈ 0.65 for both CW and CCW rotation with a spatial phase of 9° , which is close to 6° observed before plugging. The spatial roll aVOR gain was 0.33 for CW and 0.26 for CCW rotation with a spatial phase of 70° and 87° , respectively. Thus, the yaw and roll aVOR gains were close to normal when tested with thrusts of acceleration, but were substantially reduced in gain when tested with low accelerations.

To verify the effects of thrusts of head acceleration on the aVOR after canal plugging, the animals in this and a previous study were tested by rotating them about a spatial vertical axis while in upright, left side down, and prone (face down) positions. Among these animals were five animals with various types of canal plugging tested before and after surgery. There was no difference in the yaw ($P = 0.98$, *t*-test), pitch ($P = 0.15$), and roll ($P = 0.29$) aVOR gains in response to thrusts of high acceleration between the normal and canal-plugged animals. On average, aVOR gains were 0.97 ± 0.11 for yaw and pitch and 0.58 ± 0.13 for roll in all animals. These data confirm that plugged canals can be activated by high-acceleration stimuli.

Physiological and histological analyses

The extent of the vestibular ablations was verified both physiologically and by histological analysis. Canal nerve section was verified physiologically by the loss of responses to rotation in the horizontal plane as well as the loss of horizontal optokinetic after nystagmus (OKAN) (Cohen et al. 1983).

When M97050 and M98079 were rotated in head tilted 40° forward orientation with the thrusts of acceleration, there were no responses from either lateral canal (Fig. 5a, b compare blue and red traces, Table 1). This shows that the lateral canals had been inactivated by canal nerve section in both animals and that there was no recovery of high frequencies even up to almost a year.

The integrity of the vertical canals was verified by rotating the animals around the normals to the LARP and RALP planes. Eye movements evoked by these rotations are composed of both vertical and torsional components. When M98079 was rotated in a plane that excited the left anterior canal, the postsurgical gain was reduced from 0.45 to 0.34 (*F* test, $P < 0.05$; Fig. 5c). This indicates that the function of the left anterior canal was at least partially damaged in this animal. The response of the other three vertical canals in this animal and all vertical canals in M97050 were normal (not shown).

Changes in OKAN were reported earlier for the same animals (Yakushin et al. 2005). Horizontal (yaw) OKAN was lost in both directions immediately after nerve section in M98079. Animal M97050 had some yaw OKAN in both directions for the first 3 months after surgery (Fig. 2 in (Yakushin et al. 2005)). Later, it could no longer be evoked. There was also no neural response associated with lateral canal activation in the medial vestibular nucleus in these animals (Yakushin et al. 2005).

Histological analysis of the temporal bones of M98079 (Fig. 6) demonstrated that left and right anterior canal ampullae were collapsed (Fig. 6a, b, inset). Additionally, the right anterior canal was plugged (Fig. 6b, black triangular marks). Both posterior canal ampullae were normal (Fig. 6c, d, inset), although the right posterior canal was plugged close to the

common crus. The lateral canal nerves were sectioned on both sides (Fig. 6e, f, arrows) leaving the hair cells and both cupulae intact. There was partial degeneration of the hair cells on the left anterior canal crista, indicating partial damage to this canal nerve. Thus, histological analyses in animal M98079 showed that only the posterior canals were functioning normally. Histological analysis was not available for animal M97050.

Discussion

This study shows that no eye velocities were induced by steps and thrusts of rotation in the plane of the lateral canals long after bilateral lateral canal nerve section. The results were the same in two nerve canal-sectioned animals, confirming that there was no spatial adaptation for the loss of lateral canal input in these animals. Responses obtained in these animals were predicted by the model, which considered that each canal contributed to the total response according to its geometrical orientation relative to the axis of rotation and that input from the plane of the canals whose nerves were sectioned was just eliminated. The model predicted that peak responses occur when animals are tested with their heads tilted back by 50° in an orientation that optimally activates the intact vertical canals. The gains of the responses were predicted from canal gains obtained from the intact animals. The spatial responses to thrusts in the nerve-sectioned animals show that it is not necessary to have high-frequency capability to obviate spatial adaptation. Rather, the coordinate frame imposed on the central vestibular system by canal orientation is invariant. This study also shows that spatial responses to thrusts of accelerations were normal in canal-plugged animals. This finding is consistent with the idea that canal plugging does not eliminate canal function but rather reduces its dominant time constant from 4 s to 0.07 s (Yakushin et al. 1998; Rabbitt et al. 1999).

The responses obtained within the first week after canal plugging (acute state) were low in some animals, but they recovered to levels predicted by the model of the aVOR after several weeks (chronic state) (Yakushin et al. 2011). The early loss of response is probably due to detachment of the cupula from the roof of the ampulla, with reattachment at a later time, as found in the toadfish (Rabbitt et al. 1999, 2009). The changes in gain over time in the toadfish are similar to responses to sinusoidal oscillation in the rhesus monkeys (Yakushin et al. 2011). As our results demonstrate, there were no changes in spatial orientation of the canal responses after canal plugging, whether from single canals or from all six canals. Previous studies with unilateral posterior canal occlusion in humans had substantial reduction in the aVOR gain for head thrusts toward plugged canal, which persisted (Aw et al. 1995a, b; Cremer et al. 1998). One possible reason for differences in our and previous results is differences in canal plugging technique. Our studies and studies of the others indicate that the time constant of the plugged canal is dependent on the location of the plug. In our study, each canal was blocked over a distance ≈ 1 mm, while in patient, canal walls were occluded over ≈ 3 mm (Pohl 1996). The extended plug is closer to the cupula, blocking a longer portion of the canal duct. This in turn may have reduced the time constant of the plugged canal further than it is in our study. A plugged canal with a smaller time constant may become unresponsive even to short thrusts of head velocity that have broader frequency characteristics (Rabbitt et al. 1999).

After inactivation of the lateral canals by nerve section, the responses obtained during the recovery period were within the predicted range, and the average gains in yaw and roll were at the lower level of the limits predicted by the model. The reason for this could be that both anterior canals were not functioning in one of the lateral canal nerve-sectioned animals (M98079). This was probably related to damage to the adjacent anterior canal during the lateral canal nerve section. Although the function of one canal of an anterior–posterior canal pair was lost, the fellow canal in the same plane could partially compensate for head

movement in that plane. As was found during testing, the responses were somewhat smaller than from the intact canal pair. This would explain why the spatial responses were also somewhat smaller than predicted.

Although the histology was not available in M97050, it seems likely that the anterior canals were at least partially damaged in this animal, as well, because the spatial gains were also lower than predicted. Regardless, the data indicate that after sectioning of the lateral canal nerves, the nervous system does not accommodate to the loss, and their function is not compensated by the remaining intact semicircular canals, even over the long term. Rather, the spatial responses are consistent with hypothesis that each individual canal pair contributes according to its geometrical orientation to the axis of rotation (Yakushin et al. 1998).

Previous studies indicate that although the lateral canal-related input is dominant among neurons located in the medial vestibular nuclei (MVN) (Fuchs and Kimm 1975; Keller and Kamath 1975; Searles and Barnes 1977; Ishizuka et al. 1980; McCrea et al. 1980, 1987; Furuya and Markham 1981; Chubb et al. 1984; Reisine and Raphan 1992; Scudder and Fuchs 1992; Cheron et al. 1996; Newlands and Perachio 2003), many neurons receive convergent inputs from the vertical canals (Curthoys and Markham 1971; Markham and Curthoys 1972; Baker et al. 1984a, b; Fukushima et al. 1990; Brettler and Baker 2001; Dickman and Angelaki 2002; Sato et al. 2002; Yakushin et al. 2006; Eron et al. 2008). The behavioral data obtained in this study are consistent with the spatial responses of individual neurons recorded in the superior vestibular nuclei in these two animals after all behavioral tests were completed 13 months after surgery in M98079 and 19 months afterward in M97050 (Yakushin et al. 2005). As expected, none of the neurons were related to lateral canal activation. There were many vertical canal-related neurons that had peak sensitivities when the head was tilted back 50°. The spatial phases of the individual neurons in M98079 were very close to the 50° plane, while in M97050, the neurons deviated up to 15° from the 50° plane. These deviations are also consistent with the distribution of the spatial phases of vertical canal-related afferents (Reisine et al. 1988).

One of the animals in this study (M97050) had gradual recovery of the gain over the first month after surgery. This was consistent with our observations in cynomolgus and rhesus monkeys after canal plugging (Yakushin et al. 1995, 1998, 2011). This could be explained by the fact that drilling close to the semicircular canals can induce sudden changes in pressure in the endolymph, which could cause the cupula to detachment from the ampullary wall (Rabbitt et al. 1999, 2009). The second animal (M98079) had virtually no responses immediately after surgery, and its first spatial responses that were measurable did not occur until more than 7 months after surgery.

In conclusion, we have shown that regardless of the type of surgical ablation (plugging or nerve section) or the type of a functional deficit (high frequency or all frequency), each functional canal pair is an independent sensor of the head rotation, and final eye velocity, in response to the particular angular stimulus, is a summation of the responses evoked in all three functional canal pairs. The central representation of the spatial orientation of the remaining canals is unaffected, and the response plane that has been compromised remains uncompensated.

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Fig. 1.

Yaw (a) and roll (b) aVOR gains obtained from M97050 before surgery with the high-acceleration head thrusts (gray symbols) and step (black symbols) stimuli. Vertical lines are ± 1 SD about the mean values. Insets below are the head tilt relative to the spatial vertical axis of rotation

Fig. 2.

The yaw (a–c) and roll (d–f) spatial responses of the animals M97050 (a, b, d, e) and M98079 (c, f) tested with the steps (ramps) of velocity 10 days (a, d), 1 month (b, e), and 7 months (c, f) after surgery. Filled symbols are average values. Vertical lines are ± 1 SD about mean. Black curve is cosine fit to the data. Gray lines are a model prediction of the responses obtained after the surgery. Insets below are the head tilt relative to the spatial vertical axis of rotation

Fig. 3. Spatial yaw (a–b) and roll (c–d) gains obtained in animals M97050 (a, c) and M98079 (b, d) by rotation with head thrusts at different times after surgery (filled circles). Vertical lines are ± 1 SD about mean. Black curve is cosine fit to the data. Gray lines are a model prediction of the responses obtained after the surgery. Insets below are the head tilt relative to the spatial vertical axis of rotation

Fig. 4.

a, b, Yaw eye velocities (*red*) evoked by the thrusts of head rotation (*black*) about spatial vertical axis in upright position for clockwise (CW, **a**) and counterclockwise (CCW, **b**) directions in all six canal-plugged animal. **c, d**, Yaw eye velocities evoked in similar condition by rotation with the steps of head velocities (*black*) before (*dark blue*) and after all six canal plugging (*light blue*). Traces at **a–b** are synchronized to the peak head velocities, while at **c–d** to the onset of head rotation. **e–h**, Yaw (**e, f**) and roll (**g, h**) aVOR gains obtained in different head orientations in pitch (see insert on the bottom). *Red* symbols and curves in **e–h** are gain values and fits through the data, respectively, obtained with thrusts of head velocity. *Light blue* symbols and curve are similar data obtained with the steps of head

velocities. *Black* curve is model fit through the data obtained before canal plugging. *Vertical lines* are ± 1 SD about the mean. *Gray vertical lines* indicate time point at which aVOR gains were measured

Fig. 5.

The oculomotor responses in the planes of the canal before (*blue traces*) and after (*red traces*) surgery. **a, b**, Eye velocity evoked by rotation about spatial vertical axis with head tilted forward 40° in M97050 (**a**) and in M98079 (**b**). **c, d**, Responses obtained in the LARP (**c**) and RALP (**d**) planes in animal M 98079. *Dashed line* on each graph represents unity gain line for yaw (**a, b**) and roll (**c, d**) responses

Fig. 6. Histological analyses of the semicircular canals of animal M98079. **a–b**, Collapsed ampullae of the left (**a**) and right (**b**) anterior canals. Additionally, the duct of the right anterior canal was plugged, which is marked by the *black triangles* (**b**). **c, d**, Intact ampullae of the left (**c**) and right (**d**) posterior canals. Right posterior canal was plugged on the side away from ampulla, next to the common crus (**d**, area surrounded by the *black triangles*). **e, f**, Intact ampullae of the lateral canals. *Black arrows* are pointing to the spots in which the lateral canal nerves were sectioned

Table 1

Yaw aVOR gains tested with animal tilted 40° forward before and after lateral canal sectioning

Monkey	Tested canal	Surgery	After surgery	
			Thrusts $\approx 3000^\circ/s^2$	Steps $\approx 300^\circ/s^2$
M97050	RL Canal	0.71 ± 0.07	-0.010 ± 0.06	0.02 ± 0.05
	LL Canal	0.61 ± 0.09	0.016 ± 0.07	0.03 ± 0.04
M98079	RL Canal	0.44 ± 0.05	0.048 ± 0.05	0.001 ± 0.03
	LL Canal	0.48 ± 0.07	0.054 ± 0.08	0.06 ± 0.03

LL left lateral, *RL* right lateral