Spatial Properties of Central Vestibular Neurons

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Yakushin, Sergei B., Theodore Raphan, and Bernard Cohen. Spatial properties of central vestibular neurons. J Neurophysiol 95: 464–478, 2006. First published September 28, 2005; doi:10.1152/jn.00459.2005. We studied the spatial characteristics of 45 vestibular-only (VO) and 12 vestibular-plus-saccade (VPS) neurons in two cynomolgus monkeys using angular rotation and static tilt. The purpose was to determine the contribution of canal and otolith-related inputs to central vestibular neurons whose activity is associated with the central velocity storage integrator. Lateral canal-related neurons responded maximally during vertical axis rotation when the head was tilted 25 ± 6 and 22 ± 3° forward relative to the axis of rotation in the two animals, and vertical canal-related neurons responded maximally with the head tilted back 63 ± 5 and 57 ± 7°. The origin of the vertical canal–related input was verified by rotation about a spatial horizontal axis. Thirty-one percent of cells received input in a single canal plane. Sixty-seven percent of canal-related cells received otolith input, 31% of vertical canal neurons had lateral canal input, and 43% of lateral canal neurons had vertical canal input. Twenty percent of neurons had convergent input from the lateral canals, the vertical canals, and the otolith organs. Some VO and VPS cells had spatial-temporal convergent (STC) properties; more of these cells had STC properties at lower frequencies of rotation. Thus VO and VPS neurons associated with velocity storage receive a broad range of convergent inputs from each portion of the vestibular labyrinth. This convergence could provide the basis for gravity-dependent eye velocity orientation induced through velocity storage.

INTRODUCTION

Angular rotation in darkness at a constant velocity evokes nystagmus during which the slow phase eye velocity gradually declines to zero as rotation continues. Because of the contribution of the velocity storage integrator, the declining time constant (Tc) of the nystagmus is longer than the Tc of the neural activity from the semicircular canals that responded to this rotation (Raphan et al. 1979). A number of neuronal classes are activated in the vestibular nuclei by the angular rotation (Chubb et al. 1984; Fuchs and Kimm 1975; Miles 1974; Scudder and Fuchs 1992; Tomlinson and Robinson 1984). Of these, the declining time constants of the vestibular-only (VO) and vestibular-plus-saccade (VPS) neurons are closely correlated with the time constants of per- and postrotatory nystagmus and optokinetic after-nystagmus (OKAN) (Reisine and Raphan 1992; Waespe and Henn 1978, 1979). The time constants of other neurons in the vestibular nuclei vary from 3 to 80 s (Henn et al. 1980; Miles and Henn 1976; Waespe and Henn 1977a,b; Waespe et al. 1977). This may reflect the distributed nature of the cellular network that implements velocity storage in three dimensions (Raphan and Sturin 1991).

A striking property of velocity storage is its spatial orientation in three dimensions. If subjects are rotated in yaw about an axis that is tilted from the spatial vertical, the postrotatory nystagmus, rather than being purely in yaw, develops pitch or roll components depending on head orientation to gravity when stopped (Dai et al. 1992). Neurons that support such spatial orientation require information that reflects head position in space. An important step in understanding the neuronal basis for this spatial orientation would be to clarify the convergence from the otolith organs and semicircular canals onto the VO and VPS neurons over a wide range of tilt angles. This was the primary aim of this study.

VO and VPS neurons are located in the rostral medial and superior vestibular nuclei (MVN and SVN) (Chen-Huang and McCrea 1999; Chubb et al. 1984; Dickman and Angelaki 2002, 2004; Fuchs and Kimm 1975; Keller and Kamath 1975; Lisberger and Miles 1980; Miles 1974; Reisine and Raphan 1992; Scudder and Fuchs 1992; Tomlinson and Robinson 1984; Zhang et al. 1995), although VO neurons that receive convergent neck proprioceptive input are located caudally in the MVN (Gdowski and McCrea 1999, 2000). Both types of neurons receive semicircular canal input and are excited and inhibited by rotation over a wide range of frequencies. Some VO neurons receive monosynaptic input from primary afferents (Cullen and McCrea 1993; Dickman and Angelaki 2002; Gdowski and McCrea 1999; McCrea et al. 1999). Their activity is unrelated to eye position during sinusoidal pursuit or optokinetic stimulation at high frequencies, but both VO and VPS neurons respond to movement of the visual surround at frequencies below 0.1 Hz (Boyle et al. 1985; Waespe and Henn 1977a,b; Waespe et al. 1977). VPS neurons pause during saccades in one or several directions. If these pauses are disregarded, the VPS and VO neurons have a similar relationship to vestibular nystagmus, optokinetic nystagmus (OKN), and OKAN (Reisine and Raphan 1992). A signal feature of VO, but not VPS neurons, is that their activity is sustained when eye movements disappear during drowsiness (Reisine and Raphan 1992). This shows that their activity is more closely related to estimation of head velocity in space through the velocity storage integrator than to oculomotor commands.

The existence of canal–canal and canal–otolith convergence onto central vestibular neurons was first suggested by Duensing and Schaefer (1958). Curthoys and Markham (1971) showed that this convergence was a general phenomenon. A number of studies have determined characteristics of this convergence (Baker et al. 1984; Brettler and Baker 2001;
Fukushima et al. 1990; Graf et al. 1993; Perlmuter et al. 1998), but the quantitative contribution of individual canals has not been determined. Recently, using a combination of linear and angular accelerations, it was shown that there are classes of non-eye movement-related units distributed over the vestibular nuclei that have considerable canal-otolith convergent properties (Dickman and Angelaki 2002). Because a limited range of head orientations were tested with rotation about a spatial vertical axis (±45°), the maximal vertical canal sensitivity and the head orientation at which this occurred was extrapolated, but not actually measured. In the present study, we determined the canal and otolith contribution of each canal-related neuron over a wider range of tilt angles (±90°) to understand how static otolith information is integrated with canal input.

McCrea and colleagues have shown that neck convergent input to the lateral canal-related neurons also modulates unit activity in-phase with stimulus velocity (Gdowski and McCrea 1999, 2000; Gdowski et al. 2001). If the same were true for vertical canal-related VO units, it would complicate the quantitative analysis of the canal-related convergent inputs to central vestibular neurons because the head could move on the neck during tilt or translation, activating neck proprioceptors. Therefore to reduce the number of variables in this study, we also tested each neuron for its response to neck proprioceptor activation. Only units that did not receive convergent input from neck proprioceptors were included in the analysis.

METHODS

Two cynomolgus monkeys (Macaca fascicularis) were used in this study. 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.

Surgical procedures

The surgical procedures have been described in detail (Yakushin et al. 2000b). Briefly, a head mount developed by Sirota (Sirota et al. 1988; Yakushin et al. 2000b) was implanted under anesthesia. This mount held the animal’s head in stereotaxic coordinates painlessly during the experiment. An aluminum cap protected the head mount between experiments. Two coils were implanted on the left eye at a second surgery. A perlimbal coil measured horizontal (yaw) and vertical (pitch) eye position (Judge et al. 1980; Robinson 1963). The second coil, placed on top of the eye approximately orthogonal to the perlimbal coil, measured roll (torsional) eye position (Dai et al. 1994).

Unit recording

Details of the technique of unit recording are provided elsewhere (Yakushin et al. 2005). Briefly, a Delrin block was installed in stereotaxic coordinates inside the head mount, 1–2 mm above the skin (Yakushin et al. 2000b). The block had a grid of 0.64-mm-diameter holes at each mm. Sterile 80-μm, varnish-covered, tungsten microelectrodes were installed in a guide tube and inserted just above the vestibular nuclei. The microelectrodes were advanced with a lightweight, mechanical micromanipulator fixed to the head mount (Sirota et al. 1988). The abducens nucleus was identified first (Smith et al. 1972). VO and VPS neurons in medial vestibular nucleus (MVN) were located about 1 mm caudal and 0–2 mm lateral from the caudal end of the abducens (Reisine and Raphan 1992). The superior vestibular nucleus (SVN) was located about 2–4 mm lateral to the center of the abducens nucleus. We intended to record units in both the left and right MVN and SVN in M9357, and in the right MVN in M96012, although some neurons in M96012 may have been located in the right SVN. Histological analyses is not available because both animals are still alive.

Data collection and processing

Animals were tested in a multi-axis vestibular stimulator (Reisine and Raphan 1992). The stimulator had three gimbaled axes for rotation, a horizontal axis parallel to the spatial horizontal, a nested yaw axis, and a doubly nested, inner pitch/roll axis. The yaw and pitch/roll axes were enclosed in a light-tight optokinetic cylinder, 91 cm in diameter with 10° black and white stripes. The axis of the cylinder was collinear with the yaw axis. Each axis went through the center of rotation of the head. Eye movements were calibrated by rotating the animals in light at a constant velocity of 30°/s about the pitch, roll, and yaw axes. It was assumed that horizontal and vertical gains were unity and roll gain was ~0.6 in this condition (see Yakushin et al. 1995, for details). In this paper, we use the terms “horizontal” or “yaw” and “vertical” or “pitch” interchangeably.

Voltages related to eye position and to chair rotation about each axis were recorded with amplifiers with a band-pass of DC to 40 Hz. Voltages were digitized at 600 Hz/channel with 12-bit resolution and stored for later analysis. Eye position voltages were smoothed and digitally differentiated by finding the slope of the least squares linear fit, corresponding to a filter with a 3-dB cut-off >40 Hz, the cut-off frequency of the filters used for data acquisition. Unit activity was converted into pulses (BAK Electronics) of standard amplitude (5 V) and duration (0.5 ms). Pulses were delayed relative to action potentials by 0.5 ms. The time of the spike occurrence was stored relative to the nearest sampling time with the assumption that only one spike could occur within each sampling period (1.67 ms) or a frequency of 600 Hz.

Classification of VO and VPS

Units with discharges related to eye position were excluded from the analysis. We first detected relations between eye position or eye velocity and unit discharges on the oscilloscope or with an audio monitor, and these units were not recorded. The recorded units were also tested off-line. Each cell was recorded for 1–5 min while the animal looked at objects presented in various portions of the visual field. Average horizontal and vertical eye positions and the instantaneous frequencies were averaged over 25-ms periods. The average firing frequencies were color-coded on an X-Y plot of horizontal versus vertical eye positions with higher firing rates represented by darker colors. If there was a relationship to eye movements in a particular direction, e.g., up and to the right, the graph would show a color gradient with an increase in darkness as the eyes moved up and to the right. The same was done to identify the relationship of unit activity to eye velocity. The sensitivity of this technique was determined by simulation using artificially created unit activity. If a unit had consistent change in its firing rate of about 3 imp over a ±30° position range, the change could be detected by the alteration in color. Therefore the accuracy of this method of identification was about 0.05 imp · deg⁻¹.

VO and VPS neurons were identified by their response characteristics (Dickman and Angelaki 2002; Fuchs and Kimm 1975; Keller and Kamath 1975; Lisberger and Miles 1980; Reisine and Raphan 1992; Scudder and Fuchs 1992; Waespe and Henn 1977a,b). When tested at 0.2 Hz, VO neurons respond only to vestibular stimulation, and their activity was not related to eye position or to eye velocity. Activity of VPS units was similarly related to head velocity, but VPS units also paused in association with saccades in one or more directions. To identify VPS neurons, unit activity was synchronized with the beginning of 10–50 saccades of approximately identical amplitude (25 ± 3°) in the left, right, upward, or downward directions. In some
units pauses were only present for saccades to the left or right but not during vertical saccades. Other neurons had pauses associated with saccades in all directions.

During OKN at constant velocity in the direction that excited the unit shown in Fig. 1, the frequency of firing changed slowly, reaching a stable level. During OKAN, the firing frequency returned to its resting level with a time constant (Tc) similar to that of the OKAN (Reisine and Raphan 1992; Waespe and Henn 1977a,b). In this study, each unit was tested either during OKN/OKAN at 60°/s (Fig. 1A) and/or with sinusoidal oscillation of optokinetic drum. When the visual surround was oscillated at 0.2 Hz, no modulation of unit activity was induced (Fig. 1B). However, as the frequency of oscillation was decreased below 0.05 Hz, the activity of the unit was modulated in phase with the OKN stimulus velocity (Fig. 1C). Thus the activity of this unit was related to velocity storage (Boyle et al. 1985).

Each unit was also tested for convergent inputs from muscle proprioceptors by pressing on the muscles in the neck, arms, legs, and body and listening for changes in firing rate on an audio monitor or by noting changes in firing frequency on an oscilloscope. All units that had detectable convergent proprioceptive input were not considered to be VO or VPS units and were not studied further. This technique does not guarantee that all units with neck proprioceptive input were excluded from the analysis (Roy and Cullen 2001), but it eliminated a significant number of such neck-related neurons. Therefore VO and VPS neurons tested in this study may represent a specific subgroup of units tested by others (Dickman and Angelaki 2002; Gdowski and McCrea 2000).

Coordinate notation and classification of convergent inputs to neuron

The head coordinate frame was defined by three axes: x (naso-occipital, positive direction back-to-front), y (interaural, positive from the left ear), and z (body axis, positive up) (Fig. 2A). Positive directions for eye movements were defined by the right hand rule:

![Image](http://jn.physiology.org/)

**FIG. 1.** A: typical activity of a type I vestibular-only (VO) neuron located in the right medial vestibular nuclei (MVN) during optokinetic nystagmus (OKN)/optokinetic after-nystagmus (OKAN) evoked by rotation of the visual surround at 60°/s. The unit firing rate decreased during OKN to the right and increased during OKN to the left. During OKAN, the firing rate returned to the resting level with approximately the same time constant as the decaying slow phase eye velocity. The sudden drops in eye velocities are periods of drowsiness. The VO neurons were not susceptible to changes in alertness and there were no pause or change in firing frequency. OKAN stimulus ON represent rotation of the OKN drum in light. B and C: activity of another type I VO neuron tested with sinusoidal OKN of 60°/s peak velocity at 0.2 (B) and 0.01 Hz (C). The firing rate was unrelated to the OKN drum velocity at 0.2 Hz but was modulated at 0.01 Hz. Positive eye velocities correspond to eye velocity to the left.
tortion toward the right ear (clockwise from the animal’s point of view), vertical down and left horizontal.

To assign unit activity to a particular semicircular canal, we assumed that convergent inputs from the canals to central vestibular neurons were excitatory. It is possible that crossed activity could be inhibitory (Abend 1977; Goldberg et al. 1987; Kasahara and Uchino 1974; Shimazu and Precht 1966), but excitation, which we measured, would not be produced by such a crossed inhibitory input unless there was a second inhibitory linkage in the pathway to the canal-related neuron. It is also possible that if several inputs converged on a single neuron, some of them could be excitatory while other were inhibitory. For purposes of quantifying the extent of convergence, this would not negate our simplifying assumption that they behaved as excitatory inputs.

Thus if a unit increased its firing rate when the head was rotated to the left in the lateral canal plane, we assumed it was related to the left lateral canal. Lateral and/or vertical canal-related units were first identified by sinusoidally rotating the animal about a spatial vertical axis at 0.2 Hz, peak velocity 60°/s with the animal’s head and body aligned with the axis of rotation or statically tilted forward and backward at increments of 15° up to ±90° (Fig. 2). This range of tilt angles allowed us to assess the spatial orientation of the unit’s response. Unit sensitivity to rotation at each head orientation (temporal sensitivity) was defined as the amplitude of the sine fit through the response. Unit sensitivity to rotation at each head orientation (temporal phases of the modulation in unit activity were considered to be zero when peak unit activation occurred in phase with the peak of head velocity in the ipsilateral direction and −180° when the unit was modulated out-of-phase with the stimulus (Fig. 2D). The orientation of the canals to the axis of rotation is dependent on the angle of head tilt. Consequently, the direction of head rotation that excited canal-related units in some head orientations could be the reverse of the activity with the animal upright (Figs. 2C and 3, A–D). The temporal sensitivities (gains) at each head orientation were plotted as a function of head tilt and fitted with a sinusoid

\[ y = A \times \cos (x + B) \]  

The spatial sensitivity, A, was the amplitude of the sinusoidal fit and the spatial phase, B, was the head orientation at which the peak amplitude occurred. Thus a lateral canal unit would be maximally activated when the head was tilted forward −30° so that the average plane of the lateral canals lay in the plane of rotation (Figs. 3, A and B, gray lines) (Baker et al. 1984; Yakushin et al. 1995). Activation would be type I (Fig. 3A) if the input came from the contralateral lateral canal and type II (Fig. 3B) if it came from the contralateral lateral canal (Duensing and Schaefer 1958). If the unit received input only from one vertical canal the modulation in unit activity would be maximal when the animal oscillated with the head tilted 50° backward (−50°), so that the average vertical canal plane was in the plane of rotation (Fig. 2B) (Yakushin et al. 1995). The activation would be type I if there was excitatory input from the contralateral vertical canal (Fig. 3C, gray line) and type II if the input was from the ipsilateral vertical canal (Fig. 3D, gray line). Thus if a unit received input from vertical canal afferents, rotation about a spatial vertical axis could only indicate the vertical canal origin of the responses, but could not specify particular canal. If there were excitatory inputs from a vertical canal on one side and the lateral canal on the opposite side, the total

![Diagram of vestibular system](http://www.jn.org)
FIG. 3. Model predictions (gray lines; Yakushin et al. 1995, 1998) and experimental data (symbols) for spatial sensitivities (A–E) and temporal phases (F–J) of central vestibular units that received semicircular canal inputs from only a lateral canal (A, B, F, and G), a vertical canal (C, D, H, and I), or equal convergent inputs from the ipsilateral lateral and contralateral vertical canals (E and J). Black lines in A–E are sine fits to the data. Insets on the bottom are the approximate head orientation indicated on the abscissas. Open symbols represent data values where modulation was not significant (see Statistical analysis).
response would have a spatial sensitivity in the upright position. The spatial sensitivity would be positive if it were activated by ipsilateral lateral canal (type I) and contralateral vertical canal (type I; Fig. 3E, gray line). We use the terms sensitivity and gain of the unit responses interchangeably.

To identify specific vertical canal inputs, each unit was tested by sinusoidal oscillation about a spatial horizontal axis at 0.25 Hz over ±17° or 0.05 Hz over ±80° with the head in different orientations relative to the axis of rotation from 180 to 360° in 15° increments (Fig. 5B). As in the previous test, unit sensitivity, plotted as a function of head orientation, was fitted with a sinusoid (Eq. 1) to determine the spatial sensitivity (gain) and phase. Units related to the right anterior canal would be maximally activated at 45° (Fig. 6D, insets). Units related to the right posterior canal would have maximal activation at 135°, whereas cells related to the left posterior canal would be maximally activated at 225° and to the left anterior canal at 315°.

The maximum activation, i.e., the spatial gain of individual canal afferents can deviate as much as 10–12° from the average canal planes, and a single pair of reciprocal canals can deviate about 6° from being coplanar in the rhesus monkey (range, 3–18°) (Reisine et al. 1988). From this, we assumed that ±15° of deviation of the spatial phases of VO and VPS neurons from lateral and vertical canal planes could be caused by normal variation of the data. If the spatial phases lay more than ±15° from canal plane, we assumed that the unit had convergent inputs from another canal and/or from the otolith organs.

Static otolith sensitivity was determined by tilting the head 30 or 60° with the head oriented from 180 to 360° in 15° steps relative to the spatial horizontal axis and holding it in this position for ≥20 s (Fig. 5B). The last 10 s of the response were analyzed to eliminate possible dynamic inputs. Sensitivity to tilt, expressed as imp · s⁻¹ · g⁻¹, was plotted as a function of head orientation and fit with a sine function (Eq. 1). This determined the orientation of the response vector, which is the projection of the otolith polarization vector to the X-Y plane (Schor et al. 1984). Convergent dynamic otolith inputs to VO and VPS neurons would not be identified by this test, but a study of this is beyond the scope of this paper.

Statistical analysis of data

The significance of the sinusoidal fit through the data were tested with a F-statistic, which is a reduced case of the general ANOVA (Yakushin et al. 1995). For 10 cycles of oscillation with each head orientation (n = 13), the mean square error for the numerator was computed as an average instantaneous frequency of the neuron over 20 ms (1/100 of cycle) period compared with the average activity over the full 10 cycle period. The mean square error for the denominator was computed by comparing actual data to the sinusoidal fit through the data. The computed ratio was compared with the critical value of the F distribution. Units were considered unrelated to a particular stimulus if the modulation was not significant in more than one-half (n = 7) of the head orientations.

A standard two-tail t-test was used to compare two groups of data. An ANOVA was used to compare more than two groups of data. If the general ANOVA showed significant differences between data sets, each between-group degree of freedom was analyzed separately by developing orthogonal contrasts. In this case, the results of the test were adjusted with a Scheffe approach (Keppel 1991). The data in this paper are described by means and ±SD.

RESULTS

Data derived from rotation around spatial vertical and horizontal axes were obtained from 31 units in M9357 and 26 in M96012. Forty-five cells were VO and 12 were VPS neurons. Each unit was sensitive to low frequency optokinetic stimulation (Fig. 1) and had activity associated with the declining slow phase eye velocity during OKAN. Some of the recorded neurons did not respond to horizontal OKN/OKAN, but their activity was correlated with the vertical OKN/OKAN (data not shown). Therefore these cells were related to velocity storage in the vestibular system (Reisine and Raphan 1992). The relation of the unit responses to velocity storage has been presented in preliminary form (Yakushin et al. 1996). There was no observable difference in the spatial characteristics of the VO and the VPS neurons, and their data were combined in the analysis. The average resting discharge of the recorded units in M9357 was 41.3 ± 20.3 imp · s⁻¹, ranging from 0 to 77.1 imp · s⁻¹. The average activity in M96012 was 70.6 ± 17.1 imp · s⁻¹, ranging from 43.2 to 104.3 imp · s⁻¹. These levels of activity are close to those reported in other studies (Chen-Huang et al. 1997; Chubb et al. 1984; Waespe and Henn 1977a, 1978, 1979; Zhang et al. 1993).

Relationship of unit activity to the lateral and/or vertical canals

A typical VPS unit, tested by rotation about a spatial vertical axis with the head at different pitch angles relative to the axis of rotation, recorded in the right MVN, is shown in Fig. 2B. With the animal upright, the unit increased its firing rate when rotated to the contralateral (left) side (Fig. 2B; 0°), i.e., it had type II activation (Duensing and Schaefer 1958). When the head was tilted −90° (animal on back), the firing rate increased with contralateral rotation. The modulation in unit activity increased as the head was reoriented −60° and −30° relative to the axis of rotation. There was no modulation when the head was tilted forward 30°. When the animal was tilted farther forward, to +60 and +90°, the modulation reappeared, but the phase was opposite to that observed before, and the activity increased as the animal was rotated to the ipsilateral side. The temporal sensitivity of this unit as a function of head position with regard to gravity was fitted with a sinusoid (Eq. 1) to obtain the spatial sensitivity and phase of the response (Fig. 2C). The spatial phase was −62°, which is close to the orientation of the average plane of the vertical canal (−50°).

The logic that was used to determine whether units received input from a single lateral or vertical canal or had convergent inputs is shown in Fig. 3. The spatial phases of two units were 17 and 23° (Fig. 3, A, B, F, and G), indicating lateral canal input (compare symbols and gray curves). One was a type I cell (Fig. 3A). If its convergent input was excitatory, this unit was related to the ipsilateral lateral canal. The other was a type II cell (Fig. 3B), related to excitatory input from the contralateral lateral canal. The spatial phases of two other units were −58 and −63°, which indicated activation by a vertical canal (Fig. 3, C, D, H, and I; compare symbols and gray curves). One had type 1 behavior (Fig. 3C), indicating input from a contralateral vertical canal. The second had type II activation (Fig. 3D) and therefore had input from an ipsilateral vertical canal. The type I unit shown in Fig. 3, E and J, had a spatial phase of 10°, which was significantly different from the predicted lateral and vertical canal planes. This indicated that it received convergent inputs of comparable amplitude from the ipsilateral lateral canal and a contralateral vertical canal (Fig. 3E, compare symbols and gray curves).

As determined by this test, 22 neurons in the two animals were lateral canal units (Fig. 4, triangles). Fifteen (68%)
received input from the ipsilateral (open triangles), and 7 (32%) from the contralateral lateral canal (filled triangles). Twenty of 24 (83%) vertical canal-related neurons received input from an ipsilateral vertical canal (Fig. 4, open circles and diamonds) and 4 (17%) from a contralateral vertical canal (filled circles and diamonds). Another two units had activity associated with both lateral and vertical canal activation (Fig. 4, open squares). The combined sensitivities of lateral canal units were $0.61 \pm 0.07 \text{ imp} \cdot \text{s}^{-1} \cdot \text{deg} \cdot \text{s}^{-1}$ in M96012 and $0.37 \pm 0.13 \text{ imp} \cdot \text{s}^{-1} \cdot \text{deg} \cdot \text{s}^{-1}$ in M9357. This difference was probably caused by natural variation and sampling. The sensitivity of the vertical canal-related units was similar for the two animals ($0.46 \pm 0.15 \text{ imp} \cdot \text{s}^{-1} \cdot \text{deg} \cdot \text{s}^{-1}$, M9357; $0.66 \pm 0.32 \text{ imp} \cdot \text{s}^{-1} \cdot \text{deg} \cdot \text{s}^{-1}$, M96012; $P = 0.105$), and there was no difference in spatial sensitivity of the lateral and vertical canal-related units ($P = 0.152$).

The average plane for best activation of the lateral canal-related units (average spatial phase) was $25 \pm 6$° in the first monkey and $22 \pm 3$° in the second animal. The average planes of the vertical canal-related units were $-63 \pm 5$° and $-57 \pm 7$°. Thus the central spatial orientation of the VO and VPS vertical canal units were $\approx 90$° from the plane of the lateral canal-related neurons.

**Activation of the central canal-related units by static tilts**

Sixty-seven percent of canal-related units received static otolith-related convergent input (Table 1). The discharge rate of the lateral canal-related VPS neuron shown in Fig. 5A was maximally reduced when the head was tilted with the ipsilateral (right) ear down (90°), and the decrease was smaller when prone (0°). The discharge rates were unchanged when supine (180°) and left ear down (270°). When the unit response was plotted as function of head orientation (Fig. 5B), otolith input response vectors could be derived from the phase of the sinusoidal fit. In one unit, the response vector lay along 48° (Fig. 5C, inset), close to the plane of the ipsilateral (right) anterior canal. In another cell, the response vector was along 317° (Fig. 5D, inset), close to the plane of the contralateral (right) anterior canal. The average amplitude of the response vectors for 21 units, was $\approx 10$ imp $\cdot$ s$^{-1}$/g. Spatial responses of units were converted with regard to the coordinate notation used in this study as if all neurons were located in the left vestibular nuclei. There was substantial scatter in the response vectors, and, in general, there was no alignment with either canal or head coordinates (Fig. 5, E and F).

**Activation by the vertical canals**

Inputs from the vertical canal were also verified by sinusoidal oscillation about the spatial horizontal with the head in different orientations relative to the axis of rotation. This gave the added capability of identifying the specific vertical canal, which provided input to the neurons. Because the lateral canals were tipped up $\approx 30$° in the null position used in this study (Yakushin et al. 1995, 1998), these canals were also activated when animals were oscillated about a naso-occipital axis. Consequently, units with and without convergent input from the lateral canals were analyzed separately. Units unrelated to the lateral canals were modulated during oscillation when the head was oriented 180° relative to the axis of rotation, and the modulation essentially disappeared at a head orientation of 225° (Fig. 6A). As the head was reoriented further toward the 360° head position, the modulation reappeared, but the temporal phases were reversed. The spatial sensitivity of this unit was $0.94 \text{ imp} \cdot \text{s}^{-1} \cdot \text{deg} \cdot \text{s}^{-1}$, with a spatial phase of 148° (Fig. 6, B and C), indicating that the ipsilateral (right) posterior canal had likely activated this unit.

Twenty-six vertical canal-related units were classified in terms of their relation to the anterior or posterior vertical canal. In this analysis, we assumed that all of the cells were located on the left side of the brain. Most vertical canal-related neurons (92%) received ipsilateral input (24 of 26 cells), and a contralateral vertical canal activated only 13% of the population. The spatial sensitivities of the ipsilateral anterior and posterior canal-related unit populations were comparable ($P = 0.06; 0.50 \pm 0.32$ and $0.73 \pm 0.54 \text{ imp} \cdot \text{s}^{-1} / \text{deg} \cdot \text{s}^{-1}$, respectively). Seventy-three percent (19/26) received input from individual vertical canals (Fig. 6, D and E, filled symbols), and 27% (7/26) of units had spatial

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**Table 1. Units with single or multiple convergent inputs**

<table>
<thead>
<tr>
<th>Type of convergence</th>
<th>Number of Identified Units</th>
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<tbody>
<tr>
<td>Lateral canal only</td>
<td>M9357 3  M96012 3  Both Animals 11%</td>
</tr>
<tr>
<td>Vertical canal only</td>
<td>M9357 6  M96012 5  Both Animals 20%</td>
</tr>
<tr>
<td>Lateral canal + vertical canal</td>
<td>M9357 1  M96012 0  Both Animals 2%</td>
</tr>
<tr>
<td>Lateral canal + otolith</td>
<td>M9357 6  M96012 4  Both Animals 18%</td>
</tr>
<tr>
<td>Vertical canal + otolith</td>
<td>M9357 6  M96012 10  Both Animals 29%</td>
</tr>
<tr>
<td>Lateral canal + vertical canal + otolith</td>
<td>M9357 8  M96012 3  Both Animals 20%</td>
</tr>
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**Fig. 4.** Polar plots of the spatial sensitivities and phases of units tested by rotation about a spatial vertical axis with the head in different orientations relative to the axis of rotation in M9357 and M96012. Average planes of the lateral and vertical canal-related units ($\pm$SD) are shown next to the plots. Insets show approximate head orientations at these angles. Bold lines on the heads in the insets indicate the semicircular canals that are predominantly activated at this head orientation.
phases deviated >15° from any canal plane (Fig. 6, D and E, open symbols). This indicated that these cells received more than one convergent vestibular input.

**Prediction of temporal and spatial responses**

Rotation about a horizontal axis not only activates the semicircular canal afferents but also generates input from the otolith organs. We used three different analyses to evaluate whether the unit responses to spatial vertical and horizontal axes were internally consistent. By comparing results obtained from rotation about spatial horizontal axis with those obtained from rotation about a spatial vertical axis, which does not dynamically activate the otolith organs, it was possible to determine whether otolith input had altered the temporal and spatial phases and sensitivity of the 23 vertical canal-related neurons that did not have lateral canal input. The temporal phases of the sinusoids fitted to the unit discharge rate relative to the stimulus velocity, measured in the two tests were correlated, and the slope of the regression line for 23 tested cells was close to unity (Fig. 7A; P < 0.01). Some data points substantially deviated from the line, suggesting that otolith input may have affected the temporal responses of these units. However, the unity slope indicates that, on average, convergent input from the otoliths had no effect on the phase of the recorded neurons (6.6 ± 13.5° for the horizontal axis rotation vs. 3.2 ± 19.1° for the vertical axis rotation, P = 0.161).

This question was explored further by determining if spatial sensitivities obtained by oscillating the head about a spatial horizontal axis (H) could predict the spatial sensitivities from oscillation about spatial vertical axis (V). When an animal is oscillated about spatial vertical axis with the head tilted back 60°, the vertical canals are rotated 45° about the spatial horizontal from their plane of maximal activation. Therefore...
The measured and predicted spatial sensitivities for $V$ were correlated for 16 of the 23 vertical canal units that had complete testing of spatial sensitivities in the two tests. The regression line was close to unity ($P < 0.01$; Fig. 7B). These data show that, on average, otolith input at this frequency of oscillation had no significant effect on the spatial sensitivities of the neurons in this series determined by rotation about a horizontal axis, which is consistent with the previous conclusion of Baker et al. (1984).

Substantial deviation of individual data from the average slope in Fig. 7B, however, could have been caused by convergent input from the otolith organs. To test this hypothesis, we calculated the difference between the predicted and actual value of the spatial gain obtained from rotation about a spatial vertical axis and expressed it as a percent error, where positive values represented overestimation in the predicted values and 0% represented ideal prediction. The percent errors varied from −8 to 73%. If we assumed that prediction was accurate if the error was <10%, the spatial sensitivities of 8 of the 16 vertical canal neurons (50%) were accurately predicted.

To test the hypothesis that inaccurate prediction in the remaining eight units was caused by the additional convergent inputs, we calculated the angles between the plane of the vertical canal that provided the convergent input and the head orientation in which the individual neuron were maximally activated by rotation about spatial horizontal axis (spatial phase). The percent error was correlated with this angular deviation (Fig. 7C). The inaccuracy of gain prediction was larger for larger deviations of the spatial phase of the unit from the corresponding vertical canal plane. Five of these units (Fig. 7C, filled symbols) received static otolith input (Dickman and Angelaki 2002), and the directions of the otolith response vectors were consistent with the angular deviations from the corresponding vertical canals. Three other units (○) were not modulated by static head tilt, and it is possible that they received dynamic otolith input (Dickman and Angelaki 2002), which was not tested in this study.

In conclusion, the correlation between the temporal phases of the data obtained for the vertical canal-related neurons from vertical and horizontal axis rotation was high.
was detected. Thus oscillation about a spatial horizontal axis of the 16 vertical canal units for which static otolith input was accurate in identifying convergent inputs from the vertical canals for the large majority of neurons.

**STC**

There were eight units that had approximately constant temporal gains when the animals were oscillated about a spatial horizontal axis at 0.2 Hz (±17°; peak velocity = 23°/s) in different head orientations (Fig. 8A). Their temporal phases changed monotonically with head orientation, being in-phase with head velocity for one particular orientation (Fig. 8B, phase 0°) and with head position (Fig. 8B, phase 90°) in another head orientation. These are typical STC units (Angelaki 1992a, 1993a,b; Baker et al. 1984; Schor et al. 1984; Siebold et al. 1999, 2001; Yakushin et al. 1999). The majority of these units (6/8) also had lateral canal input, which dominated the vertical canal input when animals were rotated about a spatial vertical axis (Fig. 4, open triangles).

The phases related to head orientation during horizontal axis rotation could be fit by a straight line from which the head orientation that corresponded to 0 (180°) and 90° (270°) phase shifts were determined (Table 2). The head orientations at which the units fired in phase with head position (90°) were plotted against the head orientations at which it fired in phase with head velocity (0°; Fig. 8C). The data were fit by a straight line (P < 0.01) with a slope of 1.05. This indicated that there was a 90° spatial difference between the head orientations where the units fired in phase with head velocity (0°) and in phase with head position (90°) for all of the units (Fig. 8C). Five of the eight STC units had their velocity vectors aligned within ±15° of the naso-occipital or interaural axes (Table 2).

STC characteristics were rare in the VO and VPS neurons when tested at 0.2 Hz, but were frequently encountered when the animals were tested at lower frequencies (Fig. 9). The temporal sensitivities of these units varied with head orientation (Fig. 9C), and their temporal phases were in- or out-of-phase with stimulus velocity at 0.25 Hz (Fig. 9D). An example is shown in Fig. 9, A and B. At 0.05 Hz, the unit had STC characteristics. The sensitivity was approximately the same in all head orientations (0.28 ± 0.07 imp · s⁻¹/deg · s⁻¹, Fig. 9A), but the temporal phases varied from being in-phase with stimulus velocity to in-phase with stimulus position depending on the head orientation to tilt (Fig. 9B).

Seven other VO and VPS units were identified that had convergent lateral and vertical canal inputs but did not have the phase relationship as a function of head orientation associated with STC characteristics. These neurons had their maximal sensitivity when oscillated about a spatial vertical axis with the head pitched forward in the lateral canal plane (0.53 ± 0.08 imp · s⁻¹/deg · s⁻¹). The vertical canal sensitivities were smaller (0.27 ± 0.10 imp · s⁻¹/deg · s⁻¹), but these sensitivities lay within 2° of a vertical canal plane in six of seven of the units. Of interest, the polarities of the lateral and vertical canals during oscillation about a naso-occipital axis were in opposite directions and would subtract from each other during rotation about a naso-occipital axis. Thus the opposing activations could have contributed to the reduced sensitivity of the vertical canal input in these units and also could have helped tune the maximal activation planes when the head was rotated about these different axes.

**FIG. 7.** A: temporal phases of the units measured at head orientations at which maximal sensitivities occurred for rotation about spatial horizontal and vertical axes. B: experimental and computed spatial sensitivities, for vertical canal-related units tested with head oscillation about a spatial vertical axis. Spatial sensitivities are the maximal modulation in unit activity over all tested head orientations. Different symbols represent units in which activity was modulated (•) or not modulated (○) by static tilt.
In summary, the canal and otolith convergent inputs identified in the three tests described above are shown in Table 1. Convergent input from the lateral semicircular canals was present in 31% of vertical canal cells, and 43% of lateral canal cells had vertical canal input. Among the canal-related units, 31% had input from a single semicircular canal (11% lateral and 20% vertical canal-related). Most canal-related neurons also received otolith input (67%), of which 18% were lateral canal-related, 29% were vertical canal-related, and 20% received both lateral and vertical canal-related inputs. Thus convergent inputs from several semicircular canals and/or the otoliths were common in the VO and VPS neurons.

**Modeling of STC behavior**

To test our hypothesis about STC behavior, a simple model was devised that had orthogonal otolith and canal convergence that activated an STC cell (Fig. 10). We chose the angle for the activation of the canal component of the artificial STC cell approximately in accord with the angle found for the unit shown in Fig. 9, and thus the unit vector for canal activation, $\hat{\alpha}_c$, was chosen to be maximal with the head oriented at $-45^\circ$ (Fig. 10A).

The otolith component, $\hat{\alpha}_o$, was orthogonal to the canal vector, being maximally activated for oscillation with the head oriented about $45^\circ$ (Fig. 10A), consistent with the data of Fig. 9.

When the head is oscillated about spatial horizontal axis in a particular orientation, the axes of maximal canal and otolith activation deviate from the $x$-axis, $\hat{a}_x$, and $y$-axis, $\hat{a}_y$, respectively, by an angle $\theta$. The activation of the otolith vector, $\hat{\alpha}_o$, can be given as a complex phasor, $r_o \hat{\alpha}_o$, where $r_o$ is a real number given by

$$ r_o = A \cos \theta $$

(2)

The activation of the canal vector is a simplified single time constant transfer function

$$ H_c = \frac{j2\pi f T_v}{1 + j2\pi f T_v} B $$

where $f$ is the frequency of the oscillations and $A$ and $B$ are the weights of the otolith and canal contributions to the STC cell firing, respectively. Because the STC VO neurons that we recorded all had the long time constant associated with velocity storage, these two time constants were lumped into a single dominant time constant, $T_v$, for simplicity. A more complete model would consider a two time constant transfer function that included the contribution of the canals and velocity storage integrator (Raphan et al. 1979).

The canal contribution to the STC cell is $r_c \hat{\alpha}_c$, where $r_c$ is the complex phasor given by

$$ r_c = H_c \cos \theta $$

(5)

The summation of these two orthogonal signals can be expressed as

$$ r_{STC} = r_c + r_o $$

(4)

A program that implemented Eqs. 2–4 was written in Matlab to simulate STC behavior (Fig. 9, symbols). The weighting of the

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**TABLE 2. Units with STC characteristics**

<table>
<thead>
<tr>
<th>Head Orientation</th>
<th>LC Input</th>
<th>Monkey No.</th>
<th>Unit No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 0°</td>
<td>Phase 90°</td>
<td>Ipsi</td>
<td>M96012</td>
</tr>
<tr>
<td>258</td>
<td>150</td>
<td>Contra</td>
<td>M96012</td>
</tr>
<tr>
<td>287</td>
<td>177</td>
<td>Contra</td>
<td>M9357</td>
</tr>
<tr>
<td>351</td>
<td>259</td>
<td>Contra</td>
<td>M9357</td>
</tr>
<tr>
<td>360</td>
<td>277</td>
<td>No</td>
<td>M9357</td>
</tr>
<tr>
<td>228</td>
<td>138</td>
<td>?</td>
<td>M9357</td>
</tr>
<tr>
<td>93</td>
<td>5</td>
<td>Contra</td>
<td>M9357</td>
</tr>
<tr>
<td>205</td>
<td>60</td>
<td>Contra</td>
<td>M9357</td>
</tr>
<tr>
<td>298</td>
<td>207</td>
<td>Ipsi</td>
<td>M9357</td>
</tr>
</tbody>
</table>

STC, spatial-temporal convergent; LC, lateral canal.
canals (Fig. 9B) was chosen as 0.21, while the otolith weighting (Fig. 9A) was 0.07, which approximately equalized the canal and otolith contributions at a frequency of 0.05 Hz, the lowest frequency used in this study. The time constant of the unit, $T_V$, was chosen as 30 s for this unit, consistent with the average time constant observed for the STC units during OKAN. The simulations show that, for an oscillation frequency of 0.05 Hz, there was a small modulation of amplitude of 0.01 at a level of 0.2 (Fig. 9A, gray line). The phase varied linearly as a function of head orientation from $-40$ to $-220^\circ$ (Fig. 9B, gray line). When the frequency was 0.25 Hz and all other parameters were kept the same, the model predicted that the gain would vary as a function of head orientation from $-0.21$ to 0.21 (Fig. 9G). This was because of the increased contribution of the canal response, which tunes the unit along the canal vector. The model also predicts that the phase would no longer have a linear change as a function of head orientation, but rather would change abruptly from about $-180$ to $0^\circ$ as a function of head orientation (Fig. 9D, gray line). These changes in gain and phase of the hypothetical unit as a function of stimulus frequency is similar to the behavior of the unit shown in Fig. 9 (symbols). Thus the model shows that STC behavior in VO neurons could be caused by approximately orthogonal convergent inputs from the canal and otolith afferents.

**DISCUSSION**

The major findings of this study were: 1) there is extensive convergence from the semicircular canals and otolith organs onto VO and VPS neurons in the vestibular nuclei, which are closely linked to velocity storage; 2) some lateral and vertical canal-related neurons were activated by the corresponding lateral or vertical contralateral canals, and therefore were true type II neurons, suggesting that the velocity storage integrator is implemented as a bilateral system; and 3) STC-related VO and VPS units can be modeled as receiving approximately orthogonal convergent inputs from the otolith organs and semicircular canals to implement the frequency-dependent STC characteristics.

The presence of extensive convergence in the VO and VPS neurons recorded in this series is in general agreement with the findings of Dickman and Angelaki (2002) in non–eye move-
ment-related neurons and with Curthoys and Markham (1971) in a general population of central vestibular neurons. The lateral and vertical canal convergence would substantially increase the range of rotation axes over which the VO and VPS neurons respond. The strength of the input was essentially equivalent in only 2 of 17 neurons with lateral and vertical canal inputs (Fig. 4A, □). The remaining 15 neurons had predominant input from the lateral canals. It has been shown that there are central otolith neurons whose dynamic properties could mimic vertical canal inputs when tested with rotation about a spatial horizontal axis (Angelaki and Dickman 2000), and this concept has been implemented in a recent model (Green and Angelaki 2004). Results obtained in our study with rotation about a spatial vertical axis, which would not activate otolith inputs, were internally consistent with results obtained from horizontal axis rotation and support our model of canal-otolith interaction. Regardless, the presence of the neurons that respond to rotation about any axis in both studies implies that most VO and VPS neurons receive information about head rotation and orientation in many dimensions.

It is now well accepted that velocity storage contributes to the slow phase velocity of both optokinetic and vestibular nystagmus and that velocity storage is responsible for the reorientation of eye velocity when the head is tilted relative to gravity. In this paper, we show that VO and VPS neurons, which are related to velocity storage and have STC characteristics because of canal and otolith convergence, are likely to contribute to the spatial orientation properties of velocity storage, and hence to the nystagmus that results from activation of velocity storage (Angelaki and Hess 1994; Dai et al. 1991; Gizzi et al. 1992; Moore et al. 2004; Raphan and Cohen 2002; Raphan and Sturm 1991; Raphan et al. 1992; Wearne et al. 1999). That is, at high frequencies, the STC neurons reflect the canal input, but at low frequencies, they are strongly tuned to the otolith input, which represents head position in space. The spatial orientation has been modeled as a change in the system matrix of velocity storage and is produced by changes in the time constants and cross-coupling between the horizontal, vertical and roll angular vestibulo-ocular reflexes (aVORs), mediated through the nodulus and uvula (Cohen et al. 1992; Waespe et al. 1985; Wearne et al. 1997, 1998). These changes in time constant of the aVOR could be produced by altering the time constants of the lateral- and vertical canal-related VO and VPS neurons according to head position with regard to gravity, thereby reorienting slow phase eye velocity to gravity when the head is tilted during postrotatory nystagmus, OKN, or OKAN.

The extensive convergence onto VO and VPS neurons could also play a role in implementing the gain adaptation in the aVOR, which is dependent on head position with regard to gravity (Tiliket et al. 1993; Yakushin et al. 2000a, b, 2003a, b). The convergence from static input from the otolith organs, which establishes head orientation relative to gravity, could set the context for the gain adaptation of the aVOR for any head position. Although the VO and VPS cells do not project directly to the oculomotor nuclei, they do send projections to the flocculus (Zhang et al. 1993), which is critically involved in gain adaptation (Luebke and Robinson 1994; Partsalis et al. 1995; Zee et al. 1981), and the otolith convergent input to the VO and VPS neurons could affect alterations in gain of the aVOR through this pathway.

Some VO and VPS units recorded in this study had STC characteristics at 0.2 Hz, whereas others had no STC behavior when tested at this frequency but had STC characteristics for rotation at 0.05 Hz (Fig. 9). Thus the STC properties of the central vestibular units may be much more common than previously described, and cells that receive canal and static otolith convergent inputs may be tuned to specific frequency bands. This finding sheds light on the unexplained differences in the number of central vestibular units with STC characteristics that have been reported (Baker et al. 1984; Kasper et al. 1988; Siebold et al. 1999, 2001; Wilson et al. 1996; Yakushin et al. 1999). We hypothesize that the STC behavior of the VO and VPS units that received canal and otolith input in orthogonal planes does not become apparent until the otolith input becomes manifest mainly at low frequencies when the strength of the vertical canal input is reduced by decreasing the frequency of rotation. This hypothesis is supported by the fact that sensitivity to static tilt of the canal related units recorded in this study was lower than 10 imp s−1/g, which is smaller than the otolith sensitivity of the central otolith-related neurons located in the lateral and descending vestibular nuclei (Schor et al. 1985; Yakushin et al. 1999). The hypothesis is further supported by the findings that the majority of the VO neurons in the rostral fastigial nucleus had STC characteristics at low frequencies of rotation (Siebold et al. 2001).

It has been proposed that the STC characteristic is caused by the convergence of canal and otolith inputs or to the convergence of two otolith inputs (Angelaki 1992a, b; Baker et al. 1984; Bush et al. 1992; Wilden et al. 2002; Yakushin et al. 1999). Our results are in agreement with this. In addition, the model shows that projection of the canal and otolith sensitivity vectors to the head coronal plane are orthogonal to each other. These transformations, which are coded in VO and VPS units, could contribute to the implementation the spatial orientation properties of velocity storage (Raphan and Sturm 1991).

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