Properties of Cerebellar Fastigial Neurons During Translation, Rotation, and Eye Movements

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Shaikh, Aasef G., Fatema F. Ghasia, J. David Dickman, and Dora E. Angelaki. Properties of cerebellar fastigial neurons during translation, rotation, and eye movements. J Neurophysiol 93: 853–863, 2005. First published September 15, 2004; doi:10.1152/jn.00879.2004. The most medial of the deep cerebellar nuclei, the fastigial nucleus (FN), receives sensory vestibular information and direct inhibition from the cerebellar vermis. We investigated the signal processing in the primate FN by recording single-unit activities during translational motion, rotational motion, and eye movements. Firing rate modulation during horizontal plane translation in the absence of eye movements was observed in all non-eye-motion-sensitive cells and 26% of the pursuit eye-motion-sensitive neurons in the caudal FN. Many non-eye-motion-sensitive cells recorded in the rostral FN of three fascicularis monkeys exhibited convergence of signals from both the otolith organs and the semicircular canals. At low frequencies of translation, the majority of these rostral FN cells changed their firing rates in phase with head velocity rather than linear acceleration. As frequency increased, FN vestibular neurons exhibited a wide range of response dynamics with most cells being characterized by increasing phase leads as a function of frequency. Unlike cells in the vestibular nuclei, none of the rostral FN cells responded to rotational motion alone, without simultaneously exhibiting sensitivity to translational motion. Modulation during earth-horizontal axis rotation was observed in more than half (77%) of the neurons, although with smaller gains than during translation. In contrast, only 47% of the cells changed their firing rates during earth-vertical axis rotations in the absence of a dynamic linear acceleration stimulus. These response properties suggest that the rostral FN represents a main processing center of otolith-driven information for inertial motion detection and spatial orientation.

INTRODUCTION

Orientation and motion in space are sensed by vestibular end organs (semicircular canals and otoliths) as well as visual and proprioceptive signals. The vestibular afferents innervating each semicircular canal are spatially tuned to provide a three-axis head-reference frame representing rotational movements (Dickman 1996; Estes et al. 1975; Goldberg and Fernandez 1971a,b; Haque et al. 2004; Rabbitt 1999; Reisine et al. 1988). Otolith afferents are uniquely tuned to linear accelerations along different directions throughout three-dimensional space (Fernandez and Goldberg 1976a,b,c). Primary vestibular afferents project to both the vestibular nuclei (VN) in the brain stem and the vestibulo-cerebellum, including the anterior and posterior cerebellar vermis and the fastigial nuclei (Carleton and Carpenter 1984; Newlands et al. 2003).

Specifically, the fastigial nucleus (FN), the most medial of the deep cerebellar nuclei, receives both sensory vestibular signals (Kotchabhakdi and Walberg 1978; Noda et al. 1990) and cerebellar cortex projections related to motion processing (Wylie et al. 1994). Anatomical and physiological studies have separated the fastigial nucleus into rostral and caudal subdivisions, the two being characterized by different afferent and efferent connectivities, as well as neural sensitivities to eye movement and motion stimuli (Buttner et al. 1991; Garder and Delgado-Garcia 1994; Noda et al. 1990). Neurons of the caudal FN, known as the fastigial oculomotor region, are under strong inhibitory control from the oculomotor vermis (lobules VI–VII) (Armstrong and Schild 1978; Noda et al. 1990) and are modulated during saccadic (Fuchs et al. 1993; Helmchen et al. 1994) or smooth-pursuit eye movements (Buttner et al. 1991; Garder and Fuchs 1975; Garder and Delgado-Garcia 1994). Pursuit eye-movement neurons in the caudal FN also modulate during suppression of the rotational vestibuloocular reflex (RVOR). The few studies that have characterized pursuit-related FN neurons only used rotational stimuli (Buttner et al. 1991; Garder and Fuchs 1975; Garder and Delgado-Garcia 1994). Very little is known at present regarding how caudal FN neurons respond during the translational VOR (TVOR).

In contrast to the caudal FN where eye-movement-sensitive neurons are encountered, the rostral division of the fastigial nuclei is populated by neurons that are modulated by vestibular stimulation but do not show sensitivity to eye movements (Buttner et al. 1991; Garder and Fuchs 1975; Garder and Delgado-Garcia 1994; Siebold et al. 1997). These neurons are called “vestibular-only” (VO) cells and are believed to be involved in vestibulospinal control, including regulation of gait and postural mechanisms (Buttner et al. 1991; Garder and Fuchs 1975; Siebold et al. 1997; Thach et al. 1992). Neurons in the rostral FN receive sensory vestibular signals and strong inhibitory inputs from Purkinje cells in the anterior and posterior cerebellar vermis (lobules I–V and X) (Armstrong and Schild 1978; Wylie et al. 1994). Mossy fiber projections arise from the VN bilaterally as well as other premotor areas, including the perihypoglossal and pontine nuclei (Gonzalo-Ruiz and Leichnetz 1990; Noda et al. 1990). Occasional collaterals to FN from primary vestibular afferents have also been reported (Newlands et al. 2003; Sato et al. 1989). Previous studies have established that rostral FN neurons respond to sinusoidal vestibular stimulation in horizontal and vertical planes (Garder and Fuchs 1975; Siebold et al. 1997, 1999). Pure translational stimuli have only been used to characterize
rostral FN responses by Zhou et al. (2001). Yet characterization of neural responses during translation is important as vertical plane rotations can activate both otolith and semicircular canal afferent sensors and result in activities that are difficult to interpret.

Using discrete rotational and translational stimuli, we have recently quantified the properties of neurons in the vestibular nuclei. In these studies, three groups of neurons were identified in the VN, otolith-only, canal-only, and otolith + canal cells, each being characterized by different response properties to rotational and translational movements (Angelaki and Dickman 2000; Dickman and Angelaki 2002). Because of the strong interconnectivity between the fastigial and vestibular nuclei (Noda et al. 1990) and because neurons in both areas have been shown to process vestibular information for inertial motion detection (Angelaki et al. 2004), a comparison between the neural response properties in these nuclei is important. Thus the main goal of the present study was to characterize the properties of FN neurons with motion stimuli similar to those previously used in the VN (Angelaki and Dickman 2000; Dickman and Angelaki 2002). We also recorded from eye-movement-sensitive neurons in the caudal FN during translation as the animal either generated compensatory eye movements during fixation of a space-fixed target or suppressed the TVOR. We found that, unlike VN cells, none of the FN VO neurons were modulated by rotational motion alone. Thus canal-only cells were not encountered in the FN. In terms of spatial and temporal response properties, however, no prominent differences were seen between FN and VN neurons, suggesting a similar, but distributed, processing of otolith-driven motion information. Results of this work have previously appeared in abstract form (Shaikh et al. 2004a).

METHODS

Three juvenile fascicularis monkeys (Macaca fascicularis) were chronically implanted for head stabilization with a circular delrin ring using stainless steel inverted T-bolts, secured to the skull with dental acrylic. A guide tube platform (3 × 3 × 0.5 cm) constructed of delrin was stereotaxically secured to the skull inside the head ring. The platform had a staggered array of holes (spaced 0.8 mm apart) (for details, see Angelaki and Dickman 2000; Dickman and Angelaki 2002). Stereotaxic placement of the platform was such that the staggered array of holes covered the bilateral fastigial nuclei. For all three animals, the platform was slanted relative to the frontal plane, 10° from anterior to posterior. For one of the animals (monkey 1), in addition to the antero-posterior slant, the platform was also tilted relative to the sagittal plane, 10° from left to right. This allowed exploration of cerebellar areas close to the midline. The animals were also implanted with scleral search coils to measure eye movements (Judge et al. 1980; Robinson 1963). All surgical procedures were performed under sterile conditions in accordance to institutional and National Institutes of Health guidelines.

During experiments, the monkey was seated in a primate chair with its head positioned such that the horizontal stereotaxic plane was aligned with the earth-horizontal. The primate chair was then secured inside the inner frame of a vestibular turntable consisting of a three-dimensional rotator atop a 2-m linear sled (Acutronics/Neuro-kinetics, Pittsburgh, PA). The linear acceleration of the head was measured with a three-axis accelerometer (NeuwGhent Technology, La Grangeville, NY) mounted on the head ring support structure. For each recording session, the eye-coil signals, the three output signals of the linear accelerometer as well as velocity tachometer and position feedback signals from the rotator were low-pass filtered (200 Hz, 6-pole Bessel), digitized at a rate of 833.33 Hz (Cambridge Electronics Design, model 1401, 16-bit resolution), and stored for off-line analysis.

Extracellular recordings from single FN neurons were obtained with epoxy-coated tungsten microelectrodes, inserted into 26-gauge guide tubes, advanced through a predrilled hole, and manipulated vertically with a remote control microdrive. Neural activity was amplified, filtered (300 Hz to 6 kHz) and passed through a BAK Instruments dual time-amplitude window discriminator. Single-unit spikes triggered acceptance pulses (BAK window discriminator) that were stored on computer using the event channel of the 1401. Stimulus protocols and data acquisition were computer-controlled with the 1401 using scripts written for the Spike2 (CED) software environment.

During initial experiments in each animal, we first identified the abducens nuclei bilaterally. The recording sites in the fastigial nuclei were then identified by neuronal firing characteristics (Buttner et al. 1991; Gardner and Fuchs 1975; Siebold et al. 1997, 1999) and their location relative to the fourth ventricle and the abducens/vestibular nuclei. After termination of all recording sessions for animal 1, horseradish peroxidase-wheat germ agglutinin (HRP-WGA) was injected into the same location where many of the VO neurons were recorded. Histological reconstruction verified that the injection was made within the rostral FN (Fig. 1B). For animal 2, recording location and electrode tracks were also verified histologically (Fig. 1C). No histology is yet available for monkey 3.

During recording sessions, once in the vicinity of the FN, a stimulus consisting of both translational motion, rotational motion, or smooth pursuit/saccadic eye movements was used to search for responsive neurons. Once a vestibular or eye-movement cell was isolated, it was characterized using standard motion protocols, including translation along different horizontal directions as well as earth-vertical axis and earth-horizontal axis rotations (Dickman and Angelaki 2002).

Protocols for the eye-movement-sensitive neurons

Monkeys were trained to follow a target back-projected onto a screen located at a distance of 33 cm from the animal in an otherwise dark room. The target was moved sinusoidally at 0.5 Hz, eliciting ±10° horizontal or vertical smooth-pursuit eye movements. Neurons were also tested during fixation and saccades to multiple horizontal and vertical targets. Neurons responsive to saccadic but not pursuit eye movements were not further analyzed here as they were never modulated during the slow phase of either the RVOR or TVOR. Pursuit-responsive cells were also characterized during both the RVOR (yaw and pitch, at 0.5 Hz, ±10°) and the TVOR (0.5 Hz, ±0.2 G) as animals fixated a near (33 cm) target using a space-fixed servo-controlled laser. Whenever unit isolation was maintained, pursuit-sensitive neurons were also tested during RVOR and TVOR cancellation as animals fixated a head-fixed target. This protocol was delivered first during lateral motion, next during fore-aft motion, and finally during translation along in between directions.

Motion protocols for FN VO neurons

A more extensive battery of tests was delivered for cells without any eye-movement sensitivity. VO cells were tested in complete darkness, using the experimental protocol outlined in the following text.

First, to characterize their otolith-driven responses, neurons were tested during translation along different directions in the horizontal plane. The FN VO neural responses were first obtained during 0.5-Hz (±0.2 G) translation with the animal oriented at 0° (lateral motion), 30, 45, 60, 90 (fore-aft motion), 120, 135, and 150° relative to the linear sled. Neurons were also tested during translation at different frequencies (0.16 Hz, ±0.1 G; 0.3 Hz, ±0.19 G; 1, 2, and 5 Hz at ±0.2–0.3 G, where G = 9.8 m/s²) along different directions in the
horizontal plane. Each cell was typically tested at a minimum of three different frequencies and at least two different orientations (lateral and fore-aft motion).

Second, neural responses to earth-horizontal axis (EHA) rotations (when both otolith and semicircular canals afferents were simultaneously activated) were characterized during 0.5-Hz (±10°) rotations in the pitch, roll, right-anterior/left-posterior (RALP), and left-anterior/right-posterior (LARP) canal planes.

Third, earth-vertical axis (EVA) rotations were used to quantify the neuron’s rotational sensitivities due to stimulation of the semicircular canals with minimal simultaneous dynamic otolith afferent activation. To quantitatively characterize the maximum sensitivity vector in the pitch plane, EVA rotations were delivered by reorienting the animal relative to the axis of rotation. These included EVA rotations (0.5 Hz, ±10°) first delivered with the animal upright and then while it was pitched 30° nose-up and 30° nose-down.

**Data analyses**

Neural activities were analyzed off-line using custom-written scripts in Matlab (Mathworks). For each neuron, the instantaneous firing rate (IFR) was computed as the inverse of interspike interval and assigned to the middle of the interval. For each experimental run, data were folded into a single cycle by overlaying neural IFR from each response cycle. The neural response amplitude and phase during rotation/translation were determined by fitting a sine function (1st and 2nd harmonics and a DC offset) to both response and stimulus using a nonlinear least-squares minimization algorithm (Levenberg-Marquardt). For rotational stimuli, neural gain was expressed in units of spikes/s per °/s, whereas phase was expressed as the difference (in degrees) between peak neural activity and peak angular head velocity. For translational stimuli, neural gain was expressed in spikes/s (G = 9.81 m/s²). Phase was reported as the difference (in degrees) between peak neural activity and peak linear acceleration.

The spatial and dynamic properties of each neuron during translational and rotational motion were computed using a spatiotemporal function that allows for nonzero minimum response gain and phase that could vary as a function of stimulus direction. As described in detail in previous work (Angelaki 1991; Angelaki and Dickman 2000; Bush et al. 1993), such gain and phase behavior can be modeled by two sensitivity vectors (rather than the single vector that characterizes cosine-tuned neurons). Several studies to date have demonstrated the existence of spatiotemporal convergence in the central otolith system (Angelaki and Dickman 2000; Angelaki et al. 1992, 1993; Bush et al. 1993; Zhou et al. 2001) and canal/otolith interactions (Baker et al. 1984a,b; Siebold et al. 1999). Such fitting allowed estimation of four parameters describing each cell’s properties: maximum response gain and phase, the maximum response direction, as well as tuning ratio (ratio of minimum over maximum neural response gains). For cosine-tuned neurons, the last two parameters assume nearly zero values.

**RESULTS**

Extracellular single-unit responses were recorded from 126 VO and 55 eye-movement-sensitive neurons located in the

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**FIG. 1.** Stereotaxic and histological reconstruction of recording locations. A: 3-dimensional location of all neurons recorded in monkey 1 (right side view). Grid orientation is aligned with electrode track direction, which in this monkey had a double angle tilt of 10° in both the lateral/medial and anterior/posterior directions. Neurons in the fastigial nucleus (FN) have been classified as vestibular only (VO, ●) or eye-movement-sensitive (○). VO neurons were mainly encountered in the rostral FN, whereas eye-movement-sensitive neurons were restricted to the caudal FN. ● VO cells encountered ventral to the eye-movement-sensitive cells in the cerebellar cortex (lobule X). B: a cross-section of the brain stem and cerebellum of monkey 1 illustrating the center of a horseradish peroxidase-wheat germ agglutinin (WGA-HRP) injection (marked as 1) as well as three additional electrode tracks through the nucleus (marked as 2–4). C: recording sites in monkey 2 are illustrated in a cross-section through the deep cerebellar and brain stem vestibular nuclei. Illustrated electrode tracks in the FN were identified histologically: IntP, interpositus posterior; IntA, interpositus anterior; Dent, dentate; Y, Y-group vestibular nuclei; MVN, medial vestibular nucleus; DVN, descending vestibular nucleus; MLF, medial longitudinal fascicules; IV, fourth ventricle; CN, cochlear nucleus; FL, flocculus.
responses for motion along that direction, as well as the ratio of amplitude and phase of spatiotemporal model fits: the direction of maximum response et al. 2001). Four response parameters were estimated from the 1993; Dickman and Angelaki 2002; Shaikh et al. 2004b; Zhou (Angelaki 1991; Angelaki and Dickman 2000; Bush et al.

as a function of stimulus direction and fitted with a spatiotemporal model fit (Angelaki 1991). Examples of such fits to the gain and phase of the cell whose responses are illustrated in Fig. 2 have been plotted in Fig. 3. This cell (and many other FN VO neurons) was cosine-tuned, as evident by the nearly zero minimum gain and the lack of any strong dependence of response phase on stimulus orientation. Indeed, the tuning ratios computed for this cell were 0.05 and 0.04 for translation and rotation, respectively.

Only neurons the responses of which were tested along a minimum of two directions for each motion type (e.g., lateral/fore-aft translation and pitch/roll rotation), such that their spatiotemporal properties could be characterized, were included for further analysis. In the next sections, we summarize the properties of FN VO cells, first during translation, followed by a summary of cell responses during rotation.

Neural response properties during translation

Most of the FN VO neurons were cosine-tuned during horizontal plane translation. As illustrated in Fig. 4A, 61% (59/96) of the FN neurons had tuning ratios <0.2. There was no difference (χ²-test) in either tuning ratio or response phase for the FN neurons during 0.5-Hz translation when compared with the respective distribution from a population of vestibular nuclei neurons (Angelaki and Dickman 2000). Similar to the VN, unlike primary otolith afferents that exhibit small phase leads relative to linear acceleration (e.g., Fernandez and Goldberg 1976b; see also Angelaki and Dickman 2000; Si et al. 1997), the majority of FN cells modulated in phase with head velocity during horizontal plane translation at 0.5 Hz (Fig. 4B). Of 101 neurons, 55 (55%) exhibited response phase values within ±45° of head velocity (−90° in Fig. 4B), whereas only 46 (45%) exhibited response phase values within ±45° of head acceleration (0° in Fig. 4B).

When the minimum response gain of the cells with tuning ratios >0.2 was plotted as a function of the respective maximum gain, a significant correlation was revealed (Fig. 5A, R² = 0.59, P < 0.05). This significant correlation was also seen at other motion frequencies. The slope of these linear regression lines (which can be thought of as a mean tuning ratio for these neurons) increased with frequency (Fig. 5B).

VO neurons

All (126/126) of the FN VO neurons were modulated during translational motion in the horizontal plane. In contrast, of 72 cells that were tested, only 47 neurons changed their firing rates during sinusoidal roll or pitch rotation. Responses from one representative VO neuron during lateral and fore-aft translation, as well as roll and pitch rotations, are illustrated in Fig. 2. Common to the majority of FN VO neurons, this cell exhibited a sinusoidal modulation of its firing rate during all four stimuli. Typically, the depth of modulation was stronger for translational rather than rotational stimuli.

To quantify the properties of these neurons for all motion directions tested, neural response gain and phase were plotted as a function of stimulus direction and fitted with a spatiotemporal model that represents an extension of cosine tuning (Angelaki 1991; Angelaki and Dickman 2000; Bush et al. 1993; Dickman and Angelaki 2002; Shaikh et al. 2004b; Zhou et al. 2001). Four response parameters were estimated from the spatiotemporal model fits: the direction of maximum response in the respective plane of testing, the amplitude and phase of responses for motion along that direction, as well as the ratio of the minimum (Smin) over the maximum (Smax) response amplitude (tuning ratio = Smin/Smax). The later provides a measure of how close the cell follows cosine-tuning (Angelaki and Dickman 2000). Examples of such fits to the gain and phase of
However, this increase was less than a 10-fold change per decade of frequency, as would have been expected if a derivative relationship characterized the dynamics along these two vector orientations (see DISCUSSION).

Preferred directions for FN VO cells were scattered throughout the horizontal plane. The distribution of maximum response directions during 0.5-Hz translation is illustrated in Fig. 6. Here each dot represents a single cell, with its distance from the center illustrating neural response gain and its angular orientation corresponding to the direction of the stimulus that elicited maximum response (Fig. 6A). Although distributed throughout the horizontal plane, there was a clear bias of FN cell preferred response vectors to be oriented close to the 0°/180° lines, suggesting a preference for lateral motion directions. This difference is better illustrated in Fig. 6B, where the number of cells preferring motion directions within ±30° of the interaural axis composed 56% of the whole VO population. A preference for lateral motion directions was also reported for vestibular nuclei neurons (Angelaki and Dickman 2000; Dickman and Angelaki 2002).

Further similarities between FN and VN neurons were also seen in their response dynamics. The neural response gain for all FN neurons tested along a minimum of two different directions for at least three frequencies have been plotted in Fig. 7A (n = 47). The corresponding phase has been illustrated in Fig. 7B. Cells exhibited widely different dynamics with neurons having increasing, decreasing, or relatively flat gains as a function of frequency (Fig. 7A) with the most dramatic frequency-dependent changes being observed for the response phase (Fig. 7B). Similarly to VN cells (Angelaki and Dickman 2000; Dickman and Angelaki 2002), the phase for the majority of FN neurons increased with frequency. Also, in contrast to the otolith afferent population, FN neuron phase changed steeply as a function of frequency. At low frequencies, the response phase for the majority of the neurons was close to velocity (−90° in Fig. 7B; see also Fig. 4B). At higher stimulation frequencies, neural response phase shifted toward being in phase with linear acceleration. There was no dependence of the direction of maximum sensitivity for FN cells on frequency [F(5,50) = 1.7, P > 0.05, repeated-measures ANOVA], as illustrated in Fig. 7C. In contrast, both the gain and phase of the neurons significantly depended on frequency [F(5,50) = 10.8 and 18.9, P < 0.05, repeated-measures ANOVA].

Neural response properties during EHA rotation (e.g., dynamic pitch/roll tilts)

Thirty-one FN VO cells were recorded for a minimum of two stimulus orientations during EHA rotations (typically pitch/roll, although in-between directions were also tested, as illustrated in Fig. 3). Of those cells, 24 (77%) neurons modulated their firing rates during at least one EHA rotation direction at 0.5 Hz. Following a similar analysis to that used for translation, population response properties have been summa-

**FIG. 4.** Histograms of tuning ratio (A) and maximum response phase (B) for all recorded FN VO neurons during 0.5-Hz translation. A phase of 0° corresponds to a response in phase with linear acceleration. A phase of −90° corresponds to a response in phase with linear velocity (- - -).

**FIG. 5.** Relationship between neural response gain along the maximum and minimum response directions (S_max and S_min). A: 0.5-Hz gains for broadly tuned neurons (tuning ratio >0.2) are linearly correlated with a slope of 0.24 ± 0.07 (95% confidence interval; R² = 0.59, P < 0.01; ■). □, cosine-tuned neurons (tuning ratio < 0.2). B: the slopes of the regression lines computed for all neurons with tuning ratio >0.2 has been plotted as a function of frequency. Error bars represent the 95% confidence intervals.
rized in Fig. 8. Similar to translation responses, most cells had small tuning ratios (Fig. 8A). Neural response phase also varied across neurons, with some cells leading and some cells lagging rotational head velocity (Fig. 8B). The majority (18/24) of the neurons were within $\pm 45^\circ$ of being in phase with head velocity as previously reported (Siebold et al. 1997). The preferred axes of EHA rotation spanned the whole horizontal plane (Fig. 8C).

During EHA rotations, both otolith and semicircular canal afferents are simultaneously activated. In contrast, the translational responses of these neurons reflect the sole contribution of otolith system activation. Thus we compared whether neural response gain, phase and maximum response direction during 0.5-Hz rotation correlated with the respective values during translation (Fig. 9). Neural response gain and phase (but not maximum response direction) were significantly correlated ($P < 0.05$) during EHA rotation (tilt) and translation. Notably, most cells had higher gains during translation than during EHA rotation. The ratio of the tilt versus the respective translation gain averaged $0.7 \pm 0.3$ (mean $\pm$ SD, $n = 24$). The slope of the regression line was statistically different from unity ($0.68 \pm 0.19$, 95% confidence interval). Thus the presence of semicircular canal signals during EHA rotations appears to decrease the responsiveness of the neurons to linear acceleration. The significance of this observation will be explored in the Discussion.

Responses to earth vertical axis rotations

The canal-driven responses of central cells were also tested with earth-vertical axis (EVA) rotations. With the animal upright, such rotations would deliver a purely yaw stimulus, activating mostly the horizontal semicircular canals. To stimulate vertical canals during EVA rotations, animals were also tested in nose-up and nose-down orientations. Of 47 cells tested with these EVA rotation stimuli, 22 (47%) cells exhibited clear response modulation (i.e., neural gain $>0.2$ spikes/s per $^\circ$/s) during EVA 0.5-Hz rotation in at least one of three static pitch orientations (yaw, $30^\circ$-nose-up-yaw and $30^\circ$-nose-down-yaw). The gain and phase have been plotted as a function of static pitch angle in Fig. 10A. Some cells were characterized

![FIG. 6. Distribution of maximum response directions during translation in the horizontal plane (0.5 Hz). A: polar plot of vector distribution. Concentric rings represent response sensitivity (spikes/s/$^\circ$/G$^{-1}$). Thus the distance of each dot from the center corresponds to neural response gain, whereas its angular position illustrates the spatial direction preference of each neuron (VO cells: ●, eye-movement-sensitive cells: ○). Inset: the corresponding motion direction relative to the animal. B: distribution of preferred vectors within three $\pm 30^\circ$ intervals centered around lateral motion ($0^\circ$, 180$^\circ$, light gray bar), fore-aft motion ($\pm 90^\circ$, dark gray bar), and oblique motion directions (white bar).]
by different phases for the nose-up and nose-down orientations, suggesting an input from the vertical semicircular canals. The distribution of response phase is illustrated in Fig. 10B. In contrast to translation and EHA rotation, neuronal responses during EVA rotations had a narrow phase distribution, with most cells being in phase, or slightly leading, rotational head velocity (mean of 22.8° ± 28.5°, n = 22). This phase distribution was similar to that reported for VN cells during EVA rotation (Dickman and Angelaki 2004).

FIG. 8. Summary of responses during earth-horizontal axis (EHA) rotations (0.5 Hz). A and B: histograms of tuning ratio (A) and phase (B). C: distribution of maximum response orientation. Concentric rings represent response sensitivity (spikes/s per °/s). The distance of each dot from the center corresponds to neural response gain, whereas its angular position illustrates the spatial rotation preference of each neuron. Cells with dots along the 0°/180° or 90°/270° orientations correspond to those with maximum response sensitivities during roll and pitch rotations, respectively (inset).

FIG. 9. Comparison of neural responses during translation and EHA rotation. Maximum response gain (A: in units of spikes/s°/s), phase (B: in units of °), and maximum response direction (C: in units of °) during earth horizontal axis rotations are plotted vs. the corresponding values during translation. — and - - - in A and B, the best-fit lines and 95% confidence intervals (A: slope = 0.68 ± 0.19, r² = 0.70, P < 0.01; B: slope = 0.85 ± 0.40, r² = 0.47, P < 0.01).
Eye-movement-sensitive neurons

Among the 55 eye-movement-sensitive neurons encountered in the caudal FN, 21 exhibited modulation during smooth pursuit eye movements, whereas the remaining 34 exhibited bursts in activity during saccadic eye movements (and were not further characterized here). Of the pursuit-sensitive cells, 19 were also characterized when the animal generated or cancelled the TVOR. All but one of these neurons modulated during the TVOR, although only 5/19 neurons exhibited modulation during the TVOR cancellation task in the absence of eye movements. The five cells with response modulation during TVOR suppression had sensitivities averaging $235 \pm 83$ compared with $218 \pm 152$ (SD) spikes/s$^{-1}$G$^{-1}$ for VO cells.

DISCUSSION

Here we have characterized the response properties of fastigial neurons during translation as well as during earth-vertical and earth-horizontal axis rotations. This characterization of otolith/canal convergence in the FN allowed a direct comparison of the neural response properties in the deep cerebellar nuclei with vestibular nuclei cells. We found that all FN VO neurons modulated their firing rates during translation, in contrast to brain stem neurons, where approximately one-fourth of the cells only modulated during rotation and were characterized as “canal-only” neurons (Dickman and Angelaki 2002). This striking difference between FN and VN cell populations might reflect a functional specialization of the rostral fastigial nuclei (see following text). Other response properties of FN neurons were similar to those in the VN. We will first summarize the present results in relationship to previous studies and then speculate on the potential functional role of the fastigial nuclei in vestibular signal processing.

Properties of FN neurons during translation

Previously there had been only a single report (Zhou et al. 2001) describing the properties of rostral fastigial neurons to translational motion. The study focused primarily on the spatiotemporal properties of FN VO neurons and characterized the distribution of tuning ratios, i.e., the ratio of the minimum over the maximum sensitivities of FN VO neurons during horizontal plane translation. Tuning ratios close to zero would characterize cells with cosine-tuning properties. In contrast, large tuning ratios would be indicative of spatiotemporal convergence, including a lack of zero (null) response during motion in the horizontal plane. Zhou et al. (2001) reported that only about one-third (5/17) of the recorded FN neurons had tuning ratios $<0.2$, an observation that is consistent with the present results from a larger cell population (Fig. 4A). Similar to the Zhou et al. study, we also found that there was a linear relationship between the minimum and maximum response gains of FN neurons (Fig. 5A). This result, which was first reported in the VN of decerebrate rats (Bush et al. 1993), is in contrast to the primate VN population, where no such correlation was found (Angelaki and Dickman 2000; Dickman and Angelaki 2002). In the rat VN, the linear correlation between the two sensitivity vectors arose because of a derivative relationship between the neural response dynamics during translation along each of these two orthogonal directions (Angelaki et al. 1993; Bush et al. 1993). If such a derivative relationship existed for the primate FN VO neurons, the slopes of these regression lines would be expected to exhibit a tenfold increase per decade of frequency (Angelaki et al. 1993; Bush et al. 1993). As the regression line slopes did not increase as steeply with frequency (Fig. 5B), we conclude that no such derivative relationship exists in primate broadly tuned translation-sensitive neurons.

In addition to similar spatiotemporal tuning characteristics, FN and VN VO cells also share several other response properties during horizontal plane translation. Perhaps the most
striking resemblance, which exists in sharp contrast to the primary afferent population, relates to the temporal properties of these neurons. Unlike primary otolith afferents, the majority of FN and VN cells had response phases that were closer to head velocity than linear acceleration during low frequency motion (e.g., 0.5 Hz; see Fig. 4B) (see also Angelaki and Dickman 2000; Dickman and Angelaki 2002; Zhou et al. 2001). Neural response phase increased with frequency, often steeply, with many neurons exhibiting phase differences of ∼180° between 0.2 and 5 Hz. Therefore central translational responses in both the VN and FN have been temporally processed compared with the primary afferent population (Angelaki and Dickman 2000). Such an extensive temporal processing, part of which might involve a neural integration, has been proposed to be important for central otolith processing and the discrimination of gravitational from translational components of acceleration (Green and Angelaki 2004).

Despite a strong frequency dependence of both response gain and phase, the preferred motion direction did not depend on frequency (Fig. 7C). A similar conclusion was also previously made for VN responses (Angelaki and Dickman 2000; Dickman and Angelaki 2002). In contrast, during EHA rotations, rostral FN neurons exhibited a frequency dependence of optimum response orientation (Siebold et al. 1999). Such discrepancy could be due to a difference in the nature of stimuli used in the two sets of experiments. Siebold et al. (1999) used EHA rotations, which evoke combined otolith and canal-driven responses, in contrast, translations in the earth horizontal plane (used in current experiments) evoke purely otolith-driven signals (see next section).

The directional preferences of FN VO neurons were distributed throughout the horizontal plane; however, more than half of the neurons had preferred vectors that clustered within 30° of the interaural axis. A preference of maximum response directions of FN neurons to cluster around the interaural, as opposed to the naso-occipital axis of the head, appears to be a common property in the central coding of translational motion. Such a preferred vector distribution has been reported in both the vestibular nuclei (Angelaki and Dickman 2000; Dickman and Angelaki 2002) and the medial superior temporal cortical area (Gu et al. 2004). The functional implications of these directional preferences are unclear. It is interesting to note though that, although lateral motion directions would be an advantage in terms of amplitude detection, direction discrimination (i.e., how small differences in the direction of motion can be detected by individual cells) could be small during left/right movements. The reverse would be true for forward/backward movements. Because the majority of the cells prefer orthogonal (lateral) directions of motion, they would operate at the steepest (e.g., most sensitive) slope of their spatial tuning curves during fore-aft movements. Consistent with these expectations, direction discrimination thresholds during translation are significantly lower for forward rather than lateral heading directions (Smith et al. 2002).

With the head fixed relative to the body, it is unclear if the preferred vector distributions reported here for FN VO neurons represent directional preferences regarding motion of the head or motion of the body. One way to distinguish whether neurons encode the translation of the head or body through space would require that the response tuning of the cell be characterized at different head-on-trunk orientations. When this protocol was tested in a subpopulation of FN VO neurons, cells in this area encoded either motion of head or motion of the body (Kleine et al. 2004; Shaikh et al. 2004b). In this respect, FN VO cells were different from VO neurons in the rostral medial VN, where a head reference frame was prevalent (Shaikh et al. 2004b).

Properties of FN neurons during EHA and EVA rotations

The majority of previous studies characterizing FN VO responses utilized earth-horizontal axis (EHA) rotations, where both otolith and semicircular canal afferents are simultaneously activated (Gardner and Fuchs 1975; Siebold et al. 1997, 1999, 2001). During sinusoidal motion, the neural activations due to either one of the sensory inputs alone would appear as a sinusoidal modulation of firing rate. Thus it is virtually impossible using EHA rotations to distinguish the specific sensory contributions. Nevertheless, previous attempts to distinguish FN cells into otolith-only, canal-only, and otolith + canal neurons were based on neural response phase during EHA rotation as well as on the cell’s static tilt sensitivity (pure translation stimuli were not used) (Siebold et al. 1997, 1999). Only neural responses in phase with head position and cells with static tilt sensitivity were considered to receive otolith inputs. Based on these assumptions, the authors reported that the vast majority of FN VO cells were “vertical semicircular canal-related,” whereas only 22% of neurons were “otolith-related” (Siebold et al. 1997). The authors further concluded that “canal-related responses were much more common than otolith-related responses” in the rostral FN. In the present study, all neurons modulated during translational motion and none modulated during rotational motion alone. Thus no FN neurons were canal-only cells.

This discrepancy simply reflects the inadequacy of the previously used assumptions to perform such a characterization solely from rotational responses. In fact, it is clear from the phase distribution of Fig. 8B that the majority of FN VO cells (all of which modulated during translation) responded in phase with head velocity, rather than position, during EHA rotations. Thus it is simply incorrect to conclude that neurons are otolith- or canal-related based on response phase during EHA rotations, a point previously also demonstrated for VN cells (Angelaki and Dickman 2000; Dickman and Angelaki 2002). It is notable that the response phase during EHA, although centered around velocity, exhibited a wide distribution, similar to response phase during translation (compare Fig. 8B with 4B). This is so because EHA rotation responses reflect both otolith and semicircular canal contributions. In contrast, response phase during EVA rotation had a much narrower distribution and were clustered around a phase lead of 30–40° relative to head velocity as previously also reported for VN neurons (Dickman and Angelaki 2002).

In a more recent study, Siebold et al. (2001) have attempted to characterize the otolith contribution to rostral FN neuron responses by comparing neural activities during EHA and EVA rotations. The rationale behind this approach is the following: EVA rotations only dynamically activate semicircular canal afferents, thus allowing for the canal response of a given neuron to be determined in isolation. These canal responses were then subtracted from the response during EHA rotation to obtain the otolith contribution. This analysis yielded a higher
percentage (74%) of “otolith” FN neurons. Although this approach might appear sounder than the previous classification based on phase values, it is not without caveats. Extracting otolith contribution using rotation responses makes multiple assumptions: First, it assumes that otolith and canal contributions to the given cell interact linearly. Second, it assumes that the canal signal contribution to a cell’s response does not change as a function of static head orientation relative to gravity. Third, it assumes that central otolith-related neurons respond similarly to gravitational and translational accelerations, as is the case for primary otolith afferents (Angelaki and Dickman 2000; Dickman et al. 1991; Fernandez et al. 1972; Fernandez and Goldberg 1976a,b,c; Loe et al. 1973; Si et al. 1997; Tomko et al. 1981).

Unfortunately, all of these three assumptions have been recently shown to be incorrect. First and foremost, there are strong theoretical reasons to expect that central canal/otolith interactions might be nonlinear if neurons were to compute gravitational and translational accelerations (Green and Angelaki 2003, 2004; Merfeld et al. 1999; Merfeld and Zupan 2002; Zupan et al. 2002). The fact that otolith/canal convergence in central neurons is nonlinear has been recently demonstrated in the VN, where neural predictions based on this subtraction method did not match cell responses during translation (Dickman and Angelaki 2002). Second, one aspect of these nonlinear canal/otolith interactions that is needed to separate net gravito inertial acceleration into gravitational and inertial components is the fact the central canal responses are predicted to modulate as a function of static head orientation relative to gravity (Green and Angelaki 2004). This complexity makes it impossible to combine EVA rotation responses from different static head orientations relative to gravity to estimate a global canal contribution to cell firing. Finally, central otolith-related neurons have been shown not to encode net gravito inertial acceleration (as primary otolith afferents do) but rather reflect an intermediate stage of processing. Specifically, the majority of rostral FN neurons are closer to encoding translational rather than net gravito inertial acceleration (Angelaki et al. 2004).

The hypothesis that FN VO neurons represent processed vestibular information that is closer to encoding translation as opposed to net gravito inertial acceleration is also supported by the results of the present study. Only 77% of the translation-sensitive FN VO neurons exhibited significant modulation during EHA rotations. In addition, neurons with clear modulation during EHA rotation had response gains that were typically smaller than the respective gain during translation (Fig. 9A). Hence, the responses of FN VO neurons during EHA rotations, reflecting either absence of modulation or relatively low response gains, could be due to convergent canal inputs affecting dynamic otolith processing.

Is there a functional role of FN on otolith signal processing?

The rostral fastigial nucleus has been typically implicated in vestibulospinal function. Rostral FN neurons project directly to the ventral horn in the upper cervical region (Asanuma et al. 1983) and the medial and superior vestibular nuclei (Homma et al. 1995; Noda et al. 1990). Lesions in the FN lead to a falling tendency to the ipsilateral side (Kurzan et al. 1993; Thach et al. 1992). In addition, muscimol injection into the anterior vermis, the major output of which is the rostral FN, has been shown to alter the gain and spatiotemporal properties of vestibulospinal reflexes (Manzoni et al. 1997). In cats, inactivation of the rostral FN with muscimol has also been shown to affect the initiation and the control of combined eye-head gaze shifts (Pelisson et al. 1998).

The present results, showing that all vestibular neurons in the FN are sensitive during translation and that canal-only neurons might not exist in the rostral FN, suggest that this area could represent an important processing stage for otolith signals. In addition to the present results, such a hypothesis is also supported by the findings of two recent studies: first, some neurons in the rostral FN encode translation in a head reference frame, whereas others in a body reference frame (Shaikh et al. 2004b). Second, rostral FN neurons are closer to detecting the true translational component of the motion compared to either primary otolith afferents or VN cells (Angelaki et al. 2004). In fact, the tendency of FN-lesioned animals to fall toward the ipsilateral side might represent an inability of the brain to react distinctly to gravity and inertial forces. However, otolith signal processing in the FN might be important for more than just vestibulospinal function. VO cells in the rostral FN project to several premotor eye-movement-related areas in the brain stem, including the medial and superior VN, where many oculomotor-projecting neurons are found. It will be important that future studies investigate the functional consequences of rostral FN inactivation on tilt/translation discrimination, the TVOR, as well as spatial orientation tasks related to linear acceleration.

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