Responses of Primate Caudal Parabrachial Nucleus and Kölliker-Fuse Nucleus Neurons to Whole Body Rotation

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Balaban, Carey D., David M. McGee, Jianxun Zhou, and Charles A. Scudder. Responses of primate caudal parabrachial nucleus and Kölliker-Fuse nucleus neurons to whole body rotation. J Neurophysiol 88: 3175–3193, 2002. The caudal aspect of the parabrachial (PBN) and Kölliker-Fuse (KF) nuclei receive vestibular nuclear and visceral afferent information and are connected reciprocally with the spinal cord, hypothalamus, amygdala, and limbic cortex. Hence, they may be important sites of vestibulo-visceral integration, particularly for the development of affective responses to gravitoinertial challenges. Extracellular recordings were made from caudal PBN cells in three alert, adult female Macaca nemestrina through an implanted chamber. Sinusoidal and position trapezoidal angular whole body rotation was delivered in yaw, roll, pitch, and vertical semicircular canal planes. Sites were confirmed histologically. Units that responded during rotation were located in lateral and medial PBN and KF caudal to the trochlear nerve at sites that were confirmed anatomically to receive superior vestibular nucleus afferents. Responses to whole-body angular rotation were modeled as a sum of three signals: angular velocity, a leaky integration of angular velocity, and vertical position. All neurons displayed angular velocity and integrated angular velocity sensitivity, but only 60% of the neurons were position-sensitive. These responses to vertical rotation could display symmetric, asymmetric, or fully rectified cosinusoidal spatial tuning about a best orientation in different cells. The spatial properties of velocity and integrated velocity and position responses were independent for all position-sensitive neurons; the angular velocity and integrated angular velocity signals showed independent spatial tuning in the position-insensitive neurons. Individual units showed one of three different orientations of their excitatory axis of velocity rotation sensitivity: vertical-plane-only responses, positive elevation responses (vertical plane plus ipsilateral yaw), and negative elevation axis responses (vertical plane plus negative yaw). The interactions between the velocity and integrated velocity components also produced variations in the temporal pattern of responses as a function of rotation direction. These findings are consistent with the hypothesis that a vestibulorecipient region of the PBN and KF integrates signals from the vestibular nuclei and relay information about changes in whole-body orientation to pathways that produce homeostatic and affective responses.

INTRODUCTION

Recent anatomic and physiologic studies have demonstrated direct connections between the vestibular nuclei and brain stem regions that influence sympathetic and parasympathetic outflow (review: Balaban 1996). These pathways originate from a region within the vestibular nuclei that includes the dorsal aspect of the superior vestibular nucleus, the caudalventral aspect (pars α) of the lateral vestibular nucleus, and the caudal half of the medial vestibular nucleus and the inferior vestibular nucleus (Balaban 1996; Balaban and Beryozkin 1994; Porter and Balaban 1997; Ruggiero et al. 1996; Yates et al. 1994, 1995). The caudal medial vestibular nucleus and the inferior vestibular nucleus can influence parasympathetic and sympathetic outflow, either directly or indirectly, via ascending projections to the nucleus of the solitary tract, dorsal motor vagal nucleus, nucleus ambiguus, and rostral ventrolateral medullary reticular formation. An ascending pathway also originates from the dorsal aspect of the superior vestibular nucleus, pars alpha of the lateral vestibular nucleus, and caudal half of the medial vestibular nucleus and the inferior vestibular nucleus. This ascending projection terminates densely in the caudal third of the parabrachial nucleus, which has reciprocal connections with the amygdala, hypothalamus, and prefrontal cortex. These pathways have been suggested as substrates for vestibular contributions to cardiovascular control, respiratory patterns, gastrointestinal function, and anxiety disorders (Balaban 1999; Balaban and Thayer 2001; Balaban and Yates 2002). In particular, this pathway may participate in the anxiety and panic associated with losing one’s balance, optic-flow-induced illusions of drifting or falling backward, and vestibular system dysfunction.

The parabrachial nucleus is generally recognized as a major relay for ascending visceral (including gustatory) and nociceptive information in central autonomic pathways (Bernard et al. 1993, 1995; Feil and Herbert 1995; Fulweiler and Saper 1984; Jasmin et al. 1997; Pritchard et al. 2000) with modality-specific regions such as a “gustatory region” (Grigson et al. 1998; Nishijo and Norgren 1997; Spector et al. 1992). The anatomical distribution of vestibulo-parabrachial fibers raises the further hypothesis that there may be a distinct “vestibular” or “body/head motion”-sensitive region within the parabrachial nucleus and the Kölliker-Fuse nucleus. Although anatomical evidence indicates that the vestibular nuclear projections are confined within the caudal aspect of the lateral, medial, and external lateral parabrachial nucleus and the Kölliker-Fuse nucleus, there is no physiological information regarding re-
Response properties of neurons in these regions to head and/or whole-body rotation. This study provides the first demonstration that a discrete region in the caudal parabrachial nucleus contains neurons that show complex responses to rotations in three dimensions in alert primates.

**METHODS**

**Surgical procedures**

All surgical procedures were conducted under aseptic conditions in an animal surgical suite at the Central Animal Facility of the University of Pittsburgh. Three female macaque monkeys (*Macaca nemestrina*) were premedicated with atropine (0.05 mg/kg im) and ketamine (12 mg/kg im). After endotracheal intubation, anesthesia was maintained by inhalation of a 1–1.5% halothane-nitrous oxide-oxygen mixture. Three dental acrylic lugs were implanted for secure but painless head stabilization during recording sessions. One lug, positioned centrally on the top of the skull, served as a pedestal for electrical connectors; the other two lugs were positioned behind the ears. At the site of each lug, a 15 × 20-mm patch of skin and periosteum was removed, and small holes were drilled in the skull with a dental burr. Small stainless steel screws were tapped into these holes, and the lug was constructed by applying layers of dental acrylic around the screws to a height of approximately 9 mm.

A “search coil” was implanted on the right eye to measure eye movements, based on the technique of Judge et al. (1980). The conjunctiva was cut at the limbus, and a preformed 16-mm-diam coil (3 turns of Teflon-insulated stainless steel wire) was sutured to the sclera. Lead wires were passed subcutaneously to a connector on top of the skull. The conjunctiva was sutured with 7-0 vicryl to cover the coil. A 20-mm-diam, 10-mm-high stainless steel recording chamber was implanted surgically over a hole that was trephined in the parietal bone to permit the chamber to contact the intact dura mater. The chamber was centered at 1 mm left of the midline and +1 to +3.5 mm anterior to the ear bar in different monkeys, angled 15° posteriorly. This approach permitted complete exploration of the left parabrachial nucleus and access to the medial edge of the right parabrachial nucleus. Stainless steel screws were anchored within the surrounding bone through small burr holes, and dental acrylic applied to fix the chamber to the skull. The chamber was filled with “triple antibiotic ointment” and covered with a tightly fitting metal cap.

**Recording sessions**

Recording sessions began after at least a 2-wk recovery period. The monkeys were seated in a primate chair with their heads fixed to the chair in the stereotaxic plane. They were placed in a two-axis rotation device enclosed in a soundproof, lightproof, and shielded booth. Horizontal rotation about a (vertical) yaw axis was driven by an 80 ft-lb servo-controlled motor (Contraves), which reliably produced waveforms ranging from velocity trapezoids of unlimited duration to sine waves exceeding 10 Hz. The stimulator had an inner axis for producing oscillations in a vertical plane or static deviations up to 90°. With the monkey facing forward, the oscillations were oriented in the pitch plane. Rotating the primate chair 90° in the apparatus allowed oscillations in the roll plane. Intermediate angles produced oscillations in the planes of the vertical semicircular canals.

Eye movements were measured with the magnetic search coil technique (CNC Engineering). Because the transmitting coils for generating the magnetic fields do not rotate, search-coil signals are demodulated with the “phase angle” method (Collewijn 1977).

Extracellular single-unit recordings were obtained with standard 0.005-in tungsten electrodes purchased from Microprobe and were positioned with a Trent Wells X-Y stage on top of the chamber and Trent-Wells microdrive. A guide tube protected the electrode as it was lowered through the dura mater. Signals from the electrode were amplified conventionally, filtered, and monitored. Unit, eye-movement, and vestibular data were encoded and recorded on videotape with a Vetter PCM recorder for off-line analysis.

The left abducens nucleus and left trochlear nerve root were first identified as landmarks by their characteristic burst-tonic properties during eye movements (Fuchs and Luschei 1970). Single units in the parabrachial nucleus were identified initially in the dimly illuminated booth using a search stimulus of 0.7-Hz oscillation in the pitch plane (±12 or 53/8 peak velocity) and 0.7-Hz oscillation about the yaw axis (±60/8 peak velocity). Units that showed any modulation with the stimulus were then tested during 0.3-Hz sinusoidal (±12°), 0.7-Hz sinusoidal (±12°), and 0.3 Hz position trapezoid (±9–13°, peak velocity 95–100°/s) rotation in the dark booth in the following planes: (1) pitch plane; (2) an approximate left anterior-right posterior semicircular canal plane (LARP, animal rotated 45° rightward from pitch axis); (3) an approximate right anterior-left posterior semicircular canal plane (RALP, animal rotated 45° leftward from pitch axis); (4) roll plane (animal rotated 90° rightward from the pitch axis); (5) yaw plane with head level (i.e., utricular and horizontal semicircular canal oriented about 25° upward); and (6) yaw plane with the monkey rotated 25° nose-down (utricular and horizontal semicircular canal plane).

The spike times were identified with 0.1-ms precision and the firing rates were digitized at 5 ms/sample. Each stimulus cycle was divided into 64 equally spaced time bins, and the number of neuronal spikes in each bin was averaged to compute the firing rate across an average stimulus cycle. These 64-bin average responses were used for further analyses. The body position signal relative to gravity was obtained directly from the averaged position signal from the vertical plane rotation device; horizontal rotational velocity, and vertical and horizontal eye position signals were also saved.

The approach to analysis of the responses is described in detail in the presentation of the results. Briefly, least-squares methods (Marquardt-Levenberg algorithm) were used to estimate the baseline firing rate and unit sensitivities to angular velocity, angular position, and a leaky integration of angular velocity (with 250-ms exponential decay). As described in results, the inclusion of an empirically determined leaky integration of angular velocity in the analysis was sufficient to represent the responses of all neurons in all directions tested. This was not true if an acceleration or jerk component (peak velocity occurred 250–300 ms after stimulus onset, whereas peak acceleration occurred within 100–150 ms after stimulus onset) was substituted for integrated velocity in the analyses. Least-squares methods were then used to estimate the spatial tuning sensitivity of velocity, integrated velocity, and position sensitivity parameter for each unit during vertical plane and yaw rotations. These sensitivities were then used to reconstruct three-dimensional plots of velocity and integrated velocity sensitivity as a function of the orientation of axes of rotation based on the assumption of a linear summation of vertical plane- and yaw-related responses. Statistical tests such as ANOVA, least-significant differences (LSD), and Bonferroni post hoc tests and probability plots were performed with SYSTAT (SPSS, Evanston, IL). Directional statistics (Mardia and Jupp 2000) were employed to perform tests of significance on angular measurements that avoid analytical problems that are inherent in “cutting” data distributed around a circle at an arbitrary point (e.g., at 0°) and performing linear statistics. The algorithms for these methods were taken from Mardia and Jupp (2000) and implemented in MATLAB. Finally, multivariate analyses for vectorial data (e.g., Hotelling’s $T^2$ test) (e.g., Anderson 1958) were implemented in MATLAB.

Rotation axes for unitary responses were calculated using a right hand rule convention, with $\theta$ designating azimuth (“longitude”) and $\phi$ (referenced to the horizontal semicircular canal plane) designating elevation, based on the observed cosine-like spatial tuning of the units (see RESULTS). Because all recordings were performed from the left parabrachial complex, nose-up pitch was produced by right-handed
rotation about an axis pointing out the right (contralateral) ear, defined as \((\theta, \phi) = (-0.5\pi \text{ rad}, 0 \text{ rad})\). Nose-down pitch was defined accordingly as right-handed rotation about the axis \((\theta, \phi) = (0.5\pi \text{ rad}, 0 \text{ rad})\), directed out of the ipsilateral (left) ear. Left ear down (LED) rotation was defined accordingly as right-handed rotation about the axis \((\theta, \phi) = (\pm \pi \text{ rad}, 0 \text{ rad})\); right ear down (RED) right-handed rotation as \((\theta, \phi) = (0 \text{ rad}, 0 \text{ rad})\). Therefore nose-up and nose-down right-handed rotation in the RALP plane are defined right-handed rotation about the axes \((\theta, \phi) = (-0.75\pi, 0)\) and \((0.25\pi, 0)\) radians, respectively, while nose-up and nose-down rotation in the LARP plane are defined as right-handed rotation about the axes defined by \((\theta, \phi) = (-0.25\pi, 0)\) and \((0.75\pi, 0)\) radians, respectively. Excitation to leftward yaw was defined as \((\theta, \phi) = (0 \text{ rad}, 0.5\pi \text{ rad})\); excitatory responses to rightward yaw were represented as \((\theta, \phi) = (0 \text{ rad}, -0.5\pi \text{ rad})\).

After completion of PBN recording sessions, a tungsten electrode was used to verify the location and depth of the superior vestibular nucleus. A quartz-glass pipette 10-15 um (ID tip) containing biotinylated dextran-amine (BDA, 7.5% in 10 mM phosphate buffer containing 0.5 M NaCl, pH 7.0) was introduced into the superior vestibular nucleus. A quartz-glass pipette containing bio- tinylated dextran-amine (BDA, 7.5% in 10 mM phosphate buffer containing 0.5 M NaCl, pH 7.0) was introduced into the superior vestibular nucleus, and the BDA was ejected iontophoretically (4 \(\mu A\) tip positive square wave, 15-s duty cycle, 30 min). During the ensuing survival time of 17 days, a series of small electrolytic lesions (25-30 \(\mu A\), 20-30 s) was placed above and below the borders of the PBN region that contained responsive units. At the conclusion of the survival period, the monkeys were killed with a pentobarbital overdose and perfused transcardially with 50 mM phosphate-buffered saline (PBS, pH 7.2-7.4) or stored at -20°C in a solution of 30% sucrose-30% phosphate buffer and 30% ethylene glycol.

For visualizing BDA transport, the sections were rinsed successively in distilled water (3 x 10 min), 0.9% H2O2 and distilled water to suppress endogenous peroxidase activity, followed by a preincubation for 2 h at room temperature in 0.5% Triton X-100 in PBS. After rinsing in PBS, the sections were incubated for 1 h in ABC reagent, rinsed in buffer, and reacted for visualizing sites of peroxidase activity with either a nickel-enhanced DAB or a standard DAB (2 mg DAB, 8.3 \(\mu l\) H2O2 in 10 ml 500 mM sodium acetate buffer, pH 6.0) chromogen. After extensive rinsing, sections were mounted on subbed slides, cleared in xylene and coverslipped with a nonfluorescent DPX mounting medium.

**RESULTS**

**Location of parabrachial nucleus units and confirmation of afferent projections from the superior vestibular nucleus**

The physiological data were obtained from 85 units that were confirmed histologically to be within the borders of the lateral or medial parabrachial nucleus or the caudal aspect of the Kölliker-Fuse nucleus (Fig. 1). Fifty-four of these units were infiltrated with a 30% sucrose-4% paraformaldehyde solution overnight at 4°C, then cryoprotected in 30% sucrose in PBS until they sank. Frozen sections (40 \(\mu m\), transverse plane) were cut on a sliding microtome in a transverse plane at the same orientation as the electrode tracks. Sections were either placed in 50 mM phosphate buffered saline (PBS, pH 7.2-7.4) or stored at -20°C in a solution of 30% sucrose-30% phosphate buffer and 30% ethylene glycol.

**FIG. 1.** Location of units in the parabrachial nucleus. The location of each unit is plotted on a series of transverse sections [from rostral (1) to caudal (4)]. The mesencephalic trigeminal nucleus (Mes V) and brachium conjunctivum (BC) are also indicated. These units are all located in the caudalmost 2 mm of the parabrachial and Kölliker-Fuse nuclei, which lies immediately caudal to the level of the trochlear nerve exit.
(64%) were tested in multiple rotation conditions for characterization of the spatial tuning of the responses. The tracks were reconstructed from histological sections on the basis of marking lesions and the location of physiologically mapped borders of the abducens nucleus, spinal trigeminal nucleus, and trochlear nerve. The units were located between the caudal border of the trochlear nerve root and the caudal border of the parabrachial nuclear complex.

Anatomical tracing evidence confirmed that axons from the superior vestibular nucleus terminate within these regions of the parabrachial nucleus. Figure 2 shows a biotinylated dextran amine-labeled terminal in the lateral parabrachial nucleus at the level of section 3 from Fig. 1. Terminals were distributed throughout the region containing rotation responsive units.

Temporal response properties

RESPONSES TO POSITION TRAPEZOID STIMULATION. The responses to position trapezoid stimulation have provided the greatest insight into temporal characteristics of the responses of parabrachial nucleus neurons to whole body rotation in vertical planes and the horizontal plane. The parabrachial nucleus units in this study were unresponsive to eye position and eye velocity during spontaneous saccades interspersed with periods of fixation. Subsequent data from another trained monkey indicate that they are unresponsive during sinusoidal smooth pursuit (unpublished observations). Four examples of single-unit responses to vertical position trapezoidal wave stimulation are shown in Fig. 3 and responses of two units to vertical and horizontal position trapezoidal stimuli are shown in Figs. 5 and 6. All units responded vigorously during the dynamic phase of whole-body position trapezoid rotation (Figs. 3–6). Responses during vertical rotation could be either unrectified (increased discharges in 1 direction, decreased discharges in the opposite direction), fully rectified (increased discharges in both directions), or biphasic (increased followed by decreased discharges in 1 direction, decreased followed by increased discharges in the opposite direction). Further, the discharges of the same unit could vary both from a biphasic response to a monophasic response pattern and in degree of rectification as a function of the stimulus direction (e.g., Fig. 6).

All rotation-responsive parabrachial nucleus neurons were
sensitive to vertical rotation. Analyses of the data indicated that the unit discharges during vertical rotation reflect baseline activity, whole-body velocity, whole-body position, and a response that resembled a leaky integration of rotational velocity. The presence of position sensitivity was tested by comparing the results of a model with a fixed position gain of zero versus a model with a free parameter for position gain; units fit by the former model were termed position-insensitive. In addition, 30/70 units tested with sinusoidal or position trapezoid stimulation in yaw showed significant responses to horizontal rotation, which reflected baseline activity, whole-body velocity, and a response that resembled a leaky integration of rotational velocity. There was no empirical evidence supporting acceleration-related unit responses. This communication classifies the units on basis of the spatial properties of velocity and position-related components of the responses.

A simple iterative modeling approach was used to quantify the contributions of these stimulus components to the neuronal firing rates. The vertical body position signal relative to gravity was obtained directly from the averaged position signal from the vertical plane rotation device. The body vertical velocity signal was calculated by a discrete differentiation of the averaged vertical body position signal, which was then transformed to simulate primary vestibular afferent discharges using the MATLAB function “lsim” and the transfer function

\[
\frac{16s}{16s + 1}
\]

Two approaches were used to model the residual responses after subtraction of the components related to baseline activity, velocity sensitivity, and position sensitivity. The first approach was to use whole-body acceleration, calculated as a discrete
derivative from the head-velocity information. The inclusion of whole-body acceleration produced a satisfactory fit for biphasic and narrow monophasic response (e.g., Fig. 4, bottom), but could not fit the broader monophasic responses (e.g., Fig. 4, top). The second approach was to empirically model the residual response as a leaky integration of whole-body velocity. The time constants were rounded from the median values obtained from a set of representative residual traces and fixed for the final model. The leaky integrator component was defined as 

\[ v_i = R_{\text{int}} - R_{\text{leak}} \]

where \( R_{\text{int}} \) is integrated (primary afferent transformed) head velocity with a transfer function \( \frac{1}{0.2s} \) and \( R_{\text{leak}} \) is result of inputting \( R_{\text{int}} \) to a first order low pass filter with transfer function. 

**FIG. 4.** Representative performance of models of unit responses. This figure compares the ability of a model incorporating whole-body angular acceleration and a model incorporating a leaky integration of whole-body angular velocity to explain the position trapezoid responses of 2 units from Fig. 3. Both models represented the firing rate of the cell as the sum of baseline firing rate, angular position sensitivity, whole-body angular velocity sensitivity, and either acceleration (thin line) or a leaky integration of velocity (thick line). Note that the latter model was capable of describing both responses, but that the acceleration-based model could not adequately describe the monophasic response of unit g1901. Thus the leaky integrator model was used as a parsimonious description of the cellular responses for further analyses.
Because the responses to velocity transients of many cells were not directionally symmetric (see following text), separate gain parameters were estimated for upward and downward velocity and integrated velocity sensitivity. The model incorporating a leaky integration of velocity was sufficient to account for all monophasic and biphasic neuronal response patterns of the units (Fig. 4). Because individual units could display monophasic responses in one direction and biphasic responses in other directions (e.g., Fig. 6), this approach was selected as the simplest comprehensive model for unit responses.

The units in Fig. 3 represent the range of different combinations of responses shown by parabrachial nucleus neurons during vertical position trapezoid rotation. Unit g1901 showed a prolonged monophasic excitatory response to both upward and downward rotation. This response is produced by a summation of positive position gain (increased firing rate for upward displacement) with rectified velocity and integrated velocity responses (increased firing rate for both upward and downward velocity). Unit a5603, on the other hand, displayed a biphasic inhibitory-excitatory response during ipsilateral-ear up roll rotation and a biphasic excitatory-inhibitory response during ipsilateral-ear down roll rotation. This response is produced by a summation of an ipsilateral ear-downward symmetric velocity sensitivity and an ipsilateral ear upward symmetric integrated velocity sensitivity but no position sensitivity. Unit a7102 showed a monophasic increase in firing rate to upward rotation in the ipsilateral anterior-contralateral posterior SC plane and a narrower decrease in firing rate (followed by a brief increase) during downward rotation. This response reflected a summation of upward symmetric position and velocity responses with a rectified response to integrated velocity. Finally, unit a5901 showed a low-amplitude prolonged increase in firing during ipsilateral-ear up roll and larger prolonged increase in firing during ipsilateral ear-down roll rotation. The response pattern is a summation of a rectified velocity response with a downward integrated velocity response. Thus the position, velocity, and integrated velocity components appear to behave as independent signals across neurons.

Individual neurons also showed different temporal profiles of position trapezoid responses as a function of the axis of rotation (Figs. 5 and 6, top). The responses could range from monophasic and broad to monophasic and narrow to a biphasic response. Analyses of the spatial properties of the unit responses revealed that these variations in the temporal response profiles could be explained parsimoniously as a summation of position, vertical velocity, and vertical integrated velocity signals with cosine-like spatial tuning. As illustrated in Figs. 5 and 6, bottom, the gain estimates of position, velocity, and vertical integrated velocity response components displayed cosine-like tuning as a function of the orientation of the rotation plane. These position, velocity, and integrated velocity responses could be summarized by the orientation of a maximum sensitivity axis for responses to rotation in a vertical plane (θo) and the sensitivity of the unit response to the magnitude of the stimulus. For the velocity and integrated velocity components, separate magnitudes were fitted by least-squares methods to half cycles of a cosine function. The largest magnitude sensitivity parameter that produced increased discharges was defined as the sensitivity in the excitatory (or preferred) direction and the sensitivity parameter that produced decreased (or smaller peak) discharges was designated as sensitivity in the nonpreferred direction. These summary analyses showed that velocity and integrated velocity responses could be symmetric, asymmetric, or, less frequently, rectified fully. A symmetric cosine function provided an adequate characterization of the spatial tuning of the position sensitivity (e.g., Fig. 6).

BASELINE FIRING RATE. The baseline firing rates of parabrachial nucleus neurons ranged from 1.3 to 87.0 spikes/s and their distribution was positively skewed (Fig. 7A). The baseline firing rate did not appear to differ as a function of either the magnitude or best orientation of the velocity (Fig. 7B), integrated velocity (Fig. 7C), or position sensitivity of individual neurons or with the symmetry or rectification of the responses. Distributions with this degree of positive skew are typically described well by gamma functions. Maximum likelihood estimation methods indicated that the baseline firing rates are consistent with a random sample from a gamma distribution with a shape parameter of 2 and a scale parameter of 16.7 (Fig. 7A, —).

VELOCITY SENSITIVITY FROM SINUSOIDAL RESPONSES. The analysis of sinusoidal responses was complicated by the fact that approximately 60% of the neurons had position sensitivity. For cells with both position and integrated velocity sensitivity, the relative contributions of the position and integrated velocity components of the sinusoidal responses cannot be separated uniquely. Therefore the unit responses were first classified as position-sensitive or -insensitive on the basis of responses to position trapezoids. The responses of position-insensitive units were then analyzed in the same manner as the responses to position trapezoids but with the position gain fixed at zero. Least-squares methods were used to estimate upward and downward gains for velocity and integrated velocity sensitivity of only the position-insensitive neurons during sinusoidal oscillation.

The vertical velocity sensitivities of individual neurons were correlated highly for the 0.3-Hz sinusoidal, 0.7-Hz sinusoidal, and position trapezoid responses. One-way repeated-measures ANOVA, followed by Bonferroni and Dunn-Sidak corrected t-tests, indicated that estimates of preferred velocity sensitivity and the direction for maximal excitation of did not differ significantly during vertical 0.3-Hz sinusoidal, 0.7-Hz sinusoidal, and 0.25- or 0.3-Hz position trapezoid stimulation. However, estimates for velocity sensitivity in the nonpreferred direction [F(2,52) = 5.61, P < 0.01] showed significant differences across stimulus profiles. Post hoc tests (least-significant differences) revealed that the velocity sensitivity in the nonpreferred direction to a 0.7-Hz sinusoidal stimulus was less than the response to either a 0.3-Hz sinusoid (P < 0.01) or a 0.3-Hz position trapezoid (P < 0.01). The velocity responses in the nonpreferred direction to the 0.3-Hz sinusoid and the 0.3-Hz position trapezoid did not differ significantly. The bases for these statistical differences in frequency response characteristics of preferred and nonpreferred direction response components will require further investigation.
Three-dimensional organization of velocity sensitivity

The three-dimensional rotational velocity sensitivity of both the yaw-responsive and -insensitive units was estimated from relative magnitudes of the unit sensitivity to yaw and to vertical plane rotation. The spatial tuning of the velocity response of each unit was expressed as an axis of rotation in modified spherical coordinates using a right-hand rule for both the excitatory (or, for rectified cells, preferred) and inhibitory (or for rectified cells, nonpreferred) directions. In this coordinate system, \( r \) designates the magnitude of the rotation vector. The azimuth (\( \phi_{\text{vel}} \) or \( \phi_{\text{int}} \)) designates the orientation of the vertical rotation component with respect to the head. The elevation (\( \theta_{\text{vel}} \) or \( \theta_{\text{int}} \)) designates the orientation of the yaw-sensitive component [0 indicates no yaw sensitivity, \( \pi/2 \) indicates a strictly ipsilateral (left) yaw response and \( -\pi/2 \) designates a purely contralateral (right) yaw response]. The responses were also represented graphically as response surfaces, which plot the rotational velocity or integrated velocity sensitivity (the projection of \( r \)) as a function of azimuth and elevation (Fig. 10). The plots assume a linear addition of yaw and vertical axis rotational sensitivity across all azimuths and elevations, which permit a direct comparison of rotational spatial tuning properties of velocity and integrated velocity response component.

The elevation (\( \phi_{\text{vel}} \)) of three-dimensional angular velocity sensitivity axes and the presence of inhibitory (nonrectified) or excitatory (rectified) responses in the nonpreferred direction of rotation were sufficient to distinguish five populations of parabrachial nucleus neurons (Fig. 8). These categories are described in the sections that follow.

**vertical-plane-only response neurons.** Thirty-two neurons responded to whole body angular velocity in a vertical plane (i.e., \( \phi_{\text{vel}} = 0 \)). Twenty-one cells showed a nonrectified response pattern with a maximum excitatory response during rotation in one direction in a vertical plane and an inhibitory response during rotation in the opposite direction. Cells with rectified responses (11 units), on the other hand, showed excitatory responses for rotation in either direction within a best plane.

The vertical-plane-only neurons could be subdivided into three groups of cells on the basis of velocity sensitivity in the excitatory (preferred) and inhibitory (or nonpreferred) directions of rotation (Fig. 9A). High-velocity-sensitivity neurons (\( n = 6 \)) had responses more than 0.70 spikes/s per \(^\circ/\text{s}\) to rotation in the excitatory direction (preferred direction for rectified cells). Five of these cells showed a nonrectified response and one had a rectified response. Neurons with intermediate velocity sensitivity (\( n = 11 \)), on the other hand, showed responses in the range 0.25–0.7 spikes/s per \(^\circ/\text{s}\) to rotation in the preferred excitatory direction. Finally, neurons that responded with sensitivity \(<0.25\) spikes/s [per] \(^\circ/\text{s}\) (\( n = 15 \)) were termed low velocity sensitivity neurons. There was no preferred direction for responses of neurons as a function of velocity sensitivity (Rayleigh tests, NS).

The integrated velocity sensitivities in the preferred and nonpreferred directions (Fig. 9B) divided these neurons almost equally into cells displaying fully rectified (17 cells) and unrectified (15 cells) responses. However, these two types of integrated velocity responses were distributed equally across the neurons with rectified and unrectified velocity responses. Rectified integrated velocity responses were displayed by only 6 of the 11 units with rectified velocity responses and by 11 of the 21 units with unrectified velocity responses. Ten units had unrectified velocity and unrectified integrated velocity response; the remaining 5 units have unrectified velocity responses and rectified integrated velocity responses. Regression analysis indicated that the velocity and integrated velocity sensitivities in the excitatory response direction were roughly equal (\( r = 0.639, \text{slope} = 0.98 \pm 0.22 \)) among the vertical plane only units.

Approximately two-thirds (20/32) of the units with strictly vertical plane velocity sensitivity were also sensitive to static position displacement during position trapezoidal stimulation. The best position response sensitivities and directions (Fig. 9, C and D) tended to cluster between nose-up pitch and left ear-up roll. The rotation axes for best position sensitivity (\( \theta_{\text{pos}} \)) of the eight units with highest position sensitivities (range: \( 0.72–1.80 \) spikes \( \cdot s^{-1} \cdot \circ^{-1} \)) were distributed nonuniformly but broadly (Rayleigh test statistic: 11.36, \( P < 0.01 \)), with a mean direction of \(-0.83\) rad [near the nose-up ipsilateral anterior-contralateral posterior (LARP) semicircular canal plane, circular SD = 0.59 rad, von Mises \( \kappa = 0.83 \)]. By contrast, the preferred position response axes of the 12 lowest sensitivity neurons (0.18–0.56 spikes \( \cdot s^{-1} \cdot \circ^{-1} \)) were distributed uniformly (Rayleigh test statistic: 3.55, NS).

The \( \theta_{\text{vel}} \) values for the position-sensitive neurons (Fig. 9E) were distributed uniformly (Rayleigh test statistic: 2.58, NS). By contrast, the \( \theta_{\text{vel}} \) values of the position-insensitive, vertical-plane-only units were focused near nose-down pitch (Rayleigh test statistic: 9.7, \( P < 0.01 \)). The mean \( \theta_{\text{vel}} \) for position-insensitive units was 1.65 rad (von Mises dispersion: \( \kappa = 0.84 \); circular SD: 0.95 rad). The distributions of \( \theta_{\text{vel}} \) for the position-insensitive and position-sensitive units differed significantly (\( U \)-scores test statistic = 11.2, \( P < 0.01 \)).

The best axes for the position (\( \theta_{\text{pos}} \)) and the velocity (\( \theta_{\text{vel}} \)) sensitivities were nearly identical in the majority of the position-sensitive units (Fig. 9F). There was no significant relationship between the magnitudes of the velocity and position sensitivities of these neurons. Analysis with the Spurr and Koutbeij algorithm indicated that the distribution of \( \theta_{\text{vel}} \), \( \theta_{\text{pos}} \) was consistent with a mixture of two von-Mises-distributed populations. The majority of the units (estimate: 66%) formed sharply focused distribution near a zero difference between \( \theta_{\text{vel}} \).
and $\theta_{\text{pos}} (\mu = -0.01 \text{ rad}, \kappa = 5.92)$, indicating that the excitatory discharges reflect position and velocity information.

VERTICAL ROTATION PLUS YAW VELOCITY-SENSITIVE NEURONS. Three populations of neurons had preferred response axes with nonzero elevation ($[\phi_{\text{vel}}] > 0$). These populations (Fig. 8) have been designated positive elevation axis neurons, negative elevation axis neurons, and rectified neurons. The velocity and integrated velocity sensitivity of these units to rotation about axes with different azimuths and elevations is plotted for one positive elevation axis neuron ($a6301$), one negative elevation axis neuron ($a5902$), and two rectified neurons ($a5801$ and $a5901$) in Fig. 10.

Nearly half (10/22) of the nonzero elevation neurons also had position sensitivity, which had sinusoidal spatial tuning about a best vertical rotation plane. The position sensitive neurons had significantly lower velocity sensitivity than the position-insensitive cells in both excitatory and inhibitory (or nonpreferred) directions of rotation [Fig. 11D, repeated-measures ANOVA, $F(1,20) = 5.02, P < 0.05$]. However, there was no significant difference in integrated velocity gain among position-sensitive and position-insensitive units [repeated-measures ANOVA, $F(1,20) = 0.22, P > 0.5$].

Positive elevation axis neurons. Eleven units showed a maximum velocity-related excitation during both vertical position trapezoid rotation and ipsilateral (leftward) yaw position trapezoid rotation (i.e., $\phi_{\text{vel}} > 0$). These units also had inhibitory (or absent) responses for rotation in the opposite direction. The values of $\phi_{\text{vel}}$ (elevation) for excitation were focused tightly (Rayleigh test statistic: 20.08, $P < 0.01$) around a preferred direction of 0.97 rad (56° upward, circular SD: 0.30 rad, von Mises $\kappa = 0.78$ rad) from the horizontal. The values of $\theta_{\text{vel}}$ (azimuth) for the preferred responses showed no significant preferred direction across units (Rayleigh test statistic: 3.58, NS).

The $\phi_{\text{vel}} > 0$ cells (Fig. 11A) showed relatively symmetric excitatory and inhibitory response sensitivities (excitatory: $1.00 \pm 0.47$ spikes/s per $^\circ$/s; inhibitory: $.85 \pm 0.72$ spikes/s per $^\circ$/s, mean $\pm$ SD), both of which were distributed normally (Kolmogorov-Smirnov test, Lilliefors standardization, $P > 0.4$). The angle between the excitatory and inhibitory best rotation axes (calculated as the inverse cosine of the dot prod-

FIG. 6. Summary of whole-body rotation responses of unit $a6301$. Top: the average firing rate during a cycle of position trapezoid rotation in the RALP SC, pitch, LARP SC roll, and yaw (horizontal SC) plane. The duration of the upward and downward movements are shown by solid bars at the top of each graph. The solid trace represents the model fit of each response. Bottom: the directional tuning of the sensitivity of the position, angular velocity, and leaky integration of angular velocity response components to vertical rotation. The solid line in each panel represents the fit of an asymmetric cosine function (see text) to characterize the directional tuning.
rad (Rayleigh test, 6.39, $P < 0.01$), indicating that the units are excited and inhibited by rotations in opposite directions about a single preferred axis. Hence, the angular velocity responses of these neurons [Figs. 6 and 10 ($\alpha_{6301}$)] show approximately symmetric maximum excitatory and inhibitory sensitivities during rightward versus leftward rotation about a single preferred axis, with the sensitivity varying according to a cosine rule for other orientations.

Six of the 11 neurons (Fig. 11C) were position-sensitive [0.46 ± 0.27 (SD) spikes \cdot s^{-1} \cdot \circ^{-1}]. The values of $\theta_{\text{pos}}$ (azimuth) for the plane of best position sensitivity of these cells ranged between $-3.13$ and $-0.63$ rad with a mean of $-1.82$ rad (Rayleigh test, 6.39, $P < 0.05$, circular SD: 0.79 rad, $\kappa = 0.85$). The azimuth for best position sensitivity ($\theta_{\text{pos}}$) was not correlated significantly with the azimuth for best rotational velocity sensitivity ($\theta_{\text{vel}}$) among these neurons.

Negative elevation axis neurons. Seven cells showed a maximum velocity-related excitation during vertical rotation combined with contralateral (rightward) yaw (i.e., $\theta_{\text{vel}} < 0$) and inhibitory responses for rotation in the opposite direction about the preferred axis (Fig. 8). The values of $\theta_{\text{vel}}$ (elevation) were focused tightly (Rayleigh test statistic: 13.80, $P < 0.01$) around a preferred direction of $-0.42$ rad (circular SD: 0.12 rad, von Mises $\kappa = 0.76$ rad). The values of $\theta_{\text{vel}}$ (azimuth) had a preferred response orientation for nose-down ipsilateral (left) anterior canal-contralateral posterior canal plane to nose-down pitch rotation (Rayleigh test statistic: 9.35, $P < 0.01$, von Mises $\mu = 2.13$ rad, $\kappa = 0.84$ rad; circular SD: 0.64 rad). This

FIG. 8. Three-dimensional best response axis for excitatory responses of parabrachial nucleus neurons. The axis of rotation for the greatest excitatory response of each parabrachial nucleus neuron is expressed in modified spherical coordinates using a right hand rule. In this coordinate system, $r$ designates the magnitude of the rotation vector. The azimuth ($\theta$) designates the orientation of the vertical rotation component with respect to the head (0 indicates nose-up pitch, $-\pi/2$ designates ipsilateral (left) ear-down roll, $\pi/2$ indicates contralateral (right) ear-down roll and $\pi = -\pi$ indicates nose-down pitch). The elevation ($\phi$) designates the orientation of the yaw-sensitive component (0 indicates no yaw sensitivity, $\pi/2$ indicates a strictly left yaw response and $-\pi/2$ designates a purely right yaw response). The neurons could be classified by the elevations ($\phi$) of their 3-dimensional angular velocity sensitivity axes as: vertical-rotation-only cells ($\phi = 0$), vertical rotation plus ipsilateral yaw cells (or positive elevation axis neurons, $\phi > 0$) with unrectified responses, vertical rotation plus ipsilateral yaw cells (or negative elevation axis neurons, $\phi < 0$) with unrectified responses, and $|\phi| > 0$ cells with rectified responses.

FIG. 9. Properties of angular velocity and “leaky integrator” responses of neurons with $\phi = 0$. A: 3 classes of neurons could be differentiated by rotational velocity sensitivity independent of rectification of responses. However, velocity gain was unrelated to integrated velocity responsiveness ($B$). C: polar plot of the vertical angular position sensitivity of parabrachial nucleus neurons with $\phi = 0$. The axis of rotation is represented by a right-hand rule; the length of the vector is the sensitivity of the cell in spikes/s. D: distribution of the best orientations for position sensitivity of $\phi = 0$ neurons. E: distribution of the best orientations for angular velocity sensitivity of position-insensitive $\phi = 0$ neurons. F: the differences between the preferred (excitatory) response directions for velocity sensitivity ($\theta_{\text{vel}}$) and for position sensitivity ($\theta_{\text{pos}}$) were distributed bimodally for position-sensitive units with $\phi = 0$. The estimated underlying von Mises distributions for the bimodal data are also plotted.

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population of neurons had high to very high velocity sensitivity (Fig. 11A), with a mean response of 1.34 ± 0.63 spikes/s per °/s for rotation in the excitatory direction and a sensitivity of 0.98 ± 0.56 spikes/s per °/s for rotation in the inhibitory (i.e., opposite) direction. The sensitivities in both directions were distributed normally (Kolmogorov-Smirnov test, Lilliefors standardization, P > 0.2). The angle between the excitatory and inhibitory best rotation axes (calculated as the inverse cosine of the dot product of unit vectors of the axes for each response) was focused at 2.78 rad (Rayleigh test statistic: 12.09, P < 0.01, circular SD: 0.38 rad, von Mises κ = 0.80 rad). This finding indicates that the rotation axes are in opposite directions about the same axis. The angular velocity responses of these neurons, then, show relatively symmetric maximum excitatory and inhibitory responses during rightward versus leftward rotation about a single preferred axis [Figs. 5 and 10 (α5902)], with the sensitivity varying according to a cosine rule for other orientations.

Only two of the $\varphi_{vel} < 0$ cells had nonzero position sensitivity [Fig. 11C, 0.89 ± 0.05 (SD) spikes ⋅ s$^{-1} ⋅ °^{-1}$]. The $\theta_{pos}$ (azimuth) values for these cells (−0.818 and −1.269 rad) were of opposite polarity to the $\theta_{vel}$ values (2.04 and 2.25 rad) for their high sensitivity velocity responses (1.40 and 1.26 spikes/s per °/s). Hence, the response during rapid movements will reflect predominantly velocity while slow movements (e.g., less than 1°/s) will be reflected predominantly in position sensitivity.

Rectified elevation axis neurons. Four neurons had both a nonzero elevation ($\varphi_{vel} > 0$) for the axis of maximum rotational velocity sensitivity (the preferred excitatory direction) and only excitatory responses in a nonpreferred direction. One of these neurons (Fig. 10, a5801) had an excitatory rotation axis with positive elevation ($\varphi_{vel} > 0$), but it displayed a completely rectified response for both vertical and horizontal components of rotation. The remaining three neurons had preferred axes with a negative elevation ($\varphi_{vel} < 0$). The rotational velocity responses of one of these neurons were nearly a mirror image of responses of unit a5901. The other two neurons showed rectified yaw rotation sensitivity but reasonably symmetric excitatory and inhibitory responses to opposite directions of rotation at a best azimuth.

Discussion

This study provides the first electrophysiological demonstration that neurons the parabrachial nucleus respond to whole-body rotation. The responses were restricted to neurons in the caudal aspect of the lateral parabrachial, medial parabrachial, and Kölliker-Fuse nuclei of these head-restrained monkeys. The responses were all confined to the region caudal to the root of the trochlear nerve. Because these neurons were circumcribed in a region that receives terminals from the superior vestibular nucleus, it seems likely that these responses reflect inputs from vestibu-lo-parabrachial relay neurons. More rostral electrode penetrations yielded only units that were unresponsive to whole-body rotation. These data, then, support the existence of a functional “vestibulo-receptive” region of the parabrachial nuclear complex.

The limited tracing data from this study in monkeys are consistent with previous anatomical evidence from rabbits (Balaban 1996) and rats (Porter and Balaban 1997) that demonstrated that the caudal aspect of the lateral parabrachial, medial parabrachial, and Kölliker-Fuse nuclei receive projections from the vestibular nuclei. However, vestibular nuclear afferents are only one of the known sources of input to this region. Anatomical tracing studies in rats indicate that these caudal regions of the parabrachial and Kölliker-Fuse nuclei also receive presumptive body and head nociceptive and thermal input from contralateral spinal cord laminae 1–3 and the spiral trigeminal nucleus (Feil and Herbert 1995), somatosensory input from the oral cavity, upper alimentary tract, and upper respiratory tract from the paratrigeminal nucleus (Feil and Herbert 1995), and visceral sensory inputs from the rostral and ventrolateral nucleus of the solitary tract (Herbert et al. 1990). Data from rats indicate that descending projections to this region originate in the central amygdaloid nucleus and the prefrontal, insular and infralimbic cortex (Moga et al. 1990); a central amygdaloid nucleus projection to the parabrachial nucleus was also reported earlier in primates (Price and Amaral 1981). Hence, it is important to recognize that the responses to rotation of these neurons may be altered by other sensory information and descending limbic projections under other experimental conditions.

The data from this study are consistent with the hypothesis that the caudal region of the parabrachial nucleus is a source of information about whole-body motion to limbic pathways (Balaban and Thayer 2001). Anatomical studies have shown that the caudal parabrachial nuclei project to the central amygdaloid nucleus (Norita and Kawamura 1980; Pritchard et al. 2000), the lateral bed nucleus of the stria terminalis (“extended amygdala”) (Pritchard et al. 2000), the frontal pole and anterior cingulate cortex (Porrino and Goldman-Rakic 1982), and the hypothalamus (Pritchard et al. 2000). Thus these neurons may convey information about body (and/or head) rotation to pathways that produce homeostatic and affective responses to body motion.

Three response components of parabrachial nucleus neurons were identified unambiguously from discharges during position trapezoid, whole-body rotation. First, the firing rates of all neurons were sensitive to rotational velocity in a plane with a prominent vertical component. Second, all cells displayed a signal that could be modeled parsimoniously as a leaky integration of rotational velocity in a plane with a vertical component. The leaky integrator component also showed cosine-like or rectified cosine-like directional tuning, but the spatial

**FIG. 10.** Static spatial tuning characteristics of units with non-0 elevation rotation axes for excitatory velocity responses. Top: the responses of the units shown in Figs. 5 and 6 are represented as response surfaces. Graphs plot the rotational velocity or (leaky) integrated velocity sensitivity as a function of azimuth and elevation and permit a direct comparison of rotational spatial tuning properties of velocity and integrated velocity response components. These response surfaces are termed static tuning characteristics because they show the response for rotation about any fixed axis. The velocity and integrated velocity sensitivity of these units to rotation about axes with different azimuths and elevations is plotted for 1 positive elevation axis neuron (a6301), 1 negative elevation axis neuron (a5902), and 2 rectified neurons (a5801 and a5901).
tuning was not correlated with the velocity sensitivity of the unit. Finally, approximately 60% of the cells also displayed vertical position sensitivity with cosine-like tuning as a function of the orientation of the rotation plane relative to the head. These tuning properties are consistent with inputs from the vestibular nuclei, which show cosine-like spatial tuning of responses to otolith, semicircular canal, and proprioceptive neck afferents (Graf et al. 1993; Kasper et al. 1988; Schor and Angelaki 1992). The rotational velocity sensitivity of these units was consistent with the reported velocity sensitivity of units from the vestibular nuclei in alert primates (e.g., Gdowski and McCrea 1999; Roy and Cullen 2001; Scudder and Fuchs

FIG. 11. Properties of angular velocity and vertical position responses of neurons with $\phi \neq 0$. A: positive elevation axis neurons ($\theta_{vel} > 0$, ●), negative elevation axis neurons ($\theta_{vel} < 0$, ■), and rectified elevation axis neurons (×) varied in the symmetry of velocity sensitivity during rotation about the preferred axis. B: polar plot of the magnitude of the 3-dimensional velocity response vector ($r$) as a function of its azimuth ($\theta_{vel}$). The population of negative elevation neurons (■) had a preferred $\theta_{vel}$ (azimuth) centered near nose-down ipsilateral (left) anterior canal–contralateral posterior canal plane to nose-down pitch rotation (Rayleigh test statistic: 9.35, $P < 0.01$). By contrast, the population of positive elevation axis neurons (●) showed no significant preferred direction. C: polar plot of the magnitude and best excitatory response direction ($\theta_{pos}$) for position-sensitive positive elevation axis neurons ($\theta_{vel} > 0$, ●), negative elevation axis neurons ($\theta_{vel} < 0$, ■), and rectified elevation axis neurons (×). D: the position-sensitive nonzero elevation axis neurons had significantly lower velocity sensitivity than the position-insensitive cells in both excitatory and inhibitory [nonpreferred] directions of rotation [repeated-measures ANOVA, $F(1,20) = 5.02$, $P < 0.05$].
1992), and all units displayed either cosine-like or rectified cosine-like tuning as a function of the orientation of the rotation axis. The leaky integrator response pattern has not been described in previous studies of the vestibular nuclei in primates, possibly as a consequence of the predominant use of sinusoidal velocity stimulation. The position sensitivity of the responsive units (range: 10.4 – 103.9 spikes · s⁻¹ · G⁻¹), though, was similar to reported position sensitivity of vestibular nucleus units in alert monkeys (Angelaki and Dickman 2000; Yakushin et al. 1999). Because parabrachial nucleus units were insensitive to eye movement, it is logical to suggest that they reflect input from eye-movement-insensitive vestibular nucleus neurons. Despite these similarities to the properties of vestibular nucleus neurons, it is important to note that neither the sources of the velocity, integrated velocity, and position signals nor relative contributions of semicircular canals, otolith organs, proprioceptors, or enteroreceptors to these responses can be resolved unambiguously by the experimental paradigm.

There are three basic orientations for excitatory rotational velocity responses of the sampled parabrachial nucleus neurons. The first population of neurons is excited by rotation about an axis with zero elevation; this is equivalent to a best response in a purely vertical rotation plane. The second group of cells showed maximum excitation to rotational velocity about an axis that produced both vertical and ipsilateral yaw rotation components. The best axes were centered at 0.97 rad of elevation but showed no preference in azimuth. Finally, a third population of neurons was excited best by rotation about an axis that included a contralateral yaw component. These axes were focused at an elevation of −0.42 rad and showed a preferred azimuth that produced best responses for nose-down rotation in ipsilateral anterior canal-contralateral posterior canal plane to pitch planes. In addition, nearly half of the neurons showed position sensitivity with maximal excitation for nose-up rotation between the vertical semicircular canal planes. It is suggested that these signals may contribute to detection of changes in body trajectory relative to gravity during loss of balance, which may trigger homeostatic and affective (e.g., panic responses). For example, an unexpected fall will produce a change in vertical angular velocity and in the position of the head and body relative to gravity. Similarly, generation of a righting response will produce a yaw axis rotation of the body toward a nose-down orientation, resulting in changes in both angular velocity (i.e., velocity and direction of rotation about a body or head axis) and orientation of the head and body relative to gravity. It is suggested that these types of behavioral contingencies can be discriminated by a comparison of signals from position-sensitive and -insensitive neurons with similar dynamic responses to rotation. These comparisons would presumable occur at sites receiving parabrachial nucleus input, such as the central amygdaloid nucleus and limbic regions of neocortex.

The common feature of all sampled PBN neurons was prominent vertical angular velocity sensitivity and a response resembling a leaky integration of velocity sensitivity during whole-body rotation. The dynamic pattern of responses is determined as a summation of spatially independent often rectified velocity and integrated velocity signals. As a result, the responses of a single cell may vary according to the stimulus orientation from a monophasic response to a biphasic response. A monophasic response may reflect velocity alone, integrated velocity alone, or a sum of velocity and integrated velocity components of the same polarity. A biphasic response is produced by velocity and integrated velocity components of opposite polarity. The net result of this phenomenon is that the temporal profile of the response to a position trapezoid often varies with the axis of rotation (e.g., Figs. 5 and 6).

The different patterns of summation of velocity and leaky integrated velocity signals displayed by parabrachial nucleus units produce different temporal filtering characteristics during movements. The responses of simulated units with the either the same or an opposite polarity of velocity and (leaky) integrated velocity responses are shown in Fig. 12A, which simulates responses to rotation about a best axis. The excitatory and
inhibitory responses were assumed to be symmetric. Based on the properties of units with a zero elevation best rotation axis, the velocity and integrated velocity gains were assumed to be equal. The simulated unit responses (Fig. 12A, top and middle) are shown for Gaussian velocity profiles ($\sigma = 0.04, 0.12,$ and $0.24$ s) with equal peak velocities (normalized to 1). For biphasic unit response (opposite polarity velocity and integrated velocity signals; Fig. 12A, top), the simulated response closely parallels the velocity of the displacement for narrow pulses but becomes attenuated and shifted in phase toward acceleration for wider pulses (associated with larger displacements). Thus cells with opposite polarities of velocity and integrated velocity responses display a quasi-high pass behavior relative to peak acceleration (Fig. 12B). By contrast, the simulated unit with velocity and integrated velocity responses of the same polarity (Fig. 12A, middle) shows a monophasic response that is broader than the velocity of the displacement, with a magnitude that increases for wider pulses (and greater displacements). Hence, it shows a quasi-low pass behavior relative to peak accelerations (Fig. 12B) but yields transient information about the magnitude of the displacement. Both types of component interactions, though, show equivalent velocity-related responses for rapid, brief perturbations.

It is important to note that velocity and leaky velocity integrator responses displayed by PBN neurons are frequently clipped (or even fully rectified) in the inhibitory (or nonpreferred) direction of rotation. Further, because the spatial tuning differs between these components, the population of neurons displays a wide diversity of patterns of variation in temporal filtering properties as a function of the axis of rotation. At this early stage of investigation, these properties clearly indicate that the neuronal response patterns have the capability to encode complex spatiotemporal characteristics of whole-body motion. It is suggested that these spatiotemporal filtering properties may be important for discrimination of situations requiring homeostatic and affective responses. However, a larger sample size will be needed to determine whether specific patterns of spatiotemporal filtering define distinct neuronal populations.

In conclusion, neurons in the caudal pole of the primate PBN and Kölliker-Fuse nucleus receive axonal projections from the superior vestibular nucleus and show characteristic spatially tuned responses to three-dimensional whole-body rotation with sensitivities similar to vestibular nucleus neurons. Because the responses of all neurons reflect an interaction between spatially distinct signals related to angular velocity and a signal resembling a leaky integration of angular velocity, both the spike rate and the temporal properties of discharges may encode the direction of whole-body rotation. Thus a vestibular-recipient region of the PBN and the Kölliker-Fuse nucleus is a potential relay of body-orientation information to pathways that produce homeostatic and affective responses.

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