Firing Behavior of Vestibular Neurons During Active and Passive Head Movements: Vestibulo-Spinal and Other Non-Eye-Movement Related Neurons

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McCrea, Robert A., Greg T. Gdowski, Richard Boyle, and Timothy Belton. Firing behavior of vestibular neurons during active and passive head movements: vestibulo-spinal and other non-eye-movement related neurons. *J. Neurophysiol.* 82: 416–428, 1999. The firing behavior of 51 non-eye movement related central vestibular neurons that were sensitive to passive head rotation in the plane of the horizontal semicircular canal was studied in three squirrel monkeys whose heads were free to move in the horizontal plane. Unit sensitivity to active head movements during spontaneous gaze saccades was compared with sensitivity to passive head rotation. Most units (29/35 tested) were activated at monosynaptic latencies following electrical stimulation of the ipsilateral vestibular nerve. Nine were vestibulo-spinal units that were antidromically activated following electrical stimulation of the ventromedial funiculi of the spinal cord at C1. All of the units were less sensitive to active head movements than to passive whole body rotation. In the majority of cells (37/51, 73%), including all nine identified vestibulo-spinal units, the vestibular signals related to active head movements were canceled. The remaining units (n = 14, 27%) were sensitive to active head movements, but their responses were attenuated by 20–75%. Most units were nearly as sensitive to passive head-on-trunk rotation as they were to whole body rotation; this suggests that vestibular signals related to active head movements were cancelled primarily by subtraction of a head movement efference copy signal. The sensitivity of most units to passive whole body rotation was unchanged during gaze saccades. A fundamental feature of sensory processing is the ability to distinguish between self-generated and externally induced sensory events. Our observations suggest that the distinction is made at an early stage of processing in the vestibular system.

INTRODUCTION

An accurate view of the external world depends on the ability to distinguish between sensory experiences produced by external forces and sensory events that are produced by self-generated movements. The distinction presumably is made by comparing sensory signals with an internal estimate of the sensory consequences of self-generated movements (Grüsser 1986; Mergner et al. 1997; von Helmholtz 1867; von Holst and Mittelstaedt 1950). The internal estimate generally is considered to be constructed from efference copy signals and proprioceptive reafferent sensory inputs (von Holst and Mittelstaedt 1950). The interaction between efference copy and sensory reafferent signals clearly occurs at cognitive levels of sensory processing (Anderson et al. 1997; von Helmholtz 1867). However, the interaction also may occur at early stages of sensory processing (Bell et al. 1997; Duffy and Lombrosco 1968; Ghez and Pisa 1972; von Holst and Mittelstaedt 1950). The best known example of such early interaction occurs in muscle spindles, where the signals carried by gamma motoneurons related to active muscle contractions modify signal transduction within the spindle itself and allow it to respond primarily to external forces that stretch it (Burke et al. 1980; Vallbo 1981).

In the vestibular system, the distinction between sensory events that are related to active, voluntary head movements and passive head movements is important for perception of spatial orientation and for postural control (Blouin et al. 1998; Howard 1997; Merfeld et al. 1993; Mergner et al. 1997; von Holst and Mittelstaedt 1950). For example, the sensory signals transduced in the crista ampullaris of the semicircular canal are related to angular head rotation (Goldberg and Fernandez 1971), but these signals are processed in different ways during active and passive head movements. Active head rotation in the dark is usually not accompanied by a sense of self-motion, but passive rotation of the head or body produces a subjective sensation of self-motion (Howard et al. 1998; Mergner et al. 1983). Passive rotation of the head in space produces reflexive eye, neck, and limb movements (Wilson and Melvill Jones 1979), but reflexive movements are usually absent during active head movements (von Holst and Mittelstaedt 1950). These behavioral and psychophysical observations suggest that semicircular canal vestibular signals are modified by efference copy and/or proprioceptive signals related to active head movements. One question is whether this interaction occurs at an early stage of sensory processing—at secondary vestibular neurons in the vestibular nuclei that receive direct inputs from the vestibular nerve.

This paper focuses on the processing of vestibular signals by non-eye movement related vestibular neurons, including antidromically identified vestibulo-spinal neurons, during active head rotations generated during gaze saccades. We present evidence that vestibular reafferent signals related to active self-generated head movements are canceled or attenuated, whereas signals related to passive head movements are largely unaffected by active head movements. A preliminary report has been published elsewhere (Boyle et al. 1996).

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METHODS

Surgical preparation

Three adult squirrel monkeys were prepared for chronic recordings of eye and head movements, single-unit activity, and electrical stimulation of both labyrinths. Most methods are described in detail elsewhere (Gdowski and McCrea 1999). A small bolt was attached to the cranium with dental acrylic so that the head could be restrained during experiments. Labyrinthine stimulating electrodes were implanted bilaterally in the middle ears. A scleral search coil was implanted on one eye so that eye movements could be recorded with the magnetic search coil technique. Stimulating electrodes made of Teflon-coated platinum wire (75 μm), exposed ~1 mm from their tips, were implanted through a small opening in the dura into the ventromedial funiculus of the spinal cord on both sides of the midline at C1 (Boyle 1993; Boyle et al. 1996) in two animals. The electrodes were attached to the dura with a spring interface and cemented to the occipital bone. The location of the spinal electrodes in both animals was verified histologically.

Experimental setup

The experimental apparatus is illustrated in Fig. 1*A*. The monkey was seated in a Plexiglas box on a vestibular turntable (a) that was surrounded by a cylindrical screen (not shown). The head was attached to a rod that rotated within a ball bearing assembly (f) that was fixed to the turntable. The rod's rotational axis was coincident with the turntable's rotational axis and was positioned at the level of the external auditory meatus within 5 mm of C1–C2 axis of rotation. The apparatus allowed the monkey to generate angular head movements (±40°) in the plane of the horizontal semicircular canal. A harness (c) was placed over the animal's shoulders to restrict body movements and to align its trunk toward the screen. Slight pitch and roll postural adjustments were accommodated with a universal joint (e) that was located in-line with the rod above the animal's head (7 cm). Passive whole body rotation with the head-fixed was accomplished by preventing the rod from rotating during turntable rotation (Fig. 1*A, center inset*). Active head movements were prevented by locking the rod in place with a block (i) and by disabling the universal joint with a rigid sleeve (h). Passive head on trunk rotation was produced by rotating the rod manually or with a motor (j) mounted on the ceiling (Fig. 1*A, right inset*). Head position was measured with a search coil (k) placed on the rod below the universal joint. Angular turntable velocity was recorded with an angular velocity sensor (Watson). Animals were trained to fixate and pursue visual targets that were laser projected onto the screen from the turntable with mirror galvanometers. Head, eye, turntable and target position signals were sampled at 200–500 Hz and saved on a computer for off-line analysis.

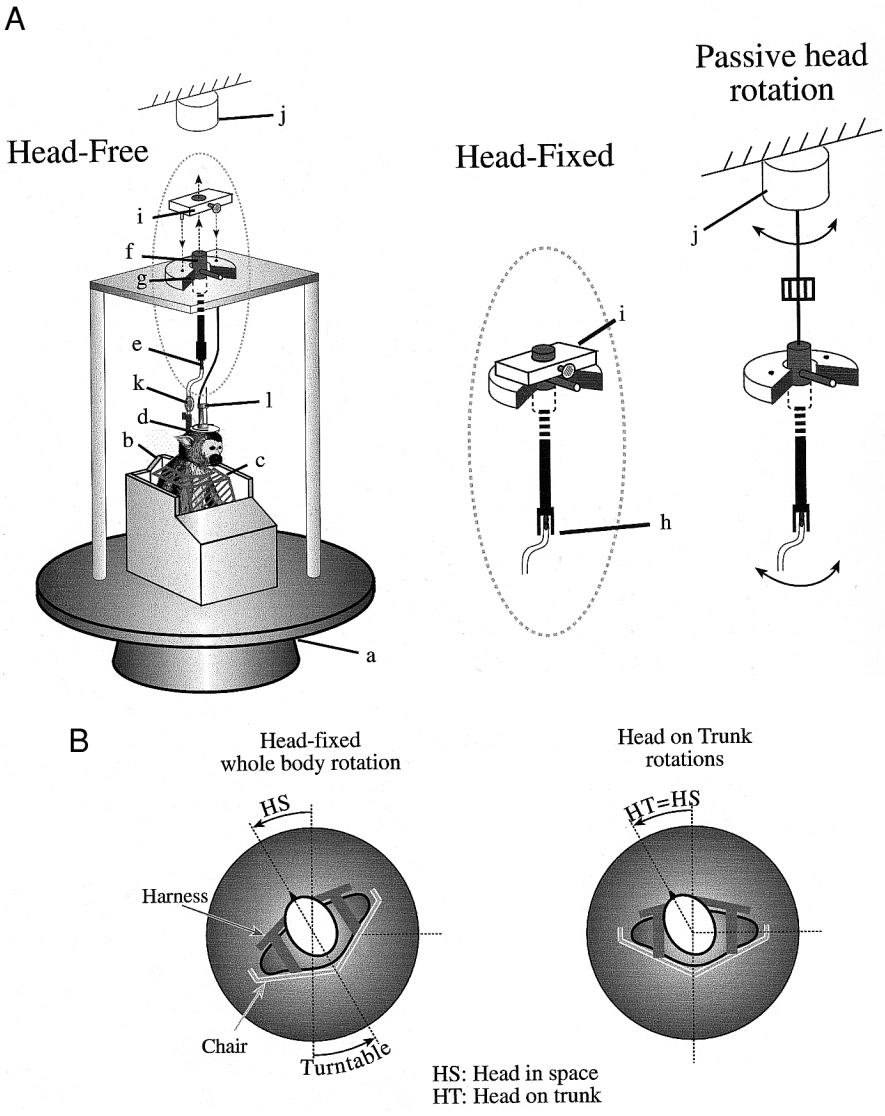

FIG. 1. *A*: experimental setup. Squirrel monkeys were seated in a Plexiglas chair on a vestibular turntable (a) and faced a cylindrical screen. A harness was placed over the animal's shoulders (c) that aligned its trunk forward by keeping it against the back of the chair (b). Animal's head was attached to a rod (d) that rotated within a ball-bearing assembly (f). In the head-free condition (exploded view), the animal was allowed to make voluntary head movements in the yaw plane, which were limited to ±40° (g). Slight postural adjustments were accommodated with a universal joint (e) mounted in-line with the rod. Head movements could be restrained (*center inset*) by fixing the rod in place by attachment of a block that was keyed to the table (i), and by covering the universal joint with a rigid sleeve (h). Animal's head could be passively rotated (*right inset*) by rotating the rod by hand or by attaching it to a motor (j) on the ceiling. Head position was monitored with a search coil (k). Microelectrodes were advanced with a remotely controlled hydraulic microdrive (l). *B*: top-view illustrations of the experimental paradigms. Shown are the position of the animal's head and trunk and the table. *Left*: whole body rotation with the head fixed. *Right*: passive or active head-on-trunk movements. HS, head velocity in space; HT, head-on-trunk velocity in space.

Single-unit recording

A micromanipulator was used to stereotaxically insert an epoxy-insulated tungsten microelectrode (4–7 MΩ) attached to a hydraulic microdrive into the cerebellum through a guide tube (22G). The electrode and microdrive were then secured to the skull. Microelectrode location in the vestibular nuclei was determined by monitoring the synaptic field potentials evoked by shocking the ipsilateral vestibular nerve (0.1 ms monophasic perilymphatic cathodal pulses, 50–300 μA). The relative location of the microelectrode within the vestibular nuclei was estimated based on the location of other identified physiological landmarks in the brainstem such as the vestibular nerve, the abducens nucleus, and the nucleus of the solitary tract. Most of the units included in this study were estimated to be located in regions of the vestibular nuclei approximately 0.5–3 mm caudal to the abducens nucleus and 3–5 mm from the midline (see Gdowski and McCrea 1999 for details). Units were considered to receive monosynaptic input from the vestibular nerve if spike potentials were evoked at latencies ≤1.3 ms with currents that were at the threshold of evoking responses. Units were tested for antidromic activation following electrical stimulation of the spinal cord (0.1-ms monophasic pulses, 50–250 μA). They were considered to be activated antidromically if spikes were evoked at constant latencies near the threshold current and collided with synaptically evoked spikes or spontaneously occurring spikes.

Action potentials (AP) of single units were time marked with a real time clock (0.1 ms resolution) after they were amplified conventionally and discriminated with a dual window discriminator (Bak). Unit recordings were discontinued if the signal-to-noise ratio was low (<2). Unit discharge rates were computed for each A/D sample (binwidth 2–5 ms) using a time-symmetric algorithm in which discharge rate was computed from the occurrence of spikes immediately before, after, and during the sample.

Experimental protocol

Whole body rotation (WBR) was used as a search stimulus as the electrode was advanced toward the vestibular nuclei. The firing behavior of single units was studied during passive WBR with the head restrained and with the head free to move. Unit responses during active head movements typically were recorded for several minutes while the monkey generated spontaneous gaze saccades in the absence of a target. The head movements generated during gaze saccades had peak head velocities ≤400°/s. The distribution of peak head velocity and acceleration of gaze saccades recorded concomitantly with single-unit recordings in the three animals is illustrated in Fig. 2.

Unit responses during active gaze shifts were compared with responses during passive whole body rotation and passive forced head and neck rotation (Fig. 1*B*). Ideally, the unit response during active head movements produced during gaze saccades would have been compared with the unit's response during a step change in turntable position that had a similar acceleration and velocity. However, this was not possible because the turntable's maximum acceleration (~350°/s^2) was significantly lower than the peak head acceleration of most gaze saccades. Alternatively, the active head movement responses were compared with responses recorded during sinusoidal WBR at 0.5 Hz (peak velocity 40°/s) and 2.3 Hz (20°/s). The higher frequency stimulus had the higher peak acceleration (289°/s^2) and was used to estimate unit sensitivity to passive head movement. The responses of most units also were recorded during passive sinusoidal head on trunk rotation. In some units, passive head on trunk velocity trapezoids (50–100°/s peak velocity, 1,200–3,700°/s^2 peak acceleration) were produced with the ceiling motor.

Data analysis

Unit sensitivities to head and eye position were assessed from 40 to 120 records of steady fixation when the head was free and when the head was restrained. Eye position sensitivity was assessed with a multiple regression analysis of the mean firing rate against vertical and horizontal eye position. Unit sensitivity to eye velocity was assessed from records of ocular saccades and from records of sinusoidal (typically 0.5 Hz, 40°/s peak velocity) smooth pursuit eye movements. The firing rate of the units included in this study was poorly correlated with eye position during periods of steady fixation and was not modulated during smooth pursuit eye movements. Sensitivity to head position was assayed in non-eye movement related neurons by linear regression of firing rate versus horizontal head position.

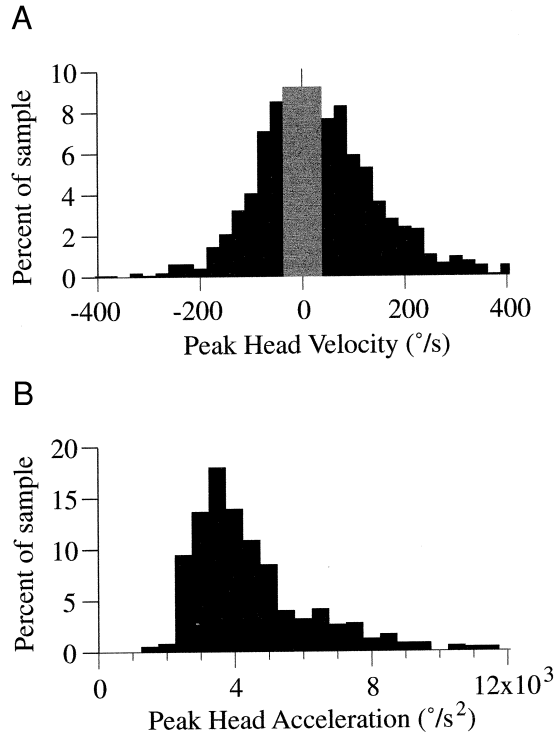

FIG. 2. Dynamic characteristics of saccade-related head movements that were included in analysis of single unit firing behavior. *A*: peak head velocity of saccades included in analysis. Saccades in which head velocity was <40°/s (gray bins) usually were excluded from analysis. Positive values are rightward saccades. Negative values are leftward. *B*: peak head acceleration of saccades whose peak head velocity was >40°/s.

UNIT SENSITIVITY TO PASSIVE HEAD ROTATION IN SPACE DURING WBR. Unit sensitivity to passive horizontal head rotation was assessed from responses during 2.3 Hz whole body rotation. The records were edited to include only epochs when the monkey was alert and to eliminate records related to quick phases of nystagmus. The gain and phase of unit responses were determined by regressing a sinewave function to an average of ≥25 stimulus cycles. The rotational response was expressed as a first-order differential equation based on head velocity (g_v) and head acceleration (g_a).

$$\mathrm{FR}(t) = k_0 + g_v H_v(t) + g_\alpha H_a(t) \qquad (1)$$

where FR is unit firing rate, k_0, is spontaneous rate, H_v is head velocity, and H_a is head acceleration. The estimates of head velocity sensitivity obtained with a regression of *Eq. 1* to the unit's responses were nearly identical to the estimates derived from decomposition of the sinusoidal fit to the unit responses into velocity and acceleration components based on the phase of the unit's response. However, the addition of a head acceleration term improved the fit to responses evoked by the slightly distorted sinusoidal stimulus that was used at 2.3 Hz. The improvement was particularly apparent for units with large response phase leads.

UNIT SENSITIVITY TO ACTIVE HEAD ROTATION DURING GAZE SACCADES. Spontaneous saccades were identified as gaze shifts with high peak accelerations (>1,000°/s^2). A database of the gaze saccades recorded with each unit was compiled that included the starting eye and head positions, direction, final eye and head position, peak head and gaze velocity, time-to-peak head and gaze velocity, and duration of the gaze and head movements. Groups of saccades that had similar characteristics were aligned and averaged with respect to saccade onset, peak gaze velocity, peak head velocity, or the end of the saccade. In this study, unit responses were quantified primarily by averaging responses during saccades with similar peak head velocity.

The active head movement responses were usually assessed during gaze saccades that had peak head velocities between 50 and 150°/s. Unit discharge rate during active head movements was modeled with *Eq. 1*. Since units were less sensitive to active head movement than to passive head movement, a quantitative estimate of the attenuation (A) in sensitivity to head rotation during active head movements was made with the following equation:

$$\mathrm{FR}(t) = k_0 + (1 - A)[g_v H_v(t) + g_\alpha H_a(t)] \quad (2)$$

The population statistics quoted in this paper are means ± SE.

RESULTS

The majority (43/51) of the horizontal canal-related vestibular nucleus units included in this study had discharge rates that were not correlated with eye position or with eye velocity during fixation, saccades, or pursuit eye movements. Eight units also were included that were inhibited weakly during most ocular saccades but were not otherwise sensitive to eye movements. Approximately half of the units (26/51) were related to ipsilateral head velocity during WBR (type I units), and the remaining 25 units were related to contralateral head velocity (type II units).

Most units tested (29/35; 16/17 type I, and 13/18 type II) were monosynaptically activated following electrical stimulation of the ipsilateral vestibular nerve. Nine units, including four type I units and five type II units, were antidromically activated following electrical stimulation of C1. Three of the antidromically identified vestibulo-spinal units were inhibited during saccades. Orthodromic and antidromic evoked spikes of a vestibulo-spinal unit are illustrated in Fig. 3. Stimulation of the ipsilateral vestibular nerve evoked short-latency spikes (0.7–1.3 ms), which suggested that the cell received monosynaptic inputs from the vestibular nerve. Spikes also were evoked at a constant latency (0.5 ms) following stimulation of the ventromedial funiculus of the spinal cord at C1. These were considered to be evoked antidromically because they were blocked by spontaneous or vestibular nerve evoked spikes that occurred just before the C1 stimulus (Fig. 3, dashed trace). The records illustrated in Figs. 4, 7, and 10*A* were from this cell. The records illustrated in Figs. 5, 6, and 10*B* were obtained from other vestibulo-spinal units. Most units were estimated to be located in the midregion of the vestibular nuclei, just caudal to the entrance of the vestibular nerve (for details, see Gdowski and McCrea 1999).

Unit responses to WBR

All units in this study were sensitive to angular head velocity (>0.2 sp/s/1/°/s re head velocity in space) during passive WBR in the plane of the horizontal semicircular canals. WBR responses usually were recorded at two frequencies (0.5 and 2.3 Hz). Type I units tended to be more sensitive to WBR than type II units. At 2.3 Hz, type I units had an average gain of 0.99 ± 0.15 sp/s/°/s re head velocity, whereas the average gain of type II units was 0.57 ± 0.06 sp/s/°/s. The rotational responses typically phase led head velocity. The mean phase lead was 16.9 ± 3.0° for type I units and 21.7 ± 4.3° for type II units.

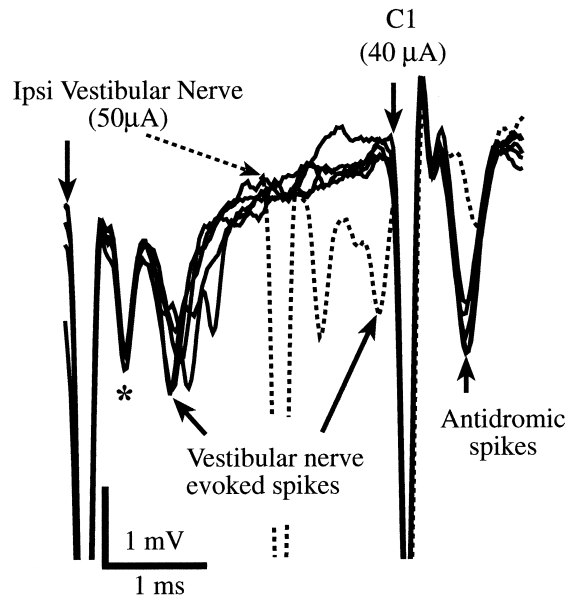

FIG. 3. Electrophysiological identification of a secondary vestibulo-spinal neuron. Electrical stimulation of the ipsilateral vestibular nerve evoked orthodromic spikes at monosynaptic latencies (0.7–1.3 ms). Stimulation of the C1 spinal cord evoked antidromic spikes at a constant latency (0.5 ms). Shortening the interval between vestibular nerve evoked orthodromic spikes and stimulation of the spinal cord blocked antidromic invasion of the C1 evoked spike (dashed trace). Asterisk indicates the field potential associated with the vestibular nerve fiber volley. The relatively large amplitude of this potential suggests that the recording site was in the ventral portion of the lateral vestibular nucleus at the level of afferent entry into the vestibular nuclei.

Active head movement responses

Vestibular units were less sensitive to horizontal head movements during gaze saccades than during WBR or during forced head on trunk rotation. In most (37/51) units, sensitivity to active head movements during gaze saccades was reduced by ≥80%. These units will be referred to as canceled units. The remaining 14 units were sensitive to active head movements during gaze saccades, but their vestibular signals were attenuated by 20–75% during active head movements in one or both directions. These units will be referred to as attenuated units. Each of the two unit classes is described in detail below.

CANCELED UNITS. Most of the 37 units whose head movement signals were canceled during gaze saccades were activated at a monosynaptic latency after electrical stimulation of the ipsilateral vestibular nerve (19/24 tested). Sixteen of the units had type I responses during WBR and 21 had type II responses. The secondary canceled units included all nine of the antidromically identified vestibulo-spinal neurons. On average, the responses of canceled units to WBR at 2.3 Hz had a gain of 0.77 ± 0.08 sp/s°/s and phase led head velocity by 22 ± 4°.

The firing behavior of a vestibulo-spinal neuron during passive and active head movements is shown in Fig. 4. Figure

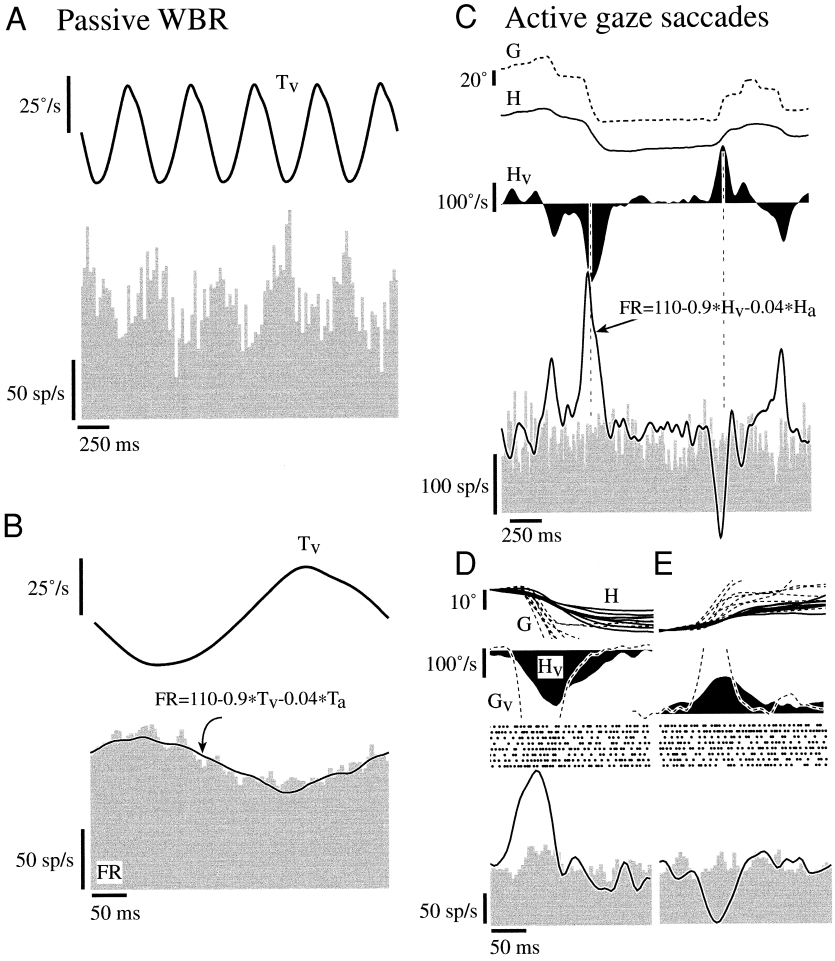

FIG. 4. Response of a canceled vestibulo-spinal unit during passive whole body rotation (*A* and *B*) and spontaneous gaze saccades (*C*–E). *A*: whole body rotation (WBR) with head restrained. *Top*: turntable velocity (T_v). *Bottom*: unit firing rate. *B*: averaged WBR response (88 cycles). Sinusoidal fit to discharge rate is superimposed. *C*: firing behavior during spontaneous gaze saccades. *Top* to *bottom*: gaze position (G, dashed trace), head position (H, solid trace), head velocity (H_v filled area), discharge rate (FR, gray histogram), and expected response (superimposed line). *D* and *E*: averaged unit responses ($n = 8$) during gaze saccades in the unit's vestibular ON-direction (*D*) and OFF-direction (*E*). Records were averaged with respect to peak head velocity (dashed vertical lines in *C*). Records of gaze position and gaze velocity (G_v) have been truncated. A model based on the rotational response during WBR is shown superimposed on the discharge rate (*C–E,* solid traces superimposed on discharge rate histograms). Upward is ipsilateral in all traces.

4*A* shows the unit's response during five WBR cycles while head movements were restrained. The averaged response recorded over 88 stimulus cycles is shown in Fig. 4*B*. The peak velocity of the sinusoidal rotation was 21°/s, and the peak modulation in unit firing rate was 20.6 sp/s. The unit's response phase led head velocity by 29.3°. The solid line superimposed on the unit histogram in Fig. 4*B* is a model of firing rate based on estimated sensitivity to head velocity ($g_v = 0.86$ sp/s/°/s) and head acceleration ($g_a = 0.042$ sp/s/°/s^2).

The unit's firing behavior during spontaneous gaze saccades is shown in Fig. 4*C*. The *top three traces* are records of gaze (dashed trace, G) and head (solid trace, H) position and head velocity (filled trace, H_v) during eight gaze saccades. The expected change in discharge rate, based on the unit's passive WBR response, is superimposed on the firing rate histogram (solid black line in Fig. 4, *C–E*, *bottom*). Averages of eight large gaze saccades made in the unit's ON- and OFF-direction are shown in Fig. 4, *D* and *E,* respectively. In both panels, records were aligned at peak head velocity. Records of averaged head velocity and gaze velocity are also shown. Firing rate essentially was unaffected by head movements generated during both ipsilateral and contralateral saccades; even though the average peak head velocity exceeded 100°/s, and the expected changes in firing rate were more than 100 sp/s.

Cancellation of vestibular signals during active head movement was rarely complete. Units whose vestibular signals were canceled during saccades in one direction always had highly attenuated responses in the opposite direction. However, vestibular signals in the ON- and OFF-directions were not always equally attenuated. The unit illustrated in Fig. 4 was insensitive to active head movements during OFF-direction saccades (attenuation factor $A = 1.0$, *Eq. 2*). Its responses during ON-direction saccades were reduced by 81% ($A = 0.81$), but not abolished. In a few units ($n = 3$) the highly attenuated response recorded during gaze saccades was reversed in direction from the predicted response ($A > 1.0$). The cancellation of vestibular signals during gaze saccades was not dependent on saccade amplitude, but some units had a small residual signal related to head acceleration during very large head movements. On average, units with canceled active head movement signals were more attenuated during OFF-direction saccades ($A = 0.99 \pm 0.05$) than during ON-direction saccades ($A = 0.86 \pm 0.06$).

Eight units with canceled vestibular signals exhibited a reduced firing rate during gaze saccades, regardless of their direction. The inhibition tended to be stronger during large saccades than during small saccades and was related temporally to the duration of the head shift. The firing rate of five of the eight units also decreased during ipsi- and contralateral ocular saccades. The other three inhibited units were not inhibited during ocular saccades and were activated antidromically following electrical stimulation of C1. Figure 5 shows averaged records of a vestibulo-spinal unit that fired in phase with ipsilateral head velocity during passive WBR (Fig. 5*A*)

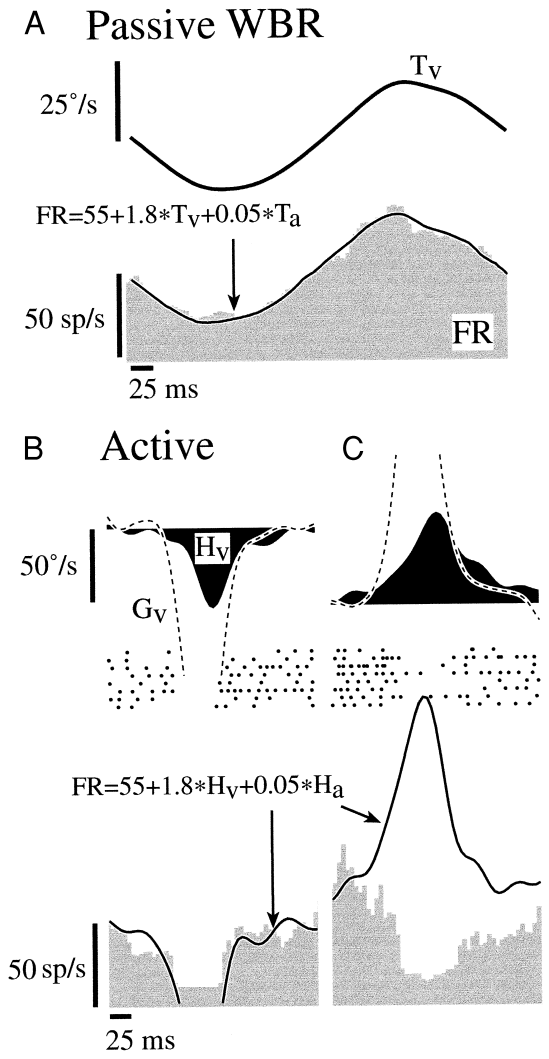

FIG. 5. Canceled vestibulo-spinal unit that was inhibited during gaze saccades. *A*: averaged WBR response with head restrained (136 cycles). Unit was inhibited during saccades in the vestibular OFF-direction (*B*) and ON-direction (*C*). All records are averages. Spike rasters for each of the 8 saccades averaged are illustrated in *B* and *C*. Trace superimposed on the average unit response is the expected response. Abbreviations and conventions are the same as in Fig. 4.

and was inhibited during both OFF-direction (Fig. 5*B*) and ON-direction (Fig. 5*C*) gaze saccades. The expected change in discharge rate, based on the unit's passive WBR response, is superimposed on the firing rate histogram.

Sensitivity of canceled units to passive forced head movement. Neck afferent inputs to secondary vestibular units were evaluated from responses during passive head-on-trunk rotation and during passive trunk rotation while the head was fixed in space. Figure 6 shows the head-on-trunk rotation responses of another vestibulo-spinal unit. The unit was modulated strongly in phase with ipsilateral head velocity during passive WBR (Fig. 6*A*). The unit's response during comparable (≈100°/s peak head velocity and ≈2,000°/s^2 peak head acceleration) passive (Fig. 6*B*) and active (Fig. 6*C*) head-on-trunk movements was quite different. Its firing rate was modulated strongly during passive, forced head-on-trunk rotation, but it was weakly inhibited during active head movements.

Because neck proprioceptive inputs failed to inhibit the unit during passive head on trunk rotation, it is unlikely that the unit's lack of response to active head movement was due to neck reafference. Most canceled units (8/13 tested) exhibited similar behavior during passive forced head movement; i.e., they did not have canceled responses during passive head on trunk rotation. Thus, the neck proprioceptive inputs alone were usually not sufficient to account for the reduction in sensitivity of canceled units to head movements during gaze saccades.

Sensitivity of canceled units to passive head movement during gaze saccades. Canceled vestibular units were not sensitive to rotations of the head in space that were self-generated, but they remained sensitive to passive head rotation in space during saccades. Figure 7 shows an analysis of the passive head movement sensitivity of a secondary vestibulo-spinal unit during active head movements produced during head-free WBR (2.3 Hz, 20°/s). The canceled responses of this unit during spontaneous gaze saccades were illustrated in Fig. 4. The averaged responses during passive head-restrained WBR are shown in Fig. 7*B*. The unit's sensitivity to passive WBR during active head movements was estimated by averaging only the responses that occurred during quick phases of nystagmus that were accompanied by active head movements (see arrows and included regions denoted in Fig. 7*A*). These saccade-related responses were averaged with respect to the stimulus frequency and are shown in Fig. 7*C*.

The function fit to the averaged response of this vestibulo-spinal unit during active head movements was indistinguishable from the fit to the response recorded in the absence of active head movements (Fig. 7*B*) even though the active head-on-trunk movements significantly altered head velocity in space (dotted trace in Fig. 7*C*) during gaze saccades. Thus, the unit was insensitive to active head movements, but it remained sensitive to passive head movement in space during active head movements.

Most of the units with canceled responses during gaze saccades exhibited were as sensitive to passive head movement in space during active head movements as they were when head movements were restrained. Two units were more sensitive to passive rotation during quick phases, and one unit was significantly less sensitive to passive head rotation during quick phases. The eight canceled units that were inhibited during gaze saccades were less sensitive to passive head movements than active head movements. But the reduction was largely attributable to asymmetric inhibition during active head movements and to their low firing rate during quick phases that occurred during passive rotation in the off-direction. The ratio of the sensitivity of the other cancelled units to table velocity during quick phases (g_q) and during head-restrained WBR (g_v) was near unity ($g_q/g_v = 0.96 \pm 0.08$, $n = 18$). The difference between the unit response phase with respect to turntable velocity during quick phases (θ_q) and during WBR (θ_v) was also small ($\theta_q - \theta_v = -9.58 \pm 11.6°$). The effect of quick phases of head nystagmus on the passive head movement sensitivity of canceled units during 0.5 Hz WBR ($g_q/g_v = 0.99 \pm 0.14$, $\theta_q - \theta_v = 13.6 \pm 7.0°$, $n = 11$) was qualitatively similar to that observed during 2.3 Hz WBR.

ATTENUATED UNITS. Fourteen units (11 type I and 3 type II) were sensitive to active head movements during gaze saccades, although the head movement response was attenuated. Most

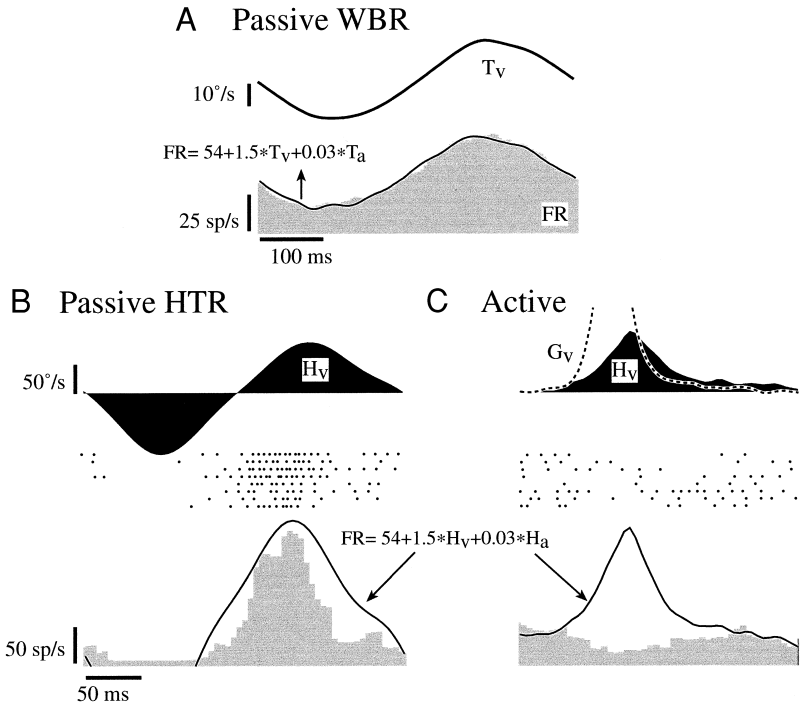

FIG. 6. Firing behavior of another vestibulo-spinal unit during passive and active head-on-trunk rotations. *A*: rotational response during WBR with head-on-trunk rotation prevented (average of 99 cycles). *B*: passive head-on-trunk rotations (3.4 Hz. 90°/s, 8 cycles). *C*: averaged responses during gaze saccades in the unit's vestibular ON-direction. Spike rasters for each cycle (*B*) and each of the 8 saccades averaged (*C*) are illustrated. Calibrations in *B* also apply to *C*. Unit was sensitive to ipsilateral head velocity evoked by passive WBR and head-on-trunk rotation but not during ipsilateral active head movements. A model based on the unit's response during WBR is superimposed on discharge rate histogram. Abbreviations and conventions are the same as in Fig. 4.

attenuated units were activated monosynaptically following electrical stimulation of the ipsilateral vestibular nerve (10/11 tested), and none of the three units tested was antidromically activated after electrical stimulation of the spinal cord. On average, the WBR responses of attenuated units at 2.3 Hz had a gain of 0.67 ± 0.10 sp/s/°/s and phase led head velocity by 18 ± 4°.

The type II unit, illustrated in Fig. 8, was more sensitive to active head movements than any other unit, but its response was attenuated during active head movements in one direction. The neuron was activated at a monosynaptic latency after electrical stimulation of the vestibular nerve. A model derived from its WBR response (Fig. 8*A,* solid line) is superimposed on its responses during active head movements produced during gaze saccades (Fig. 8, *B* and *C*). During contralateral, vestibular ON–direction gaze saccades (Fig. 8*B*), the unit's firing rate was close to the response predicted from its sensitivity to passive head movement. However, during OFF-direction saccades (Fig. 8*C*), the unit's response was smaller than predicted. The reduction in head movement sensitivity of all attenuated units ranged from 20 to 75%. Most units had attenuated responses during both ipsi- and contralateral saccades but half of the units had asymmetric attenuations. In those cells, like the unit illustrated in Fig. 8, the response attenuation was 15–40% greater during OFF-direction gaze saccades than during active head movements in the ON-direction. On average, the response attenuation of attenuated units was larger for head movements in the vestibular OFF-direction ($A = 0.46 \pm 0.05$; $n = 14$) in comparison with the response attenuation for head movements in the ON direction ($A = 0.29 \pm 0.05$). In most attenuated units, attenuated responses during saccades could be reasonably fit by assuming the reduction in response was produced by the addition or removal of an input whose dynamic characteristics were similar to WBR signals.

The reduction in response amplitude of attenuated units during gaze saccades was attributable, in part, to asymmetric neck proprioceptive inputs. Most units (6/8 tested) were sensitive to head rotation during passive head on trunk rotation. Figure 9 shows the firing behavior of the unit illustrated in Fig. 8 during passive and active neck rotation. The unit's firing rate was modulated weakly in phase with ipsilateral neck velocity (N_v) during sinusoidal rotation of the trunk while the head was held fixed in space (Fig. 9*A*). The neck rotation signal was smaller and opposite in direction to the unit's vestibular signal evoked during WBR (Fig. 8, *A* and *B*). Figure 9, *B–E,* shows the unit's responses during passive forced head on trunk rotation and gaze saccades. The solid black traces are the responses expected from the unit's sensitivity to WBR (equation in Fig. 8*A*). The solid red traces are the responses expected from the unit's sensitivity to both neck and vestibular inputs. The unit's responses during head-on-trunk rotation (Fig. 9*B*) and gaze saccades (Fig. 9*C*) in the vestibular ON-direction were best predicted by the model based on sensitivity to passive WBR (i.e., vestibular inputs) alone. During head-on-trunk rotation, the unit's response in the vestibular OFF- direction (Fig. 9 *D* and *E,* respectively) was better fit by a model that included the unit's sensitivity to both vestibular and neck rotation, but both models predicted more inhibition during OFF-direction active head movements than was observed.

Effects of saccade amplitude on unit discharge rates

In Fig. 10, the discharge rates of a canceled unit (*A*), a canceled unit that was inhibited during gaze saccades (*B*), and an attenuated unit (*C*) are plotted as a function of peak head velocity during gaze saccades of different amplitudes made in both directions.

In the plots, each point is the unit discharge rate at the time of the peak head velocity during a gaze saccade; dashed line in each of the figures indicates spontaneous firing rate (labeled SR). The expected responses based on each unit's sensitivity to head velocity during WBR are plotted as solid line. The can-

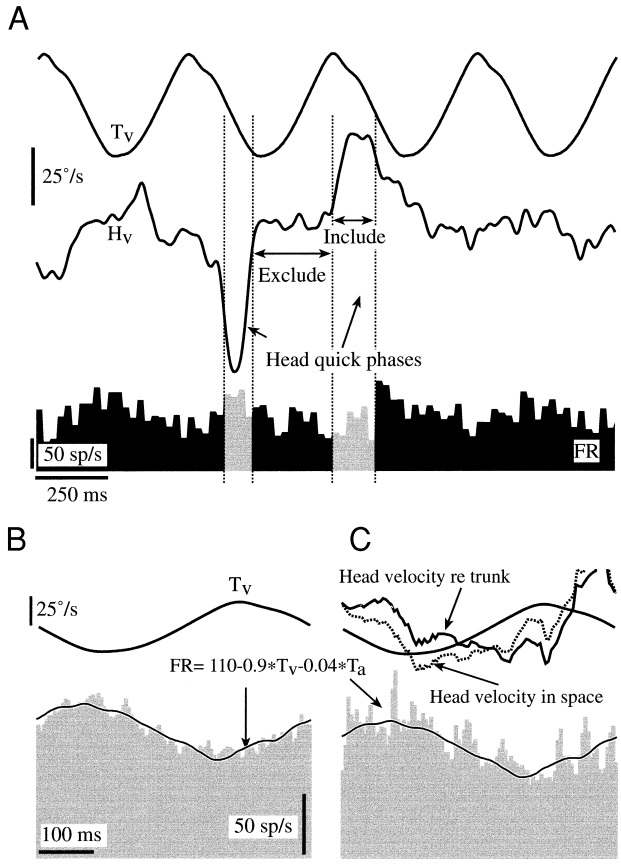

FIG. 7. Responses of a vestibulo-spinal unit to passive WBR during active head movements. Monkey was free to move its head in the yaw plane while being passively rotated on the turntable. *A*: sample records of a canceled unit during head-free WBR. Dashed vertical lines demarcate epochs related to active head movements (arrows) that were averaged with respect to the stimulus frequency. *B*: averaged response to passive rotation when the head was restrained. *C*: averaged response to passive rotation during active head movements. Sinusoidal fit to the unit's discharge rate during head-fixed WBR is superimposed on the unit responses in *B* and *C*. Number of cycles in averages was 88 (*B*) and 48 (*C*). Abbreviations and conventions are the same as in Fig. 4.

celed vestibulo-spinal unit (Fig. 10*A*) was insensitive to saccades in either direction, regardless of their peak head velocity, and had peak firing rates that were distributed about its spontaneous rate. The discharge rate of the inhibited vestibulo-spinal unit (Fig. 10*B*) was usually less than the spontaneous rate regardless of the peak head velocity of the active head movement. The attenuated unit (Fig. 10*C*) had responses that changed proportionally with changes in head velocity in space, but these responses were smaller than would have been predicted from the unit's WBR response during large head movements in the units ON-direction and larger than predicted during many OFF-direction saccades.

DISCUSSION

The main finding in this study is that the vestibular signals carried by secondary non-eye movement related neurons in the vestibular nuclei are modified during active head movements. The sensory signals related to active head movements were effectively canceled in most of these neurons, including all of the vestibulo-spinal neurons that were identified. Sensitivity to passive head rotation was preserved. Some units were sensitive to active head movements, but their responses were attenuated and directionally asymmetric. Thus, the head movements that accompany voluntary gaze shifts strongly affect sensory processing in the vestibular nuclei.

The change in unit sensitivity to vestibular stimulation was in part due to neck proprioceptive reafferent inputs that were demonstrable during passive head-on-trunk rotation. However, these proprioceptive inputs were usually too weak to account for the suppression of vestibular signals in canceled units. An additional input, presumably an efference copy of neck motor commands, is apparently also used to cancel vestibular signals related to self-generated head movements.

In the following discussion, we briefly review previous studies of vestibular unit responses during gaze saccades. We then will discuss the possible mechanisms responsible for modifying vestibular signals during active head movements and the role non-eye movement units may have in different central vestibular functions. We will focus particularly on the

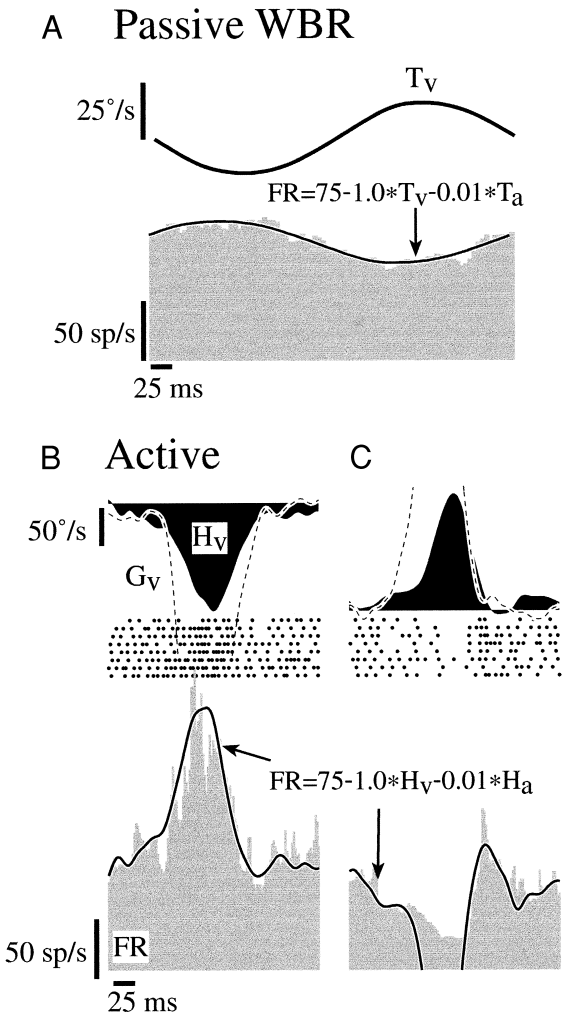

FIG. 8. Response of an attenuated unit during passive WBR and spontaneous gaze saccades. *A*: averaged WBR response with head restrained (62 cycles). *B* and *C*: averaged responses during vestibular ON- and OFF-direction gaze saccades. A model based on the unit's rotational response during WBR is superimposed on discharge rate histograms. Unit usually continued to fire during off-direction active head movements, although the model predicted that the unit would pause. Abbreviations and conventions are the same as in Fig. 4.

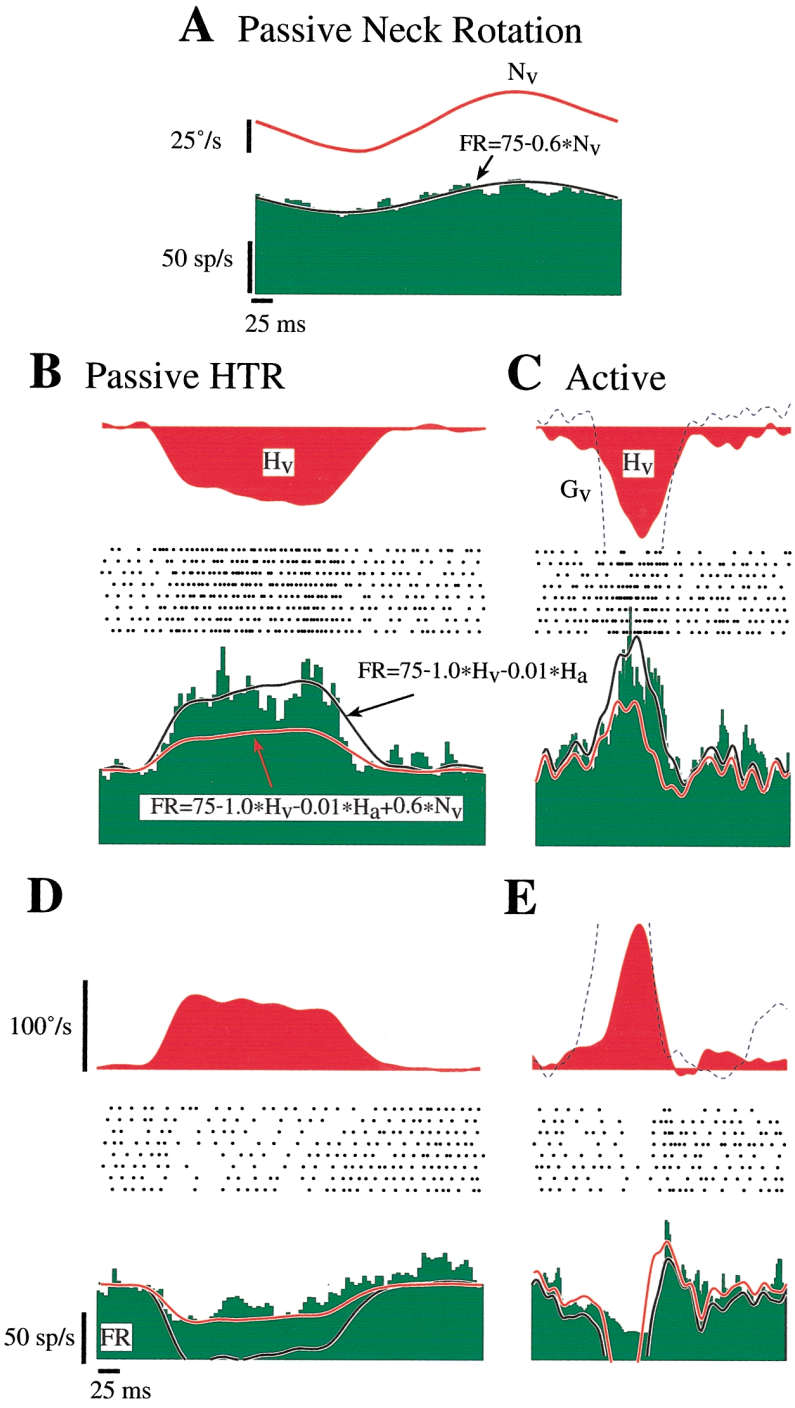

FIG. 9. Asymmetric contribution of neck proprioceptive inputs to head on trunk movement responses of an attenuated unit. Passive and active head movement responses of this unit also are illustrated in Fig. 8. *A*: sinusoidal modulation of unit firing rate during passive rotation of the trunk with the head held stationary in space. *Top red trace* is neck velocity (N_v). An average of 78 cycles is shown. Unit was approximately half as sensitive to neck velocity as it was to head velocity in space (compare sinusoidal fit in *A* to fit in Fig. 8*A*). *B* and *C*: averaged unit responses during passive (*B*) and active (*C*) head-on-trunk rotation in the unit's vestibular ON-direction. An average of 8 cycles is shown in *B–E*. Unit's discharge rate during both passive and active head-on-trunk rotation was more closely fit by a model based on head velocity sensitivity alone (black traces superimposed on unit histograms) than by a model that included its sensitivity to neck rotation (red traces). *D* and *E*: averaged unit responses during passive (*D*) and active (*E*) head-on-trunk rotation in the unit's vestibular OFF-direction. Unit's discharge rate was more closely fit by a model that included head velocity and neck velocity sensitivity (red traces superimposed on unit histograms). However, both models overestimate the inhibitory of effects of active head rotation in the unit's vestibular OFF-direction.

mechanisms involved in canceling vestibular signals on vestibulo-spinal neurons and the functional implications of this cancellation for the vestibulo-collic reflex.

Previous studies of vestibular unit responses during gaze saccades

Attenuation of the responses of non-eye movement vestibular units during gaze saccades has been described in several previous studies. Fuller (1978, 1988, 1992) found that units in the vestibular nuclei exhibited a variety of responses during gaze saccades and noted that most units received neck proprioceptive inputs that could add destructively with vestibular signals during active head saccades. He also observed that units remained sensitive to passive perturbations of the head during gaze saccades. Khalsa and colleagues (1987) described several non-eye movement related vestibular units and a cerebellar unit that had head movement related signals during gaze saccades. Although they stressed the similarity of unit responses during active and passive head movements, they found that the slope of the regression of firing rate versus peak head velocity was smaller during active than during passive

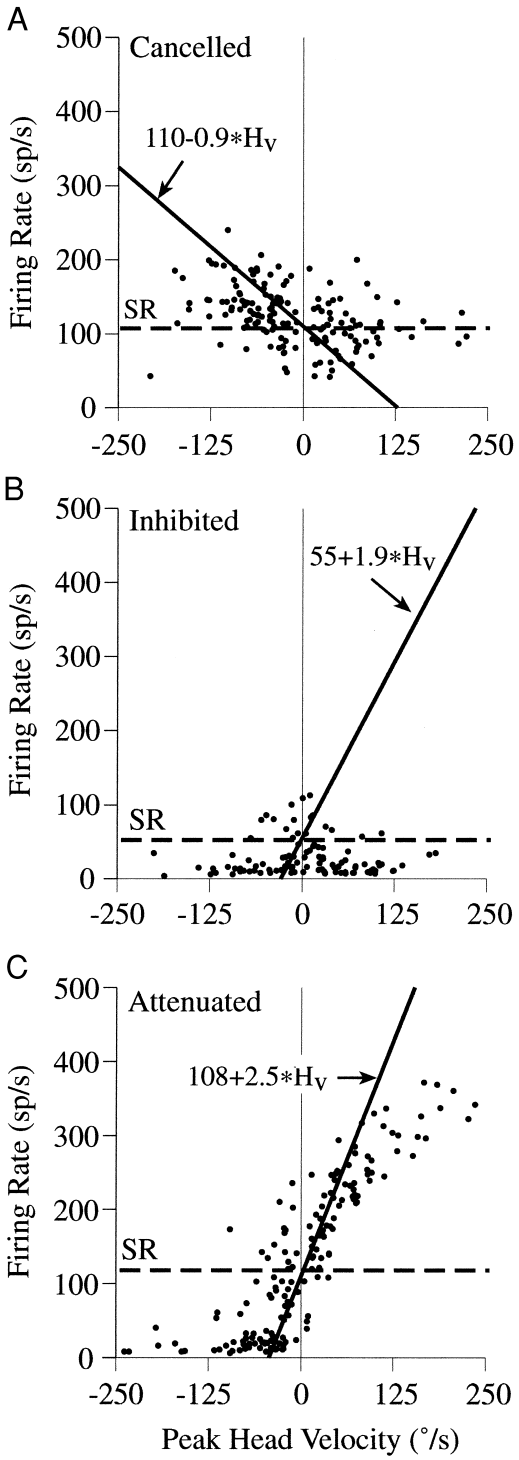

FIG. 10. Discharge rate recorded during peak active head velocity in 3 units. *A*: cancelled vestibulo-spinal unit illustrated in Fig. 4. Each point represents the unit firing rate at the time peak head velocity was reached during a saccade. *B*: discharge rate during peak head velocity of the inhibited vestibulo-spinal unit illustrated in Fig. 5. *C*: an attenuated unit that was highly sensitive to passive head velocity during WBR. Solid line, expected unit response based on its sensitivity to head velocity during passive WBR. Dashed line, spontaneous firing rate (SR).

head movements. The regression of firing rate versus peak head velocity for a ''pure'' vestibular unit they illustrated (Khalsa et al. 1987, Fig. 4) was similar to the attenuated units of this study (Fig. 10*C*). This group also presented evidence that some primate vestibular neurons receive neck proprioceptive inputs (Khalsa et al. 1988). Phillips and colleagues (1996) described the firing behavior of four pure vestibular neurons in the rhesus monkey. They found that the average head-velocity sensitivity of those units was reduced during active gaze saccades compared with their response during passive WBR, but that their sensitivity to head acceleration was increased. The result suggested that the neck movement input to those cells had different dynamic characteristics than their vestibular inputs.

The firing behavior of eye movement related vestibular neurons during active head movements also has been studied (Fuller et al. 1983; Khalsa et al. 1987, 1988; McCrea et al. 1996; Phillips et al. 1996; Roy and Cullen 1998). Eye movement related neurons carry information regarding vestibular signals and in addition also carry signals related to ocular saccades, smooth pursuit eye velocity, eye position, neck position, retinal image slip, and viewing distance. Consequently, the assessment of their vestibular sensitivity during gaze saccades is much more complex than the analysis of non-eye movement units. It is sufficient to note that in the squirrel monkey eye movement related secondary vestibular neurons receive neck proprioceptive inputs and inputs related to active head movements that effectively cancel or attenuate vestibular signals during gaze saccades (Gdowski and McCrea 1997; McCrea et al. 1996).

How are the vestibular signals of non-eye movement units modified during gaze saccades?

There are several ways vestibular signals could have been attenuated or canceled during gaze saccades.

NECK REAFFERENCE. Most vestibular neurons receive neck proprioceptive inputs whose dynamics are such that they reduce the response to head rotation during passive head on trunk movements (Anastasopoulos and Mergner 1982; Boyle and Pompeiano 1981; Fuller 1988; Wilson et al. 1990). In this study, passive head-on-trunk rotations at frequencies comparable with head saccades usually evoked responses in canceled units, including units whose signals were canceled during gaze saccades (Fig. 6). Therefore it is unlikely that proprioceptive inputs from the neck alone were responsible for the large reduction in sensitivity observed in most units during gaze saccades.

PRESYNAPTIC AND POSTSYNAPTIC INHIBITION. Presynaptic inhibition is another mechanism that may be responsible for some of the reduction in vestibular sensitivity during gaze saccades. Such interactions could occur as early as the vestibular sensory epithelium or within the vestibular nuclei itself. Efferent vestibular pathways from the CNS to the vestibular sensory epithelium are known to modify the vestibular sensory signals transmitted by primary afferents (Boyle and Highstein 1990; Brichta and Goldberg 1996; Goldberg and Fernandez 1980; Highstein 1991; Highstein and Baker 1985). Efferent activation also directly hyperpolarizes horizontal canal hair cells and reduces their receptor potential modulation to canal stimulation (Boyle et al. 1998). Efferent vestibular neurons in the toadfish and guinea pig are sensitive to behavioral arousal, and stimulation of neck and body proprioceptors (Highstein 1991; Mar-

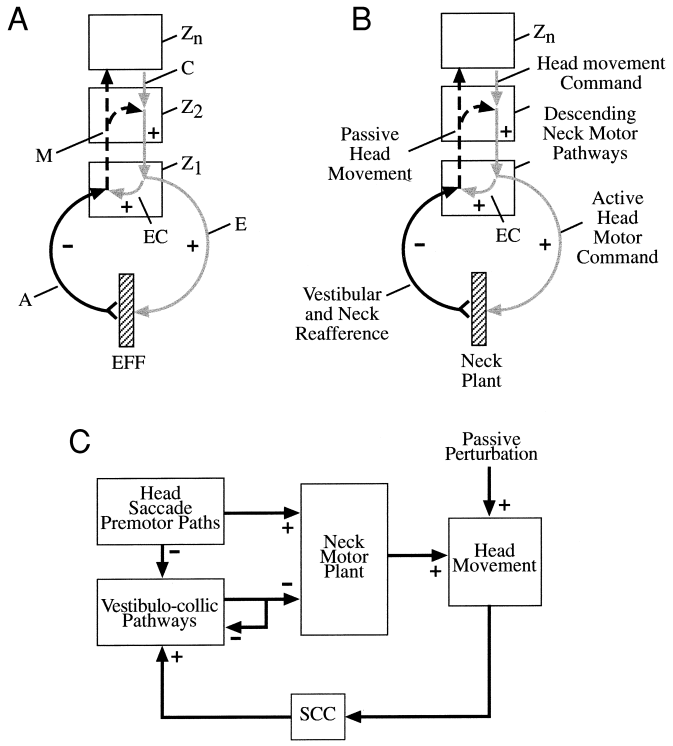

FIG. 11. Modification of sensory processing in the vestibular nuclei by neck reafferent and efference copy signals. *A*: reafference principle of von Holst and Mittelstaedt (1950; adapted from Fig. 4). *B*: reafference principle in the context of these experiments. *C*: simplified diagram of vestibulo-collic reflex pathway contributions to the control of head movements. EFF, effector; $Z_1 \ldots Z_n$, hierarchical stages of sensory-motor control; E, efferent command; A, sensory reafference; EC, efference copy; M, difference between the sensory signals related to active and passive movements; SCC, semicircular canals. See text for further explanation.

linsky 1995). Thus some of the neck movement sensitivity apparent in the vestibular nuclei could be due to the effect of vestibular efferents on vestibular afferent signals.

The vestibular sensitivity of secondary vestibular neurons also could be modified centrally by pre- or postsynaptic mechanisms. The latter idea is supported by the observation in the frog that semicircular canal-related secondary vestibular neurons receive monosynaptic excitatory and disynaptic inhibitory inputs from the same semicircular canal (Straka et al. 1997). On the other hand, it is unlikely that presynaptic mechanisms alone are responsible for reducing the vestibular sensitivity of secondary vestibular units during active head movements. The sensitivity of many units to passive head rotation was not modified during gaze saccades (see Fig. 7*C*). If the synaptic efficacy of vestibular afferent inputs to secondary neurons had been presynaptically modified, then responses to passive and active head movement would have been equally affected.

EFFERENCE COPY. von Holst and Mittelstaedt (1950) suggested that the computation of the difference between sensory afferent information and the expected sensory reafference produced by voluntary movement was a fundamental feature of sensory processing. Sensory processing of vestibular information in the context of postural reflexes was one of several examples used by von Holst and Mittelstaedt to describe their reafference principle, which is schematically illustrated in Fig. 11*A*. The descending central command used to produce an active movement of an effector (EFF) was viewed as being controlled by several hierarchical stages ($Z_1 \ldots Z_n$). The output of these stages generated an efferent command (E) that produced movement of the effector and in addition produced sensory reafference signals (A). To prevent reflexive movements from being generated as a consequence of these sensory reafference signals, they were canceled by subtraction of an efference copy (EC) of the expected sensory reafferent signal produced by the voluntary movement. The difference between the sensory signals related to active and passive movements (M) is computed by subtraction of efference copy from the sensory reafference. Von Holst and Mittelstaedt suggested that the difference was often computed at the lowest, or earliest, stage of central processing (Z_1), and it represented an internal estimate of sensory inputs produced by external forces or perturbations. This estimate then could be used to adjust or correct the central command, if necessary. We suggest that the firing behavior of most canceled units during gaze saccades can be explained as the difference between sensory reafferent inputs produced by active head movements and an efference copy of neck motor commands (Fig. 11*B*).

The evidence that units received neck efference copy inputs was indirect. If vestibular signals were canceled by a signal that was an internal estimate of active head movement, the gain and dynamic responsiveness of the estimate would have to be matched to vestibular afferent inputs. But the match was often less than perfect in individual units. The dynamics, direction, and latency of these small residual active head movement signals varied; which suggests that they might cancel one another when the entire population of non-eye movement units is considered. Their existence possibly reflects the imperfect process of canceling vestibular and neck proprioceptive reafferent signals with a signal that is a central estimate of the expected head movement. This internal estimate of expected vestibular reafference could be constructed from neck reafferent inputs, efference copy signals, or some combination of both. The evidence suggests that both mechanisms were used. Since most units were more sensitive to passive forced head and neck rotation than to head and neck rotation during gaze saccades, it seems likely that the estimate of vestibular reafference during gaze saccades was constructed primarily from an efference copy of neck movement commands.

The role of non-eye movement units in different vestibular functions

Approximately half of the semicircular canal-related units we encountered in the vestibular nuclei were non-eye movement units (Gdowski and McCrea 1999). There is little evidence that these cells participate directly in producing the vestibulo-ocular reflex, but they may be involved in several other important vestibular functions. They probably contribute to vestibulo-thalamic pathways because neurons in the vestibular cortex and associated regions of the thalamus typically have discharge rates that are not related to eye movements (Akbarian et al. 1993 1994; Büttner and Lang 1979; Büttner et al. 1977; Grüsser et al. 1990; Magnin and Fuchs 1977). Canceled units would contribute to the perceptual ability to distinguish passively induced movement of the head or body in space from self-generated movements. Non-eye movement related neurons also are thought to contribute to vestibular pathways related to velocity storage (Reisine and Raphan 1992;

Yokota et al. 1992) and to vestibulo-cerebellar pathways (Waespe et al. 1981, Zhang et al. 1993). Finally, many of the units that project to the spinal cord appear to be non-eye movement units (Boyle 1993).

The role of vestibulo-spinal units in producing the vestibulo-colic reflex

Vestibular reflexes tend to stabilize posture and oppose voluntary movements (von Holst and Mittelstaedt 1950). These reflexes need to be suppressed during active movements. The simple solution would be to cancel the self-generated component of head movement signals carried by vestibulo-spinal reflex pathways. The results of this study suggest that vestibular signals related to self-generated movements of the head on the trunk are canceled on many vestibulo-spinal units.

The antidromically identified vestibulo-spinal units reported here probably were related to the vestibulo-collic reflex (VCR). Horizontal canal-related units that mediate the VCR have axons that descend to cervical segments in the medial longitudinal fasciculus and the ventral funiculus of the cervical spinal cord. The stimulating electrodes were located in the ventral-medial funiculus and most of the identified units were activated with low stimulus currents. In addition, the units appeared to be located in the ventral lateral vestibular nucleus, which is the region that contains medial vestibulo-spinal tract neurons in the squirrel monkey (Boyle 1993; Minor et al. 1990).

The VCR produces a compensatory head movement that tends to stabilize the position of the head in space during passive whole body rotation. A simple model of the role of the VCR in head movement motor control is illustrated diagrammatically in Fig. 11*C*. The figure illustrates the concept that VCR pathways construct an estimate of passive motion of the head in space that sums at segmental levels with active head movement commands to produce different combinations of voluntary and reflexive head movement. The estimate of passive head motion is constructed by subtracting an efference copy of saccade and reflex premotor commands from a semicircular canal estimate of the movement of the head in space. The diagram does not attempt to model all of the factors that contribute to compensatory VCR head movements. Many other factors, including neck stiffness, the inertial load of the head, and the position of the neck undoubtedly, play an important role in the VCR. Moreover, the medial vestibulo-spinal tract is not the only descending pathway that is involved in producing the VCR. Nevertheless it seems likely that the reflex was designed to compensate for passive external forces that perturb the stable posture of the head and deflect the trajectory of planned movements. Summation of vestibular and neck efference copy signals would allow the reflex to perform this function in a variety of behavioral circumstances.

Conclusion

The brain must distinguish between sensory events that are externally induced and those that are self-generated to develop an accurate perception of the external world and produce coordinated behavior. In the vestibular system, the distinction appears to be made by the first neurons in the brain that receive input from the vestibular nerve. Apparently, the recognition of self-generated and non-self-generated head movements is too important to be postponed until a later stage of sensory processing.

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