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INPUT/OUTPUT PROPERTIES OF THE LATERAL VESTIBULAR NUCLEUS

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INTRODUCTION

The lateral vestibular nucleus (LVN) is one of the four main cellular masses of the brainstem in the floor of the fourth ventricle collectively known as the vestibular nuclei complex. Gravito-inertial accelerations of the head are sensed by the otolith structures of the inner ear, transformed into a neural code and carried by vestibular nerve afferents to the LVN. The acceleration signals are used either alone, in combination with events from other sensors or derived internally into a signal to excite the extensor musculature and regulate body posture. Based on input and output properties the LVN can be portioned into a dorsal cell group, called dorsal Deiters', which contains the conspicuously giant cells of Deiters', and into a ventral area (vLV) comprised of small – to medium-sized neurons. Classic anatomical and physiological investigations (2, 23, 49, 71, 77, 91) clearly showed that the lateral vestibulospinal tract (LVST) originates from both the dorsal and ventral cell groups and that the pathway is somatotopically organized: neurons in the vLV innervate the upper and lower cervical spinal segments and those in dorsal Deiters' supply the lumbosacral cord. The LVST descends over slow to fast fibers ranging from 25 to 140 m/sec (2, 16, 49, 91, cf. 77) ipsilaterally to their target sites primarily in laminae VII, VIII and IX of the ventral horn (48, 72). Neurons participating in both the medial vestibulospinal tract (MVST), vestibulo-ocular-collic (VOC) and vestibuloocular reflex (VOR) pathways originate from the vLV as well as the medial nucleus (9, 16).

Three principal sources provide afferent input to the LVST pathways: vestibular, cerebellar and proprioceptive sources. Vestibular nerve afferents supply the angular and linear acceleration sensors, and differ in their discharge regularity and response dynamics. This diversity likely has a functional significance. Semicircular canal fibers with a regular spacing of action potentials have rotational responses that parallel angular head velocity, whereas canal fibers with an irregular discharge are more phasic, showing a phase advance and gain enhancement that increase as the frequency of head movement is raised (37-39). Similar differences are seen in otolith fibers (31). A discussion of the functional significance of afferent diversity also can be found in our pervious work (16). Inertial acceleration and gravity signals are conveyed to dorsal Deiters' neurons (23), and modulate the firing rate of identified

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LVST neurons (13, 15, 16, 52, 61); semicircular canal input is sparse or absent. The dorsal Deiters' also receives cerebellar input from the fastigial nucleus and vermal cortex (spinocerebellum part), which play an important role on vestibulospinal reflexes (59, 60, 89). The vLV receives a powerful short-latency input from the vestibular nerve afferents, originating from the semicircular canals, in particular the horizontal canal, and utricle. It also receives inputs from the cerebellum, mainly from the vestibulocerebellum, and it is likely that this input assists in gaze orientation during more complex movements. The vLV also receives commissural inputs from the contralateral vestibular nuclei, and signals related to the movement and position of the eye in orbit. The other main afferent input to the cervical and lumbosacral LVST pathways involves a return pathway from receptors that are directly activated by the compensatory and stabilizing movements generated by LVST influences on spinal motor circuits (3, 55). Proprioceptive signals generated during axial and limb movements are conveyed over spinovestibular pathways to the dorsal Deiters' (76, 78), and can modulate the firing rate of identified LVST neurons (13-15, 20, 21, 53). Regional differences in response characteristics of neurons in dorsal Deiters' were found during independent sinusoidal stimulation of macular labyrinth and neck receptors (12, 13; cf. 74). The proportion of responsive units and their sensitivity to both inputs were greater in the vLV than in dorsal Deiters' nucleus. Parameters such as differences in secondary neuronal size as well as differences in quantitative and qualitative distribution of synaptic contacts of primary macular afferents (cf., Brodal, 1974) and proprioceptive neck afferents to the two regions of the LVN contribute to the differences in responsiveness of vestibulospinal neurons (14, 15).

The present study will encompass several studies employing adult squirrel monkeys, cats, and hooded rats to investigate the input and output properties of the LVN. The first study will examine the synaptic inputs to identified vestibulospinal neurons in the squirrel monkey using orthodromic and antidromic stimulation techniques. We determined if the proportions of regular (tonic, or thin) and irregular (phasic, or thick) direct vestibular nerve inputs were similar for secondary neurons descending in the MVST and LVST and destined for different segments of the spinal cord were similar. Our goal was to test the prediction that vestibular afferents and secondary neurons form functional subgroups, with regular afferents providing the main input for vestibuloocular neurons and irregular afferents doing the same for the vestibulocollic neurons. To test this prediction, we used the fact that the electrical activation thresholds of vestibular nerve fibers are systematically related to discharge regularity (40).

The second study used intracellular recording and biocytin labeling techniques in the squirrel monkey (11) to investigate whether individual LVST neurons projecting to the lumbosacral spinal segments issue collaterals more rostrally to exert an influence on the cervical ventral horn. This information is of particular interest since the LVST is one of the major descending pathways controlling the extensor musculature of the body. The axon course through the brainstem and cervical spinal cord was examined in 37 LVST neurons.

The third set of experiments focuses on the unit activity of 136 dorsal Deiters' neurons projecting to the lumbosacral spinal cord of cats. Their response characteristics to sinusoidal stimulation of labyrinth and neck receptors were related to cell size inferred from the conduction velocity of the corresponding vestibulospinal axons. Vestibulospinal neurons with faster conduction velocity and, by inference, having thicker axons and larger cell bodies differed from those neurons having lower axonal conduction velocity. These finding were presented and discussed in terms of reciprocal distribution of synaptic contacts of vestibular and neck afferent on vestibulospinal neurons as a function of cell size (15). For example, if response characteristics are determined by neuronal properties related to cell size, then they should be invariant despite difference in input drive (cf. 44, 45). On the other hand if response characteristics depend mainly upon synaptic organization, then differential control of particular neuronal groups could result, provided the relevant input systems distribute to pooled neurons with differing patterns (cf. 24).

The last set of experiments to be described, examined the spatio-temporal properties of LVN neurons in the decerebrated rat in response to dynamic acceleration inputs. The dynamic responses of central vestibular neurons receiving otolith inputs were systematically characterized using sinusoidal linear translation in the horizontal head plane.

Early descriptions of the vestibular system's response to otolith input treated the otolith organ's response as a simple linear accelerometer encoding a limited amount of information. Accordingly, the response gain of the neuron was proportional to the cosine of the angle between the applied stimulus vector and the direction of the cell's maximum response while the response phase was independent of stimulus orientation. This one-dimensional behavior was originally attributed to the spatial and mechanical properties inherent in the hair cells (87), observed in the measured responses of otolith afferents (30, 31, 56) and described in central otolith neurons (33, 67, 79, 83, 93). More complex behaviors were observed (7, 54, 84), however, and the experiments described by Bush et al. (25) using pure linear translation described the spatio-temporal properties of central vestibular neurons that could not be described by a generalized one-dimensional response. The complex behavior was described as a two-dimensional response based on an analysis developed by Angelaki (4) and when applied to the observed response properties of vestibular nuclei neurons (5) was shown to be a more accurate quantitative description of the spatio-temporal properties. These results had broad implications for the diverse nature of canal and otolith inputs onto central vestibular neurons.

METHODS

Methods to identify vestibular input to identified secondary vestibulospinal neurons.

Surgical procedures are described in detail elsewhere (16, 41). Intrasomatic recordings were made from neurons in the vestibular nuclei of 16 immobilized squirrel monkeys using glass microelectrodes filled with a salt solution with or without biocytin. Neurons were identified as receiving a short-latency input, i.e. monosynaptic, from the ipsilateral vestibular labyrinth (V_i). In most

cases the synaptic relationship to the contralateral vestibular labyrinth (V_c) was also examined. Projection pathways were determined by antidromic testing with stimulating electrodes placed in the rostral medial longitudinal fasciculus (MLF) near the caudal end of the oculomotor nucleus (III) and in the spinal cord at segments C_1, C_{5-6}, and T_{12}-L_1. Secondary neurons were classified by their patterns of antidromic activation into four categories: 1) MVST, 2) LVST, 3) VOC, or 4) VOR. To determine the tract of a spinal-projecting neuron, we adapted a previously described procedure (2). Detailed description of classification of relay cells has been previously described (16). After orthodromic and antidromic identification, a two-shock paradigm was used to characterize the monosynaptic V_i input to each neuron (41). Shock strengths were normalized in terms of the threshold strength (T) required to evoke a field potential in the vestibular nuclei, which corresponds to the strength needed to activate 10% of the afferents (41). The first or conditioning shock was set at 16 X T. A second shock or test shock was applied 4 ms later and was varied in strength from 0 to 16 X T. It was found that >90% of irregular afferent were recruited by test shocks below a value of 4 X T, whereas > 90% of regular afferents were first recruited between 4 and 16 X T (41). These observations provide a means of determining the relative proportion of V_i inputs contributed to a secondary neuron by the different afferents. This is done by comparing the size of the monosynaptic V_i EPSPs evoked in the neuron by test shocks at 4 and at 16 X T. To determine the locations of recorded cells, drawings of the cerebellum and brain stem, including nuclear boundaries and the course of electrode tracks, were made from projected sections.

Methods to identify dorsal Deiters' neurons in the squirrel monkey.

To determine whether individual dorsal Deiters' neurons terminating in the lumbosacral spinal segments issue collaterals more rostrally to exert an influence on the cervical ventral horn, intracellular recording and biocytin labeling techniques were used in the adult squirrel monkey (11). Details regarding surgical preparation, recording, stimulation, staining, and histological procedures have been detailed previously (11). Stimulating electrodes were placed in the middle ear space to orthodromically excite V_i and V_c vestibular nerve afferent that project to the LVN. Secondary vestibular neurons were identified by their short-latency response to pulses applied to stimulating electrodes that electrically excited fibers in both the superior and inferior divisions of the vestibular nerve. To identify any possible ascending projection from bifurcating neurons stimulating electrodes were lowered in to the brain to straddle the MLF between the IIIrd and IVth cranial nuclei. Dorsal laminectomies were done to expose the spinal segments of C_1-C_3 for recordings from single axons and neurons and at T_{12} for placement of stimulating electrodes in the ventrolateral funiculi of both sides for antidromically activating the neuron's descending axon. Only neurons related to the 8th nerve at monosynaptic latencies and antidromically identified to project below T_{12} were selected for study. Laterality of the vestibular nerves with respect to the recorded axon as V_i or V_c was later determined by the identification of the labeled axon from stained sections.

Methods to identify relation between cell size and response characteristics of vestibulospinal neurons to labyrinth and neck inputs.

The surgical procedures, experimental conditions, methods of recording extracellular unit activity, and marking of the locations of recording sites have already been described in detail, as have the anatomical identification of the vestibular nuclei and subdivisions of the LVN into dorsal Deiters' and vLV (12, 13). Rotations of the neck, whole animal (roll tilt), or head alone were accomplished by independent servo-driven hydraulic systems (29). Rotation of the neck clamp and table simultaneously in both directions of the coronal plane beneath a stationary head produced stimulation of neck receptors (neck input). Rotation of the entire stereotaxic equipment and table together about the longitudinal axis produced stimulation of labyrinth receptors (labyrinth input). Finally, rotation of the head about the same axis, while the C2 vertebral clamp and table remained stationary in the horizontal position, elicited co-stimulation of both receptors (neck + labyrinth inputs). Sinusoidal waveforms of 0.026 Hz, 5 or 10° peak amplitude, were used. Electric pulses were applied in a bipolar manner to wire electrodes implanted into the ventral quadrant of the spinal cord between L_1 and L_2 to antidromically excite the neuron. In agreement with the known

anatomical projections from the LVN (77), 78.7% and 21.3% antidromically identified vestibulospinal neurons were located histologically in the dorsal and ventral regions of the nucleus, respectively.

Methods to determine the spatio-temporal response properties of rat LVN neurons to sinusoidal linear translation.

Extracellular recording techniques were employed to examine the three-dimensional characteristics of central vestibular neurons in hooded rats. Each animal was prepared with a stimulating electrode cemented to the bone adjacent to the oval window of the labyrinth ipsilateral to the recording site. Anesthetic effects were minimized by decerebrating the animal prior to beginning the experiment. Upon isolating a neuron, its response latency to electrical stimulation was determined at a suprathreshold current intensity level. The vestibular input to each neuron was first evaluated according to its response to angular rotations around the yaw, pitch and roll axes. Next, the neuron was tested for its response to sinusoidal linear translation in the horizontal head plane. The stimulus frequency was varied from 0.2 to 1.4 Hz with peak accelerations of ± 0.10 g. Because response gain and phase were found to vary as a function of the orientation of the stimulus force vector, each cell was tested to vectors oriented at 15° intervals at 0.2 Hz and every 30° for the frequencies 0.4 to 1.4 Hz over a range of 180°. A dye mark was placed at the end of each penetration that permitted the approximate location of isolated cells to be determined based on the reconstructed electrode tracks following histological processing of the tissue.

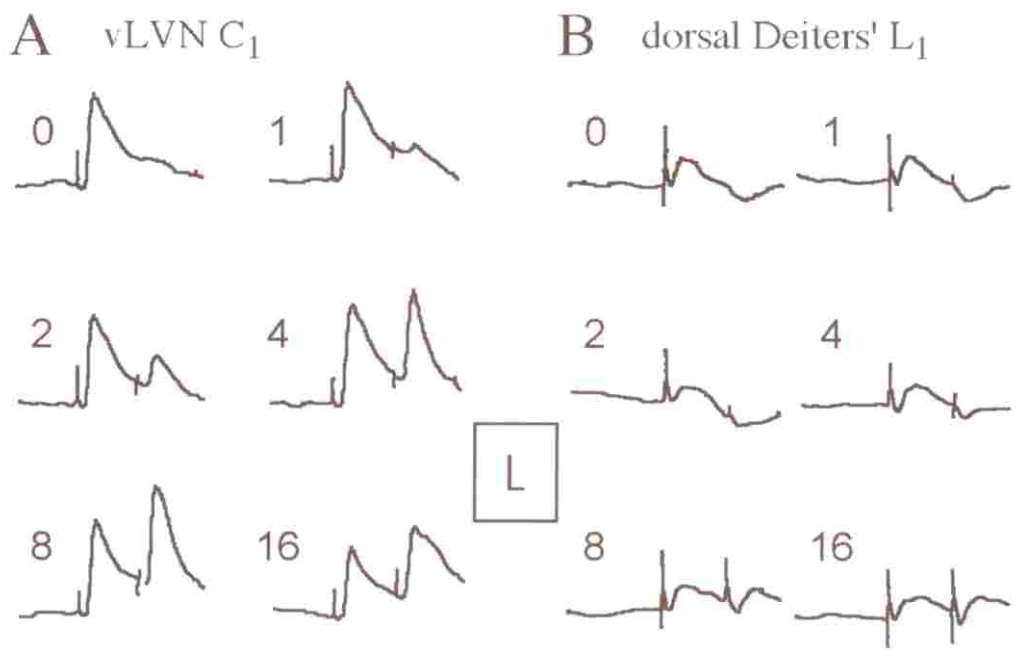

Fig. 1. - *Electrophysiological records from 2 secondary vestibular neurons.*

A: vLV neuron innervating the upper cervical segments (antidromically activated from cervical segment C_1). B: dorsal Deiters' neuron projecting to the lumbosacral spinal cord. Computer averages, based on 8 repetitions, of excitatory postsynaptic potentials evoked from the ipsilateral vestibular labyrinth. Two-shock paradigm, with 1st shock set to 16 X threshold strength (T) and 2nd shock (X T) as stated to the left of each record. Calibration bars: 1mV, 1ms. Data from Boyle et al. (1992).

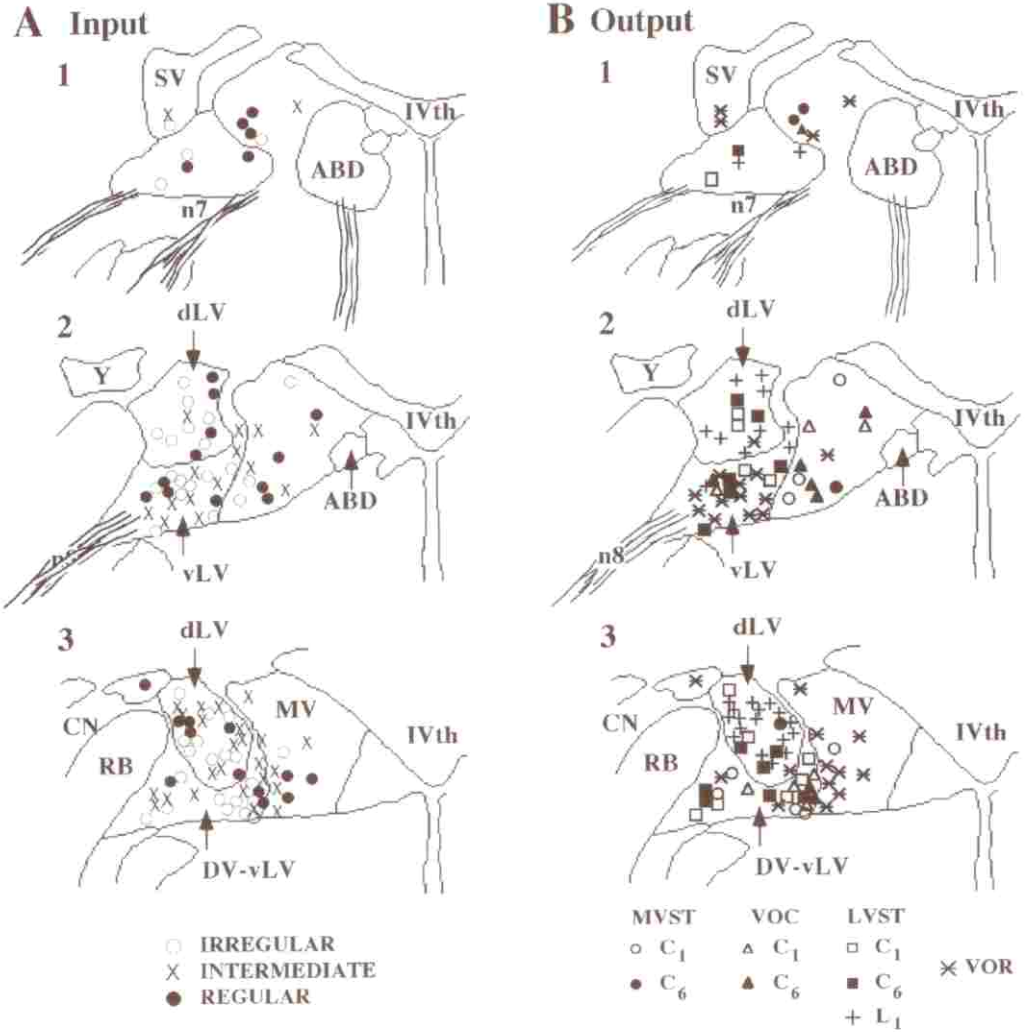

Fig. 2. - *Input/output mapping of the LVN.*

A: Anatomic locations of recorded cells classified by their on the basis of their %I indexes, the percentage of their total monosynaptic ipsilateral vestibular nerve (V_1) input contributed by irregular afferents. Neurons are designated as regular, intermediate, or irregular depending on whether their %I indexes (the normalized amplitude ratio with a test shock of 4 X T; measures the percentage of the input attributable to irregular afferents) were < 25%, 25-75%, or > 75%, respectively. B: Anatomic locations of recorded cells classified by their projection pathways into medial vestibulospinal tract (MVST), lateral vestibulospinal tract (LVST), vestibulo-ocular-collic (VOC), or vestibuloocular (VOR). For spinal-projecting neurons, the caudal most spinal segment from which they could be antidromically activated (C_1, C_6, or L_1) is also indicated. Three standard sections are shown from the rostral (1) to the caudal (3) end of the LVN. ABD, abducens nucleus; CN, cochlear nucleus; dLV, dorsal lateral vestibular nucleus (dorsal Deiters'); DV, descending vestibular nucleus; MV, medial vestibular nucleus; n7 and n8, seventh and eighth cranial nerves, respectively; RB, restiform body (inferior cerebellar peduncle); SV, Superior vestibular nucleus; vLV, ventral lateral vestibular nucleus; Y, group Y of the vestibular nuclei; IVth, fourth ventricle. Figure modified from Boyle et al. (1992).

RESULTS

Input/Output Relationships of the LVN.

Thick or irregular fibers provide a predominant synaptic input to the vLV (Fig. 2A), and particularly to neurons that project by way of the MVST and LVST to innervate the upper neck segments (Fig. 2B). The electrophysiological response of a vLV neuron projecting in the LVST and terminating in the upper cervical segments is shown in Figure 1A. Excitatory postsynaptic potentials (EPSPs) appear at 1 X T and are nearly full amplitude at 4 X T (Fig. 1A). The % I index (the normalized amplitude ratio with the test shock of 4 X T) measures the percentage of the input attributable to irregular afferents. In this case > 95% of the neuron's Vi input came from irregular afferents. Thin or regular fibers project throughout the LVN (Fig. 2A), and onto dorsal Deiters' neurons projecting in the LVST to the lumbosacral ventral horn (Fig. 2B). The electrophysiological response of a lumbar-projecting dorsal Deiters' neuron is shown in Figure 1B. The monosynaptic EPSPs appear at 8 X T and are full amplitude at 16 X T (Fig. 1B). In this case 100% of the neuron's Vi input came from regular afferents.

The majority of the output from dorsal Deiters' was found to project to the lumbosacral segments (Fig. 2B). The output from the vLV is mixed, pathways to the cervical segments are found, via both the MVST and LVST, as well as by way the bifurcating VOC pathway, and VOR-projecting neurons are intermingled with the spinal-projecting cells. Figure 3 shows an extracellular field potential study as the electrode is lowered through the cerebellum and into the vestibular nuclei about 3 mm lateral to the midline. Shocks are applied at specific delays to wires implanted in LVST (C1L) and MVST (C1M) at C1, at C6, at L1, and in the MLF near the oculomotor (IIIrd) nucleus (Oc); the two-shock paradigm was examined at the conditioning shock of 16 X T followed by the test strength of 4 x T; and lastly the contralateral vestibular nerve was shocked (Vc) to examine commissural input at different levels in the nuclei. The dorsal Deiters' appears at around 10.0 mm below the cerebellar surface, and vLV at around 11.0 mm. Near this location of the vLV the cervical vestibulospinal and oculomotor pathways are heavily activated. The Vi synaptic input intensifies as the electrode is lowered, reaching its maximum in the vLV. Commissural inputs are absent in dorsal Deiters' and appear in the vLV. If we consider input as a function of output a pattern emerges. Irregular input preferentially targets neurons projecting to the upper cervical segments by way of the MVST and LVST and to C6-projecting LVST cells. Regular input is distributed throughout the vestibular nuclei, but preferentially targets the VOC neurons and the C6-projecting MVST cells. It was also found that about half the neurons receive a mixed input, thus carrying a combined signal from both afferents.

Morphology of Secondary Lumbar-projecting LVST Neurons.

Lumbar-projecting dorsal Deiters' neurons receiving monosynaptic input from the ipsilateral 8th nerve were found not to target cell groups in the caudal brainstem or in the ventral horn of the cervical spinal cord as they course through the brainstem

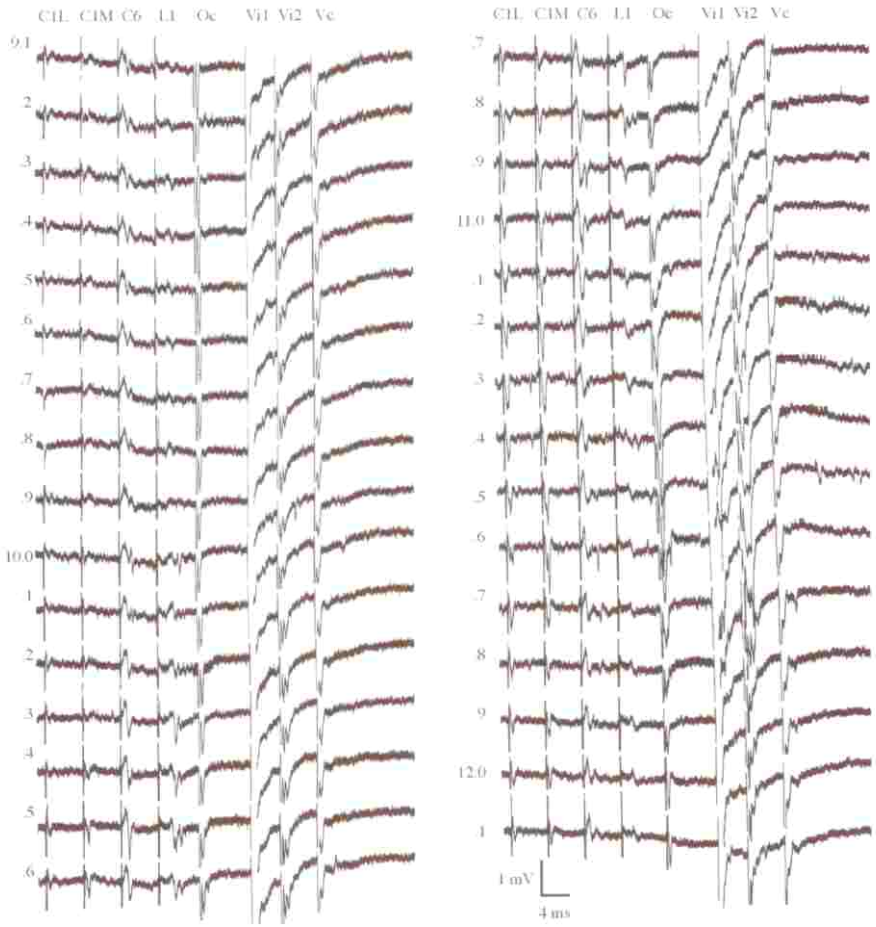

Fig. 3. - *Field potential study showing input/output properties of neurons along a 3 mm dorsoventral pass through the vestibular nuclei.*

Numbers at left indicate distance in mm beneath the cerebellar cortex from 9.1 to 12.1. Shocks are applied at specific intervals, indicated by the shock artifact, to implanted wires to examine the output pathways and input profiles from the ipsilateral (Vi) and contralateral (Vc) vestibular nerves. Shocks are: C1L (LVST at C1), C1M (MVST at C1), C6 (both MVST and LVST are activated), L1, Oc (oculomotor), Vi1 (2-shock paradigm, the conditioning or 1st shock set at 16 x T), Vi2 (2-shock paradigm, the test or second shock set at 4 x T), and Vc. Data from Boyle et al. (1992).

(Fig. 4A) to lower segments of the spinal cord (Fig. 4B). In addition, the dorsal Deiters' neuron appears to be the only central vestibular neuron that does not, at least in a portion of the population sharing morphological or physiological characteristics or both, collateralize within the brainstem. The average distance of recovered axon was 17.3 mm (4.5-31.7 mm), and thus it is possible that collaterals might have been issued beyond the point where the label faded. None of our sample could be antidromically activated from shocks applied to the rostral medial longitudinal fas-

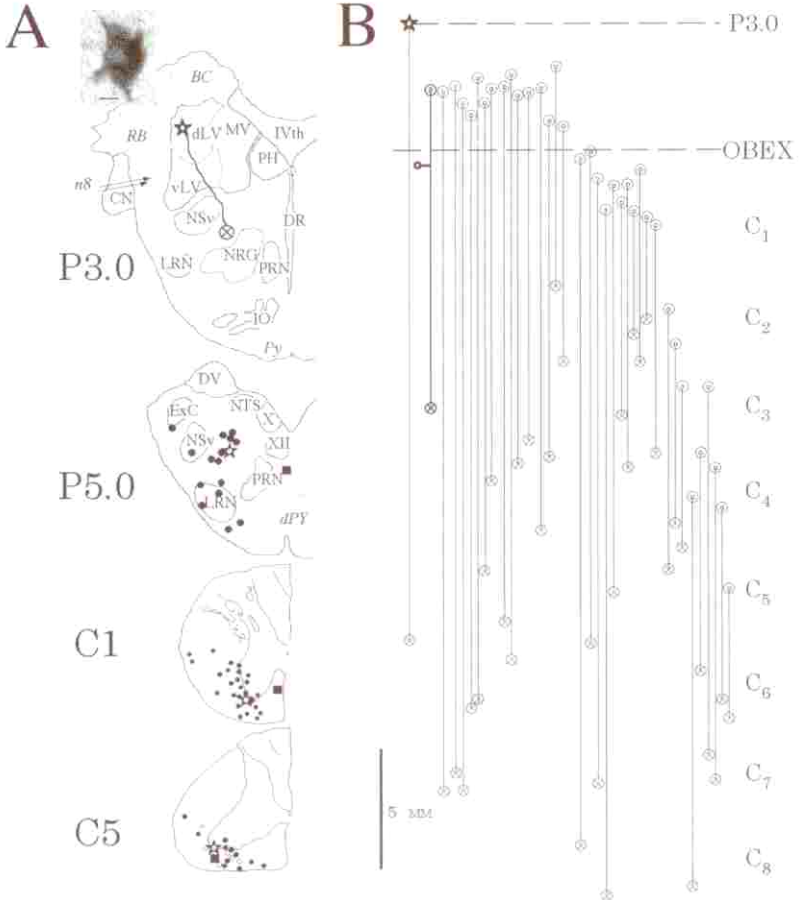

Fig. 4. - A: *Axon trajectory of lumbar projecting dorsal Deiters' neurons through the cervical segments of the spinal cord.*

A: Four drawings (rostral to caudal) show the recovered location of the individual L-LVST axons in the brainstem at P3.0 and P5.0 (upper two) and in the cervical spinal cord at C_1 and C_5 (lower two). Insert shows a photomicrograph of the soma of a labeled L-LVST neuron in dorsal Deiters' nucleus; a star in the caudal drawings represents this neuron. With one exception the other L-LVST neurons are symbolized by a filled circle. The exception is the one L-LVST neuron marked by the filled square: the axon of this L-LVST neuron traveled in the descending MLF through the caudal brainstem and beyond the first cervical segment, but left the ventromedial funiculus between C_1 and C_2 to assume a projection course more typical of the other L-LVST neurons. BC, brachium conjunctivum; CN, cochlear nuclei; n8, eighth nerve; dLV, dorsal lateral vestibular nucleus (dorsal Deiters'); vLV, ventral lateral vestibular nucleus; MV, medial vestibular nucleus; DV, descending vestibular nucleus; PH, prepositus hypoglossi; IVth, fourth ventricle; RB, restiform body; NSv, nucleus tractus spinalis n. trigemini; LRN, lateral reticular nucleus; IO, inferior olive; Py, pyramidal tract; NTS, nucleus tractus solitaire; X, dorsal nucleus of vagus; XII, nucleus hypoglossi; ExC, external cuneate nucleus; dPy, decussation of pyramidal tract. B: Extent of recovered projection of 37 L-LVST axons. Each vertical line represents the recovered labeling of the individual L-LVST neurons. Neuron mark by the star is similarly represented in panel A. Only one L-LVST neuron issued a collateral to the cervical cord (second cell from left), and its single branch is given. Fading of the labeled axon along its rostral and caudal projection is represented by a circle within and circle and an X within a circle, respectively. Figure modified from Boyle (2000).

ciculus near the 3rd nuclei, thus ruling out the possibility of a bifurcating axon. Of the 37 neurons labeled, only 1 axon issued a collateral to innervate the cervical ventral horn, primarily in the region of the spinal accessory motoneurons. This signal collateral provided a relatively minor input compared to that of LVST neurons terminating in the cervical cord. This arrangement is suggestive of a fast and private signaling pathway for reflex control of the lower limbs.

Convergence and Interaction of Neck and Macular Responses.

Figure 5C illustrates the relationships between the ratio of gain of neck response and labyrinth response of 36 dorsal Deiters' units in the study conducted by Boyle and Pompeiano (15). The 10 units located on the extreme right side of the figure showed, on average, a 4-fold greater gain to labyrinth input than to neck input and had relatively faster axonal conduction velocities and lower resting firing rates. The 11 units on the extreme left side of the plot showed the opposite findings, i.e., a 4-fold greater gain to neck input that to labyrinth input, slower conduction velocities, and higher resting firing rates. These relationships are of particular interest because no reliable correlations were found between the gains of both the labyrinth and neck responses and the other physiologic properties when studied individually. However, a strong relationship was observed when their ratio of gains was considered: the greater the gain of neck response over labyrinth response, the higher was the resting discharge rate (paired rank, $p < 0.001$) and the slower was the conduction velocity of unit's axon (same test, $p < 0.001$) and vice versa. It is possible, although still a speculation, that regular to mixed vestibular afferent input targets the neck-dominated neurons for posture stability and that irregular vestibular input targets the labyrinth-dominated neurons to drive the compensatory reflexes.

In a previous account (15), the responses of LVN neurons to head rotation, leading to co-stimulation of both neck and labyrinth receptors, were shown to be the result of a linear vectorial summation of the individual responses. For the 11 neurons studied during head rotation in Boyle and Pompeiano (15) a high degree of correspondence was observed between the actual gain and phase angle of response and the component values of the predicted vector ($x^2 < 0.01$). Further, this additive mode of interaction of inputs was maintained over the frequency domain of stimulation from 0.015 to 0.15 Hz, 10° (with a range of maximum angular acceleration from 0.09 to 8.9°/sec^2) for examined units.

Figure 5 (A) illustrates the responses of a lateral vestibulospinal neuron to the three modalities of sensory stimulation and summarizes the above findings. The unit represents (i) a relatively irregular unit discharge (CV = 0.378), (ii) a lower mean firing rate (22.7 impulses/sec), (iii) a faster conduction velocity of its axon (102.8 m/sec), (iv) a peak firing rate during side-down roll tilt (alpha response), and (v) a 4-fold greater gain to labyrinth than neck input ($G_N/G_L = 0.233$). The unit responses were out of phase by 162.20, but due to the imbalance of response gains, the resulting unit response during head rotation closely mimicked that observed during labyrinth stimulation alone (polar diagram in Fig. 5B).

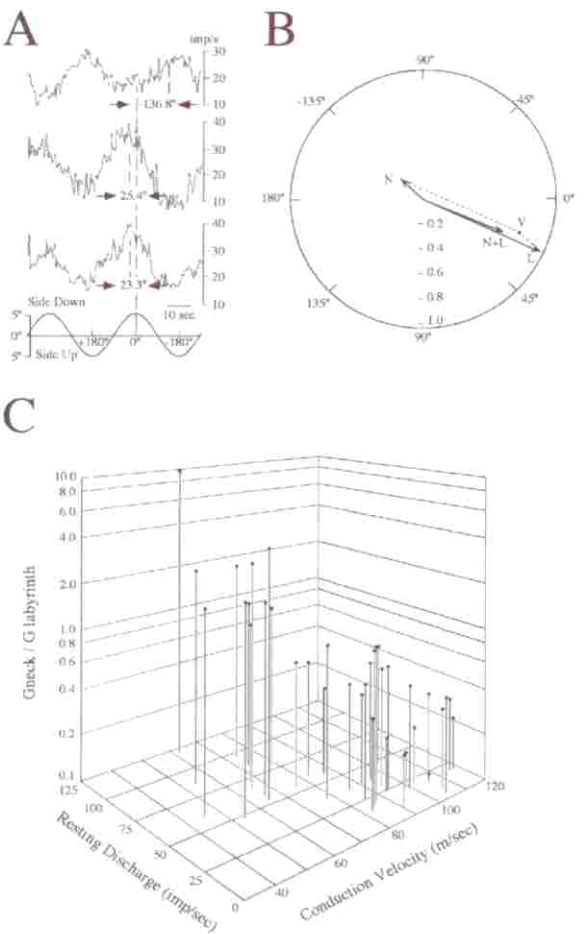

Fig. 5. - *Data of vestibulospinal neuron located in LVN. Unit was tested to rotations at 0.026 Hz, 5 or 10°, and response histograms for each record were averaged over four sweeps (128 bins, 0.6 sec/bin width).*

A & B: The average resting discharge rate, CV, and the conduction velocity of its axon were 22.7 impulses/sec, 0.38, and 102.8 m/sec. The gain, phase angle, and coherence coefficient to neck input (upper trace) were 0.24, -136.8° lag, and 0.92, respectively, and those values to labyrinth input (second trace) were 1.03, +25.4° lead, and 0.93, respectively. The response to head rotation (third trace) had a gain of 0.69, a phase lead of +23.3°, and a coherence coefficient of 0.95. As illustrated in the polar diagram, the gain (0.80) and phase angle (+20.2°) of the predicted vectorial response (V) were comparable to those obtained experimentally during head rotation (N+L). C: Three-dimensional diagram relating the ratio of response gains (G_N/G_L) to the physiologic properties of LVN neurons. The 36 units received convergent inputs from both labyrinth and neck receptors at standard parameters of testing. The ratio of gains of neck response (G_N) to the labyrinth response (G_L) (y axis) is plotted against both the resting discharge rate (measured in impulses per sec; x axis) and the conduction velocity of its axon (z axis) for each unit. The negative correlations between G_N/G_L and the conduction velocity and between the resting discharge rate and the conduction velocity and the positive correlation between G_N/G_L and the resting discharge rate were significant. Figure modified from Boyle and Pompeiano (1981).

Dynamic Responses to Natural Activation of Utricular Receptors.

Bush et al. (25) studied the spatio-temporal response properties of central vestibular neurons to sinusoidal translation. Figure 6 shows a neuron located in the LVN that responded to 0.2 Hz sinusoidal translation. The cell's spatial response was characterized by systematically measuring its response to sinusoidal translation as a function of the orientation of the stimulus force vector. Two methods were used to fit the data shown in panel B of Figure 6. The first method fit the data with a cosine function (*dashed line*) while the second fit the data utilizing the two-dimensional analysis developed by Angelaki (4). The direction of maximum sensitivity for this cell was measured to be 68° with respect to the nasooccipital axis and ipsilateral to the recording site. Based on the two-dimensional analysis developed by Angelaki (4), this cell had an S_{max} vector of 19.1 spikes/sec/g and an S_{min} of 4.0 spikes/sec/g.

Therefore, this cell would be classified as a narrowly tuned neuron based on the ratio of S_{min}/S_{max}. It can be seen that this cell is adequately described by the one-dimensional fit and the similarity of the one-dimensional and two-dimensional fits (solid line and dotted line) also supports this result. Within the LVN, the majority of the neurons isolated were shown to receive monosynaptic inputs based on their latencies to electrical stimulation. The neuron shown in Figure 6 had a latency of 1.6 msec.

DISCUSSION

Vi Input to Secondary Vestibular Neurons.

Vestibular afferents vary in fiber diameter, conduction velocity, and dendritic morphology, and have a wide range of background discharge properties and response characteristics to stimulation of vestibular receptors (see 37, 38), they are commonly termed regular and irregular based on the spacing of the interspike intervals (40). Based on an electrophysiological paradigm developed by Goldberg et al. (41), the contribution of the regular to irregular afferent input to the secondary vestibular neurons were assessed (Figures 1-3; 16). We found that the afferent input from these fibers remain partially segregated within the vestibular nuclei. Mixed

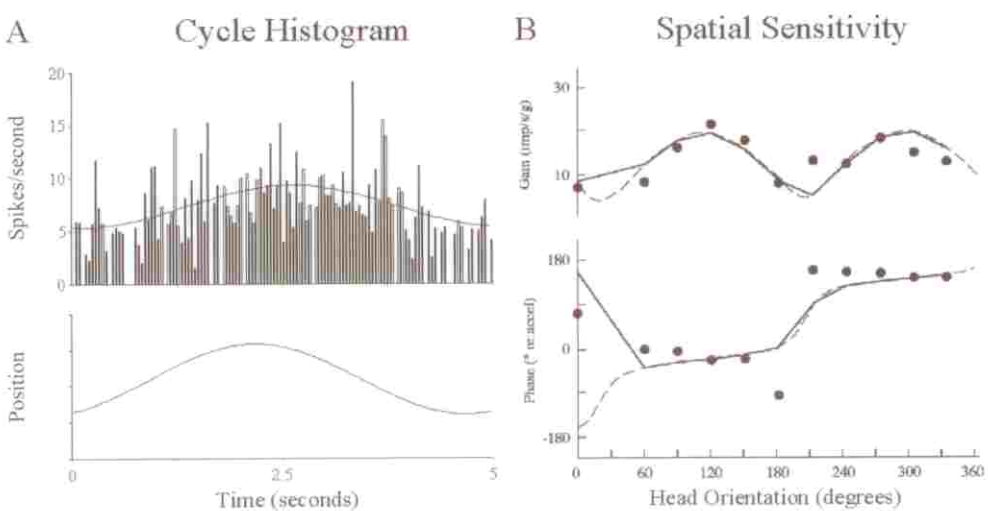

Fig. 6. - *Response of an identified LVN neuron to sinusoidal linear translation.*

A: Cycle histogram of LVN unit responding to a 0.2 Hz sinusoidal stimulus. The *upper panel* shows the average spike histogram to 6 cycles of sinusoidal translation. The superimposed solid line represents the least-square fit for estimating the response gain and phase. The *lower panel* shows the 0.2 Hz stimulus. B: Complete set of data for cell shown in *Panel A* gathered for 0.2 Hz stimulus. Response gain (*upper panel*) and phase (*lower panel*) as a function of the applied stimulus vector angle. Solid circles represent the gain and phase values fit to the data. The solid lines through the points represent the 2-dimensional fit to the data. The dotted lines are the 1-dimensional fits of the data for comparison. The 2-dimensional fit of this cell gave a S_{max} = 19.1 spikes/sec/g and S_{min} = 4.0 spikes/sec/g at an orientation of 112°.

input neurons make up slightly over half of the neurons encountered (16, 46). By the same token, almost half of the neurons received a predominant input from one or the other afferent class. The presence of neurons with mixed inputs is consistent with the morphology of secondary vestibular neurons and with the patterns of afferent termination in the vestibular nuclei. Secondary relay neurons typically have dendritic trees extending 500-2000 μm in all directions (46, 64, 65, 69, 70, 73). Intra-axonal labeling of physiologically characterized horizontal canal afferents of the cat show that there is an almost complete overlap in the terminal fields of regular and irregular afferents in each of the major subdivisions of the vestibular nuclei (82). From the large size of the dendritic trees and the degree of afferent overlap, one might suppose that the vast majority of secondary cells would receive a convergent input from the two kinds of afferents. The physiological techniques used in our studies have the advantage over purely neuroanatomic methods of allowing us to determine afferent inputs on a cell-by-cell, rather than a regional, basis. Our results show that a large fraction of secondary cells get a predominant input from thick or thin afferent classes. This implies a relatively high degree of specificity in the connections between groups of afferents and secondary neurons.

Vestibulospinal Pathways to the Lumbosacral Spinal Cord.

Monosynaptic Vi EPSPs were recorded from nearly two thirds of our sample of lumbar-projecting dorsal Deiters' neurons. The amplitude of the monosynaptic Vi EPSPs was often small, < 1 mV, and did not drive the neuron to discharge. This finding is consistent with the anatomical evidence showing the dorsal Deiters' is the one region of the vestibular nuclei almost devoid of vestibular nerve terminations (26, 34, 82). Presumably, the monosynaptic Vi inputs to these neurons are made on distal dendritic branches, which may be located outside the boundary of the dorsal Deiters' (46).

The heterogeneous input from regular, mixed and irregular afferents and efferent organization of dorsal Deiters' nucleus places it as a central player in the descending control of spinal segmental and inter-segmental mechanisms that maintain posture and regulate movement. In the lumbosacral spinal segments LVST neurons exert an excitatory influence directly (and indirectly) on both alpha (43, 57, 58) and gamma (27, 42) motoneurons. Using electrical stimulation techniques in the cat, Abzug et al. (1) presented suggestive evidence that half the lumbosacral projecting LVST neurons exert an action more rostrally to their site of termination, in the cervical segments of the spinal cord, explicitly implying that these neurons issue collateral from the parent axon. Shinoda et al. (86) found that 36% (4 out of 11) of the cat LVST axons that projected at least to segmental level T2 had axon collaterals to the lower cervical segments between C4 and C8. There are two ways to view these data. One, the somatotopy of efferent connection of the lateral nucleus is functionally blurred or irrelevant. Or two, the multi-segmental distribution of the same signals to both limbs on one side is an essential component of coordinating stance or compensatory reflex movement in quadrupeds.

Using intracellular recording and biocytin labeling techniques, we investigated this question in the primate and found that secondary, lumbar-projecting LVST neu-

rons do not target cell groups in the caudal brainstem or in the ventral horn of the cervical spinal cord as they course to lower segments of the spinal cord. In the squirrel monkey vestibular neurons projecting by way of the LVST to the ipsilateral cervical cord (10) and those sending their axons into the descending medial longitudinal fasciculus (64, 65, 68) to innervate either side of the cervical cord (17, 18) frequently collateralize caudal to their cell body and before reaching the spinal cord. This also appears to a feature of vestibular neurons studied in the cat (50, 51, 62, 63). Hence, for the squirrel monkey it appears that the caudal projection of the dorsal Deiters' neurons, in essence, is a private, and mostly rapid, communication pathway between the brainstem and the motor circuits controlling the lower limbs and tail. It is important to note that our conclusion that the lumbar-projecting dorsal Deiters' neurons do not target the cervical cord is reserved only for secondary neurons. We cannot discount the possibility that higher-order neurons might distribute collateral inputs to the cervical cord; and this might account for the high percentage of synaptic action in the cervical ventral horn from electrically stimulating L-LVST axons described by Abzug et al. (1).

Vestibulospinal Pathways to the Cervical Spinal Cord.

Vestibulospinal fibers contributing to the vestibulocollic reflex (VCR) travel in the LVST and MVST and make monosynaptic connections with motoneuron pools in the upper cervical cord (32, 90). Our observation that secondary MVST and LVST neurons terminating at this level get most of their monosynaptic Vi input from irregular afferents is consistent with the conclusion that these afferents provide the major input to the VCR (8, 75, 85, 92). There are several factors that complicate the interpretation, however. One of these is the presence of VOC neurons largely carrying regular Vi inputs. Because VOC neurons make monosynaptic connections with neck motoneurons (47, 88) and are likely to carry head velocity signals (50), they probably participate in the VCR. Other potential sources of vestibular inputs are C6 MVST and LVST neurons, which have been shown to send collateral projections to motoneurons in the upper cervical gray matter (80, 81). According to our data (16) the MVST and LVST cells would provide mainly regular and irregular Vi inputs, respectively. In short, neck motoneurons may receive a convergent input from several classes of vestibulospinal neurons, some of them having a regular and others irregular afferent profile. The situation would appear similar to that for the VOR because, in both cases, the afferent profiles of secondary neurons contributing to the reflex may be more heterogeneous than is the net afferent input to the overall reflex. Irregular afferents have been suggested to provide the viewing distance-related gain in the angular VOR, perhaps working through an inhibitory interneuron (28). It is interesting to speculate that not only do the response dynamics of the various afferents might be matched on the dynamic requirements of the reflex pathways to which they contribute, but the afferents also participate in the execution of other behaviors. The other behaviors might include sustaining the excitability of the motoneuronal pools required for "vestibular tonus" and operations of the vestibular commissural

pathways in the case of regular afferents, and the modification of the central estimates needed during the performance of voluntary movements in the case of irregular afferents.

Reponses of Vestibulospinal Neurons to Neck Afferent Stimulation.

In our previous study (15) no correlation was found between gain, sensitivity, or phase of the neck or labyrinth response and conduction velocity. Nevertheless, if we consider the units receiving a convergent input form both receptors, a close relation was found when the ratio of gain of neck response (GN) and labyrinth response (GL) was compared to cell size. The smaller the size of the vestibulospinal neuron, the more prominent was the relative gain of neck response with respect to labyrinth response (i.e., high GN/GL); the opposite was true for larger neurons. This finding indicates a size-dependent arrangement affecting either the density or efficacy of the synaptic organization of labyrinth and neck afferent signals on this population of vestibulospinal neurons controlling the hindlimb muscles and posture. These reciprocal differences in gain of vestibulospinal neurons as a function of cell size, coupled with the significant differences in phase characteristics and the predictable vectorial addition of response to the two afferent inputs, will allow a precise definition of the output of vestibulospinal neurons during simultaneous stimulation of both receptors elicited by head rotation.

More recently, Gdowski and McCrea (35) studied the action of neck rotation on the firing behavior of vestibular neurons. As in the cat, the neck proprioceptive inputs varied from cell to cell, and usually combined linearly with vestibular inputs. Typically, the neck input was "antagonistic" with respect to the same cell's vestibular sensitivity and, consequently, reduced the response during combined head-on-trunk rotation. Of the sample, the non-eye-movement related neurons and eye-head-velocity neurons had the highest sensitivity to passive rotation of the neck and their response was related to the velocity. This is of particular interest because many of these cells are likely to participate in the MVST or LVST input to the neck segments (9, 10). In a separate study by Gdowski et al. (36) secondary vestibular neurons responded to combined labyrinth and neck stimulation evoked by head on trunk rotation during reflex-induced and voluntary head movements. During passive whole body rotation in the head unrestrained condition, the animal may counter-rotate the head by executing the vestibulocollic reflex or perform any other behavior. It was seen that the interaction of head on trunk signals related to the vestibulocollic reflex with vestibular signals during passive whole body rotation increased the gain of many secondary vestibular neurons, including many that project to the spinal cord. During self-generated head movements, inputs related to head on trunk movement combined destructively with the vestibular signals, and often canceled the sensory reafferent consequences of self-generated movements. Cancellation of sensory vestibular signals was observed in all of the antidromically identified secondary vestibulospinal units (19, 66), even though reflexive head on trunk movements did not significantly affect many of these units. The results suggest both head on trunk and body in space are sensed by the vestibular nuclei, perhaps separately, and this

information is conveyed to the vestibulospinal pathways that control the posture of the neck and body.

Spatial Responses of LVN Neurons.

Central vestibular neurons receive a wide variety of inputs, including those arriving from the vestibular end organ. The inputs to a single cell may originate from a unique vestibular receptor or involve a convergence from several different vestibular receptors. While a limited sample of neurons recorded from the LVN showed primarily narrow tuning characteristics, a larger sample might have revealed a range of tuning characteristics within the population. In addition, pure otolith neurons identified within the MVN (6, 25) also showed predominantly narrow tuning characteristics. These results have posed the following questions. What determines a neuron's spatio-temporal characteristic and what is its function? Its possible that central vestibular neurons that demonstrate narrow spatial tuning are involved in encoding direction of heading or changes in heading, while neurons that are broadly tuned are involved in the various compensatory tasks related to the vestibuloocular, vestibulocollic and vestibulospinal reflexes.

SUMMARY

This article is a review of work in three species, squirrel monkey, cat, and rat studying the inputs and outputs from the lateral vestibular nucleus (LVN). Different electrophysiological shock paradigms were used to determine the synaptic inputs derived from thick to thin diameter vestibular nerve afferents. Angular and linear mechanical stimulations were used to activate and study the combined and individual contribution of inner ear organs and neck afferents. The spatio-temporal properties of LVN neurons in the decerebrated rat were studied in response to dynamic acceleration inputs using sinusoidal linear translation in the horizontal head plane. Outputs were evaluated using antidromic identification techniques and identified LVN neurons were intracellularly injected with biocytin and their morphology studied.

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