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# Are There Parallel Channels in the Vestibular Nerve?

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***A popular concept in neurobiology is that sensory information is transmitted to the central nervous system over parallel channels of neurons that play different functional roles. But alternative organizing schemes are possible, and it is useful to ask whether some other framework might better account for the diversity of vestibular primary afferents.***

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*"In vision... pattern and movement are analyzed by parallel systems..."*

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In sensory systems, incoming information is sometimes carried over parallel populations of neurons that differ from each other and appear to encode separate stimulus attributes. For example, nociceptive and tactile information is conveyed from body surface to spinal cord over different populations of somatosensory afferents; signals from these afferent populations are routed over

distinctive, parallel chains of neurons from spinal cord to brain stem and cortex. In vision, similarly, information about pattern and movement is analyzed by parallel systems of neurons that are said to be separable from retina to visual cortex.

Characterization of such "parallel channels" is a popular and intuitively attractive framework for sensory system analysis, and several investigators have wondered whether a similar paradigm might usefully be applied to the vestibular system. This review summarizes evidence for parallel information channels in the first and most thoroughly

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characterized neurons of the vestibular system: primary afferents. It emphasizes afferents from the semicircular canals because they are the best understood. There are significant lacunae in this evidence, in particular, an exceedingly sketchy understanding of how signals from afferents are routed in the central nervous system. Nevertheless, a fairly mature body of information exists about the peripheral morphology and physiological properties of canal afferents in several species, so we can begin to ask if there are parallel channels in the vestibular nerve.

## What are parallel channels?

Where parallel channels have been identified in the periphery of other sensory systems they usually share the following characteristics.

1) The peripheral neurons are heterogeneous. Anatomic and physiological parameters describing these neurons, e.g., axon diameter or resting discharge rate, assume a wide range of values.

2) These parameter values covary in orderly ways. Among somatosensory afferents, for example, receptor type and axon diameter are clearly related.

3) Parameter values tend to cluster into groups. Individual variable distributions may or may not be bi- or multimodal, but where peripheral neurons are described by  $n$  parameters, their parameter values form clusters in  $n$ -dimensional space. For example, different ganglion cell types at a single retinal locus clearly vary in axon and soma diameter, dendritic structure, spatial filtering properties, temporal dynamics, and central targets.

4) The neurons described by different variable clusters appear to play qualitatively different functional roles in the sensory system. For example, afferents arising from free nerve endings and Pacinian corpuscles in the skin encode quite different somatosensory attributes. Attributes here, and elsewhere in this review, mean subcategories or submodalities of a stimulus that are perceived to have qualitatively different information content, e.g., pattern vs. movement or temperature vs. touch.

To what extent do vestibular afferents share these characteristics?

## Properties of vestibular afferents

*Are vestibular afferents heterogeneous?* Vestibular afferents are unquestionably diverse; they differ structurally and physiologically.

**ANATOMIC PARAMETERS.** Like other primary afferents, vestibular afferents have a three-part structure: 1) a peripheral process that arborizes in one of the semicircular canals or otolith organs of the

inner ear and transmits signals from vestibular hair cells toward the brain stem, 2) a cell body in the vestibular (Scarpa's) ganglion, and 3) a central process that enters the brain stem and synapses on vestibular nucleus neurons and other central nervous system (CNS) targets.

Differences in peripheral terminal morphology can be dramatic, and these are the basis of most morphological classifications (2, 3, 6, 9, 11). In amniotes (reptiles, birds, mammals), the terminal arbor may bear a cluster of boutons (bouton afferents; Fig. 1, A and B), one or more calyceal endings (calyceal afferents; Fig. 1C), or both (dimorphic afferents; Fig. 1D); these calyceal and bouton endings contact different receptor (hair cell) types (for review, see Ref. 14). Anamniotes (fish and amphibians) appear not to have calyceal endings; however, some anamniotes (toadfish, bullfrog) and turtles may have structurally distinct subpopulations of bouton afferents (Fig. 1, A and B). The axon diameters of afferents can differ by an order of magnitude or more, and soma diameters are almost as variable (2, 3, 6, 9, 11). Finally, terminal location has aroused substantial interest during the last decade because several physiological parameters vary systematically with the position of the terminal on the neuroepithelium (2, 3, 5, 9, 11; see *Do structural and physiological parameters covary?*)

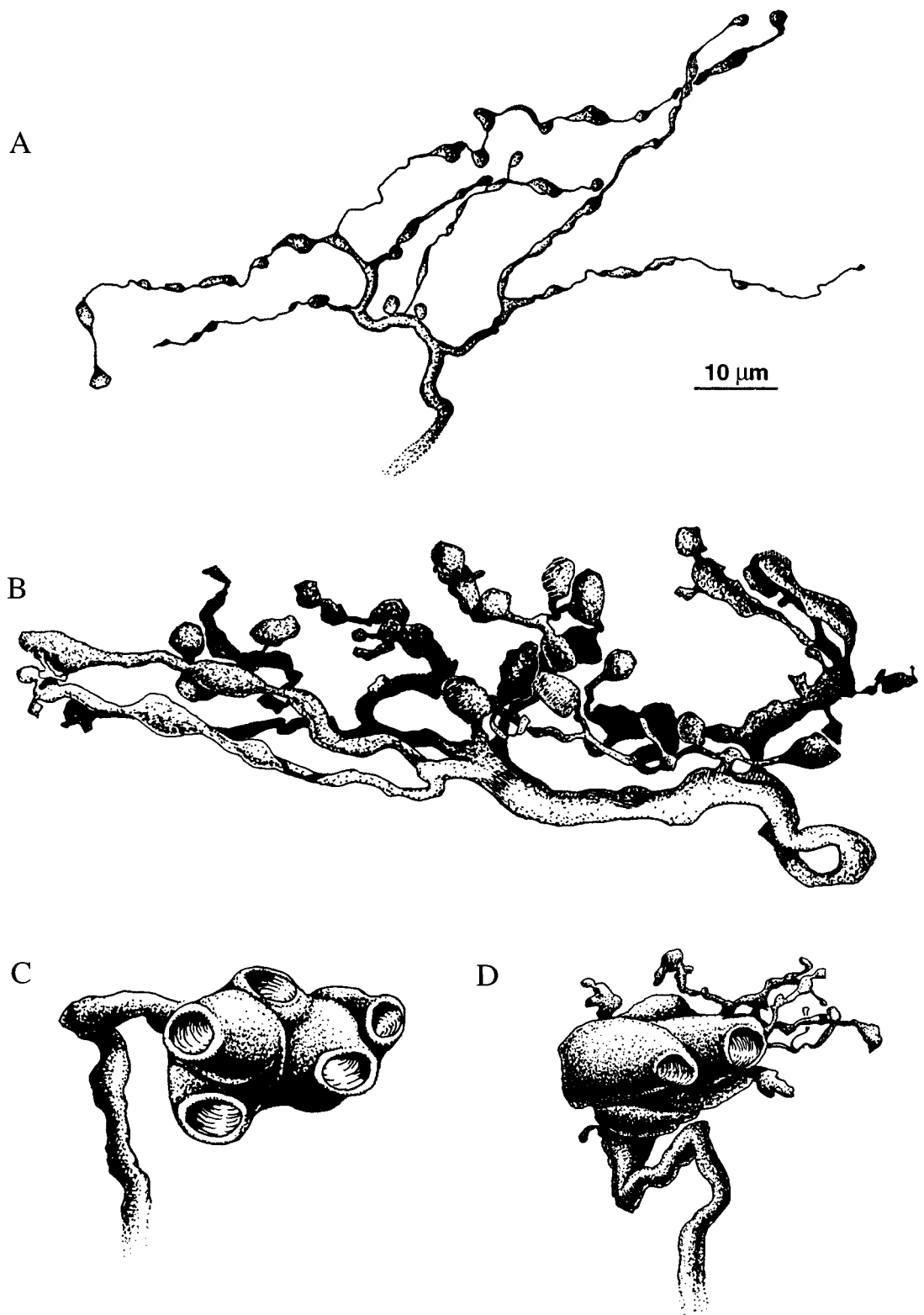
**PHYSIOLOGICAL PARAMETERS.** Canal afferents are most commonly characterized by their resting discharge as regularly or irregularly firing (Fig. 2) (1–5, 7, 9, 11, 13, 15); sometimes an “intermediate” category is recognized, and some authors emphasize that discharge regularity is a continuum. If the head is sinusoidally rotated at or near the plane of the canal, afferents can also be described by their “response dynamics” (Fig. 2): gain [incremental sensitivity to changes in head velocity (in spikes  $\times$  s<sup>-1</sup>/degrees  $\times$  s<sup>-1</sup>)], and the phase of the afferent's response (in degrees) relative to the head's sinusoidally oscillating velocity. An afferent's gain or phase may change with the frequency of oscillation, and some afferents exhibit a pronounced gain increase and phase advance at higher frequencies (2, 3, 5, 11). Afferents also differ in their sensitivity to electrical currents (4, 13), the time constant of their responses to velocity ramps or rapid head turns (i.e., they are relatively tonic or phasic; e.g., Ref. 7), and in their operating range and sensitivity to head speed [rate-intensity function (5)].

*Do structural and physiological parameters covary?* Clearly, they do. In mammals (2, 7, 11), irregularly discharging afferents have relatively phasic responses to rapid head turns and response phases shifted toward head acceleration; regularly discharging afferents have more

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*“Differences in peripheral terminal morphology can be dramatic. . . .”*

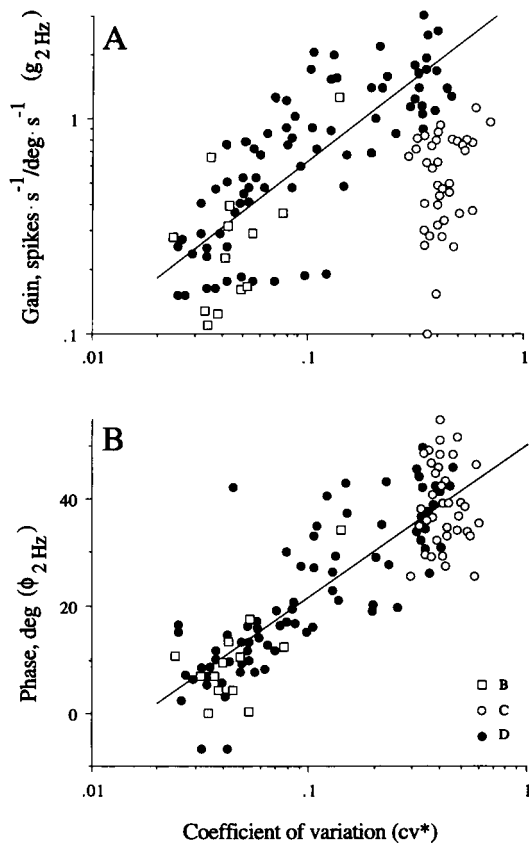
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**FIGURE 1.** Peripheral terminals of vestibular afferents in posterior semicircular canal of a turtle, *Pseudemys scripta*. Bouton afferents, which receive their input from type II hair cells (A, B), vary considerably in axon diameter and terminal morphology; multivariate statistical analyses suggest that they may be divisible into 2 groups based on their size and location on the neuroepithelium (6). Calyceal afferents (C) bear 1 or more cuplike endings that enclose type I hair cells. Calyx-bearing afferents that also bear bouton sprays are called dimorphs (D). Such differences in terminal structure and receptor (hair cell) type have led investigators to ask whether these afferents might play distinctive roles in vestibular signaling. Drawings by Alan Brichta.

tonic responses to rapid head turns and firing rates in phase with head velocity (Fig. 2). The relation between discharge regularity and

response phase also holds for afferents in toadfish (3) and bullfrog (9) and for bouton afferents in turtle (5).



**FIGURE 2.** Relationship between resting discharge regularity ( $CV^*$ ) and gain (A) or phase (B; re. head velocity) of the response to 2-Hz sinusoidal head rotations.  $CV^*$ , normalized coefficient of variation for resting interspike interval, i.e., a measure of discharge regularity. Note that the response phase of more irregular afferents (high  $CV^*$ ) is advanced by  $45^\circ$  or more toward head acceleration; in some nonmammals, afferents are phase advanced by almost  $90^\circ$ , firing maximally with peak head acceleration (3, 5, 9). Vestibular afferents ( $n = 125$ ) have been sorted into 3 morphological classes (B, bouton; D, dimorph; C, calyx). Lines are the best-fitting power law for bouton and dimorphic units (A) and best-fitting semilogarithmic relation for all units (B). [From Lysakowski et al. (11).]

Discharge regularity and response phase also covary with the location of the afferent terminal on the canal neuroepithelium. In mammals, for example, average discharge regularity increases and response phase advances as one moves from peripheral to central zones of the sensory surface (2, 11). Similarly, toadfish (3) and turtle (5) exhibit finely graded changes in discharge regularity and response phase, as well as several morphological parameters (6), as one moves from the periphery to the center of the canal.

In contrast, some afferent parameters follow this pattern of covariation less clearly if at all. Terminal morphology (and by implication, receptor type) is less tightly correlated with discharge regularity, response phase, and epithelial location. For example in mammals, in which the distinctive physiological properties of bouton, calyceal, and dimorphic canal afferents have been most fully

characterized, both calyceal and dimorphic afferents occupy the epithelial center, where they can be equally irregular (2, 11). Indeed, of the common physiological descriptors, only afferent gain appears linked to terminal type in mammals: calyceal afferents clearly have lower gains than dimorphic afferents even though they may have similar discharge regularities, response phases, and epithelial locations (2, 11).

Thus structural and physiological properties of vestibular afferents covary in orderly ways, but the pattern of variation is complex. If we think of  $n$  afferent parameters plotted in  $n$ -dimensional space, the resulting data cloud is structurally more intricate than the familiar X-Y plots of introductory statistics texts.

*Do afferents cluster into groups?* Orderly covariation of afferent properties is not a sufficient reason to posit parallel channels. It may simply reflect a gradient, e.g., a spatial gradient, that encodes a continuously variable stimulus attribute such as frequency in hearing or spatial acuity in vision or touch. Faced with a heterogeneous population of afferents, how do we decide whether the observed variation reflects distinct afferent classes, which may play different functional roles in vestibular signaling? One approach has been to focus on apparent discontinuities in peripheral terminal morphology and suggest that bouton, dimorphic, and calyceal afferents represent different classes of afferents. But detailed anatomic analyses suggest that there may be a continuous gradation of terminals, with pure calyceal and bouton endings at the extremes, and between them a series of dimorphic terminals with different proportions of the two ending types [turtle (6); mammals (2, 11)]. Several other afferent parameters, e.g., axon diameter, sensitivity to electrical currents, and response dynamics, appear to have continuous distributions; only discharge regularity tends to be bimodal (2, 5, 7, 11). So with few, sometimes arguable, exceptions, individual parameters provide little evidence for multiple classes of vestibular afferents.

A second approach has been to control for the role of spatial gradients in afferent heterogeneity (see *Do structural and physiological parameters covary?* above) and ask whether afferent properties differ if one holds terminal location constant (2, 3, 5, 6, 11). Such studies suggest two possible instances of heterogeneity that may be independent of epithelial location. First, in mammals, both calyceal and irregular dimorphic afferents occupy the epithelial center and there exhibit different axon diameters and different incremental sensitivities to head rotation (2,11). Second, in toadfish (3), bullfrog (9), and turtle (5, 6), two classes of bouton afferents with different mor-

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phologies and/or response dynamics have been described; some evidence suggests they occur side by side near the center of the canal [i.e., that they differ, even when location is held constant (3, 6)], but this is not yet firmly established (5). Thus calyceal and irregular dimorphic afferents provide the only clear evidence for afferent heterogeneity that is independent of epithelial locus.

A third approach has been to capitalize on the large number of available afferent parameters and use statistical methods, for example, principal components or discriminant analysis, to ask whether afferents fall into distinct groups when multiple parameters are considered simultaneously (5, 6). Such studies have revealed tendencies for afferents to cluster into groups based on their parameter values, but separation between groups tends to be modest.

Thus there is presently no clear answer to the question of whether afferents can be subdivided into groups based on their anatomic and physiological parameter values. There is a limited amount of positive evidence for distinct groups (i.e., groups that are separable in  $n$ -dimensional parameter space). On the other hand, there is ample evidence that afferent heterogeneity takes the form of spatial gradients (see *Do structural and physiological parameters covary?*).

*Do different afferents play distinctive functional roles in vestibular signaling?* It is well established that canal afferents signal temporal characteristics of head movement. Some afferents modulate their firing frequency in phase with head velocity and so are said to be “velocity signaling.” Other afferents have their response phase advanced toward head acceleration (Fig. 2). In all vertebrates for which data exist, these two “groups” represent the extremes of a continuous phase distribution that, as noted above, is tightly correlated with epithelial locus but not with terminal type (2, 3, 5, 9, 11).

The functional significance of different terminal types (Fig. 1) remains unclear, but recent experimental and modeling results suggest some new possibilities (8, 14). The unusual geometry of calyceal endings and their enclosed type I hair cells may increase the ability of calyx-bearing afferents to reach high firing rates and so extend the range over which spike frequency is a linear function of head velocity (8). Other work indicates that type I hair cells in turtles may have ciliary bundle morphologies that are significantly different from those on type II hair cells, and computational analyses suggest that one consequence may be increased stiffness of type I ciliary bundles (14). This could make calyceal afferents relatively insensitive to low head velocities but enable calyx-bearing afferents to respond to higher head velocities without saturating. These

modeling studies require experimental verification, but both suggest that one function of calyceal terminals and their associated type I hair cells may be to extend the dynamic range of the canals. Thus differences in terminal type and their associated hair cells could simply reflect the need to encode a continuous range of stimulus intensities (e.g., head velocities), rather than distinctive stimulus attributes.

### How are afferent signals routed in the central nervous system?

The argument for distinctive functional roles of vestibular afferents would be materially strengthened if we knew that different afferents are routed into distinctive central circuits. In vision, for example, the concept that different ganglion cell types play different functional roles was greatly reinforced when it was discovered that the axons of ganglion cells with different receptive field properties project to different central targets. In vestibular neuroscience, work addressing this issue has taken two forms.

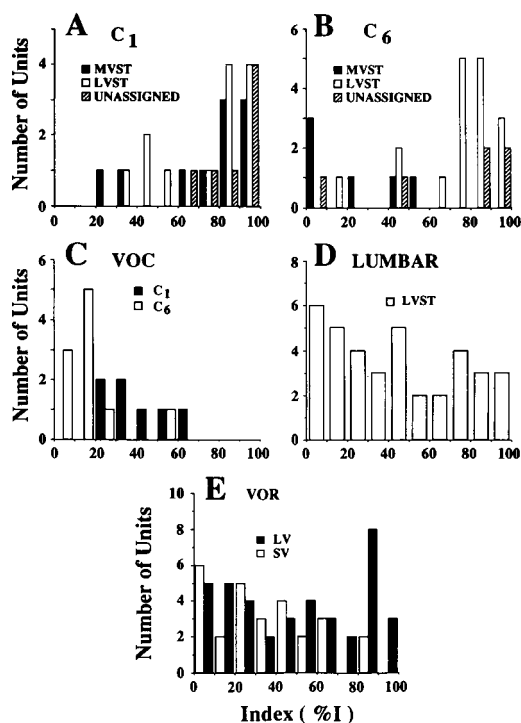
Several recent studies have used physiological methods to assess the contribution of regular and irregular afferents to vestibuloocular and vestibulospinal reflexes (see Refs. 4, 7, 13 for reviews). Most of these have taken advantage of the fact that irregularly discharging afferents, which tend to have the largest axon diameters, are more susceptible than regular afferents to externally applied currents. Thus irregular afferents can be preferentially stimulated by low depolarizing currents or “ablated” by hyperpolarizing currents (13). These studies suggest that there may be only limited segregation of regular and irregular afferents within the CNS. For example, it has been argued that the evoked discharge characteristics of regular (tonic) and irregular (phasic) afferents are best matched to the mechanical demands of the vestibuloocular and vestibulocollic reflexes, respectively and that as a result, vestibuloocular reflex (VOR) neurons might receive their peripheral inputs from regular afferents, whereas vestibulocollic reflex (VCR) neurons might receive irregular inputs.<sup>1</sup> Several physiological experiments have been designed to test this hypothesis, but their results have provided limited support for this hypothesis. Intracellular recordings in the vestibular nuclei (see Ref. 4 for review) suggest that, whereas VOR neurons are more likely to receive regular than irregular mono-

<sup>1</sup> The VOR assists in stabilizing gaze during head movement by producing eye rotation at approximately the same speed but opposite in direction to the head rotation. Vestibulospinal reflexes include “postural” reflexes of the limbs triggered by head movement (e.g., antigravity reflexes), and the vestibulocollic (neck) reflex, which acts with the VOR to help stabilize gaze.

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“...canal afferents signal temporal characteristics of head movement.”

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**FIGURE 3.** Distributions of %I (index), the percentage of total monosynaptic ipsilateral vestibular nerve input contributed by irregular afferents for various classes of secondary vestibular neurons. *A:* vestibulocollic cells to cervical segment C1, projecting in the medial (MVST, solid bars) or lateral (LVST, open bars) vestibulospinal tracts or else unassigned to a tract (hatched bars). *B:* vestibulospinal cells projecting to C6 and assigned to a projection pathway as in *A*. *C:* vestibulo-ocollic (VOC) cells projecting as far caudal as cervical segments C1 (solid bars) or C6 (open bars). *D:* LVST cells projecting to the lumbar segment (L1). *E:* vestibuloocular (VOR) cells projecting to the oculomotor nucleus, recorded in and around the ventral lateral vestibular nucleus (LV, solid bars) or the superior vestibular nucleus (SV, open bars). [From Boyle et al. (4).]

synaptic inputs, most monosynaptic inputs from the vestibular nerve are mixed (Fig. 3); conversely, some spinal-projecting vestibular neurons are dominated by irregular inputs, but inputs to most of these secondary neurons come from a range of afferent types (Fig. 3). Behavioral assays of afferent input to the monkey VOR have further complicated the issue by suggesting that irregular inputs to the VOR are negligible (13), significant (7), or dependent on conditions of stimulation (1). It does appear that pure calyceal afferents in monkeys do not contribute to the VOR, i.e., that irregular inputs, if indeed they are present, probably arise from dimorphs (7, 13). But with this potential exception, the available physiological data suggest that segregation of regular and irregular canal afferents in the central nervous system is limited at best.

Anatomic analyses present a similar picture of overlapping central trajectories, at least at the light microscopic level. In toadfish, the three physiological classes of afferents have largely (but not exclusively) overlapping central axons, with few

statistically significant differences in morphology (12). Similarly, the central axons of regular and irregular afferents in cats appear quite similar at the light microscopic level (see Ref. 15 for review), even though only the extremes of the available intracellular sample were compared (i.e., afferents with intermediate discharge regularities were not analyzed). The only statistically significant differences between regular and irregular afferent structure in cats are in axonal and varicosity size, number of varicosities per afferent, and mitochondrial shape. Furthermore, regular and irregular afferents have comparable proportions of terminals in the various vestibular nuclei, except for the lateral nucleus where regular terminals are rare.

Even when afferent axons appear to be completely filled and the full range of afferent sizes is included in the analysis (10), the central axons of afferents appear similar (Fig. 4). There are some clear qualitative differences; for example, some afferents project to the cerebellum and some do not (Fig. 4, single arrowheads). But, at least in turtles and at the present level of analysis, most differences between central axons are quantitative. For example, the tendency in cats (15) for larger diameter afferents to have more terminals in the lateral vestibular nucleus is also seen in turtles (10), but this appears to reflect a gradient in which afferent terminals are emitted more caudally as parent axon size decreases, not an identifying feature of a distinct afferent group (Fig. 4).

Thus the available anatomic and physiological data provide only limited support for the hypothesis that different afferents are routed into idiosyncratic central circuits, and this weakens any argument that there are parallel channels in the vestibular nerve. Still, our understanding of afferent central circuitry is relatively immature. There are intriguing suggestions of central differences at the ultrastructural level; for example, irregular afferents in cats are significantly more likely than regular afferents to contact large vestibular nucleus cells and to have a higher fraction of their synapses on somata and proximal dendrites (15). It is also possible that one of several afferent inputs to a vestibular secondary neuron may somehow be selected according to behavioral state (4).

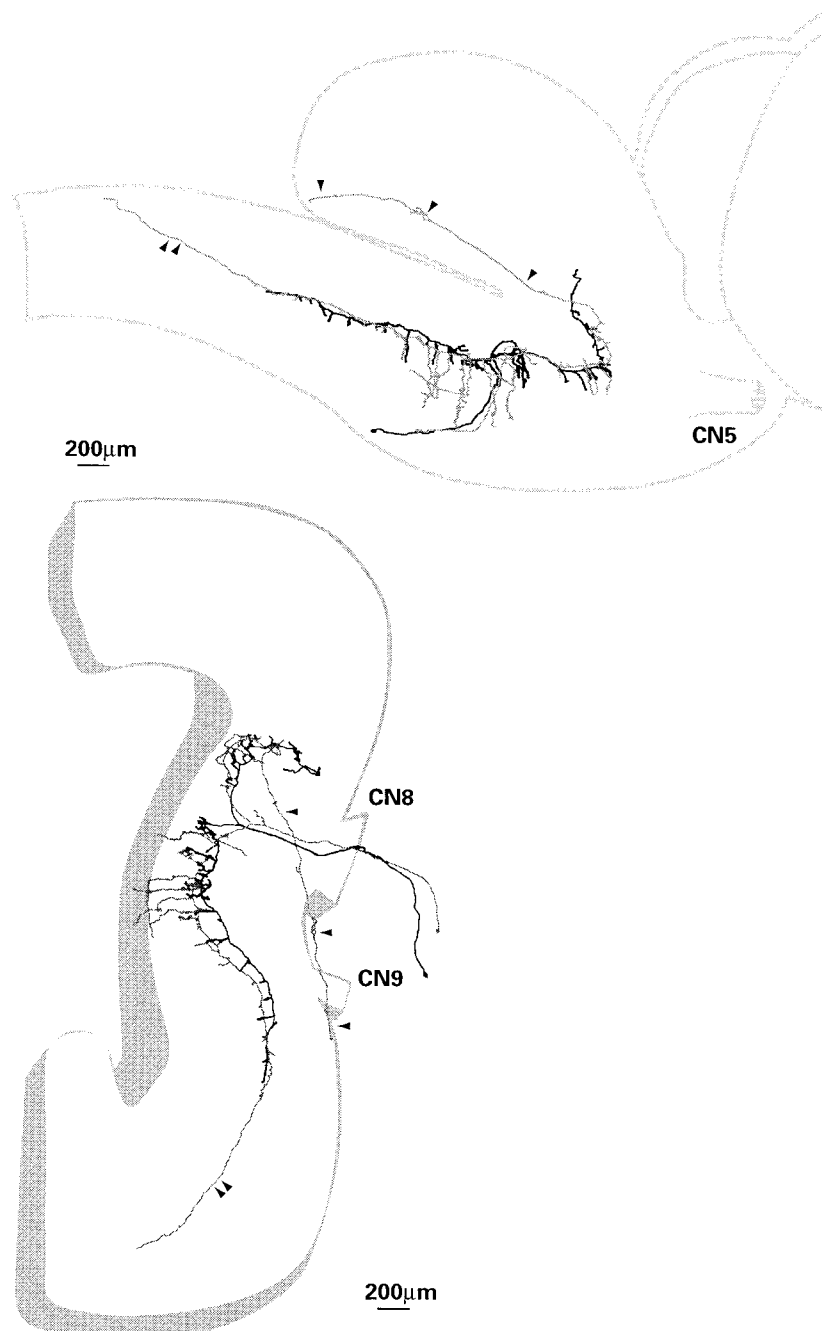
## Conclusion

Are there parallel channels in the vestibular nerve? Of the four characteristics outlined above (see **What are parallel channels?**) only the first two are clearly shared by vestibular afferents. 1) Vestibular afferents are heterogeneous and 2) their anatomic and physiological parameters covary in orderly, if sometimes complex, pat-

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*"...our understanding of afferent central circuitry is relatively immature."*

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**FIGURE 4.** Computer reconstructions of the central axons of 2 vestibular afferents from a turtle posterior canal. Afferents enter brain stem from vestibular nerve (CN8) and bifurcate into ascending and descending limbs that emit transversely oriented collaterals. *Top*: lateral view of turtle brain stem showing the 2 afferents in situ. *Bottom*: horizontal view of the same 2 afferents; cerebellar outline has been removed for clarity. Both views show considerable overlap between the 2 afferents as well as some differences, including 1) a long descending limb that almost reaches the spinal cord (double arrowheads), 2) a long ascending limb that traverses cerebellar cortex (single arrowheads), and 3) long ventromedially oriented collaterals that extend toward somatic motor column. These features are present in 1 afferent (gray) but not the other (black). The 2 descending limb morphologies are part of a structural continuum that is correlated with the diameter of afferent's parent axon (10). Axonal reconstructions by Janice Huwe.

terns. It is much less clear 3) whether this heterogeneity takes the form of gradients or distinct afferent groups and 4) the extent to which different afferents play idiosyncratic roles in vestibular signaling.

The issues surrounding *characteristics 3* and *4* are closely linked, and they are important as we develop hypotheses about the information car-

ried by canal nerves. Separable groups raise the possibility that these groups play different functional roles (*characteristic 4*); a gradient, for example, in response phase or terminal morphology, suggests that a continuous variable may be encoded. Thus the pattern of variability influences the functional questions we ask. Many authors have made it clear that dividing afferents

into morphological or physiological "types" is more a convenience for communication and analysis than a reflection of reality, but one unintended consequence may be to obscure a pattern of continuous variation that has important functional significance. This may be part of the reason we have not yet achieved a satisfying picture of the information content in canal signals and how this information content is related to observed heterogeneity in canal afferents.

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