6.26 Vestibulo-spinal Pathways in Tetrapods

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Synopsis: The vestibulospinal system provides the spinal motor circuits controlling head/neck and limb movements and body posture with rapid reflex adjustments to maintain equilibrium and stability and with a continuous essential excitatory drive, called tonus, to enhance reactive responses to perturbations that force the animal off normal posture. A striking observation in understanding the functional organization of this sensory-motor system is both that the driving sensory input can be dynamically modified by the behavioral context in which the sensation is made and that it remains able to quickly respond to an external force during self-generated head movements.

Abstract

The vestibulospinal system provides the spinal motor circuits controlling head/neck and limb movements and body posture with rapid reflex adjustments to maintain equilibrium and stability and with a continuous essential excitatory drive, called tonus, to enhance reactive responses to perturbations that force the animal off normal posture. The sensory signals to these reflex circuits originate from hair cells in the inner ear of otolith structures, namely the utricle and saccule, that transduce inertial acceleration and orientation of the head with respect to gravity and in the three orthogonally arranged semicircular canals that transduce angular head rotation.

The principal vestibulospinal pathways are 1) the medial vestibulospinal tract that descends in the ventromedial funiculus and innervates inter- and motoneurons located mainly in lamina VII, VIII, and dorsomedial IX throughout the cervical segments; and 2) the lateral vestibulospinal tracts that course in the lateral to ventrolateral funiculi and are distinguished by two divisions: i) a cervical-projecting tract that overlaps many of the targets of medial vestibulospinal tract neurons including the motoneurons in ventromedial IX and also contributes to reflex control of shoulder and forelimb (arm) muscles; and ii) a lumbosacral-projecting tract that provides a rapid input to maintain stable posture and reflex control of the lower body. A striking observation in understanding the functional organization of this sensory-motor system is both that the driving sensory input can be dynamically modified by the behavioral context in which the sensation is made and that it remains able to quickly respond to an external force during self-generated head movements. The structural basis for vestibulospinal inputs to spinal motor control circuits in quadrupeds and bipeds rely in part on the animal's need for coordination between fore- and hind-limb reflex movements. Understanding the sensory-to-

motor transformations in the diverse species rely on the correlations of the conserved and unique

species behavior, morphology and physiologic function.

The vestibulospinal system provides the motoneuronal (direct) and interneuronal (indirect) motor circuits of the ventral spinal cord with reflex control of head/neck and limb movements and body posture. This descending information helps to maintain the organism's equilibrium and stability with rapid reflex adjustments as needed. The reflex control mechanisms operate on top of a separate and continuous essential excitatory drive to the spinal motor pools. The tonic excitation raises the resting voltage level of the neuron so that new synaptic currents imparted by vestibulospinal terminals readily bring the neuron to discharge, and thereby enhances the reactive responses to perturbations that force the animal off normal posture. Ewald (1882) first convincingly demonstrated that the inner ear vestibular labyrinth exerts constant excitatory tonic influences within the central nervous system and musculature, and coined the term "Tonus Labyrinth".

When our head is perturbed, say for example during locomotion, signals arising in the vestibular endorgans and neck proprioceptors are generated to produce the vestibulocollic reflex (VCR), the vestibuloocular reflex (VOR), and to a lesser extent the stretch reflex-like cervicoocular reflex (Cohen 1974; Barnes and Forbat 1979; Wilson et al. 1995). These reflexes adequately stabilize the head in space and hold images of stationary objects steady on the retina (Grossman et al. 1988). However, when we voluntarily move both our eyes and head (gaze) together, say in acquiring and tracking visual objects of interest, there is a necessity to adjust, or even suppress, these compensatory reflexes to bring the head and eyes in the direction of intended gaze. At the same time, when the head is moved by either a perturbation or voluntarily, other vestibulospinal pathways are activated that influence alpha and gamma motoneurons to fore- and hindlimb muscles (Grillner et al. 1970, 1971; Pompeiano 1972).

The key sensory signals originate from vestibular hair cells in the inner ear otolith structures, namely the utricle and saccule, that transduce inertial acceleration and orientation of the head with respect to gravity and in the three orthogonally arranged semicircular canals that transduce angular head rotation. In early vertebrates central vestibular neurons are organized in well conserved and distinct neuroepithelial segments, and the projections to the oculomotor complex originate from the rostral rhombomeres and the origins of the ipsi- and contralaterally projecting vestibulospinal pathways are found in the more caudal rhombomeres (Straka and Baker 2013). This conservation of the compensatory reflexes mediated by the vestibulospinal system was established early in vertebrate evolution (Diaz and Glover 2002; Straka and Baker 2013). The influence of the vestibulospinal system can be detected in the appearance of the arm-hanging posture as early as 11 weeks of gestation in the human fetus (Ohmura et al. 2018). At birth the inner ear vestibular sensory structures are morphologically established and the descending tracts from axons of vestibular nuclei neurons, and particularly lateral nucleus neurons, to the cervical, thoracic and lumbosacral spinal cord are largely complete (reviewed by Jamon 2014). Within an hour after birth a foal will typically right itself in direct opposition to the force of gravity and start to correct body sway. These striking behaviors immediately after birth are possible due to existence of otolith and canal signals delivered by the vestibulospinal system to the relevant motor effectors. Functional maturation of the vestibular-mediated drive to the cervical motoneurons continues rapidly in the first weeks postnatally in mice (Lambert et al. 2016). It is reasonable to postulate that the ontogeny of motor behaviors associated with the vestibulospinal system reflects survival pressures among the prey and predator species.

Vestibulocollic Reflex. The VCR stabilizes the head in space during motion or intended motion

by activating the neck muscles that pull in the direction opposite of the head movement. This reflex also serves as a protective measure to help prevent head injury during a fall. The head is massive and behaves as an unstable inverted pendulum posture under most conditions. The fossil evidence shows the evolution of skull of hominids has benefitted head and neck stability in modern human by having center of gravity of the head only slightly in front of the occipital condyles (the fulcrum) (Tobias, 1992). As early as 1830, Flourens conducted pioneering studies examining head movements in pigeons and established for the first time the role of the vestibular structures in equilibrium and position and reflex movement of the head. Fifty years later and clearly influenced by Flourens' work Ernst Mach recognized the semicircular canals as providing a complete coordinate system for head rotations in three-dimensional space (Mach, 1875; Henn, 1974). In that same period Retzius (1881, 1884) was examining the anatomy of the inner ear in diverse lower vertebrates species, establishing the basis for later advancements with improved imaging techniques.

The predominant direct pathways from the semicircular canals and otolith organs to the spinal axial motoneurons and their associated interneuronal pools controlling head rotation, dorsal extension and ventral flexion of the head, and head stability are the three-neuron reflex arcs though the medial vestibulospinal tract (MVST) and a subset of lateral vestibulospinal tract (LVST) (Wilson and Maeda 1974; Fukushima et al. 1978; Wilson and Peterson 1988; Wilson et al. 1995; Peterson and Boyle 2003). The MVST descends bilaterally through the brainstem medial longitudinal fasciculus (MLF) and into the ventromedial funiculi on both sides of the spinal white matter as far as the upper thoracic enlargements. The axons of the LVST neurons course more lateral to the MLF in the brainstem and descend in the ipsilateral lateral and ventrolateral funiculi and target the upper cervical segments controlling head and neck reflexes

and extend into the cervical enlargement to target shoulder and forelimb (arm) motor pools (Wilson and Yoshida 1969; Brodal 1974). Another possible link of the VCR is made by vestibulo-ocular-collic neurons, which have dual destinations: one to the cervical spinal cord via the descending medial longitudinal fasciculus (MLF), like MVST axons, and the other to the oculomotor nuclei via the ascending MLF (Isu and Yokota 1983; Uchino and Hirai 1984; Isu et al. 1988; Minor et al. 1990). In addition to direct VCR pathways, there are other direct and indirect pathways that contribute to head and neck posture, such as the vestibulo-reticulo-spinal (Peterson and Boyle 2003). These reticulospinal neurons can excite motoneurons at all levels of the spinal cord and are particularly powerful on neck motoneurons (Wilson and Peterson 1988).

Figure 1 shows a schematic representation of the major projections of the crossed and uncrossed MVST (left diagram) and the uncrossed cervical-projecting LVST (right diagram) pathways in cat and squirrel monkey (Isu and Yokota 1983; McCrea et al. 1987a,b; Isu et al. 1988, 1991; Shinoda et al. 1988, 1992a,b; Minor et al. 1990; Boyle et al. 1992; Boyle and Moschovakis 1993; Wilson et al. 1995; Boyle 2001). Some vestibulospinal axons in cat might provide a bilateral input to cervical cell groups (Shinoda et al. 1992); they appear to be few in number and were not included in the figure. The center cartoon gives a representative transverse section of an upper cervical segment; the general location of MVST axons in the ventromedial funiculus and their terminal synaptic fields in the ventral horn are in red (left side of spinal cord) and the general location of LVST axons in the lateral to ventrolateral funiculi and their terminal synaptic fields in the ventral horn are in blue (right side of spinal cord). Principal neuronal targets of both crossed and uncrossed MVST axons are 1) the medial wall of lamina VIII, which contains dorsal suboccipital motoneurons (more rostrally) and intervertebral muscles (more caudally), the dorsal neck motoneurons such as the splenius capitis (Richmond et al. 1978), and

interneurons including commissural cells (Szentágothai 1951; Bolton et al. 1991); 2) lamina VII, which contains mostly interneuron circuits including propriospinal neurons and scattered motoneurons supplying the ventral as well as the dorsal neck muscles; and 3) the lateral motoneuronal groups of lamina IX (labeled IXA in Fig. 1) and particularly the spinal accessory (SA) neurons supplying the sternocleidomastoid and trapezius muscles that rotate the head and flex the neck. A major feature of crossed MVST axons in the primate is the high degree of collateralization in the cervical segments, and contrasts with the fewer collaterals issued from uncrossed MVST fibers. VOC neurons are particularly of interest because of their dual inputs to oculomotor and neck neurons. They resemble other crossed MVST fibers in the extent of their branching and terminations in the ventral horn; except, VOC cells also target the precerebellar Roller's nucleus in the caudal brainstem and the central cervical nucleus in the upper cervical segments, which receive neck proprioceptive inputs (Hongo et al. 1988) projecting to the cerebellar cortex and deep cerebellar nuclei (Matsuhita and Yaginuma (1995). Uncrossed MVST cells contact these proprioceptive nuclei sparingly or usually not at all. This finding indicates that signals carried by VOC cells are widely distributed to include extraocular motor nuclei, medially located cervical motoneurons, interneuronal segmental circuits, and likely propriospinal neurons, and proprioceptive pathways to the cerebellum; and suggests a generalized role of VOC cells in vestibular control of movement. In cat and monkey crossed and uncrossed MVST axons can target both the medially-located and lateral motor nuclei.

Pompeiano and Brodal (1957a) made the classic observations that lesions of the spinal cord produce retrograde changes in the vestibular nuclei complex, particularly in the region containing the conspicuous giant cells of Deiters, confirming the early study by von Monakow (1883). These investigators clearly showed that the LVST originates from the lateral vestibular

nucleus, and that the pathway is somatotopically organized: neurons in the more ventral and rostral parts of the nucleus project to the cervical spinal segments and those in the dorsal (dorsal Deiters') and caudal regions innervate the ventral horn of the lumbosacral cord. Like crossed MVST and VOC fibers LVST neurons distribute extensive collaterals into ventral horn of the cervical spinal course along their trajectory (Fig. 1). Principal neuronal targets of cervical-projecting LVST axons are 1) the alpha, gamma and beta neck motor neurons in lamina IXa along the lateral wall, including the spinal accessory motoneurons, 2) lamina VII and VIII, which contain mixtures of moto- and interneuron circuits; and 3) the ventral motoneuronal groups of lamina IX (labeled IX VM in Fig. 1) innervating neck muscles rostrally and shoulder, proximal and distal limb motorneurons more caudally. At the level of the lower segments of the cervical spinal cord, MVST and LVST axons appear to be distinct (Shinoda et al. 1986). Thus, the morphological division between crossed MVST and LVST neurons is relatively minor, with MVST neurons innervating the more medial and dorsal regions of the ventral horn whereas the LVST neurons innervating the more lateral and ventral regions of the ventral horn. In general, MVST and LVST neurons largely share the same synaptic target areas along the cervical spinal cord. This organization might be structured to ensure that the wide variety of control signals carried by vestibulospinal pathways include those originating from the semicircular canals and otolith organs (McCollum and Boyle 2004; Chartrand et al. 2016).

The major of specific information we have concerning the behavior of the VCR has come largely from studies of the connectivity within the VCR circuitry of the rabbit (Akaike et al. 1973a,b) and cat (Rapoport et al. 1973a,b; Wilson and Maeda 1974; Wilson et al. 1979; Baker at al. 1985; Uchino 2001), and the responses of cat neck motoneurons and muscles (Eazure and Sasaki 1978; Dutia 1985; Shinoda et al. 1994, 1996, 1997), and head movements of rabbits

(Fuller 1981), cats (Goldberg and Peterson 1986;) and squirrel monkeys (Kubo et al. 1981) to vestibular stimulation. The connections between the semicircular canals and spinal neurons are largely organized in synergies based on spatial function (McGillum and Boyle 2004; McCollum 2007). For example, motoneurons of the obliquus capitis superior, splenius, longissimus, and sternocleidomastoid muscles were excited by stimulation of each of the three contralateral canal nerves and inhibited by stimulation of each of the three ipsilateral canal nerves (Shinoda et al, 1996, 1997). In contrast, motoneurons of obliquus capitis inferior muscle were excited by stimulation of the ipsilateral anterior (ACN), posterior (PCN), and contralateral LCN and inhibited by stimulation of the contralateral ACN, PCN, and ipsilateral LCN (Shinoda et al, 1994, 1996).

Vestibulo-limb reflexes

The sole vestibulospinal pathway to the lumbosacral spinal cord is the LVST originating predominantly in dorsal Deiters' (lateral) nucleus of the vestibular nuclei complex. Three principal sources provide afferent input to this LVST pathway. Inertial and gravitational accelerations are sensed by hair cells of the utricular macula, and these signals are conveyed by the nerve afferents mainly to the entire lateral nucleus (Brodal et al., 1962), and modulate the firing rate of identified LVST neurons (Rapoport et al., 1977; Boyle and Pompeiano, 1980a, 1981a,b; Marchand et al., 1987; Kasper et al., 1988a). The fastigial nucleus and vermal cortex of the paleocerebellum comprise a significant postural input to Deiters' nucleus (Walberg et al., 1962; Walberg, 1975), and can play an important modulatory role on vestibulo-limb reflexes (Manzoni et al., 1997, 1998; Pompeiano et al., 1995). The other main afferent input to the 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

(Lindsay et al., 1976; Andre et al., 1993). Proprioceptive signals generated during axial and limb movements are conveyed over spinovestibular pathways to Deiters' nucleus (Pompeiano and Brodal, 1957b; Pompeiano, 1972), and can modulate the firing rate of identified LVST neurons (Boyle and Pompeiano, 1980b, 1981a,b; Brink et al., 1980, 1981; Kasper et al., 1988b).

This afferent 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 upright posture (Forbes et al. 2016), make corrective adjustments (Forbes et al. 2017), and regulate locomotion (Orlovsky 1972; Rossignol et al. 2006). In the lumbosacral spinal segments LVST neurons exert an excitatory influence directly (and indirectly) on both alpha (Lund and Pompeiano, 1965, 1968; Wilson and Yoshida, 1968; Grillner et al., 1970) and gamma (Carli et al., 1967; Grillner et al., 1969) motoneurons (see Pompeiano, 1975, for a review of the synaptic actions of LVST stimulation on spinal neurons). Using electrical stimulation techniques in the cat, Abzug et al. (1974) presented suggestive evidence that half the lumbosacral projecting LVST neurons exerted a collateral action in the cervical spinal segments. Shinoda et al. (1986) found that 36% (4 out of 11) of the cat LVST axons that projected at least to segmental level T_2 had axon collaterals to the lower cervical cord. To view these data in functional terms it was argued that 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.

However, this organization was not confirmed in the squirrel monkey (Boyle 2000): LVST neurons classified as second-order neurons by their short latency, monosynaptic input from the 8th nerve, identified to project to the lumbar segments by their antidromic responses, and intracellularly labeled with biocytin to permit a direct visualization of their axon trajectory in the cervical spinal cord revealed little to no collateralization in their trajectory in the cervical

segments. Of the 37 secondary LVST neurons, only 1 axon issued a collateral to innervate the ventral horn, primarily in the region of the spinal accessory motoneurons; this single collateral provided a relatively minor input compared to that of LVST neurons terminating in the cervical cord. Thus, secondary, caudal-projecting LVST neurons represent a more private, and mostly rapid, communication pathway between dorsal Deiters' nucleus and the motor circuits controlling the lower limbs and tail.

Vestibular Inputs to Identified Vestibulospinal Neurons

Primary vestibular afferents can be classified as regular or irregular based on their interspike intervals (Goldberg and Fernández 1971, Goldberg et al. 1984). These afferents differ in other aspects, most importantly in their response sensitivities and dynamics to rotational stimuli (Fernández and Goldberg 1971). Irregular afferents have a high frequency gain enhancement and phase advance, whereas regular afferents have dynamics more closing related to head velocity. The relation between the afferent's peripheral dendritic morphology and its physiology has been shown using intracellular recording and labeling techniques (Baird et al. 1988; Boyle et al. 1991). Is the peripheral organization spurious or does it serve a purpose? The dynamic elasto-viscous and inertial properties associated with movements of the eyes (VOR), head (VCR), and limbs (VSR) are different. Do the different afferents preferentially distribute onto secondary vestibular neurons that participate in different reflex mechanisms? This hypothesis was tested using an electrophysiological paradigm in the squirrel money (Goldberg et al. 1987): secondary VOR neurons receive a predominant synaptic input from regular afferents (Highstein et al. 1987), and cervical projecting MVST and LVST neurons receive almost exclusively an irregular afferent input (Boyle et al. 1992). This synaptic input from irregular

afferents may contribute to the presumed dynamic load compensation of the VCR (Wilson and Peterson 1988) and the vestibular forelimb reflexes, whose dynamics can resemble those of the VCR (Schor et al. 1988). In contrast, vestibulo-ocular-collic (VOC) neurons, which project both rostrally to the IIIrd (oculomotor) nucleus and caudally to the cervical spinal cord, receive their major synaptic input from velocity-encoding regular afferents.

Vestibulospinal responses to head movement in the alert primate

Central vestibular neurons carry a wide variety of movement related signals, from a sole labyrinthine signal reflecting a single canal or an otolith origin to a more integrative signal that incorporates not only the labyrinthine input(s) but also the position or velocity of the eyes, or both, in the absence of head movement (Miles 1974; Chubb et al. 1984; Tomlinson and Robinson 1984; McCrea et al. 1987a,b; Iwamoto et al. 1990a,b; Scudder and Fuchs 1992). Eye position-related signals were found in the electromyographic activity of some neck muscles in the alert cat, such as suboccipital and longissimus capitis muscles (Vidal et al. 1982), indicating a coordinated organization in gaze control. Both reticulospinal (for review see Grantyn and Berthoz 1988; Grantyn et al. 1992) and vestibulospinal (Peterson et al. 1981; Iwamoto et al. 1990a; Boyle 1993) are the likely principal sources of eye movement-related signals to cervical motoneurons. In the alert squirrel monkey secondary vestibulospinal neurons, identified to receive direct monosynaptic input(s) from the labyrinth and to project in the ventromedial funiculi at C_1, and thus presumably MVST cells, were found to carry head velocity signals during rotation, but also position or velocity of the eyes, or both, during fixation of an eccentric stationary visual target or voluntary tracking of a moving visual target (Boyle 1993). Thus, MVST cells likely contribute a variable input to neck excitation that is synthesized to participate

both in more global functions such as postural stability of the head on neck and neck on trunk, the existing movement and position of the eyes in orbit during moment-to-moment purposeful activity, and in the execution of more specific motor tasks such as the VCR (Goldberg and Cullen 2011). This is borne out by the following observations: MVST cells distribute axon terminations to multiple moto- and inter-neuronal cell groups in the ventral horn of the cervical spinal cord, including spinocerebellar neurons, and can excite or inhibit neck motoneurons (Wilson and Peterson 1988); they receive short-latency inputs from vestibular-nerve afferents across the continuum of response and discharge behavior; and they display an assortment of head and eye movement-related discharges (reviewed above).

The spatiotemporal transformations of target location in visual and auditory space to the generation of activation patterns of large numbers of extraocular and neck skeletomotor muscles are highly complex CNS processes. And yet some of our most routine activities executed thousands of time each day involve the coordinated movements of the eyes and head. Voluntary head pursuit of visual targets and intended head movement to external cues, such as localizing a sound source, require different control and feedback strategies than the reflex responses to perturbations. When we voluntarily move our eyes and head together, say in acquiring and tracking visual targets, there is a necessity to modify, or even eliminate, the compensatory reflexes to bring the eyes and head in the direction of intended gaze. The stable position of the head near the horizontal plane is integral to the vestibular system's ability to differentiate self- from externally-induced head motion by providing a steady gravitational reference and an optimal otolith sensitivity; in addition a stable head reference is beneficial to the saccade generator which is driven by a neural reconstruction of target position in space, i.e. in head coordinates (Daemi and Crawford 2015). As we walk or run and execute orienting eye and head

movements, an unexpected external perturbation is a constant threat to postural stability. Disorders of the vestibular system and cervical spine affect head stability, and can dramatically alter the patient's willingness to induce self-motion and can lead to trepidation of normal activities (Agrawal et al. 2009; Strupp et al. 2019).

Before the development of recording neural responses in alert animals performing natural behaviors it was reasoned that saccadic eye and vestibular commands summed linearly during voluntary gaze shifts. It is now accepted that the vestibular component of the VOR is actually weakened or turned off during large amplitude gaze saccades (Guitton and Volle 1987; Laurutis and Robinson 1986; Pélisson and Prablanc 1986; Tomlinson and Bahra 1986b; Tomlinson 1990). Self-generated head movements can reach velocities up to 350–400 °/s for extremely rapid gaze saccades. However, normal exploratory gaze saccades are made in the range <100 °/s. The main neuron making up the middle leg of the VOR is the position-vestibular-pause (PVP) neuron (McCrea et al. 1987a,b). The discharge of the secondary PVP neuron is completely turned off or paused during the execution of a saccade, particularly for saccades made in the direction ipsilateral to the cell's soma, thereby releasing the opposing reflex drive to the extraocular muscles. This is *not* the case for middle leg of the VCR. Saccadic eye movements in the head-fixed (Boyle 1993) and head-free (Boyle et al. 1996: McCrea et al. 1999) conditions did not influence the discharge behavior of secondary MVST cells. Although neurons' projection pathway(s) were not identified, these findings were confirmed and extended in Old World primates by Roy and Cullen (2001, 2004). While the MVST cell does not encode head velocity in space for self-generated movements, it nevertheless conveys perturbations of the head, <u>even during large voluntary gaze saccades</u> (Boyle et al. 1996; Boyle 2001). The functional importance of this finding is clear: to maintain head stability a perturbation of the head must be

detected, encoded as a signal independent of the signals associated with the self-generated movement, and transmitted to the cervical spinal segments for reflex compensation. A hyperpolarized MVST cell, silenced to permit a voluntary head movement, would be at a disadvantage to carry this signal. Thus, the MVST cell continues to discharge normally during voluntary head movements, without any modulation related to that movement but capable to convey the perturbation information. This finding also indirectly speaks against an exclusive peripheral mechanism that blinds the MVST cell to active head movements. Many MVST cells carry an eye movement-related signal that influences the outflow of the MVST pathway and receive convergent angular and linear inputs (Boyle 1993, 1997).

A simple conceptual model of the voluntary and reflex control of head movement is given in Fig. 2. External perturbations are the critical events that must be encoded and properly processed in the vestibulospinal pathways. The involuntary perturbations force the head to move, with or without an ensuing displacement of the body, which in turn activate the inner ear semicircular canal and otolith receptors. At this point in time the labyrinthine control signals are unambiguous and provide input to the VCR pathways originating in the vestibular nuclei. Command signals of self-generated or voluntary head movements are constructed in separate premotor centers of the cerebral cortex and distributed to the appropriate effectors, for example those located in the superior colliculus and in the midbrain and brainstem reticular formations. Based on the reafference theory of von Holst and Mittelstaedt (1950) an "efference copy" or corollary discharge of the constructed motor command is sent to the VCR pathways to modify or even cancel the expected (or redundant) head acceleration signals transmitted by the labyrinth during self-generated head movement. Sensory reafference signals, arising from the neck muscles and joints (Boyle and Pompeiano 1981; Wilson et al. 1990) may also participate directly

in extracting the active components of the head movement from the VCR pathways or indirectly by constructing a head posture reference upon which both the active and passive head movements act. Viewed in this context, it is also not surprising to see why some patients suffering from cervical trauma mimic the behavior of vestibular patients.

One of the most striking observations made in understanding the functional organization of a sensory system is that the interpretation of the prime sensory input can be dynamically modified by the behavioral context in which the sensation is evoked. Starting in the 1960's many laboratories experimentally investigated the extraordinary interaction of the electric fish's sensory reception and perception with its environment (Watanabe and Takeda 1963; Bullock et al. 1972; Heiligenberg 1976; Bell, 1982). Most electric fish rely on active electrolocation based on the returned distortions caused by external objects from their own self-generated electric field. The motor command that elicits the discharge from the electric organ sends a corollary signal to the neural electrosensory lobe to *in essence* null the powerful and redundant self-generated discharge to permit electroreception of its environs and most importantly the desired and meaningful inputs related to predators and prey. In mammals the ensuing signals associated with voluntary head movements to track visual targets or locate objects on interest (or threat) in space interact with the compensatory mechanism(s) to counter the ensuing head movement. The vestibulospinal reflexes must be suppressed or nulled to release the spinal motor circuits to permit the execution of the intended head movement and thus allow accurate gaze shifts. Importantly, in the case of the vestibulospinal system sensory receptors in the inner ear labyrinth still transduce the head acceleration signals. The vestibular nerve afferents transmit these precise head movement-related into the brain where they can enter the output pathways to rapidly activate the compensatory head/neck and body/limb reflexes during large and, particularly

unexpected, perturbations. Of particular significance the vestibulospinal neuron remains able to quickly respond to a passive stimulus during voluntary head movements to protect the organism from injury from a fall. This establishes the physiological basis for the trepidation seen in vestibular patients for generating active orienting movements during normal behaviors such as walking on uneven ground or in a crowd.

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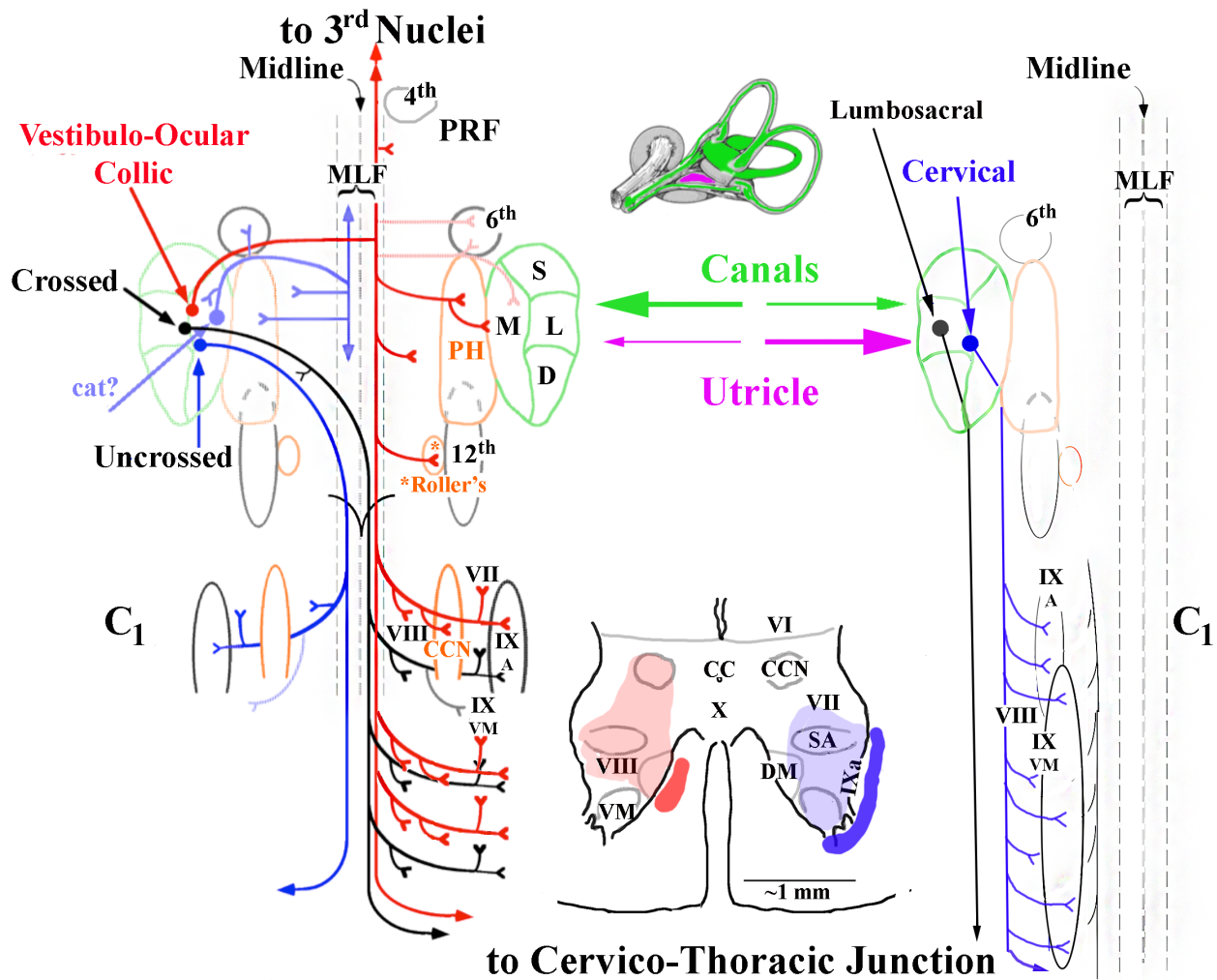
Figure 1. Schematic representation of the major projections of crossed and uncrossed MVST (left side) and cervical-projecting LVST (right side) VCR pathways drawn without respect to vestibular input specificity. Vestibular inputs (cartoon in upper center) both from the semicircular canals carrying angular head rotation information and from the otolith organs carrying inertial acceleration and head orientation with respect to gravity information provide powerful inputs into both pathways, that vary from a single source or convergence from multiple receptors. Transverse section of the ventral horn (below lamina VI) shows an idealized axon

location (solid) and synaptic terminal field (shaded) of MVST (red) and cervical-projecting LVST (blue) neurons. LVST projecting to lumbosacral segments of the caudal spinal cord bypass the cervical segments (see text for more details). Abbreviations used are: 3rd cranial nerve, oculomotor (medial, inferior and superior recti and inferior oblique extraocular muscles) nuclei; 4th, fourth cranial nerve or trochlear (superior oblique extraocular muscle) nucleus; PRF, pontine reticular formation; MLF, medial longitudinal fasciculus' 6th cranial nerve, or abducens (lateral rectus extraocular muscle) nucleus; S, superior vestibular nucleus; M, medial vestibular nucleus; L, lateral vestibular nucleus; D, descending vestibular nucleus; 12th, twelve cranial nerve or hypoglossal nucleus; CC, central canal of spinal cord; VI, VII, VIII, IX and X, grey matter layers of Rexed (1952); CCN, central cervical nucleus; DM, dorsomedial motoneuronal pool; VM, dorsomedial motoneuronal pool; SA, spinal accessory motoneuronal pool supplying sternocleidomastoid and trapezius muscles.
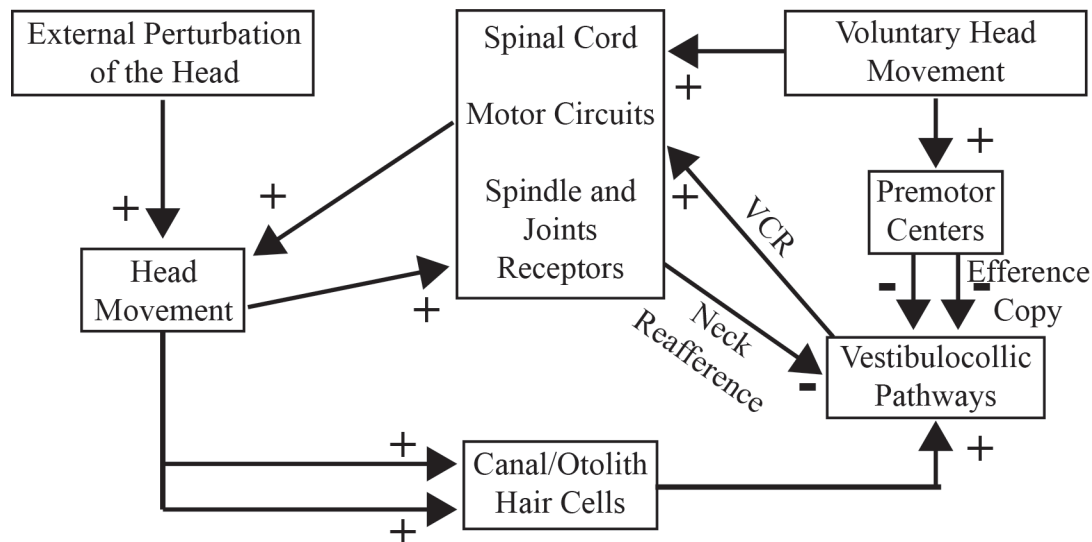
Figure 2. Simple model of active and passive contributions to the vestibulospinal control of reflex head movement and posture. The precise source and mechanism by which responses to active, self-generated components of a head movement are suppressed or nulled on vestibular neurons are as yet undefined but is modeled here as an efference copy signal, as postulated by von Holst and Mittelstaedt (1950), that effectively cancels the resultant input from the labyrinth onto the secondary vestibulospinal neurons, thus removing the redundant information and permitting throughput of external perturbations. The role of spinal afferents, such as those arising from muscle spindles and joints, which are activated by both active and passive head movements, remains unresolved.