

# How Actions Alter Sensory Processing

## Reafference in the Vestibular System

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Our vestibular organs are simultaneously activated by our own actions as well as by stimulation from the external world. The ability to distinguish sensory inputs that are a consequence of our own actions (vestibular reafference) from those that result from changes in the external world (vestibular exafference) is essential for perceptual stability and accurate motor control. Recent work in our laboratory has focused on understanding how the brain distinguishes between vestibular reafference and exafference. Single-unit recordings were made in alert rhesus monkeys during passive and voluntary (i.e., active) head movements. We found that neurons in the first central stage of vestibular processing (vestibular nuclei), but not the primary vestibular afferents, can distinguish between active and passive movements. In order to better understand how neurons differentiate active from passive head motion, we systematically tested neuronal responses to different combinations of passive and active motion resulting from rotation of the head-on-body and/or head-and-body in space. We found that during active movements, a cancellation signal was generated when the activation of proprioceptors matched the motor-generated expectation.

**Key words:** vestibular nucleus; self-motion; reafference; efference copy; gaze shift; vestibular reflexes; head-unrestrained

### Introduction

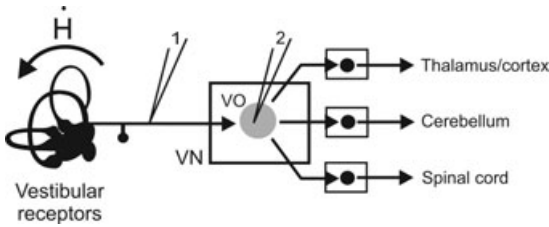
The sensors of the vestibular system are stimulated by active as well as passive (i.e., externally produced) movements. Yet, the ability to navigate and orient through the environment requires knowledge of which components of vestibular activation result from active versus passive head motion. The processing of vestibular information, at the level of single neurons has been well characterized in experiments in which head movements are passively applied.<sup>1,2</sup> Until recently, however, the way in which the brain distinguishes between vestibular stimulation resulting from passive (i.e., vestibular exafference) and active (i.e., vestibular reafference) motion was not known. To address this question, we have completed a

series of experiments that have provided novel insights into how the brain differentiates between vestibular inputs that arise from changes in the world and those that result from our own voluntary actions. In this chapter we discuss some of our recent findings. We first summarize work addressing how primary afferents and central neurons in vestibular nuclei (VN) (Fig. 1) respond to active head motion. We then explore how vestibular information converges with proprioceptive and other extravestibular signals to distinguish active from passive head movements at the first stage of central processing. Finally, we report our recent results showing that a cancellation signal is generated only in conditions where the activation of neck proprioceptors matches the motor-generated expectation.

### Methods

Rhesus monkeys (*Macaca mulatta*) were prepared for chronic extracellular recording in the

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**Figure 1.** Vestibular pathway: Vestibular receptors are activated by head movements and are innervated by primary afferent fibers that project directly to neurons in the vestibular nuclei. In turn these central neurons project to the (i) cervical spinal cord to activate the neck musculature, (ii) the vestibulo-cerebellum, and (iii) thalamo-cortical system. In this study we recorded from the vestibular afferents (1) and “vestibular-only” neurons of the vestibular nuclei (2).

vestibular nerve and nuclei using aseptic surgical techniques similar to those previously described by Roy and Cullen.<sup>3,4</sup> All experimental protocols were approved by the McGill University Animal Care Committee and were in compliance with the guidelines of the Canadian Council on Animal Care. Monkeys were trained to follow a target light (HeNe laser) to generate pursuit and gaze-shift movements. During the experiments, the monkey sat comfortably in a primate chair, placed on a servo-controlled vestibular turntable. Neuronal activity was initially recorded in the head-restrained condition during voluntary eye movements and passive whole-body and head-on-body rotations. After a neuron was fully characterized in the head-restrained condition, the monkey's head was slowly and carefully released so that the neuron's activity could be characterized during voluntary head movements.

Extracellular single-unit activity, horizontal gaze and head positions, target position, and vestibular turntable velocity were recorded and stored on digital and tape (DAT) tape for playback.<sup>5,6</sup> Action potentials were first discriminated during playback using a windowing circuit (BAK), and then spike density was calculated by convolving a Gaussian function with the spike train (SD of 10 msec).<sup>7</sup> Subsequent analysis was performed using custom algorithms.<sup>4</sup>

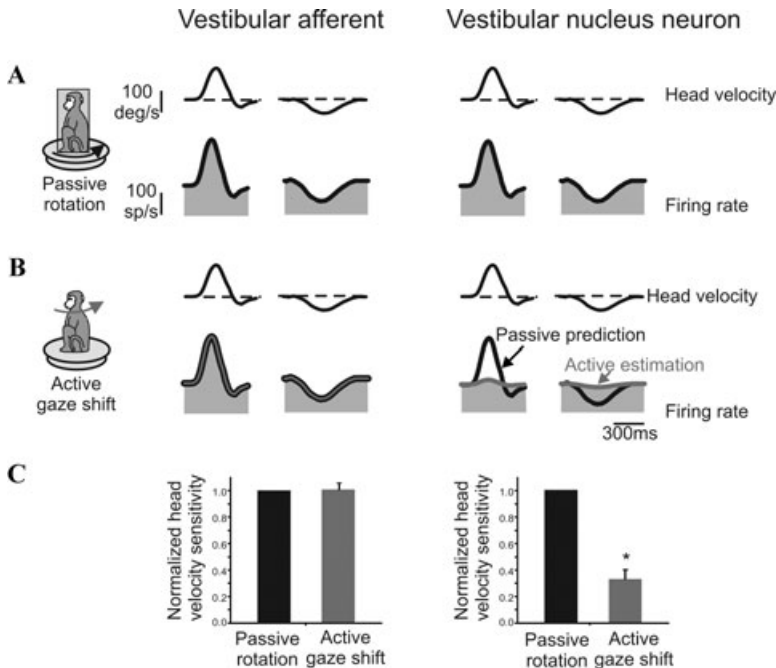
## Results

### Differential Processing of Actively-Generated versus Passive Head Movement First Occurs in the Vestibular Nuclei

Recordings were made from the vestibular nerve afferents, as well as from neurons in the brain stem vestibular nuclei that receive direct vestibular afferent signals, and in turn process and distribute information to the skeletomotor, vestibular-cerebellar, and thalamo-cortical systems. As shown in Figure 2A and B, while vestibular semicircular afferents reliably encode active rotations,<sup>4,6</sup> the responses of the target neurons in the vestibular nuclei can be dramatically attenuated.<sup>3,8</sup> This is summarized for the population of neurons (afferents:  $n = 67$ , VN:  $n = 28$ ) in Figure 2C. What is even more striking is that the same second-order vestibular neurons continue to selectively respond to passively applied passive whole-body rotations when a monkey simultaneously generates active head-on-body movements.<sup>3,8</sup> Thus, vestibular information arising from voluntary movements is selectively suppressed early in sensory processing in order to create a neural representation of the outside world. Notably, the differential processing of active and passive motion is specific to a class of neurons in the vestibular nuclei that have been classically termed “vestibular-only (VO) neurons,” on the basis of their lack of eye movement-related responses in head-restrained animals.<sup>9</sup> Given, however, that these neurons reliably encode only passively applied head velocity (i.e., vestibular exafference), this nomenclature is misleading.

### Neither the Activation of Neck Proprioceptors nor a Neck Motor Command Alone Explains the Decreased Sensitivity to Active Head Movements

Since the voluntary head movements shown in Figure 2 were produced by activation of the neck musculature, neck proprioceptors as well



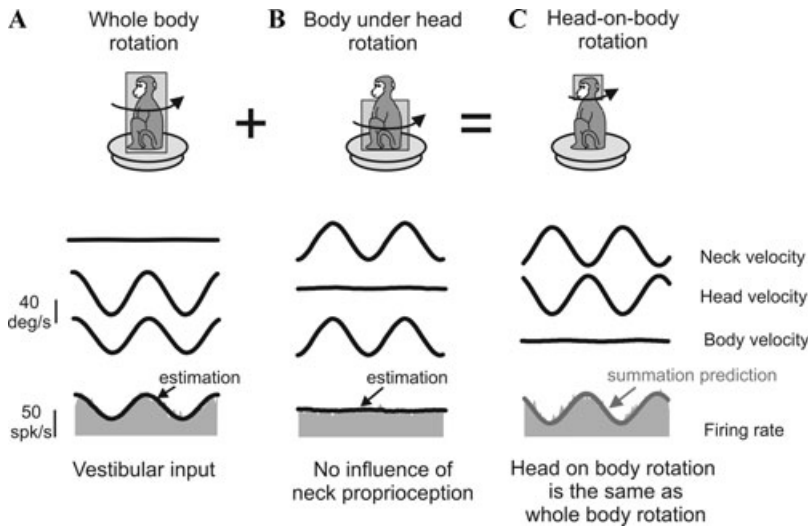
**Figure 2.** Vestibular afferents and vestibular nuclei neurons during active and passive head movements: An example canal afferent (left panel) and vestibular nuclei neuron (right panel) during **(A)** passive head movements and **(B)** active head motion. Thick black lines **(A, B)** show the firing rate predicted based on responses to passive head motion, and gray lines **(B)** show the best fits to the firing rate during active motion. Afferents reliably encode head motion in both conditions, while central neurons show significantly attenuated responses to active of head motion **(C)**.

as vestibular receptors were stimulated during the movements. In turn, the activation of neck-muscle spindle afferents has long been known to influence the activity of VN neurons in decerebrate animals.<sup>10,11</sup> This raises the question of whether the extra-vestibular information that is provided by the activation of the proprioceptive system might contribute to the suppression of vestibular sensitivity at the first stage of central processing. In alert rhesus monkeys, however, passive activation of neck proprioceptors alone does not significantly alter neuronal sensitivities to head rotation (Fig. 3B).<sup>5</sup> Thus, the responses of a neuron to passive whole-body rotation is comparable to its sensitivity to passive head-on-body rotation (compare panels A and C of Fig. 3), even though neck proprioceptors are robustly stimulated in the latter condition. Similarly, the production of a motor command to move the neck (efference copy

command) is not sufficient to influence neuronal responses. Even when the generation of neck torque reached levels comparable to those issued to produce large active head movements, neuronal responses were not altered (data not shown).<sup>5</sup> In summary, neither neck motor efference copy nor proprioception cues alone are sufficient to account for the attenuation of neuronal sensitivity to active head rotation in rhesus monkeys.

### The Selective Suppression of Sensitivity to Active Head Movements Occurs Exclusively When Activation of Neck Proprioceptors Matches the Motor-Generated Expectation

A common feature of both the experiments described in the section above was that activation of neck proprioceptors and generation of

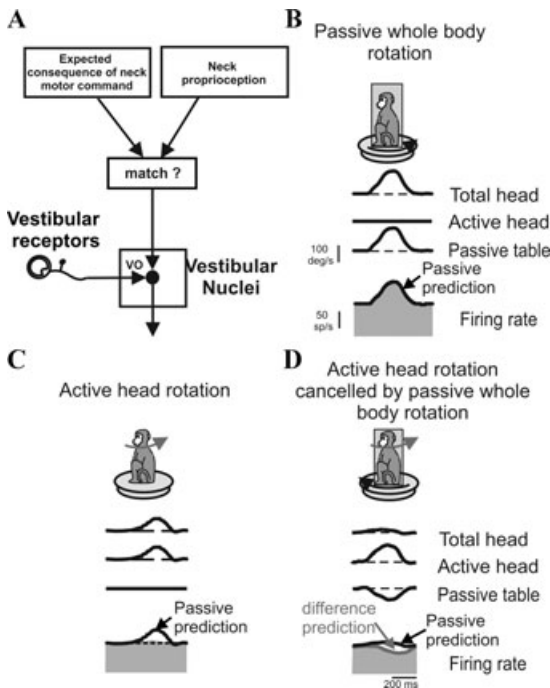


**Figure 3.** Responses of a vestibular nuclei neuron to vestibular, neck proprioceptive, and combined stimulation: Example responses to passive whole-body (A), passive body under head (B), and passive head-on-body (C) rotations. Black lines show the best fit of the head (A) and neck (B) velocity to the firing rate; the gray line (C) shows the predicted firing rate for passive head-on-body rotation based on vestibular and neck proprioception sensitivities estimated during whole body rotation and body under head rotation respectively.

motor efference copy signals was not matched as they typically are during normal active head movements. This is because in one experiment, the proprioceptive system was activated via passive manipulation of the head (i.e., Fig. 3B), while in the second the head-on-neck movement that was commanded by the neck motor system was prevented because the head was restrained. By systematically controlling the correspondence between the intended and actual head movement, we have shown that a cancellation signal is exclusively generated in conditions where the activation of neck proprioceptors matches the motor-generated expectation (Fig. 4A).<sup>5</sup>

Figures 4B–D show this for a typical VO neuron. The neuron was strongly modulated in response to passive whole-body rotation (Fig. 4B), during which the vestibular sensors are activated but no proprioceptive or motor efference copy signals are present. During active head-on-body movements, the same neuron was less sensitive to vestibular stimulation (Fig. 4C) as described above. Note that in this condition, the active head movement activated propriocep-

tive as well as vestibular afferents. Finally, the neuron was also recorded during a condition in which the monkey made active head movements, but velocity of the head in space (Fig. 4D; gray arrow in schema) was experimentally cancelled by simultaneously (and passively) rotating the monkey in the opposite direction (black arrow in schema). Consequently, the head moved relative to the body but not to space. As a result, the neck proprioceptors were activated in a manner that matched the motor generated expectation (as during the normal gaze shifts shown in Fig. 4B), but vestibular afferent input was greatly reduced. In response, the neuron's modulation showed a marked inhibition, in excellent correspondence to that predicted from the difference in response during passive versus active (Fig. 4B versus C) head movements (gray superimposed trace). Thus, this result is consistent with the schema illustrated in Figure 4D; vestibular input from the vestibular afferents is suppressed only when the activation of neck proprioceptors matches the motor-generated expectation (as is the case in Fig. 4C and D, but not Fig. 3C).



**Figure 4.** An internal model of the sensory consequences of active head motion is used to suppress reafference selectively at the vestibular nuclei level. **(A)** Schematic to explain the selective elimination of vestibular sensitivity to active head-on-body rotations. **(B)** An example VO neuron (gray filled trace) during passive whole body rotation. **(C)** Activity of the same neuron during active-head-on body rotation. Neuronal modulation predicted from the neuron's response to passive head motion is superimposed (black trace). **(D)** Activity of the same neuron when active head-on-body motion (gray arrow in schema) is experimentally cancelled by simultaneously rotating the monkey in the opposite direction (black arrow in schema). In this condition the monkey generates an efference copy signal and the neck proprioceptors are activated, but vestibular afferent input is greatly reduced. The inhibition of response matches that predicted based on the difference in response during passive **(B)** versus active **(C)** head movements (gray superimposed trace).

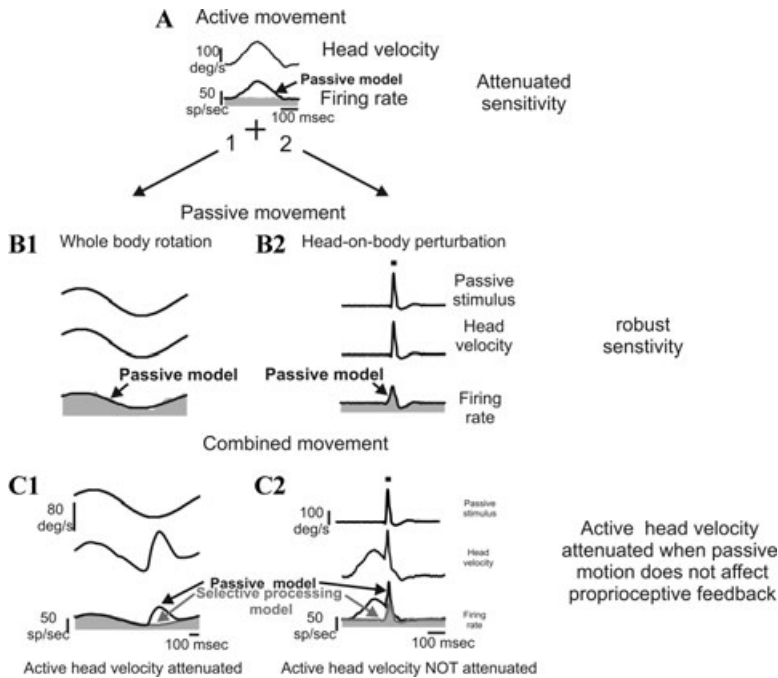
### A Test of Our Working Model

To test our working model we have begun a series of experiments designed to compare neuronal responses when active head movements (Fig. 5A) are made simultaneously in combination with two different kinds of passive stimu-

lation (Fig. 5B1, 2). First, as shown in the left panel, passive stimulation was applied by rotating the head and body together in space using the vestibular turntable (Fig. 5B1). Second, as shown in the right panel, passive stimulation was applied by rotating the head relative to the body to produce a brief head-on-body perturbation (Fig. 5B2). The black lines show that the same head velocity-based model can describe the firing rate in both passive conditions. Finally, the monkey made an active movement while undergoing one of the two types of passive movements depicted in panel B (Fig. 5C1, 2). Notably when the passive stimulation consisted of whole-body rotation, neurons were insensitive to the active head-on-body movements, while continuing to selectively encode the passive portion of the movement. In contrast, when the passive stimulation consisted of a head-on-body rotation, neurons were no longer able to distinguish between active and passive components of head velocity and encode both components of head velocity.<sup>12</sup> This is what we expected since in this condition, the neck proprioceptive feedback is the result of both active and passive movement and so does not match the motor-generated expectation. Thus, taken together these preliminary results provide support for our proposal that a cancellation signal is only generated in conditions where the activation of neck proprioceptors matches the motor-generated expectation.

## Discussion

Von Holst and Mittelstaedt initially proposed that an internal model of the sensory consequences of voluntary behavior is used to selectively suppress reafference.<sup>13</sup> Our recent work had provided evidence for this proposal at the level of single neurons in the vestibular nuclei. This differential processing of vestibular information during active versus passive head movements is essential for ensuring accurate motor control. This point can be easily appreciated by considering that many of the same neurons



**Figure 5.** Model confirmation: vestibular nuclei neurons do not always distinguish between active and passive head motion: Active head movements (**A**) were made in combination with two different kinds of passive stimulation: (**B1**) whole body and (**B2**) head-on-body ( $N = 2$ ) rotation. The black lines (**B1**, **B2**) show best fit of the head velocity to the firing rate when either type passive stimulus was delivered in isolation, as well as the predicted response during active head movements (**A**). When an active head-on-body movement was combined with passive whole-body rotation, neurons selectively encode the passive component of head velocity (**C1**). When an active head-on-body movement was combined with passive head-on-body rotation, however, neurons encode the summed stimulation (**C2**). Black lines indicate predicted firing rates based on passive stimulation; gray lines in panel C indicate the predicted response if VO continued to be have attenuated sensitivity to the active movement.

that distinguish actively generated from passive head movements control the vestibulo-collic reflex (VCR) via their projections to the cervical segments of the spinal cord.<sup>14,15</sup> The vestibular drive to this reflex pathway would command an inappropriate head movement during active movements, since the reflex would normally cause a compensatory head movement in the opposite direction. Suppression of the neuronal response to head motion suggests that reflex function is reduced during active movements. Nevertheless, our findings also suggest that these neurons would continue to encode robust information about passive head-on-body rotations that occur during locomotion. This selectivity is fundamental, since recovery from tripping

over an obstacle while walking or running requires a selective but robust postural response to the unexpected vestibular stimulation.

The finding that vestibular reafference is suppressed early in processing also has important implications for understanding higher-level vestibular function. First, the vestibular nuclei neurons are reciprocally interconnected with the fastigial nucleus<sup>16-18</sup> and nodulus/uvula<sup>19-21</sup> of the cerebellum, suggesting that the differential processing of vestibular reafference is most likely essential for the computation of spatial orientation as well as for the regulation of gait and posture. Second, the vestibular nuclei send information to the thalamo-cortical system via their projections to the vestibular

thalamus.<sup>22,23</sup> Regions of the cortex and thalamus that receive inputs from the vestibular nuclei are not sensitive to eye movements,<sup>24–28</sup> suggesting that the vestibular information could arrive via VO neurons. Furthermore, vestibular projections to the hippocampus are of considerable interest because this structure produces an estimate of current orientation for navigation.<sup>29</sup> It is commonly thought that on-line integration of the head velocity signal generated by the vestibular nuclei is required for the estimation of head direction by the hippocampal system.<sup>30,31</sup> Future studies will be required to understand how the gated information encoded by these neurons of the vestibular nuclei is used by these higher-order structures to provide perceptual stability during natural behaviors.

### Conflicts of Interest

The authors declare no conflicts of interest.

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