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Sensory signals during active versus passive movement

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Our sensory systems are simultaneously activated as the result of our own actions and changes in the external world. The ability to distinguish self-generated sensory events from those that arise externally is thus essential for perceptual stability and accurate motor control. Recently, progress has been made towards understanding how this distinction is made. It has been proposed that an internal prediction of the consequences of our actions is compared to the actual sensory input to cancel the resultant self-generated activation. Evidence in support of this hypothesis has been obtained for early stages of sensory processing in the vestibular, visual and somatosensory systems. These findings have implications for the sensory-motor transformations that are needed to guide behavior.

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Abbreviations

fMRI function magnetic resonance imaging

Introduction

Most of our sensory experiences are gained by active exploration of the world, for example, by locomotion, eye movement and touch. Normally, we can readily distinguish between sensory signals that register changes in the external world (exafference) and those that result from our own actions (reafference). The ability to make this distinction is essential both for our perceptual stability and for spatial orientation and the construction of neural representations of the environment to guide behavior accurately. When we make eye movements, for example, the world moves across our retinas, but we do not perceive the world as moving. How do we distinguish sensory events resulting from our own actions from those that arise externally?

So far, most analyses of sensory processing have been done in an experimental framework that is designed to

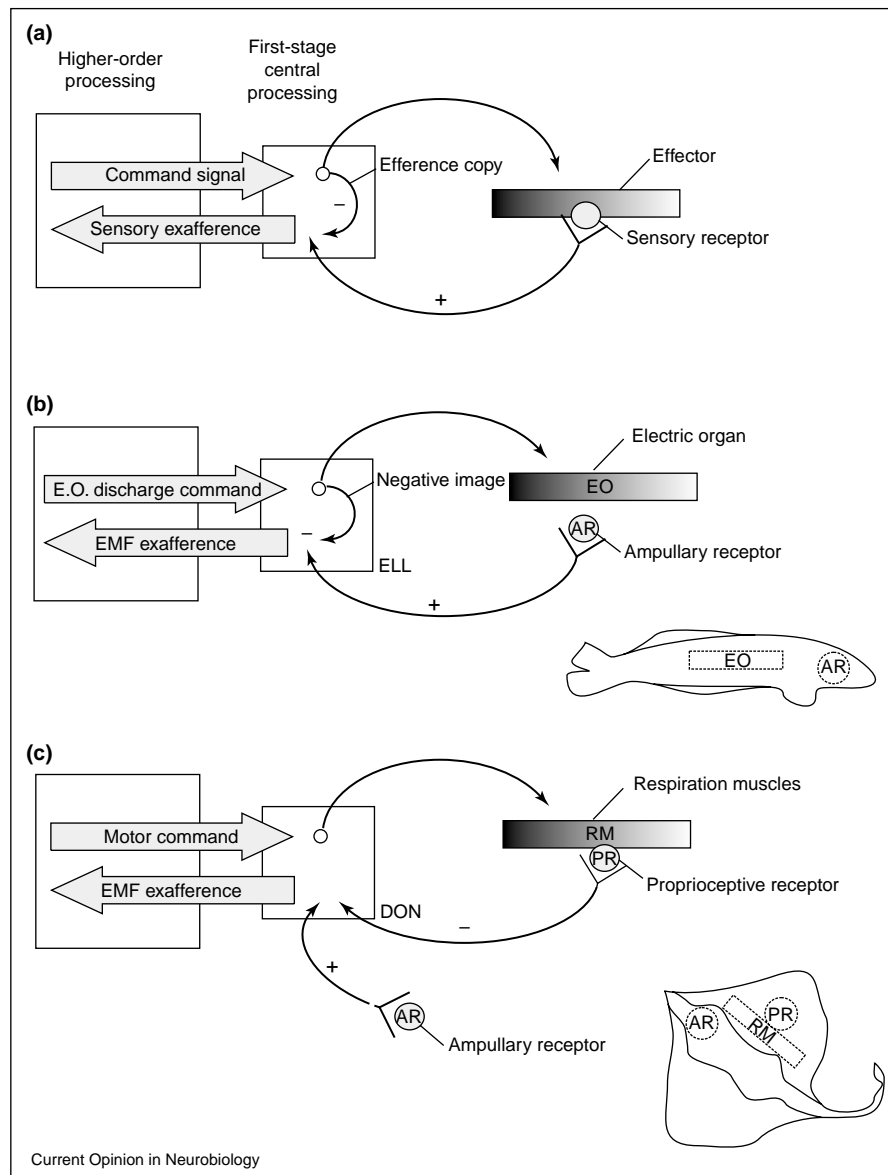
test passive rather than active sensation. Recent results from several laboratories have, however, yielded major insights into our understanding of how sensory signals are processed during movement. In this review, I consider recent advances in this field, focusing on experiments in the vestibular system that have provided evidence for the differential processing of reafference early in sensory systems [1[•],2,3^{••}]. Parallels between findings in this system and those emerging from recent studies of the visual [4,5,6[•]] and somatosensory [7^{••},8,9^{••}] systems are also considered. This body of work is discussed in relation to prominent theories of motor control and addresses the following questions. What information or cues are available to achieve perceptual stability? At what level in sensory processing are active and passive sensory signals differentially encoded? What mechanisms underlie differential sensory processing? Finally, I consider the implications of these results in relation to how the processing of sensory signals during motion is reflected in the sensory-motor transformations that are needed to guide behavior.

Conceptual frameworks and model systems

Historically, the idea that animal behavior is triggered by stimuli and based on reflex elements that are linked together in a chain of activations has provided an important conceptual framework in neurophysiology. The focus on relationships between afferences and efferences follows logically from the influential theory of a reflex chain first made popular by Sherrington in 1906 [10]. In classical reflex theory, any given stimulus results in a predictable motor response (i.e. a reflex), and complex behavior can be explained as the combined effect of a chain of reflexes. Although this conceptual framework remains to be abandoned completely, it is clear that the ‘cause’ of every response cannot be solely attributed to a sensory stimulus.

In 1950, two separately but simultaneously published studies by Von Holst and Mittelstaedt [11] and Sperry [12] re-evaluated this dominant model and demonstrated a need for the traditional perspective to be reversed. Classical reflex theory asks what is the relationship between afference (sensory information) and efference (motor output)? These investigators argued, however, that it is necessary to ask what happens when efference causes changes in the state of an organism that are then reverberated back into the nervous system as reafference? To avoid responding to sensory inputs that arise from self-generated actions, the sensory system needs to know what the motor system has done. On the basis of their observations, Von Holst and Mittelstaedt [11] proposed the ‘principle of reafference’ (Figure 1a), in which a copy

Figure 1



(a) Simplified scheme of the refference principle of von Holst and Mittelstaedt [11]. The motor command is sent to the effector muscle and in turn sensory activation, resulting from the activation of sensory receptors by an effector, is returned. This refference is then compared to an efference copy of the original motor command. Here, refference is arbitrarily marked '+' and the efference copy is marked '-'. When the refference and efference copy signals are of equal magnitude they cancel, and no sensory information is transmitted to the next levels of processing. By contrast, a difference between the refference and the efference copy indicates an externally generated event (i.e. exafference) that is considered behaviorally relevant and thus is processed further. **(b)** Primary afferent fibers from electroreceptors project to the cerebellum-like electrosensory lobe (ELL) of mormyrid electric fish. Descending motor commands result in the generation of electric organ discharge, which results in the activation of ampullary afferents (i.e. refference). Corollary discharge signals associated with the motor command that elicits the electric organ discharge are prominent in the mormyrid electrosensory lobe and are used to reduce the central effects of activity in ampullary receptors evoked by the electric organ discharge (i.e. exafference) of the fish. Abbreviation: EMF, electromagnetic field. **(c)** Skate do not generate electric fields but can detect them. The first-order neurons in this system are the principal cells of the dorsal octavolateral nucleus (DON). These neurons receive proprioceptor inputs from the parallel fibers inputs of the dorsal granular ridge, which cancel electric magnetic field refference in the DON during respiration.

of the expected sensory results of a motor command, which they termed the 'efference copy', is subtracted from the sensory signal to eliminate reafferent information. More recent behavioral investigations have general-

ized this original proposal by suggesting that an internal prediction of the sensory consequence of our actions, derived from the motor efference copy, is compared to the actual sensory input [13–15].

In some model systems, including the electrosensory systems of mormyrid fish [16,17] and elasmobranchii (sharks, skates and rays [18]), the mechanosensory system of the crayfish [19,20], and the auditory system of the cricket [21[•]], evidence indicates that sensory information arising from self-generated behaviors is selectively suppressed at the level of afferent fibers and/or the central neurons to which they project. The mechanisms by which suppression occurs can differ. Bell and co-workers [16,17] have provided concrete support for Von Holst and Mittelstaedt's principle of reafference in their investigations of the electrosensory system in mormyrid fish. In this system, a negative image of the predicted reafference is generated and added to neurons at the first stage of central processing (Figure 1b). As a result, the fish does not respond to the discharge from its own electric organ. In the skate, by contrast, information from proprioceptive inputs alone can generate a negative image of self-motion during respiration [18]. This negative image is then used at the first central stage of electrosensory processing to remove the modulation of its electroreceptors that results from its own motion (Figure 1c).

Vestibular processing during active head movements

The vestibular system provides information about head motion relative to space that is necessary for maintaining posture, computing spatial orientation and perceiving self-motion. The differential processing of actively versus passively generated vestibular stimuli is crucial, however, for controlling eye, neck and body movements, as well as for perceptual stability (reviewed in [1[•]]). This point can be easily appreciated by considering the simple example of a vestibularly driven spinal reflex — the vestibulo-colic reflex — which, in response to head motion, stabilizes the head in space via activation of the neck musculature (Figure 2a). The compensatory head movements produced by this reflex are clearly beneficial when the behavioral goal is to stabilize head position in space. When the behavioral goal is to make an active head movement, however, the vestibular drive to the reflex pathway would command an inappropriate head movement to move the head in the direction opposite to the intended goal.

At what level are the vestibular signals that arise from passive versus active head movement first differentially encoded? In the alert primate, the vestibular system does not seem to distinguish between active and passive head movements at the level of the vestibular afferents (Figure 2b; [2]), but the differential treatment of vestibular signals is evident at the next stage of processing. The head-velocity-related modulation of one population of vestibular nuclei neurons, which receive direct inputs from the vestibular afferents, is markedly attenuated in response to vestibular inputs that result from active head movements (Figure 2c; [22,23]). Notably, these same neurons con-

tinue to respond selectively to passive head motion when a monkey generates voluntary head movements while undergoing passive whole-body rotation.

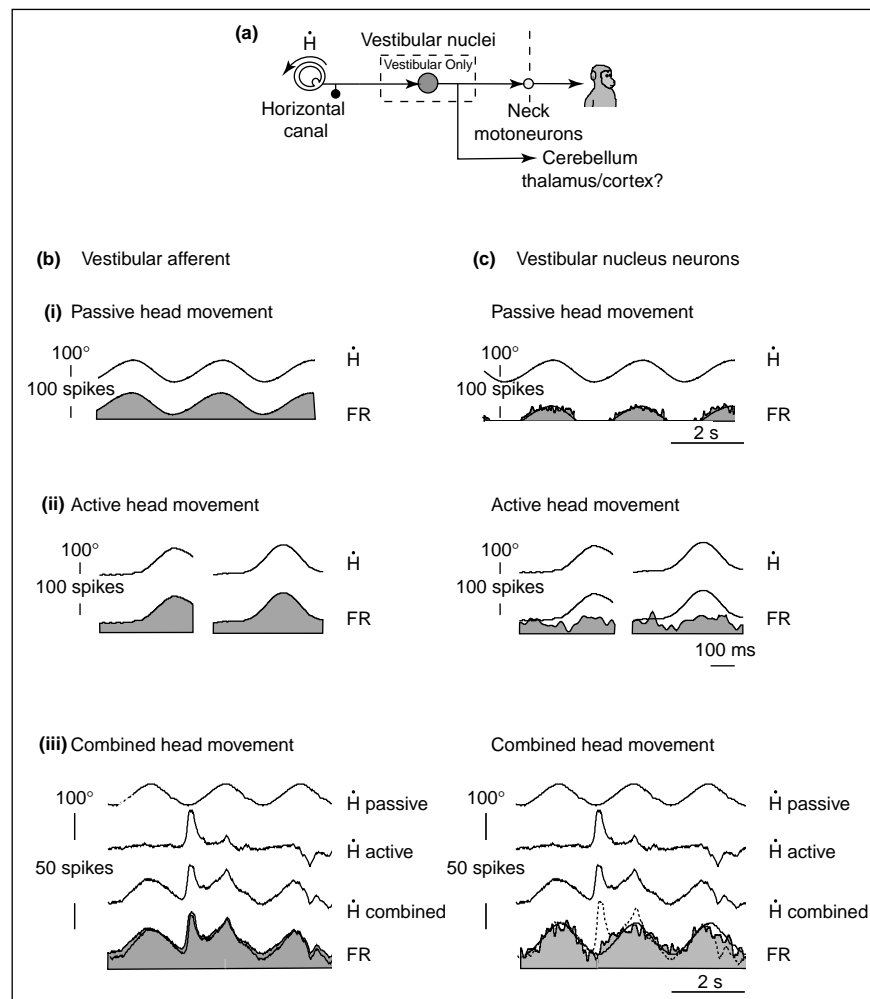
There are at least three extravestibular cues that could contribute to canceling reafference at the level of the vestibular nuclei. First, inputs from neck proprioceptors; second, knowledge of the self-generated motion; and third, neck efference copy signals. Roy and I [3^{••},23] have explored each of these possibilities in the rhesus monkey. First, we found that the activation of neck proprioceptors is not sufficient for suppressing vestibular reafference: neurons in the vestibular nuclei encode head velocity similarly during passive rotations of the head relative to the body and during passive rotations of the head and body together.

Second, higher-order areas, such as parietoinsular vestibular cortex, that are involved in the perception of self-motion [24] are known to send substantial projections to each of the vestibular nuclei [25]. We found, however, that knowledge of self-generated head motion alone is not sufficient to suppress vestibular reafference. Neurons respond robustly to head velocity when monkeys drive themselves through space by rotating a steering wheel connected to the motor controller of a vestibular turntable [23]. Third, a copy of the command to the neck muscles (i.e. a motor efference signal) could be used to cancel vestibular inputs during active head movements. We found, however, that when head-restrained monkeys attempted to move their heads, generating levels of neck torque comparable to those issued during large active head movements, neuronal responses were not modulated [3^{••}].

Further exploration has provided evidence for Von Holst and Mittelstaedt's principle of reafference in the primate vestibular system [3^{••}]. The activity of individual neurons in the vestibular nuclei was recorded in monkeys making active head movements and the correspondence between intended and actual head movement was experimentally controlled. We found that a cancellation signal was generated only when the activation of neck proprioceptors matched the motor-generated expectation during active head movements (Figure 3). This mechanism functions to eliminate selectively self-movements from the subsequent computation of orientation and posture control. These findings are the first to confirm Von Holst and Mittelstaedt's proposal at the level of single neurons in a mammalian system.

Correlates for the differential processing of active and passive vestibular inputs have been identified upstream of the vestibular nuclei. Head direction cells in several areas of the classic limbic circuit discharge preferentially when a monkey or rat orients its head in a specific preferred direction. These neurons, which are important

Figure 2



In the vestibular system, second-order neurons distinguish between sensory inputs that result from self-actions and sensory inputs that arise externally. (a) A subclass of neurons in the vestibular nucleus, named vestibular-only neurons on the basis of their responses in head-restrained models, receive direct projections from the semicircular canals and in turn project bilaterally to spinal motor neurons to activate the neck musculature. These neurons probably also send projections to the cerebellum, thalamus and cortex. (b) Activity of an example horizontal canal afferent during (i) passive head movements, (ii) active head movements and (iii) combined active and passive head-in-space motion. Afferents reliably encode head-in-space motion in all conditions. (c) Activity of an example VO neuron in the vestibular nucleus during the head movements described in (b). Neuronal responses to the active component of head-in-space motion are significantly attenuated; by contrast, the neurons show no attenuation in response to the passive rotation component. Abbreviations: FR, firing rate; \dot{H} , horizontal head velocity. Afferent responses are based on data from [2], and (c) is modified from data reported in [23].

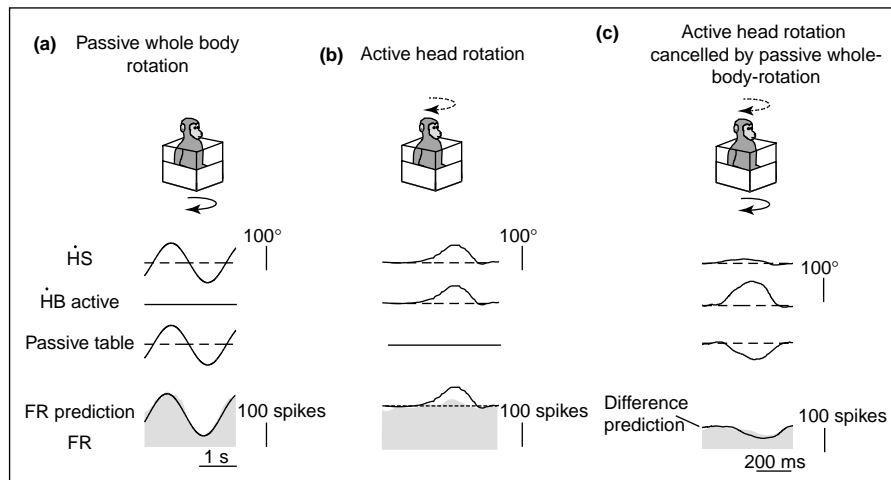
for spatial memory and navigation, respond more robustly during active than during passive head rotations [26]. In addition, neurons in the ventral interparietal area, one of several 'vestibular' areas identified in the parietotemporal cortex, have been studied during active and passive head movements. The results show that there are considerable differences in neural responses during active versus passive head movements [27]. This differential processing of vestibular inputs most probably reflects the integration of information from an efference copy of motor commands and from proprioceptive and vestibular sources required for the perception of self-motion and for the representa-

tion of extrapersonal space. I take this point up again further below.

Visual processing during voluntary eye movements

How the visual world is perceived as stable despite movements of the eyes, head and body is an issue that concerned many eminent scientists of the last century including von Helmholtz, Hering, Mach and Sherrington. Although targets rapidly jump across the retina as we move our eyes to make saccades, we never see the world move over our retina. Helmholtz [28] made the salient,

Figure 3



In the vestibular system, an internal model of the sensory consequences of active head motion is used to selectively suppress reafference at the level of the vestibular nuclei. **(a)** Activity of an example VO neuron (gray-filled trace) during passive whole-body rotation. In this condition, only vestibular inputs are available to the central nervous system and there is no motor efference copy signal because the monkey does not actively move its head. **(b)** Activity of the same neuron during active head-on-body movements. In this condition, the monkey commands an active head movement and thus an efference copy signal is theoretically available. In addition, the movement of the head activates vestibular and proprioceptive afferents as a result of the head-in-space (\dot{H}_S) and head-on-body (\dot{H}_B) movement, respectively. A prediction of the activity of the neuron, based on its response to passive head motion, is superimposed (bold trace). **(c)** The neuron is recorded as the monkey actively moves its head; however, the head-in-space velocity (\dot{H}_S) that is generated by the monkey (broken arrow) is experimentally cancelled by simultaneously rotating the monkey in the opposite direction (unbroken arrow). Consequently, in this condition the head moves relative to the body (\dot{H}_B), but not to space (\dot{H}_S); as a result, an efference copy signal is generated and the neck proprioceptors are activated, but vestibular afferent input is greatly reduced. This approach reveals a cancellation signal that is sent to the vestibular nuclei in conditions in which neck proprioceptive inputs match those expected based on the neck motor command, but not when these inputs are vastly different. Indeed, the marked inhibition in the response of the neuron shows excellent correspondence to that from the difference in response during passive (a) versus active (b) head movements. Abbreviation: FR, firing rate. Modified from data reported in [3**].

and easily replicated, observation that tapping on the canthus of the eye to displace the retinal image, for example during a saccadic eye movement, results in an illusory shift of the visual world. How can continually changing retinal inputs to the visual system thus result in the perception of a stable visual world during eye movements?

Our visual sensitivity is reduced during and just before a saccadic eye movement — a phenomenon that is referred to as ‘saccadic suppression’. Psychophysical data have shown that suppression is strongest for stimuli that would preferentially activate the magnocellular dorsal visual processing stream, which carries transient, motion-related visual information (e.g. see [29]). Neural correlates for saccadic suppression have been now identified at several stages of visual processing. Significant saccade-related responses can be observed early in visual processing at the level of the dorsal lateral geniculate nucleus of the thalamus [4,5]. Reppas *et al.* [5] found that the most common effect was a biphasic modulation of response strength (weak suppression followed by strong enhancement), which was far more prominent for neurons in the magnocellular than the parvocellular layer. Moreover,

correlates of saccadic suppression are most evident in magnocellular recipient areas including medial temporal and medial superior temporal cortex of rhesus monkey [30].

Results of studies in humans are remarkably consistent with these findings. For example, functional magnetic resonance imaging (fMRI) studies show saccade-related changes in areas that receive magnocellular input including medial temporal cortex, V7 and V4 [31]. In addition, transcranial stimulation studies in humans have provided evidence that saccadic suppression occurs via extraretinal mechanisms in the thalamus or primary visual cortex [6*]. Note, however, that there might be differences in the strategies adopted across species (e.g. see the work of Olveczky *et al.* [32*] in rabbit).

The mechanisms that underlie saccadic suppression remain to be fully elucidated. Proprioceptive information from the stretch receptors in the extraocular muscles could be used for this purpose; however, the relative timing of saccadic suppression and eye movement suggests that inputs from saccadic planning centers (e.g. an efference copy or corollary discharge signal) are crucial.

Somatosensory processing during active touch

Touch is also clearly an active process. Fingers or whiskers, like eyes, move as they scan the external world. These movements thus determine the nature of the sensory input that will be encountered. As pointed out by Gibson [33], the constancy of the tactual world is characterized by the stability of an object. For example, movement of a skin surface over a corner of an object does not usually give rise to recognition of the 'tactile motion'.

The whiskers (vibrissae) system in rats has proved to be an excellent experimental model of active touch. During whisking, the responses of first-order neurons in the trigeminal ganglion of the vibrissae system cannot be inferred from their responses to comparable passive whisker deflection. Ahissar and co-workers [7**] have recently shown that, during intervals of whisking, these neurons carry both a reference signal that encodes the current position of the rat's vibrissae and a more 'typical' sensory signal that encodes contact of the vibrissae with an object. Timing differences between the reference and the contact signals carried by neurons can be used to compute the position of an object in space. In this system, the position of vibrissae within a cycle could be encoded primarily through direct sensory activation rather than via central pathways. Nevertheless, there is some evidence for the existence of a modulatory efference copy at the cortical level that might influence the amplitude of whisking [34]. Central information of this kind can be used to tune large-scale feedback loops in the vibrissae sensorimotor system to optimize sensory processing [8].

In primates, correlates for the differential active processing of touch have been found in somatosensory cortex, where neuronal responses are attenuated for self-produced versus externally produced tactile stimuli [35]. In humans, self-generated tactile stimulation does not result in the same tickling sensation that arises when the stimulation is externally produced [36–38]. Blakemore *et al.* [37] have shown, however, that when an artificial delay or trajectory perturbation is introduced between a movement and the resultant tactile stimulation, self-generated stimulation is rated as more ticklish. Thus, as in the vestibular system, when the sensory sensation no longer corresponds to the motor command, the predicted image of the afferent signal (in this case a tickle stimulus) does not fully cancel the distorted refference. The analogy between findings in these two systems implies that the vestibular system is effectively 'ticklish'.

Common strategies?

Studies of the primate vestibular system have shown that a cancellation signal is used at the first level of central processing to suppress vestibular activation resulting from active head movements. An investigation by Roy and myself [3**] found that this cancellation signal is gener-

ated only when the activation of neck proprioceptors matches the motor-generated expectation, thereby eliminating vestibular signals that result from active head-on-body movements. Such a mechanism has clear analogies to that used by the electrosensory system of the mormyrid fish to cancel refference. In addition, recent behavioral studies in humans have shown that a similar strategy is used by the somatosensory system.

Where is the essential cancellation signal actually computed for each system? Evidence from work in electric fish indicates that the cerebellum-like electrosensory lobes provide the signal that is used to cancel the sensory response to self-generated stimulation [39]. Moreover, fMRI studies have suggested that the cerebellum has a similar role in the suppression of tactile stimulation during self-produced tickle [36–38]. More recently, however, the results of a fMRI study of active hand movements has led to the proposal that efference copy information is not located in the cerebellum *per se*, but instead is implemented via interactions between perceptual areas and motor areas in a task-dependent way [40*]. Identifying the neural representations of efference copy information in different tasks promises to be an interesting area of investigation.

It remains to be determined whether a comparable framework can be used to describe the processing that selectively suppresses refference across all or even most modalities. It is now clear that other mechanisms can contribute to the differential processing of refference. For example, peripheral mechanisms have an essential role in processing touch during active whisking, as described above. In addition, a recent study has shown that during active wrist movements in primates, cutaneous inputs are presynaptically inhibited at the level of the spinal cord afferents [9**]. The timing of the attenuation suggests that descending motor commands, rather than peripheral feedback from the movement, generate the inhibition. This strategy is markedly different from that used by the vestibular system: vestibular afferents do not differentially encode active versus passive head movements; instead, refference is distinguished only at the next stage of processing in the vestibular nuclei.

Implications: consequences for motor control

The differentiation of sensory stimulation that arises from passive versus active movement is not only crucial for perceptual stability but is also required to produce accurate neural representations of the environment to guide behavior accurately. The implications of this are particularly obvious for the vestibular system, where the second-order sensory neurons function as both sensory and premotor neurons. Second-order vestibular neurons, which are differentially sensitive to active and passive head movements, project to the spinal cord and mediate

postural reflexes such as the vestibulo-colic reflex (Figure 2a). Accordingly, their reduced sensitivity during active head movements is consistent with their functional role in head stabilization, because their modulation is actually counterproductive during these self-generated movements. The fact that these same neurons continue to encode information faithfully about passive head rotations that occur during the execution of voluntary movements [22,23] is also important. As a person explores the environment, these neurons will selectively respond to adjust postural tone in response to any head movements that the brain does not expect. This selectivity can be crucial, for example, in recovering from tripping over an obstacle while walking or running, which requires a robust postural response.

Vestibular pathways that control postural responses must combine vestibular inputs with information from other sources, such as neck and body proprioceptive information, to generate appropriate motor responses. This can be easily appreciated by considering two subjects: one whose head is pointing forward, and another whose head is rotated 90° to one side. To ensure postural stability, the same vestibular stimulus will need to activate different muscle combinations in each subject. In this example, combining neck proprioceptive information with head-referenced vestibular inputs to the brain will provide information about motion of the body in space and, indeed, there is recent evidence for such a multimodal integration of vestibular and proprioceptive inputs. Some neurons in the rostral fastigial nucleus of alert primates encode movement of the body rather than the head in space during passively applied rotational [41] and translational [42] motion. Thus, during passive movements these neurons encode movement in a body-referenced coordinate system.

To date, coordinate transformations, which have been observed in many brain areas, have been characterized in studies designed to test passive rather than active sensation. What do these neurons encode during active movements? The rostral fastigial nucleus is a particularly interesting example to consider with regard to this question. It is thought to be important in vestibulo-spinal control, including the regulation of gait and postural mechanisms. Thus, the same arguments made above for the utility of selective gating of vestibular reafference at the level of the vestibulo-spinal neurons could be applied to the rostral fastigial nucleus. By extension, a similar logic can be applied to areas that have been implicated in higher-order perceptual functions. Spatial perception is more accurate in response to active than to passive rotations [43–45]. The absence of a signal related to motor efference copy, at the level of higher-order vestibular areas such as parietal cortex might prevent the complete updating required for accurate spatial localization [46], consistent with the differences in the pro-

cessing of active and passive movement that can be found at these higher levels of processing.

Conclusions

Over 50 years ago, Von Holst and Mittelstaedt [11] proposed that the brain generates a sensory expectation based on the motor command, compares it with the actual sensory feedback, and subtracts the self-generated sensation. In this way, the nervous system could theoretically differentiate sensory inputs that arise from external sources from those that result from self-generated movements. Recent work in several systems has provided evidence in support of this hypothesis, as well as evidence for other mechanisms that suppress reafference in the early stages of sensory processing. It remains a challenge to understand how the differential processing of sensory inputs in the early stages is used by the upstream networks that mediate perceptual stability and guide behavior.

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