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Sympathetic responses to vestibular activation in humans

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Carter JR, Ray CA. Sympathetic responses to vestibular activation in humans. Am J Physiol Regul Integr Comp Physiol 294: R681–R688, 2008. First published January 16, 2008; doi:10.1152/ajpregu.00896.2007.—Activation of sympathetic neural traffic via the vestibular system is referred to as the vestibulosympathetic reflex. Investigations of the vestibulosympathetic reflex in humans have been limited to the past decade, and the importance of this reflex in arterial blood pressure regulation is still being determined. This review provides a summary of sympathetic neural responses to various techniques used to engage the vestibulosympathetic reflex. Studies suggest that activation of the semicircular canals using caloric stimulation and yaw rotation do not modulate muscle sympathetic nerve activity (MSNA) or skin sympathetic nerve activity (SSNA). In contrast, activation of the otolith organs appears to alter MSNA, but not SSNA. Specifically, head-down rotation and off-vertical axis rotation increase MSNA, while sinusoidal linear accelerations decrease MSNA. Galvanic stimulation, which results in a nonspecific activation of the vestibule, appears to increase MSNA if the mode of delivery is pulse trained. In conclusion, evidence strongly supports the existence of a vestibulosympathetic reflex in humans. Furthermore, attenuation of the vestibulosympathetic reflex is coupled with a drop in arterial blood pressure in the elderly, suggesting this reflex may be important in human blood pressure regulation.

sympathetic nerve activity; blood pressure; head-down rotation

THE VESTIBULAR APPARATUS HAS long been recognized for its role in equilibrium and orientation, but it is only beginning to be recognized as an important regulator of autonomic activity. The vestibular apparatus is part of the fluid-filled membranous labyrinth located in the inner ear and consists of two major parts: the semicircular canals and the otolith organs. The semicircular canals are sensitive to angular acceleration whereas the otolith organs are sensitive to both gravity and linear acceleration. Both the semicircular canals and the otolith organs have specialized hair cells capable of sensing these accelerations. These hair cells contain two kinds of hairs: numerous stereocilia and single kinocilium. When stereocilia are bent toward the kinocilium, the hair cell is depolarized, and when the stereocilia are bent away from the kinocilium, the cell is hyperpolarized (19). Thus, each hair cell acts as its own accelerometer and depending on the type of acceleration and the placement of the kinocilium, hair cells in the vestibular apparatus can be depolarized, hyperpolarized, or both.

Although the neural signals generated from the hair cells of the otolith organs and semicircular canals are important in the maintenance of equilibrium and orientation, they are not the only signals that contribute to this homeostatic mechanism. Individuals that experience damage to the vestibular apparatus eventually adapt and learn to function without it, demonstrating that other systems play a vital role in maintaining equilibrium (36). For example, signals from both neck proprioceptors and visual receptors integrate with signals from the vestibular apparatus in the vestibular nuclei before an effector signal is sent to various motoneurons in the body. If damage occurs to the vestibular apparatus, these other systems begin to contribute more to the maintenance of equilibrium (36).

More recently, the vestibular system has been shown to influence autonomic control, and evidence suggests that the vestibular system plays a role in postural-related adjustments in blood pressure. Much like equilibrium, blood pressure regulation involves multiple feedback systems. The most recognized feedback system for blood pressure regulation is the baroreflex, an autonomic reflex that senses mechanical changes in the blood vessels of the aortic arch and carotid bodies. However, evidence suggests that the vestibular apparatus also assists in blood pressure regulation.

The Role of the Vestibular System in Autonomic Regulation

Changes in posture can profoundly impact the cardiovascular system. Standing from a seated or supine position causes a gravitationally induced fluid shift from head to foot. This fluid shift can lead to decreases in cerebral perfusion and cardiac output and can ultimately lead to lightheadedness or even syncope if rapid autonomic neural adjustments do not occur.
Parasympathetic activity must decrease and sympathetic activity must increase during an orthostatic challenge. This shift in autonomic balance from predominantly parasympathetic to sympathetic control is normal and necessary and is an important compensatory mechanism that allows humans to contend with fluid shifts associated with postural change.

The most recognized autonomic reflex engaged during orthostasis is the baroreflex. Unloading either the arterial or cardiopulmonary baroreceptors leads to an increase in heart rate, muscle sympathetic nerve activity (MSNA), and vascular vasoconstriction of the limbs (5, 38). However, in addition to unloading the baroreceptors, a change in posture from the supine to upright posture also engages the vestibular apparatus. Doba and Reis (15) provided direct evidence that the vestibular system is important in postural blood pressure regulation in animals. They recorded blood pressure responses in anesthetized cats during whole body tilt before and after bilateral transection of the vestibular nerve (VIII cranial nerve). Removing the vestibular nerve exaggerated the drop in blood pressure during whole body tilt and the normal recovery of blood pressure was blunted. Jian et al. (21) reported similar results using awake cats. These studies clearly demonstrate that the vestibular apparatus plays a significant role in postural blood pressure control in animals.

Whether the vestibular apparatus contributes significantly to postural blood pressure control in humans is equivocal. Evidence from several laboratories suggests that stimulation of the otolith organs in humans activates the sympathetic nervous system (9, 20, 22, 24–30, 33). The sudden surge in peripheral sympathetic neural activity associated with otolithic activation leads to vasoconstriction and an increase in total peripheral resistance (37), thus leading some to suggest that the vestibular-mediated increase in sympathetic activity, commonly referred to as the vestibulosympathetic reflex, helps maintain arterial blood pressure. To date, only six techniques have been used to examine the effect of vestibular activation on sympathetic outflow, and discrepancies exist. The remainder of this review will present the various techniques that have been developed to examine the vestibulosympathetic reflex in humans and discuss sympathetic responses associated with each technique. We will also discuss how this autonomic reflex may contribute to regulating arterial blood pressure in humans.

**Sympathetic Responses to Activation of the Semicircular Canals in Humans**

**Caloric stimulation.** Caloric stimulation is a technique used to activate the horizontal semicircular canals of the vestibule. This technique exposes the tympanic membrane to cold and/or warm water and often results in nystagmus. Briefly, this technique produces a thermal gradient within the semicircular canals that leads to increased endolymphatic flow and vestibular stimulation. This vestibular stimulation is maximized by tilting the head up 30°, a position that places the horizontal semicircular canals in the vertical plane. Because of the close proximity of the horizontal semicircular canals to the external auditory canal, the largest thermal gradient is produced in the horizontal semicircular canals. Caloric stimulation does lead to some stimulation of the vertical semicircular canals, but the stimulation of the horizontal semicircular canals is much more prominent.

Costa et al. (10) were the first to examine the influence of caloric stimulation on sympathetic activity in humans. In this study, 37°C water was irrigated into the left ear at a rate of 450 ml/min for 5 min. Following a 5-min rest period (or until nystagmus ceased), the water temperature was lowered by 7°C, and the protocol was repeated. This continued until either the subjects reported intolerable side effects or until a temperature of 16°C was reached. Subjects were asked to score the discomfort level during the varying levels for caloric stimulation on a scale from 0 (no dizziness or nausea) to 10 (intolerable dizziness or nausea). Costa et al. (10) reported no change in either MSNA or plasma norepinephrine during or after caloric stimulation, even when subjects reported increased dizziness or nausea. Therefore, early evidence suggested that caloric stimulation does not alter sympathetic neural outflow to the leg.

In contrast, Cui et al. (14) reported that caloric stimulation enhanced MSNA. In this study, caloric stimulation was evoked for 1 min with either 50 ml of cold (10°C) or 50 ml of warm (44°C) water. A total of nine irrigations were performed (separated by 7 min), and both the temperature (cold vs. warm) and the ear irrigated (left vs. right) were alternated. Nystagmus was evoked after all cold water irrigations (49/49 irrigations) and after many of the warm water irrigations (27/56). MSNA was elevated after either cold or warm water irrigation, but MSNA enhancement was more pronounced after cold water irrigation. Therefore, it was concluded that caloric stimulation increases MSNA and that this response is proportional to the level of nystagmus.

In another study, Cui et al. (13) examined the effect of caloric stimulation on skin sympathetic nerve activity (SSNA) and demonstrated a suppression of SSNA during nystagmus and an enhancement of SSNA after nystagmus. The experimental design was enhanced for this study by having a control stimulation in which water was irrigated into an ear in which the external meatus was plugged with cotton. Nystagmus was evoked after all cold water irrigations (22 of 22 irrigations) and most warm water irrigations (18 of 23), but it was not evoked after any of the plugged-control irrigations (13 cold-water trials and 14 warm water trials).

The discrepant MSNA response to caloric stimulation between Costa et al. (10) and Cui et al. (14) is unclear. It is possible that differences are due to the protocol for caloric stimulation. Costa et al. (10) only stimulated with cold water and progressively lowered the temperature to a low of 16°C in just one subject. Cui et al. (14) stimulated with colder water (10°C) and also stimulated with warm water (44°C). Nevertheless, cold water caloric stimulation evoked no change in MSNA in one study (10), while it evoked an increase in MSNA in another study (14). Unfortunately, neither study (10, 14) included a plugged-control similar to the SSNA study (13). Cui et al. (13) justified the plugged-control for the SSNA study because SSNA is “very sensitive to mental or somatosensory (sound, touch, light, or electrical) stimulation.” MSNA might not be very sensitive to mental or somatosensory stimulation, but it is sensitive to mental stress (1, 6, 9, 18, 41); thus it would appear that a plugged-control might be appropriate when examining MSNA responses to caloric stimulation.

**Yaw rotations.** In addition to caloric stimulation, sinusoidal yaw head rotation is a technique used to activate the semicircular canals in humans. Ray et al. (32) examined the effects of yaw head rotation on both MSNA and SSNA. Subjects were
seated comfortably with the head facing forward. Sinusoidal yaw head rotation was performed at 0.1, 0.6, and 1.0 Hz with the assistance of an auditory signal (i.e., metronome). An investigator manually moved the head for the subjects during the 0.1 Hz yaw head rotation, while subjects voluntarily moved their heads at 0.6 and 1.0 Hz. In this study, Ray et al. (32) report that yaw head rotation did not significantly alter heart rate, mean arterial pressure, MSNA, or SSNA at any of the head rotation frequencies. These results indicate that stimulation of the horizontal semicircular canals does not alter sympathetic nerve activity to either the muscle or skin. Wilson et al. (42) has also reported no change in SSNA during yaw head rotation before and after whole body heating.

The findings of Ray et al. (32) and Wilson et al. (42) conflict with the caloric stimulation studies by Cui et al. (13, 14) but are in agreement with Costa et al. (10), who reported that stimulation of the horizontal semicircular canals via caloric stimulation did not alter MSNA in humans. It should be noted that the yaw head rotation model used by Ray et al. (32) is limited to stimulation of the horizontal semicircular canals. It is possible that stimulation of the vertical (anterior and posterior) canals may produce different results, but these vestibular receptors cannot be selectively stimulated in humans without simultaneous stimulation of the otolith organs. Furthermore, it is important to note that caloric stimulation and yaw head rotations activate the semicircular canals differently. Caloric stimulation is normally applied to one ear to establish conflicting inputs between the right and left vestibules, whereas yaw head rotations produce bilateral activation. In summary, we conclude that the semicircular canals do not modulate sympathetic nerve activity based on evidence from caloric stimulation (10) and yaw head rotation (32, 42) studies. However, it should be recognized that some studies suggest that both MSNA (14) and SSNA (13) are altered by caloric stimulation. Table 1 summarizes the sympathetic responses to activation of the semicircular canals in humans.

### Sympathetic Responses to Activation of the Otolith Organs in Humans

**Head-down rotation.** The otolith organs are sensitive to both gravitational and linear accelerations. The head-down rotation (HDR) maneuver is the most extensively used technique to create an altered gravitational input to the otolith organs. This maneuver initially activates both the otolith organs and the semicircular canals, but upon completion of the rotation, the influence of the semicircular canals is eliminated. Briefly, the baseline requires the subject to lie prone with the neck extended and the chin or forehead supported. This position approximates the normal orientation of the head while standing upright. During HDR, the head is passively lowered by an investigator until the chin touches the chest. Following the HDR, the head is returned to the baseline position (i.e., head-up) for a recovery period. Shortt and Ray (37) were the first to demonstrate that HDR increases MSNA (Fig. 1). To date, 16 studies have confirmed the findings of Shortt and Ray (37) by demonstrating an increase of MSNA during HDR (7–9, 16, 20, 24–30, 32–34, 37, 43). Increases in MSNA are graded to the degree of head rotation and persist for prolonged periods of time (i.e., 30 min) (20). Furthermore, studies comparing MSNA in the arm and leg demonstrate comparable responses to the limbs (25). In contrast to the reliable MSNA response, HDR does not increase SSNA (31). Thus, human studies indicate that the vestibulosympathetic reflex is complex, eliciting both differential (i.e., muscle vs. skin) and nondifferential (i.e., arm vs. leg) outflow of sympathetic nerve activity. Fig. 2 illustrates original nerve tracings during baseline and HDR in a representative subject.

In addition to stimulating the otolith organs, HDR activates several nonvestibular mechanisms capable of increasing sympathetic outflow. Therefore, Shortt and Ray (37) performed a series of controlled studies to determine whether these nonvestibular mechanisms were influencing HDR-mediated increases of MSNA. First, it was determined that baroreflexes are not responsible for the sympathoexcitation during HDR because this maneuver does not alter central blood volume and does not elicit reductions in arterial blood pressure. Second, blindfolding subjects during HDR had no effect on MSNA compared with eyes-open trials, indicating that altered visual input (i.e., inverted field) is not a mechanism for increases in MSNA during HDR (37). Third, Ray and Hume (30) reported an increase in MSNA during HDR, but no change during head rotation in the lateral decubitus position, indicating that neck afferents do not regulate MSNA during HDR in humans. Fourth, it was determined that central command is not responsible for the increase in MSNA during HDR because there was no increase in SSNA during HDR (31).

### Table 1. Sympathetic neural responses to various techniques used to activate the vestibular system

<table>
<thead>
<tr>
<th>Study</th>
<th>Technique</th>
<th>MSNA</th>
<th>SSNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costa et al. (1995)</td>
<td>Caloric stimulation</td>
<td>No change (n = 5)</td>
<td></td>
</tr>
<tr>
<td>Cui et al. (1997)</td>
<td>Caloric stimulation</td>
<td>Increase (n = 14)</td>
<td>Decrease (n = 9)</td>
</tr>
<tr>
<td>Cui et al. (1999)</td>
<td>Caloric stimulation</td>
<td>No change (n = 33)</td>
<td>No change (n = 25)</td>
</tr>
<tr>
<td>Ray et al. (1998)</td>
<td>Yaw head rotation</td>
<td>Increase (n = 9)</td>
<td>No change (n = 10)</td>
</tr>
<tr>
<td>Wilson et al. (2004)</td>
<td>Yaw head rotation</td>
<td>Increase (n = 16)</td>
<td>No change (n = 12)</td>
</tr>
<tr>
<td>Shortt &amp; Ray (1997)**</td>
<td>Head down rotation</td>
<td>Decrease (n = 4)</td>
<td></td>
</tr>
<tr>
<td>Ray et al. (1997)</td>
<td>Head down rotation</td>
<td>Decrease (n = 16)</td>
<td></td>
</tr>
<tr>
<td>Cui et al. (1999)</td>
<td>Sinusoidal linear acceleration</td>
<td>Decrease (n = 7)</td>
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</tr>
<tr>
<td>Cui et al. (2001)</td>
<td>Sinusoidal linear acceleration</td>
<td>Increase (n = 12)</td>
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<tr>
<td>Kaufmann et al. (2002)</td>
<td>Off-vertical axis rotation</td>
<td>Increase (n = 7)</td>
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<tr>
<td>Bolton et al. (2004)</td>
<td>Galvanic stimulation</td>
<td>Increase (n = 11)</td>
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<tr>
<td>Voustianiouk et al. (2006)</td>
<td>Galvanic stimulation</td>
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<tr>
<td>Bent et al. (2006)</td>
<td>Galvanic stimulation</td>
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MSNA, muscle sympathetic nerve activity; SSNA, skin sympathetic nerve activity. **The increase of MSNA during head-down rotation is a consistent finding and has been replicated in 16 other studies (not included in this table but included in the text).
Central command typically increases SSNA (39). Finally, head-down neck extension from the supine position did not alter MSNA, indicating that increased cerebral pressure does not mediate the increase in MSNA during HDR (20). Therefore, evidence strongly indicates that the HDR model elicits increases in MSNA through activation of the otolith organs. It should be noted that sex does not appear to affect the vestibulosympathetic reflex, because MSNA responses to HDR are comparable in men and women (27).

In addition to establishing that HDR elicits a consistent increase of MSNA, Ray and coworkers also examined the neural interaction of the vestibulosympathetic reflex with other autonomic reflexes (Fig. 3). It was determined that the vestibulosympathetic reflex has an additive MSNA interaction with baroreflex unloading (29), skeletal muscle reflex (28), arterial chemoreflex (24), and mental stress (9). Collectively, these studies indicate that MSNA activation by the vestibular system is a powerful autonomic reflex, capable of stimulating MSNA in the presence of other sympathetic activators. More recently, Dyckman et al. (16) examined the vestibulosympathetic reflex during baroreceptor unloading (nitroprusside infusion) and loading (phenylephrine infusion). HDR elicited increases in MSNA during the nitroprusside trial but did not change MSNA during the phenylephrine trial (16). The preservation of the vestibulosympathetic reflex during nitroprusside infusion (16) is consistent with prior studies using lower body negative pressure to unload the baroreceptors (29). Furthermore, the inability to activate the vestibulosympathetic reflex during phenylephrine infusion (16) is consistent with animal studies that have shown an abolishment of the vestibulosympathetic reflex after arterial blood pressure was increased by infusion of an α-agonist (23). It is important to note that HDR increases MSNA during other interventions that increase arterial blood pressure, such as isometric handgrip (28), mental stress (9), and hypoxia (24). It is not entirely clear why the vestibulosympathetic reflex remains preserved during some, but not all, conditions that increase arterial blood pressure, but it may be important to consider the nature of the stimulus. Nevertheless, it appears that the vestibulosympathetic reflex retains the ability to increase MSNA during baroreceptor unloading, regardless of the stimulus type (16, 29).

The ability of the vestibulosympathetic reflex to activate sympathetic outflow (37), coupled with an ability of the vestibulosympathetic reflex to consistently increase MSNA during baroreceptor unloading (16, 29), makes it reasonable to speculate that the vestibulosympathetic reflex may contribute importantly to maintaining orthostasis in humans. To date, no evidence directly links the vestibulosympathetic reflex to the maintenance of blood pressure during a postural change in humans. However, Ray and Monahan (33) have reported a blunted vestibulosympathetic reflex in elderly (64 ± 1 years) compared with young individuals (26 ± 1 years; Fig. 4). More importantly, engagement of the otolith organs during HDR elicited a drop in arterial blood pressure in the older but not the young subjects (33). It was determined that the attenuation of
MSNA during HDR was not due to a ceiling effect in the elderly who have a greater resting MSNA, as both populations demonstrated comparable increases in MSNA during cold pressor test. Aging is associated with increased prevalence of orthostatic intolerance (35). These findings indicate that aging alters the vestibulosympathetic reflex and suggests that the vestibulosympathetic reflex may play an important role in regulating arterial blood pressure.

Linear accelerations—sinusoidal vs. off-vertical axis rotation. Whereas the HDR model uses gravitational acceleration to activate the otolith organs, other methods are available for activating the otoliths via linear accelerations. For example, Cui et al. (11) examined MSNA responses to sinusoidal linear acceleration in humans and reported a decrease in MSNA using this technique. In this study, subjects were seated in a linear accelerator (sled) that produced accelerations using a magnetic levitation system. The subjects were strapped to a chair on the linear accelerator with their body and head firmly restrained to prevent unplanned movement. Acceleration was applied along the anteroposterior directions over a fixed distance of 14 m. A total of three stimulations were applied, with each stimulation consisting of five cyclic movements with the same peak acceleration (±0.10 Gx, ±0.15 Gx, or ±0.20 Gx). The authors concluded that otolithic activation via sinusoidal linear acceleration decreases MSNA and suggested that differences observed between this technique and the head-down rotation model are due to 1) different baseline positions (sitting vs. prone), 2) sinusoidal stimulation vs. sustained stimulation, 3) activation of primarily utricular afferents, whereas head-down rotation activates both the utricles and saccules, and 4) different intensities of the stimulations (11).

One limitation of the sinusoidal linear acceleration study by Cui et al. (11) was the limited number of MSNA subjects (n =
4). Furthermore, MSNA responses were examined during forward and backward linear accelerations, but lateral linear accelerations (left and right) were not examined. Therefore, Cui et al. (12) performed a more comprehensive study to determine MSNA responses to dynamic stimulation of the otoliths in the forward, backward, left, and right directions in seated humans. A significant decrease of MSNA was reported during anteroposterior acceleration (n = 10) and lateral acceleration (n = 6). Because mean arterial blood pressure did not change significantly during the four linear accelerations, the authors argued that the reductions of MSNA could not be attributed to arterial baroreflex modulation (12). In conclusion, the two studies by Cui et al. (11, 12) indicate that linear accelerations of the vestibule decrease MSNA, regardless of the direction.

In contrast to the studies by Cui et al. (11, 12), Kaufmann et al. (22) reported an increase in MSNA during linear acceleration via off-vertical axis rotation (OVAR). During OVAR, subjects are rotated about an axis tilted 15° from the vertical. At the onset of OVAR, the semicircular canals are initially activated, but this response disappears after ~10–12 s. In the steady state, OVAR projects 0.26 g onto all axes in the coronal plane via a rotating gravity vector that circles the head in a direction opposite the body rotation (2, 17). As a control, earth-vertical axis rotation (EVAR) was performed because the position of the head does not change with respect to gravity; thus this rotation does not stimulate the otolith organs. Kaufmann et al. (22) reported an increase in MSNA during forward linear acceleration along the naso-occipital axis and demonstrated that the latency of this sympathetic outflow was too short to be accounted for by the arterial baroreflex. EVAR did not change MSNA. These results provide support for the presence of an otolithic-mediated vestibulosympathetic reflex in humans.

It is not entirely clear why the sled linear acceleration model used by Cui et al. (11, 12) elicits a decrease in MSNA while the OVAR linear acceleration model of Kaufmann et al. (22) increases MSNA. Kaufmann et al. (22) has suggested that otolith-sympathetic reflexes are directionally sensitive and that the experimental protocol by Cui et al. (11, 12) did not account for this. Cui et al. (11, 12) averaged MSNA during the sinusoidal movement (i.e., forward and backward) and reported that total integrated MSNA decreased throughout the entire stimulus cycle as the peak linear acceleration increased. This analysis did not allow for discrimination between changes in MSNA specific to the direction of movement. In contrast, Kaufmann et al. (22) discriminated between positive and negative linear accelerations along the naso-occipital axis. The argument that otolith-sympathetic reflexes are directionally sensitive is also supported by the HDR model. Hum and Ray (20) demonstrated that rotating the head from the prone position increases MSNA, while head rotation from the supine position does not elicit increases in MSNA. Thus, it appears that otolith-sympathetic reflexes are directionally sensitive as suggested by Kaufmann et al. (22). Furthermore, OVAR uses a continuous stimulus in which the body is subjected to different angles, whereas sinusoidal linear accelerations produce abrupt, brief accelerations. It is possible that the abrupt, brief accelerations evoke a startle or other alerting response that could influence MSNA differently than a continuous stimulation.

**Sympathetic Responses to Galvanic Stimulation in Humans**

Galvanic stimulation is different from the other five techniques for activation of the vestibular apparatus (i.e., caloric stimulation, yaw rotation, HDR, sinusoidal linear acceleration, OVAR) because electrical stimulation of the mastoid results in an overall activation of the vestibule. Therefore, this technique cannot be used to discriminate between the otolith organs and semicircular canals. Galvanic stimulation also results in some stimulation of cutaneous afferents immediately under the electrodes. However, this technique does offer the advantage of stimulating the vestibule without: 1) modulating neck afferents as occurs during HDR and 2) causing fluid shifts in the body which occurs during both linear sinusoidal acceleration and OVAR. Furthermore, evidence suggests that the semicircular canals do not modulate sympathetic activity (10, 32, 42); thus, any changes in sympathetic outflow during galvanic stimulation can be inferred to be otolithic in origin.

Bolton et al. (4) were the first to examine the effect of galvanic stimulation on MSNA. In this study, brief galvanic...
stimulation (30 ms, 333 Hz) did not alter MSNA. However, another study by Voustianouk et al. (40) demonstrated that pulse trains of electrical stimulation to the mastoid (300–700 ms delay after the R wave) significantly increased MSNA. These findings suggest that the mode of delivery (brief stimulation vs. pulse train stimulation) may be important in modulating sympathetic outflow via the galvanic stimulation model. To confirm this concept, Bent et al. (3) examined MSNA stimulation (30 ms, 333 Hz) did not alter MSNA. However, evidence suggests that galvanic stimulation is a reliable technique for examining vestibular mediated increases in MSNA if there is a dynamic component to the galvanic stimulation (i.e., pulse train or sinusoidal). Because studies indicate that semicircular activation does not change MSNA (10, 32, 42), increases in MSNA during galvanic stimulation are likely otolithic in origin.

Perspectives and Significance

Over the past 10 years, the role of the vestibular system on regulating sympathetic outflow has become well established. Activation of the otolith organs through either HDR (7–9, 16, 20, 24–30, 32–34, 37, 43) or OVAR (22) increases MSNA, whereas otolithic activation using sinusoidal linear acceleration decreases MSNA. In contrast, activation of the semicircular canals via caloric stimulation (10) and yaw rotation (32, 42) do not appear to alter MSNA, although some studies have reported an increase in MSNA during caloric stimulation (13, 14). More recently, galvanic stimulation has been shown to increase MSNA (3, 40). It appears that the vestibulospinal reflex is a robust autonomic reflex in humans, but the role of the vestibulospinal reflex in human blood pressure regulation is not as clear. Doba and Reis (15) provided convincing evidence that vestibular input plays a critical role in blood pressure regulation of cats, but this has not been confirmed in humans. Ray and Monahan (33) reported an attenuation of MSNA during HDR in elderly subjects with a subsequent decrease in arterial blood pressure, suggesting that the vestibulospinal reflex may play a key role in acute regulation of arterial blood pressure. In fact, the vestibulospinal reflex may serve as the first line of defense in regulating arterial blood pressure during orthostasis by eliciting an increase in MSNA prior to actual baroreceptor unloading (Fig. 5). To date, only the HDR model has been studied extensively and has systematically eliminated several nonvestibular mechanisms that could potentially influence MSNA during the maneuver. Carefully designed experiments are needed to determine whether nonvestibular mechanisms are influencing techniques such as linear sinusoidal acceleration and off-vertical axis rotation (which both result in fluid shifts) and galvanic stimulation (which activates cutaneous afferents immediately under the electrodes and does not allow for discrimination of the otolithic organs and semicircular canals).

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