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The clinical significance of vestibular system hemodynamic control

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Abstract

Aims: The otoliths of the vestibular system in the inner ear not only provide sensory information for body movements and balance but also have indirect autonomic effects. Vestibular dysfunction has clinical significance in a wide range of disorders including bone hemostasis, cognitive function, and cardiovascular system. This study aimed to discuss only the clinical significance of vestibular system hemodynamic control and the consequences of its dysfunction in orthostasis.

Methods: The time window for this review was 1990-2024, and the databases used included Google Scholar, PubMed, Scopus, and Web of Science. Only full-text articles in English were cited.

Findings: Recent evidences indicated vestibular-induced sympathetic activation and shifted the hypothesis of vestibular feed-forward control of blood pressure during orthostasis toward a well-documented fact. As an input source for cardiovascular reflexes, the vestibular system must be considered in etiologies, pathogenesis, diagnosis, and therapeutic interventions of orthostatic intolerance states.

Conclusion: The vestibular system by itself has clinical significance in managing patients suffering from orthostatic hypotension and syncope. Vestibular dysfunction may be one of the underlying causes of orthostatic hypotension.

Keywords: *Hypotension, Orthostatic, Reflex, Vestibular System, Hemodynamics, Autonomic Nervous System.*

Introduction

Vestibular sensory function provides conscious and subconscious information about linear and angular body accelerations, head tilt, compensatory eye movements, gravity, postural equilibrium, and spatial orientation (1-5). Vestibular inputs supply the vestibulospinal and the vestibuloocular reflexes (6-7). The signals from type 1 and type 2 hair cells of the five vestibular sensory organs including the otoliths (utricle and saccule) and the three semicircular canals modulate also other neural pathways. These pathways extend from the medulla to the cortex (8-10). The so-called vestibular cortex does not apply to a specific anatomic location and its concept is a cortical neural network that has extensive connections among the frontal, temporal, occipital, and parietal cortices. The vestibular cortex works bi-directionally with subcortical centers in the limbic system and brain stem (11-13).

Discharges of autonomic sensory afferent and autonomic motor efferent fibers are directly/indirectly modulated by vestibular signals. The first and the most well-known example of this interaction is the motion sickness. (14-16) However, unlike motion sickness which is due to discrepancies between movement-induced vestibular signals and visual sense of the same movement, in normal hemostasis, the best concordant example of the vestibulo-autonomic interaction may be the blood pressure control during orthostasis (17-19). The etymology of orthostasis consists of ortho and stasis which means vertical and stability respectively. However, orthostasis is ordinarily used for orthostatic hypotension (20-24).

The effect of gravity on blood volume redistribution during the transition from supine to sitting or standing positions (or from sitting to standing) must rapidly be compensated. This prompt and neurally mediated

hemodynamic adjustment will be started through the fast, predictive, and anticipatory feed-forward mechanism because the closed feedback loop needs an error signal and this innate delay is unable to compensate for orthostatic changes in nearly the same time window of orthostasis. Indeed the feedback control comes into the act after the open-loop feed-forward control to complete the orthostasis hemodynamic compensations (25-28).

Blood pressure is one of the most important vital signs. Increase or decrease in systolic, diastolic, mean, and pulse pressure and also the dynamic changes of blood pressure in orthostasis that can be in the form of orthostatic hypotension (OH) or orthostatic hypertension (OHT) are clinically important in diagnosis, treatment, and prognosis of patients (29-31). Almost immediately after changing the position from lying down to standing, 500 ml of blood is transferred from the thoracic vessels to the subdiaphragmatic veins. This reduction in the blood volume in the thoracic vessels reduces the preload of the ventricles and stroke volume, leading to a decrease in arterial blood pressure if there are no compensatory responses. Compensatory reactions usually provide sufficient compensation simultaneously or in less than a minute and prevent pressure drop (32).

Intolerance of the standing position because of the autonomic system disorder is called orthostatic intolerance and includes three disorders orthostatic hypotension, postural tachycardia syndrome, and reflex syncope. Orthostatic hypotension has two forms: primary and secondary, each with acute and chronic forms (33). Orthostatic hypotension is a common phenomenon, and it is classified into three different types: classical, delayed, and initial orthostatic hypotension, according to the time of its occurrence and its duration (34-35).

Recent evidences indicated vestibular feed-forward control of blood pressure during orthostasis. The vestibular system as an orthostasis sensory detector is one of the input sources for cardiovascular reflexes and acts through sympathetic activation. This study aimed to discuss the clinical significance of vestibular hemodynamic adjustment and the consequences of its dysfunction in orthostasis and include the following topics: hemodynamic changes in orthostasis, vestibular neural connections, vestibular modulation of autonomic discharges, and cardiovascular consequences of vestibular dysfunction.

Hemodynamic changes in orthostasis

Orthostasis is a frequent daily activity and causes a gravity-induced volume shift in the vasculature and transient venous pooling of blood in the lower extremities. The subsequent unloading of high and low-pressure baroreceptors decreases their afferent firing discharges which results in the escape of sympathetic efferent from their inhibitory effects (36). The enhanced sympathetic tone keeps the central volume and blood pressure in the normal physiological range by increasing the total peripheral resistance, effective circulatory volume, and heart performance (lusitropy, bathmotropy, dromotropy, chronotropy, inotropy) and decreasing vascular compliance (37-41). The pooling volume ranges between 300 to 800 mL; on average, it is considered 500 mL in an adult person (21, 32). Other physiologic responses to central hypovolemia include muscle pumps and reverse delayed compliance, but their efficiencies and speeds are not important in general orthostasis hemodynamic adjustment. They are limited to specific vascular beds (42). Orthostatic hypotension and orthostatic hypertension are representations of inadequate and exaggerated sympathetic reflexes to orthostasis respectively (29, 43). However, the pathogenesis and predisposing factors to orthostatic hypertension are not well documented and other factors like impaired Baroreflex and vascular dysfunctions may also be important (44).

Vestibular neural connections

The vestibular sensory system has some unique properties and is different from other sensory systems (45). Laterality, multimodality, multi-sensory integrations, viscera-somatic connections, structural corticocortical networks, and hierarchical bidirectional communication between lower-level (caudal) and higher-level (rostral) brain regions cause the link of the vestibular system to a wide higher central nervous system functions (1, 10-11, 46-51). Recent evidence highlights the effect of normal vestibular inputs on cognition and also the consequence of vestibular dysfunction on cognition impairment (8, 52-56). There are many reports about the relation of vestibular function with sleep (57-61). These wide central vestibular networks trivialize the traditional and anatomical basis for differentiating central versus peripheral vestibular disorders (45). In the classic anatomic view, the vestibular cortex is limited to the parietoinsular cortex, mainly consisting of the posterior insula and the parietal operculum (47). There are various non-vestibular responses after vestibular cortex stimulation (11). They may be interpreted as a result of bidirectional vestibular pathways to the brain stem, cerebellum, limbic system, and complex corticocortical networks and

also as a result of the modulation of the upper centers especially the prefrontal cortex on vestibular signal processing (12).

Another property of the central vestibular signals is related to their interactions with autonomic centers including the nucleus tractus solitarius, the lateral medullary reticular formation, and the rostral ventrolateral medulla (62). The so-called vestibulo-autonomic system has ascending projections to the thalamus and insular cortex and descending projections to some brain stem autonomic centers including the vasomotor, respiratory, nausea-vomiting centers, and also to the rostral ventrolateral medulla neurons (63).

Vestibular modulation of autonomic discharges

Vestibular autonomic effects have been known for more than 50 years ago, first as motion sickness and soon after in cardiovascular regulation (62, 63). Recently these effects have also been discovered in bone hemostasis and bone remodeling. Normal and abnormal vestibular function are reported to have associations with bone metabolism, but a causal relationship is still not proven (64-71).

Skeletal muscle neural fiber discharges are modified by vestibular stimulation. This effect is limited to vasoconstrictors and is not observed in fisimotor fibers. Vestibular afferent stimulation by electrical currents causes both increase and decrease and mix responses in sympathetic fiber discharges. It is suggested that these differential effects obey an anatomical distribution and there is a kind of patterning (72-78).

Animal models show that even an isolated stimulation of one semicircular canal can change the sympathetic and parasympathetic discharges and will cause a decrease in heart rate and blood pressure (79). It must be emphasized that the vestibular modulation of autonomic discharges involves both divisions of the autonomic nervous system and, it is recommended to be referred to as vestibulo-autonomic rather than vestibulo-sympathetic reflex (80, 81).

Cardiovascular consequences of vestibular dysfunction

Orthostasis is associated with vestibular system activity. Vestibular stimulation changes the visceral autonomic nerves' discharges (82, 83). Ageing hurts this relationship and decreases its efficacy in hemodynamic adjustment during orthostasis (84-86). The vestibular-evoked potentials provide a dynamic spatiotemporal map regarding the central processing of vestibular signals. These potentials are induced by different methods including caloric, auditory, tactile (shaker), magnetic, galvanic and natural (rotating chair, tilt, motion platforms) vestibular stimulation. Some cortical vestibular potentials have a very short latency of about 6 ms indicating trisynaptic vestibulo-thalamo-cortical pathways (87, 88). The recent experimental data indicates that the origin of the hemodynamic effect of the vestibular system may be otoliths organ or semicircular channels and both divisions of the autonomic nervous system are involved. Indeed, the pharmacological block of sympathetic or parasympathetic receptors eliminates the vestibuloautonomic changes in heart rate and both the heart rate and blood pressure respectively. The changes in the low and high-frequency spectral heart rate variability indices also indicate a simultaneous increase in sympathetic activity and a decrease in parasympathetic activity in the vestibuloautonomic reflex. There is approximately 1 second time gap between electrical baroreceptor afferent stimulation and changes in blood pressure. In addition, the baroreceptor feedback closed-loop control of blood pressure needs an error signal. During orthostasis, the vestibular system provides a rapid and open-loop feed-forward control of blood pressure at less than 100 ms. This rapid vestibular control then is completed and maintained by baroreceptor control (89). Postural orthostatic tachycardia syndrome is characterized by an exaggerated increase in heart rate and the absence of orthostatic hypotension. An inappropriate higher level of vestibular-induced sympathetic stimulation is reported as the underlying mechanism. This imbalance between appropriate paradoxical changes in sympathovagal autonomic tone may be due to enhanced utricular inputs (90). Utricular dysfunction also is reported to be related to orthostatic hypotension (91). The interaction of the vestibular and autonomic systems is more complex. The effect of vestibular signals on blood pressure and heart rate is mediated by different autonomic neurons including the rostral ventrolateral medulla neurons. These neurons are linked to the sympathetic preganglionic neurons that regulate heart rate and constriction of vascular smooth muscle. However, there are differential responses of the rostral ventrolateral medulla neurons to vestibular signals. When the intensity of the natural vestibular stimulus is low and the orthostasis or other movements have little or no impact on intravascular blood pooling there are no changes in rostral ventrolateral medulla neuron discharges. This phenomenon only exists in the conscious animal and does not exist in a decerebrate condition. This state may probably indicate a vestibular signal gating. Therefore, the

vestibuloautonomic reflex for hemodynamic adjustment during orthostasis occurs merely when the tilt or other positional changes cause physiologically significant blood volume pooling. The vestibuloautonomic reflex is also different from central command-induced autonomic activities. In voluntary or active movements especially during exercise, the central commands will cause anticipatory feed-forward cardiovascular responses. This autonomic adjustment is due to the effect of central commands on rostral ventrolateral medulla neurons and does not exist in passive movements. In contrast, the vestibuloautonomic reflex starts only after the activation of vestibular sensory afferents and exists in both active and passive movements because both conditions will cause afferent vestibular signals (92). It must be emphasized that the relationship between blood pressure and vestibular function is bi-directional. The vestibular system controls orthostatic blood pressure, but on the other hand, hypotension by itself can induce ischemic excitation of central vestibular neurons, which may cause dizziness in hypotensive states and may cause a secondary compensatory hypotensive-induced vestibuloautonomic reflex (93).

Conclusion

Vestibular sensory signals compensate for blood pooling likely in a gated and threshold-sensitive manner, nearly simultaneously during active or passive orthostasis. There is a bi-directional relationship between blood pressure and vestibular function. Vestibular dysfunction may be one of the underlying causes of orthostatic hypotension and by itself has clinical significance in managing patients suffering from orthostatic hypotension and syncope. Ischemic excitation of vestibular neurons in hypotensive states may cause a secondary compensatory hypotensive-induced vestibuloautonomic reflex that usually is associated with dizziness. However, the primary vestibuloautonomic reflex is a normal physiological compensation and is not associated with dizziness or other symptoms.

Compliance with ethical guidelines

This research is a review article with no human or animal samples.

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Conflicts of interest

The authors declared no conflict of interest.

Authors' contributions

All authors have contributed to the design, execution, and writing of all sections of the current study.

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