CLINICAL EVIDENCE THAT THE VESTIBULAR SYSTEM PARTICIPATES IN AUTONOMIC CONTROL

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Abstract — The vestibular system, including both the peripheral vestibular system, that is, the labyrinth, and the central vestibular system, is known to influence autonomic function in several ways that have clinical implications. This paper discusses evidence for vestibular influences on autonomic control from normal human subjects, evidence for vestibular influences on autonomic control from patients, clinical implications of vestibulo-autonomic regulation, and speculations regarding possible clinical implications of vestibulo-autonomic control. Situations that provoke vestibular-induced autonomic responses in normal subjects include vestibular laboratory testing, vehicular motion, simulators, and, possibly, exposure to microgravity. Patients with peripheral and central vestibular abnormalities manifest both symptoms and signs of autonomic dysfunction presumably via vestibulo-autonomic connections. Vestibulo-autonomic regulation impacts vestibular diagnostic testing, clinical diagnosis of balance disorders, and treatment of balance disorders. In addition to well-recognized peripheral and central vestibular disorders, anxiety disorders have recently been linked to vestibular dysfunction in a subset of patients. In particular, vestibular dysfunction has been linked to panic disorder and agoraphobia. Vestibular-autonomic connections may form a basis for an association between vestibular dysfunction and panic attacks. The importance of vestibulo-autonomic regulation in the clinical arena is not fully known. Two speculative areas discussed in this paper include vestibular-induced orthostatic intolerance and the role of vestibular—respiratory pathways on sleep apnea. © 1998 Elsevier Science Inc.

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Introduction

The vestibular system, including both the peripheral vestibular system, that is, the labyrinth, and the central vestibular system, is known to influence autonomic function in several ways that have clinical implications. Figure 1 illustrates diagrammatically how input from the vestibular labyrinth and other sensory systems combine in the vestibular nuclei to influence so-called vegetative symptoms such as nausea, vomiting, and changes in heart rate and blood pressure. Additionally, sensory signals important for spatial orientation, through the vestibular nuclei, also influence the locus coeruleus, a noradrenergic structure thought to be important in panic disorder and agoraphobia (1). Another important structure for vestibular autonomic regulation is the cerebellum, which is known to influence the cardiovascular system (2).

This paper is concerned with the clinical implications of vestibular autonomic regulation and will be organized as follows. There will be a discussion of evidence for vestibular influences on autonomic control from normal human subjects, evidence for vestibular influences on autonomic control from patients, clinical implications of vestibulo-autonomic regulation and,
Figure 1. An overview of vestibular influences on autonomic control. Ascending projections from the vestibular nuclei to the parabrachial nucleus may participate in producing affective and emotional responses, and dysfunction in this pathway may lead to psychiatric disorders such as agoraphobia. A descending pathway from the vestibular nuclei to brainstem centers that control respiration and circulation may be responsible for adjusting blood pressure and respiration during movement and changes in posture.

Evidence for Vestibular Influences on Autonomic Control from Normal Human Subjects

The vestibular system is known to influence the sympathetic nervous system, the parasympathetic nervous system, and the respiratory system. Although the respiratory system is not formally part of the autonomic nervous system, the involuntary nature of respiratory control and its importance in vomiting prompted its inclusion herein. Evidence for vestibular influences on autonomic control from normal human subjects includes the occurrence of both autonomic "symptoms," that is, perception on the part of subjects, and "signs," that is, objective findings that can be observed. Vestibular-induced autonomic symptoms include nausea, malaise, drowsiness, abdominal awareness, anxiety, distress, dread, and reduced vigilance. Vestibular-induced autonomic signs include changes in salivation, changes in gastric motility, vomiting, endocrine responses, "cold" sweating, pallor, increased blood flow to skeletal muscles, and changes in heart rate and heart rate variability.

Situations that provoke vestibular-induced autonomic responses include clinical vestibular laboratory testing, research vestibular laboratory testing, vehicular motion, simulators, and exposure to microgravity. The latter three circumstances can lead to motion sickness, simulator sickness, and space sickness, respectively. The term "sickness" refers to the autonomic signs and symptoms that result from a combination of vestibular stimulation, visual motion, and visual–vestibular interaction. Vestibular-induced motion sickness has been conceptualized as a "poison response" that includes a combination...
of “stomach emptying” and a “stress response” (3). Stomach emptying includes a combination of symptoms of the act of vomiting, arginine-vasopressin (AVP) release, and increased activity in the parasympathetic nervous system. The “stress response” includes symptoms of anxiety or discomfort, endocrine release, and predominantly sympathetic nervous system changes.

There are several issues regarding vestibular-induced autonomic changes that are unresolved. These include individual variability in the susceptibility to vestibular-induced autonomic changes, the relative influence of the semicircular canals compared with the otolith organs, and the cause of delayed or prolonged autonomic symptoms following vestibular stimulation.

Evidence for Vestibular Influences on Autonomic Control from Patients

Evidence for vestibular influences on autonomic control from patients includes the effects of acute unilateral peripheral vestibular loss, vestibular compensation for unilateral peripheral loss, and the effects of central vestibular lesions on autonomic control including lesions both of the brainstem and of the cerebellum. Acutely, unilateral peripheral vestibular disease causes vegetative symptoms such as nausea, vomiting, and malaise. These symptoms and signs are unquestionably related to direct and indirect connections from the vestibular system to the autonomic nervous system (4). The usefulness of these symptoms and signs physiologically is uncertain. With the process of “vestibular compensation” (5), which results in a resolution of vestibulo-ocular and vestibulo-spinal imbalances, patients typically have a resolution of their vegetative symptoms and signs. In particular, vomiting typically resolves over a period of hours. Nausea and malaise may be more long-standing and can continue for days to weeks, even in patients who eventually fully recover their functional abilities.

Many patients with central nervous system disorders that adversely affect central vestibular structures have accompanying autonomic symptoms and signs that may be related to the disorder primarily, or may be related to the effect of the disorder on central vestibular function. Such disorders as brainstem or cerebellar infarction (6), migraine (7,8), the effects of neurotoxins (9), and neurodegenerative disorders (10), all can affect central vestibular function and/or autonomic function. For example, the highly prevalent nausea and occasional vomiting that accompanies migraine headache (11) may be due, in part, to abnormalities in vestibulo-autonomic connections during a migrainous episode. Similarly, the autonomic symptoms and signs associated with lateral medullary infarction (Wallenberg’s syndrome) may be a result of direct damage to the brainstem autonomic centers or may relate to autonomic dysfunction due to infarction of the vestibular nuclei (6).

Clinical Implications of Vestibulo-Autonomic Regulation

Diagnostic Testing of the Vestibular System

Current diagnostic testing methods used in the evaluation of vestibular disorders include caloric testing, rotational testing, and platform posturography. A limitation of each of these methods pertains to autonomic symptoms induced by vestibular stimulation. For caloric testing, in our experience, nausea is induced in most patients and vomiting occurs in about 5% of patients. Autonomic symptoms require discontinuation of caloric testing prior to completion of binocular infrared testing in about 5% of our patients. Conventional rotational testing, wherein patients are gently spun while seated in a computer-controlled chair, rarely results in autonomic symptoms that are severe enough to warrant discontinuation of testing. Another type of rotational testing, still in the development stage, is designed to assess the otolith-ocular reflex and uses off-vertical axis rotation. For this test, patients are tilted while rotating. Off-vertical axis rotation leads to significant autonomic symptoms that ultimately may limit the clinical applicability of this new technique (12). Measures to reduce autonomic symptoms include ensuring that the ambient temperature in
Balance Disorders and Anxiety Symptoms

Many vestibular disorders are associated with autonomic symptoms and signs. For example, peripheral vestibular disorders, such as Meniere's disease, are often associated with nausea and vomiting in addition to vertigo. As noted above, presumably, the nausea and vomiting are a result of the influence of peripheral vestibular signals on the autonomic nervous system. Also, as noted above, central vestibular disorders can lead to abnormal autonomic nervous system activity.

In addition to well-recognized peripheral and central vestibular disorders, certain anxiety disorders recently have been linked to vestibular dysfunction in a subset of patients (14,15). In particular, vestibular dysfunction has been linked to panic disorder and agoraphobia (16-21). Panic attacks are characterized by sudden onset of autonomic symptoms, hyperventilation, and dizziness. The autonomic symptoms include heart palpitations, sweating, trembling, hot or cold flashes, and gastrointestinal distress; the symptoms of hyperventilation include shortness of breath, feeling like choking, chest discomfort, and numbness or tingling sensations (concomitantly with autonomic symptoms and signs). For example, the autonomic symptoms include heart palpitations, sweating, trembling, hot or cold flashes, and gastrointestinal distress; and also, as noted above, central vestibular disorders can lead to abnormal autonomic nervous system activity.

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Current theories of the epidemiology of panic disorder include (1) dysregulation of brainstem noradrenergic systems (for example, 27-29); (2) involvement of central serotonergic pathways (30); and (3) respiratory dysfunction (31,32). Recent advances in our understanding of vestibular disorders and anxiety disorders are uncertain, possibly, it is mediated by autonomic circuits involving the locus coeruleus, a structure that influences almost every part of the brainstem and spinal cord (1).

A commonly used diagnostic term for patients with dizziness and anxiety without concomitant symptoms that clearly define a vestibular syndrome such as Meniere's disease or migraine is "psychogenic dizziness" (22). Nedzelski and colleagues (23) have offered a definition of psychogenic dizziness. Their definition is problematic because many patients labeled as psychogenic may have vestibular system abnormalities (22). Based upon the symptoms of patients with anxiety, many are likely to be suffering from alterations in vestibulo-autonomic regulation. This idea is supported by the knowledge that patients with bonafide panic attacks have autonomic symptoms as an accompaniment of their attacks.

Patients with panic disorder often develop agoraphobia, characterized by avoidance of situations such as heights, elevators, supermarkets, shopping malls, crowds, theaters, stadiums, traveling, bridges, and tunnels (24). The high prevalence of vestibular dysfunction in panic disorder with agoraphobia suggests a functional relationship between these conditions. The presence of such a relationship is also supported by findings that panic attacks and agoraphobic avoidance are prevalent among otoneurological patients with balance complaints and objectively demonstrated vestibular dysfunction. Eagger and colleagues (25) found that one third of patients with peripheral vestibular disorders had panic and agoraphobic symptoms. Similarly, Stein and colleagues (26) found a prevalence of panic disorder of 41% in patients with vestibular disorders; Clark and colleagues (14) found panic attacks in 37% of patients with vestibular disorders as compared to a 0% prevalence of panic in patients with mild hearing loss.

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tutres of the limbic system, including the amygdala (45). The amygdala and other parts of the limbic system are known to be essential for the conditioning of fear responses (46).

Although these neuroanatomical findings suggest a relationship between vestibular dysfunction and panic attacks, they may not easily account for the observations, within patients with panic disorder, of a specific relationship between vestibular dysfunction and agoraphobic avoidance. However, “pseudo-agoraphobic” syndromes in patients with vestibular disorders have long been recognized. including “street neurosis” (47), the “supermarket syndrome” (48,49), the “wallpaper, or traffic patterns. We believe that in patients with anxiety disorders selected for prominent SMD showed an increased postural sensitivity to optic flow stimuli (57), and (2) agoraphobics, known to have high levels of SMD (56), exhibited a surface-dependent sway pattern on computerized dynamic posturography (59).

To summarize, central vestibulo-autonomic relationships, along with the situational specificity of vestibular symptoms leading to SMD, provide the basis for the role of the vestibular system in certain anxiety disorders. Specifically, vestibular-autonomic connections may form a basis for association with panic attacks. Also, mediated by space and motion discomfort, the development of certain phobic avoidance patterns is facilitated, including agoraphobia. Figure 2 (1) summarizes these relationships, embedded with other possibilities not specifically discussed here. For example, increased arousal and the behavior of hyperventilation, both common in panic disorder, may affect vestibular function (60–62).

The model depicted in Figure 2 (1) is still incomplete. Importantly, we need to further develop our understanding of why vestibular dysfunction contributes to anxiety disorders in some individuals and not in others. The nature of the underlying vestibulopathy (that is, whether acute or chronic, compensated or uncompensated) and the degree of anxiety proneness (as indicated, for example, by a family history of anxiety disorders) are likely moderators of the relationship. Even though vestibular dysfunction may not be the ultimate cause of panic disorder, it appears to contribute to its phenomenology, particularly the development of agoraphobia.

Treatment of Patients with Balance Disorders

Treatment for vestibular disorders currently includes pharmacotherapy, physical therapy, and surgery. An emerging technology that may be applied to the treatment of patients with dizziness and balance disorders is that of virtual environments (63). Autonomic side effects from physical therapy can be a limiting factor in treatment options. Similarly, as virtual environments evolve as an additional treatment modality, au-
Vestibular Dysfunction

Other Visceral Input

Autonomic Activity

Hyperventilation

Space / Motion Discomfort

Panic Disorder

Other Agoraphobic Mechanisms

Height Phobia

Agoraphobia without Panic

Panic Disorder with Agoraphobia

Figure 2. Overview of relationships between vestibular dysfunction and certain anxiety disorders. From Jacob and colleagues (1).

Further Speculations Regarding Clinical Implications

The importance of vestibulo-autonomic regulation in the clinical arena is as yet unknown. Two speculative areas of application include vestibular-induced orthostatic intolerance and the role of vestibular-respiratory pathways on sleep apnea. Although these issues are only being explored in a very preliminary fashion, orthostatic intolerance experienced by astronauts returning to Earth (65) may have as a component abnormal vestibulo-autonomic regulation. Further research regarding vestibulo-autonomic connection, particularly otolith-autonomic influences, may improve our understanding of “Earth sickness.” Also, although patients with vestibular disorders rarely complain of orthostatic hypotension, they avoid making sudden changes in posture that would require rapid readjustments in circulation.

Upper airway muscle tone is known to be influenced by head position (43,66–68). Such influences may be mediated by vestibulo-respiratory circuits. Possibly, by altering the activity in such circuits, pharmacological hypotonia, which often underlies obstructive sleep apnea, may be ameliorated by vestibular stimulation.

Conclusions

In conclusion, vestibulo-autonomic pathways impact the field of vestibular and balance disorders. In particular, patients with either peripheral and central vestibular abnormalities manifest both symptoms and signs of autonomic dysfunction. Vestibular autonomic regulation affects the assessment, diagnosis, and treatment of patients with vestibular disorders.
REFERENCES


