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The Potential Role of Joint Injury and Eustachian Tube Dysfunction in the Genesis of Secondary Ménière's Disease

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Abstract: Ménière's disease not only includes the symptom complex consisting of attacks of vertigo, low-frequency hearing loss, and tinnitus but comprises symptoms related to the eustachian tube, the upper cervical spine, the temporomandibular joints, and the autonomic nervous system. Quantifiable experience shows that the insertion of a middle-ear ventilation tube can alleviate Ménière's disease symptoms, suggesting that eustachian tube dysfunction is a contributing feature. Clinical practice also shows that treating disorders of the upper cervical spine and temporomandibular joints can lessen Ménière's disease symptoms, suggesting a relationship. Similarly, stellate ganglion blocks can be beneficial in controlling Ménière's disease symptoms, highlighting the influence of the autonomic nervous system. Thus, contrasting symptoms associated with the eustachian tube, the upper cervical spine, the temporomandibular joints, and the autonomic nervous system relate to Ménière's disease, but the possible reflex pathway by which a link is established is unclear. We made an attempt in this study to describe a hypothetical reflex pathway that links joint injury and the autonomic nervous system, where eustachian tube function is under their influence and is the critical link. In this hypothetical reflex pathway, irritation of facet joints can first lead to an activated anterior cervical sympathetic system via an independent pathway in the mediolateral cell column; it can simultaneously lead to an axon reflex involving nociceptive neurons, resulting in neurogenic inflammation and the prospect of a eustachian tube dysfunction. The eustachian tube dysfunction is responsible for a disturbed middle ear–inner ear pressure relationship, circumstances that have the potential to develop into secondary Ménière's disease. This reflex pathway is supported by recent animal experiments.

Key Words: autonomic nervous system; cervical spine; eustachian tube; Ménière's disease; neurogenic inflammation; temporomandibular joint

Ménière's disease is characterized by intermittent attacks of vertigo, low-frequency hearing loss, and tinnitus. Apart from this classical symptom triad, a diverse range of other symptoms is regularly reported. These include disorders of the cervical spine and temporomandibular joints, the eustachian tube, and the autonomic nervous system. Each of these symptoms has been targeted, with some success, in an effort to alleviate the main symptoms of Ménière's disease. Thus, reducing functional disorders of the cervical spine or temporomandibular joints can lessen Ménière's disease symptoms, as does insertion of a middle-ear ventilation tube. Disorders of the autonomic nervous system have been treated with stellate ganglion blocks or acupuncture, and we have recently investigated how the motor or sensory components of the autonomic nervous system may influence eustachian tube function in rats.

Though circumstantial evidence suggests that joint disorders, eustachian tube dysfunction, and the autonomic nervous system are involved in the genesis or

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maintenance of at least some forms of secondary Ménière's disease, a theory that explains how these seemingly disparate symptoms contribute to Ménière's disease is completely absent. This study first examines the evidence that joint disorders, eustachian tube dysfunction, and the autonomic nervous system are involved in Ménière's disease. Then we describe some theories as to how these conditions may interact to cause secondary Ménière's disease. It is hoped that these theories will stimulate further research that may lead to new ways to treat this vexing disease.

EUSTACHIAN TUBE DYSFUNCTION AND MÉNIÈRE'S DISEASE

Clinical experience shows that Ménière's disease patients frequently complain of a blocked ear and the annoying feeling of fluid in the middle ear. These symptoms suggest eustachian tube dysfunction. Consequently, reduced middle-ear ventilation has been regarded as a threat to the inner ear [1].

Addressing improved middle-ear ventilation by inserting a ventilation tube was not very successful in treating Ménière's disease symptoms [2], and it was suggested that a relationship between middle-ear pressure and function of the inner ear is unlikely, thus questioning the rationale of inserting middle-ear ventilation tubes [3]. This view seemed to be supported by studies that showed that eustachian tube dysfunction is not prevalent in Ménière's disease patients [4]. However, none of these studies employed specific eustachian tube function tests.

Demonstrating eustachian tube dysfunction can be difficult when the eardrum is intact, and tympanometry alone is insufficient to demonstrate it. However, specific eustachian tube function tests have been developed that reveal the inability of Ménière's disease sufferers to equalize middle-ear pressure when mild negative pressure is present in the middle ear [5,6]. These specific tests showed that normal middle-ear function, as revealed by tympanometry, does not exclude eustachian tube dysfunction. However, as middle-ear function appears to be normal, it might be more reasonable to speak of eustachian tube hypofunction.

In contrast to negative experiences with the insertion of middle-ear ventilation tubes, other investigators could demonstrate that eustachian tube dysfunction is a feature of Ménière's' disease and that treatment with middle-ear ventilation tubes has benefits [6,7]. The symptoms were explained by exaggerated pressure sensitivity [7]. The latter is supported by studies that reveal a change of electrophysiological parameters of the inner ear with various pressure constellations of the middle ear [8].

It appears that eustachian tube function is important for the integrity of the inner ear, and secondary Ménière's disease could develop in patients with exaggerated pressure sensitivity. Looking at diverse experiences with eustachian tube function in Ménière's disease, one is inclined to assume that Ménière's disease is prevalent in geographical regions where the eustachian tube is more frequently challenged. In fact, a report praising the benefits of middle-ear ventilation tubes in the management of Ménière's disease symptoms is from hilly and mountainous regions [7].

DISORDERS OF THE CERVICAL SPINE AND MÉNIÈRE'S DISEASE

The suggestion that the cervical spine is involved in Ménière's disease is not new [9,10], and a number of studies have confirmed the higher prevalence of cervical spine disorders in patients with diagnosed Ménière's disease as compared to control subjects from the general population [11]. In this context, "neck disorder" is usually taken to be a joint injury, but Decher [12] points out that, in the context of the vestibular organ, the cervical spine is not just a bony structure and needs to be viewed as a whole, including muscles, ligaments, and the vascular and nervous system.

As would be expected, if cervical injury plays a role in Ménière's disease, treating the cervical injury should alleviate Ménière's disease symptoms. Chiropractic manipulation of disorders of the cervical spine has been successfully used to treat patients with vestibular symptoms [13,14]. Franz et al. [6] described a syndrome—the *cervicogenic otoocular syndrome*—that has the potential to develop into Ménière's disease. Adequate physiotherapeutic treatment of the associated neck disorder can prevent the development of Ménière's disease in these patients.

The relationship between cervical disorders and Ménière's disease is commonly explained by either a "vascular" or a "neural" theory. The vascular theory is based on the observation that the vertebral artery supplies the inner ear, the vestibulocochlear nuclei, and the reticular system, and a cervical joint injury could affect the artery and compromise blood supply to these regions. The neural theory is based on the belief that the vertebral nerve, in close association with the vertebral artery and containing sympathetic axons, may be irritated by cervical injury and become dysfunctional.

In support of the vascular theory, Klausberger and Samec [15] described the foramen retroarticulare atlantis as a possible source compromising the vertebral artery. The reduction in blood supply might result from osseous deformities of vertebrae compromising the

lumen of the supplying blood vessel. In support of the neural theory, the Barré-Liéou syndrome or posterior sympathetic syndrome has often been mentioned. Its mechanism is, however, uncertain and has been discredited, allowing misuse of this eponym [16]. This so-called posterior sympathetic syndrome has recently been challenged, as vestibulocochlear symptoms can be explained by the "anterior sympathetic" system comprising the superior cervical ganglion and its postganglionic neurons, with branches to the eustachian tube and inner ear [17].

Overall, evidence suggests that disturbances of the cervical spine can be associated with Ménière's disease symptoms and that their adequate management can lessen inner-ear symptoms.

DISORDERS OF THE TEMPOROMANDIBULAR JOINTS AND MÉNIÈRE'S DISEASE

A correlation between ear disorders and the temporomandibular joints almost seems to be mandatory, owing to their close anatomical proximity. Chole and Parker [18] found that aural symptoms of tinnitus and vertigo are more frequently found in patients with temporomandibular disorders than in a comparable age-matched population. Bjorne and Agerberg [19] could demonstrate that the costs of sick leave and disability pension due to Ménière's disease could significantly be reduced by treatment of the temporomandibular and cervical spine joints.

The Costen syndrome is a well-recognized disorder predicated on the very close relationship between the temporomandibular joints and middle-ear and inner-ear function [20]. Costen speculated that pressure from the condyle could cause eustachian tube blockage, which could result in hearing loss and tinnitus.

Some researchers speculated that hyperactivity of masticatory muscles could induce a secondary reflex contraction of the tensor veli palatini muscle, thereby causing ineffective eustachian tube opening [18,21–23]. Because the trigeminal nerve also innervates the tensor tympani muscle, it was speculated that a similar secondary reflex causes contraction of the tensor tympani muscle, which can lead to tinnitus.

A neurologically based hypothesis is derived from the concept that the middle ear and the inner ear receive input from the trigeminal and sympathetic nerves through the tympanic plexus. An irritation could be the result of the Costen syndrome, and this can lead to tinnitus. Consequently, some patients responded to tinnitus treatment that involved sectioning the tympanic plexus in the middle ear [24].

Though it is not quite clear by which reflex mechanism vestibulocochlear symptoms develop, temporomandibular disorders are likely to be present in Ménière's disease.

THE AUTONOMIC NERVOUS SYSTEM AND MÉNIÈRE'S DISEASE

It has been suggested for some time that a disorder of the autonomic nervous system is a possible cause of Ménière's disease [25]. One telling clinical observation is an enlarged pupil on the side of the affected ear, particularly during an attack of vertigo. There is some discrepancy as to whether such pupillary enlargement represents paralysis of parasympathetic innervation or is due to hyperactivity of the sympathetic portion of the autonomic nervous system [6,26,27].

Some clinical evidence shows the efficacy of ganglion stellate blocks or that the removal of the cervical sympathetic system can have a beneficial effect on the symptomatology in Ménière's disease [28,29].

The effect of the sympathetic nervous system is believed to be its influence on stria vascularis circulation [24]. However, as ample evidence supports autonomic representation in the middle ear and the eustachian tube, sympathetic hyperactivity could also lead to dysfunction through changes of gland secretions in the eustachian tube and thus could influence middle ear–inner ear pressure relationships.

In short, the autonomic nervous system, and particularly the sympathetic portion of that system, could influence physiological events in the inner ear by changing the blood supply. Physiological events might also be influenced by changing middle ear–inner ear pressure relationships via the alteration of eustachian tube function through changes of gland secretions.

A HYPOTHETICAL LINK

Unquestionably, the upper cervical spine, the temporomandibular joints, the eustachian tube, and the autonomic nervous system can contribute to the global symptom complex of Ménière's disease. It can be demonstrated that Ménière's disease symptoms improve with physiotherapy directed to the upper cervical spine and temporomandibular joints. Similarly, treatment with stellate ganglion blocks or dissection of the tympanic plexus can be beneficial and demonstrates autonomic involvement. Equally, Ménière's disease symptoms can improve with the insertion of a middle-ear ventilation tube, suggesting eustachian tube dysfunction.

The recent development of positive-pressure pulse therapy in the management of Ménière's disease

highlights the importance of a balanced middle ear–inner ear pressure relationship [30,31]. Clinical experience with positive-pressure pulse therapy suggests pressure sensitivity and supports the idea that good middle-ear ventilation is vital. In this context, the eustachian tube that provides ventilation to the middle ear is most likely the critical link.

Evidence also corroborates that the autonomic nervous system can influence eustachian tube function. This is not surprising, as the mucosa of the eustachian tube requires lubrication provided by glands that are below the epithelium and are under the influence of sympathetic and parasympathetic innervation.

A study of the influence of the autonomic nervous system in short-term experiments in an animal model of active eustachian tube function could demonstrate that parasympathetic stimulation leads to a dysfunction [32]. Stimulating the sympathetic portion of the autonomic nervous system had no influence on eustachian tube function by itself. However, by simultaneously stimulating the anterior cervical sympathetic system electrically and the sensory system through the application of capsaicin, a eustachian tube dysfunction could be observed [33].

It was assumed that capsaicin released inflammatory mediators in sensory and nociceptive neurons surrounding the eustachian tube, with the potential of neurogenic inflammation. Capsaicin alone had no effect on eustachian tube function but operated only in conjunction with an cervical sympathetic system.

The observed aggravation of eustachian tube function, though simultaneously stimulating the cervical sympathetic system and applying capsaicin, could be explained by the sympathetic effect of enhancing neurogenic inflammation, and the associated edema in the eustachian tube could render middle-ear ventilation difficult. This concept is supported by recent findings that activation of sympathetic neurons can enhance neurogenic inflammation via $alpha_1$ receptors [34]. This would also explain the frequent complaints by patients of having a wet ear.

Hence, an activated sympathetic system could seemingly have an adverse effect on eustachian tube function. This effect is generated through modulation or interaction with the sensory system. An explanation remains to be found for the simultaneous activation or sensitization of the sensory system such that a eustachian tube dysfunction could develop through this pathway.

In our view, the clinical observation of an enlarged pupil on the side of the affected ear in Ménière's disease patients is due to an activated cervical sympathetic system rather than paralysis of parasympathetic innervation, as has been suggested in the past. Thus, a stellate ganglion block can be beneficial. A stellate ganglion block will have the effect of a Horner complex, an observation always made when treating Ménière's disease patients with this treatment modality. It is difficult to imagine that a true Horner's syndrome can be observed when the parasympathetic system is paralyzed in these circumstances. There might be a change in pupil size, but meiosis, as is expected in Horner's syndrome, would be missing when the parasympathetic system is paralyzed. One would also suspect that paralysis of parasympathetic innervation would facilitate eustachian tube function, as its activation causes an aggravation.

Though an enlarged pupil is consistent with an activated cervical sympathetic system, indications suggest that it can also be linked to an upper cervical spine disorder. Mydriasis can be physiological when normal pupil reflexes are observed. Further enlargement of the pupil during a shoulder turn may also be observed, but this typically occurs in the end position, when there is strain on the facet joints and neck muscles. Immediate enlargement of the pupil while turning the shoulder is abnormal and points to an irritation in the upper cervical facet joints. This clinical observation links the cervical sympathetic system with the upper cervical spine. Physiological studies support the innervation of cervical facet joints by sensory and sympathetic neurons [35].

It is unclear whether functional disorders of the temporomandibular joints are capable of activating the cervical sympathetic system and cause an enlargement of the pupil. Clinical experience shows that functional disorders of the temporomandibular joints are likely to cause a functional disorder of the upper cervical spine and vice versa. This reciprocal behavior is explained by the association of cervical spine and temporomandibular joints as components of the so-called upper quarter, a phenomenon leading to the involvement of the other unit when one unit is compromised [36]. Physiotherapists are familiar with this phenomenon and take it into consideration when treating disorders of the cervical spine and temporomandibular joints, respectively.

The eustachian tube is suspected to be the critical link. It has quite a remarkable representation of sensory neurons. This system could be activated through an axon reflex of the mandibular branch of the trigeminal nerve that innervates the temporomandibular joints and upper cervical facet joints. The autonomic nervous system, particularly the sympathetic portion of the autonomic nervous system, can be activated by a neck and temporomandibular joint disorder, and this combination can have the effect of neurogenic inflammation in the eustachian tube, with the consequence of reduced middle-ear ventilation.

Anatomical studies demonstrate that an independent sympathetic pathway exists in the mediolateral cell column of the spinal cord, stretching from C2 to T2,

bypassing the stellate ganglion and linking up with the superior cervical ganglion [37]. These findings suggest that it is not necessarily the posterior cervical sympathetic system—which, in the Barré-Liéou syndrome, has thus far garnered all the attention—but rather the anterior cervical sympathetic system is involved in the symptomatology of Ménière's disease.

The anterior cervical sympathetic system sends postganglionic neurons from the upper cervical ganglion, innervating the eye and organs of the ear. Postganglionic neurons link up with the eustachian tube and the inner ear, reaching it via the tympanic plexus and via the labyrinthine artery [38].

We hypothesize that one possible reflex pathway consists of an irritation of a cervical facet joint or a temporomandibular joint that can lead to the release of inflammatory mediators in sensory and nociceptive neurons of the eustachian tube via an axon reflex. Independently, this might not necessarily result in eustachian tube dysfunction. When, however, the joint injury also leads to an activated anterior cervical sympathetic system, the combination could result in a eustachian tube dysfunction due to enhanced neurogenic inflammation. An enlarged pupil on the side of the affected ear is the clinical observation of activated postganglionic sympathetic neurons (Fig. 1). The eustachian tube dysfunction is hypothesized to disturb middle ear–inner ear pressure relationships, which has the potential to lead to secondary Ménière's disease.

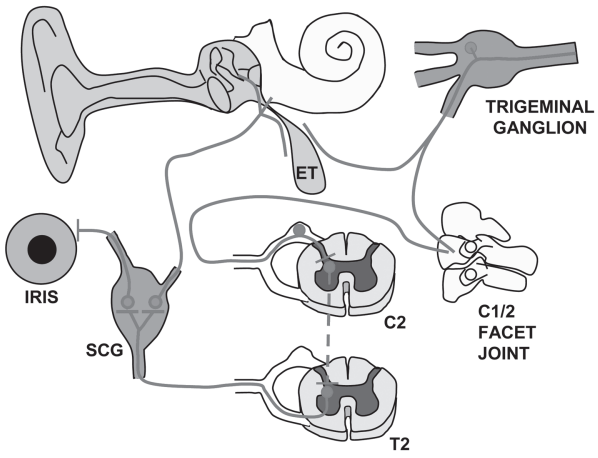

Figure 1. Hypothetical reflex pathway in secondary Ménière's disease. An upper cervical facet joint disorder (or temporomandibular joint disorder) could simultaneously release inflammatory mediators in the eustachian tube via an axon reflex and activate the anterior cervical sympathetic system, the latter enhancing neurogenic inflammation in the eustachian tube and resulting in reduced middle-ear ventilation. This imbalance of a middle ear–inner ear pressure relationship has the potential to develop into secondary Ménière's disease. (*SCG* = superior cervical ganglion; *ET* = eustachian tube; *C1/2* = cervical segments one and two of spinal cord; *C2* = cervical segment two of spinal cord; *T2* = thoracic segment two of spinal cord.)

This hypothetical reflex pathway describes one possible mechanism that can lead to secondary Ménière's disease. Other pathways may exist. The critical link in this reflex pathway is the eustachian tube. Thus, we hypothesize further that any treatment that improves middle-ear ventilation or any treatment that addresses neurogenic inflammation in the eustachian tube will alleviate Ménière's disease symptoms. This could lead to new treatment concepts.

SUMMARY

A hypothetical reflex pathway has been described as linking upper cervical facet joints and temporomandibular joints with the autonomic nervous system and resulting in eustachian tube dysfunction, a constellation that has the potential to develop into secondary Ménière's disease.

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