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Letter to the Editor

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Gender differences in audio-vestibular disorders

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Abstract

In the last years, the attention to the role of gender in physiopathology and pharmacology of diseases in several medical disciplines is rising; however, the data on the relationship between gender and audio-vestibular disorders are still inconclusive and sometimes confusing. With this letter to the editor, we would like to review the role of gender in audio-vestibular disorders. Literature data show that anatomic variances of the inner ear do exist in men and women and that the different physiology and/or hormonal influence between genders could produce different clinical outcome of routine audiological and vestibular tests. Beyond the epidemiological gender-related differences, the clinical data suggest that the gender has a potential role as an etiopathogenetic factor in audio-vestibular disorders and it is probably responsible for the different clinical features observed between male and female subjects.

Keywords

audiology, cochlea, gender, gender differences, inner ear, sensorineural hearing loss, sex, vestibule

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Dear Editor,

We would like to review the role of gender in audio-vestibular disorders, since the attention to gender differences in physiopathology and pharmacology of several medical conditions is rising, in the recent years.

Gender Medicine is an emerging discipline which focuses on investigating the role of gender in human health, analysing the gender-related effects on anatomy, physiology, biology and pharmacology across male and female subjects.[1] Gender-related aspects represent key health factors, which are broader than the mere sex-related differences.[1] There is a precise distinction between gender and sex: *sex* comprises the aspects related to the biological differences between male and female subjects (involving genetic and epigenetic, anatomic, physiologic and metabolic factors, proteins arrangement, sex hormones levels, body composition and pathophysiology of diseases).[1] *Gender*, according to the World Health Organization (WHO) definition, involves behavioural, psychological, cultural aspects and the personal and social

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perception of male and female, which necessarily influence the adaptation strategies towards health.[1]

Gender is considered one of the individual lifestyle determinants of health, and it is an independent risk factor (such as age, ethnicity and comorbidities) for several diseases.[1] It has been reported that sex and gender differences have a significant impact on the pathophysiology, the clinical onset and the treatment of several diseases.[1] Gender medicine aims to ensure the best medical practice and the most appropriate available therapeutic approach for both genders, particularly establishing a personalized/targeted treatment.[1] Many authors have already examined the role of gender in several medical disciplines, such as cardiology, pulmonology, gastroenterology and rheumatology. The interest on the relationship between gender and audio-vestibular disorders is still growing.

Gender-related differences of the inner ear and of the auditory pathway

Anatomical and physiological differences among the auditory system of male and female subjects have been already described. The male cochlea was found to be longer than the female cochlea of approximately 1.11 mm.[2] It has been hypothesized that variations in the cochlear length can influence the rigidity of the basilar membrane (BM).[2] In this context, the shorter cochlear length in women could be related to a greater BM stiffness.[2] This cross-gender anatomical difference has been considered to have possible physiological implications on the dynamics of the von Békésy travelling wave.[2]

In order to explain gender-induced differences in otoacoustic emissions (OAEs) data, hormonal imbalances have been hypothesized to influence the micro-mechanics of the outer hair cells on the organ of Corti.[2] A higher occurrence of spontaneous otoacoustic emissions (SPOAEs) and a greater amplitude of transient-evoked OAEs (TEOAEs) have been described among women than in men.[2] Interestingly, the observed OAE gender differences are reverted in menopausal women.[2] Studies on female mice also demonstrated differences in distortion product otoacoustic emission (DPOAEs) levels, higher in premenopausal and lower in postmenopausal subjects, despite the fact that in young male and female mice the DPOAE levels are quite similar.[2]

Click-evoked auditory brainstem response (ABR) recordings also show gender differences. Recordings from female subjects seem to have shorter mean peak latencies in comparison to those from male subjects.[2] Both the absolute and the inter-wave latencies were significantly shorter in female subjects in comparison to males.[2] Data in the literature suggest numerous hypotheses in order to explain these electrophysiological ABR differences, such as (1) the head size, (2) the body temperature and (3) the subject's hormonal features.[2] The different anatomical dimension of the head and the different length of the cochlea between genders did not explain adequately the clinical observations, although a smaller head and a shorter travelling time (in the smaller cochlea) could account for the observed shorter ABR latencies in women. Surely, the hormonal influence in women has been hypothesized to be responsible for these ABR results, as oestrogen could facilitate the synaptic transmission and accelerate neural conduction.[2] Data from mice models demonstrated differences between genders using the age as a co-factor; for instance, ABR thresholds vary with age in female mice compared to males.[2]

Gender-related differences have been observed in data from the central auditory system. Studies on functional magnetic resonance imaging (MRI) described in females a higher and earlier activation of the cortical areas involved in the processing of an acoustic signal and in the language development, compared to males.[3] These aspects could be a possible explanation of the earlier development of verbal and written language observed in females. Moreover, differences in the functional organization of the phonologic processing between men and women have been reported.[3] More specifically, when studying the cortical processing of an acoustic signal, a bilateral activation can be registered in female subjects, instead of a unilateral (and mostly left) activation in males.[3]

Gender-related differences and audiological disorders

There is evidence in the literature that sex and gender may influence the development of sensorineural hearing loss (SNHL). The prevalence of hearing impairment is higher among older men than older women.[4] In Europe, the prevalence of

presbycusis, the most common sensorial impairment in the elderly, is estimated to be approximately 20% in female and 30% in male subject, aged >70 years.[4] Clinical data suggest a peculiar gender-related trend in presbycusis, with an earlier deterioration of hearing threshold in men than in women.[4] Nonetheless, understanding the role of sex and gender-related factors in the presbycusis onset is complex since the multifactorial pathogenesis of the age-related hearing loss. A different tonal audiometric threshold shape between men and women has been highlighted: male subjects showed a larger mean hearing loss above 1 kHz, while female subjects showed a mean hearing loss below 1 kHz.[4] This difference was found to increase according to the subject's age and the degree of hearing loss.[4] A number of hypotheses have been proposed to explain this gender difference. Men could have higher hearing threshold deterioration at high frequencies due to noise exposure in their workplace, while women have higher hearing threshold deterioration at low frequencies caused by the atrophy of the stria vascularis.[4] However, in later long-term, longitudinal epidemiological studies on age-related hearing loss, these gender-related audiometric findings were minimized.[4] In more recent studies, the gender-related variance of the audiometric shape in elderly is significantly reduced, possibly due to the lifestyle and environmental changes among the sexes in the last two decades.[4]

The gender-related differences on the audiometric shape may have an implication on the audiological rehabilitation of presbycusis. Women with severe-to-profound hearing loss are more likely to receive a specific rehabilitation strategy (i.e. hearing aids) than men.[4] A probable reason for this observation is that for women hearing loss has a more significant and negative impact on the daily life, which might motivate female subjects to seek a resolute solution. Also, women were found to be more methodical in the use of hearing aids compared to men.[4]

The influence of sex and gender on the sudden sensorineural hearing loss (SSNHL) development and prognosis is a topic which receives a lot of attention in the literature. In the United States, the incidence of SSNHL is reported to be 5–20 out of 100,000 with an overall male preponderance, and approximately 90% of the SSNHL cases remain idiopathic.[5] For the latter, a number of etiopathogenetic hypotheses have been suggested, such as vascular disorders, viral infections, immunological diseases, endolymphatic hydrops, labyrinthine membrane ruptures and electrolytic anomalies.[5] Data from studies investigating the prognostic role of gender on hearing recovery after SSNHL show a correlation with a higher hearing threshold improvement in men compared to women, although not statistically significant.[5]

Also autoimmune inner ear disease, a progressive bilateral and not always symmetric SNHL progressively developing over weeks to months, which typically benefits from a steroid and immunosuppressive therapy, has been reported to be more prevalent in women, and women have often been reported to show the most severe clinical features.[6]

Tinnitus has been reported to have a higher prevalence in men, although the data in the literature do not suggest a significant correlation between gender and the severity of tinnitus.[4] However, a possible relationship between tinnitus annoyance and gender has been found, since women appeared more irritated and distressed than men.[4] Furthermore, a gender-related difference in coping strategies and habituation methods has been observed, as women present fewer proactive coping strategies and resources than men.[4] This gender difference suggests that new personalized treatments might produce better results in women, who are better involved with relaxation exercises, cognitive behavioural or group tinnitus therapy.[4]

Sex and gender should also be considered as risk factors in the ototoxicity cases, since data in literature increasingly suggest significant sex and gender differences in drug induced ototoxicity.[7] Despite the data in the literature, the role of gender in cisplatin ototoxicity remains controversial.[7] Although a declined hearing function and a higher number of apoptotic neurons have been found in the spiral ganglia and in the brainstem of cisplatin-treated female rats, in comparison to male treated groups, the gender effect in the mouse model needs additional verification data.[7]

Gender-related differences and vestibular disorders

A hormonal influence was hypothesized to be responsible for the higher preponderance in

women of Meniere's disease (MD).[8] MD is an idiopathic hydropic disorder of the inner ear which typically causes hearing loss and vertigo; a possible relationship between the occurrence of endolymphatic hydrops and the menstrual cycle has been observed, possibly related to a fluid redistribution; this relationship has been clinically observed particularly in women suffering from a premenstrual syndrome.[8]

The role of *RANTES* (regulation upon activation normal T cell expressed and secreted) gene polymorphism has been studied in patients affected by MD. *RANTES* gene polymorphisms have been correlated to susceptibility to several inflammatory and autoimmune diseases (such as sarcoidosis, asthma and rheumatoid arthritis); a significant correlation between RANTES gene polymorphism and MD has been found in male, highlighting a protective role only in men.[9]

The benign paroxysmal positional vertigo (BPPV), the most frequent cause of peripheral vertigo, is reported to be more prevalent in women, with an overall female:male ratio of (2.2–1.5):1.[10] Since a definite BPPV etiology has not been established yet, a hypothesis of a hormonal influence may be taken into account: data in the literature show that the female patients treated with oestrogen for menopausal symptoms presented fewer BPPV recurrences.[10] Accordingly, a reduction of oestrogen levels during the menopause could be hypothesized to represent a risk factor for BPPV occurrence.[10] Furthermore, this possible estrogenic-related etiopathogenesis for BPPV may influence the development of new therapeutic and/or preventive strategies based on oestrogen restoration.

Conclusion

Gender represents an increasingly important variable in the medical practice. The anatomic and physiologic differences existing between men and women may determine different manifestations of inner ear diseases.

A major drawback of this review is the lack of reliable data, despite the clinical end experimental evidence available in the current literature, so far. However, in our opinion, it is crucial to clarify the role of sex and gender in the pathogenesis of audiovestibular disorders, particularly aiming to (1) evaluate correctly the clinical features of the disease and (2) possibly establish a personalized/targeted treatment. The latter postulate stems from recent data in the literature reporting the different gender effects of ototoxic drugs in women and men. The data suggest that there are different pharmacokinetic and pharmacodynamic profiles across genders, a fact reflecting the various biological and physiological differences between men and women.

In order to establish clear-cut gender-based protocols for audiovestibular disorders, further research is undoubtedly necessary.

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