Review Article

Endocrine-Auditory Interactions: A Comprehensive Review of Hormonal Effects on Auditory Physiology and Pathology

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Short running title: Endocrine-Auditory Interactions: A…

Highlights:

- Hormones directly or indirectly affect auditory system function
- Hormones have protective roles, but their imbalance may contribute to hearing loss
- Hormonal modulation may serve as a future therapy for hearing loss

ABSTRACT

Background and Aim: Hormones have various effects on different parts of the body, including the auditory system. This study aimed to review the effects of various hormones on the auditory system.

Recent Findings: Various hormones, including estrogen, progesterone, prolactin, oxytocin, aldosterone, growth hormone, dopamine, Thyroxine (T4), Triiodothyronine (T3), parathyroid hormone, cortisol, norepinephrine, insulin, and melatonin, affect the auditory system. Estrogen, aldosterone, norepinephrine, melatonin, and oxytocin have a protective effect against noise. Growth hormone has a positive impact on the development of hair cells. High or low levels of thyroid hormones and low levels of parathyroid hormone, insulin, melatonin, and dopamine can cause sensorineural hearing loss. High levels of cortisol can cause tinnitus and hyperacusis. Also, the presence of prolactin is related to early-onset presbycusis in women.

Conclusion: Hormones play an important role in the function of the auditory system and can affect the development and maturation of auditory structures and their function. Any disruption in hormonal balance may lead to temporary or permanent changes in the auditory system.

Keywords: Auditory system; hormone; endocrine glands

Introduction

In a proper body functioning, various organs and systems need to coordinate and interact with one another in order to maintain a stable internal condition (i.e., homeostasis). Two systems contribute to this interaction: the nervous system and the hormonal system. Hormones are molecules produced by endocrine glands. The endocrine glands include the hypothalamus, pituitary gland, adrenal glands, gonads (i.e., testes and ovaries), thyroid gland, parathyroid glands, and pancreas, as well as the pineal gland [1]. The hypothalamus acts as the main connector between the nervous system and the endocrine system. Corticotropin-releasing hormone, gonadotropin-releasing hormone, thyrotropin-releasing hormone, growth hormone-releasing hormone, somatostatin, and dopamine are secreted by the hypothalamus; adrenocorticotropic hormone, gonadotropins, thyroid-stimulating hormone, growth hormone, prolactin, antidiuretic hormone, vasopressin, and oxytocin by the pituitary gland; melatonin by the pineal gland; cortisol, aldosterone, epinephrine, and norepinephrine by the adrenal glands; estrogen, progesterone, and testosterone by the gonads; Thyroxine (T4), Triiodothyronine (T3), and calcitonin by the thyroid gland; parathyroid hormone by the parathyroid glands; and insulin and glucagon by the pancreas [1]. Some of these hormones have pivotal roles in the function of the auditory and vestibular systems [2-4].

Numerous studies have shown the role of growth hormone in auditory development during the embryonic stage, as well as its protective function and involvement in auditory processing [5-7]. Estrogen has been identified as a protective factor in auditory and balance functions, modulation of vestibular symptoms in vestibular migraine and Meniere's disease [8, 9], and in auditory processing of sounds [10]. Associations between hearing loss and reduced T4 levels [11], hypothyroidism, and vestibular disorders have also been reported [12]. Given the importance of the auditory system in communication, speech perception [13], prevention of emotional disorders, depression [14], and increasing quality of life [15], this study aimed to review the effects of different hormones on the auditory system, aiming to enhance our understanding of the physiological impact of these hormones on auditory processing.

Methods

In this narrative review, human and animal studies published from 1989 onwards were searched in multiple databases, including Medline (PubMed), Google Scholar, Science Direct, and the Cochrane Library. The keywords used in the search were hormones, auditory system, vestibular system, and endocrine glands. In addition to the database search, the reference list of the included articles was checked to identify additional eligible studies. The articles with an abstract or accessible full text, those related to auditory and vestibular system, and those written in English were included.

Results

Initially, we found 84 relevant articles. Of these, 68 articles met the inclusion criteria. This comprehensive search and screening process allowed us to compile a strong body of literature, enhancing our understanding of how hormones impact the health of both the auditory and vestibular systems.

Various hormones influence the auditory system. Among them, sex hormones, thyroid hormones, growth hormone, and aldosterone have been studied more extensively. In contrast, fewer studies have investigated hormones such as prolactin, epinephrine, parathyroid hormone, and oxytocin. Figure 1 illustrates the endocrine glands and the hormones that affect the auditory system.

Discussion

Thyroid gland: thyroxine and triiodothyronine hormones

The thyroid gland is the primary regulator of the endocrine system in the body. It produces two related hormones, T4 and T3, which play crucial roles in cellular differentiation during growth and development, maturation of the central nervous system, and maintaining thermogenic and metabolic homeostasis. A long-standing relationship between thyroid hormone levels and the development of the auditory system was recognized in patients with congenital hypothyroidism [16]. Thyroid disorders can affect middle ear, cochlear and retro cochlear [17], and lead to manifestations of hearing loss and tinnitus. Hearing loss is considered the main clinical symptom and can be in the form of conductive, mixed, and Sensorineural Hearing Loss (SNHL) [18]. In acquired hypothyroidism,

hearing loss is gradual, symmetrical, and mild to moderate, and occurs at frequencies 2000, 4000, and 8000 Hz [11, 16, 19]. There is a strong correlation between the degree of hypothyroidism and the associated hearing loss. In other words, the more severe the hypothyroidism, the greater the hearing impairment. Hearing loss in hypothyroidism is treatable and even reversible with appropriate replacement therapy [11]. Brainstem electrophysiological findings showed prolonged absolute latency of wave V, interpeak latency of I-III, I-V, and reduced amplitude of waves I, II, and V in adult patients, indicating retro cochlear dysfunction. After treatment with levothyroxine, statistically significant improvements in hearing thresholds and tympanogram pattern were observed [17].

Conductive, mixed, and sensorineural hearing loss was observed in 20% of children with congenital hypothyroidism, mainly those with high-frequency SNHL. Delay in starting thyroid therapy, even by a few days, was a significant factor in the occurrence of hearing loss. In addition, language difficulties, auditory discrimination problems, and poor reading skills persisted into the early school years. A study emphasized that hearing evaluation is essential for all patients with congenital hypothyroidism, even if initial hearing tests are normal, to prevent long-term consequences [20]. A study of patients with hyperthyroidism showed a lower prevalence of SNHL in this group [21]. Additionally, research on Graves' disease, an autoimmune disorder characterized by elevated T3 and T4 levels and suppression of thyroid-stimulating hormone, showed that Graves' disease can lead to high-frequency SNHL [22]. These findings suggest that both forms of thyroid dysfunction can have adverse effects on the auditory system, although the severity and pattern of these effects are different.

Sex glands: estrogen, progesterone, and testosterone hormones

Sex hormones are steroid hormones primarily produced in the gonads (testes in males and ovaries in females) and, to a lesser extent, in the adrenal glands and adipose tissue. The three main sex hormones are estrogen, progesterone, and testosterone. Estrogen and progesterone are typically predominant in females [8]. The normal menstrual cycle in women consists of three phases: follicular, ovulation, and luteal phases [23]. The follicular phase begins with the onset of menstrual bleeding and lasts an average of about 15 days. During this phase, estrogen and progesterone levels are at their lowest level. Then, estrogen levels gradually increase, reaching a peak on day 13 or 14, just before ovulation. The ovulation phase lasts about three days, after which the luteal phase begins and lasts for 14 days, when progesterone levels rise. Progesterone levels peak about seven days after ovulation [24, 25]. Several studies using immunohistochemistry reported the presence of estrogen receptors α (ERα) and β (ERβ) in the adult human cochlea; ERα is found in the spiral ganglion, and ERβ is located in the stria vascularis. Changes in ion and water reabsorption that occur during the ovarian cycle can affect the function of specific parts of the peripheral auditory system. Most physiological changes occur in women during the luteal phase, and endolymphatic hydrops due to sodium retention and increased endolymphatic pressure has been reported during this phase [24, 26].

Hormone Replacement Therapy (HRT) is a treatment that enables women to overcome the adverse consequences associated with decreased estrogen levels and to maintain their feminine characteristics. Various pharmaceutical formulations are available for HRT, including estrogens, progestins, and combined estrogen-progestin preparations [27]. A study aimed at investigating the effect of estrogen therapy on hearing in postmenopausal women found that estrogen therapy may slow the progression of hearing loss in older postmenopausal women [28]. In another study aimed at investigating the effects of sex hormones, especially progesterone, on the auditory system, the results showed that the group receiving combined estrogen and progesterone therapy showed greater peripheral and central hearing impairments, and their ability to understand speech in noisy environments was significantly reduced [29]. In assessing the effects of HRT on Auditory Brainstem Responses (ABRs) in postmenopausal women, it was shown that the latency times of waves I, III, and V as well as the interpeak intervals I-III, I-V, and III-V, were shorter in women treated with estrogen replacement alone compared to those receiving combined HRT [30]. These findings suggest that, unlike estrogen, progesterone, as a component of HRT, has a significant negative impact on the hearing health of older women [29]. Another study that examined the effects of testosterone and estrogen found that, although total testosterone levels were relatively higher in people with hearing loss, they did not have an independent impact on hearing loss. In contrast, decreased levels of estradiol (a type of estrogen) were correlated with an increased risk of hearing loss, especially in postmenopausal women. Therefore, low estradiol levels may act as an independent risk factor for hearing loss and play an important role in screening and preventing hearing disorders, especially among the older female population [31].

Evidence about the effect of sex hormones on central auditory and cognitive processing is contradictory. In a study by Sajadian et al. aiming to investigate the effect of menopause on working memory in women, it was shown that menopause in the age range of 50–59 years had no effect on verbal auditory memory [32]. Furthermore, a study that examined auditory processing abilities in women at different stages of the menstrual cycle showed no significant differences in the dichotic vowel-consonant test, speech in noise test, interval recognition test, and working memory test across the three stages of the menstrual cycle [10]. Research should examine the combined effects and role of sex hormones in maintaining hearing health with more comprehensive approaches.

Adrenal gland: aldosterone, cortisol, norepinephrine, and epinephrine hormones

The adrenal gland is located directly above the kidney and secretes hormones such as aldosterone, cortisol, norepinephrine, and epinephrine [1]. Aldosterone is a vital mineralocorticoid hormone in the renin-angiotensin system that plays an important role in regulating cardiac, renal, and vascular physiology [33]. Aldosterone is a naturally occurring steroid hormone that influences the regulation of Na^+/K^+ ions in the cochlea of mammals. A decrease in aldosterone concentration with aging can cause atrophy and degeneration of the lateral wall of the inner ear, including the stria vascularis blood vessels [34]. Among older adults, a significant difference in serum aldosterone levels was found between those with normal hearing and those with hearing loss, and serum aldosterone concentration showed a strong correlation with pure-tone hearing thresholds and scores in the hearing-in-noise test. Therefore, serum aldosterone concentration may have a protective effect on hearing at older ages. Aldosterone's primary effect is exerted on the peripheral auditory system, especially on inner hair cells, with less impact on outer hair cells [35]. Important advances in biomedical research are mainly the outcome of animal models, increasing our understanding of the etiology, pathology, physiology, and various conditions that affect humans and animals [36]. However, the results of animal studies are contradictory. A study in mice showed the positive effect of aldosterone in increasing sensitivity to soft sounds and improving the acoustic reflex response; in addition, long-term treatment with aldosterone improved behavioral and physiological measures of hearing, including ABR thresholds. Aldosterone treatment in aged animals also improved some aspects of presbycusis [37]. However, another animal study showed no significant difference in ABR thresholds before and after aldosterone administration. Furthermore, one month after treatment, mild endolymphatic hydrops was observed in the basal turn region in 9 out of 12 cases, suggesting that aldosterone can induce mild hydrops in a considerable portion of the cochlea, particularly in the basal turn [4].

Cortisol is a glucocorticoid hormone that primarily functions to raise blood glucose levels. This hormone is secreted by the adrenal gland, located above the kidneys, along with norepinephrine and epinephrine, which are known as stress hormones [1, 38, 39]. An increased level of cortisol was reported in patients with tinnitus-related conditions [39]. Hébert et al. conducted a study aimed at examining the relationship between tinnitus-related distress severity, cortisol levels, and hyperacusis in individuals with and without tinnitus. The results showed that individuals experiencing severe tinnitus-related distress exhibited higher levels of chronic cortisol and greater intolerance to external sounds compared to both the mild-distress group and the control group, whereas no statistically significant difference was found between the mild-distress and control groups [40].

Tian et al. in a study on the effect of norepinephrine on noise-induced hearing damage, evaluated the protective role of this hormone through α_2A-adrenergic receptors. Animal models were used to assess the expression levels of receptors and the extent of outer hair cell damage after exposure to loud sounds. The results demonstrated that the activation of α_2A adrenoceptors by norepinephrine significantly reduced damage to outer hair cells and lower levels of hearing loss after noise exposure [41]. These findings clearly indicate that the noradrenergic system protects the inner ear against damage caused by acoustic stress.

Pancreas gland: insulin hormone

Insulin is the only hormone that lowers blood sugar levels [1]. It plays a significant role in storing excess energy [42]. It promotes the transport of amino acids to the skeletal muscle and liver [1]. Type 1 diabetes is caused by the destruction of insulin-producing pancreatic cells [43, 44]. Significant long-term complications of insulin resistance include the development of type 2 diabetes mellitus (type 2 diabetes mellitus), cardiovascular disease, obesity, and some malignancies associated with insulin resistance (such as colon, breast, and endometrial cancer) [45]. Complications of this disease include retinopathy, nephropathy, and neuropathy [46]. In diabetic patients, the prevalence of hearing loss is notably high, as evidenced by a study conducted by Al-Rubeaan et al. [47],

where more than 60% of patients with type 2 diabetes aged 30–60 had hearing loss of varying degrees, with 50% having moderate to severe hearing loss. Hearing loss in children with insulin-dependent diabetes mellitus is bilateral and symmetrical sensorineural and is related to the duration of the disease. The duration of the disease affects the severity of hearing loss at some frequencies [46], especially at high frequencies (4–8 kHz) [48]. In the study, people with a long history of diabetes showed significantly higher hearing thresholds at frequencies of 8 and 12 kHz compared to those with a shorter history of diabetes. Also, the risk of more severe hearing impairment was higher in diabetic patients in each age group than in the control group [49]. Since hearing loss in diabetes is similar to presbycusis, age-related hearing loss in diabetic patients is earlier and more severe than in the general population [48]. Medications and agents that reduce insulin resistance may play a role in slowing the progression of age-related hearing loss [50].

Pineal gland: melatonin hormone

Melatonin is a hormone produced in the pineal gland from the amino acid tryptophan. Melatonin is a primary regulator of circadian sleep cycles that primarily affects sleep and circadian rhythms. This hormone is not produced in significant amounts in other parts of the body. After removal of the pineal gland, melatonin levels drop to zero, and circadian rhythms are disrupted [1]. Melatonin has a protective effect against damage to outer hair cells in the process of age-related hearing loss [51]. In a research conducted to evaluate circulating melatonin concentrations in patients with idiopathic sudden SNHL, circulating melatonin concentrations were lower in the patient group compared to the control group, and an inverse relationship was observed between circulating melatonin concentrations and the degree of hearing loss [52]. Song et al. investigated the role of oxidative stress (the imbalance between the production of free radicals and antioxidants) in idiopathic sudden SNHL and evaluated the protective impact of melatonin on hearing in individuals with idiopathic sudden SNHL. Their findings indicated that oxidative stress can be involved in the etiopathogenesis of idiopathic sudden SNHL. Also, melatonin levels, reactive oxygen species, and the presence of vertigo can be predictive indicators for the effectiveness of hearing restoration following idiopathic sudden SNHL [53]. Serra et al., in an animal study on the effect of melatonin on the prevention of outer hair cell dysfunction in presbycusis, showed that from the tenth month onward, the group receiving melatonin had higher Distortion-Product Otoacoustic Emission (DPOAE) amplitudes in all examined frequencies compared to the control group [51].

Pituitary gland: growth hormone

Growth hormone is a multifunctional hormone produced by somatotroph cells in the pituitary gland [1, 54]. Growth hormone production begins during the embryonic stage [1] and plays a significant role in auditory development during this period. Growth hormone deficiency leads to hearing loss [5, 55] or central auditory processing disorders [5]. Guerra et al. conducted a study on a 3.5-month-old infant diagnosed with cerebral palsy and bilateral SNHL. The child underwent treatment with growth hormone, melatonin, and rehabilitation for 14 months. At discharge, the infant's hearing had improved, which was attributed to the regeneration of hair cells from stem cells in the cochlear sensory epithelium. It was suggested that hearing loss is common in children with growth hormone deficiency and is often bilateral [7]. In an animal study conducted on zebrafish, damage to auditory hair cells was induced by exposing the fish to loud sounds. Following the injection of growth hormone, cell proliferation was observed in the saccule and utricle [6]. These results indicate that exogenous growth hormone accelerates the regeneration of auditory hair cells after acoustic trauma by promoting cell proliferation and reducing apoptosis (programmed cell death). Moreover, the presence of endogenous growth hormone signaling during the regeneration process confirms the critical role of this hormone in auditory recovery and rehabilitation.

Anterior pituitary gland: prolactin hormone

Lactotrophs in the anterior pituitary gland are responsible for the production of Prolactin [1]. The main function of prolactin is related to pregnancy and lactation, and it contributes to the development of the mammary glands, the synthesis of milk, and the sustenance of its secretion. Circulating prolactin concentrations are increased rapidly during pregnancy, and this increase is accompanied by an increase in the number and size of lactotroph cells. During lactation, infant's suckling leads to a rapid secretion of prolactin through a neuroendocrine reflex pathway [56]. In a study by Horner et al. on the impact of prolactin on hearing, hyperprolactinemia (increased prolactin levels) was experimentally induced in guinea pigs using estrogen. Chronic estrogen-induced

hyperprolactinemia caused significant hearing loss at all frequencies (30–40 dB) after two months, which was more severe in males. Microscopic examinations showed pathological changes in the bony cochlear bulla (the bony part of the middle ear). Damage to hair cells and delicate structures of stereocilia was also seen [57]. Their results indicate that long-term estrogen-induced prolactin elevation can cause disruption of the bone structure and sensory cells of the inner ear, which ultimately leads to hearing loss. Marano et al. conducted a study to investigate the relationship between hearing loss, prolactin level, and cochlear bone metabolism. Mice at 6 months of age (middle-aged mice) and 12 months of age (old-aged mice) were evaluated for hearing ability using the ABR test. Their findings showed that prolactin production in the cochlea was only present in female mice, and that the production of this hormone was associated with a decrease in bone mineral density and higher hearing thresholds. This was also associated with a greater change in hearing thresholds for females aged 6–12 months. At 6 months of age, female mice had lower hearing thresholds than males, but showed earlier hearing loss at some frequencies in comparison with males aged 6–12 months. The bone density of the auditory ossicular capsule was significantly reduced in female mice compared to male mice. However, this reduction was small, and it was unclear whether it would have a significant impact on hearing [58].

Hypothalamus gland: dopamine and oxytocin hormones

The hypothalamus gland contains various hormones. The effects of dopamine and oxytocin on the auditory system have been proven. Dopamine is a key molecule in the human body, which is released by the hypothalamus and is delivered to the pituitary gland [1]. Dopamine regulates nuclear activity within both ascending and descending auditory pathways. Multiple nuclei in the central auditory system contain a source of dopamine that is capable of dopaminergic neurotransmission [59]. The dopaminergic projections from the lateral lemniscus to the inferior colliculus have also been reported. Tyrosine hydroxylase-labeled terminals in the inferior colliculus colocalize with glutamate and glycine terminals [59]. Garasto et al. suggested that the association between auditory function and basal ganglia dopamine transporter availability supports the hypothesis that the decline in peripheral auditory function associated with dopamine depletion plays a role in the pathogenesis of Parkinson's disease, and that there is an important difference between patients with left and right-dominant motor symptoms. According to their findings, assessment of peripheral auditory function and its lateralization may serve as key components for subclassification of the disease [60]. Auditory nerve fiber activity is modulated by lateral olivocochlear efferent neurons using a large repertoire of neurotransmitters, such as dopamine and acetylcholine. However, our understanding of the dynamic utilization of individual neurotransmitter systems remains limited. Wu et al. provided quantitative evidence that the dopaminergic lateral olivocochlear input to auditory nerve fibers is modulated according to the animal's recent acoustic experience. Sound exposure upregulates tyrosine hydroxylase, an enzyme responsible for dopamine synthesis, in cholinergic lateral olivocochlear intrinsic neurons, suggesting co-release of acetylcholine and dopamine. They demonstrate that dopamine reduces the firing rate of auditory nerve fibers by simultaneously decreasing the release rate from hair cells and diminishing the magnitude of synaptic events. Electrophysiological recordings showed that two distinct mechanisms through which dopamine lowers the firing rate of auditory nerve fibers were as follows: decreasing the frequency of synaptic events, and reducing the amplitude and overall charge of excitatory postsynaptic currents [61]. These results suggest a dynamic, experience-dependent reconfiguration of lateral olivocochlear neurotransmitter identity, enabling modulation of auditory gain and potentially protecting the auditory nerve from excitotoxic damage.

Oxytocin is a neuropeptide produced primarily by neurons in the paraventricular and supraoptic nuclei of the hypothalamus. The axons of these neurons project to the posterior pituitary, and they secrete oxytocin into the bloodstream to enhance parturition and lactation [62]. Akin Ocal et al. in assessing DPOAEs and ABRs in rats, demonstrated that intratympanic administration of oxytocin exerted a therapeutic effect in rats exposed to acoustic trauma. The findings of this study indicated that oxytocin, when administered via the intratympanic route, could exert a protective effect against inner ear damage induced by acoustic trauma in rats. Electrophysiological evaluations revealed that, in animals receiving oxytocin, both hearing thresholds and signal-to-noise ratios showed significant improvement during the post-injury period. Furthermore, immunohistochemical analyses demonstrated that treatment with oxytocin led to a reduction in apoptotic processes within both outer and inner hair cells [63]. Overall, these data suggest that oxytocin possesses therapeutic potential for mitigating or preventing noise-induced ototoxicity and may be considered as a treatment option in animal models. Nevertheless, additional clinical research is required to evaluate the generalizability of these findings to humans.

Parathyroid gland: parathyroid hormone

Parathyroid hormone is the main regulator of calcium and phosphate homeostasis in the human body [1]. This hormone is the most important endocrine regulator involved in maintaining calcium levels in humans [64]. The parathyroid gland secretes this hormone to regulate serum calcium, which affects the bones, kidneys, and intestines. Parathyroid disorders can cause excessive secretion of parathyroid hormone, leading to hyperparathyroidism [65]. The most common symptoms of hyperparathyroidism include brittle bones, joint pain, and kidney stones [66]. Few studies have investigated the relationship between parathyroid disorders and hearing. Djian et al. investigated predictive factors of hearing loss in patients with Pseudohypoparathyroidism (PHP)/inactivating parathyroid hormone/parathyroid hormone-related protein signaling disorders (iPPSD), a rare genetic disorder caused by dysfunction in the parathyroid hormone signaling pathway. The most common form of hearing loss observed was non-progressive, unilateral, or bilateral SNHL across all frequencies. Endocochlear damage was the most probable pathophysiological mechanism. The results confirmed the presence of hearing loss in patients with PHP/iPPSD, with a reported prevalence of 39% [67]. Hypoparathyroidism is also associated with hearing loss in some conditions, including Barakat syndrome, which is characterized by hypoparathyroidism, SNHL, and renal dysplasia [68].

Discussion

The findings showed that various body hormones, including estrogen, progesterone, prolactin, oxytocin, aldosterone, growth, dopamine, T4, T3, parathyroid, cortisol, norepinephrine, insulin, and melatonin, each individually or in interaction with other factors, affect the auditory system. Estrogen has a protective role on the cochlea, and its reduction during menopause is associated with hearing loss. Unlike estrogen, progesterone level is related to hearing impairment at high frequencies. Prolactin secretion leads to faster hearing loss in women. Oxytocin is related to hearing loss associated with acoustic trauma. Aldosterone helps maintain hearing function by regulating the balance of electrolytes in the endolymph fluid of the cochlea and also has a protective effect on the cochlea against sound. Growth hormone plays an important role in the growth and development of the nervous system, including auditory pathways. Growth hormone deficiency in childhood is associated with delayed development of the peripheral and central auditory systems, and some studies have shown that its administration can be effective in improving hearing thresholds. Dopamine plays an inhibitory role in auditory pathways, likely serving a protective function for auditory synapses against acoustic noise, and its reduction is associated with hearing loss. Thyroid hormones (T3 and T4) play a vital role in the maturation of the auditory nervous system and cochlear function, and hypothyroidism or hyperthyroidism can alter hearing thresholds. Parathyroid hormone is effective in maintaining the function of electrolytes essential for sound transmission by regulating the levels of calcium and phosphorus in body fluids, especially in the endolymph fluid of the inner ear. Chronic increase or decrease in parathyroid hormone or dysfunction can cause an electrolyte imbalance and impair the function of cochlear hair cells. High levels of cortisol increase hyperacusis and tinnitus. Norepinephrine is essential for plasticity and plays a role in the activity of the auditory cortex. In addition, it has a protective effect on inner and outer hair cells when exposed to noise. Insulin acts on auditory cells by regulating blood sugar metabolism, and a high prevalence of hearing loss has been reported in diabetic patients. Melatonin, with its antioxidant properties, has regulatory effects on neurotransmitters, and recent studies have shown the protective effect of this hormone against damage to outer hair cells in the process of age-related hearing loss. This evidence suggests that hormonal adjustments in the body can directly affect the functioning of the auditory system and, in some cases, lead to the development or exacerbation of disorders such as hearing loss, tinnitus, or sensitivity to sound. Further research should be conducted to accurately explain the mechanism of the effects of hormones on the auditory system. Perhaps in the future, hormones can be used for therapeutic purposes in auditory disorders, and by designing interdisciplinary protocols, a safe and effective clinical basis for this approach can be provided.

Ethical Considerations

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Authors' contributions

NG: Study design, acquisition of data, interpretation of the results, statistical analysis, and drafting the manuscript; SGR: Interpretation of the results and drafting the manuscript; MK: Study design, interpretation of the results, and drafting the manuscript.

Conflict of interest

The authors declare no competing interests.

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Table 1. Summary of studies on the effects of hormones on the auditory system

Source	Year	Hormone	Population	Population sample size	Main findings
Lakshmi and Jein [10]	2020	SEX	Male and female	N=21	Central auditory processing abilities do not show significant differences in the three different phases of the menstrual cycle
Sajadian et al. [32]	2019	Estrogen	Female	N=25	Menopause between the ages of 50 and 59 does not affect auditory verbal memory
Kilicdag et al. [28]	2003	Estrogen	Female	N=109	Estrogen therapy may be able to slow the process of hearing loss in older postmenopausal women
Caruso et al. [30]	2000	Estrogen	Female	N=50	Women who received estrogen replacement therapy showed shorter latency times compared with women who received combined hormone replacement therapy
Yang et al. [31]	2023	Estrogen and testosterone	Male and female adult	N=3558	People with the highest estradiol levels had a lower risk of hearing loss than those with the lowest. However, total testosterone levels had no effect on the risk of hearing loss
Tadros et al. [35]	2005	Aldosterone	Male and female	N=47	Serum aldosterone concentrations may have a protective effect on hearing in old age. The effect of aldosterone is primarily on the peripheral auditory system, and in particular the inner hair cells
Zhong et al. [4]	2023	Aldosterone	Animal	N=12	There was no significant difference in ABRs thresholds before and after aldosterone injection in any of the groups
Halonen et al. [37]	2016	Aldosterone	Animal	N=18	Positive effect of aldosterone on hearing
Muus et al. [55]	2017	GH	children	N=209	Hearing loss is common in children with growth hormone deficiency and is often bilateral
Guerra et al. [7]	2019	GH	children	N=1	Improved hearing caused by the production of hair cells from stem cells (in young adults) in the sensory epithelium of the cochlea
Sun et al. [6]	2011	GH	Animal	N=76	Growth hormone accelerates the regeneration of auditory hair cells after acoustic injury and plays an important role in hearing repair and rehabilitation
Nedunchezhian et al. [18]	2019	Thyroid (T3, T4, TSH)	Male and female (thyroid disorder)	N=106	The most common type of hearing loss is bilateral, symmetrical, high-frequency SNHL
Berker et al. [22]	2012	Thyroid (T3, T4, TSH)	Male and female (Graves disorder)	N=44	Hyperthyroidism is associated with hearing impairment at high frequencies
Tian et al. [41]	2024	Norepinephrine	animal	N=24	The noradrenergic system protects the inner ear from damage caused by sound
Hébert et al. [40]	2004	Cortisol	Male and female	N=36	People suffered from severe distress due to higher chronic cortisol levels and greater intolerance to external sounds. People with tinnitus had slightly higher hearing thresholds
Okhvat et al. [46]	2010	Insulin	Male and female	N=200	Correlation of hearing loss with period of diabetes. The type of hearing loss in children is also bilateral and symmetrical sensorineural
Sachdeva and Azim [48]	2018	Insulin	Male and female	N=92	The relationship between diabetes and hearing threshold levels, especially at high frequencies. Hearing loss in diabetic patients increases more with age than in the general population
Chang et al. [50]	2014	Insulin	Male and female	N=169	Insulin resistance is associated with changes in high-frequency hearing levels. Insulin resistance is associated with accelerated hearing loss
Das et al. [49]	2018	Insulin	Male and female	N=142	A long-term history of diabetes is associated with increased thresholds at 12 and 8 kHz
Song et al. [53]	2023	Melatonin	Female and male	N=58	Oxidative stress may play a role in the idiopathogenesis of idiopathic sudden SNHL, and melatonin and reactive oxygen species levels and the presence of vertigo may be considered as predictive indicators of the effectiveness of hearing treatment after idiopathic sudden SNHL
Baki et al. [52]	2019	Melatonin	Female and male	N=44	Serum melatonin levels in the patient group were lower than the control group, and a negative correlation was observed between serum melatonin levels and hearing loss severity
Serra et al. [51]	2020	Melatonin	Animal	N=32	Melatonin has a protective effect against outer hair cell damage in the process of age-related hearing loss
Marano et al. [58]	2013	Prolactin	Animal	N=9	Female mice had lower hearing thresholds than males at 6 months of age, but showed more rapid hearing loss compared to males between 6 and 12 months of age at a number of frequencies
Garasto et al. [60]	2023	Dopamine	Female and male	N=39	Decreased peripheral auditory function associated with dopamine depletion plays a role in the development of Parkinson's disease
Aken Ocal et al. [63]	2019	Oxytocin	Animal	N=28	Therapeutic effect of oxytocin after acoustic trauma

GH; growth hormone, T3; triiodothyronine, T4; thyroxine, TSH; thyroid stimulating hormone, SNHL; sensorineural hearing loss

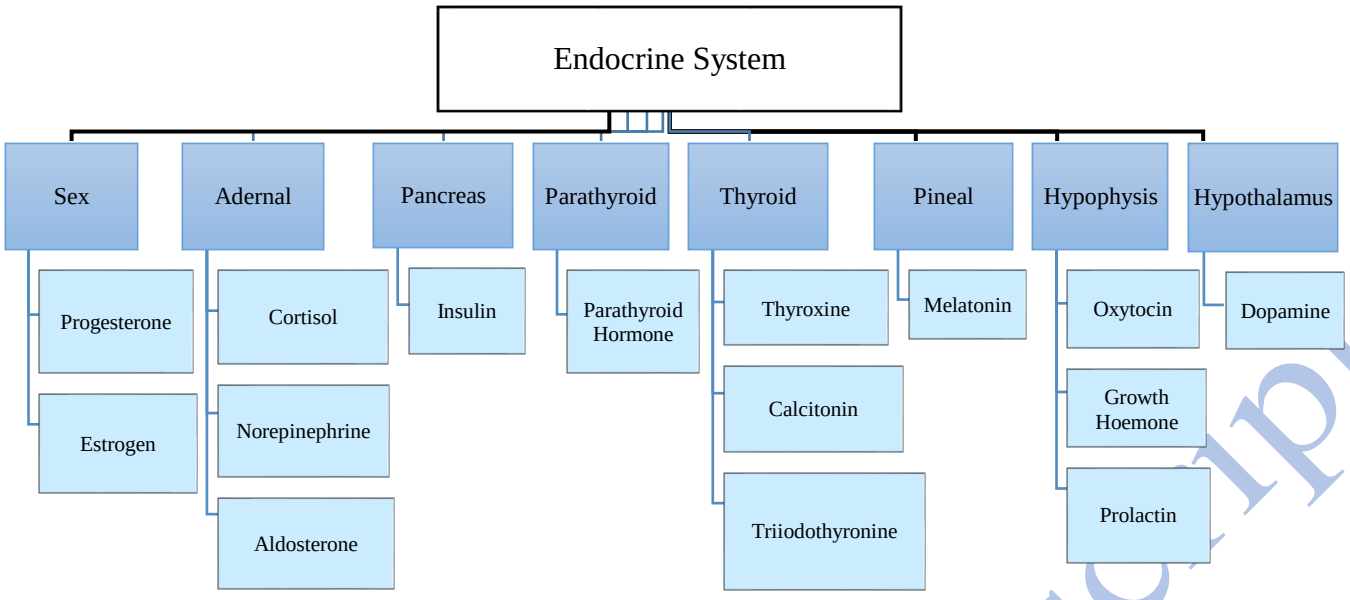

Figure1. Schematic illustration of endocrine glands and hormones that affect the auditory system