COMPREHENSIVE REVIEW ON TINNITUS

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***Abstract*- The perception of sound when there are no external stimuli present is known as tinnitus. One of the main disorders of the hearing that affects a large segment of the aging population is tinnitus. Comorbidities such as sadness, anxiety, difficulty concentrating, insomnia, resignation, helplessness, headaches, or social isolation are common. There is no known treatment for tinnitus, despite numerous therapy treatments being tried with a range of symptoms. Even though various models of tinnitus formation are available and discussed, the lack of a complete understanding of these mechanisms has hindered the search for a viable treatment. Tinnitus treatment was not effective, and the etiology of the condition is poorly understood. To investigate tinnitus more thoroughly, several animal models have been created. Tinnitus and hearing loss are linked to a higher frequency of emotional distress. Preclinical trials including a variety of herbal remedies were conducted to treat tinnitus. Research on the pathophysiology of tinnitus in basic neuroscience has been made easier using animal models. Several investigations have discovered that a variety of neurotransmitters or modulators contribute to the development of tinnitus. This article provides an overview of pathophysiology, animal behavioral models and its assessment, induction of tinnitus in rodents.**

***Keywords*: Auditory Brain Stem Response (ABR), SPIAC, Cognitive Behavioral Therapy (CBT).**

INTRODUCTION:

The term “tinnitus” which comes from the Latin word “tinnire” (to ring) refers to the experience of sound near the head when there is no external sound present. It can be complicated and varied, and it may sound like buzzing, ringing, roaring, whistling or hissing [1]. Tinnitus can be pulsatile, intermittent or continuous; the latter is frequently highly distressing. The prevalence of tinnitus is thought to be 15-20% of the global population, 1-3% of instances have a serious impact on quality of life and 25% of affected individuals find that the diseases interfere with daily activities. Anxiety, sleeplessness and depression are commonly linked to severe tinnitus [3].

Hearing loss and Morbus Meinere are two common disorders that are associated with tinnitus. Numerous symptoms, including depression, anxiety, difficulty in concentrating, insomnia, helplessness, headaches, bruxism and social isolation, are among the diverse range of comorbidities or variables linked to tinnitus [2]. Unfortunately, these aftereffects may exacerbate tinnitus and interfere with a person's capacity to live a normal life, in extreme circumstances, they may even lead to suicide [3]. Preclinical models are a valuable experimental tool for evaluating the role of various systems in the pathophysiology of diseases and for generating concepts for innovative therapeutic approaches [2].

Understanding the neurological correlates of tinnitus has advanced throughout time through the application of electrophysiology, cell biology, molecular biology and other methods. Numerous techniques, such as auditory masking techniques, electrical stimulation, and pharmaceutical treatment, have been employed to lessen tinnitus symptoms [6]. The development of hearing loss brought on by ototoxic medicines or excessive noises stimulation triggers the phantom of perception of tinnitus [5]. But the precise reasons of tinnitus are still mostly unknown. In animal models of tinnitus, several intriguing neurophysiological alternations have been found [6]. As an illustration, tinnitus is hypothesized to be associated with an increase in neuronal spike synchrony that has been seen in the auditory cortex. Furthermore, tinnitus has also been linked to an increase in the spontaneous firing rates of the inferior coliculus and auditory cortex. But unless a behavioral test is performed to determine whether tinnitus is present or absent it is impossible to determine whether changes are connected to tinnitus [3] [4]. Consequently, to ascertain if tinnitus is present or absent at a given moment, it is crucial to utilize behavioral techniques that enable tinnitus to be assessed in individual animals treated with a specific tinnitus inducing agent [10]. Tinnitus can be challenging to measure in an animal model since it is subjective in nature and lacks an objective test. To investigate the underlying brain mechanism and possible treatments for tinnitus, a number of helpful animal behavioral models are currently available. These models take advantage of “animal behavioral changes” that may be associated with tinnitus [3] [4] [9].

Objective tinnitus is the term used to describe sound detected from physical sound sources within the body, such as blood flow and middle ear muscle twitches. The most common causes of tinnitus are exposure to noise and hearing impairment. Although tinnitus is only related to the ear, most chronic cases have a central origin in the brain [1] [6]. Increased neuronal synchronization, tonotopic map reconfiguration, and increased spontaneous firing rates (SFR) in the

auditory system are suggested to be potential neural correlates of tinnitus by electrophysiological and functional imaging measures in people and animals. Tinnitus most likely results from the central nervous system's maladaptive plasticity. After being diminished in the frequency range of the hearing loss, the central nervous system seeks to raise these levels of evoked neural activity back to normal [6] [8]. The synaptic efficacy of central auditory neurons increased to achieve this. However, the absence of a physical sound source causes the SFR to alter as well, leading to an increase in the SFR known as tinnitus, this is perceived as sound.

A malfunction of several neurotransmitters and their receptors may be a major factor in the development of tinnitus [5]. The neurotransmitter release from neuron presynaptic sites and the reaction in postsynaptic structures play a significant role in auditory signal production, transmission and perception [6].

CLASSIFICATION:

Objective tinnitus is linked to the production of noise close to the ear, which the examiner may occasionally be able to hear using a stethoscope. Objective tinnitus is an infrequent event characterized by a pulsating, audible hum, which can be brought on by turbulent blood flow via the jugular vein or carotid artery [5]. Other potential causes of objective tinnitus include dural arteriovenous malformations and highly vascular middle ear tumors, such as glomus jugulare tumors [37].

Subjective tinnitus can arise from nearly any ear condition [1]. The following are common causes: cerumen blockage of the ear canal, infections (such otitis media), medicines like salicylates, and sensorineural hearing loss (like acoustic trauma) [37].

CAUSES:

Otosclerosis, otitis, impacted cerumen, abrupt deafness, Meniere's disease, noise-induced hearing loss, and other causes of hearing loss are examples of otologic causes [5] [44]. Cerebellopontine-angle tumors, vestibular schwannoma (also known as an acoustic neuroma), multiple sclerosis, head trauma, and whiplash are among the neurologic causes. Meningitis, syphilis, otitis media, and other infectious or inflammatory diseases that impact hearing are examples of infectious causes. Meningitis is also a possible contributing factor [34] [37].

Other oral medications that might cause tinnitus include salicylates, nonsteroidal anti-inflammatory drugs, aminoglycoside antibiotics, loop diuretics, and chemotherapeutic treatments (such vincristine and platins) [10]. Tinnitus can also be brought on by temporomandibular-joint dysfunction and other oral conditions. Other potential risk factors include obesity, smoking, alcohol use, head injuries in the past, history of arthritis, and hypertension. Some research has also suggested a slight hereditary tendency (tinnitus) [34].

First-class models postulate that injury to the cochlea's peripheral receptor epithelium causes an imbalance in the connections between excitatory and inhibitory signals along the auditory pathway [5]. This, in turn, leads to a disinhibition of auditory neurons, which is then perceived as increased activity, or tinnitus.

Second-class models postulate a homeostatic response of the central auditory system that aims to raise response gain to compensate for decreased cochlear input. This increase in spontaneous activity could potentially be experienced as tinnitus [9].

A third category of models suggests that the auditory system is continuously trying to maximize the transmission of information through stochastic resonance. In this case, tinnitus is thought to be experienced as an internally generated neural noise that is required for the stochastic resonance-based optimization process [11].

PATHOPHYSIOLOGY:

To better understand the pathophysiology of tinnitus, researchers have focused on the internal ear, cochlear nerves, and the auditory system. More recently, attention has turned to tinnitus networks and how they interact with other brain regions (the pathological mechanism and treatments of tinnitus). Numerous risk factors have been linked to tinnitus, such as extended noise exposure (22% of cases), head/neck injuries (17% of cases), and infections (10% of cases). According to the most recent pathophysiologic theory, tinnitus originates from or is "generated" by the central nervous system [1]. As of right now, it is estimated that abnormalities within the otoacoustic periphery (i.e., the vestibulocochlear nerve and inner ear) account for about 24% of instances; acoustic pathways account for 35% of cases, and supratentorial structures account for 41% [31]. Since one of the main risk factors for tinnitus is otological problems, particularly high-frequency hearing loss, the auditory phantom feeling is frequently thought to be a neuroplastic reaction to sensory deprivation [37]. While cochlear defects may be the first cause of tinnitus, it is more likely that the disease will be sustained by a series of later neuronal changes in the central auditory system [31]. The excitatory-inhibitory imbalance that results from a decrease in inhibition or an increase in excitation can cause neuronal hyperexcitability in certain areas, which can cause tinnitus to be perceived. Potential pharmaceutical targets, however, include several neurotransmitters and neuromodulators that operate on voltage- or ligand-gated channels to alter neuronal changes [1]. Tinnitus could be caused by an increase in the spontaneous firing rate of neurons in the central auditory system. Cochlear hearing loss lowers cochlear nerve activity, which in turn suppresses inhibitory cortical processes in the affected

peripheral auditory region. The downregulation causes hyperexcitability in central auditory tissues, including the primary auditory cortex [31]. Neural synchronization is yet another potential mechanism.

DIAGNOSIS:

For most tinnitus instances, there is no objective test available; instead, the diagnosis is based on the patient's medical history and an evaluation of the condition's impact on him or her family. The location and nature of the tinnitus are important questions, especially if it has a pulsatile or rhythmic component [45]. Since many patients report having a blocked sensation in their ears, tympanometry can be helpful in addition to pure-tone audiometry. Individuals who exhibit asymmetric tinnitus, asymmetric hearing on pure-tone audiometry, or other related neurological symptoms or indicators require additional testing, with MRI typically being the method of choice [32]. A complicated methodology that may include ultrasonography, CT, MRI, CT angiography, MR angiography, or conventional angiography is required for a more thorough assessment of patients with heartbeat-synchronous pulsatile tinnitus.

TREATMENT:

The two types of current therapies and treatments are tinnitus masking/reduction and tinnitus cessation. Since tinnitus masking treatments are more practical and easier to use for tinnitus patients, they are currently used more often in the initial line of treatment for tinnitus, improving the long-term prognosis of the patient [32]. Improved efficacy has been observed in tinnitus masking/reduction with Sound Therapy, Hearing Aids, and Cognitive Behavioral Therapy (CBT), Tinnitus Retention Therapy (TRT) and Tailor-Made Notched Music Training [31].

There aren't any pharmaceutical treatments available at the moment for tinnitus discomfort or loudness. Current guidelines recommend avoiding prescribing antidepressant, anticonvulsant, or anxiolytic medicine for individuals with troublesome tinnitus, despite the existence of tinnitus distress networks and the causal relationship between tinnitus and depression [37]. However, antidepressants and selective serotonin reuptake inhibitors can be used by individuals who already suffer from anxiety and depression to treat tinnitus. The goals of the present therapeutic approach are symptomatically lowering tinnitus perception and managing underlying problems. Therefore, rather than a 100% cure, the main objective has been to improve quality of life. Effective tinnitus management involves monitoring blood pressure, cholesterol, thyroid function, allergies, and educating patients about things like stress, caffeine, nicotine, and aspirin that might exacerbate tinnitus [22]. Important aspects of management include cochlear implants for sensorineural hearing loss, hearing aids for presbycusis, and stopping any offending medicines. Due to high serum serotonin levels, many tinnitus sufferers display symptoms of anxiety or sadness. The auditory system comprises of serotonin and GABA receptors, and anomalies in these neurotransmitters have been suggested to be a factor in certain cases [25]. Nowadays, it is understood that each tinnitus patient has a distinct medical, psychological, and social experience. Numerous recent research suggests targeted treatment plans that use multimodal techniques adjusted to each patient's unique requirements [41]. According to this research, effective tinnitus therapies require a tinnitus management team that includes an otolaryngologist, audiologist, neurologist, psychologist, and specialists in pain or sleep.

HERBAL TREATMENTS:

Herbal studies in tinnitus represent a subset of research exploring complementary and alternative medicine (CAM) approaches to manage this condition. While conventional treatments for tinnitus primarily focus on managing symptoms and addressing underlying causes, herbal remedies have been investigated for their potential efficacy in providing relief from tinnitus-related symptoms. Ginkgo biloba, derived from the leaves of the Ginkgo tree, is one of the most widely studied herbal remedies for tinnitus [10]. Several clinical trials have investigated its effectiveness, with some studies reporting modest improvements in tinnitus symptoms, particularly in individuals with age-related hearing loss or vascular-related tinnitus. However, results have been mixed, and more research is needed to establish its efficacy conclusively. Various other herbal remedies, includes Chinese herbal formulations, Korean red Ginseng have been explored in tinnitus research [22] [39]. While some preliminary studies suggest potential benefits, the evidence is often limited by methodological shortcomings, small sample sizes, and inconsistent findings. While herbal remedies are generally perceived as natural and safe, it's essential to exercise caution, as they can interact with medications and have potential side effects. Additionally, the quality and purity of herbal products can vary significantly, highlighting the importance of obtaining them from reputable sources [31]. Herbal studies in tinnitus represent a growing area of research aimed at exploring alternative approaches to manage this condition. While some herbal remedies have shown promising results in preliminary studies, further well-designed clinical trials are needed to establish their efficacy, safety, and optimal dosing regimens for tinnitus management. As with any treatment approach, individuals considering herbal remedies for tinnitus should consult with healthcare professionals to make informed decisions tailored to their specific needs and circumstances [37].

ANIMAL STUDIES:

Understanding the mechanism and possible treatments for tinnitus is greatly aided by research conducted on animals. Scholars employ several animal models, including rodents and nonhuman primates, to examine the brain circuits, cellular alterations, and behavioral reactions linked to tinnitus. In addition to offering insights into the underlying pathophysiology of tinnitus, these investigations assist in identifying possible targets for therapeutic approaches [15] [10]. Before beginning human clinical trials, researchers can also evaluate the safety and effectiveness of novel medicines using animal models. All things considered, research on animals has made a substantial contribution to our knowledge and treatment of tinnitus [17].

INDUCTION:

Like the variety of species employed in tinnitus behavioral testing, there are several approaches of tinnitus induction in animal models [16]. Tinnitus can be induced in two ways; one way is using pharmaceutical methods. On the other hand, tinnitus can be brought on by exposing the subject to intense stimulation for 30 to 60 minutes [27].

Pharmacological:

Pharmacological induction was employed in the first investigation to evaluate subjective tinnitus in an animal model. When tinnitus is evaluated in animal models using behavioral methods, salicylate and the antimalarial medication quinine are the two most often utilized drugs. Other ototoxic medications that have been studied in animal experiments include carboplatin and cisplatin (cis-diamine-dichloroplatinum (II)) [21]. Cisplatin primarily targets the outer hair cells, while carboplatin most likely affects the inner hair cells. The most often used medication in animal models is salicylate, which is the active component in aspirin. Therapeutically, it is used in anti-inflammatory therapy (e.g., against rheumatic arthritis) or as a mild analgesic [25]. One benefit of salicylate is that it can be quickly induced in only a few minutes, and its effects reverse within 72 hours after the last dosage. Salicylate was given systemically, either by injection or oral means, in most of the research mentioned above. Salicylate was also occasionally applied locally to the auditory cortex and other central regions, such as the inner ear [30].

Studies on animals have demonstrated that salicylate decreases cochlea sensitivity by obstructing the outer hair cells' prestin-based electromotility, which lowers cochlea neural output. But salicylate's effects aren't limited to cochlea [35]. High dosages of salicylate significantly decreased inhibitory postsynaptic currents in whole cell patch clamp recordings on AC brain slices, indicating a direct impact of salicylate in the CAS (central auditory system) [13]. On the other hand, the auditory cortex (AC) becomes hyperactive in response to high-level sound stimulation when a high-dose SS is administered systemically. Modified serotonin and g-aminobutyric acid (GABA) mediated neurotransmission in the central nervous system (CNS) may be connected to these alterations. Furthermore, high-dose SS enhanced the expression of the activity-dependent protein c-fos in the AC and several non-classical auditory areas (such as the amygdala) linked to stress, anxiety, and emotion [14]

Acoustic trauma:

Acoustic trauma has been shown to be the second reliable way of causing tinnitus in behavioral models [40]. In the peripheral and central nerve systems, acoustic trauma and the ensuing hearing loss cause a wide range of acute and long-term alterations. Damage to outer hair cells, cochlear dead areas (no functioning inner hair cells), damaged stereocilia in both types of hair cells, and deafferentation of auditory nerve fibers are the peripheral effects of an acoustic trauma [11].

ANIMAL BEHAVIORAL MODELS:

Animal behavioral models are employed in tinnitus research to investigate the etiology, causes, and possible therapies of the ailment. In these models, animals are usually given stimuli that resemble tinnitus, and their behavior is then observed to evaluate the impact of the condition and the effectiveness of treatments. popular behavioral models in research on tinnitus [10] [9] [35].

Gap-Prepulse Inhibition of the Acoustic Startle Reflex (GPIAS):

In this technique, animals are trained to recognize brief intervals in auditory input. Animals experiencing tinnitus symptoms may have trouble identifying these gaps. GPIAS is a behavioral paradigm that is frequently used to evaluate tinnitus-related alterations in auditory processing in both human subjects and animal models [35]. In this test, a startle-inducing stimulus (such as a sudden burst of loud noise) is either provided all at once or before a brief silent interval that is intercut with a continuous background sound. When the gap is offered, normal animals and humans show fewer startle reactions, indicating that the previous gap has inhibited the startle reflex [36]. Nonetheless, tinnitus-affected animals or people could exhibit decreased inhibition of the startle reaction, indicating a malfunction in the auditory gating systems linked to tinnitus perception.

Conditioned Avoidance Response:

Animals are taught to link a particular sound to an unpleasant stimulus (such a small electric shock). Animals will learn to avoid the tinnitus sound if they find it unpleasant, illustrating how the condition affects behavior. Animal learning, memory, and emotional responses are studied in behavioral neuroscience through the use of experimental settings called

conditioned avoidance paradigms [10] [9] [18]. Under these models, animals acquire the ability to link a neutral stimulus to an unpleasant occurrence or outcome, which results in the formation of conditioned avoidance behavior. Animals are trained by first exposing them to a neutral conditioned stimulus (CS), like a tone or light, and then an aversive unconditioned stimulus (US), such a moderate electric shock or an unpleasant air puff. The formation of conditioned avoidance behavior occurs when the animals come to identify the CS with the unpleasant US. Researchers can evaluate learning and memory in several ways using conditioned avoidance paradigms, such as acquisition, extinction, generalization, and retention of the conditioned response [22]. Researchers can examine what influences conditioned avoidance behavior by varying parameters including the time of the presentation of the US and CS, their intensity and duration, and other aspects. In the context of tinnitus research, alterations in auditory perception, learning, and emotional reactions in animal models can be evaluated using conditioned avoidance procedures. For instance, compared to normal animals, tinnitus-affected animals may display different conditioned avoidance behavior in response to auditory stimuli [27] [12]. Researchers can learn more about the cognitive and affective dimensions of tinnitus perception and its behavioral effects by examining how tinnitus influences conditioned avoidance behavior.

Startle Reflex:

Researchers measure changes in the startle reflex of animals in response to sudden loud sounds, which can be affected by the presence of tinnitus. animals with tinnitus may exhibit altered startle responses compared to controls [12] [16]. The startle reflex is a defensive reaction to sudden or unexpected stimuli; it usually manifests as a sudden, involuntary movement or jump [13]. The startle reflex is frequently examined in the context of tinnitus research to comprehend how tinnitus impacts auditory processing and sensory gating processes [21].

These behavioral models of animals offer important insights into the behavioral expressions of tinnitus and aid in the development and assessment of possible treatment approaches by researchers [16]. Though these models can simulate some features of tinnitus, it's crucial to remember that they might not be able to accurately capture the complexity of the human situation. Thus, results from research on animals should be carefully understood and verified in clinical trials involving humans [30].

Schedule-Induced Polydipsia Avoidance Conditioning:

SPIAC is a hybrid of two behavioral paradigms: shock avoidance conditioning and schedule-induces polydipsia. The delivery of food pellets on a schedule induces polydipsia, which is the term for excessive drinking [2] [10]. After two to three days on this regimen, rats lick for water on their own even if they are not dehydrated. This licking occurs spontaneously between pellet deliveries. Rats that have been trained for a week or two exhibit a high rate of licking after receiving food pellets [14]. Aversive foot shock is used in the subsequent training phase to put the licking behavior under stimulus control, with licks occurring [44]. In these circumstances, the rats learn to only lick in quiet times and to avoid seeking water when noise is present.

Auditory Brain Stem Response:

In preclinical research settings, rats' Auditory Brainstem Response (ABR) testing can be used to assess tinnitus [16]. Researchers can cause tinnitus-like symptoms in rats by a variety of techniques, including exposure to loud noises, ototoxic medications, or manipulation of the auditory system.

Baseline ABR Recordings:

Rats are given baseline ABR recordings to establish baseline auditory thresholds and general auditory function prior to generating tinnitus-like symptoms. This provides an outline for further analysis and comparisons [17].

Tinnitus Induction:

Rats are produced to exhibit tinnitus-like symptoms by means of ototoxic chemical delivery (e.g., salicylate), loud noise exposure, or surgical procedures aimed at the auditory system. These therapies may result in alterations in the auditory pathway's neuronal activity that are linked to tinnitus [17] [18].

Post-Induction ABR Recordings:

The purpose of the ABR recordings is to evaluate any differences in the rats' auditory responses from baseline recordings when tinnitus-like symptoms are induced. They might specifically search for modifications to ABR waveforms, adjustments to auditory thresholds, or adjustments to the latency or amplitude of ABR components [16].

Behavioral Testing:

Behavioral assays are frequently used by researchers to evaluate tinnitus-related behavior in rats in addition to ABR testing. Conditioned avoidance paradigms and gap-prepulse inhibition of the acoustic startle reflex (GPIAS) are common behavioral tests [41]. These experiments assess the rats' acoustic sensitivity as well as their capacity to recognize and respond to alterations in auditory stimuli, which may be suggestive of tinnitus.

In preclinical research, ABR testing in rats is a useful method for evaluating symptoms like tinnitus. It makes it possible for researchers to assess how different interventions affect the auditory system and investigate prospective treatment plans for tinnitus relief [16] [17]. Furthermore, a thorough method for researching tinnitus in animal models is offered by integrating behavioral assays with ABR testing.

IN-VITRO STUDIES:

In vitro studies for tinnitus typically involve experiments conducted outside of a living organism, often using cell cultures or tissue samples. These studies are crucial for understanding the underlying mechanisms of tinnitus at the cellular and molecular levels, as well as for testing potential treatments [4]. Here are some common approaches and findings in in vitro studies related to tinnitus.

Cell Culture Studies:

This involves exposing cultured auditory system cells such as spiral ganglion neurons, cochlear hair cells, or auditory cortex cells to a range of stimuli or environmental factors associated with tinnitus. These investigations can aid in the understanding of the cellular signaling networks, neurotransmitter activity, and altered gene expression linked to tinnitus [19].

In vitro electrophysiological recordings involve measuring the electrical activity of neurons or neuronal networks in response to different stimuli or pharmacological agents. These recordings can provide insights into the hyperactivity, synchronization, and aberrant neural firing patterns associated with tinnitus [21].

Gene Expression Profiling:

Transcriptomic and proteomic analyses of auditory tissues or cells from animal models can identify molecular changes associated with tinnitus. By comparing gene expression profiles between tinnitus and control samples, researchers can uncover potential biomarkers and therapeutic targets [27]. Overall, in vitro studies play a crucial role in advancing our understanding of tinnitus and developing effective treatments. However, findings from these studies need to be validated in animal models and clinical trials to ensure their relevance to human tinnitus pathology.

DISCUSSION AND CONCLUSION:

Preclinical models of tinnitus have been used to investigate a wide range of pharmacological techniques. Beneficial outcomes have been shown for strategies that target neurotransmission and neural excitation as well as those that exert cytoprotective, antioxidant, or anti-inflammatory effects [45].

The first steps in treating tinnitus patients include taking a thorough medical history, examining the auditory system for anomalies, determining whether there are any psychiatric problems present, and measuring the degree of discomfort associated with tinnitus using questionnaires and auditory tests [41]. Similar to other neurological conditions like epilepsy, pain, or depression, tinnitus is most likely caused by intricate and varied brain pathways. More therapeutically useful classification systems for tinnitus patients are presently being developed. These classification systems will be based on neurological imaging results, etiology, somatic, audiometric, perceptual, and psychological aspects. Improved success rates with medications developed for subpopulations are probably going to result from advancements in the classification of tinnitus sufferers [46]. Along the auditory pathway, which extends from the cochlear nucleus to the auditory cortex, tinnitus can begin at any point. Among the most popular theories are those involving damaged cochlear hair cells that repeatedly stimulate auditory nerve fibers, spontaneous activity in individual nerve fibers, hyperactivity of the brain stem's auditory nuclei, or a decrease in the central auditory cortex's typically suppressive activity on peripheral auditory nerve activity [44].Novel treatments for tinnitus will minimize the impact the condition has on sufferers' lives and may even improve the efficacy of currently available treatments. Currently, research hotspots include depression, acoustic treatment, quality of life, CBT, and TMS [47] [46]. Recently, tinnitus sufferers have become interested in acoustic therapy, low-frequency repetitive transcranial magnetic stimulation, and cognitive behavioral therapy either separately or in combination. Tinnitus treatment including multiple disciplines, such as otolaryngology, neurology, and psychology, is becoming increasingly popular in the 21st century [35] [43]. The investigation will provide further findings, and our work will serve as a valuable resource for future tinnitus research and therapeutic practice.

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