Casual Friday Series

Tinnitus and How to Support

A BIOGENETIX CLINICAL PRESENTATION

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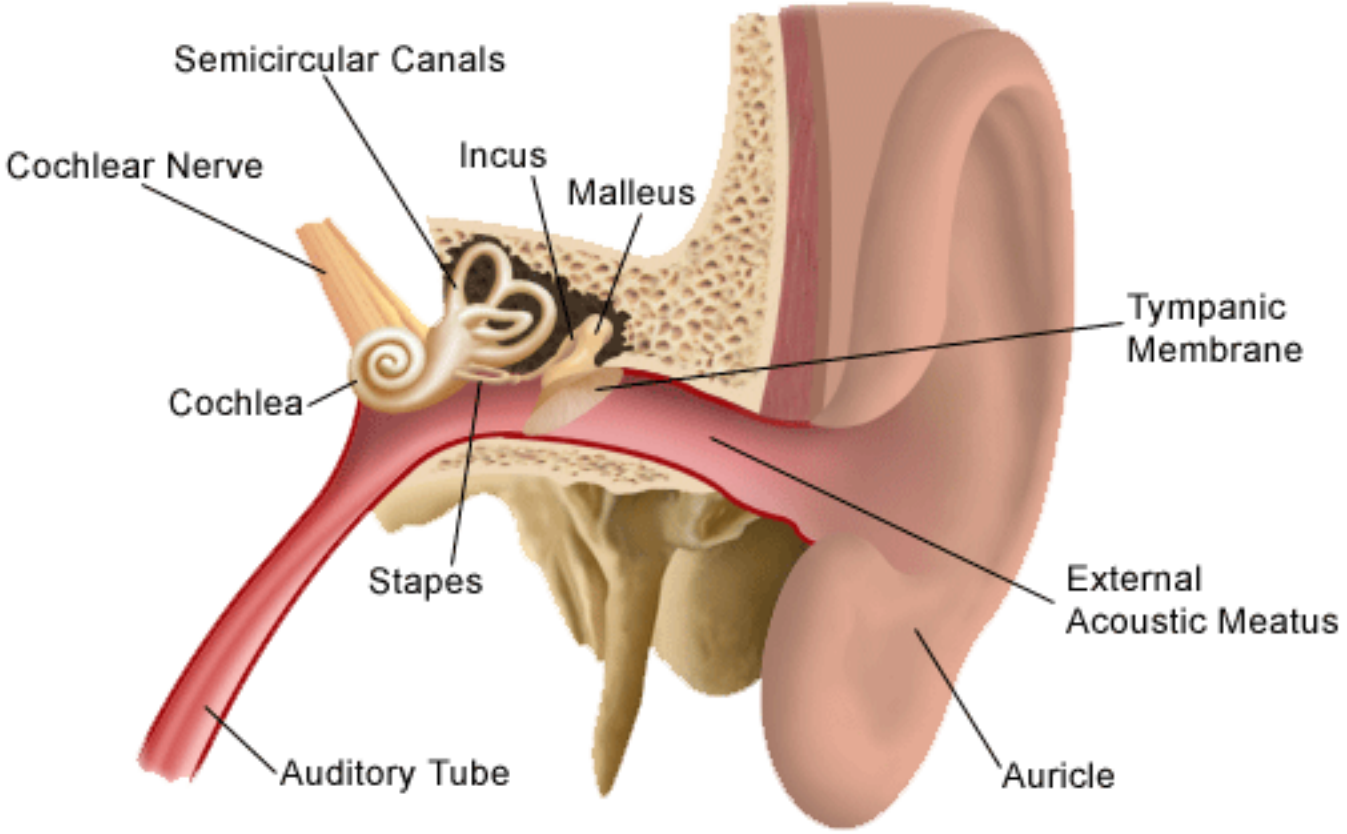
Anatomy of the Ear



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Tinnitus

Tinnitus is a sound a person hears that is generated by the body rather than by an outside source. Most tinnitus is subjective. This means the examiner cannot hear it, and there are no tools to measure or hear that sound. Objective tinnitus can arise from an aneurysm. This can be objectified and heard by the examiner. Other objective tinnitus investigations include temporomandibular joint disease (TMJD) and tensor tympani muscle spasms.

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https://www.ncbi.nlm.nih.gov/books/NBK430809/

Tinnitus

Almost everyone experiences tinnitus at some point in their lifetime. The American Tinnitus Association estimates that 10 million people suffer from tinnitus. It is also common in non-industrialized countries. Military personnel have a high incidence of tinnitus due to loud explosions and gunfire. It is also seen in the movie and stage workers who prepare scenes with explosions and gunfire. Musicians exposed to loud noise get tinnitus, such as drummers and those who perform in front of loudspeakers.

Children may have tinnitus, but it is mostly unrecognized because they do not recognize the disorder. The usual history is of a worker exposed to loud factory noises, where workers had to shout to be heard. Many workers develop high-tone hearing loss, but only a small percentage also have tinnitus. Hyperacusis also can accompany tinnitus. In these cases, certain ordinary sounds, like closing doors, moving chairs, and dropping books, are so loud and strong that they are extremely uncomfortable or sometimes unbearable.

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Tinnitus

Humans normally react with a typical fight or flight response when there is a danger or threat. This is the reason why the onset of tinnitus can be so distressing. A broken finger does not necessarily trigger this response, but tinnitus does. Cognitive therapy is done to stop the unwanted reaction. However, stress is not a cause of tinnitus. Because humans cannot objectify tinnitus, the pathophysiology is not understood. Lesions that put pressure on the eighth cranial nerve may cause tinnitus. An increase in fluid pressure in the inner ear causes tinnitus. Symptoms associated with increased inner ear pressure include hearing loss, vertigo, tinnitus, and feeling of pressure in the ear. MRI shows that many areas of the brain are involved in tinnitus, including the cognitive and emotional areas and the auditory. Sound first enters the brain via the amygdala center. Therefore, learning that tinnitus is not a danger is therapeutic.

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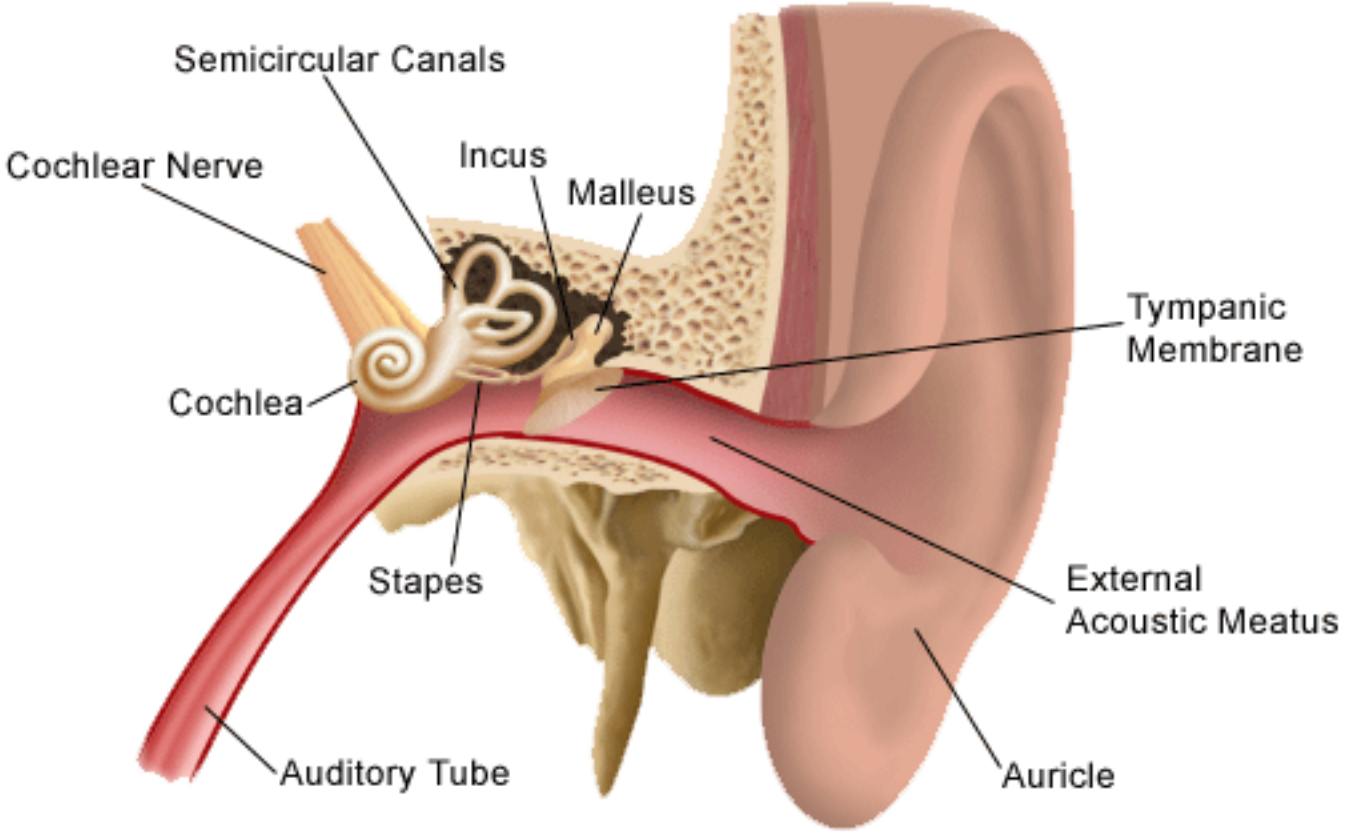
https://www.ncbi.nlm.nih.gov/books/NBK430809/

Tinnitus

Differential diagnosis for tinnitus includes:

- Cytomegalovirus
- Hypercholesterolemia
- Lyme disease
- Measles
- Meningitis
- Neoplasm
- Neurosyphilis
- Rubella
- Sickle cell anemia
- Small vessel disease
- Stroke
- Tumor

Anatomy of the Ear



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Front Pharmacol. 2023 Jan 4;13:1037528. doi: 10.3389/fphar.2022.1037528

Herbal medicines in the treatment of tinnitus: An updated review

Dongliang Liu [1,†], Yue Hu [1,†], Dali Wang [1,†], Hezhou Han [1], Yi Wang [1], Xilu Wang [1], Zhaoyu Zhou [1], Xiulan Ma [1,*], Yaodong Dong [1,*]

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PMCID: PMC9847569 PMID: 36686691

al., 2022). An early randomized study of 259 patients with tinnitus of less than 1 year duration showed that *G. biloba* extract (Meyer, 1986) reduced the severity of tinnitus in 70% of the patients. A double-blind placebo-controlled trial of 1,121 healthy subjects with tinnitus showed that 50 mg *G biloba* extract LI 1370 (containing 25% flavonoids, 3% ginkgolides, and 5% bilobalides) three times daily for 12 weeks resulted in no notable improvement in tinnitus versus placebo (Drew and Davies, 2001; Rejali et al., 2004; Polanski et al., 2016). The authors also failed to find improvement in other symptoms of cerebral insufficiency with *G. biloba* extract. Overall, *G. biloba* extract was safe and had no serious side effects. In a

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Overall, these studies demonstrated that *G. biloba* extract benefited patients with mild to moderate dementia in terms of reducing the severity of tinnitus. However, measures of tinnitus were not assessed as a primary outcome in these trials of *G. biloba* extract for dementia and the results need to be interpreted with caution. In addition, depression and anxiety are prevalent in patients with tinnitus (Ziai et al., 2017). A mediation analysis showed that *G. biloba* extract EGb 761 directly accounted for 60% of the total effect of tinnitus severity reduction while amelioration of the symptoms of anxiety and depression and improvement in cognition contributed to 40% of the total effect (Brüggemann et al., 2021). The efficacy of *G. biloba* extract in reducing tinnitus severity in mild to moderate dementia patients remains to be investigated in vigorously conducted clinical trials with measures of tinnitus as the primary study end point.

Hear Res. Author manuscript; available in PMC: 2011 Dec 1.

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The Effect of Supplemental Dietary Taurine on Tinnitus and Auditory Discrimination in an Animal Model

Thomas J Brozoski [a,c], Donald M Caspary [b], Carol A Bauer [a], Benjamin D Richardson [b]

Loss of central inhibition has been hypothesized to underpin tinnitus and impact auditory acuity. Taurine, a partial agonist at inhibitory glycine and γ-amino butyric acid receptors, was added to the daily diet of rats to examine its effects on chronic tinnitus and normal auditory discrimination. Eight rats were unilaterally exposed once to a loud sound to induce tinnitus. The rats were trained and tested in an operant task shown to be sensitive to tinnitus. An equivalent unexposed control group was run in parallel. Months after exposure, 6 of the exposed rats showed significant evidence of chronic tinnitus. Two concentrations of taurine in drinking water were given over several weeks (attaining average daily doses of 67 mg/kg and 294 mg/kg). Water consumption was unaffected. Three main effects were obtained: (1) The high taurine dose significantly attenuated tinnitus, which returned to near pre-treatment levels following washout. (2) Auditory discrimination was significantly improved in unexposed control rats at both doses. (3) As indicated by lever pressing, taurine at both doses had a significant group-equivalent stimulant effect. These results are consistent with the hypothesis that taurine attenuates tinnitus and improves auditory discrimination by increasing inhibitory tone and decreasing noise in the auditory pathway.

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Relevant to the present study, taurine has been shown to act as an inhibitory neuromodulator, although its status as a neurotransmitter is unresolved. There is evidence of taurine specific receptors (Frosini et al., 2003; Wu et al., 1992; Wu et al., 1990). Taurine has been shown to inhibit neural activity by acting at glycine (GlyR), $GABA_A$ ($GABA_AR$), and $GABA_B$ ($GABA_BR$) receptors (Albrecht et al., 2005), and is distributed throughout the central and peripheral auditory system (Contreras et al., 1979; Harding et al., 1993). In the central auditory system it has been shown to activate GlyRs in rat inferior colliculus (IC) (Xu et al., 2004; Xu et al., 2006), and may act similarly in the auditory midbrain and brainstem, including the cochlear nucleus, superior olivary complex, and nuclei of the lateral lemniscus (Friauf et al., 1997). Although the inhibitory role of taurine is widespread in the CNS, it may have an excitatory role in the periphery. Liu et al., (Liu et al., 2008; Liu et al., 2006) have shown that increased taurine elevates cochlear outer hair cell and spiral ganglion neuron Ca2+ influx.

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PMCID: PMC2997922 NIHMSID: NIHMS245865 PMID: 20868734

Three main effects were obtained with supplemental dietary taurine: (1) A significant, and reversible, tinnitus therapeutic effect was evident at the high dose level (4 mg/ml, or 294 mg/kg/da), but not the low dose level (1 mg/ml, or 67 mg/kg/da). (2) At the low dose, taurine may have exacerbated high-frequency components of the tinnitus. (3) Auditory discrimination performance was enhanced in normal-hearing rats in a dose-dependent manner.

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Assuming that taurine functions as an effective agonist at inhibitory amino acid neurotransmitter receptors in the auditory pathway, it may have the capacity to reduce background neural activity through enhanced inhibition, and thereby improving signal-to-noise separation. In the present study normal-hearing intact rats, while on a moderately-high level of supplemental taurine, improved their discrimination performance across a broad frequency range. Loss of coding fidelity is observed in aged animals in conjunction with loss of GABA and glycine function in the auditory neuraxis (Caspary et al., 2008; Hughes et al., 2009; Schatteman et al., 2008; Wang et al., 2009). Consistent with these findings, it would be expected that enhanced inhibitory amino acid neurotransmitter function would facilitate frequency detection (Gleich et al., 2003). In the present study, normal-hearing intact rats on a moderately-high level of supplemental taurine improved their discrimination performance across a broad frequency range. The same mechanism, that is, increased agonistic activity at inhibitory amino acids receptors in the auditory neuraxis, could explain the attenuation of tinnitus. This would be particularly true if tinnitus emerges from brainstem areas and derives from bursting activity with high peak discharge rates (Bauer et al., 2008). Beyond specific improvements in auditory processing, taurine and other extra-synaptic GABA agonists, including GABA itself, may play an important role generally stabilizing brain systems.

J Neurosci. 2015 Nov 4;35(44):14822-8. doi: 10.1523/JNEUROSCI.2695-15.2015.

Human Auditory Cortex Neurochemistry Reflects the Presence and Severity of Tinnitus

William Sedley [1], Jehill Parikh [2], Richard A E Edden [3], Valerie Tait [4], Andrew Blamire [2], Timothy D Griffiths [5]

Affiliations + expand

PMID: 26538652 PMCID: PMC4635131 DOI: 10.1523/JNEUROSCI.2695-15.2015

This study used magnetic resonance spectroscopy to measure GABA levels in the auditory cortex of 14 tinnitus patients and matched controls. It found reduced GABA concentrations in the right auditory cortex associated with tinnitus presence, suggesting a link to impaired inhibitory neurotransmission. Severity correlations were weaker, and the study highlights methodological challenges in isolating GABA's role.

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> Sci Rep. 2022 Mar 8;12(1):4068. doi: 10.1038/s41598-022-07835-8.

Lower glutamate and GABA levels in auditory cortex of tinnitus patients: a 2D-JPRESS MR spectroscopy study

B Isler [1 2], N von Burg [3], T Kleinjung [4 3], M Meyer [5 6], P Stämpfli [7], N Zölch [7 8], P Neff [9 10 11 12]

Affiliations + expand

PMID: 35260698 PMCID: PMC8904839 DOI: 10.1038/s41598-022-07835-8

this study compared 16 tinnitus patients (no hearing loss) to 17 controls, finding lower GABA levels in the left auditory cortex and reduced glutamate in the right. GABA findings align with theories of reduced inhibition in tinnitus, but the authors note causality is unclear and call for longitudinal studies.

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> Front Syst Neurosci. 2012 Feb 24:6:9. doi: 10.3389/fnsys.2012.00009. eCollection 2012.

Gamma-aminobutyric acid and glutamic acid levels in the auditory pathway of rats with chronic tinnitus: a direct determination using high resolution point-resolved proton magnetic resonance spectroscopy (H-MRS)

Thomas Brozoski [1], Boris Odintsov, Carol Bauer

Affiliations + expand

PMID: 22383901 PMCID: PMC3285819 DOI: 10.3389/fnsys.2012.00009

This animal study used 1H-MRS to measure GABA and glutamate in auditory brain regions of rats with noise-induced tinnitus. Decreased GABA was observed in the medial geniculate body, suggesting regional inhibitory deficits. The authors propose targeting GABA systems for therapy but note complex excitatory-inhibitory interactions.

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Randomized Controlled Trial > Otol Neurotol. 2007 Jan;28(1):11-5.
doi: 10.1097/01.mao.0000235967.53474.93.

Treatment of tinnitus with gabapentin: a pilot study

David L Witsell [1], Maureen T Hannley, Sandra Stinnet, Debara L Tucci

Affiliations + expand

PMID: 17106432 DOI: 10.1097/01.mao.0000235967.53474.93

This placebo-controlled trial tested gabapentin (up to 2400 mg/day) in 39 patients, split by acoustic trauma history. Trauma patients showed significant reductions in tinnitus loudness (subjective and psychoacoustic measures), while non-trauma patients had variable responses. It suggests gabapentin's efficacy may depend on tinnitus etiology.

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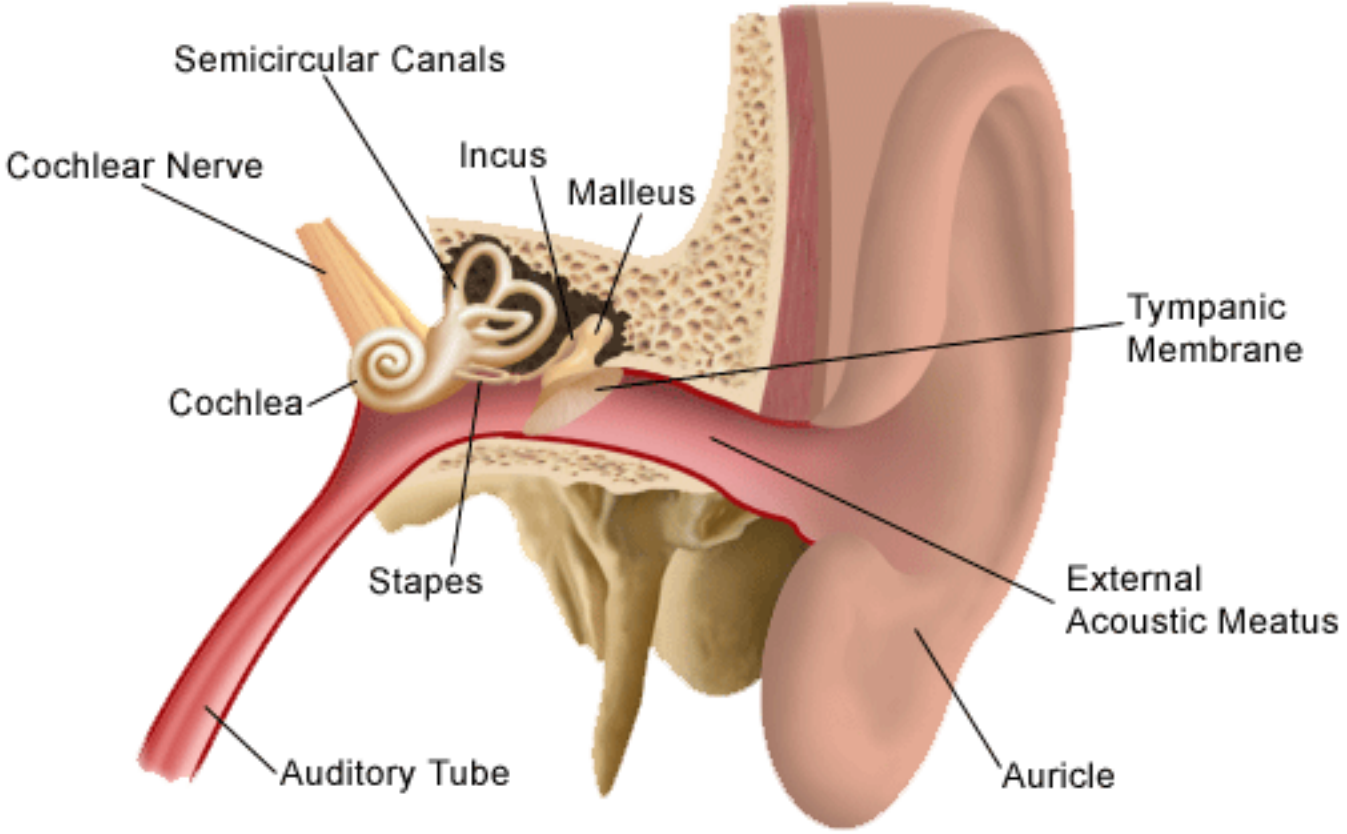

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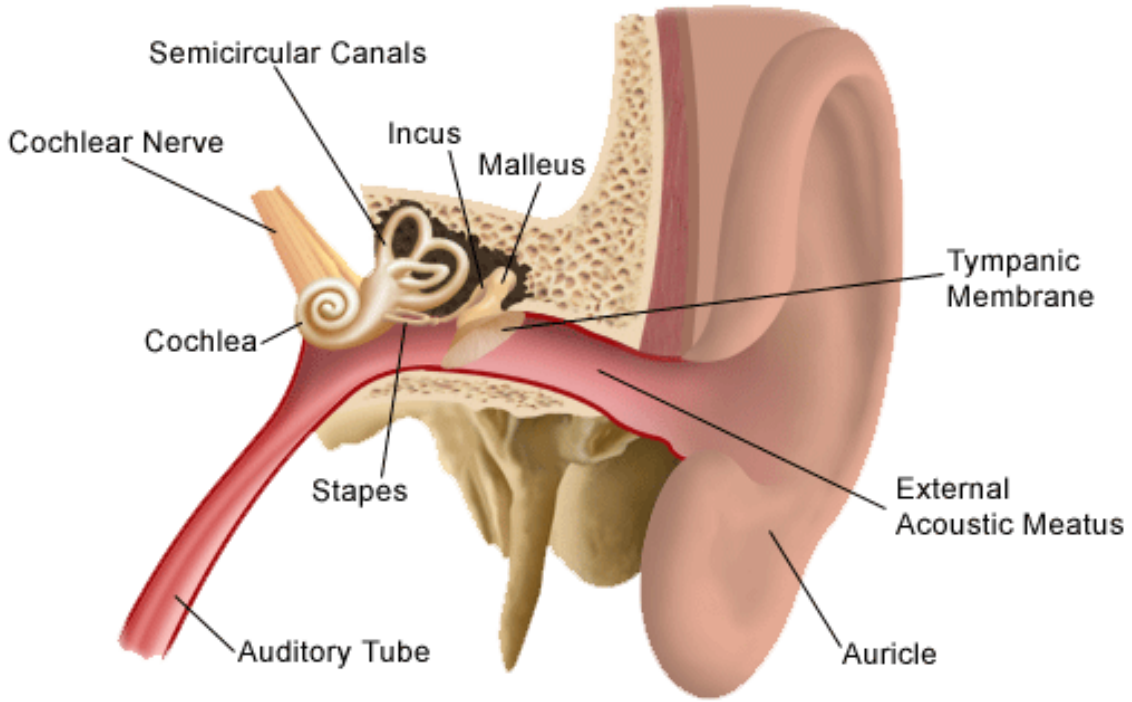
Support Strategy

1. Audiology Appt.
2. Food allergy, irritation.
3. Infection/Dysbiosis.
4. Toxicity/Drugs.
5. Injury.
6. Supplemental Support.
    - GABA
    - Taurine



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