

Cortical Plasticity in Tinnitus

Roadmap Paths: B and C; one year grant for \$99,949

By SHAOWEN BAO, Ph.D.

Intent of our Work

Recent studies reveal substantial changes in brain activity patterns in tinnitus patients and in animals with hearing loss. These brain activity changes (cortical plasticity), potentially produce hearing loss-induced tinnitus. Two different types of cortical plasticity have been implicated as causes of tinnitus etiology: *cortical map reorganization* and homeostatic regulation of cortical excitation and inhibition. Our work aims at understanding the contributions of these types of cortical plasticity in hearing loss-induced tinnitus.

Our Study

Tinnitus, the perception of sound in the absence of external sources, has been a subject of considerable research to localize the underlying *neural substrate*. Although often caused by peripheral hearing loss,

tinnitus persists after auditory nerve *transection*, suggesting involvement of central mechanisms. Recent studies reveal a correlation between abnormal *auditory cortex* activation and cortical map reorganization and the occurrence and severity of tinnitus. Elevated, spontaneous activity and map reorganization are also co-modulated – both are induced by acoustic trauma, and prevented if enriched acoustic experience follows the trauma. These findings lead to the notion that cortical map reorganization causes abnormal cortical activity and tinnitus, and that preventing and reversing such reorganization could alleviate tinnitus symptoms.

While long-term map reorganization is believed to be mediated by *Hebbian plasticity*,

non-Hebbian *homeostatic plasticity* may also be activated by altered sensory input. Cochlear *ablation*, for example, results in weakened inhibitory *synapses*; strengthened excitatory synapses; and enhanced neuronal excitabilities in the auditory cortex. These effects could potentially lead to elevated, spontaneous cortical activity and tinnitus. Because map reorganization generally increases sensory input to the previously input-deprived neurons in the reorganized zone of the cortical map, it may ease homeostatic plasticity. Thus, if tinnitus is caused by homeostatic plasticity, map reorganization should reduce it.

GLOSSARY

Ablation: Surgical removal of a body part or tissue.

Auditory cortex (AI): The highest level of the brain that receives input from its lower auditory regions, including the inner ear, and interprets that neural activity into sound.

Cortical map: Areas of mini columns in the brain cortex that perform a specific information processing function.

Cortical map reorganization: Changes to the cortical map following localized repetitive stimuli, or elimination or interruption of sensory nerve fibers.

Hebbian plasticity: Describes a basic mechanism for synaptic plasticity when an increase in synaptic effectiveness arises from the pre-synaptic cell's repeated and persistent stimulation of the post-synaptic cell.

Homeostatic plasticity: Refers to the capacity of neurons to regulate their own excitability relative to network activity.

Lesion-induced: Acoustic trauma to produce hearing loss and tinnitus effect.

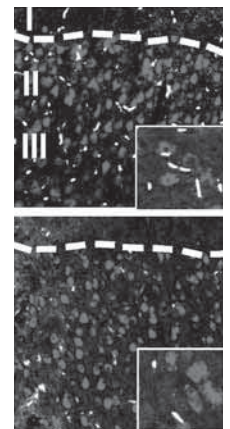
Neural substrate: A set of brain structures that underlies a specific behavior or psychological state.

Synapse: Junction, or point of connection, across which a nerve impulse passes from an axon terminal (end of a nerve fiber capable of rapidly conducting impulses away from the neuron cell body) to cells, such as a neuron, muscle or gland cell.

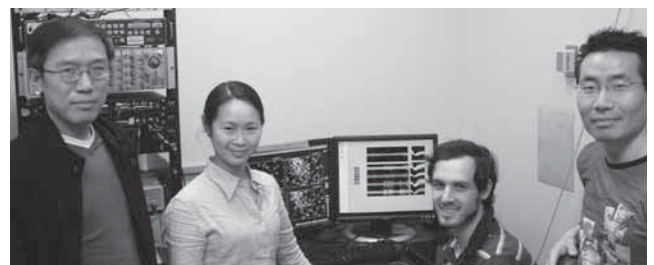
Synapse plasticity: A change in the strength of a synapse brought about by activity in another pathway.

Transection: A cross section; a division created by cutting transversely.

Top image: from a non-hearing-lesioned animal. The grey color represents all neurons. The white color is for GAD65, an enzyme that synthesizes the inhibitory neurotransmitter GABA. The I, II and III mark cortical layers. Lower image: from a hearing-lesioned animal. There are fewer white clusters in this image.



To clarify the roles of different forms of cortical plasticity in tinnitus, we examined high frequency, hearing *lesion-induced synaptic plasticity*, sensory map reorganization and tinnitus behaviors in adult rats. Both excitatory and inhibitory synaptic transmissions were enhanced in a normal hearing primary auditory cortex (AI) zone after hearing lesion. By contrast, only inhibitory synaptic transmission was down-regulated in the non-reorganized zone of the AI that used to represent the hearing-loss frequencies. Behavioral study indicated that the hearing-lesioned animals experienced tinnitus in the hearing loss-frequency



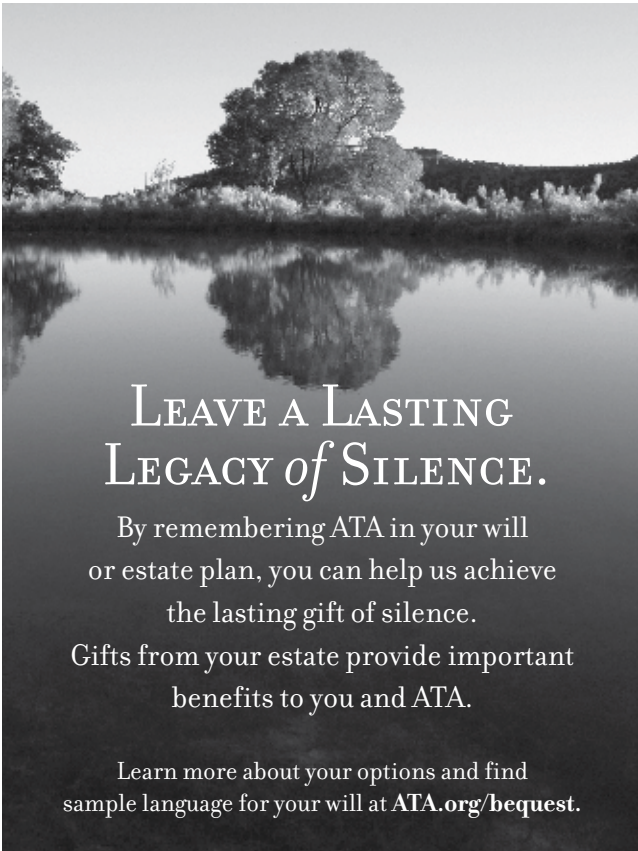
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range, suggesting a role of homeostatic down-regulation of inhibitory input in tinnitus. These results support the homeostatic plasticity hypothesis of tinnitus, and suggest a new direction for tinnitus treatment.

Conclusion

Research previously suggested two opposing mechanisms for hearing loss-related tinnitus. One is the cortical map reorganization explained above. The other is homeostatic plasticity, which is activated when map reorganization is lacking or incomplete. We found that in animals with high-frequency hearing loss, the pitch of tinnitus is in the hearing-loss frequency range. The cortical area representing the tinnitus pitch showed homeostatic plasticity but not map reorganization. These results suggest that cortical map plasticity, which would reduce homeostatic plasticity, may help relieve tinnitus. Targeting hearing loss-induced homeostatic plasticity with specific medication may also be a viable option for future tinnitus treatment. ☺

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