ROLE OF COCHLEAR NMDA RECEPTORS IN SALICYCLATE INDUCED TINNITUS

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Approximately 20 million people in the United States of America experience tinnitus (ringing in the ears) and probably two million of these individuals suffer from tinnitus that interfere substantially with their occupation and activities of daily living. Large dose of aspirin (acetylsalicylic acid) produce reversible hearing loss and tinnitus that recover after stopping treatment. These effects were attributed to the salicylate ion, the active component of aspirin (Cazals, 2000). Salicylate acts as a competitive antagonist at the anion-binding site of prestin, the motor protein of sensory outer hair cells (Oliver et al., 2001). This provides an explanation for the significantly reduced outer hair cell electromotility (Tunstall et al., 1995, Kakahata and Santos-Sacchi, 1996) that underlies the hearing loss induced by aspirin. However, the site of action and the mechanism of generation of the tinnitus induced by salicylate still remains elusive and obscure. Here, we report that application of sodium-salicylate into the cochlea elicits neural excitation in the auditory nerve fibers. Addition of NMDA receptor antagonists reverses salicylate-induced neural excitation whereas an AMPA receptor antagonists did not. Behavioral test showed that the occurrence of tinnitus induced by sodium-salicylate can be suppressed by local application of NMDA antagonists. This demonstrate that tinnitus induced by sodium-salicylate requires activation of cochlear NMDA receptors. These experiments are now extended to other types of pathologologies that induced tinnitus. Thus target cochlear NMDA receptors may present a therapeutic strategy for treatment of tinnitus.