AUT3, a Kv3.1 positive modulator, suppresses chronic noise-induced tinnitus in a rat model

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Kv3.1 channels are voltage-gated potassium channels that enable fast repolarization of the neuronal action potential, and are essential for the high frequency, high fidelity firing of neurons in the auditory brainstem and midbrain. Altered activity of these neurons has been implicated in the generation of tinnitus induced by noise exposure. Furthermore, loss of Kv3 channel function has been observed shortly after noise exposure, which may contribute to the maladaptive plasticity leading to the emergence of tinnitus. In the current study, 20 Long Evans rats (and 10 sham controls) were exposed to a unilateral 116 dB, 16 kHz octave-band noise for one hour in order to induce temporary hearing loss and chronic tinnitus. Thirty days after the noise exposure, a subset of approximately half of the noise-exposed rats demonstrated deficits in auditory gap processing, consistent with the presence of tinnitus. All 30 rats were administered 30 and 60 mg/kg of AUT3 (a Kv3.1 positive modulator) and vehicle in a counterbalanced order, with 48-hours washout between treatments. Both the 30 and 60 mg/kg doses of AUT3 abolished evidence of tinnitus, while the drug had no effect on the behavior of control animals or noise-exposed animals without tinnitus. These results suggest that AUT3 has potential in the treatment of chronic tinnitus associated with noise-induced hearing loss.