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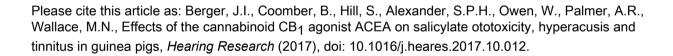
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ACCEPTED MANUSCRIPT

Effects of the cannabinoid CB₁ agonist ACEA on salicylate ototoxicity, hyperacusis and tinnitus in guinea pigs

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Abstract

Cannabinoids have been suggested as a therapeutic target for a variety of brain disorders. Despite the presence of their receptors throughout the auditory system, little is known about how cannabinoids affect auditory function. We sought to determine whether administration of arachidonyl-2'-chloroethylamide (ACEA), a highly-selective CB₁ agonist, could attenuate a variety of auditory effects caused by prior administration of salicylate, and potentially treat tinnitus. We recorded cortical resting-state activity, auditory-evoked cortical activity and auditory brainstem responses (ABRs), from chronically-implanted awake guinea pigs, before and after salicylate + ACEA. Salicylate-induced reductions in click-evoked ABR amplitudes were smaller in the presence of ACEA, suggesting that the ototoxic effects of salicylate were less severe. ACEA also abolished salicylateinduced changes in cortical alpha band (6-10 Hz) oscillatory activity. However, salicylate-induced increases in cortical evoked activity (suggestive of the presence of hyperacusis) were still present with salicylate + ACEA. ACEA administered alone did not induce significant changes in either ABR amplitudes or oscillatory activity, but did increase cortical evoked potentials. Furthermore, in two separate groups of non-implanted animals, we found no evidence that ACEA could reverse behavioural identification of salicylate- or noise-induced tinnitus. Together, these data suggest that while ACEA may be potentially otoprotective, selective CB₁ agonists are not effective in diminishing the presence of tinnitus or hyperacusis.

Keywords

Tinnitus; cannabinoids; chronic recording; auditory cortex; treatment; salicylate

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