Calcium, Vc1.1 and α9α10 nicotinic acetylcholine receptors

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Nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels involved in fast synaptic transmission. nAChRs are pentameric complexes formed from a combination of alpha and beta subunits to form heteromeric channels, or alpha subunits alone in the case of homomeric channels. Stoichiometric differences have been conclusively shown to exist with α4β2 nAChR subtypes ((α4)3(β2)2 and (α4)2(β2)3) and that calcium permeability differs between the two receptor populations (Tapia *et al.*, 2007). The α9α10 heteromeric complex is found in inner hair cells, and is potently and selectively inhibited by the conotoxins Vc1.1 and RgIA (Vincler *et al.*, 2006; Halai *et al.*, 2009). Its been shown to exist as one stoichiometric population ((α9)2(α10)3) (Plazas *et al.*, 2005). We have investigated the roles of both stoichiometry of α9α10 receptors and calcium concentration on conotoxin inhibition of ACh-evoked currents heterologously expressed in Xenopus oocytes. We have altered intracellular and extracelluar calcium concentrations, and the ratio of α9 and α10 subunit mRNA to change the relative abundance of the subunits to infer stoichiometry. Our data show that Vc1.1, but not RgIA or atropine, inhibits α9α10 receptors in a biphasic manner under the varying conditions and infer that these receptors exist in at least two stoichiometric forms.

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