



Functional characterization of alpha9-containing cholinergic nicotinic receptors in the rat adrenal medulla: implication in stress-induced functional plasticity

Submitted by Emmanuel Lemoine on Tue, 02/24/2015 - 15:29

Titre	Functional characterization of alpha9-containing cholinergic nicotinic receptors in the rat adrenal medulla: implication in stress-induced functional plasticity
Type de publication	Article de revue
Auteur	Colomer, C. [1], Olivos-Ore, L. A [2], Vincent, A. [3], McIntosh, J. M [4], Artalejo, A. R [5], Guérineau, Nathalie C [6]
Editeur	Society for Neuroscience
Type	Article scientifique dans une revue à comité de lecture
Année	2010
Langue	Anglais
Date	2010
Numéro	19
Pagination	6732 - 42
Volume	30
Titre de la revue	The Journal of Neuroscience
ISSN	1529-2401
Mots-clés	Acetylcholine/metabolism [7], Animals [8], Cold Temperature [9], diffusion [10], Excitatory Postsynaptic Potentials/physiology [11], Gap Junctions/physiology [12], In Vitro Techniques [13], Isoquinolines [14], Medulla Oblongata/physiology [15], Neural Inhibition/physiology [16], Neuronal Plasticity/physiology [17], Neurons/physiology [18], Rats [19], Rats, Wistar [20], Receptors, Nicotinic/metabolism [21], Stress, Physiological/physiology [22], Synaptic Transmission/physiology [23], Synaptophysin/metabolism [24], Time Factors [25], Up-Regulation [26]

An increase in circulating adrenal catecholamine levels constitutes one of the mechanisms whereby organisms cope with stress. Accordingly, stimulus-secretion coupling within the stressed adrenal medullary tissue undergoes persistent remodeling. In particular, cholinergic synaptic neurotransmission between splanchnic nerve terminals and chromaffin cells is upregulated in stressed rats. Since synaptic transmission is mainly supported by activation of postsynaptic neuronal acetylcholine nicotinic receptors (nAChRs), we focused our study on the role of alpha9-containing nAChRs, which have been recently described in chromaffin cells. Taking advantage of their specific blockade by the alpha-conotoxin RgIA (alpha-RgIA), we unveil novel functional roles for these receptors in the stimulus-secretion coupling of the medulla. First, we show that in rat acute adrenal slices, alpha9-containing nAChRs codistribute with synaptophysin and significantly contribute to EPSCs. Second, we show that these receptors are involved in the tonic inhibitory control exerted by cholinergic activity on gap junctional coupling between chromaffin cells, as evidenced by an increased Lucifer yellow diffusion within the medulla in alpha-RgIA-treated slices. Third, we unexpectedly found that alpha9-containing nAChRs dominantly (>70%) contribute to acetylcholine-induced current in cold-stressed rats, whereas alpha3 nAChRs are the main contributing channels in unstressed animals. Consistently, expression levels of alpha9 nAChR transcript and protein are overexpressed in cold-stressed rats. As a functional relevance, we propose that upregulation of alpha9-containing nAChR channels and ensuing dominant contribution in cholinergic signaling may be one of the mechanisms whereby adrenal medullary tissue appropriately adapts to increased splanchnic nerve electrical discharges occurring in stressful situations.

Résumé en anglais

URL de la notice <http://okina.univ-angers.fr/publications/ua8254> [27]

DOI [10.1523/JNEUROSCI.4997-09.2010](http://dx.doi.org/10.1523/JNEUROSCI.4997-09.2010) [28]

Lien vers le document <http://dx.doi.org/10.1523/JNEUROSCI.4997-09.2010> [28]

Titre abrégé J Neurosci

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