Neuronal control of localized inflammation through expressed nicotinic acetylcholine receptors: a study carried out in mice

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Abstract

Introduction Although the local inflammatory reactions are known to be regulated through cholinergic anti-inflammatory pathways, the exact subtypes of nicotinic acetylcholine receptors involved in neuroimmune modulation are not well identified.

Objectives Immunohistochemical localisation of α1 subunit of nicotinic acetylcholine receptors (α1nAChR) in sites of localised inflammation induced by injecting turpentine to the hind limbs of Balb/C mice.

Methods Localised inflammation and subsequent development of sterile abscesses was induced by injecting sterile turpentine subcutaneously into thighs of Balb/C mice. Sterile saline was used in the control.. Skin and muscle tissues of inflammatory sites were recovered from the animals after 48 hours and were stained with hematoxylin and eosin. Indirect immunohistochemistry was done using anti-α1nAChR as the primary antibody and biotinylated anti-rat IgG as the secondary antibody. Labeled streptavidin biotin (LSAB) technique was used with diaminobenzedene to detect the immunoreactivity (IR). Intensity of immunostaining was determined based upon a score of 0 - 3+ by qualitative computerised image analysis using FSX 100 Olympus microscope.

Results H and E stained slides showed polymorpho-nuclear leukocytes (PNL) infiltration at the abscess sites while the saline injected control tissue sections did not show PNL infiltration. A 2+ immunoreactivity (IR) of α1nAChRs was visible at peripheral zones of sterile abscesses where PNL infiltrations were high while the central area with necrotic tissue did not show IR. A subcutaneous lymph node found within the inflammatory region expressed IR of α1nAChR in its capsular sinuses, subcapsular sinuses and trabecular regions.

Conclusions The findings suggest the possible role of controlling localised inflammatory response by parasympathetic cholinergic nerves through α1nAChRs of inflammation sites.

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Introduction

The central nervous system is known to interact with the immune system through the autonomic nervous system and modify immune responses. Though the sympathetic system is the main component which controls the functions of lymphoid tissue, recent evidence shows significant influence by the cholinergic nervous system as well [1, 2]. Accordingly cholinergic anti-inflammatory mechanisms can inhibit the activation of macrophages and release of cytokines [2].

The cholinergic system, which uses acetylcholine as a neurotransmitter, is one of the excitatory pathways of the central nervous system [2]. Acetylcholine and multiple nicotinic acetylcholine receptor (nAChR) subunits are present on many cell types including endothelial cells and cells of the immune system [3, 4]. Thymocytes, thymic epithelial and myoid cells of immune organs express nAChRs on their cell surface [5]. Peripheral T cells express an unusual profile of muscle type nicotinic subunits, but their nAChR expression has not been identified [6]. In addition, expression of mRNA of α5, α9, α10, β1, β2, β4 nAChR subunits in the freshly isolated CD4 and CD8 T cells have been reported [7]. Gene expression of α1, α7 and α10 nAChRs also has been shown in mRNAs of primary human macrophages isolated from blood mononuclear cells [8].

Majority of the evidence shows the expression of α7nAChRs on monocytes and macrophages. [3]. α7nAChR is involved in the anti-inflammatory pathway [8]. Similarly, several studies show the crucial role of α7nAChR in the inhibition of excessive inflammation of many organs in the neuroimmune network [9, 10]. But the anatomical distribution of other nAChRs or their functional effects has not been studied.

A recent study shows that the parasympathetic cholinergic innervations are found predominantly in lymph nodes and spleen parenchyma in the supporting framework of reticulin fibres and consists mainly of α1nAChRs with minimum of α7nAChR in T cell and macrophage abundant regions of these tissues [11].

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