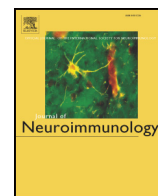




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Review article

A focus on mast cells and pain

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ABSTRACT

Mast cells (MCs) are immunocytes with secretory functions that act locally in peripheral tissues to modulate local hemodynamics, nociceptor activation and pain. They are also able to infiltrate the central nervous system (CNS), especially the spinal cord and the thalamus, but their cerebral function remains an enigma. A role in regulating the opening of the blood–brain barrier has been proposed. Paracrine-like action of MCs on synaptic transmission might also signal a modulation of the nervous system by the immune system. In this review, we examine the link between MCs and nociceptive process, at the periphery as well as in the CNS.

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Contents

Introduction	0
1. Peripheral and central mast cells	0
2. Role of peripheral mast cells in pain transmission	0
3. Do mast cells have a role in central integration of pain?	0
4. Conclusion	0
Acknowledgments	0
References	0

Introduction

Mast cells (MCs) are immune cells produced by the bone marrow (Gurish and Boyce, 2002). These cells pass the blood wall and quickly infiltrate most tissues, such as skin, mucous membranes, respiratory and gastrointestinal tracts, peritoneal cavity and meninges (Metcalf et al., 1997). MCs act by degranulation (Florenzano and Bentivoglio, 2000) and produce a plethora of mediators such as biogenic amines (histamine and serotonin), enzymes (acid hydrolases, phospholipases, chymase, trypsin and other proteases), cytokines (interleukin-1 to interleukin-6, interferon, transforming growth factor TGF, granulocyte-macrophage colony-stimulating factor, leukemia inhibitory factor, tumor necrosis factor TNF), lipid metabolites (leukotrienes, prostaglandins, platelet-activating factor), ATP (adenosine triphosphate), neuropeptides (vasoactive intestinal peptide), growth factors (nerve growth factor, NGF) and nitric oxide (Schwartz and Austen, 1980; Johnson and Krenger, 1992). MCs are also the only cells containing intracytoplasmic granules of proteoglycans, mainly heparin. Indeed, the

principle of specific staining of MCs on histological tissues is based on a metachromatic reaction of these proteoglycans with acidified toluidine blue (pH 2.3), which results in a shift of the natural color blue dye in characteristic red purple (Humason, 1972). MCs adapt and release mediators according to local tissue conditions (Lowman et al., 1988).

1. Peripheral and central mast cells

In the peripheral tissues, MCs are involved in the inflammatory reaction in response to exogenous pathogens and pro-inflammatory bioactive substances, such as cytokines and prostaglandins. They are also considered to be major effectors in IgE-associated hypersensitivity and in allergic responses such as asthma. More recently, the pathophysiological role of MCs have been recognized in various diseases affecting the periphery and/or the brain, such as atherosclerosis, pulmonary hypertension, autoimmune disorders, visceral diseases, cancer, ischemia–reperfusion injury, anxiety, Alzheimer's disease, migraine... (for review see Anand et al., 2012). In addition to the periphery, numerous data indicate that MCs are also resident in the central nervous system (CNS) of many animal species, including humans

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