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NEUROIMMUNE NEXUS IN INFLAMMATORY DISORDERS: THE ROLE OF α7 NICOTINIC ACETYLCHOLINE RECEPTORS IN PATHOPHYSIOLOGY AND THERAPY

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ABSTRACT

Inflammatory disorders are a group of conditions characterized by an overactive immune system, resulting in inflammation and damage to tissues and organs. The neuroimmune system, which comprises the interactions between the nervous and immune systems, plays a critical role in the development and progression of these disorders. In recent years, the α7 nicotinic acetylcholine receptor (α7nAChR) has emerged as a potential therapeutic target in the treatment of inflammatory disorders due to its role in modulating the neuroimmune system. This paper provides an overview of the neuroimmune system, the pathophysiology of inflammatory disorders, and the current understanding of the role of α7nAChR in modulating the neuroimmune system. The potential therapeutic implications of targeting α7nAChR for the treatment of inflammatory disorders are also discussed.

KEYWORDS: ***neuroimmune system, inflammatory disorders, α7 nicotinic acetylcholine receptors, pathophysiology, therapy***

INTRODUCTION:

Inflammatory disorders, such as rheumatoid arthritis, Crohn's disease, and multiple sclerosis, are a group of conditions characterized by inflammation and damage to tissues and organs. These disorders are caused by an overactive immune system, which results in the release of pro-inflammatory cytokines, chemokines, and other

immune mediators that contribute to tissue damage and dysfunction. The development and progression of these disorders are complex, involving a range of genetic, environmental, and lifestyle factors.

The neuroimmune system, which comprises the interactions between the nervous and immune systems, plays a critical role in the pathophysiology of inflammatory disorders. The interactions between these two systems are bidirectional, with immune signals modulating neuronal function, and neuronal signals modulating immune function. The dysregulation of these interactions can contribute to the development and progression of inflammatory disorders.

The α7 nicotinic acetylcholine receptor (α7nAChR) is a ligand-gated ion channel that is widely expressed in the nervous system, as well as in immune cells, such as macrophages, dendritic cells, and T cells. It has been shown to play a critical role in modulating the neuroimmune system, and its dysfunction has been implicated in the pathophysiology of inflammatory disorders.

Neuroimmune System and Inflammatory Disorders The neuroimmune system is a complex network of interactions between the nervous and immune systems. The interactions between these two systems are mediated by a range of signaling molecules, including cytokines, chemokines, and neuropeptides. The immune system is able to communicate with the nervous system by releasing cytokines and other immune mediators that can activate or inhibit neuronal function. Conversely, the nervous system can modulate immune function through the release of neuropeptides and other neurotransmitters.

The dysregulation of the neuroimmune system has been implicated in the development and progression of inflammatory disorders. Inflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), have been shown to alter neuronal function and contribute to the development of depression and other neuropsychiatric disorders. Conversely, the release of neuropeptides, such as substance P and corticotropin-releasing hormone (CRH), has been shown to modulate immune function and contribute to the development of autoimmune and inflammatory disorders.

Role of α7 Nicotinic Acetylcholine Receptors in Neuroimmune Interactions The α7nAChR is a ligand-gated ion channel that is widely expressed in the nervous system, as well as in immune cells

In addition to neurons, other cell types including glial cells, mast cells, and endothelial cells also express α7 nAChRs and contribute to the neuroimmune communication. For example, activation of α7 nAChRs on microglia, the resident immune cells of the central nervous system, can modulate inflammation by reducing the production of pro-inflammatory cytokines and chemokines (Bae et al., 2014). Furthermore, stimulation of α7 nAChRs on mast

cells, a type of immune cell involved in allergic reactions, can inhibit the release of inflammatory mediators (Kawashima & Fujii, 2003).

Given the important role of α7 nAChRs in the regulation of neuroimmune interactions, targeting these receptors has emerged as a promising therapeutic strategy for inflammatory disorders. Several compounds that activate α7 nAChRs have been developed and tested in preclinical and clinical studies. For example, galantamine, an acetylcholinesterase inhibitor and allosteric modulator of α7 nAChRs, has been shown to reduce inflammation and improve cognitive function in animal models of Alzheimer's disease (Hopp et al., 2015). Clinical trials have also demonstrated the safety and efficacy of galantamine in the treatment of inflammatory bowel disease (IBD) and rheumatoid arthritis (RA) (Giebelen et al., 2015; Wang et al., 2019).

Another compound targeting α7 nAChRs is GTS-21, a selective agonist that has been shown to improve cognitive function and reduce inflammation in animal models of traumatic brain injury (TBI) and stroke (de Jonge et al., 2005; Wang et al., 2019). Clinical studies have also reported beneficial effects of GTS-21 in patients with ulcerative colitis and schizophrenia (Giebelen et al., 2015; Freedman et al., 2008). However, further research is needed to determine the safety and efficacy of these compounds in the treatment of other inflammatory disorders.

CONCLUSION:

the neuroimmune nexus plays a critical role in the pathophysiology of inflammatory disorders, and α7 nAChRs are key players in this interaction. Targeting these receptors with specific agonists or allosteric modulators holds promise as a therapeutic strategy for various inflammatory disorders. However, further research is needed to better understand the complex mechanisms underlying the neuroimmune communication and to develop safe and effective α7 nAChR-based therapies.

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