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Systemic inflammation and neurodegenerative disease

Marcella Reale
University "G. D'Annunzio", Italy

Low-grade inflammatory state is a pathological feature of a wide range of chronic conditions such as neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and multiple sclerosis. The association between inflammation and chronic conditions is widely recognised, and since inflammation inducers may be generated in a disease-specific manner, the issue of causality and the degree to which inflammation contributes and serves as a risk factor for the development of disease is not fully clarified. Communication between the systemic immune system and the central nervous system (CNS) is a critical component of the inflammatory response, and there is evidence for convergence in the mechanisms responsible for the sensing, transduction, and amplification of inflammatory processes that result in the production of neurotoxic mediators. Several studies have suggested that low-grade peripheral systemic inflammation is associated with increased cognitive decline, and that increased risk of developing Alzheimer disease (AD) may be associated with increased systemic inflammation.

Increased levels of inflammatory proteins have been found in the brains and plasma samples of patients with dementia. Proinflammatory cytokines, chemokines and prostaglandins promote neuronal death and plus a role in immune to brain communication by activating the central innate immune response, including microglial cells. Recently, the ability of the nervous system to modulate the cytokine production in the immune system was studied; and the so called "cholinergic anti-inflammatory pathway" is responsible of the brain-immune system interface. Knowledge about the cholinergic antiinflammatory pathway as a specific regulator of cytokine responses makes it possible to consider the crosstalk between the CNS and the immune system. Thus, keeping in mind the role of the cholinergic system in inflammation, in addition to the proinflammatory cytokines, the cholinergic agents may be considered as new and interesting therapeutic tools in the pharmacological treatments that may have relevance in neurodegenerative diseases.

e: mreale@unich.it

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