Published in final edited form as:

Curr Immunol Rev. 2010 August 1; 6(3): 149. doi:10.2174/157339510791823736.

Immunological regulation of the central nervous system: From physiological to pathological processes

Oscar Gonzalez-Perez^{1,2}

¹ Neuroscience Laboratory, Psychology School, University of Colima, Colima, Mexico 28040

² Neuroscience Department, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara. Guadalajara, Jal. Mexico 44340

The central nervous system (CNS) is an immune-privileged organ because a selective permeability to exchange blood cells and substances from the circulatory system. Nevertheless, increasing evidence indicates that an extensive bi-directional communication takes place between the CNS and the immune system. Thus, the psyconeuroimmunology has emerged as a relative novel discipline to study interactions among psychological processes, brain functioning and the immune system. This especial issue of the **Current Immunology Reviews** contains nine comprehensive articles addressing the interactions between the immune and nervous systems in either physiological or pathological conditions.

In an excellent review, Cordiglieri and Farina explain the role of astrocytes in initiating and tuning cerebral immune responses. Authors state that astrocytes promote or confine inflammatory processes and, in consequence, play a role in neuroprotection and CNS repair. Astrocytes act as immune-competent cells by secreting cytokines and chemokines, and participating in innate immunity. As reviewed by Tian and Rauvala, the communication between immune system and CNS is bi-directional, in fact, neurons participate in immune responses by controlling responses of microglia and T lymphocytes. Interestingly, the immune system also controls proliferation, differentiation, migration and self-renewal of adult neural stem cells, which reside in the wall of lateral ventricles of brain. Modulation of neural stem cells are mainly mediated by IL-6, IL-18, TNF- α , CNTF, LIF and IFN- γ [1–3].

Neuroinflammation plays a role in the etiology and/or progression of several neurological disorders. As reviewed by Ramos and Duran, rheumatoid arthritis is a systemic inflammatory disorder that affects the central and peripheral nervous system. As in other rheumatic diseases, TNF- α is one of the main mediators of CNS damage. Orozco et al. reviewed the effects of inflammatory reactions on neuronal excitability, cell survival impairment, and permeability to blood-borne molecules and cells. These pathological events and high levels of IL-1, IL-2, and TNF- α have been associated with epilepsy development and seizures.

Cytokines and chemokines also modulate cognitive and emotional processes in the absence of overt immunological, physiological, or psychological challenges. Psychological stress and glucocorticoid-related immunosuppression is reviewed by Jauregui et al. They explain that stress increases the levels of glucocorticoids, which target resident microglia and decrease the ability of these brain cells to proliferate, to produce pro-inflammatory cytokines, and to produce toxic radicals. Brain Leonard summarizes evidence indicating that

IL-1, IL-4, IL-6, IL-10, IL-13, IFN- α and TNF- α can affect cognitive and emotional processes as observed in major depression [4,5]. Pro-inflammatory cytokines affect neuronal signaling by enhancing the glutamatergic system, which stimulates the tryptophan-kynurenine pathway. In an excellent review, Müller and Schwarz explain that high levels of IL-8 during pregnancy are associated with an increased risk for schizophrenia in the offspring. In this landmark review, the authors indicate that infections of the CNS in early childhood increase risk for developing psychoses and that IL-6 serum levels are elevated in patients with an unfavourable course of mental disease.

This issue concludes with the striking proposal of Momin et al. who addressed the oncogenic and tumor-supporting potential of mesenchymal stem cells (**MSCs**) within the context of cancer treatment. This review states the risk for malignant transformation of MSCs, the *in vivo* interactions with tumor stroma and the immunosuppressive qualities of MSCs that facilitate evasion of the immune system by tumors.

In summary, increasing evidence indicates that cytokines and chemokines modulate cerebral functions through multiple signaling pathways. All these interactions affect neural remodeling, synaptic plasticity, neurotransmitter releasing, neuronal regeneration, brain aging, cognitive and emotional processes, and mental disease progression. All these events modulate cognitive and emotional processes, and brain disease predisposition/progression.

Acknowledgments

O.G-P was supported by CONACyT's grant (CB-2008-101476); and NIH/NINDS's grant (1K08NS055851)

References

1. Bauer S. Cytokine control of adult neural stem cells. *Ann N Y Acad Sci* 2009;1153:48–56. [PubMed: 19236327]
2. Miller RJ, et al. Chemokine action in the nervous system. *J Neurosci* 2008;28(46):11792–5. [PubMed: 19005041]
3. Bonecchi R, et al. Chemokines and chemokine receptors: an overview. *Front Biosci* 2009;14:540–51. [PubMed: 19273084]
4. Duman RS, Heninger GR, Nestler EJ. A molecular and cellular theory of depression. *Arch Gen Psychiatry* 1997;54(7):597–606. [PubMed: 9236543]
5. Capuron L, et al. Neurobehavioral effects of interferon-alpha in cancer patients: phenomenology and paroxetine responsiveness of symptom dimensions. *Neuropsychopharmacology* 2002;26(5):643–52. [PubMed: 11927189]