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GUEST EDITORIAL

Cytokines in the brain: neuropathological aspects

Damage to and/or death of brain neurones and glial cells underlie most of the major neurological diseases including stroke, brain trauma, cerebral ischaemia, neural inflammatory disorders, dementias (eg Alzheimer's disease), prion diseases, bacterial and viral infections such as HIV, HSV, and meningitis. There is no effective treatment for these conditions, but mounting evidence points to common underlying features, mediators and mechanisms in these neurological diseases despite their varied pathologies and symptomatic presentation. Most remarkable is the recent explosion in research implicating immune or inflammatory processes in acute and chronic neurological disease. There is now substantial evidence that the molecules which mediate these processes, known as cytokines, participate directly in the pathogenesis of many neurological diseases.

Cytokines are proteins released by activated immune cells which play a pivotal role in the development of immunological and physiological responses of the host to infection and inflammation. Regulation of these responses is critically dependent on the balance between distinct arrays of cytokines produced by different subsets of immunocytes. There is now strong evidence that several proinflammatory and anti-inflammatory cytokines are present in the brain and that central expression and functions of these molecules can be influenced by local and systemic insults. Cytokines and their receptors are expressed in many brain regions, including the hippocampus, hypothalamus and striatum, and all resident brain cells (neurones, glia and endothelial cells) can synthesize and respond to cytokines. In response to trauma, infiltrating blood cells will also produce cytokines in affected and distal brain areas. Despite its presence in the CNS, the cytokine network has not yet been widely explored as a drug target in brain disorders and injuries. The only exception is IFNβ which is used for the treatment of multiple sclerosis and probably acts by blocking synthesis and/or actions of proinflammatory cytokines.

Much has been learned during the past 5 years on the involvement of proinflammatory cytokines in the neurodegenerative processes which result from acute insults such as brain trauma and ischaemia, and chronic neuronal diseases of unknown aetiology, including Alzheimer's disease. At the cellular level, the role of microglia activation in the defence of the brain parenchyma against these insults and the conditions which are necessary for normally trafficking immune cells to stay in the CNS and recruit other inflammatory cells are becoming gradually understood. At the molecular level, the role of cytokines in the induction of the inducible forms of nitric oxide synthase (NOS type II) and prostaglandin synthesis enzyme (COX2), the regulation of neural cell's specific splicing of the β-amyloid precursor protein, and the path to cell death are now important issues in neurosciences. In terms of animal models, the development of transgenic mice overexpressing cytokines in the CNS or lacking the gene for a given cytokine or its receptor provides valuable tools for advancing our understanding of the CNS pathobiology of cytokines.

All these issues and still many others were discussed on the occasion of an international symposium on the neuropathological consequences of the expression of cytokines in the brain which was organised in Saint-Jean-de-Luz, France, on April 26–28, 1996, within the context of the BIOMED Concerted Action 'Cytokines in the Brain' and with the financial support of Association pour la Neuropsychopharmacologie and Institut International de Recherches Servier. The present issue of *Molecular Psychiatry* contains a section entitled 'Cytokines in the Brain,' with papers presented at that symposium and will give the reader an insight into this rapidly evolving area of neurosciences.

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