Pro- and anti-inflammatory mediators in neuroinflammation: focus on interleukin-1β and interleukin-10

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Neuroinflammation, characterized by activation of glial cells and production of inflammatory mediators, is a prominent feature of various pathological conditions in the central nervous system and is considered to contribute to disease. In recent studies, we focussed on the expression and action of pro- and anti-inflammatory mediators in the central nervous system (CNS) under various inflammatory conditions.
We found that interleukin-1β, as an example of a pro-inflammatory mediator, is expressed in macrophages and microglial cells in the brains of rats injected with bacterial lipopolysaccharide (LPS), in post-mortem brains of septic patients and in spinal cord of rats suffering from chronic-relapsing experimental Multiple Sclerosis (cr-EAE). Also in a culture of mixed glial cells, LPS induced the production of pro-inflammatory mediators (IL-1β, TNF-α, IL-6, NO). Anti-inflammatory cytokines (TGFβ, IL-4, IL-10) differentially reduced the production of these pro-inflammatory mediators with IL-10 being the most general inhibitor. Indeed, increased production of cellular IL-10 by lentiviral vector mediated gene transfer, reduced LPS-induced TNF-α production in various rat cells. In vivo, IL-10 modulated the LPS-induced febrile response in rats in a site-specific way, inducing IL-10 receptor I mRNA and reducing IL-1β levels at the site of LPS injection only. In addition, using quantitative RT-PCR, we determined the expression levels of a number of inflammatory and non-inflammatory genes in the spinal cord of rats suffering from cr-EAE. Four different clusters of genes were identified among which macrophage-related genes but not T-cell-related genes correlated with the neurological score. Finally, in post-mortem spinal cord of human MS cases, mRNA levels of various inflammatory mediators were studied by quantitative RT-PCR showing that expression levels depended upon the activity state of the lesion.
Together, our studies indicate that both pro- and anti-inflammatory mediators are expressed and active in the CNS under neuroinflammatory (LPS, cr-EAE, MS) conditions.

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