LPS effect on specific interleukin (IL) mRNA expression in the spleen and brain

Patricia Szot
VA Puget Sound Health Care System, USA

Neuroinflammation is proposed to be an important component in the development of several central nervous system (CNS) disorders including depression, Alzheimer’s disease (AD), Parkinson’s disease (PD), and traumatic brain injury (TBI). The intra-peritoneal (i.p.) administration of lipopolysaccharide (LPS) induces peripheral inflammation and neuroinflammation as evident by elevations in blood and brain levels of cytokines. However, the cellular and anatomical sources of these cytokines are not known. Here, we used in situ hybridization to examine in brain and spleen the sources of cytokine production after 3-injection regime previously shown to elevate cytokine levels in brain and blood. Administration of LPS significantly increased mRNA expression of interleukin (IL)-6 and -10 in the spleen, an important organ for an immune response, consistent with increases in blood levels for these cytokines after LPS. LPS significantly decreased IL-6 receptor (-6R) mRNA in the spleen, but had no effect on IL-7 or IL-7R mRNA. In the CNS, IL-6 mRNA was expressed in neurons prior to LPS in regions that include the cortex, cerebellum and hippocampus. After LPS, IL-6 mRNA expression in these neuronal populations was unchanged, but a diffuse non-neuronal pattern appeared throughout the brain. IL-6R mRNA showed a pattern of expression similar to IL-6 mRNA and LPS significantly elevated all regions, except cerebellum, mainly in animals which expressed the non-neuronal IL-6 mRNA after LPS. IL-10 mRNA was widely expressed in neurons in many discrete brain regions, with LPS tending to decrease expression in forebrain regions and increase it in hindbrain regions. IL-7 and IL-7R had limited expression mainly to the cerebellum. LPS had no effect on IL-7 or IL-7R mRNA in the CNS. These studies indicate that LPS induced neuroinflammation has unique effects on regional and cellular patterns in the CNS and splenic cytokine expression. It is apparent that LPS can affect neuronal and non-neuronal cells in the brain, with IL-6 demonstrating the greatest change.

Recent Publications

Biography
Patricia Szot as a long-term Member of the MIRECC research team at the VA Puget Sound Health Care System has provided substantial information on the expression of receptors and transmitter-synthesizing enzymes in the human and rodent brain. This has included autopsy brain material from Parkinson’s disease and Alzheimer’s or dementia patients. Due to the in situ hybridization and slice autoradiography technical expertise he has worked on the localized quantitation of some important regulatory proteins. These studies contribute to his understanding of the mechanisms of side effects and additional symptomatology observed, e.g., in Alzheimer’s disease and Parkinson’s disease-information which is of direct clinical relevance.

szot@uw.edu