EXPRESSIONS OF INTERLEUKIN-6 AND TUMOR NECROSIS FACTOR IN PERIPHERAL TISSUES AFTER INTRACRANIAL ADMINISTRATION OF INTERLEUKIN-1

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Interleukin (IL)-1 is a key cytokine for brain-mediated acute phase responses, such as fever, sleep, anorexia and adrenocortical activation. In this study, I investigated effects of central IL-1 on peripheral cytokine synthesis. Intracerebroventricular (icv) injection of recombinant human IL-1β (200 ng/rat) produced a remarkable increase in the serum IL-6 level in 2 h. The serum tumor necrosis factor (TNF) level was also increased transiently. Intraperitoneal injection of IL-1 at the same dose had no significant effects on serum IL-6 and TNF levels. Next, to determine whether the brain is also able to regulate the expression of these cytokines in peripheral tissues, I measured mRNA levels of IL-6 and TNF in spleen, thymus, liver and lung by Northern blot analysis. The cellular level of IL-6 mRNA increased in spleen 1-2 h, in thymus 2 h and in liver 2 h after icv injection of IL-1. TNF mRNA was also found to increase in spleen and liver, but not in thymus. The mRNA of IL-6 and TNF could not be detected in lung even after IL-1 injection. The effect of central IL-1 on peripheral cytokine expression was much suppressed by the pretreatment with chlorisondamine, a ganglionic blocker. Finally, to cofirm the pathophysiological significance of the IL-1-induced IL-6 response, I examined the response of haptoglobin, one of the major acute phase proteins regulated by IL-6. Icv injection of IL-1 increased both the plasma level and hepatic expression of haptoglobin following the increase in plasma IL-6 and TNF levels. Thus, brain IL-1 raises serum levels of IL-6 and TNF, probably through stimulation of their synthesis in several organs by sympathetic nerve activation, and thereby induces acute phase responses involving hepatic acute phase protein synthesis.