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The reciprocal relationship between heme oxygenase and nitric oxide synthase in the organs of lipopolysaccharide-treated rodents

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ABSTRACT

The production of nitric oxide (NO) by inducible NO synthase (NOS) and carbon monoxide (CO) by inducible heme oxygenase (HO) contributes greatly to endotoxemia. Reciprocal relationships have been proposed between the NO/NOS and CO/HO systems. However, the interaction between these systems during endotoxemia is unclear, and it is unknown whether the interactive behavior differs among organs. Using endotoxic rats, we studied the effects of the inducible NOS (iNOS) inhibitor L-canavanine (CAN), and the HO inhibitor zinc protoporphyrin (ZPP) on gene expression and protein levels of iNOS, endothelial NOS (eNOS), inducible HO (HO-1), and constitutive HO (HO-2) in the brain, lung, heart, liver and kidney tissue. Intravenous injection of LPS significantly increased iNOS and HO-1 gene expression in all organs. The effects of LPS on eNOS gene expression differed among organs, with increased expression in the liver and kidney, and no change in the lung, brain and heart. ZPP administration down-regulated the LPS-induced increase in HO-1 expression and produced a further increase in iNOS expression in all organs. These data suggest that the CO/HO system modifies the NO/NOS system in endotoxic organs, and that there were only minor organ-specific behaviors in terms of the relationship between these systems in the organs examined.

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