PARTICIPATION OF THE NITRIC OXIDE PATHWAY IN SEPSIS-INDUCED HYPOTHERMIA

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A few mechanisms have been suggested to be involved in sepsis-induced hypothermia, but no information exists on the role of nitric oxide (NO). In the present study, we assessed the participation of NO in sepsis-induced hypothermia by means of inhibition of NO synthase (NOS). Rats were anesthetized with 2,2,2-tribromoethanol and implanted with a polyethylene catheter into the jugular vein for administration of lipopolysaccharide (LPS) and a stainless steel guide cannula (0.7 mm o.d.) into the third cerebral ventricle for administration of the non-selective NOS inhibitor N^G-nitro-L-arginine methyl ester (L-NAME). After 1week of recovery the body temperature of awake and unrestrained rats was measured over a period of 5 hours at 15 min intervals by inserting a thermoprobe into the colon. The body temperature was measured before and after administration of LPS (1.5 mg/kg), L-NAME (250µg/1µl) or both treatments together. In order to determine the effect of the NOS inhibitor on LPS-induced hypothermia, L-NAME was injected i.c.v. 30 min before LPS injection. Control animals received the same volume of D-NAME i.c.v and sterile saline i.v. Animals injected with LPS showed a significant decrease in body temperature 60 minutes after LPS administration from 37.8±0.2 to 36.9±0.15°C ($P<0.002$). In euthermic animals L-NAME caused no significant change in body temperature. However, when L-NAME and LPS were combined, a reduction in the magnitude of LPS-induced hypothermia was observed, from 36.9±0.15 to 37.9±0.08°C ($P<0.001$). In conclusion, these findings are consistent with the notion that central NO pathway plays a key role mediating hypothermia elicited by endotoxaemia.

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