THERMOREGULATORY RESPONSE TO HYPOXIA AFTER INHIBITION OF THE CENTRAL HEME OXYGENASE-CARBON MONOXIDE PATHWAY

Flávia M. Paro, Alexandre A. Steiner and Luiz G.S. Branco, Faculty of Odontology of Ribeirao Preto and Faculty of Medicine of Ribeirao Preto -University of Sao Paulo, Ribeirao Preto, SP, Brazil.

A regulated decrease in body core temperature (Tc), called anapyrexia, has been described to occur in a wide variety of species and seems to be an important adaptive response, but little is known about the mechanisms involved. Recently, carbon monoxide (CO) has been shown to be involved in thermoregulation and fever, but no report exists about its role in hypoxia-induced anapyrexia. Endogenous CO arises from the catabolism of heme to biliverdine, free iron and carbon monoxide (CO), a process catalyzed by the enzyme heme oxygenase (HO). Since it has been reported that HO is overexpressed during hypoxia, the present study was designed to test the hypothesis that the central HO-CO pathway plays a role in hypoxia-induced anapyrexia. To this end, we used intracerebroventricular (i.c.v.) injection of the HO inhibitor zinc deuteroporphyrin 2,4-bis glycol (ZnDPBG; 200 nmol). Tc was determined in awake, unrestrained rats under each of the following three experimental conditions: 1. hypoxia (7% inspired O_2) only; 2. i.c.v. ZnDPBG or its vehicle administered to rats kept under normoxia; 3. i.c.v. ZnDPBG or its vehicle administered to rats exposed to hypoxia. I.c.v. pretreatment with ZnDPBG or its vehicle did not alter Tc during normoxia, confirming our previous observations that the central HO-CO pathway plays no tonic role in the maintenance of basal Tc. However, i.c.v. ZnDPBG exacerbated the anapirexia evoked by hypoxia. These data imply that the central HO-CO pathway is an important modulator of hypoxia-induced anapyrexia in rats with a key function in the prevention of excessive decreases in Tc.

Financial support: FAPESP, CNPq and PRONEX.

lgsbranc@usp.br