

The Effect Of Methane On Hypoxia-Induced Mitochondrial Calcium Homeostasis

Anna Nászai^a, László Juhász^a, Marietta Zita Poles^a, József Kaszaki^a, Mihály Boros^a

^a Institute of Surgical Research, Faculty of Medicine, University of Szeged, Szeged, Hungary;

Background: Ca²⁺ overload is common intracellular denominator of hypoxic-ischemic pathologies, leading to the opening of mitochondrial permeability transition pores (mPTP), non-selective Ca²⁺-efflux and apoptosis-mediated cell death. Previous studies have demonstrated anti-inflammatory properties for methane (CH₄), through a possible influence on mitochondrial function. Our aim was to investigate the in vivo effect of CH₄ on mitochondrial Ca²⁺ movements in a standardized model of hypoxemic hypoxia to gain insight into the mechanism of action. **Material and Methods:** Anaesthetized Sprague-Dawley rats were mechanically ventilated for 60 min with normoxic synthetic air (controls; n=7), hypoxic air (16% O₂; n=7) or hypoxic air-methane mixture (16% O₂+2.2% CH₄; n=7). Liver biopsies were taken to measure mitochondrial respiration and Ca²⁺ flux (CalciumGreen-5N) in parallel using high-resolution fluorespirometry (Oroboros, Austria). Endogenous Ca²⁺ release under anoxia and exogenous CaCl₂-stimulated (50 μM) Ca²⁺-fluxes were also determined. **Result:** Ventilation with hypoxic air did not influence the duration of CaCl₂-induced Ca²⁺-flux (efflux: 41±5s vs 39±14s, P<0.05), whereas endogenous Ca²⁺ release was reduced (ΔF/F: 0.135±0.06 vs 0.351±0.06). CH₄ addition to the hypoxic air markedly increased the Ca²⁺ storage capacity, prolonged the duration of Ca²⁺-efflux (to 176±132s) and significantly improved the endogenous Ca²⁺ release (to 0.23±0.08). **Conclusion:** Conclusion: CH₄ inhibits the mPTP-dependent Ca²⁺ efflux and ameliorates the anoxic release of endogenous Ca²⁺. This novel inhibitory effect on mPTP contributes to the preservation of electron transport system function and Ca²⁺ homeostasis under hypoxia. Grant Support: NKFI 120232, the UNKP-18-2 New National Excellence Program of the Ministry of Human Capacities and Szeged Scientist Academy (EMMI, TSZ:34232-3/2016/INTFIN).