

In the presence of the ATP-synthase inhibitor, oligomycin, oxidative phosphorylation was inhibited but low level of substrate level phosphorylation was detected in the presence of α -KG, but not with succinate as a respiratory substrate. In the presence of oligomycin, MB stimulated respiration with α -KG and succinate, respectively. But the rate of ATP synthesis was increased only in α -KG energized mitochondria when succinyl-CoA was formed. In this case, when the ATP synthase was inhibited, the generated ATP was derived from the substrate level phosphorylation. The formed ATP can contribute to the alleviation of energetic insufficiency.

It is concluded that MB mediated stimulation of substrate level phosphorylation can be an important factor to maintain energetic competence of mitochondria.

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Succinate dehydrogenase regulation via oxaloacetate in brain mitochondria

Sváb Gergely^{1,2}, Horvath Gergo², Komlódi Tímea¹, Ádám-Vizi Veronika², Tretter László³

¹Semmelweis University, Department of Medical Biochemistry, Budapest,

²Department of Medical Biochemistry, MTA-SE Laboratory for Neurobiochemistry, Semmelweis University, Budapest,

Succinate dehydrogenase (SDH) a mitochondrial enzyme participates in the respiratory chain and also in the citrate-cycle. SDH has a well-known metabolic role but according to recent studies it also participates in hypoxia-induced cellular reactions and tumorigenesis.

We have observed earlier that at low concentrations of succinate ADP inhibited oxygen consumption in brain mitochondria, but this phenomenon was not detected in kidney and liver mitochondria.

The aim of the present study was to investigate the organ specific regulation of SDH in order to clarify the regulatory mechanisms responsible for the ADP induced respiratory depression. Experiments were carried out on isolated guinea pig brain and kidney mitochondria. Mitochondrial respiration was measured by Clark-type electrode. Multiple mitochondrial enzymes activities were determined spectrophotometrically, for example SDH, malic enzyme, phosphoenolpyruvate-carboxykinase (PEPCK) and hydroxy-oxoglutarate aldolase (HOGA) in the two organs. Oxygen consumption measurements pointed out that the maximal O₂ consumption in the presence of succinate was similar in brain and kidney mitochondria at saturating conditions. We assumed that the cause of inhibition at lower succinate concentration

was the endogenously produced oxaloacetate (OA). Inhibitor titration of SDH activity showed no difference, OA inhibited SDH in both organs to a similar extent. We also addressed the kinetics of OA elimination; therefore the role of different substrates and enzymes in the OA metabolism was investigated. Addition of rotenone, a respiratory chain inhibitor, stopped the utilization of reduced coenzymes produced by the citrate-cycle, also decreased the OA production. Adding pyruvate to the mitochondria the formation of citrate from OA increased. The mitochondrial presence of malic enzyme increased the production of pyruvate from malate. The HOGA enzyme formed pyruvate from OA. These enzymes had dual effect by decreasing the malate or OA and increasing pyruvate concentration, respectively. PEPCK directly eliminated OA and produced phosphoenolpyruvate. The enzyme activity measurements showed that HOGA and PEPCK had crucial role in the OA elimination.

The reason behind the organ specificity of ADP-mediated inhibition of succinate respiration could be the various mechanism and efficacy of OA elimination in the two organs. Our results showed that PEPCK and HOGA enzymes take part in the OA concentration regulation, which is the main metabolic inhibitor of SDH.

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Microglia: diversity in energy metabolism

Nagy Adam M¹, Toth Krisztina¹, Torok Eszter¹, Fekete Rebeka², Kornyei Zsuzsa², Koncsos Gabor³, Giricz Zoltan³, Adam-Vizi Veronika¹, Tretter Laszlo¹

¹Semmelweis University, Department of Medical Biochemistry and MTA-SE, Laboratory for Neurobiochemistry, Budapest, ²Institute of Experimental Medicine of the Hungarian Academy of Sciences, Laboratory of Cellular and Developmental Neurobiology, Budapest, ³Semmelweis University, Department of Pharmacology and Pharmacotherapy, Budapest,

Microglia are resident immune cells in the central nervous system (CNS), showing high dynamic activity. Upon chemotactic stimuli these cells can enter into metabolically different compartments of the CNS. Multiple energy compounds in the cerebrospinal fluid can serve as metabolic fuels for the brain, however, the exact compartmentation to different brain regions and cell types still remains unclear. In this study we investigated which energy substrates can support the oxidative metabolism of microglial cells.