

PhD Scientific Meeting



SUCCINATE DEHYDROGENASE REGULATION VIA OXALOACETATE IN BRAIN MITOCHONDRIA

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Introduction

Succinate dehydrogenase (SDH) a mitochondrial enzyme participates in the respiratory chain and 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.

Aim

Our goal was to investigate the SDH organ specific regulation. In our experiments we examined which regulatory mechanism stands behind the ADP induced respiratory depression.

Methods

Our experiments were done on isolated brain and kidney mitochondria from guinea pigs. The mitochondrial respiration was measured by Clark-type electrode. The SDH, malic enzyme, phosphoenolpyruvate-carboxykinase (PEPCK) and hydroxy-oxoglutarate aldolase (HOGA) was determined spectrophotometrically.

Results

Oxygen consumption measurements pointed out that the maximal respiration in the presence of succinate was similar in both organs at saturating conditions. We assumed the cause of inhibition at lower succinate concentration was the endogenously produced oxaloacetate (OA). The OA inhibited SDH in both organs to a similar extent. Addition of rotenone a respiratory chain inhibitor abolished the ADP-mediated respiratory inhibition. Mitochondria supported with low succinate and pyruvate also increased oxygen consumption after adding ADP. The mitochondrial malic enzyme activity was five times higher in brain mitochondria. Threefold higher PEPCK enzyme was measured in kidney mitochondria.

Conclusion

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

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