? -NADH REVERTS THE SUCCINATE DEHYDROGENASE ACTIVITY INHIBITION INDUCED BY METHYLMALONATE

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Methylmalonic acidemias are metabolic disorders caused by a severe deficiency of methylmalonyl-CoA mutase activity, which are characterized by neurological dysfunction including convulsions. Furthermore, it has been proposed that MMA inhibits succinate dehydrogenase (SDH) leading to ATP depletion, lactate accumulation and excitotoxic damage. In this study we investigated whether the enzymatic medium reduction alters the activity of SDH or its inhibition by MMA. SDH activity was determined in cerebral cortex homogenates, using 2-(p-iodophenyl)-3-(p-nitrophenyl)-5-phenyltetrazolium chloride, as the electorn acceptor. The reduction enzymatic medium was promoted by preincubation with ß-NADH (160 µM). The preincubation of ß-NADH reverted the MMA–induced SDH activity inhibition [F(1,5)=9,31; p=0,028]. In addition, was determined of kinetic parameters (Km, Vmax) of SDH preincubated in the presence and absence of ß-NADH. The K_m of SDH preincubated with ß-NADH (K_m=0,216 nmol INT/mg protein/min) was different of the K_m of SDH preincubated in the absence of the ß-NADH (Km=0,272nmol INT/mg protein/min) [T(2)=10,375; p=0,009]. The presence of ß-NADH in the incubation medium did not alter V_{max}= 4,72±0,28.10-8 mol INT/mg protein/min) [T(2)=-1,0; p=0,423]. Our results suggest that enzymatic medium reduction protects against MMA-induced SDH activity inhibition. Key words: L-methylmalonic acid, methylmalonic acidemias, succinate dehydrogenase,