Effect of ethylmalonic acids on acetylcholinesterase activity and expression in young rats

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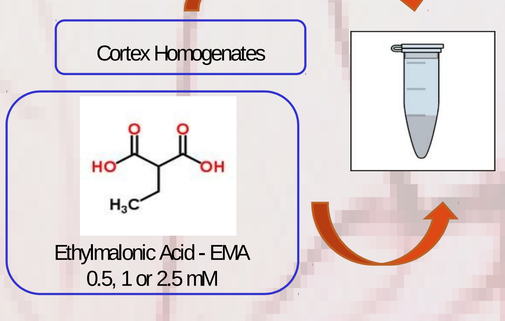
Introduction

Patients suffering from short-chain acyl-CoA dehydrogenase deficiency (SCADD) and ethylmalonic encephalopathy (EE) present high concentrations of ethylmalonic acid (EMA) in tissues and body fluids. They present neurological heterogeneous alterations, including developmental delay and neuromuscular symptoms [1]. In this work we evaluate the *in vivo* and *in vitro* effects of EMA on acetylcholinesterase (AChE) activity and its expression in cerebral cortex, striatum and hippocampus.

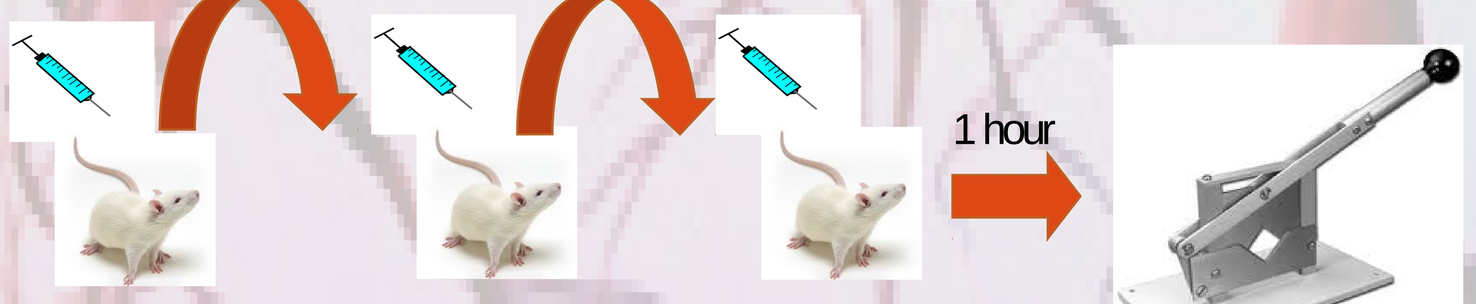
Materials and methods

In vitro experiment [2]



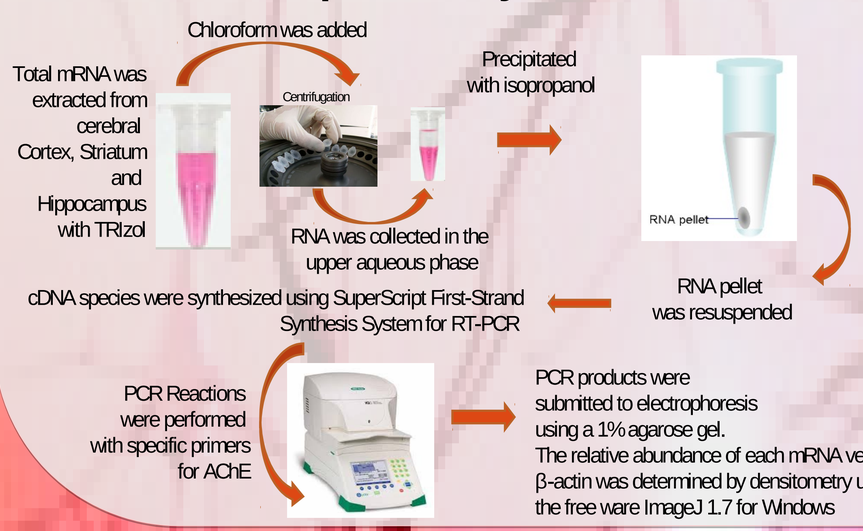
In vivo experiment [3]

- 30-day old male Wistar
- subcutaneous injections
- EMA 6 µmol/g body weight
- saline solution as control group



AChE activity and mRNA expression

AChE expression by RT-PCR [4]



Results

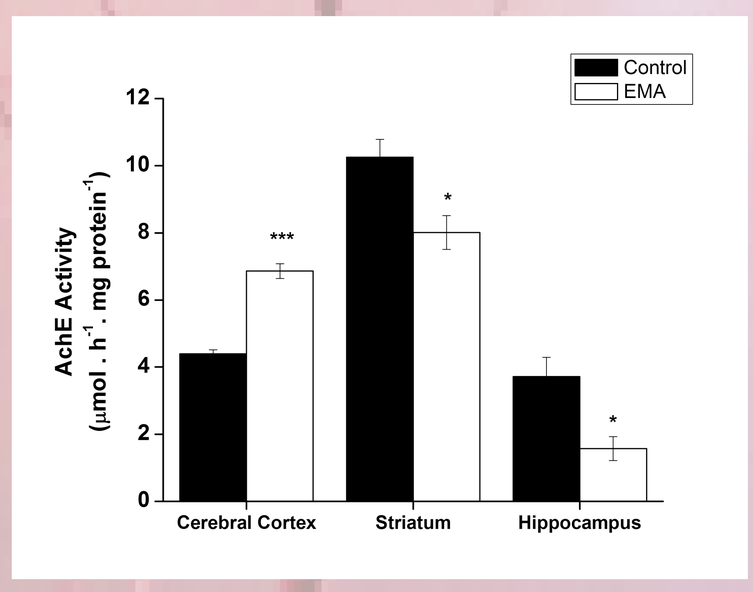


Figure 1. ***In vivo*** **effect of Ethylmalonic Acid (EMA) on AChE activity (µmol AChE . h -1 . mg protein-1) in cerebral cortex, striatum and hippocampus of 30-day-old rats. Significant difference between cortex group were detected.**

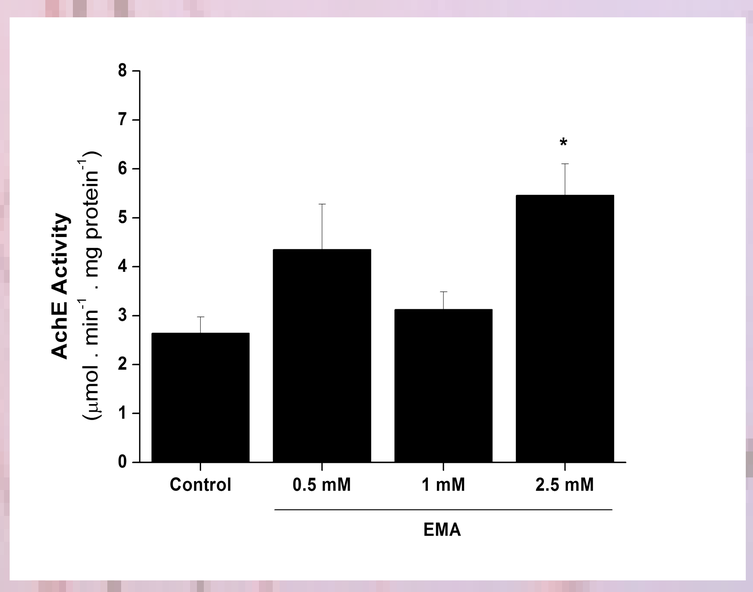


Figure 2. ***In vitro*** **effect of EMA on AChE activity (µmol AChE . h -1 . mg protein-1) in cerebral cortex homogenates preincubated at 37 °C for 60 minutes shows increase in AChE activity at 0.5, 1 or 2.5 mM EMA.**

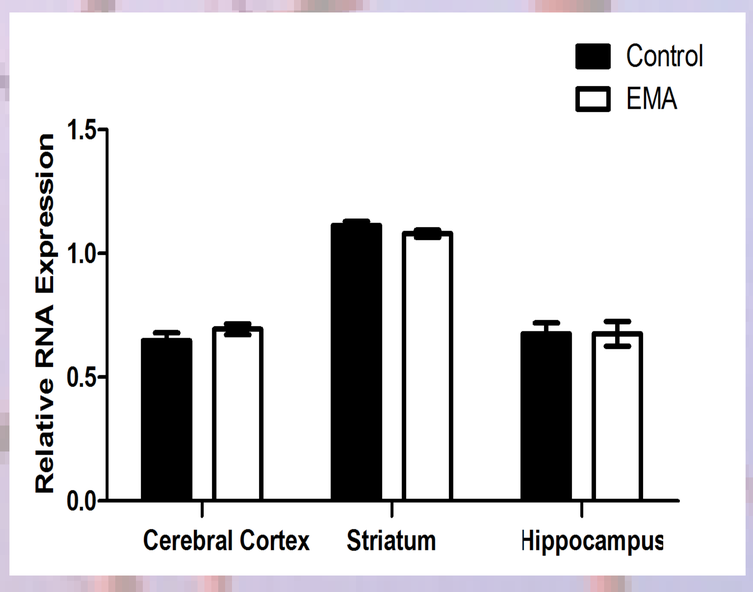


Figure 3. Relative mRNA AChE expression in cortex, striatum and hippocampus in the ***in vivo*** **experiments. No significant difference between groups was detected.**

Data are shown as mean ± standard deviation of experiments in duplicate (n=5) and are expressed in Arbritary Units (AU). ****p*<0,05 compared to control group (one-way ANOVA folowed by the Ducan's multiple range test).

Conclusions

It was observed that AChE activity was increased in cerebral cortex in both *in vivo* and *in vitro* experiments, when compared to control group. Regarding to AChE expression, it was not observed any difference between groups. Taken together, the results presented herein demonstrate that EMA caused alterations on AChE activity in cerebral cortex of young rat, which could collaborate to the brain damage found in patients affected by SCADD and EE.

CAPES Coordenação de Aprefeiçoamento de Pessoal de Nível Superior
CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico
FAPESC Fundação de Apoio à Pesquisa Científica e Tecnológica do Estado de Santa Catarina
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3) Ferreira et al. Effect of in vivo administration of ethylmalonic acid on energy metabolism in rat tissues. Metab Brain Dis. 2006. 21:29-39
4) Schuck et al Ethylmalonic Acid Modulates Na+,K+-ATPase Activity and mRNA Levels in Rat Cerebral Cortex. Synapse. 2012.