Effect of Acetyl-l-Carnitine on cerebral energy and phospholipid metabolism in adult and aged rats. Study by P-31 and H-1 NMR spectroscopy

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INTRODUCTION

Carnitine-acetylcarnitine system plays a fundamental role in the lipid metabolism, acting as carrier for the transport of long and short fatty acid chain across mitochondrial membrane. In a previous work we have reported a significant increase in the glycerophosphorylcholine (GPC) levels in aged rat brain, consistent with the hypothesis of age-dependent changes in the membrane phospholipid metabolism (1). In the present study we have investigated the effects of Acetyl-l-Carnitine (ALC) on energy and phospholipid metabolism in adult and aged rat brains P-31 and H-1 NMR spectroscopy.

MATERIALS AND METHODS

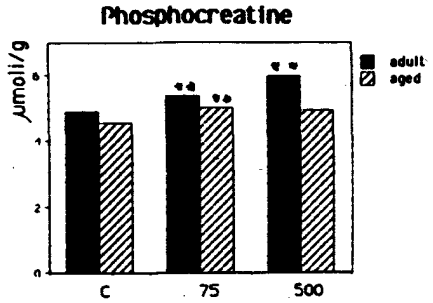
Fisher 344 male rats of 6 (adult) and 24 (aged) months old were. Both adult (n=8) and aged (n=10) rats were treated (i.p.) with 75 and 500 mg/kg b.w. of ALC; control rats received only distillated water. Anaesthesia was induced with 1.5% halothane and N_2O/O_2 70/30 and maintained with 0.5% halothane and N_2O/O_2 70/30. Animals were sacrified by funnel freeze technique as described in (1,2). Brains were extracted by modified Bligh-Dyer procedure (2). P-31 and H-1 NMR spectra were carried out on Varian XL 300 spectrometer.

RESULTS

In aged rat brains a significant increase of GPC levels has been evidenced in respect to adult ones. On the contrary no variations have been observe in phosphocreatine (PCr), creatine (Cr), ATP, ADP, Pi, lactate, glycerophosphorylethanolamine (GPE), phosphorylethanolamine (PEt), phosphorylcholine (PCho) levels. In both adult and aged rats the treatment with ALC induces a significant increase in PCr levels and a decrease in lactate and sugar phosphate levels. On the contrary, a different trend in GPC levels has been observed between adult (increase) and aged (decrease) rats depending on ALC concentrations.

DISCUSSION

The results obtained are in agreement with our previous data (1):no variations in ATP, ADP, PCr, Cr, Pi, lactate and sugar phosphate levels in aged rat brain as compared to adult ones. The changes in GPC levels observed in aged rat brain are consistent with the hypothesis of age-dependent alterations on the activity of membrane enzymes involved in the deacylation-reacylation process (1). The treatment with ALC induced a decrease in brain glucose utilization, as demonstrated by reduction of lactate and sugar phosphate levels, stimulating the utilization of alternative energy source (i.e. endogenous free fatty acid). In agree-



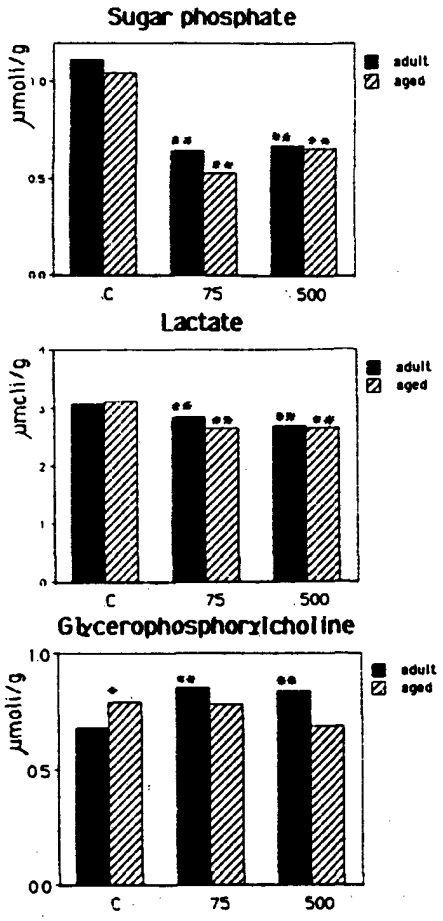


Fig. 1 Changes in PCr, lactate, sugar phosphate and GPC levels in adult and aged rat brain depending on ALC treatment. p 0.05* adult vs aged**control vs treatment.

ment with this explanation, the results show an increase in PCr levels (adult and aged rats) and GPC levels (adult), due to the treatment with ALC. Furthermore, the observed changes in GPC levels in aged rat brains could indicate a modulating effect of ALC on the activity of enzymes involved in the acylation-reacylation processes.

REFERENCES

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