The action of acetyl-L-carnitine in dopaminergic neurotransmission

Lidia Cunha [1], Krisztian Szigeti [2], Domokos Mathe [3] and Luís Metello [1]

1 Nuclear Medicine Department, IsoPor SA & ESTSP.IPP, Porto, Portugal

2 Institute of Biophysics & Radiation Biology, Semmelweis University, Budapest, Hungary

3 CROmed Ltd, Budapest, Hungary

Abstract

1807

Objectives Acetyl-L-Carnitine (ALC) has been described as playing a neuroprotective effect against a variety of substances. However, the molecular mechanisms underlying its action, particularly regarding the induction of changes in neurotransmitter system, are still not fully understood. Using both a cell line and an animal model of exposure to methamphetamine (METH), we aim to contribute to clarify the mechanism by which the administration of ALC alters neurotransmitter release.

Methods Rat pheochromocytoma PC12 cells were treated with increasing doses of ALC (0.01 to 1.0 mM) alone or in combination with METH 1.0 or 100 μM for 24h or 72h. When ALC and METH were combined, pre-treatment with ALC preceded METH exposure in 30 min. Dopamine (DA) content was determined by high performance liquid chromatography. In vivo assays using C57BL/6J mice were performed to assess DA striatal binding. Mice were divided into 4 groups, according to different treatments: group 1 (control), group 2 (ALC, 100 mg/kg), group 3 (METH, 10 mg/kg) and group 4 (ALC+METH). 123I-IBZM was injected and images were acquired in a SPECT/CT scanner (NanoSPECT/CT, Mediso, Hungary) 70 minutes after injection. Regions of interest were drawn over the left and right striatum as well as in the cerebellum in order to determine the striatal binding ratio.

Results Increased intracellular levels of DA were observed in PC12 cells at 24h and 72h after the administration of ALC. When cells were treated with METH 100 μM, intracellular levels of DA were clearly decreased. ALC was effective in preventing the METH-induced decrease

of DA concentration ($p<0.0001$). In mice, the challenge with a single dose of 10 mg/kg of METH decreased striatal D2R binding ratios relative to the control group between 20% and 30%. Interestingly, over time, ALC was able to reverse the decrease on the radiotracer binding induced by METH.

Conclusions The present study demonstrates a possible effect of ALC over METH-induced DA release.