ALC NEUROPROTECTION THROUGH AUTOPHAGY AND UPS ACTIVITY

Bravo J[1], Cunha L[1,2], Fernandes S[1,2], Binienda Z[3], SummavielleT[1,2]

1-Neuroprotection Lab, Molecular Neurobiology, IBMC, UP, Portugal;

2-ESTSP-IPP, Portugal;

3-Neurophysiology Lab., NCTR- FDA, AK, USA

Background: Acetyl–L-carnitine (ALC) has beneficial effects in neurodegenerative diseases and was shown to be protective against exposure to methamphetamine (METH) reducing mitochondrial dysfunction and oxidative stress. However, the mechanisms underlying ALC action are still unknown, limiting its putative therapeutic use.

Aims: The present study aimed to clarify the possible role of ALC in improving both ubiquitin-proteosome system (UPS) activity and autophagy. Therefore we have exposed PC12 cells to increasing concentrations of ALC (0.01, 0.1 and 1.0 mM) and METH (1 and 100 µM) for 24h or 72h and monitored by Western blot the alterations induced to α-synuclein, ubiquitin, cathepsin D and bax, keys proteins in UPS and autophagy.

Results: α-Synuclein is typically increased when there is impaired UPS function, as expected, exposure to METH 1 µM increased expression of α-synuclein both at 24h and 72h, importantly a pre-treatment with ALC 1.0 mM prevented this effect. Ubiquitin expression seems to be increased after METH exposure, however a beneficial effect of ALC in only significant for high concentrations of METH. Cathepsin D, a marker of autophagy activation, was reduced in cells exposed to METH 1µM but transitorily increased when cells were pre-treated with ALC. Bax expression was significantly decreased in cells treated with ALC even in the absence of METH, showing that ALC acts as an anti-apoptotic substance. However, the combined action of ALC and METH on Bax expression was unclear.

Conclusion: Collectively, these results are indicative that the protection conferred by ALC is probably linked to a transitory increase of autophagy and decreased protein misfolding, but not to improved UPS activity.

Relevance: These data reveals new ALC features that can be instrumental in designing future strategies for therapeutic use.

Foi decidido que não será apresentada a versão integral deste documento.

Para obtenção de mais informações:

www.nucmedonline.net

cursomedicinanuclear@gmail.com

It has been decided that it would not be shown the entire version of this document.

To obtain more informations:

www.nucmedonline.net

cursomedicinanuclear@gmail.com