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Further steps in the role of autophagy in methamphetamine toxicity

Silvio Paparelli[1], Gloria Lazzeri[1], Marco Gesi[1], Mariangela Guagnozzi[1], Fabio Concetti[2,3], Franco Venanzi[2,4] and Francesco Fornai[1]

[1] Human Anatomy-Department of Translational Research and new Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
[2] School of Biosciences and Biotechnologies, University of Camerino, Camerino, Italy
[3] I.R.C.C.S. Neuromed, Pozzilli, Italy
[4] CureLab Oncology (Boston USA)

Methamphetamine (METH) abuse is known to cause a variety of disorders Incluing depression and psychosis. METH induces nigrostriatal damage in animal models and in humans consisting of intracellular alterations in nigral DA cell bodies, degeneration of DA terminals and decreased striatal DA levels. Following METH exposure, the number of nigral cell bodies is quite preserved but autophagy-like vacuoles and cytoplamic accumulation of misfolded proteins are observed. The DA-containing PC12 cell lines represent a simple model of METH toxicity and are commonly used in vitro to understand the pathophysiology of DA neurons.

We analyzed at morphological level the effects of plasmid-dependent autophagy modulation on METH toxicity in PC12 cell line.

We profited from the high number of authophagic like vacuoles induced by low doses of METH in order to isolate cell fraction in which to study their origin, dynamic structure and molecular composition.

We found that authophagy-like vacuoles are positive both for autophagy and proteasome markers. The modulation of autophagy via a p62 containing plasmid protected from METH toxicity, while the inhibition of autophagy machinery worsened METH neurotoxicity.

The present data substantiate the protective role of the autophagy machinery in METH-induced DA toxicity where the pro-autophagy protein p62 possesses a key role.

Key words

Methamphetamine, PC12, transmission electron microscopy, autophagy.