IJAE
Vol. 117, n. 2 (Supplement): 144, 2012
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Ultrastuctural alteration after METH treatment

Silvio Paparelli[1], Carla L. Busceti[2], Cristina Demi[1], Filippo S. Giorgi[3], Mariangela Guagnozzi[1] and Antonio Paparelli[1]

[1] Department of Human Morphology and Applied Biology, University of Pisa, Pisa, Italy
[2] IRCCS Neuromed, Pozzilli (IS), Italy
[3] Department of Neuroscience, Neurological Clinic, University of Pisa, Pisa, Italy

Methamphetamine (METH) is an illicit recreational drug known to cause a variety of mental disorders, including anxiety, confusion, and hallucination. Exposure to METH induces nigrostriatal damage in experimental animal models and in humans. METH leads to cellular alterations of the dopamine (DA) system consisting of striatal DA release that produces an oxidative stress, and eventually, causes intracellular alterations in nigral DA cell bodies, degeneration of DA terminals and decreases striatal DA levels. However, the number of DA neurons in the substantia nigra pars compacta seems not to be affected by METH, but their cytoplasm features autophagic-like vacuolization and cytoplasmic accumulation of α-synuclein-, ubiquitin- and parkin-positive inclusion-like bodies.

The PC12 cell line, derived from the rat pheochromocytoma, is commonly used as an in vitro model to understand the physiology of central DA neurons. A number of factors contribute to the wide use of PC12 cells: they are not expensive, easy to handle, and mimic many features of central DA neurons. In particular they contain DA and present DA receptor on the external membrane.

In light of this evidence using the PC12 cell line we analyzed the ultrastructural alterations induced by METH treatment (0.1-10 μM for 72 h). On the other hand the electron microscopy technique represents the gold standard for the study of the cell death, apoptosis, and the occurrence of autophagy vacuoles. Although the neurotransmitter pattern of PC12 cells is close to DA neurons, ultrastructural morphometry demonstrates that, in baseline conditions, PC12 cells possess very low vesicle density and low catecholamine levels. Again, compartmentalization of secretory elements in PC12 cells is already pronounced in baseline conditions, while it is only slightly affected following catecholamine-releasing stimuli. This low flexibility is caused by the low ability of PC12 cells to compensate for sustained catecholamine release, due both to non-sufficient DA synthesis and poor DA storage mechanisms.

Moreover increasing the dose of METH leads to a higher number of apoptotic cells and an higher concentration of autophagy-like vacuoles per cell. Interestingly these vacuoles were immunoreactive for the protein of the autophagy pathway and for α-synuclein.

Noteworthy, METH induces mithocondrial alterations consisting in matrix dilution and disrupted cristae. These latter findings pose METH as a robust mitochondrial neurotoxin reminiscent of MPTP and rotenone.

Keywords: Drugs of abuse, mithochondria, dopamine, amphetamines derivatives.