IJAE
Vol. 119, n. 1 (Supplement): 78, 2014
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Impairment of the autophagic flux in astrocytes intoxicated by trimethyltin

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Autophagy is generally considered a degradation pathway involved in many neurodegenerative processes. It is induced by different stress conditions such as starvation improving cell survival. Conversely, an excess activation of autophagy can drive cells to death by a sort of self-cannibalism. Toxic compounds such as arsenic and lead have been described to affect autophagy in a different way by blocking the correct execution of this pathway. Our previous results show that in hippocampal neuronal cultures the toxic compound trimethyltin (TMT) determines the formation of autophagic vacuoles and that autophagy inducers (lithum, rapamycin) improves neuronal survival (Fabrizi et al., 2012). The present data show that in astrocytes TMT similarly activates the autophagic pathway. Differently from neurons, in astrocytes autophagy inducers are ineffective in modifying cell survival. Moreover, the analysis of the LC3B conversion show in TMT-treated astrocytes a precocious block of the late stages of autophagy which ultimately leads to p62 accumulation, nrf-2 nuclear translocation and induction of ARE-responsive genes.

References

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Keywords
Autophagy, glia, environmental neurotoxins, LC3.