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Mitophagy in post-mitotic neurons

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Mitophagy is a novel identified autophagic process through which defective and malfunctioning mitochondria are degraded or recycled. The balance between this process and mitochondrial biogenesis is crucial for post-mitotic neurons' survival, as mitochondria are the primary energetic source required for the formation and function of axon terminals and dendritic spines (Amadoro et al 2014). As other cell types, neuronal populations also continually modulate size and number of these organelles, according to the variable energy demands and metabolic states throughout the entire lifetime and/or different sub-cellular compartments. In polarized neurons removal of damaged mitochondria can be a bioenergetically demanding task because these organelles need to be actively transported from the axons and dendrites in order to fuse to cell body resident lysosomes (Wang et al 2006).

Physiologically aging as well as numerous human neurodegenerative disease, including Parkison's disease, Huntington's disease, amyotrophic lateral sclerosis and Alzheimer's disease (AD) has been associated with alterations in quality control of neuronal mitochondria (Santos et al 2010), but still now, mitophagy pathway and its dysfunction in neudegenerative disease remain undisclosed. Data from several neurotoxic models show that mitochondria undergo to selective morphological changes in distribution, shape and interconnectivity which are hallmarks of mitophagy. These changes are typically studied at the confocal and TEM microscopes and quantified through a morphometric approach. Due to their polarized nature, neurons present a loss in the neuritic domain more pronounced in respect to the cell body compartment. In addition, morphometric analysis show that the mitochondria interconnectivity, area/perimeter ratio and elongation, major/minor axis ratio, are reduced in neurotoxic models and that these changes parallel in vivo findings from tissue derived from several neurodegenerative diseases.

Thus, neurotoxic models, which are acute insults, are able to trigger mitophagy in similar way to human neurodegenerative diseases which, instead, develop the pathology in the course of several years.

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Keywords
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