Autophagic Markers in the 6-OHDA Rat Model of Parkinson's Disease

C. Marin, E. Aguilar

Laboratori de Neurologia, Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

Emerging evidence supports a critical role for autophagy in the pathogenic process of the dopaminergic neurodegeneration in Parkinson's disease (PD). However, the definitive in vivo proof of it is currently lacking. Due to the relevance oxidative stress and chaperone-induced autophagy (CMA) in PD pathogenesis, we investigated the expression of nigral autophagic markers in 6-hydroxydopamine (6-OHDA)-lesioned hemiparkinsonian rats.

Male Sprague-Dawley rats received a 6-OHDA injection (8 µg in 4 µl of saline with 0.02% ascorbate) into the left medial forebrain bundle. Following a three-week recovery period, rats exhibiting a vigorous rotational response (>100 total turns) to apomorphine (0.05 mg/kg, sc) were selected for further study. Western blottings for nigral tyrosine hydroxylase (TH, 1:5000), lysosomal membrane protein receptor type 2A (LAMP2A, 1:500), the heat shock protein 90 (HSP90, 1:500), the microtubule-associated protein 1 light-chain3 (LC3, 1:500) and the protein VPS41 (1:500) were performed.

Immunoblotting analyses showed a decrease by 88 % in nigral TH expression levels after 6-OHDA lesion (p< 0.01) associated to an increase in LAMP2A (p< 0.01), HSP90 (p< 0.01), LC3 (p< 0.01) and VPS41 (p< 0.01) levels.

The present results provide in vivo evidence of an autophagic activation in the animal model of parkinsonism in rats with a unilateral lesion of the nigrostriatal pathway induced by 6-OHDA. This widely used model offers great potential for future studies regarding new potential treatments for neurodegenerative conditions and in the investigation of signaling pathways regulating autophagy.