The Parkinsonian Mimetic, MPP+, Rapidly Activates Autophagy in Dopaminergic Neurons

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Parkinson’s disease (PD) is a neurodegenerative disorder that is characterized by the death of dopaminergic cells in the midbrain. Although the etiology of PD is still unknown, numerous studies have suggested that at least later stages of the disorder are marked by autophagy, a process in which the cell gets rid of dysfunctional organelles. The O’Malley lab has shown that LC3 aggregates, a marker of autophagy, could be visualized in dopaminergic neurons at very early stages of cell death caused by the PD-mimetic, MPP⁺. To test the hypothesis that autophagy plays a neuroprotective role in PD, midbrain cells from mouse embryos were transfected with a fluorescently-tagged LC3, DsRed-LC3-GFP. The doubly-labeled probe allowed for the distinction to be made between autophagosomes and autolysosomes, which form at different stages of the autophagic process. The cells were then fixed at different time points (2 hr., 4 hr., and 6 hr.) in order to observe how the quantities of LC3 changed over 24 hours in response to MPP⁺. The cells were analyzed using light microscopy and cells exhibiting autophagic markers were quantified at each time point. Experiments analyzed to date indicate increasing quantities of cells expressing punctuated patterns of LC3 up through the 6-hr. time period. A significant increase in autophagic markers would ultimately indicate that autophagy is being upregulated during PD and therefore plays, at least initially, a neuroprotective role.