

Mechanistic Studies on Dopaminergic Neuronal Death in Parkinson's Disease by Regulating ZBP-1

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Abstract

Background: Many studies have shown that the programmed cell death (PCD) pathway plays a crucial role in Parkinson's disease. However, in Parkinson's disease (PD), the specific mechanism of dopaminergic neuronal death has not been fully elucidated. Some scholars have recently proposed the concept of a new mode of death, PANoptosis, emphasizing the interaction and coordination between pyroptosis, apoptosis, and necroptosis. Z-DNA-binding protein 1 (ZBP-1) is essential for activating all three pathways. PANoptosis provides a new approach to study the regulation of cell death. In order to examine whether PANoptosis is present in the process of dopaminergic neuronal death, we chose Parkinson's disease as a research model to explore the role of PANoptosis in key pathological processes and to study the expression pattern of the key protein ZBP-1. **Methods:** Mouse PD models were established and randomly divided into model group and control group. The behavior of mice was evaluated by rod climbing experiment and rod rotation experiment. Immunohistochemical staining was performed to stain the brain sections of mice in each group to verify the success of the model. Immunofluorescence staining was performed to study the expression pattern of ZBP-1 in mouse brain sections. **Results:** Compared with the control group, the number of tyrosine hydroxylase (TH) staining in the substantia nigra pars compacta (SNpc) of the midbrain was significantly reduced, and the staining density of TH neuronal fibers in the striatum was significantly reduced. At the SNpc site, ZBP-1 protein was co-labeled with surviving dopaminergic neurons, Neun neurons and microglia, indicating that ZBP-1 was activated in microglia and neurons in the PD model. **Conclusion:** The results of this study found that there was activation of ZBP-1 after PD modelling, supporting the presence of PANoptosis in the process of dopaminergic neuronal death in Parkinson's disease. This may provide new insights into the underlying mechanisms of cell death in Parkinson's disease and provide new therapeutic targets for neuroprotection.

Keywords

Parkinson's Disease, PANoptosis, ZBP-1, Microglia