MEETING ABSTRACT



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Oxidative DNA damage triggers ProNGF-Mediated apoptosis in the striatum of 6-OHDA-treated rats

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Background

Oxidative DNA damage generated by 6-hydroxydopamine (6-OHDA) may initiate a programmed cell death cascade called apoptosis and plays an important role in the pathogenesis of Parkinson's disease (PD). ProNGF, a precursor of nerve growth factor (NGF), is found to be involved in neuronal apoptosis of neurodegenerative diseases such as PD. Therefore, we have tested the presumption that proNGF-mediated apoptosis might be initiated by oxidative DNA damage in 6-OHDA treated rats.

Method

Enzymatic assay, histochemistry, TUNEL and Western blot were used to investigate profiles of pro-NGF mediated apoptosis after oxidative DNA damage in a unilateral 6-OHDA treated rat model of PD.

Result

A signaling cascade of proNGF-mediated apoptosis definitely occurred in striatum of 6-OHDA lesioned rat under a circumstance of oxidative DNA damage. We confirmed the following changes: 1) activities of antioxidant defense system and levels of malondialdehyde (MDA), 2) MTH1 levels and 8-oxo-2'-deoxyguanosine (8-oxo-dG) accumulation, 3) loss of the TH-positive fiber and dopamine neurons in nigrosriatal system, 4) appearance of apoptotic body and neuronal apoptosis in striatum, 5) expression of proNGF and downstream correceptor of sportily and p75NTR, 6) activation status of c-Jun N-terminal kinase (JNK) and its target p53, 7) activation status of the intrinsic apoptotic pathway including cytochrome *c*, caspase 9 and caspase 3, 8) phosphorylation levels of Bad and ratio of Bax/Bcl-2.

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Conclusion

These results support that after exposure to the stress stimuli such as oxidative DNA damage induced by 6-OHDA, the destiny of neuronal cells in striatum finally went to apoptosis mediated by proNGF-mediated signaling and it suggests that these profiles might provide some clues for the possible molecular basis of PD etiology.

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