ABSTRACT

Neurotrophic factors are proteins that regulate the proliferation and differentiation of neurons and can protect neurons from various toxic insults. There are various neurotrophic factors known to be beneficial on dopaminergic neuron survival when given exogenously, but the endogenous expression of these neurotrophic are not well known when dopaminergic neurons are degenerating. In this study, the endogenous expression of TGF-β1 and GDNF was investigated, which are known to be important on the development and maintenance of dopaminergic neurons. Also the endogenous expression of CNTF and neuregulin, which are known as peripheral motor neuron survival factors were investigated.

The expression of neurotrophic factors were evaluated in the hemiparkinsonian model rat which was produced by striatal injection of 6-hydroxydopamine(6-OHDA). Male Sprague-Dawley rats of 9 week old were used. 6-OHDA was stereotaxically injected into the striatum and rats were sacrificed at 4, 7, 14 and 28 days after operation. The progressive degeneration of dopaminergic neuron cells was confirmed by tyrosine hydroxylase immunohistochemistry and apomorphine behavior test. RT-PCR and in situ hybridization was performed to evaluate the changes of mRNA levels and immunohistochemistry was performed to evaluate the protein levels of each neurotrophic factors.

We found that the protein expression of TGF-β1 and GDNF was not changed but the mRNA level of TGF-β1 was increased in the lesioned striatum at 4 days after 6-OHDA injection. CNTF expression
was significantly increased after 7 days in the lesioned striatum (ST) and substantia nigra (SN) compared to the intact side. Neuregulin-β expression also increased in the lesioned ST. CNTF immunoreactive cells had a similar morphological and distribution pattern with glial fibrillary acidic protein (GFAP) immunoreactive cells in the lesioned striatum.

In conclusion, the expression of CNTF and neuregulin-β was upregulated in the lesioned rat brain, while TGF-β1 and GDNF expression did not change. These results suggested that CNTF and neuregulin-β may be important neurotrophic factors associated with dopaminergic neuron death in the nigrostriatal dopaminergic pathway following 6-OHDA insult.

**Key words**: Parkinson’s disease, 6-OHDA, neurotrophic factor, CNTF, neuregulin, GDNF, TGF-β1

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