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MOLECULAR NEURODEGENERATION

MEETING ABSTRACT Open Access

N-cadherin-ERα-Src signal models mediate the synergistic potentiation of activation of PI3K/Akt signal pathway in injured dopaminergic neurons by GDNF and E2

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Background

Accumulating evidence indicates that glial cell line-derived neurotrophic factor (GDNF) synergizes with 17β-estradiol (E2) could protect dopaminergic neurons. However, the mechanisms have not yet been elucidated. Based on the fact that either E2 or GDNF can activate the intracellular PI3K/Akt signal pathway, we hypothesize that the synergic protection of dopaminergic neurons exerted by E2 and GDNF is ascribed to enhancing the activation of the cellular PI3K/Akt signal pathway in a certain way.

Method

We studied the potential mechanism under the synergistic protective effects of E2 and GDNF on dopaminergic neurons using the MN9D cell line. The MN9D cells were treated with 6-OHDA before incubating with either E2 or GDNF or both. Endogenous AKT phosphorylation and precise underlying mechanistic studies were revealed using co-immunoprecipitation(co-IP), western blot and immuno-fluorescent staining.

Result

Compared with the sole administration of GDNF or E2, the co-administration of GDNF and E2 significantly increased the Akt phosphorylation in injured dopaminergic neurons. Incubation of GDNF and E2 promoted the interaction of estrogenic α-receptor (ERα) with the intracellular N-cadherin which potentially recruited ERα to the inner surface of cell membrane. The GDNF and E2 mediated AKT phosphorylation was potentially mediated through an Src-dependent signaling pathway as inhibition of Src using specific inhibitor totally abrogated this process.

Conclusion

The above findings indicated the potential importance of AKT in GDNF and E2 mediated synergistic protective effects in 6-OHDA injured MN9D cells. E2 recruited ERα to the inner surface of the cell membrane which could at least partially participate in the downstream AKT phosphorylation. We also proposed a role of Src as a potential mediator during this process. This study further explored the underlying protective mechanism of GDNF and E2 and has important clinical relevance.

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