Morphological Changes in a Severe Model of Parkinson?s Disease and Its Suitability to Test the Therapeutic Effects of Microencapsulated Neurotrophic Factors

Requejo C.

Ruiz-Ortega J.A.

Bengoetxea H.

García-Blanco A.

Herrán E.

Aristieta A.

Igartua M.

Pedraz J.L.

Ugedo L.

Hernández R.M.

Lafuente J.V.

The unilateral 6-hydroxydopamine (6-OHDA) lesion of medial forebrain bundle (MFB) in rats affords us to study the advanced stages of Parkinson?s disease (PD). Numerous evidences suggest synergic effects when various neurotrophic factors are administered in experimental models of PD. The aim of the present work was to assess the morphological changes along the rostro-caudal axis of caudo-putamen complex and substantia nigra (SN) in the referred model in order to test the suitability of a severe model to evaluate new neurorestorative therapies. Administration of 6-OHDA into MFB in addition to a remarkable depletion of dopamine in the nigrostriatal system induced an increase of glial fibrillary acidic protein (GFAP)-positive cells in SN and an intense immunoreactivity for OX-42, vascular endothelial growth factor (VEGF), and Lycopersycum esculentum agglutinin (LEA) in striatum and SN. Tyrosine hydroxylase (TH) immunostaining revealed a significant decrease of the TH-immunopositive striatal volume in 6-OHDA group from rostral to caudal one. The loss of TH-immunoreactive (TH-ir) neurons and axodendritic network (ADN) was higher in caudal

sections. Morphological recovery after the implantation of microspheres loaded with VEGF and glial cell line-derived neurotrophic factor (GDNF) in parkinsonized rats was related to the preservation of the TH-ir cell number and ADN in the caudal region of the SN. In addition, these findings support the neurorestorative role of VEGF+GDNF in the dopaminergic system and the synergistic effect between both factors. On the other hand, a topological distribution of the dopaminergic system was noticeable in the severe model, showing a selective vulnerability to 6-OHDA and recovering after treatment.

6-OHDA

GDNF

Neuroregeneration

Parkinson?s disease

Rostro-caudal gradient

VEGF

desipramine

dopamine

glial cell line derived neurotrophic factor

glial fibrillary acidic protein

microsphere

oxidopamine

pargyline

tyrosine 3 monooxygenase

vasculotropin

glial cell line derived neurotrophic factor

neuroprotective agent

vascular endothelial growth factor A, rat

vasculotropin A

animal experiment

animal model

animal tissue

Article

brain nerve cell

caudate nucleus

cell count

controlled study

corpus striatum

disease severity

dopaminergic system

female

histopathology

immunoreactivity

medial forebrain bundle

microencapsulation

nigroneostriatal system

nonhuman

Parkinson disease

pathogenesis

protein function

putamen

rat

substantia nigra

animal

drug formulation

parkinsonism

pathology

procedures

severity of illness index

Sprague Dawley rat

treatment outcome

Animals

Drug Compounding

Female

Glial Cell Line-Derived Neurotrophic Factor

Neuroprotective Agents

Parkinsonian Disorders

Rats

Rats, Sprague-Dawley

Severity of Illness Index

Treatment Outcome

Vascular Endothelial Growth Factor A