

# Deleterious effects of VEGFR2 and RET inhibition in a preclinical model of Parkinson's disease

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Neurotrophic factors (NTFs) are a promising therapeutic option for Parkinson's disease (PD). They exert their function through tyrosine kinase receptors. Our goal was to assess the effects of administering a selective tyrosine kinase inhibitor (vandetanib) that blocks VEGFR2 and RET receptors in a preclinical model of PD. Rats underwent intrastriatal injections of 6-hydroxydopamine (6-OHDA). Two weeks later, the rats received 30 mg/kg vandetanib or saline orally. The effects were assessed using the rotational behavioral test, tyrosine hydroxylase (TH) immunohistochemistry, and western blot. In 6-OHDA-lesioned rats, motor symptoms were almost undetectable, but morphological and biochemical changes were significant. Vandetanib treatment, combined with the presence of 6-OHDA lesions, significantly increased behavioral impairment and morphological and biochemical changes. Therefore, after vandetanib treatment, the TH-immunopositive striatal volume, the percentage of TH+ neurons, and the extent of the axodendritic network in the substantia nigra decreased. Glial fibrillary acidic protein-positivity significantly decreased in the striatum and substantia nigra in the vandetanib-treated group. In addition, p-Akt and p-ERK 1/2 levels were significantly lower and caspase-3 expression significantly increased after vandetanib administration. In conclusion, we demonstrate for the first time the deleterious effect of a tyrosine kinase inhibitor on the dopaminergic system, supporting the beneficial and synergistic effect of NTFs reported in previous papers. © Springer Science+Business Media, LLC 2017.

6-OHDA



animal experiment  
animal model  
animal tissue  
Article  
biochemistry  
controlled study  
drug effect  
enzyme inhibition  
experimental behavioral test  
histology  
immunohistochemistry  
male  
nerve cell  
neuroprotection  
nigrostriatal system  
nonhuman  
Parkinson disease  
protein expression  
protein function  
rat  
signal transduction  
substantia nigra  
Western blotting  
animal  
antagonists and inhibitors  
chemically induced

metabolism

parkinsonism

pathology

Sprague Dawley rat

treatment outcome

Animals

Male

Parkinsonian Disorders

Piperidines

Proto-Oncogene Proteins c-ret

Quinazolines

Rats

Rats, Sprague-Dawley

Treatment Outcome

Vascular Endothelial Growth Factor Receptor-2