The antioxidant N-acetyl-L-cysteine exerts strong neuroprotective effects in both in-vitro and in-vivo models of Parkinson’s disease

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Introduction

Parkinson’s disease (PD) is a devastating neurodegenerative disorder for which there is no cure. It is caused by the loss of dopaminergic (DA) neurons in the striatum, responsible for disabling motor symptoms. The neurotoxin 6-hydroxydopamine (6-OHDA) is used for the modeling of Parkinson’s disease in both in-vitro and in-vivo experiments. In lab animals, 6-OHDA produces striatal dopamine depletion along with sensorimotor deficits. In cell cultures, 6-OHDA induces death of dopaminergic neurons in dose-dependent manner.

Objectives

The neuroprotective potential of 4 different treatment mechanisms including the inhibition of oxidative stress by the antioxidant N-Acetylcysteine (NAC) is evaluated in 6-OHDA-intoxicated dopaminergic neurons in culture. The most efficient treatment is then assessed 6-OHDA hemiparkinsonian rats for its ability to prevent the development of motor symptoms and dopamine depletion.

Assessment of neurotoxicity and neuroprotection in neuronal cultures

Culture of neurons from the mesencephalic brain of rat embryos (day 15 of gestation).

Measure of death of dopaminergic neurons by immunostaining of Tyrosine hydroxylase - positive neurons.

Assessment of sensorimotor motor deficit in 6-OHDA hemiparkinsonian rats


Figure 1: 6-OHDA-induced death of dopaminergic neurons

Figure 2: Neuroprotective potential of treatment mechanisms

Figure 3: Measure of the striatal level of Dopamine and its metabolites (HVA and DOPAC)

Figure 4: Cylinder test (Limb asymmetry use)

Figure 5: Beam walking test

Delayed motor initiative

Rats with delayed motor initiative are those that do not move within the 120 s after the initiation of the test and thus are considered having limb akinesia.

Walking performance

The prevalence of Akinesia was markedly high in 6-OHDA hemiparkinsonian rats. In addition, 6-OHDA hemiparkinsonian rats showed poor beam walking performance. NAC treatment markedly improved the motor deficit observed in 6-OHDA hemiparkinsonian rats.