INTRAVENTRICULAR 6-OHDA ADMINISTRATION: A PROGRESSIVE MODEL OF PARKINSON’S DISEASE IN RATS

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Parkinson’s disease (PD) is a neurodegenerative disorder characterized by the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc), and consequently a depletion of dopamine (DA) in the striatum. The origin and the neurochemical mechanisms involved in this cell loss are still unknown. Until present, the rodent models used to investigate dopaminergic cell vulnerability in PD fail to mimic the major pathological and behavioural features in PD patients. Thus, models induce an abrupt and practically complete degeneration, whereas degeneration is slowly progressive in PD patients.

Our goal was to develop a rodent model to more closely reproduce the slowly degeneration pattern of human PD. The neurotoxin 6-hydroxydopamine (6-OHDA) was administered in the third ventricle at different doses (100-1000 µg, 100 µg/day) in awake Sprague-Dawley rats for 1 to 10 consecutive days. Motor behaviour (cylinder and grid test), striatal dopamine transporter (DAT) and nigral tyrosine hydroxilase (TH) expression were measured to characterize the model. Animals developed a progressive reduction in the use of limbs in the cylinder test and catalepsy related to the dose of 6-OHDA administered (\(p< 0.05\)). Optical density showed a progressive loss of striatal DAT and nigral TH\textsuperscript{+} neurons in these animals (\(p< 0.05\)). Interestingly, some 6-OHDA-lesioned animals showed a bilateral symmetrical midbrain DA-degeneration whereas others showed an asymmetrical pattern.

The slow progressive pattern of degeneration and motor impairment recall human PD, suggesting that this model might be a useful tool in the study of cell vulnerability mechanisms involved in this neurodegenerative disorder.