cima
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Parkinson´s Disease: Animal Models

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disease that affects 1-2 per 1000 of the worldwide population. It is characterized by the presence of α-synuclein-containing Lewy bodies and loss of dopamine neurons in the substantia nigra, manifesting as motor and non-motor alterations.

Cause of PD remains unknown and it is considered a multifactorial disorder that results, in most cases, from the combined effects of multiple risk and protective factors, including genetic and environmental ones.

Although there is presently no cure for PD, there are several therapeutic options such as medication and surgery (including deep brain stimulation, DBS) to manage its symptoms. Nevertheless, PD symptoms continue and worsen over time and long-term use of pharmacological therapies cause disabling side effects that are the greatest source of impairment in quality of life for patients and families. As a result, the major outstanding challenges in PD today include:

- To stop or slow down disease progression.
- To manage (and preferably prevent) levodopa-resistant symptoms.
- To develop new pharmacological and non-pharmacological treatments.
- To treat the non-motor symptoms of the disease.

Rodent models for Parkinson´s disease

Pharmacological models

Haloperidol model (mouse and rat)

The blockade of D_2 receptors by haloperidol results in rigidity and catalepsy in rodents, mimicking the difficulties of PD patients in the initiation of movement. This is a transient model that lacks dopamine neuron degeneration.

Applications: Robust model to screen for potential symptomatic efficacy of novel anti-PD therapies (pharmacological or DBS-based) and to investigate the role of D_2 receptors in the pathophysiology of PD.

Neurotoxin-induced models

MPTP mouse model

Intraperitoneal administration of MPTP induces the specific loss of the dopaminergic neurons in the substantia nigra. Different administration regimes (acute/sub-acute/chronic) reproduce different aspects of the disease. At the end of the treatment animals present transient motor impairment and partial loss of dopaminergic neurons.

Applications: This mice model is useful in the pre-clinical research for the development of new therapies for PD. The chronic MPTP mouse model is the reference model for the development of neuroprotective treatments. MPTP administration could be combined with genetic mouse models to study the susceptibility/resistance of different genes to the dopamine neuron degeneration.

6-OHDA rat model

The 6-OHDA is injected directly into one side of the brain by stereotaxic surgery. Administration of 6-OHDA in the medial forebrain bundle induces a complete dopaminergic lesion while the intra-striatal administration induces a partial degeneration.

Applications: This model is useful in the pre-clinical research for the development of new therapies for PD. Administration of levodopa to this model reproduces abnormal movements induced by medication that resemble the levodopa-induced dyskinesias in patients. It can be used in the development of drugs to counteract these side-effects, to investigate their origin or to test the effect of new DBS approximations.

Levels of analysis

- Motor behavior: different tests to determine motor impairment.
- Synchronized video and neurophysiological recording of freely moving animals under different behavioral and motor conditions including the action of DBS and pharmacological treatments.
- Neuroprotection: immunohistochemistry followed by stereology to analyze the nigrostriatal pathway.
- Cellular and biochemical determinations including the assessment of neurotransmitter levels, real-time PCR, western blotting or flow cytometry.