THE PHENOTYPE OF A NEW MOUSE MODEL OF PARKINSON'S DISEASE EXPRESSING FULL LENGTH HUMAN LRRK2


Neurodegeneration, AFFiRiS AG, Vienna, Austria

Introduction: Mutations in Leucine-rich repeat kinase 2 (LRRK2) are frequently involved in both familial and sporadic forms of Parkinson's disease (PD). Until now, no functional murine LRRK2 transgenic model is publicly available that fully recapitulates the clinical symptoms of PD. We recently developed a novel mouse model of Parkinson's disease over-expressing human wild-type LRRK2 under the control of the neuron specific Thy1.2 promoter.

Aims: In order to determine whether neuron-specific over-expression of human wild-type LRRK2 would lead to phenotypic alterations in this novel mouse model for PD, we started to implement a battery of classical behavioural tests.

Methods: Mice were subjected to behavioural testing at 4, 8, 12 and 16 months of age. After completing a modified SHIRPA screen for general health and reflexes, animals were tested for cognitive, functional and motoric alterations assessing anosmia, nesting behaviour, memory deficits, and deficits in grip strength, endurance and motor-coordination.

Results: We found that expression of human LRRK2 under the control of the neuron specific Thy1.2 promoter results in viable offspring, which develops age dependent, progressive phenotypical alterations at around 8 months of age. Results depicting these deficits will be discussed.

Conclusions: Based on the initial findings presented, this novel transgenic model over-expressing LRRK2 could be instrumental to further elucidate the biologic and pathologic role of Leucine repeat rich kinase-2 (LRRK2) in the nervous system and could thus be a suitable tool for studying the effects of therapeutic drugs for PD in animals.