# Role of GILZ in a mouse model of Parkinson Disease and related behavioural alterations

A. Leo[1], E. Russo[1], R. Citraro[1], E. Mazzon[2], S. Bruscoli[3], C. Riccardi[3], G. De Sarro[1]

[1]University of Catanzaro, School of Medicine, Science of Health Department, Catanzaro, Italy
[2]Experimental Neurology Laboratory, IRCCS Centro Neurolesi Bonino-Pulejo, Messina, Italy
[3]Dept. of Clinical and Experimental Medicine, Section of Pharmacology, Toxicology, and Chemotherapy, Medical School, University of Perugia

Glucocorticoids (GCs) are fundamental steroid hormones for human life. They are widely used in clinics for the treatment of various diseases. Most part of the effects mediated by GCs is due to the binding with the GCs receptor (GR) and the consequent modulation of gene expression. However, GCs have also non-genomic effects. Among the genes potently and invariably regulated by GCs, the Glucocorticoid-induced leucine zipper gene (GILZ), basally expressed in central nervous system (CNS), seems to play a crucial role in the anti-inflammatory, immunosuppressive and anti-apoptotic effects of GCs [1]. Aim of this study was to investigate the involvement of GILZ in a mouse model of Parkinson's disease (PD) characterized by chronic inflammation and progressive neurodegeneration. Furthermore, we evaluated the effects of Dexamethasone (DEX) also in relation to GILZ expression. To this purpose, GILZ KO (C57BL/6j background) and GILZ WT (C57BL/6j) mice have been used to realize a mouse model of pre-motor symptoms of PD. In particular, these mice (WT and KO) have received an unilateral injection of 6-hydroxydopamine hydrochloride (6-OHDA) into the dorsal-lateral striatum. DEX administration (1mg/Kg per os) was started the same day of 6-OHDA intoxication over a period of 3 weeks. At the end of this period, several behavioural tasks have been performed to test, in the various experimental groups, anxiety/depressive-like behaviour, cognitive impairment and motor activity [2]. At the end of behavioural testing, mice were sacrificed and their brain have been used for morphological and biochemical assays.
Our results show that in WT mice the injection of 6-OHDA leads to the development of anxiety/depressive-like behaviour and cognitive impairment. Moreover, 6-OHDA injection in these groups affected vertical but not horizontal motor activity as well as turning behaviour after apomorphine administration. These behavioural evidences have been also correlated with a loss of tyrosine hydroxylase (TH) in striatum. At odds, KO GILZ mice after the injection of 6-OHDA have shown reduced striatal damage in comparison to WT lesioned mice. Accordingly, in KO GILZ lesioned mice, behavioural alterations were less marked. DEX administration, in WT lesioned mice, was able to improve depressive-like behaviour, cognitive impairment as well as motor activity, whereas it did not ameliorate anxiety-like behaviour. At odds, DEX in KO GILZ lesioned mice did not show beneficial effects on acquired behavioural alterations.
In conclusion, according to Mazzon, et al. [3], this neuroprotective phenotype in GILZ KO mice could be due, at least in part, to the fact that GILZ is able to modulate the neuroinflammation as well as immunity system. However, the administration of DEX has shown neuroprotective effects only in WT lesioned mice but not in GILZ KO lesioned mice. According to D'Adamio, et al. [4] we hypothesize that the positive effects of DEX could be mediated by the induction of GILZ expression. Therefore to better understand the complex role of GILZ, further studies need to be carried out.

**References**

[1] Ayroldi and Riccardi (2009) *FASEB J* **23**, 3649-3658.
[2] Bonito-Oliva et al., (2014). *Front Behav Neurosci* **8**, 290.
[3] Mazzon et al., (2014). *CNS Neurosci Ther* **20**, 973-981.
[4] D'Adamio et al., (1997) *Immunity* **7**, 803-812.