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N° de poster: P10.05 Globus Pallidus Contribution to Motor Behaviour in Normal and Parkinson's Disease States: Optogenetic Studies in murine models

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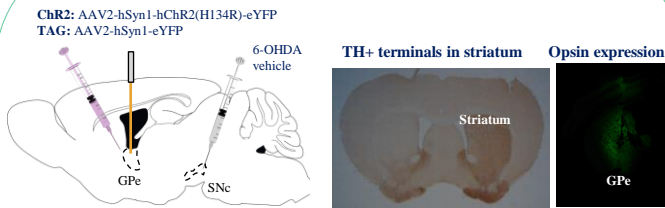
Globus Pallidus Contribution to Motor Behaviour in Normal and Parkinson's Disease States: Optogenetic Studies in Murine Models

INTRODUCTION

Excessive inhibition of external globus pallidus (GPe) by striatal GABAergic neurons is considered a central mechanism contributing to motor symptoms of Parkinson's disease (PD). While electrophysiological investigations in animal models of PD provide support for this view, behavioural studies assessing beneficial effects of global GPe stimulation in the context of dopamine (DA) depletion are scarce and the reported results are controversial. Here, we used an optogenetic approach and the standard unilateral 6-hydroxydopamine (6-OHDA) nigrostriatal dopamine (DA) lesion model of PD to assess beneficial effects of GPe stimulation on motor deficits in mice. The behavioural effects of GPe optogenetic inhibition were also studied in normal mice under the same testing conditions to verify whether reduced GPe activity reproduces the typical motor deficits of DA lesion in rodents.

METHODS & RESULTS

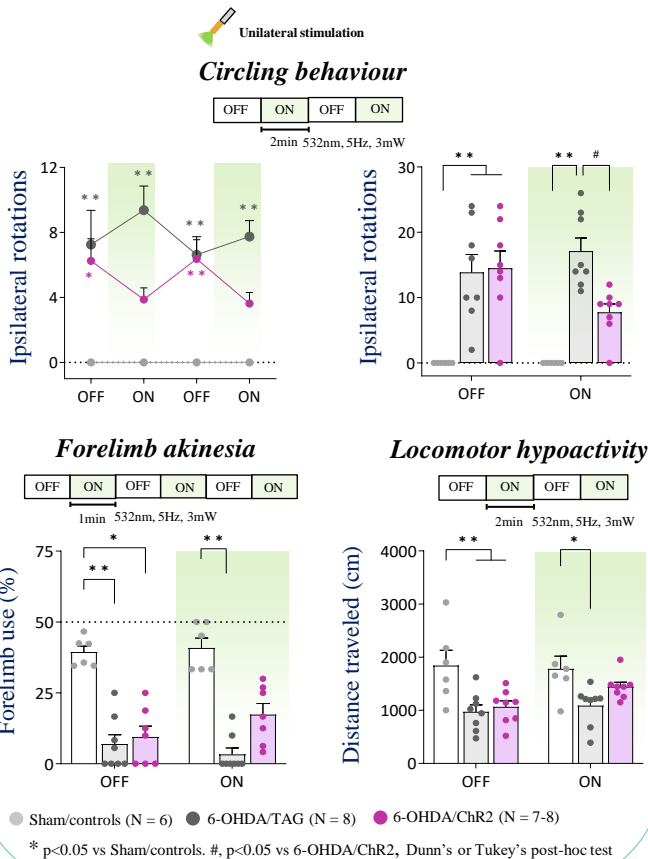
Hemiparkinsonian mice



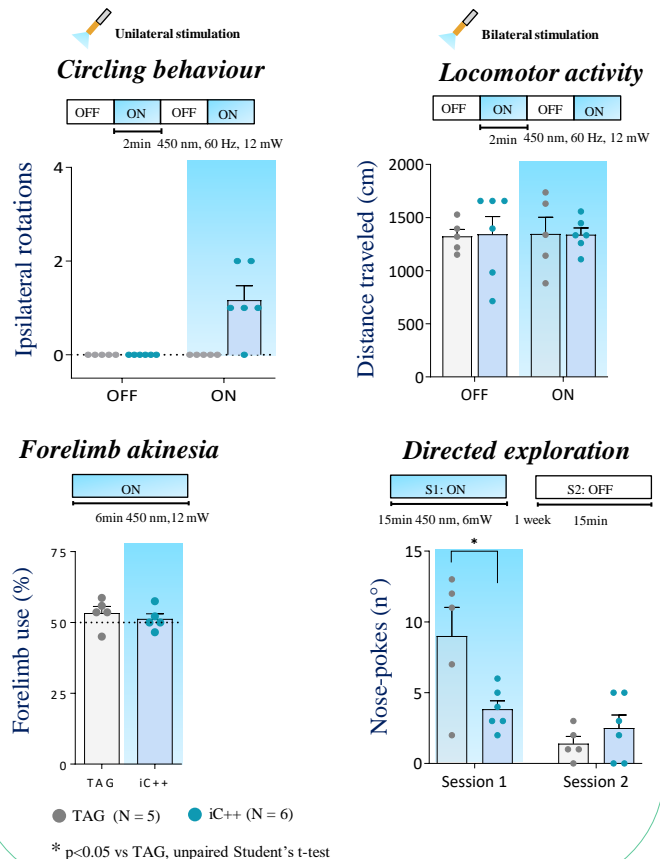
Intact mice



GPe Photostimulation



GPe Photoinhibition



CONCLUSION

- GPe photostimulation restores a range of motor deficits in 6-OHDA-lesioned mice (ipsilateral circling, forelimb akinesia and locomotor hypoactivity).
- GPe photoinhibition in normal mice has no impact on locomotor behaviour but impairs exploration directed towards salient spatial cues (nose-poke holes).
- In DA-depleted state, GPe plays a more important role in the development of motor deficits.

GPe is a promising target for neuromodulatory restoration of motor deficits in PD