Differential molecular and behavioural response to L-DOPA in mice injected with 6-hydroxydopamine in the striatum or in the medial forebrain bundle

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Differential molecular and behavioural responses to L-DOPA in mice injected with 6-hydroxydopamine in the striatum or in the medial forebrain bundle

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INTRODUCTION

Unilateral lesions of the nigrostriatal dopamine (DA) pathway with 6-hydroxydopamine (6-OHDA) can be used to obtain a model of Parkinson's Disease in the mouse. In the present study we examine two types of unilateral 6-OHDA lesions in the mouse for their ability to induce stable motor deficits and a supersensitive molecular and behavioural response to L-DOPA.

EXPERIMENTAL DESIGN

Day0: 6-OHDA lesions in the **striatum** or in the **MFB**

Day14-16: spontaneous rotations and cylinder test off L-DOPA

Day21: AIMs rating

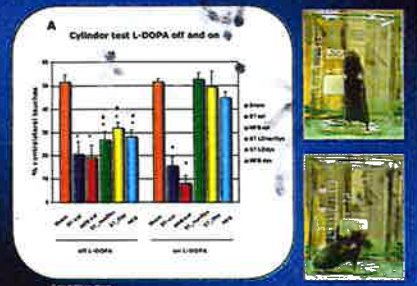
Day22: L-DOPA-induced rotations
Day23: AIMs rating
Day24: L-DOPA-induced rotations
Day25: AIMs rating
→ **L-DOPA 3mg/Kg + Benserazide 12mg/Kg**

Day26: L-DOPA-induced rotations
Day27: AIMs rating
Day28: L-DOPA-induced rotations
Day29: AIMs rating + cylinder test
Day30: L-DOPA-induced rotations
Day31: AIMs rating
Day32: L-DOPA-induced rotations
→ **L-DOPA 6mg/Kg + Benserazide 12mg/Kg**

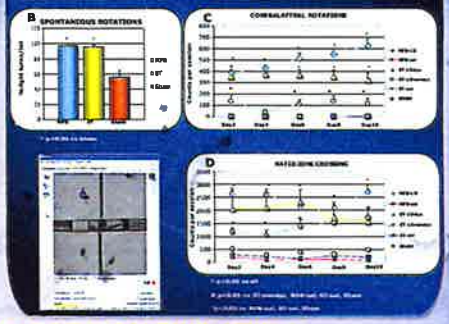
Day33: sacrifice (perfusion for IHC or decapitation for HPLC)

BEHAVIOURAL TESTS

CYLINDER TEST



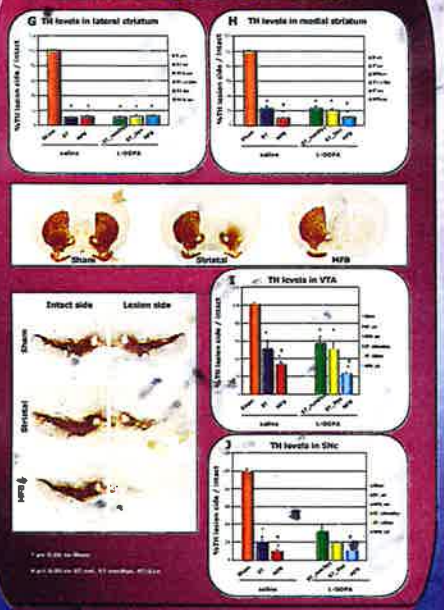
ROTATIONS and HORIZONTAL ACTIVITY



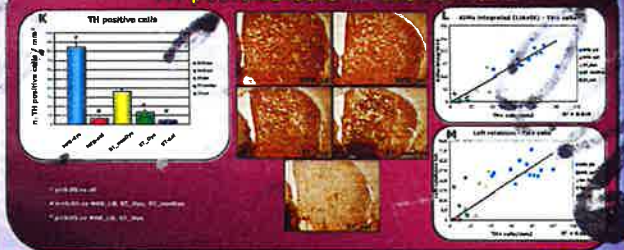
ABNORMAL INVOLUNTARY MOVEMENTS

IMMUNOHISTOCHEMISTRY

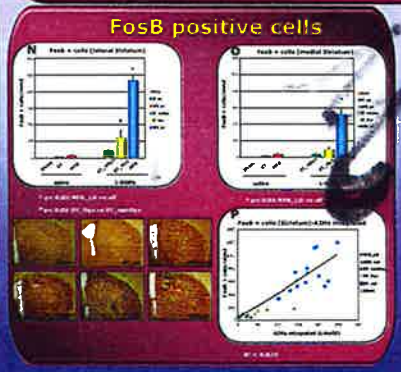
DOPAMINE DENERVATION



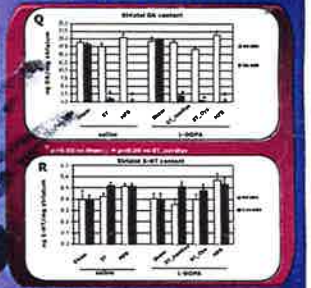
TH positive cells in the striatum



FosB positive cells



BIOCHEMISTRY



CONCLUSIONS

- **mice with 6-OHDA lesion in the MFB are very susceptible to L-DOPA-induced dyskinesia (LID). Molecular markers of LID are highly expressed and evenly distributed throughout the striatum.**

- **mice with 6-OHDA in the striatum provide a model where the susceptibility to LID differs among animals. Molecular changes associated with LID only occur in the highly denervated striatal subregions.**

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