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# Longitudinal follow-up of brain metabolism in rat models of progressive Parkinson's disease using Magnetic Resonance Spectroscopy Imaging.

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## Purpose / Introduction

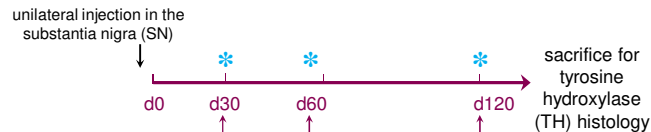
Parkinson's disease (PD) is characterized by: **i)** selective and progressive loss of nigral dopamine (DA) neurons, **ii)** unilateral to bilateral evolution pattern and **iii)** late appearance of motor deficits ( $\geq 50\%$  of DA neurons have degenerated).

The development of animal models mimicking these features has opened new possibilities to study the disease's evolution. Here, longitudinal **magnetic resonance spectroscopy imaging** was used to **follow up metabolites distribution** in key basal ganglia components in two rat models of progressive PD.

**Objective: provide novel insights onto the pathological alterations associated with the progression of the neurodegenerative process.**

## Subjects and Methods:

### ❖ Experimental design:



n=7 rats in each group

Group 1: injection of the substrate inhibitor of excitatory amino acid transporters (EAATs) = PDC (300 nmol)<sup>1</sup>

Group 2: injection of  $\alpha$ -synuclein (1  $\mu$ L of the recombinant adeno-associated virus vectors (1.5x10<sup>13</sup> vg/mL))

Group 3: sham= injection of the vehicle

**in vivo MRSI:**

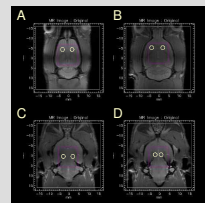
- 11.7 T (Bruker BioSpec 117/16 Ultra Shielded Refrigerated system)
- circular polarized <sup>1</sup>H RF coil for excitation and a head rat surface coil for signal reception.

\* Behavior test = cylinder test

analysis of the symmetry/asymmetry of their forepaw use during 5 min.

### ❖ NMR experiments:

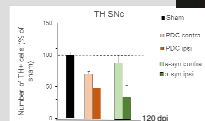
- Coronal images = fast spin echo  $T_2$ -weighted RARE; 256x256; 2 mm slice thickness
- MRSI acquisition = CSI with a semi-LASER voxel volume selection (dimensions in mm: FOV 32x32x2, voxel size = 10x10x2, image size = 20x20, resolution = 1.6x1.6x2, TR = 2000ms, TE = 24ms, VAPOR for water suppression).



T2 coronal MRI slices covering the motor cortex (Cx), the dorsal striatum (STR), subthalamic nucleus (STN) and substantia nigra (SN) in A, B, C and D respectively. CSI voxels are in purple. Yellow circles are voxels for each structure at right and left.

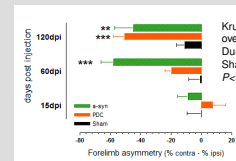
## Results

**TH immunohistochemistry** in SN of an  $\alpha$ -syn rat.

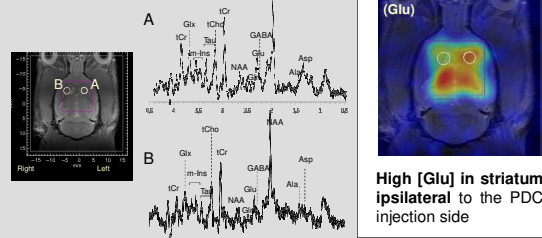


Kruskal-Wallis ANOVA, overall  $P < 0.0001$ , and Dunn's post-hoc test vs Sham: PDC ipsi  $P = 0.0025$  and  $\alpha$ -syn ipsi  $P = 0.0008$ .

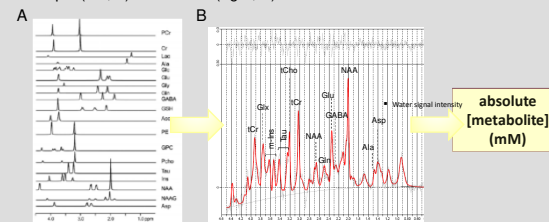
### Cylinder test.



**MRSI example:** acquisition on striata of a PDC PD rat model

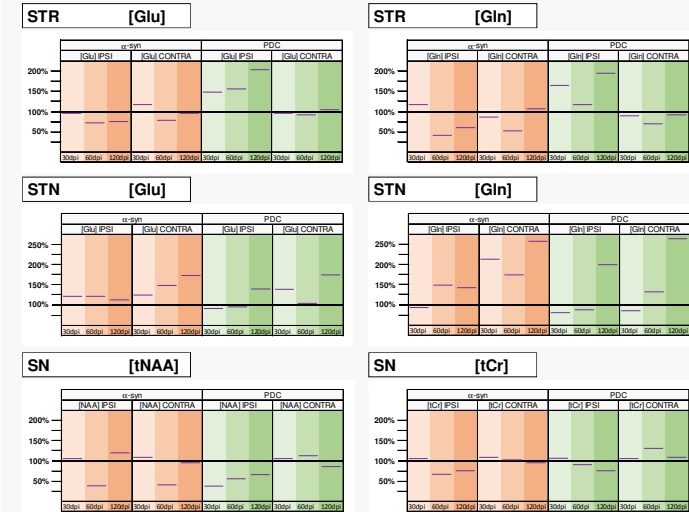


MRSI data are processed under CSIAP0<sup>2</sup>. A metabolite map is generated. Spectra from ipsi (left, A) and contra (right, B) striata of the side of lesion are extracted.



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Illustration of the evolution of selected metabolite concentrations (as % of SHAM):



## Conclusions

- ❖ MRSI = useful technique for **longitudinal characterization of metabolite profiles** in animal models of PD.
- ❖ **specificities** of the neurochemical changes within key basal ganglia components in the two PD rat models: the well-established  $\alpha$ -synuclein and a new one, the PDC model.
- ❖ Uni- to bilateral progression of neurodegeneration in the PDC model: involvement of the **subthalamic nucleus contralateral** to the PDC injection side.

1. Assous et al. Neurobiol. 2014;65:69-81
2. Le Fur et al. Magn Reson Mater Phys. 2010;23(1):23-30.
3. Provencher. Magn Reson Med. 1993;30(6):672-679.

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