Securing Bench to Bedside Translation

With Predictive EEG Biomarkers of Parkinson's disease

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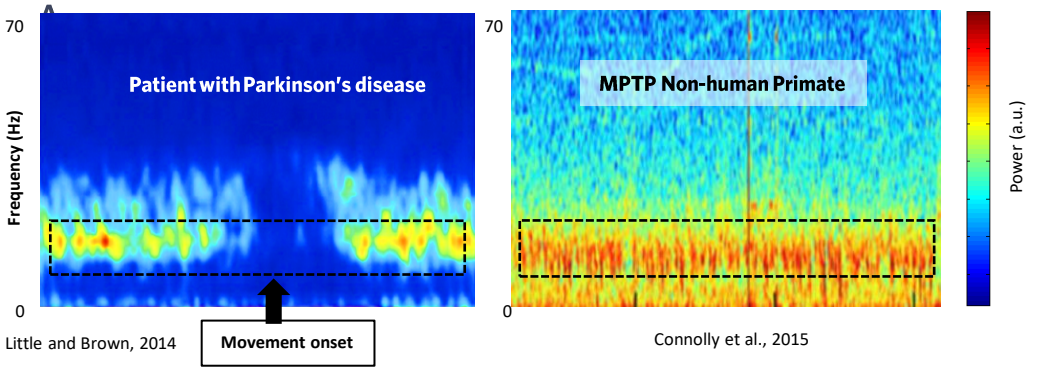
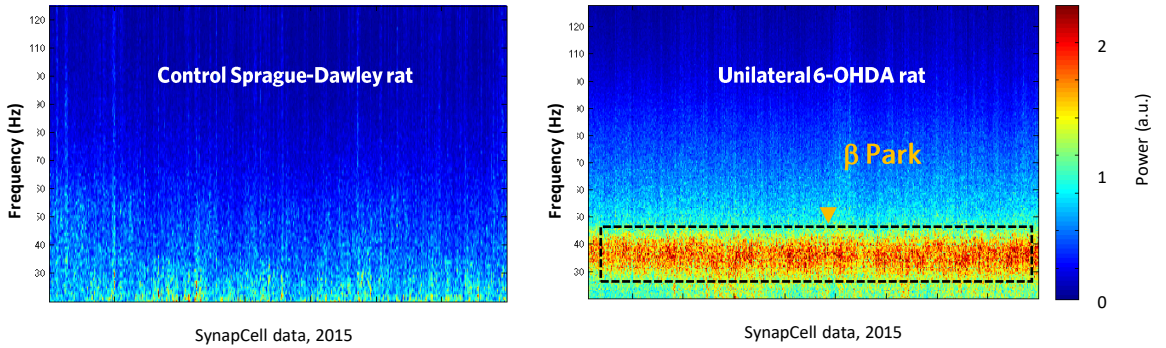
Head of Science

SynapCell's Pipeline Presentation
Predictive EEG biomarkers for PD
ASENT 2021

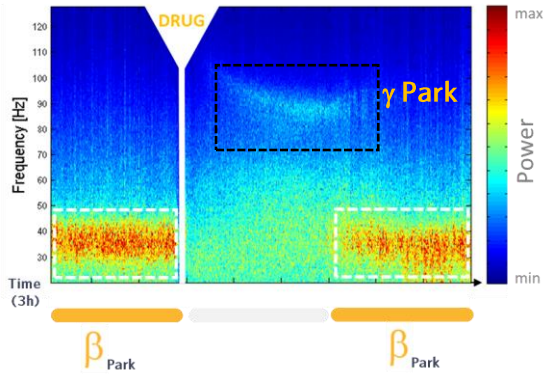
INTRODUCTION





- ✓ **A prominent aberrant Beta frequency band** characterized in PD patients and MPTP Non-human primate.

- ✓ **Similar aberrant Beta oscillations** characterized in the motor cortex of unilateral 6-OHDA-lesioned rats **(BetaPark, by SynapCell)**
- ✓ Dopamine agonists reduce BetaPark but increase high frequency oscillations **(GammaPark, by SynapCell)**



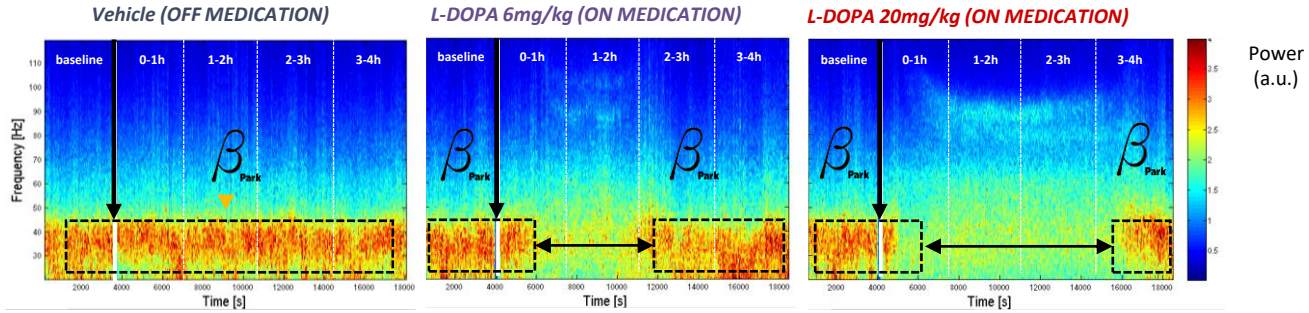
AIM OF THE STUDY

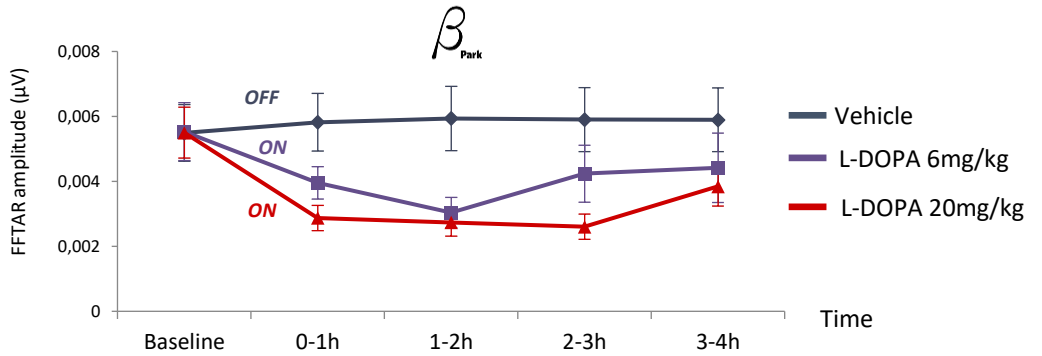
- ✓ **Evaluate the acute effect of dopaminergic agonists** on BetaPark and GammaPark in the 6-OHDA lesioned rat

- ✓ **Evaluate the acute effect of amantadine** on dyskinesia and GammaPark induced by chronic administration of L-DOPA

L-DOPA induces changes on BetaPark & GammaPark oscillations

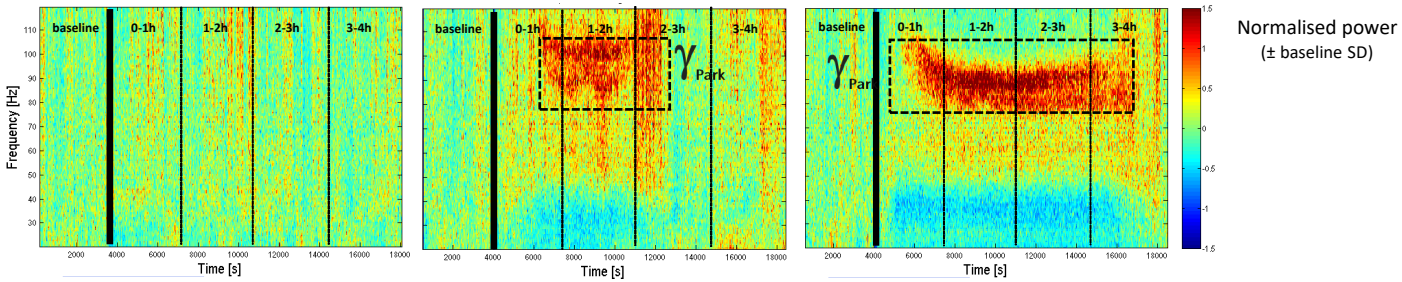
(A) BetaPark

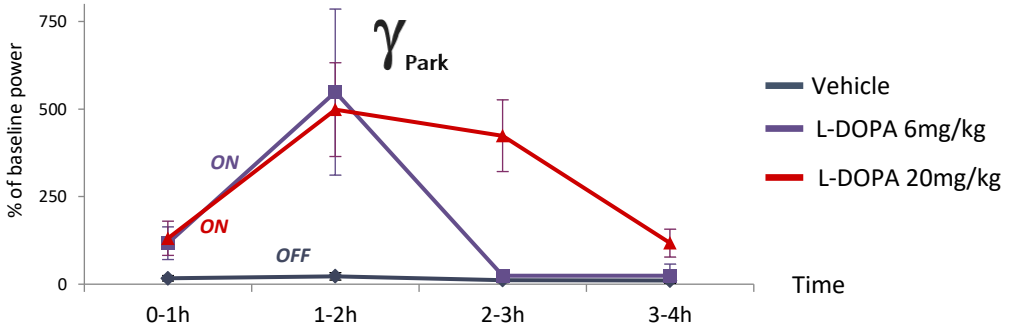




- ✓ **BetaPark remains stable over time** (3h time course) in the vehicle (OFF) group
- ✓ **L-DOPA dose-dependently and transiently decreases aberrant beta oscillations (BetaPark)**

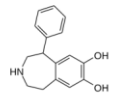
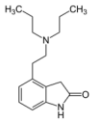
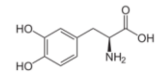
(B) GammaPark



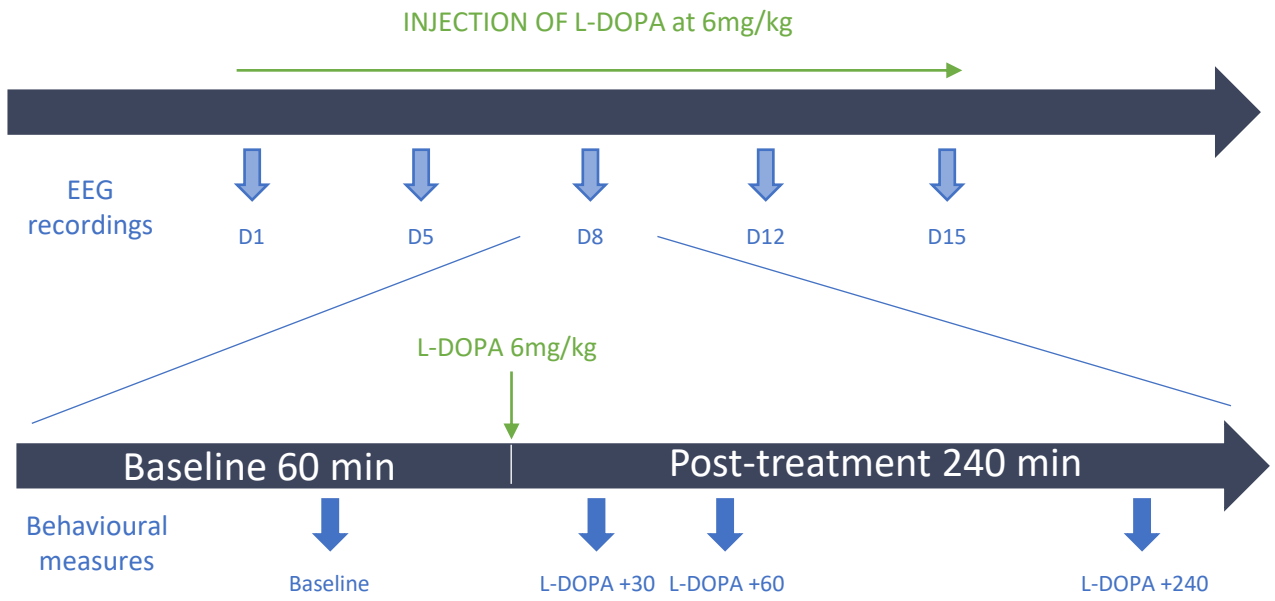


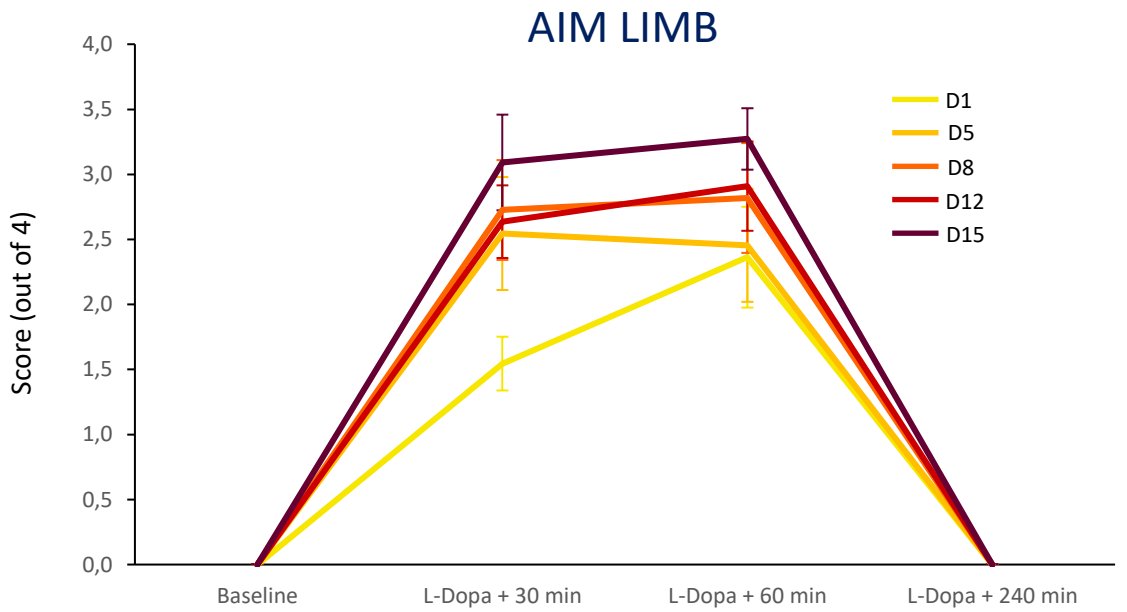
- ✓ **While decreasing BetaPark power, L-DOPA dose-dependently increases GammaPark power and duration,** whereas vehicle does not induce high frequency oscillations

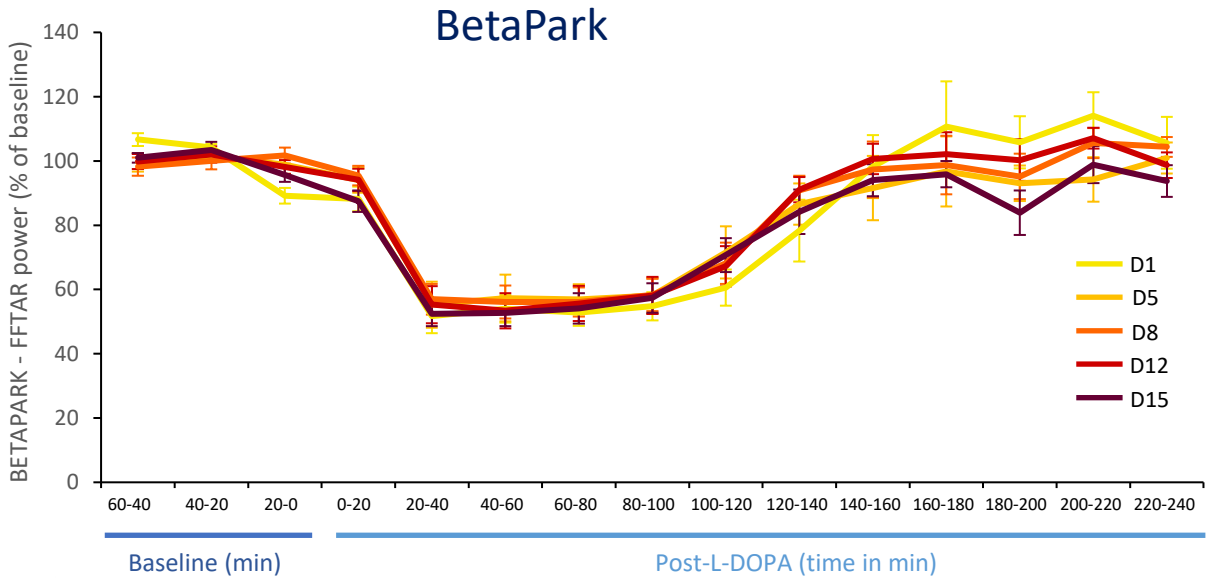
Summary of spectral effects

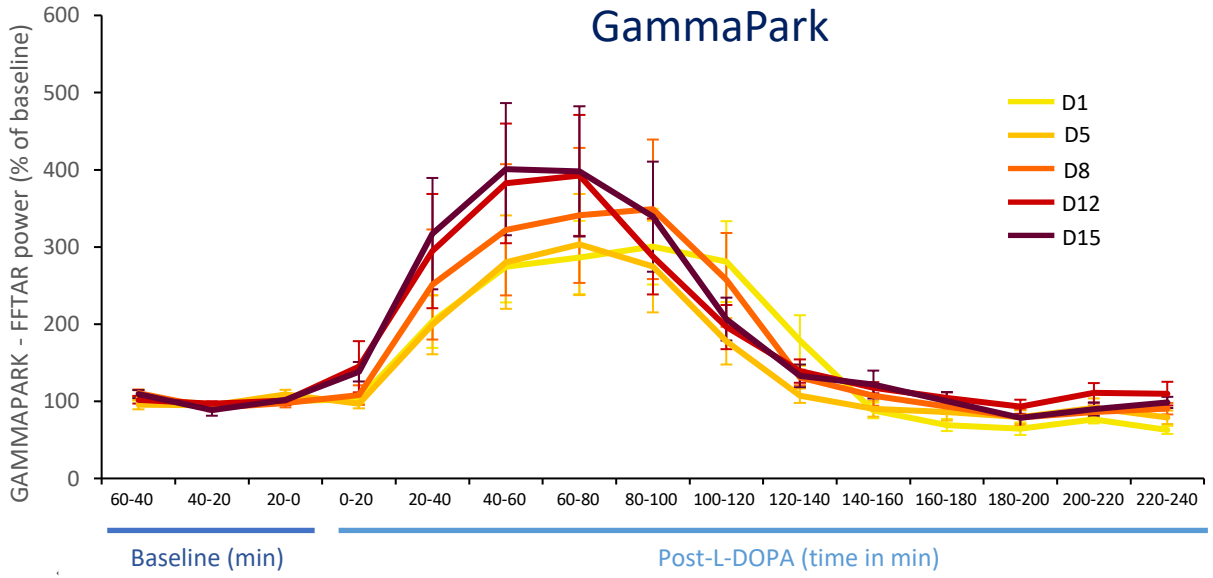
	SKF-38393	Ropinirole	L-DOPA
Chemical formula			
Target	D1/D5 (partial agonist)	D2/D3/D4 (agonist)	All dopaminergic receptors
Effect on Beta in 6OHDA rats (*)	-71%	-36%	-70%
Effect on Gamma in 6OHDA rats (*)	+1680%	+75%	+1780%
Peak effect	2 hours	0.5 hour	3 hours

CHRONIC L-DOPA induces dyskinesia + changes on BetaPark & GammaPark

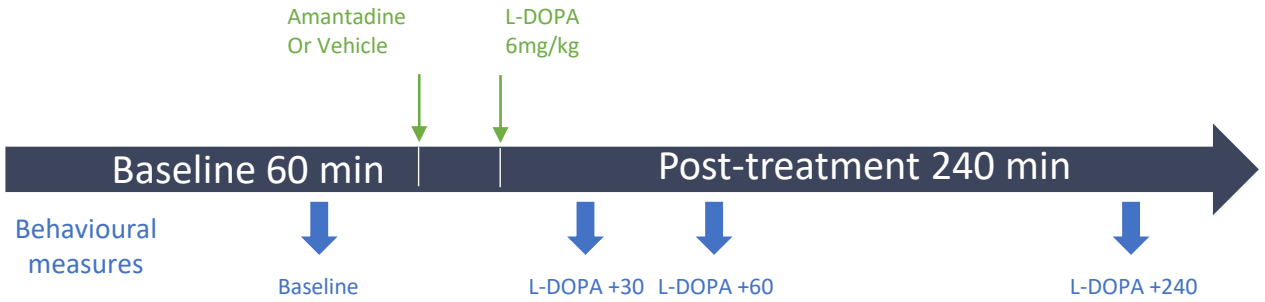


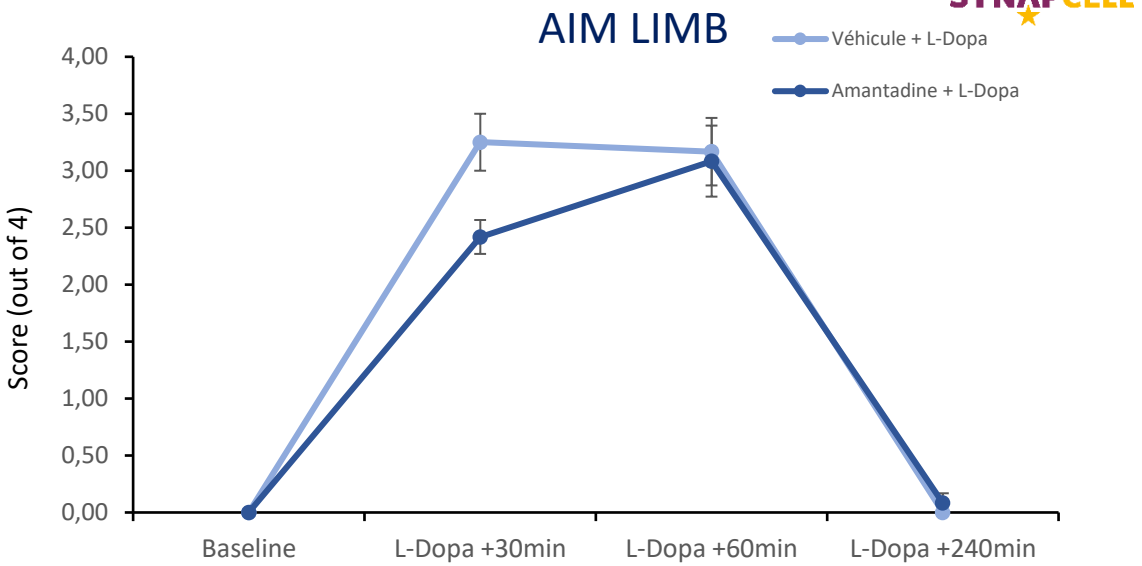


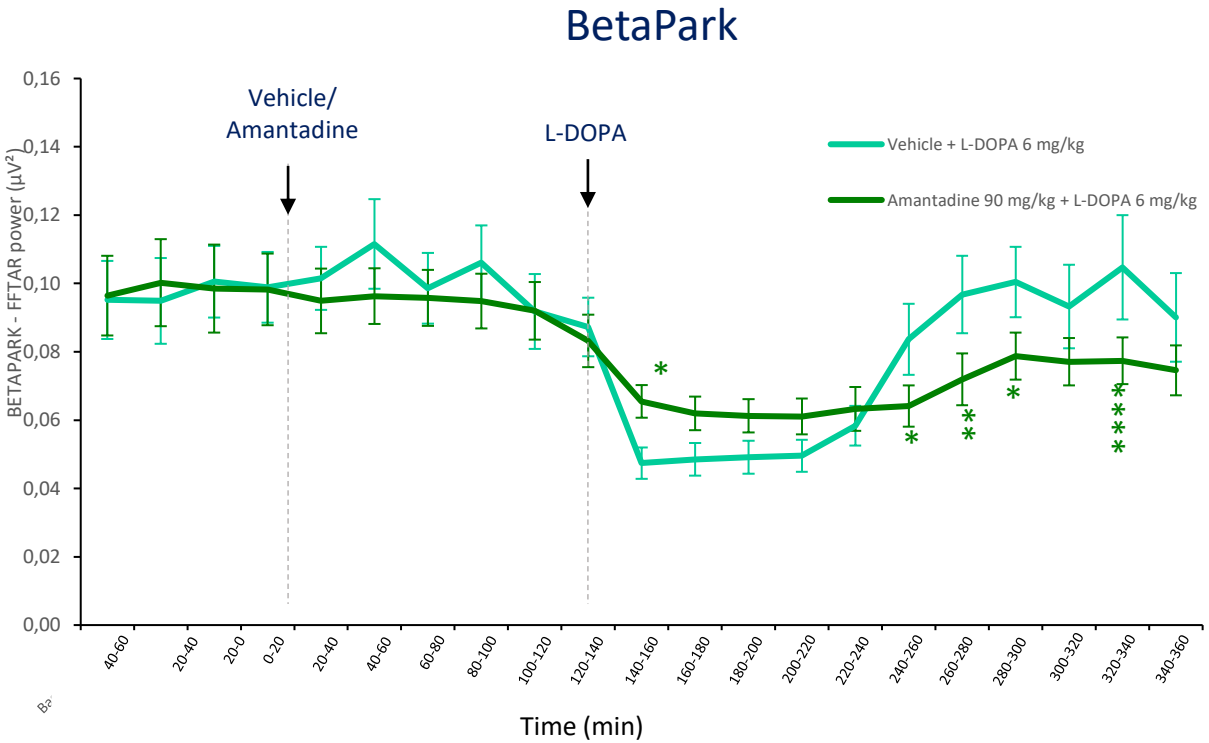


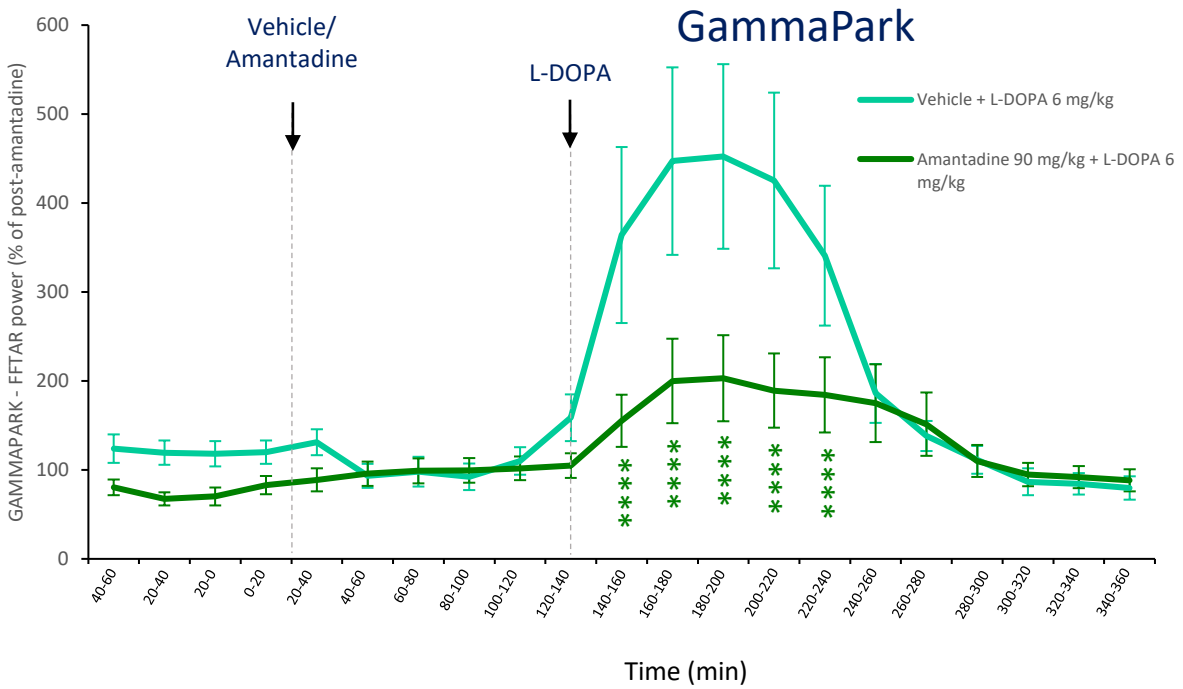


AMANTADINE reduces LID + changes on BetaPark & GammaPark









CONCLUSIONS

SYNAPCELL

- ✓ We identified **a prominent BetaPark oscillation** in the 6-OHDA model of Parkinson's Disease. This oscillation is stable, reliable, can be quantified objectively and is modulated by dopaminergic agonists.
  - ➢ ***BetaPark*** *can be used to* ***evaluate the antiparkinsonian effect*** *of newly developped Neurotherapeutics*
- ✓ We observed **a GammaPark oscillation** associated with the **development of dyskinesia** after chronic administration of L-DOPA
  - ➢ ***GammaPark*** *represents an interesting tool to* ***evaluate the antidyskinetic effect*** *of Neurotherapeutics in Parkinson's disease*

- **BetaPark and GammaPark** represent reliable, objective and clinically-relevant EEG biomarkers of Parkinson's Disease.
- **Pharmacosensitive**, these specific brain oscillatory signatures enable the quantification of anti-parkinsonian or anti-dyskinetic effect of Neurotherapeutics *in vivo*.