



**XXIX Congresso Nazionale SIPF**

*"Beyond the lockdown of the brain"*

**Palermo, 30 settembre - 2 ottobre 2021**

Aula Magna di Economia "Vincenzo Li Donni" - Università degli Studi di Palermo

## **REAL-TIME ASSESSMENT OF INHIBITORY DEFICITS IN PARKINSON'S DISEASE BY COMBINING TMS AND EEG**

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**SANTA LUCIA**  
NEUROSCIENZE  
E RIABILITAZIONE



# INTRODUCTION

## TMS-EMG-EEG CORTICAL BIOMARKERS IN PD

### EXCITABILITY



### CONNECTIVITY



### PLASTICITY



### BEHAVIORAL MEASURES

- Go/NoGo task
- Motor task

### CLINICAL MEASURES

- UPDRS-III
- AIMS
- PD-MMSE

### AIMS

- Test the **sensitivity** of TMS-EEG measures in distinguishing **PD and healthy brain dynamics**
  - Assess the **correlation** of TMS-EEG measures on **PD severity**
- Assess the **predictive value** of TMS-EEG measures on **PD progression**

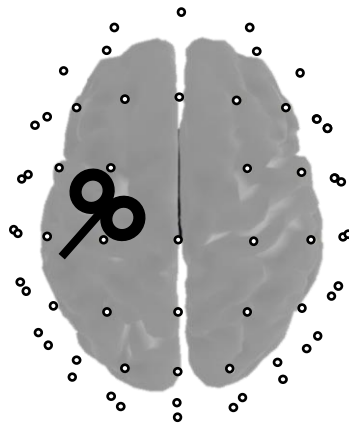
# METHODS

## Participants

	n	SEX (F)	AGE (YEARS)	UPDRS	MMSE	RMT
PD	15	5	72.2±4.8	12.3±4.7	27.3±2.5	58.2±10.5
HV	15	4	56.4±10.6	-	29.5±0.8	69.5±6.7

## TMS-EEG recordings

- 160 TMS pulses over the dominant/affected M1 during a Go/NoGo task
- 90% of RMT
- 64 channels EEG

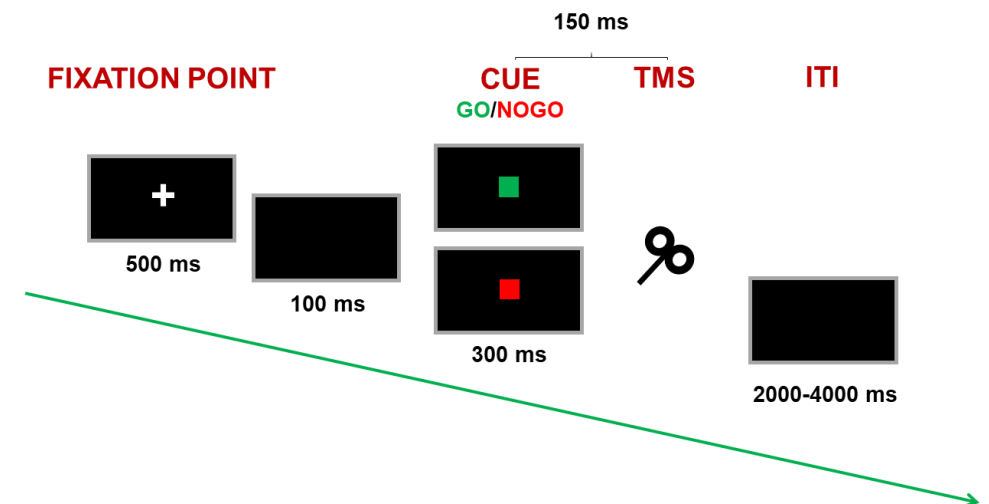


## Patients' characteristic

- Non-discinetic
- 1-3 years from onset disease
- Tested 1 h after therapy assumption (i.e. ON)

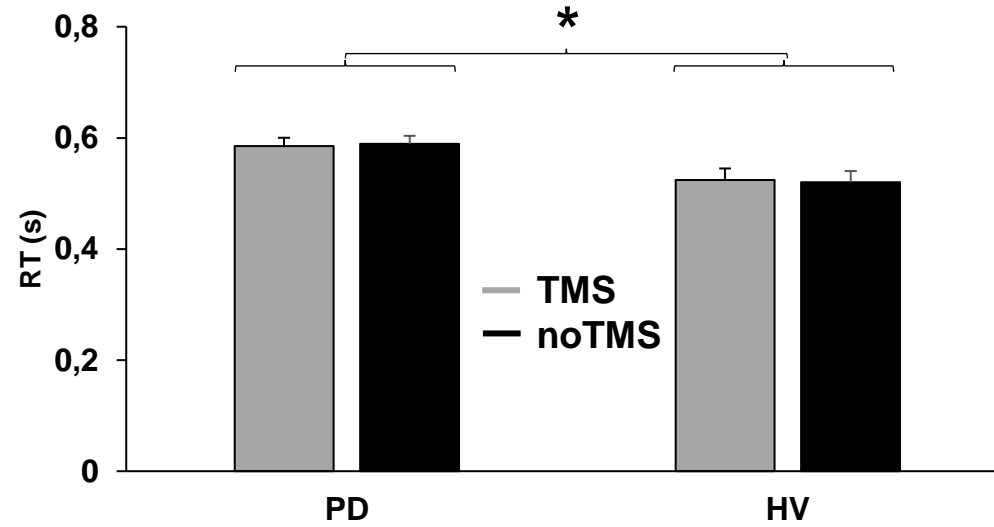
## Behavioral task

- 160 **Go** trials (80 TMS, 80 no TMS)
- 160 **NoGo** trials (80 TMS, 80 no TMS)
- Reaction Time (ms), Accuracy (%), False alarms (n), Miss (n)



# RESULTS: BEHAVIOURAL TASK

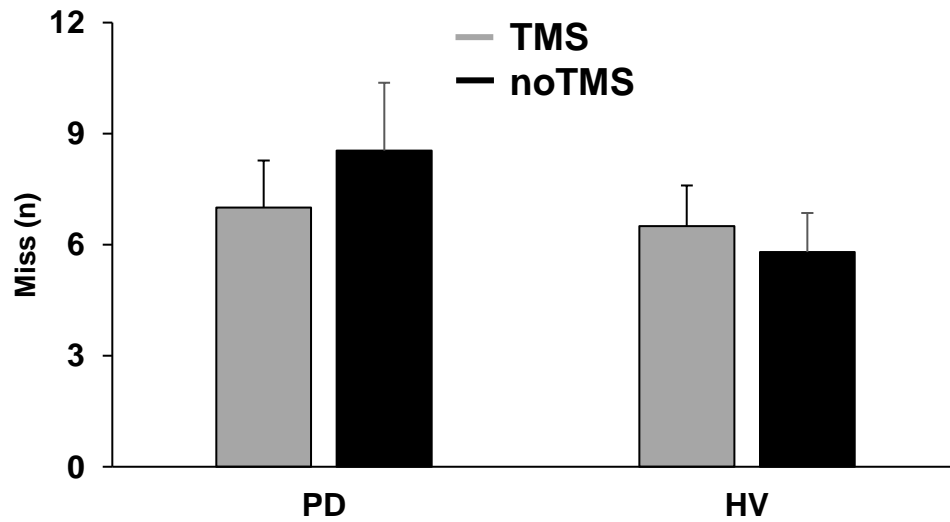
## Reaction times (RT)



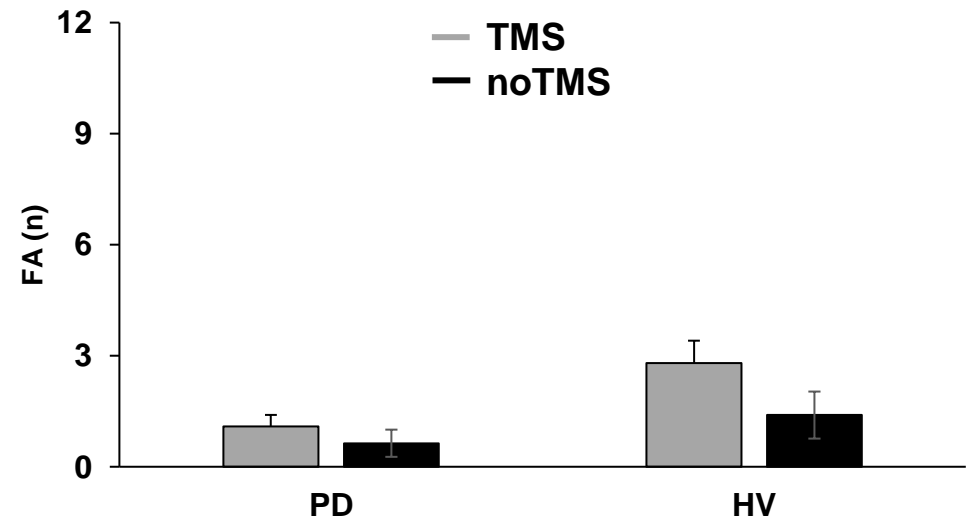
**Group main effect**

$F(1,26)=5.643$ ;  $p=0.025$

## Miss (n)



## FA (n)

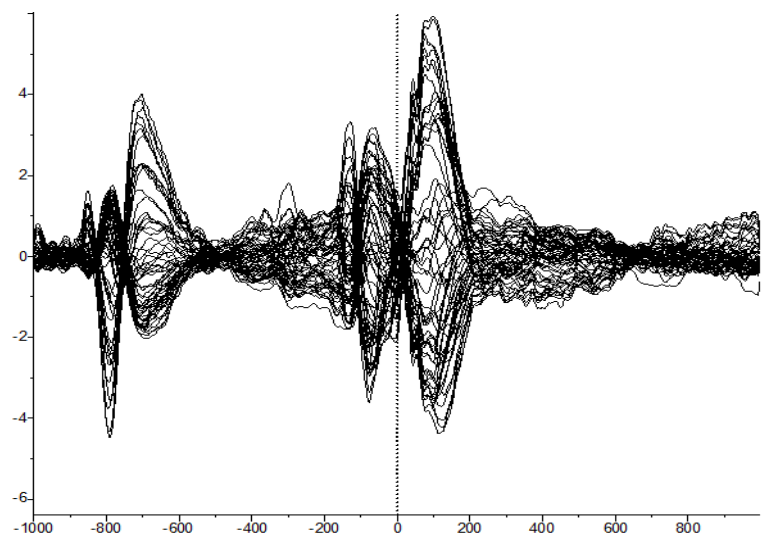
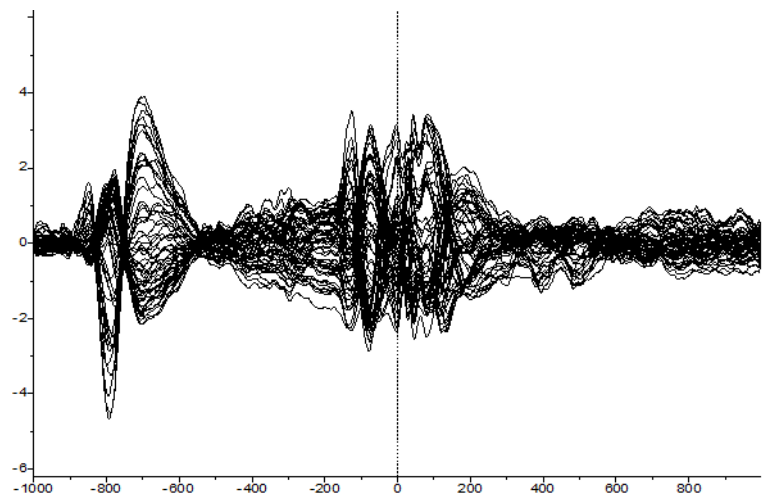


# RESULTS: ELECTROENCEPHALOGRAPHIC RECORDINGS

TMS TRIALS



TERPs



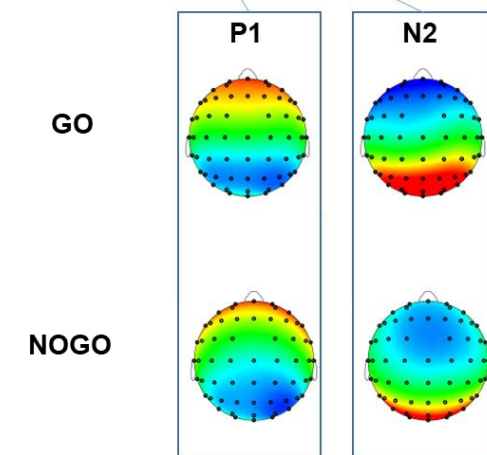
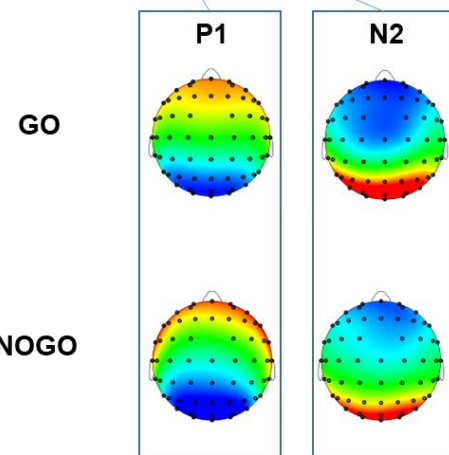
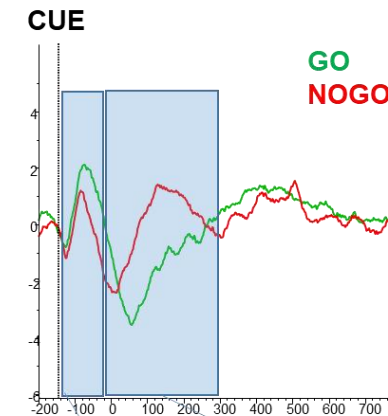
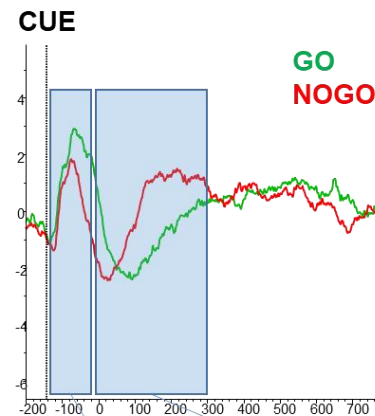
NO TMS TRIALS



ERPs



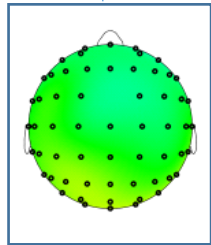
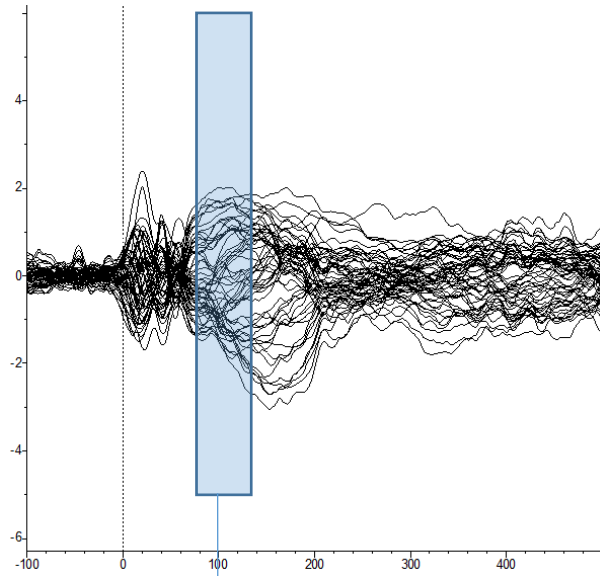
TEPs



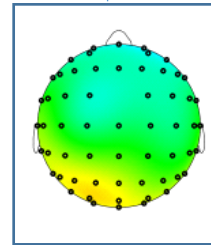
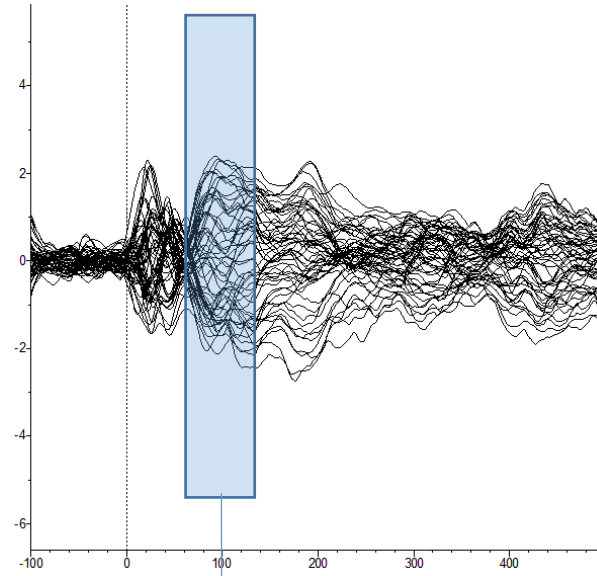
# RESULTS: TMS-EVOKED POTENTIALS

## PD

### GO

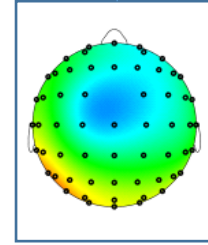
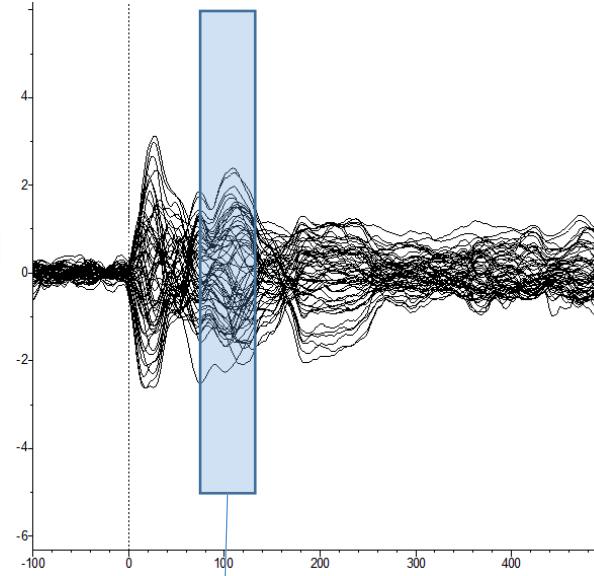


### NOGO

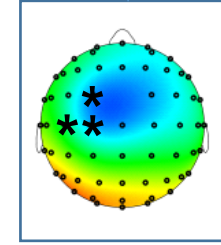
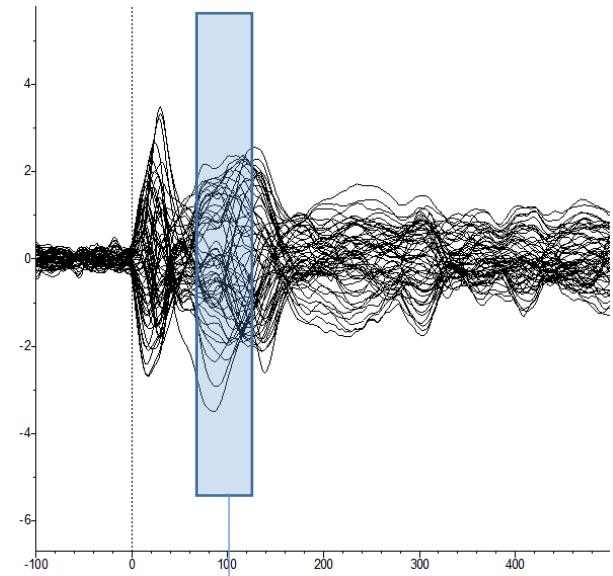


## HV

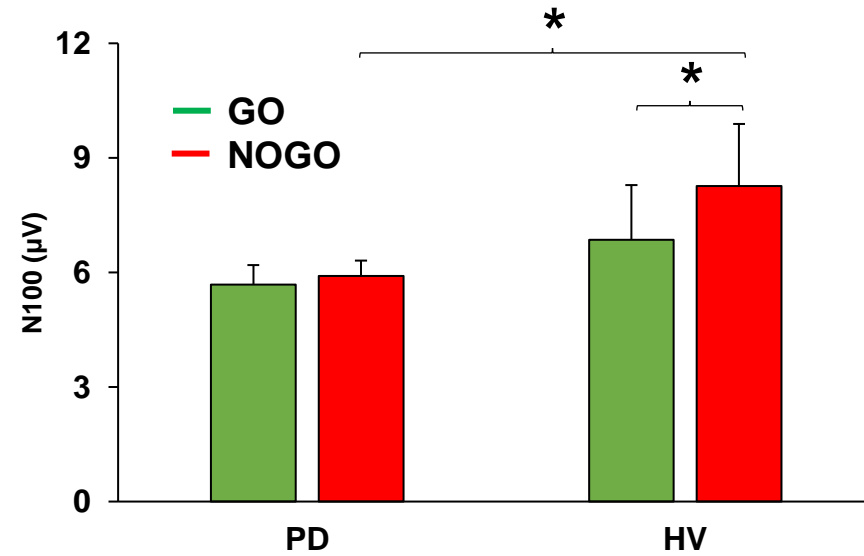
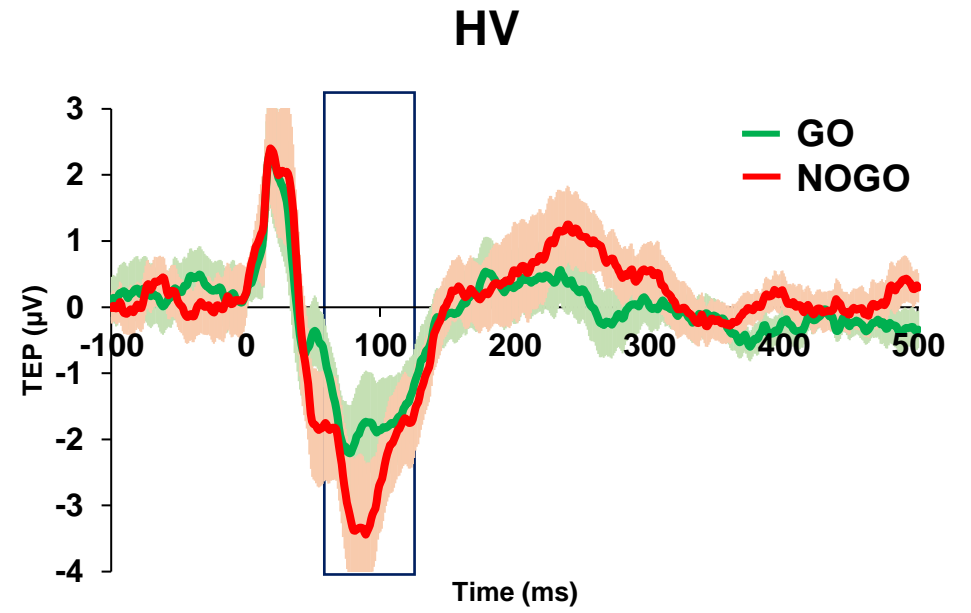
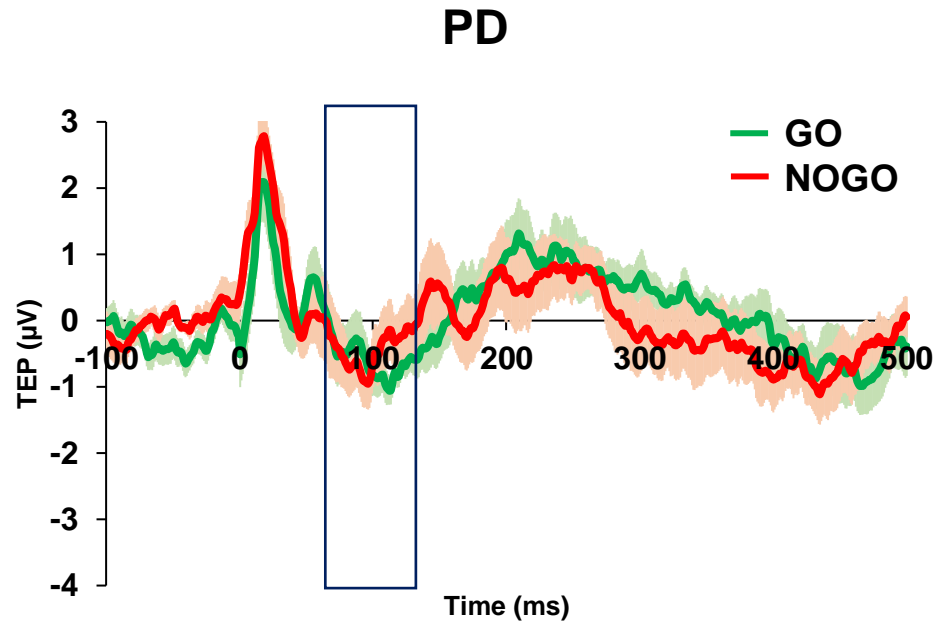
### GO



### NOGO



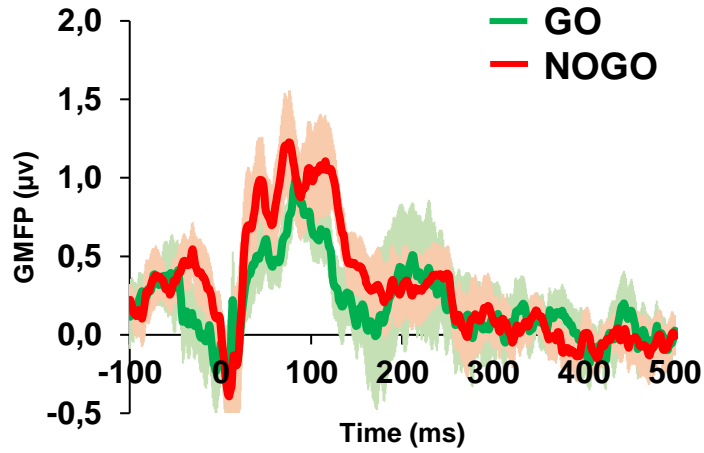
# RESULTS: LOCAL REACTIVITY



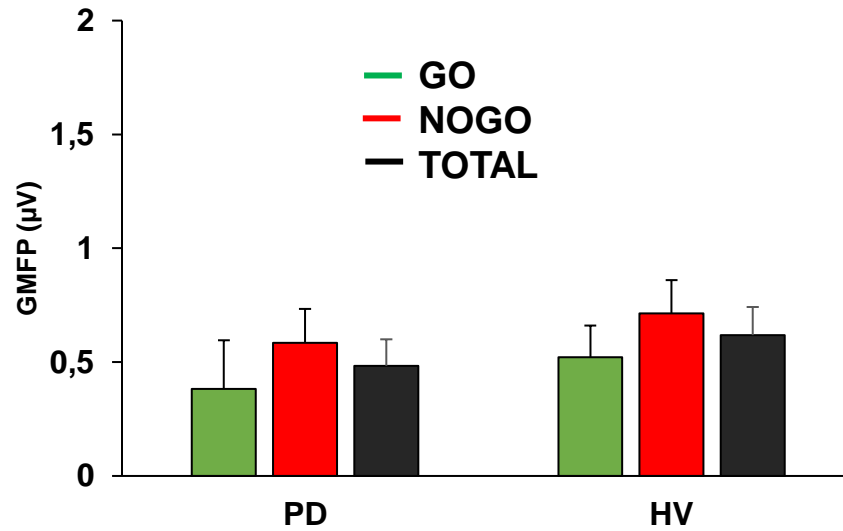
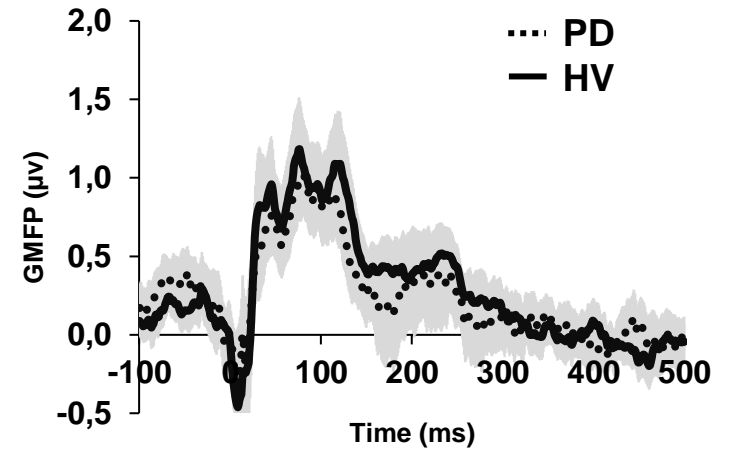
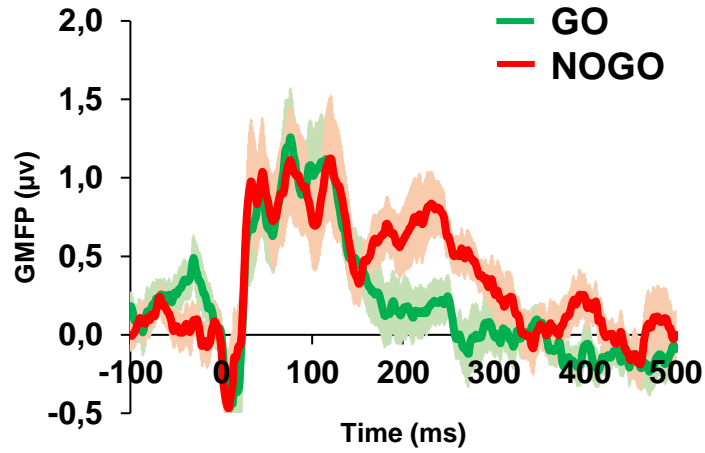
**Group\*condition interaction**  
 $F(1,26)=5.433$ ;  $p=0.028$

# RESULTS: GLOBAL REACTIVITY

## PD



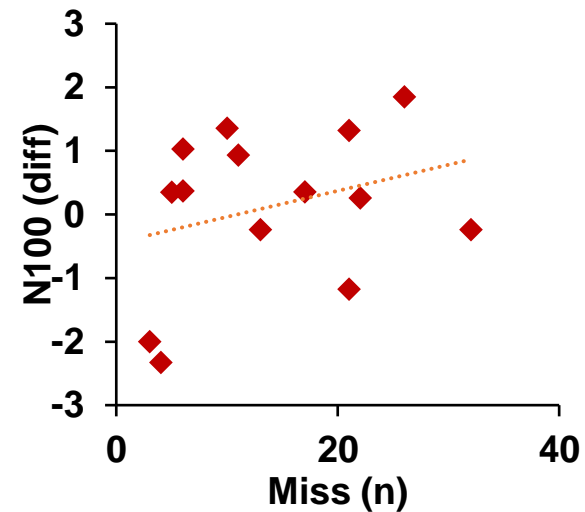
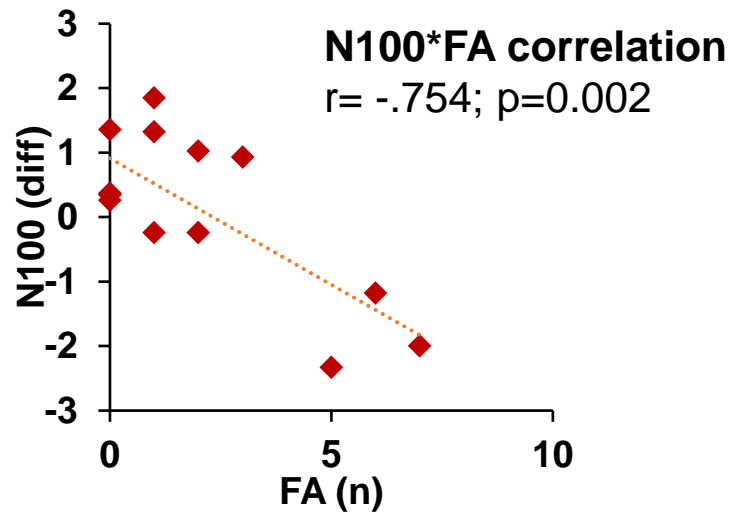
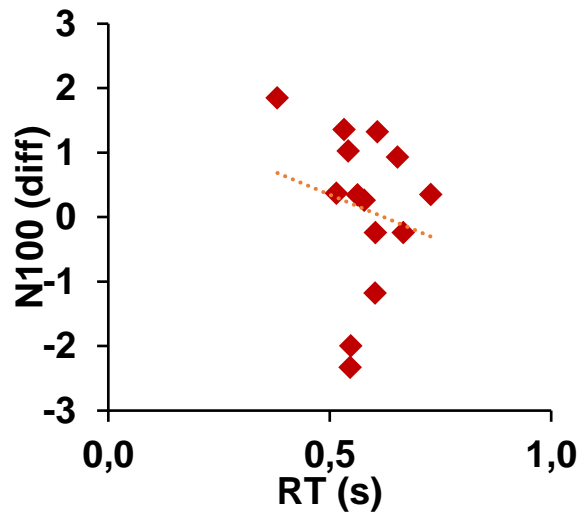
## HV



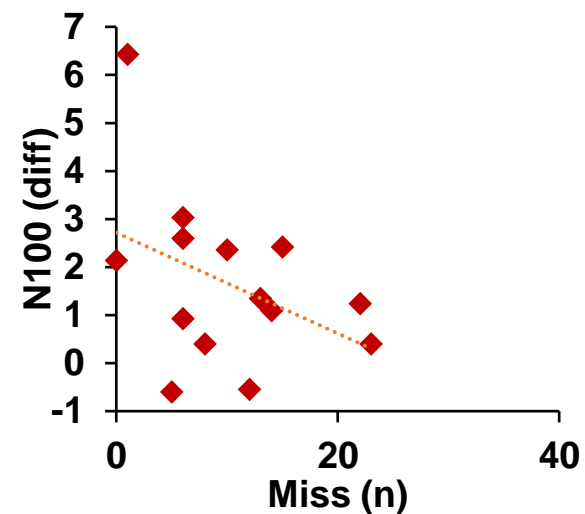
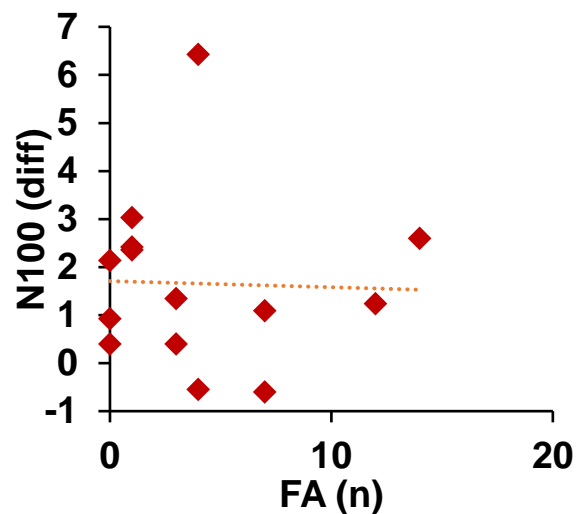
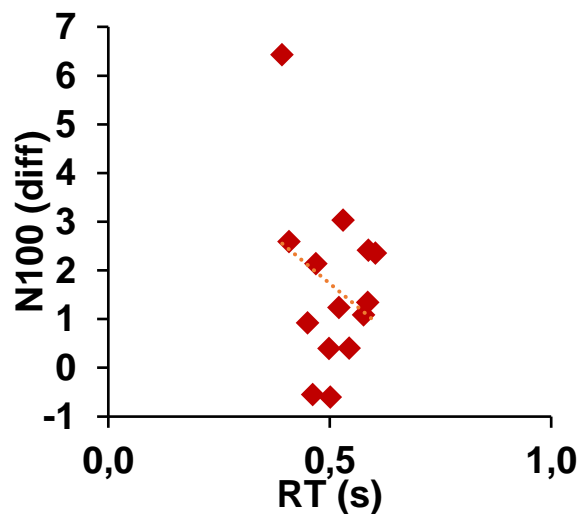


# RESULTS: GLOBAL REACTIVITY

## PD



## HV



# RESULTS: BEHAVIORAL-NEUROPHYSIOLOGICAL CORRELATIONS

1. TEP-N100 MODULATION IN HV (HIGHER IN NOGO TRIALS), BUT NOT IN PD PATIENTS
2. LINEAR RELATIONSHIP BETWEEN TEP-N100 AND FALSE ALARMS IN PD PATIENTS

## N100 AS A MARKER OF INHIBITION

### Behavioural evidence

*Nikulin et al., 2003*

*Bender et al., 2005*

*Bonnard et al., 2009*

### TMS evidence

*Daskalakis et al., 2004*

*Casula et al., 2014*

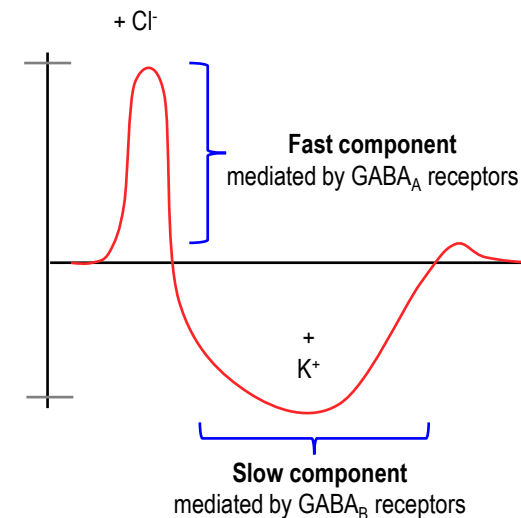
### Pharmacological evidence

*Kakhonen and Wilenius, 2003*

*Premoli et al., 2014; 2015*

The timing of the N100 coincides with slow, GABA<sub>b</sub>-mediated IPSPs observed following stimulation of cortex. N100 is likely to represent this suppression of activity.

(*Rogasch e Fitzgerald, 2012; Premoli et al., 2014; Casula et al., 2014; 2016*)



## **TAKE-HOME MESSAGES**

**1. TEP-N100 AS A RELIABLE MARKER OF INHIBITION IN PD PATIENTS**

**2. TMS-EEG AS A PROMISING TOOL TO DETECT CORTICAL BIOMARKERS IN PD**



**BOTH AT REST AND  
DURING A TASK!**

**HIGHER SENSITIVITY COMPARED TO  
STANDARD ERPs OR BEHAVIORAL  
MEASURES**

**THANKS FOR YOUR ATTENTION!**

*European Commission - Marie Skłodowska-Curie Actions*

*Experimental Neuropsychophysiology Lab, Santa Lucia Foundation (Head: Prof. Giacomo Koch)*

*Dept. of Clinical and Movement Neurosciences, University College London (Head: Prof. John Rothwell)*