PKSTIM: Rewiring dysfunctional brain circuits with personalized stimulation

Gabriel GAUGAIN[1]
Joan DUPREZ[2]
Paul SAULEAU[2,3]
Lorette QUEGUINER[1]
Denys NIKOLAYEV[1]
Julien MODOLO[2]

1 IETR, UMR CNRS 6164, Rennes 1 University
2 LTSI – INSERM U1099, Rennes 1 University
3 CHU Pontchaillou, Neurophysiology unit

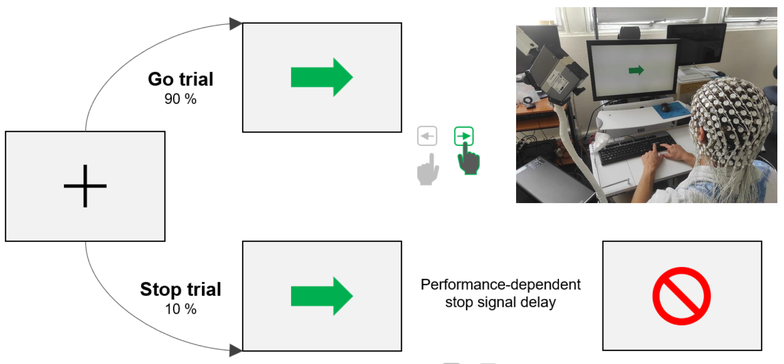
Context and objectives

- **Non-invasive brain stimulation** is a technology that holds promises for the symptomatic treatment of neurological disorders.
- **Transcranial alternating current stimulation** (tACS) has been reported to improve various cognitive functions, by targeting **specific neuronal oscillations** involved in the execution of those functions.
- Here, we propose to develop a **patient-specific tACS protocol** targeting spatiotemporally the inhibitory control circuit, a cognitive function impaired in **Parkinson's disease** (PD).
- The targeted brain region is the **right inferior frontal gyrus (rIFG)**, in which **beta-band (13–30 Hz) oscillations** underlie proper inhibitory control.
- We performed **dosimetric analyses** to optimize positioning of stimulation electrodes and achieve focal rIFG stimulation.
- We also aimed at **designing a clinical trial** aiming **to increase beta-band oscillations in the rIFG using tACS**, at a **stimulation frequency personalized for each participant** (determined using **high-resolution electroencephalography, HR-EEG**).

Clinical trial

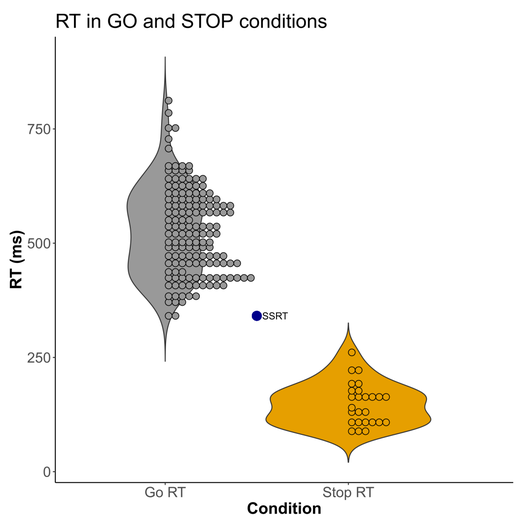
Can personalized tACS relieve inhibition deficits in patients with Parkinson's Disease (PD)?

- Inhibition evaluation (**Stop Task**) with concomitant HR-EEG recordings:



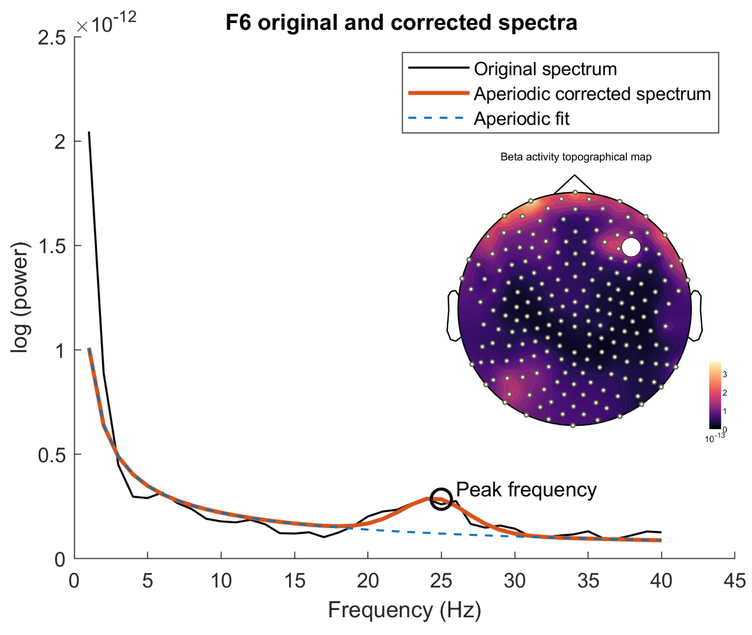
- 40 trials / block
- 25 % of Stop trials / block
- 9 blocks

- **Stop Signal Reaction Time** inferred from behavioral results:



Clinical trial (cont'd)

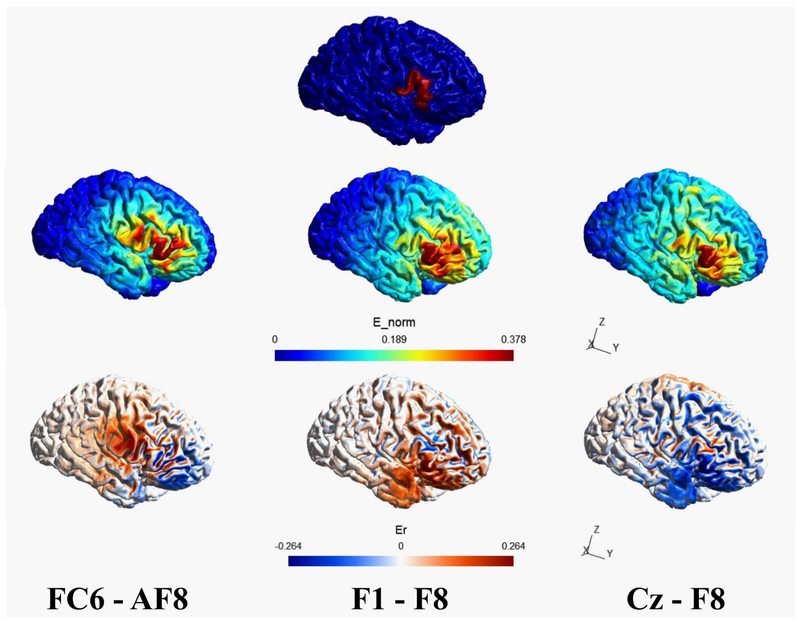
- tACS target frequency evaluated from **task-evoked EEG**:



→ In that **specific** subject, **frequency** of tACS would be set to 25 Hz.

Stimulation setup

→ Need to define a setup for stimulating the target using tACS: *a priori* **optimization** using **numerical head models**

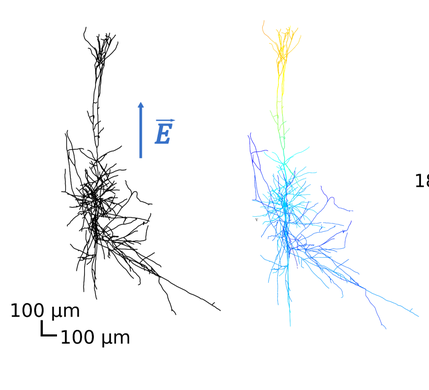


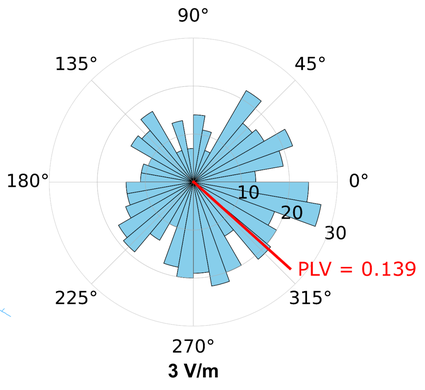
- Optimizations performed using a combination of Manual / Inhouse code and SimNIBS, to **maximize the electric field at the rIFG level**.

Neural modeling

- In addition to dosimetry, it is required to understand the impact of tACS-induced electric fields at the single-cell level (**neurofunctional models**).
- Effect of electric field on **biophysically and morphologically realistic neurons** quantified using NEURON and BBP cells.
- Could we improve our understanding of tACS effect on **spike timing** and activity of single neurons?

Neural modeling (cont'd)

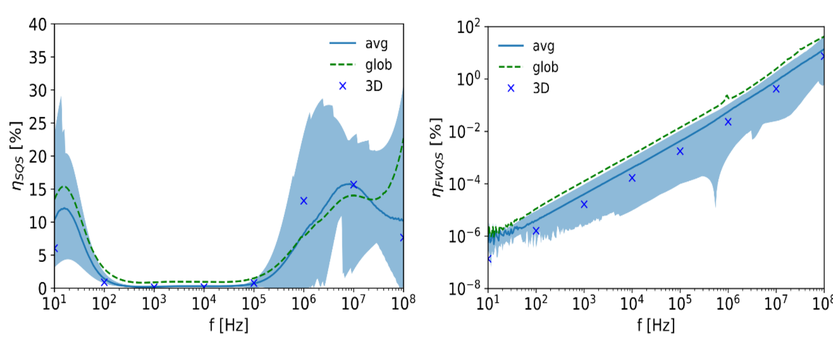




→ Quantification of electric fields effects on the **phase coherence of neuronal firing**.

Electric field modeling

Study about the accuracy of approximations made to numerically predict the *in situ* electric field.



→ Limit on the quasi-static approximation and importance of considering the **relative permittivity** of the medium.

Conclusion & future prospects

- Modeling the coupling between single neurons and electric field to understand which **mechanism** leads to tACS efficacy.
- Improve EF modeling with **new formulations**.
- Healthy **volunteers and PD patients recruitment** for individualized stimulation frequency characterization.
- **Double-blind randomized trial** with stimulation visits.

References

- Gaugain *et al.* (2021) 'Modeling accuracy of transcranial current stimumation: Static and quasi-static approximations errors', in *Proc. BioEM 2021*. *BioEM 2021*, Ghent.
- Gaugain *et al.* (2022) 'Effect of permittivity on temporal interference modeling', in *Proc. BioEM 2022*. *BioEM 2022*, Nagoya.
- Gaugain *et al.* (2022) 'Quasi-Static Approximation Error of Electric Field Analysis for Transcranial Current Stimulation'. Available at: https://doi.org/10.48550/ARXIV.2204.03555.
- Gaugain *et al.* (2022) 'Temporal interference modeling error using purely conductive medium appoximation', in *44th Annual Int. Conf. of IEEE Engineering in Medicine and Biology Society (EMBC)*, Glasgow.
- Allouch et al. (2022) 'Effect of channel density, inverse/connectivity methods on EEG resting-state networks: a simulation study'. Submitted (Neuroimage Reports). Available at: https://doi.org/10.1101/2022.06.01.494301.
- Modolo et al. (2022) 'Mechanisms and controversies of transcranial current stimulation'. In preparation.