Neurophysiological impact of a fronto-temporal tDCS in healthy humans: A multimodal PET-MR imaging approach

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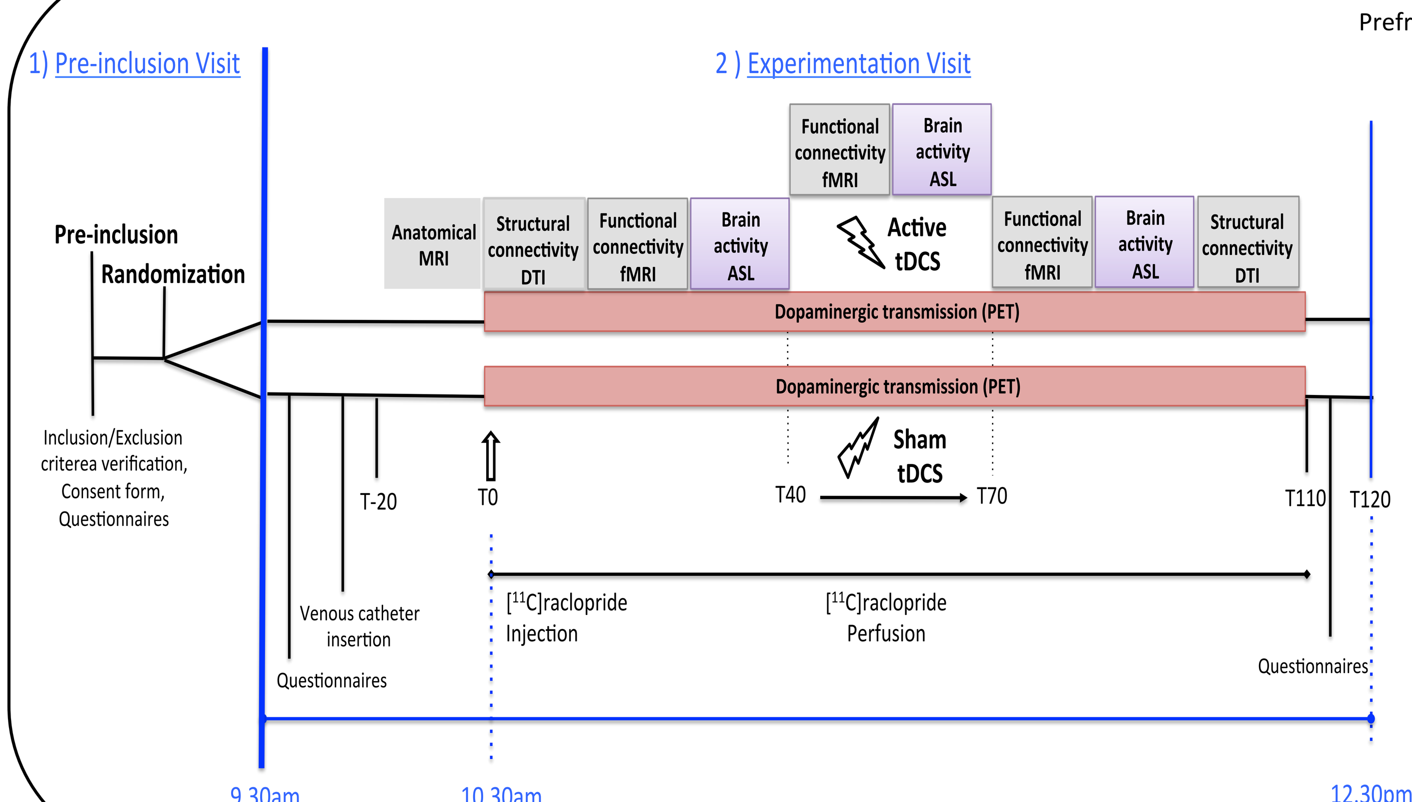
Background

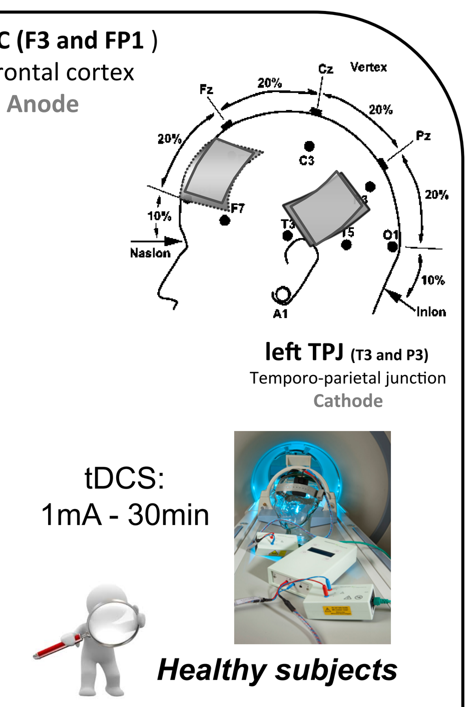
Fronto-temporal tDCS, with anodal stimulation over the left DLPFC and cathodal stimulation over the left temporo-parietal junction (TPJ), has been reported to reduce treatment-resistant symptoms in patients with schizophrenia[1]. Despite an increasing use in clinical settings, acute and subsequent effects of fronto-temporal tDCS are far from being completely understood. The few offline imaging studies and computational reports available suggest that fronto-temporal tDCS effects are not restricted to the brain areas located under the electrodes, but spread through distributed cortical networks functionally connected with the targets and reach subcortical areas, such as dopaminergic areas. Overall, these studies suggest that tDCS modulates brain activity and functional connectivity within and across resting-state networks[2]. However, these effects are currently described at different levels depending on the imaging technique used and online effects are rarely inspected.

Objectives

The aim of this study was to reveal, in healthy subjects, the combined acute and subsequent neurobiological impacts of a single-session of fronto-temporal tDCS in a unique experiment by developing a simultaneous multimodal imaging approach (PET-MR). The online implementation of the stimulation will allow deciphering changes induced during and after stimulation compared to baseline levels.

Experimental design



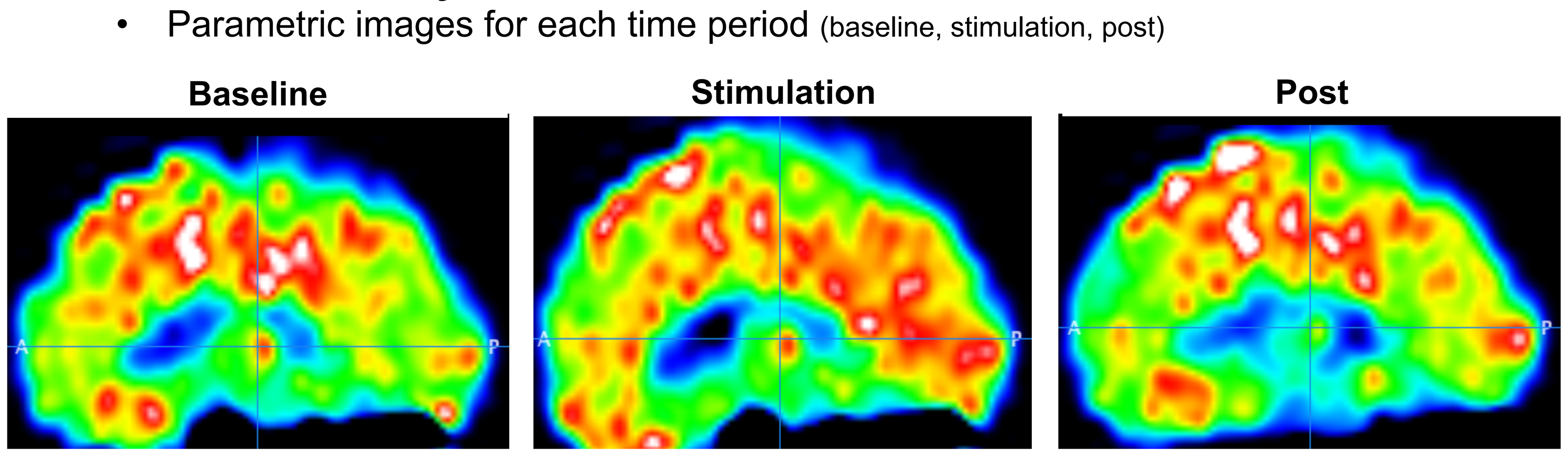


	ACTIVE	SHAM
n	15	15
Age (mean±sd)	25.00 (±2.07)	26.13 (±2.94)

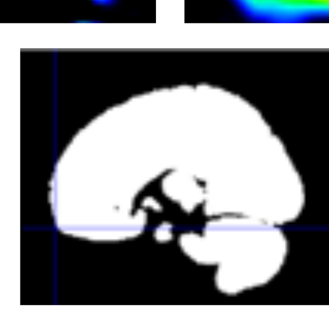
ASL – Analysis – Whole Brain Perfusion

Voxel-based analysis

- Parametric images for each time period (baseline, stimulation, post)



Flexible factorial design (Group * Time period)
Whole brain analysis

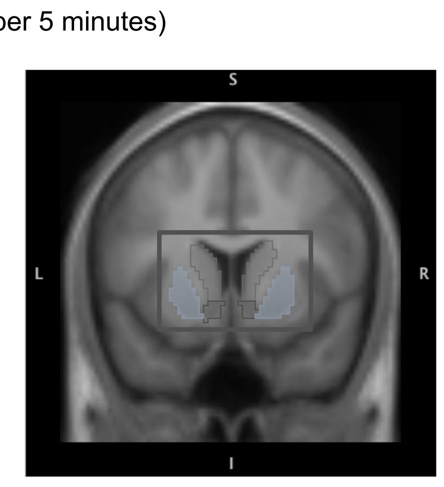


Preprocessing (movement correction, coregistration, temporal filtering, partial volume correction, normalization and smoothing-6mm) were performed using an in-house script combining SPM12 and ASL toolbox[5]
Regions were determined based on the adult brain atlas developed by A. Hammers et al. (2003)[4]

PET – Analysis - Subcortical dopamine

Kinetic Analysis (1 timepoint per 5 minutes)

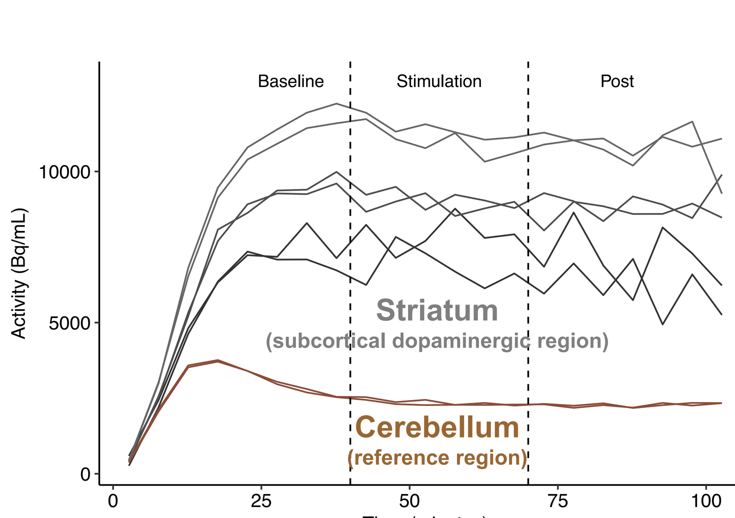
- **Extraction of time activity curve** (TACs)
  In the region of interest (**striatum**) and reference region (**cerebellum**)

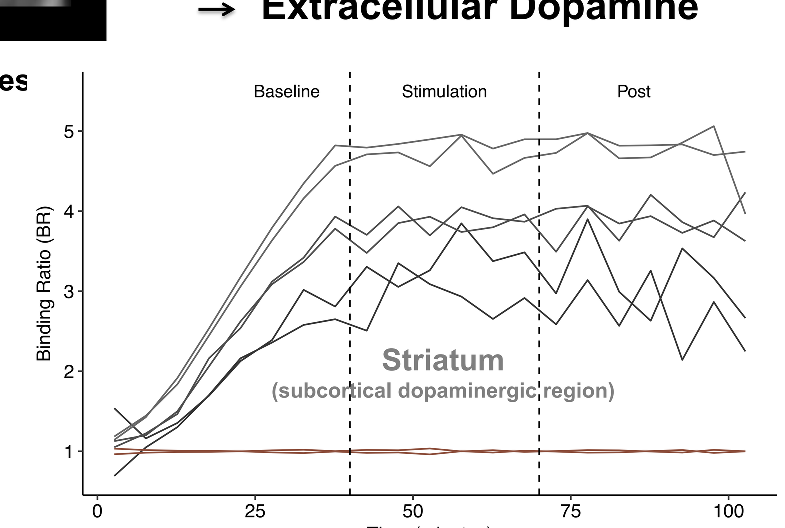


Regions of interes Atlas on MRI

- **Binding potential ratio** (BR)
  Ratio of region of interest / cerebellum activities

→ **Extracellular Dopamine**

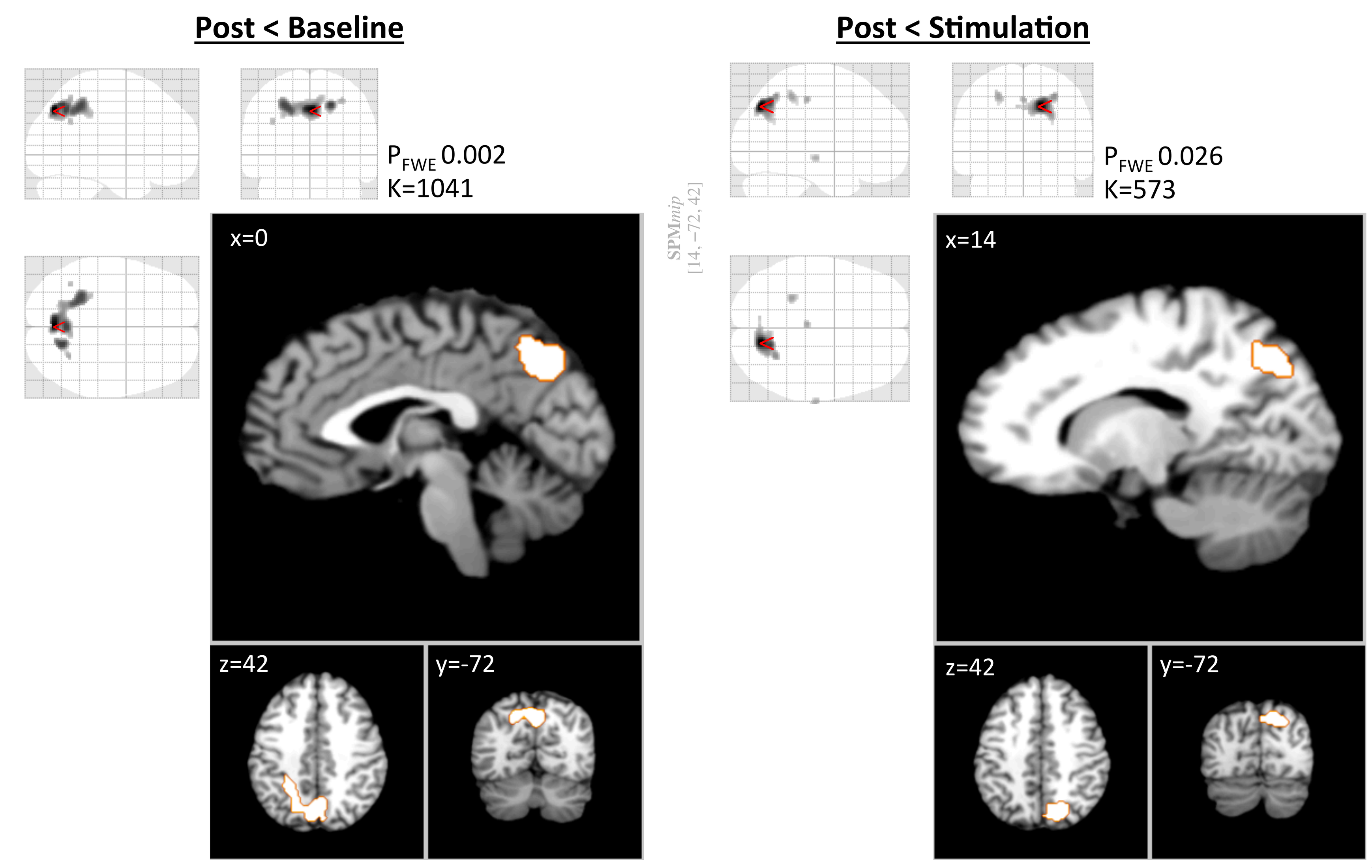




Preprocessing were performed using an in-house script combining SPM12, Turku and minc tools
Motion correction was done using EBER correction[3]
Regions were determined based on the adult brain atlas developed by A. Hammers et al. (2003)[4]

Cerebral blood flow is decreased in the precuneus after fronto-temporal tDCS

- Widespread **decrease** of CBF quantification, specifically in regions of the **superior parietal gryus** during the **20 to 30 minutes after** the end of the stimulation.



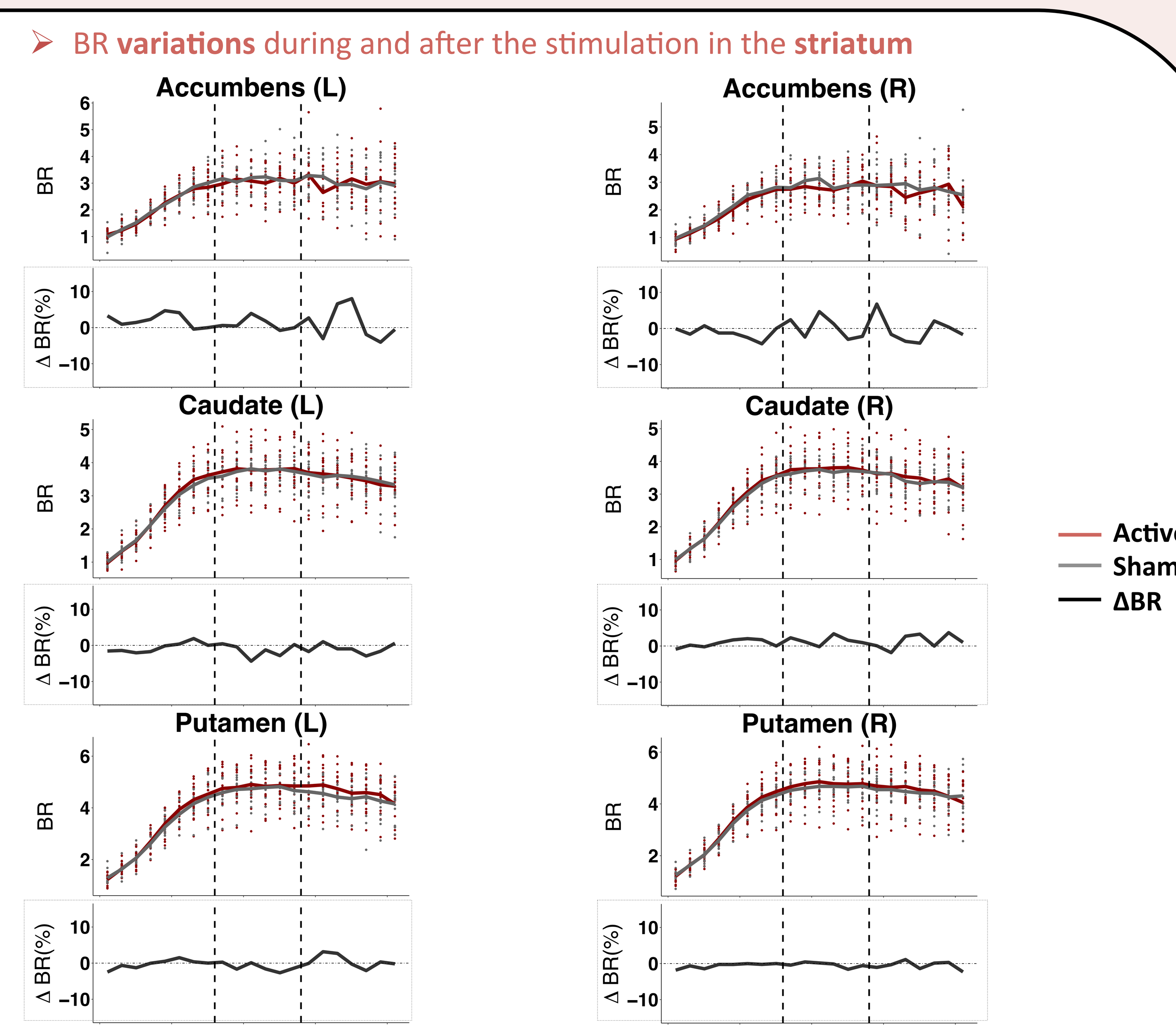
Significant clusters from the parametric analysis ($P_{uncorrected}$ < 0.001, P_{FWE} 0.05) were selected.
Active-Sham group

Heterogeneity in subcortical dopamine transmission response

LEFT HEMISPHERE BR curve

RIGHT HEMISPHERE BR curve

- BR **variations** during and after the stimulation in the **striatum**



Differences between sham and active groups were assessed in terms of BR variation (Δ) at

$$\Delta(\%) = \left(\frac{BR\{timepoint\} - BR\{baseline\}}{BR\{baseline\}} \times 100\right) - \text{Mean Sham}\,(BR\{timepoint\})$$

Discussion

When comparing the acute and subsequent effects of active and sham tDCS groups, CBF quantification showed significant decreases only after the end of the stimulation in the superior parietal gyrus. This region includes the precuneus a region connected to the stimulation sites and part of the default mode network.
In addition, fronto-temporal tDCS seems to have a heterogenous effect on the dopaminergic transmission in striatal subregions.
Further analyses are needed to create a coherent ensemble to better understand the mechanisms of fronto-temporal tDCS.

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3. EBER, Anthonin Reilhac
4. A. Hammers et al (2003) "Three-dimensional maximum probability atlas of the human brain, with particular reference to the temporal lobe," *Hum. Brain Mapp.*, vol. 19, no. 4, pp. 224–247.
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