Neurophysiological impact of a fronto-temporal transcranial direct current stimulation in healthy subjects
A multimodal PET-MR imaging approach

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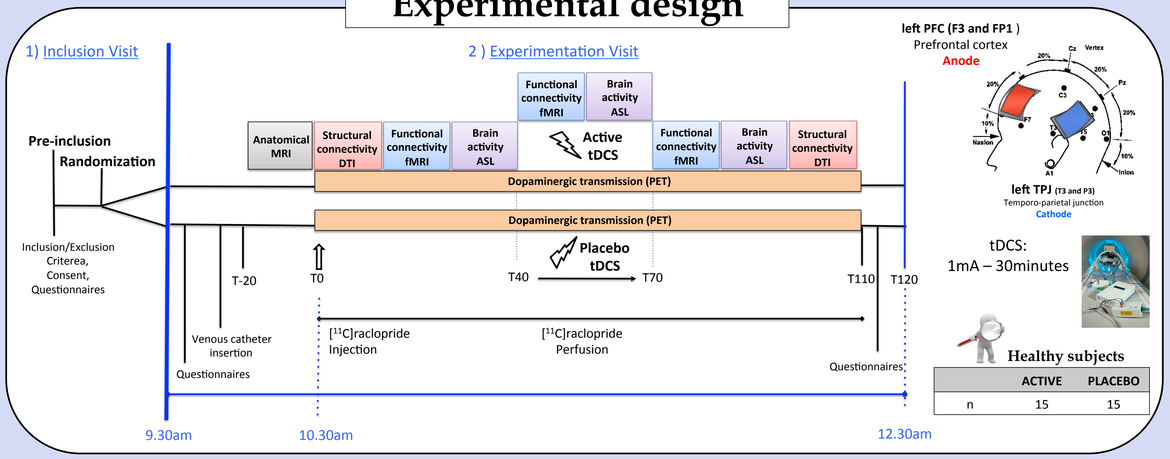
Introduction

Fronto-temporal transcranial direct current stimulation (tDCS), with anodal stimulation over the left dorsolateral prefrontal cortex and cathodal stimulation over the left temporo-parietal junction, has been reported to reduce treatment-resistant auditory hallucinations, negative symptoms and insight of the illness in schizophrenia[1]. Despite an increasing use in clinical settings, acute and subsequent neurophysiological effects of fronto-temporal tDCS are far from being completely understood. The few imaging 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. Finally, effects of the stimulation applied online are rarely inspected.

Objectives

According to the hypothesis that fronto-temporal tDCS modulates brain activity, connectivity and dopaminergic transmission, the aim of this project is to reveal the combined neurobiological impact of an online 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



Structural connectivity
Diffusion tract imaging (DTI)

Structural connectivity between the stimulated regions
- Arcuate Fasciculus
- Corpus callosum

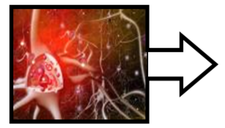
Tract based spatial statistics (TBSS) – FSL

Outcome

Mesures:
Coherent ensemble

Expected results:
Imaging biomarker

NEUROBIOLOGY



Dopaminergic transmission (PET)

NEUROPHYSIOLOGY

Structural connectivity (DTI)
Fonctional connectivity (fMRI)
Brain activity (ASL)

Before stimulation
« Normal brain »

Pathological brain

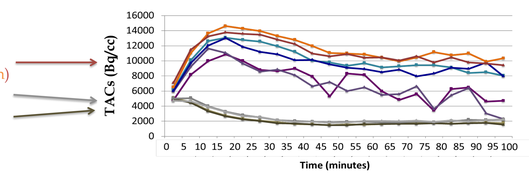
Neurophysiological effects of fronto-temporal tDCS

Improved care for patients with schizophrenia

Dopaminergic transmission
Kinetic Analysis - Example

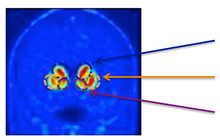
1) Extraction of time activity curve (TACs) in each region of interest in the right and left hemispheres

3 subcortical dopaminergic regions (nucleus accumbens, caudate nucleus, putamen)
1 control region (precentral gyrus)
1 reference region (cerebellum)



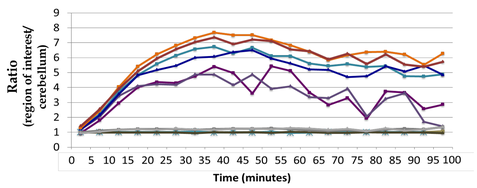
2) Binding potential (BP_R) = ratio of region of interest/mean left and right cerebellum activities

→ **Extracellular Dopamine**



PET image Regions of interest

Caudate Nucleus
Putamen
Nucleus Accumbens



Regions were determined based on the adult brain atlas developed by A. Hammers et al. (2003)[3]

Functional connectivity
Resting state fMRI

Connectivity between the stimulated regions
- DLPFC and TPJ

Impact on resting state networks
- Default Mode Network
- Fronto-Parietal Network
- Cingulo-Opercular Network

CONN toolbox

Brain activity
Pseudo-continuous arterial spin labeling (pCASL)

Quantitative and direct measure of the cerebral blood flow (CBF) between the stimulated regions
- DLPFC and TPJ

ASL Toobox

Conclusion

With the first subjects included in the study, image analysis protocols are being developed independently for each modality in order to establish correlations. Also, the combination of these modalities is being considered.
Our unique approach will create a coherent ensemble, which is a mandatory and critical step to understand the mechanisms of action of tDCS. Moreover, in the long run, we expect that it will provide an imaging biomarker essential to improve our understanding of the "normal brain" and deficient mechanisms underlying schizophrenia as well as neurological disorders.

1. Brunelin, J., Mondino, M., Gassab, L., Haesebaert, F., Gaha, L., Suaud-Chagny, M.-F., Saoud, M., Mechri, A. & Poulet, E. (2012) Examining Transcranial Direct-Current Stimulation (tDCS) as a Treatment for Hallucinations in Schizophrenia. American Journal of Psychiatry, 169, 719—724.
2. Saoite C., Turi Z., Paulus W., & Antal A. (2013) Combining functional magnetic resonance imaging with transcranial electrical stimulation. *Front Hum Neurosci*, 7, 435
3. A. Hammers, R. Allom, M. J. Koepp, S. L. Free, R. Myers, L. Lemieux, T. N. Mitchell, D. J. Brooks, and J. S. Duncan, "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, Aug. 2003.

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