

**Title: NEUROPHYSIOLOGICAL IMPACT OF A FRONTO-TEMPORAL TRANSCRANIAL DIRECT CURRENT STIMULATION IN HEALTHY SUBJECTS: A MULTIMODAL PET-MR IMAGING APPROACH**

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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 symptoms in patients with schizophrenia. 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 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. 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 is to reveal the combined acute and subsequent neurobiological effects of a single session of fronto-temporal tDCS in a unique experiment by developing a simultaneous multimodal imaging approach (PET-MR).

**Methods:** 30 healthy subjects randomly received a single-session of either active (30 min, 1mA; n=15) or sham (n=15) fronto-temporal tDCS during a simultaneous PET-MR scan. The distributed changes are explored at rest through:

- Specific and localized dopaminergic transmission evaluated by PET using dopaminergic D2 subtype receptor availability via [<sup>11</sup>C]raclopride binding. The tracer was administered intravenous, using a bolus-plus-continuous-infusion method.
- Brain activity assessed by cerebral blood flow quantitatively and directly measured by pseudo-continuous arterial spin labelling (pCASL, three 6 min-scans before, during and after tDCS).
- Spontaneous functional connectivity assessed by resting state functional MRI (rs-fMRI, three 13 min-scans before, during and after tDCS).
- Structural connectivity assessed by diffusion tensor imaging (DTI, two 10 min scans before and after tDCS).

**Perspectives:** Our unique combined approach will create a coherent ensemble, which is a mandatory and critical step to understand the mechanisms of action of fronto-temporal tDCS.