Title: **IMPACT OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON THE DOPAMINERGIC TRANSMISSION IN HEALTHY HUMANS**

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Keywords: tDCS, dopamine, subcortical, PET, DLPFC

Transcranial direct current stimulation (tDCS) is a technique emerging as a prospective therapy for neurologic and psychiatric disorders. Specifically, anodal tDCS applied over the left dorsolateral prefrontal cortex (DLPFC) is associated with improvement of symptoms, cognitive functions and mood. However, despite an increasing use in clinical settings, acute and subsequent neurobiological effects of tDCS are far from being completely understood. Some offline imaging reports suggest that tDCS neurobiological 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. Recent fMRI studies and computational model analysis highlighted subcortical effects of tDCS applied at the cortical level including modulations of cortico-striatal and thalamo-cortical functional connectivity. Moreover, some offline studies suggest that cortical stimulation by other approaches, such as transcranial magnetic stimulation may evoke a subcortical dopamine release following a single session applied over the left DLPFC. However, the online and subsequent effects of a single session of tDCS applied over the DLPFCs on dopaminergic transmission are still unknown. **Objectives:** The hypothesis is that, in healthy subjects, a single-session of tDCS applied bilaterally with the anode over the left DLPFC modulates subcortical dopaminergic transmission. These effects are explored online by positron emission tomography (PET) using dopaminergic D2 subtype receptor availability via [11C]raclopride binding. **Methods:** At the end, 30 healthy subjects randomly assigned in two groups (active, n = 15 vs sham, n=15) will receive at rest a single-session of either active or sham bifrontal tDCS during a PET scan of 100-minute duration. The tracer, [11C]raclopride, is administered intravenous, using a bolus-plus-continuous-infusion method. The stimulation starts 40 minutes after the injection of the tracer, lasts 20 minutes and is set at 2mA in active mode. PET scans are preceded by an anatomical MRI scan to control subject anatomy and electrode position. Extracellular dopamine is assessed using the binding potential (BP_{ND}) defined as the ratio of region of

interest/cerebellum activities. To investigate the changes induced by tDCS, variations of BP_{ND} are calculated before, during and after the stimulation in the right and left nucleus accumbens, caudate nucleus, putamen and precentral gyrus. **Results:** Preliminary results show that tDCS modulates BP_{ND} specifically in the nucleus accumbens. During the stimulation, the effects observed tend to be opposite in the left and right nucleus accumbens. **Conclusion:** These results suggest that tDCS rapidly impacts subcortical dopaminergic transmission.