Title: **ACUTE AND SUBSEQUENT EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON THE DOPAMINERGIC TRANSMISSION IN HEALTHY HUMANS**

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Bifrontal transcranial direct current stimulation (tDCS), applied over the dorso-lateral prefrontal cortex (DLPFC), is associated with improvement of depressive symptoms and cognitive functions. 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, such as dopaminergic areas. A recent fMRI study suggests subcortical effects of bifrontal tDCS including modulations in the caudate nucleus (Weber et al, 2014). Moreover, some offline studies suggest that cortical stimulation by other approaches, such as transcranial magnetic stimulation may evoke a subcortical dopamine release in the nucleus accumbens following a single session applied over the left DLPFC (Brunelin et al, *Schizophr Res*, 2011). However, the effect of bifrontal tDCS on dopaminergic transmission is still unknown as well as if this effect is specifically distributed across subcortical dopaminergic areas. **Objectives:** The aim of this study is to test, in healthy subjects, the effect of a single-session of bifrontal tDCS with the anode over the left DLPFC and the cathode over the right DLPFC on the subcortical dopaminergic transmission. These effects are explored online by positron emission tomography (PET) using dopaminergic D2 subtype receptor availability via [^{11}C]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, [^{11}C]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, electrode position and define the regions of interest (ROI). Extracellular dopamine concentration is assessed using simple pseudo-equilibrium 5-min ratios of ROI to cerebellum activities (B/F ratio). To investigate the changes induced by tDCS, variations of B/F ratio 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 B/F ratio 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 specifically in the nucleus accumbens.