Impact of transcranial direct current stimulation (tDCS) on the dopaminergic transmission in healthy humans

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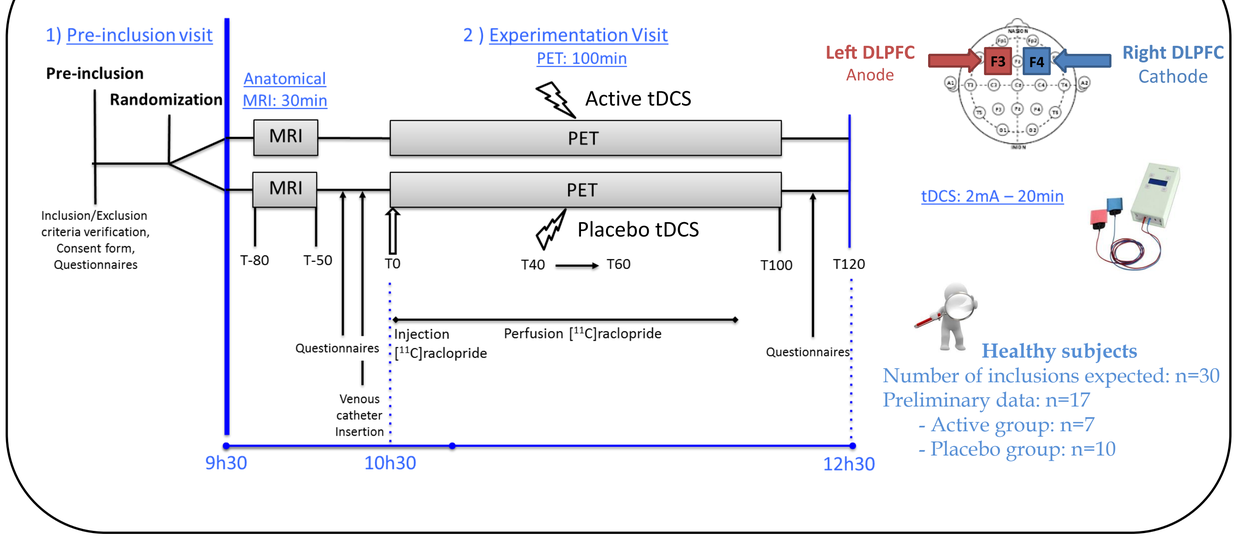
Introduction

Bifrontal tDCS is associated with improvement of depressive symptoms and cognitive functions. 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, such as dopaminergic areas. A recent fMRI study suggested 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 dorso-lateral prefrontal cortex (DLPFC) (Brunelin et al, 2011). Thus, 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

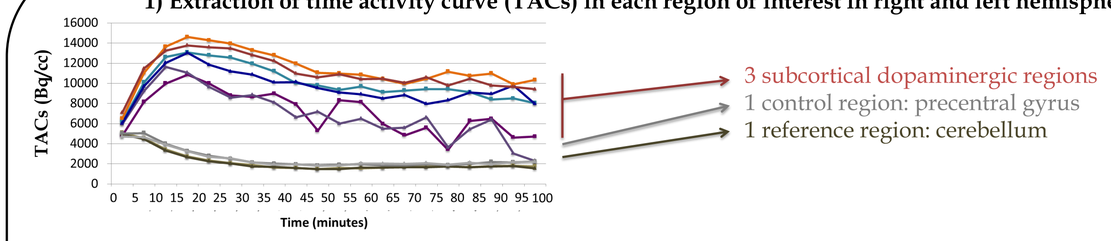
The aim of this study is to test, in healthy subjects, the effect of a single-session of bifrontal tDCS with the anode over the left DLPFC and the cathode over the right DLPFC on the subcortical dopaminergic transmission. These effects are explored online by positron emission tomography (PET) using dopaminergic D2 subtype receptor availability via [11C]raclopride binding. To investigate the changes induced by tDCS, variations of binding potentials are calculated before, during and after the stimulation in the right and left nucleus accumbens, caudate nucleus and putamen.

Experimental design



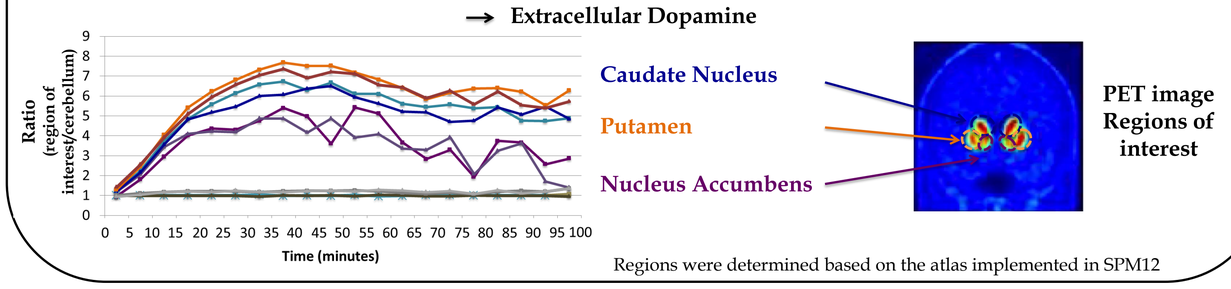
Subcortical dopamine analysis - Example

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



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

→ Extracellular Dopamine

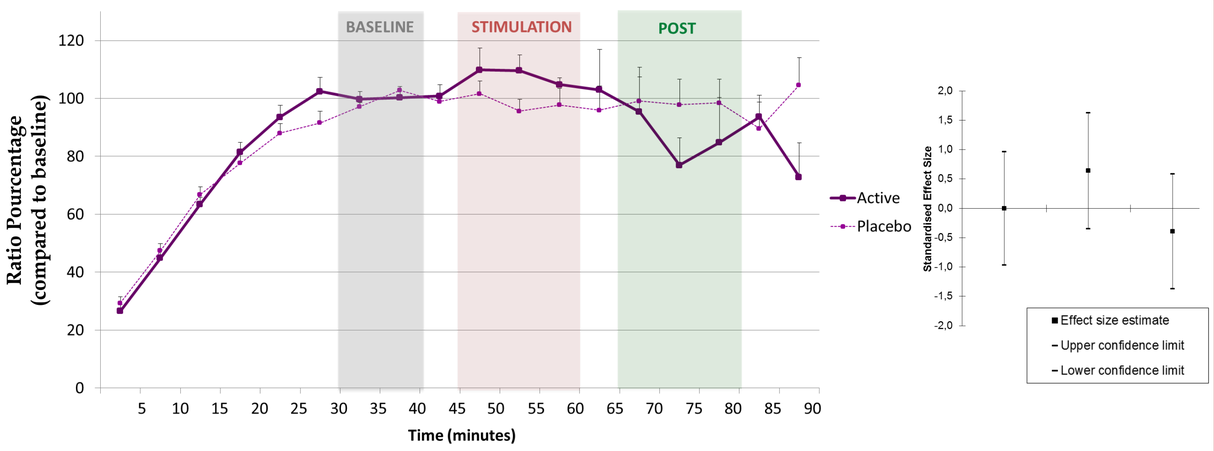


Regions were determined based on the atlas implemented in SPM12

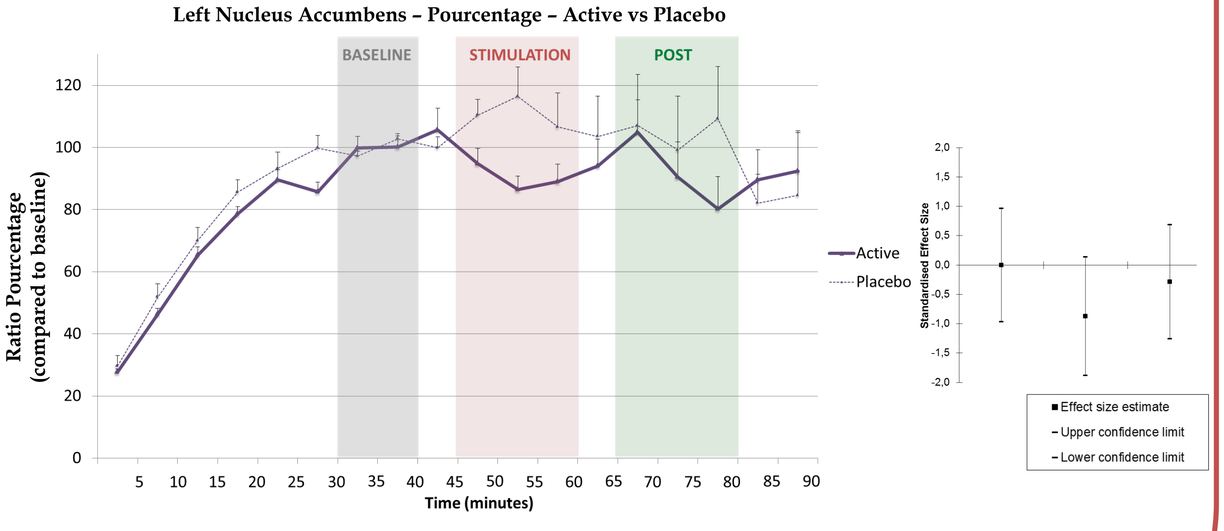
Bifrontal tDCS impacts subcortical dopamine specifically in the Nucleus Accumbens

n=7 active group/ n=10 placebo group

Right Nucleus Accumbens – Pourcentage – Active vs Placebo



Left Nucleus Accumbens – Pourcentage – Active vs Placebo



Data are expressed as mean±sem

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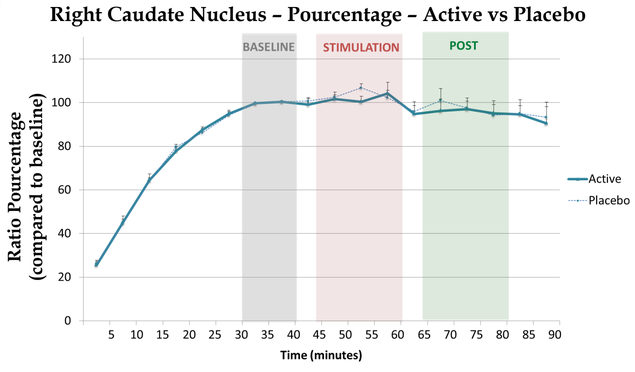
Active vs Placebo group

During the stimulation, the effects observed tend to be opposite in the left and right nucleus accumbens.

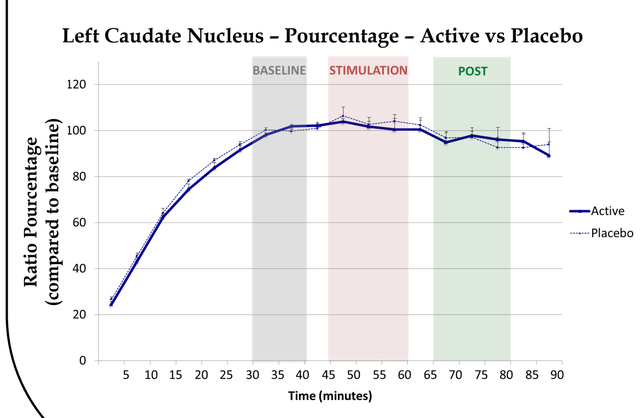
Bifrontal tDCS does not impact the caudate nucleus and the putamen

Caudate nucleus

Right Caudate Nucleus – Pourcentage – Active vs Placebo

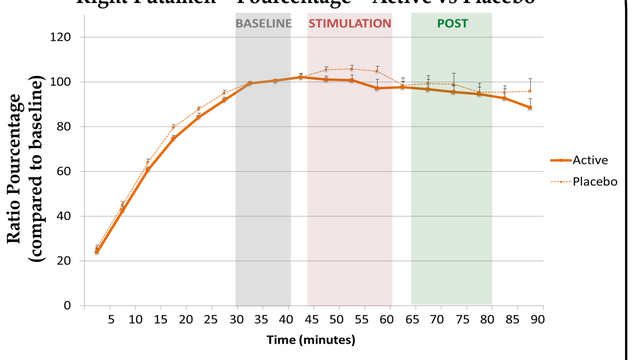


Left Caudate Nucleus – Pourcentage – Active vs Placebo

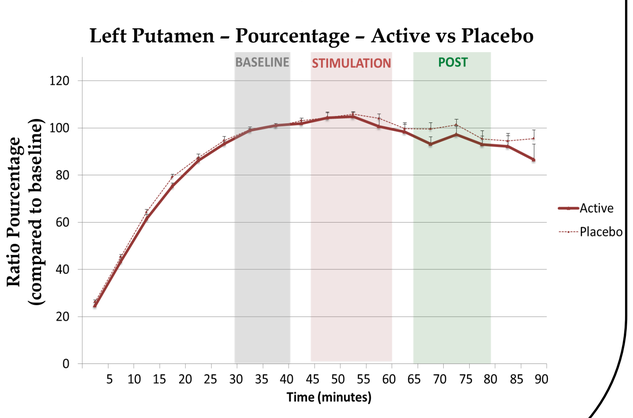


Putamen

Right Putamen – Pourcentage – Active vs Placebo



Left Putamen – Pourcentage – Active vs Placebo



Data are expressed as mean±sem

Conclusion

These results suggest that tDCS impacts subcortical dopaminergic transmission specifically in the nucleus accumbens.
Movement correction and more subject inclusions (n=30) are needed so as to validate these results.

Weber, M.J., Messing, S.B., Rao, H., Detre, J.A. & Thompson-Schill, S.L. (2014) Prefrontal transcranial direct current stimulation alters activation and connectivity in cortical and subcortical reward systems: a tDCS-fMRI study. *Hum Brain Mapp*, **35**, 3673-3686.
Brunelin, J., Szekely, D., Costes, N., Mondino, M., Bougerol, T., Mohamed, S., Suaud-Chagny, M.-F., Poulet, E. & Polosan, M. (2011) Theta burst stimulation in the negative symptoms of schizophrenia and striatal dopamine release. An iTBS- 11C raclopride PET case study. *Schizophrenia research*, **131**, 264--265.

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