Acute and subsequent effects of transcranial direct current stimulation on the dopaminergic transmission in healthy humans

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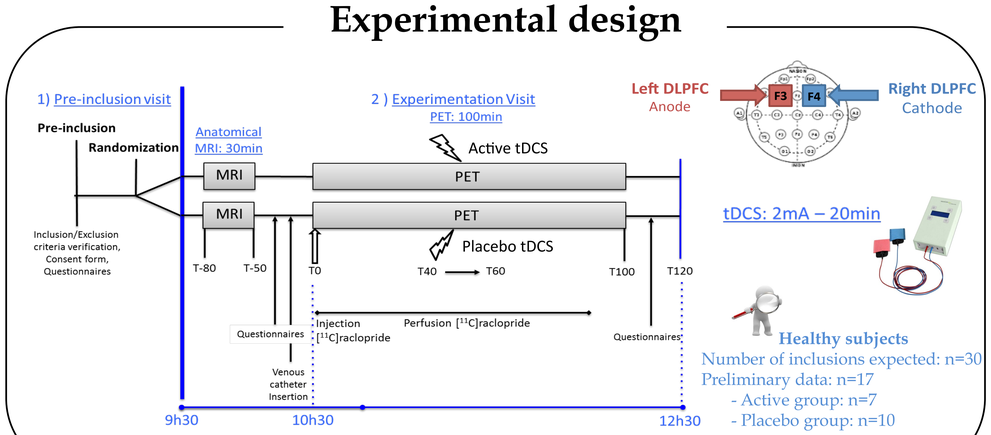
Introduction

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, 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.

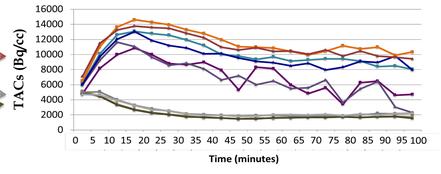
Experimental design



Subcortical dopamine analysis - Example

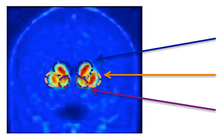
1) Extraction of time activity curve (TACs) in each region of interest in the right and left hemispheres

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



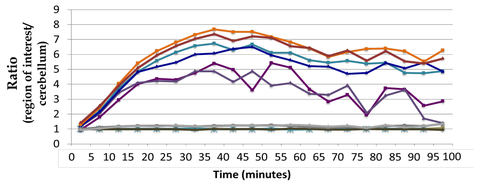
2) Binding potential (BP_R) = ratio of region of interest / mean left and right cerebellum activities

→ Extracellular Dopamine



PET image
Regions of interest

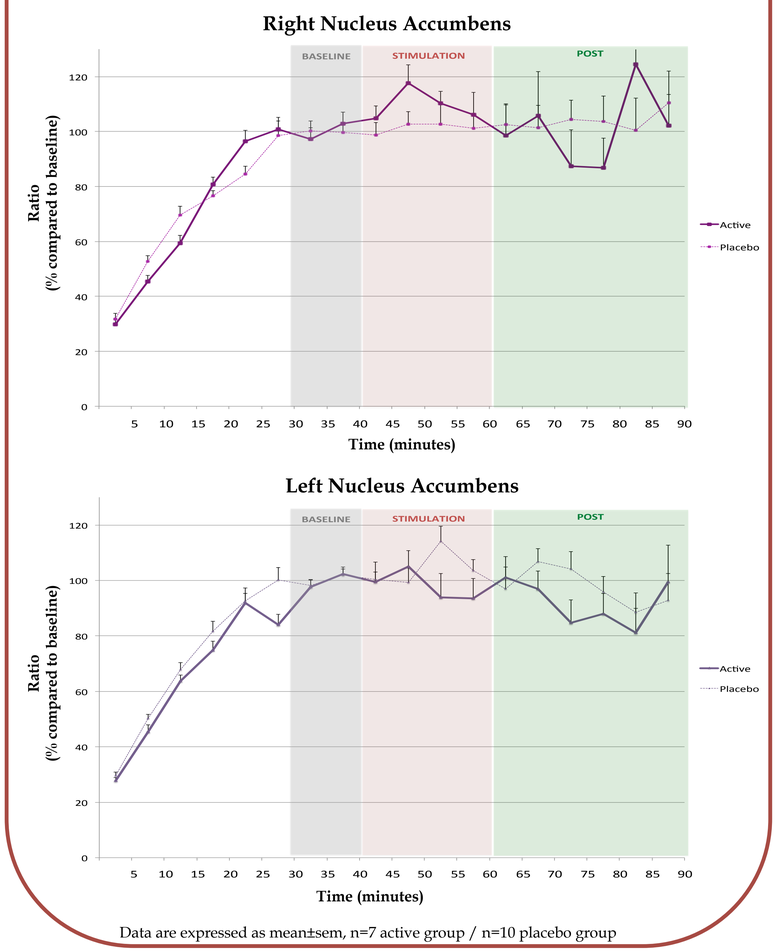
Caudate Nucleus
Putamen
Nucleus Accumbens



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

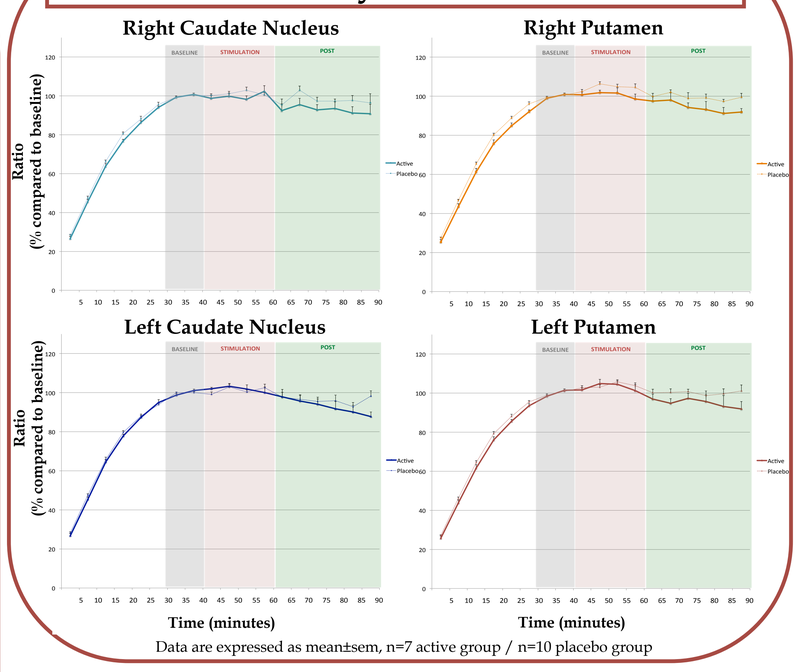
Dopamine transmission in the Nucleus Accumbens is modulated during and after bifrontal tDCS

The acute effects are opposite in the left and right hemisphere



Data are expressed as mean±sem, n=7 active group / n=10 placebo group

Dopamine transmission in the Caudate Nucleus and the Putamen is modulated only after bifrontal tDCS



Data are expressed as mean±sem, n=7 active group / n=10 placebo group

Conclusion

These results suggest that tDCS impacts subcortical dopaminergic transmission. The acute effects of tDCS are shown specifically in the nucleus accumbens. The subsequent effects of tDCS seems to be generalized in the nucleus accumbens, the caudate nucleus and the putamen.

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.
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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