**Concurrent HD-tDCS/fMRI Study Exploring Changes In Motor Network Physiology, Connectivity And Complexity**

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***Introduction*** Transcranial direct current stimulation (tDCS) applied over the primary motor cortex (M1) has been suggested to be an efficient tool to modulate the motor cortex excitability. However, recent studies demonstrated a lot of inter individual variability in the changes in behavior and neurophysiological measurements after M1 tDCS *(1,2,3)*. Accordingly, the current study explored whether another region (dorsal premotor cortex, PMd) could also modulate motor cortical excitability. We also examined changes in motor network connectivity and complexity following M1 or PMd high definition tDCS (HD-tDCS).

***Methods*** 46 healthy participants were randomized into 3 groups (left M1, left PMd or sham) in this double-blind study. A 7 min resting-state was acquired before and after a 7 min HD-tDCS (1mA) session to explore changes in motor network connectivity and complexity using a multiscale entropy (MSE) measure, which examines the changes of biological signals across a range of temporal scales (4). Changes in neurophysiology were measured using motor evoked potentials (MEP). Four regions of interest (ROIs): L M1, R M1, L PMd, R PMd, have been used to compute seed to seed functional connectivity and MSE complexity analyses.

***Results*** A two-way RM-ANOVA, with groups (active stim, sham) and time (pre, post) as factor, showed a marginal increase in cortical excitability (as measured by peak to peak MEP amplitude) (active stim: before=0.85±0.53, after=1.38±1.34; sham: before=1.15±0.84, after=1.06±0.83) following HD-tDCS (interaction Group\*time: F(1,43)=2.61, *p=*0.11; post-hoc tests active stim post > sham post (t(43)=2.32, p=0.03)). No significant difference was found between PMd and M1 groups. These marginal improvements are due to a strong inter-individual variability: 7/14 responders in M1 group whereas there are 11/15 responders in the PMd group.

The seed to seed analysis shown only a non-statistically significant trend in enhancing functional connectivity between L PMd and R PMd in the M1 group compared to sham (t(43)=1.81, *p=*0.08) and to PMd groups (t(43)=1.92, *p=*0.06).

MSE analysis demonstrated significant changes after tDCS. In the L M1 ROI, MSE increased following tDCS only in the M1 group (group\*time F(2,43)=2.5,p=0.09; post-hoc tests M1 post > M1 pre: t(43)=1.68,p=0.09), whereas in the L PMd ROI, MSE increased only in the PMd group (group\*time F(2,43)=7.5,p=0.002, post-hoc tests PMd post > PMd pre: t(43)=4.106,p=0.0002).

***Conclusion*** PMd HD-tDCS may modulate motor network neurophysiology and complexity more efficiently than M1 HD-tDCS, and multiscale entropy may be a sensitive marker of changes following noninvasive brain stimulation

**References:**

1 Lefebvre S, Liew SL. Anatomical Parameters of tDCS to Modulate the Motor System after Stroke: A Review. Front Neurol. 2017;8:29.

2 Lopez-Alonso V, Liew S-L, Fernández del Olmo M, Cheeran B, Sandrini M, Abe M and Cohen LG (2018) A Preliminary Comparison of Motor Learning Across Different Non-invasive Brain Stimulation Paradigms Shows No Consistent Modulations. *Front. Neurosci*. 12:253.

## 3 [SarahWiethoff](https://www.sciencedirect.com/science/article/pii/S1935861X14000977?via%3Dihub#!), [MasashiHamada](https://www.sciencedirect.com/science/article/pii/S1935861X14000977?via%3Dihub#!), [John C.Rothwell](https://www.sciencedirect.com/science/article/pii/S1935861X14000977?via%3Dihub#!).(2014) Variability in Response to Transcranial Direct Current Stimulation of the Motor Cortex. [*Brain Stim*](https://www.sciencedirect.com/science/journal/1935861X)*.*

# 4 [Julie Courtiol](https://www.sciencedirect.com/science/article/pii/S0165027016302011#!), Dionysios Perdikis,Spase Petkoski, Viktor Müller, Raoul Huys, Rita Sleimen-Malkoun, Viktor K.Jirsa. The multiscale entropy: Guidelines for use and interpretation in brain signal analysis.(2016)