Neurophysiological effects and behavioral outcomes after tPCS and tDCS in a patient in minimally conscious state

Alice Barra1, Sepehr Mortaheb1, Manon Carriere1, Mariachiara Luisella Binda Fossati1, Géraldine Martens1,2, Yelena Bodien2, Leon Morales-Quezada3, Felipe Fregni3, Joseph Giacino2, Steven Laureys1, Aurore Thibaut1,3

1 Coma Science Group, GIGA Consciousness - GIGA Research, University of Liège, Liège, Belgium

2 Department of Physical Medicine and Rehabilitation, Spaulding Rehabilitation Hospital and Harvard Medical School, Boston, MA

3 Neuromodulation Center, Spaulding Rehabilitation Hospital, Harvard Medical School, Boston, MA

a.barra@uliege.be, athibaut@uliege.be

**Introduction:**

Non-invasive brain stimulation (NIBS)(1-4) is a promising path in the search for treatments of patients with disorders of consciousness (DOC).

Transcranial pulsed-current stimulation (tPCS) has been used to modulate cortical and subcortical neural connectivity within 6-10Hz(5). It was successfully employed to enhance motor and cognitive functions in healthy volunteers (6) and it is theoretically able to reach deeper brain structures(7) .

On the other hand, transcranial direct-current stimulation (tDCS) over left dorsolateral prefrontal cortex (DLPFC) has shown to improve cognitive functions in DOC patients as measured by the Coma Recovery Scale-Revised (CRS-R) in about 50% of patients in minimally conscious state (MCS) (8,9).

These are preliminary results of an ongoing study that aim to investigate the effects of tPCS and tDCS on one patient with DOC.

**Methods:**

This was a randomized double-blind sham-controlled clinical trial on a patient with DOC. The Subject received 3 sessions of stimulation: active tPCS sham tDCS, sham tPCS with active tDCS, and sham tPCS with sham tDCS. Before and after each session we evaluated the patient with the CRS-R and recorded 10 minutes of resting EEG. The stimulation target for tPCS was the bimastoid line with a random frequency of 6-10Hz (2mA peak to peak), whereas the target for tDCS was the left DLPFC with 2mA of intensity. EEG data were pre-processed and the power of signal was calculated for each frequency band: Delta (0-4 Hz), Theta (4-8 Hz), Alpha (8-12 Hz) and Beta (12-25 Hz). A non-parametric corrected cluster permutation test(10) was used to statistically compare the power maps before and after each session. Electrode clusters with p-value below 0.01 were considered as significantly different.

**Results and Discussion:**

An increase of Alpha and Beta power and decrease of Theta and Delta power was observed after anodal tDCS together with an increase of behavioural responsiveness as measured by the CRS-R score.

After active tPCS, a significant increase was observed in Theta power consistently with the frequency of the stimulation (6-10Hz). However, this increase did not result in any measurable behavioural improvement maybe due to insufficient number of sessions or inadequate frequency of stimulation. Nevertheless, it could be relevant to mention that the patient’s caregivers noticed longer periods of wakefullness and higher arousal after tPCS. Therefore, it may be hypothesized that the CRS-R was not sensitive enough to capture these behavioural changes**.**

**Conclusion:**

In conclusion, here tDCS and tPCS induced distinct neurophysiological and clinical effects. So far, tDCS seems to be confirmed as a promising tool to improve behavioural responsiveness of patients with DOC. On the other hand, tPCS should be explored in larger cohorts to understand if this type of stimulation can reach similar results as the ones observed for tDCS.

**References:**

1. Buch ER, Santarnecchi E, Antal A, Born J, Celnik PA, Classen J, Gerloff C, Hallett M, Hummel FC, Nitsche MA, Pascual-Leone A. Effects of tDCS on motor learning and memory formation: a consensus and critical position paper. Clinical Neurophysiology. 2017 Apr 1;128(4):589-603.
2. Wortman-Jutt S, Edwards DJ. Transcranial direct current stimulation in Poststroke aphasia recovery. Stroke. 2017 Mar;48(3):820-6.
3. Lefaucheur JP, Chalah MA, Mhalla A, Palm U, Ayache SS, Mylius V. The treatment of fatigue by non-invasive brain stimulation. Neurophysiologie Clinique/Clinical Neurophysiology. 2017 Apr 1;47(2):173-84.
4. Lefaucheur JP, Antal A, Ayache SS, Benninger DH, Brunelin J, Cogiamanian F, Cotelli M, De Ridder D, Ferrucci R, Langguth B, Marangolo P. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Clinical Neurophysiology. 2017 Jan 1;128(1):56-92.
5. Morales-Quesada L et al. Optimal random frequency range in transcranial pulsed current stimulation indexed by quantitative electroencephalography. Neuroreport, 2015; 26(13): 747-52
6. Morales-Quezada L, Cosmo C, Carvalho S, Leite J, Castillo-Saavedra L, Rozisky JR, Fregni F. Cognitive effects and autonomic responses to transcranial pulsed current stimulation. Exp Brain Res. 2015 Mar;233(3):701-9.
7. Datta A, Dmochowski JP, Guleyupoglu B, Bikson M, Fregni F. Cranial electrotherapy stimulation and transcranial pulsed current stimulation: a computer based high-resolution modeling study. Neuroimage. 2013 Jan 15; 65:280-287.
8. Thibaut A, et al. tDCS in patients with disorders of consciousness; sham-controlled double-blind study. Neurology, 2014; 82: 1112-8
9. Thibaut, Wannez, Donneau, Chatelle, Gosserie, Bruno, Laureys. Controlled clinical trial of repeated prefrontal tDCS in chronic patients in minimally conscious state. Brain Injury, 2017; 31 (4) 466-474
10. Maris E, Oostenveld R. Nonparametrric statistical testing of EEG-and MEG- data. Journal of Neuroscience Methods, 2007 Aug 15; 164(1):177-190.