

Cortical activation following chronic transcranial direct current stimulation in patients with minimally conscious state: A NIRS-based assessment associated to behavioral and plastic response

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## Background

Near infrared spectroscopy (NIRS), a non-invasive technique measuring changes in brain tissue oxygenation, is potentially useful in the study of traumatic brain injury.<sup>1,2</sup> In a longitudinal pilot study in patients with minimally conscious state (MCS) (NCT:02288533) we assessed by NIRS the changes of cortical activation (CANIRS) following chronic transcranial direct current stimulation (tDCS) and their association with behavioral changes and biomarkers of plasticity.<sup>3</sup>

### Methods

Six male patients aged  $35\pm10$  with posttraumatic chronic ( $\geq 1$  year) MCS were enrolled to receive ten 40-minute daily sessions of 2 mA bilateral M1 anodal tDCS (Brainstim, EMS, Italy).

Before the first and last session, twentyminute NIRS monitoring was performed, with optodes placed at M1 bilaterally. Oxygenated hemoglobin was recorded, with area-under-curve calculated to determine CANIRS. Consciousness was assessed by the coma recovery scale-revised (CRS-R) total score. Two neuro-vascular biomarkers of plasticity (brain-derived neurotrophic factor and vascular endothelial growth-factor) were quantified in sera samples by proper methods.

#### Results

CANIRS increased following treatment in the whole population (+13%; P=0.60) as well the CRS-R total score (from 11 $\pm$ 3 to 12 $\pm$ 2).

CANIRS, stable in four patients (mean fold-change 0.5), was selectively increased in two subjects (mean fold-change 2.2). Interestingly, only CANIRS responders showed an increase of CRS score ( $\geq 2$  points) and variations of plastic biomarkers (Figure 1).

20000 Innt 16000 Oxy-Hb AUC (x103 arbitrary 12000 8000 4000 0 20 Recovery Scale-Revised 16 12 Coma (lm/gq) 10000 8000 ophic Factor 6000 4000 Brain-derived 2000 600 500 Vascular Endothelial Growth-Factor C (pg/ml) 400 300 200 100 No Yes NIRS-responder

Figure 1. Values of  $CA_{NIRS}$ , CRS-R, BDNF and VEGF-C at baseline and at the end of the 10 sessions of tDCS.

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# Conclusions

The study, limited by the small sample size, supports the feasibility of NIRS monitoring in MCS patients. CANIRS, with variations congruent with behavioral and plasticity changes, may represent an objective technical biomarker of response to tDCS treatment.

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