Closed-loop application of transcranial direct current stimulation (tDCS) for patients with chronic minimally conscious state

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BACKGROUND

Transcranial direct current stimulation (**tDCS**) over the dorsolateral prefrontal cortex (DLPFC) can improve behavioural responsiveness in **minimally conscious state** (MCS) patients, as assessed by the Coma Recovery Scale-Revised (CRS-R) scale. Previous research has been limited by an arbitrary timing of stimulation, while MCS patients are known to present vigilance and responsiveness fluctuations as assessed by EEG spectral entropy (ultradian cycles ≈70 min [1]) (Fig.1).

The **objective** of this randomized controlled crossover trial is to evaluate the effects of tDCS applied over the DLPFC in a **brain state-dependent** manner

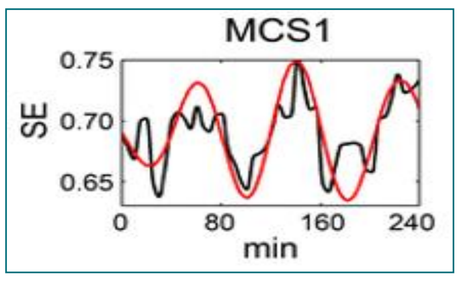


Fig.1 | Spectral entropy time course (in black) and time course of the main oscillation identified by wavelet analysis (in red) of a MCS patient [1]

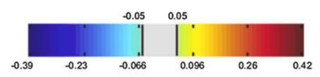
METHODS

- **12 patients** with MCS (5 women, 5 TBI, 50±17 y.)
  Time since injury: 6 ± 10 years

Crossover design 3 conditions: tDCS high vigilance – tDCS low vigilance – tDCS random vigilance

Coma Recovery Scale-Revised (CRS-R; *primary outcome*) and EEG (band power & connectivity; *secondary outcome*) before and after each session.

Intervention: customized 20-channel EEG & tDCS software (Neuroelectrics) computing spectral entropy index. Index fluctuations used to trigger tDCS application (high, low, random vigilance).



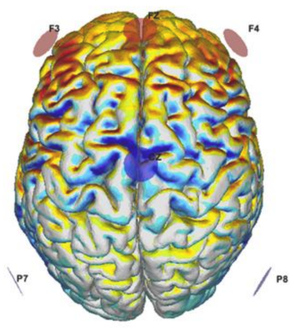


Fig.2 | Optimized stimulation montage based on current modelling targeting the bilateral prefrontal cortex [2]

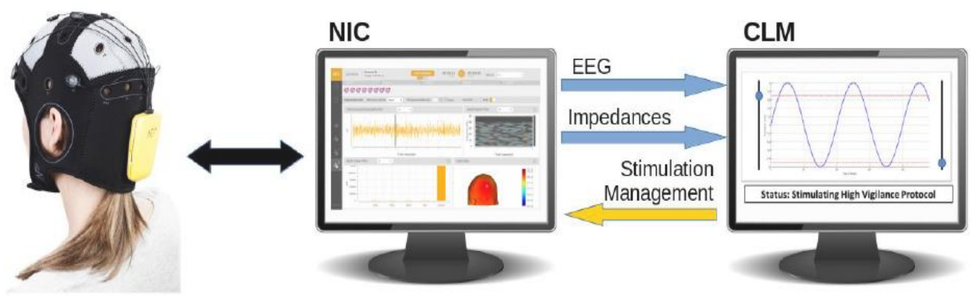


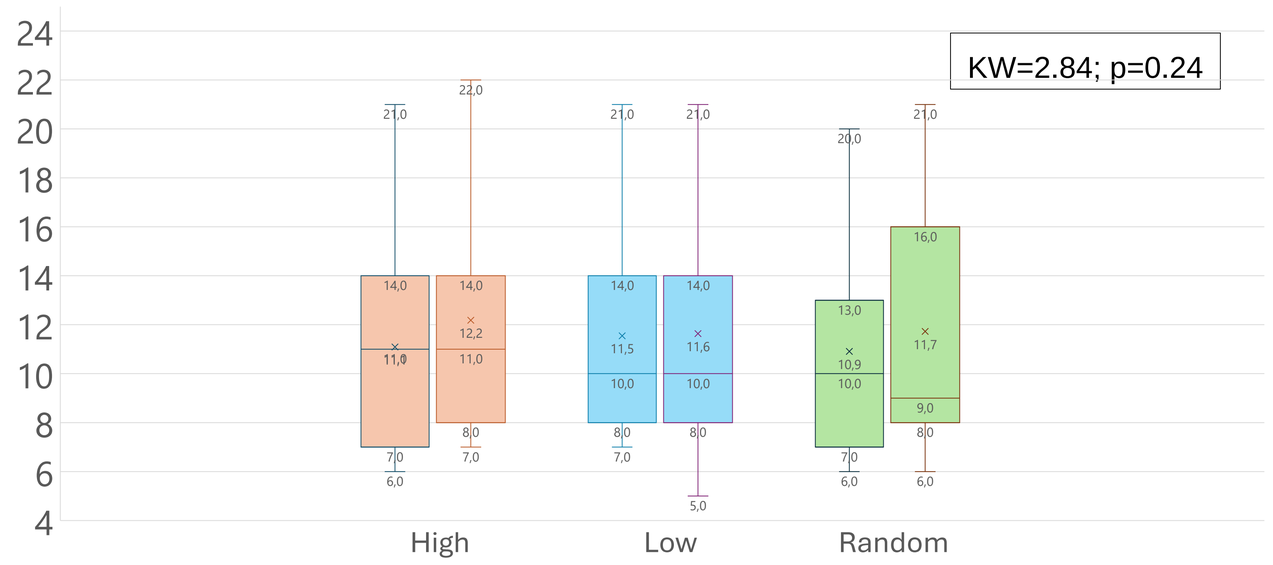
Fig.3 | Closed-loop hardware and software setting

CONCLUSIONS

- Brain-state dependent application of tDCS is feasible, even though challenging, in patients with MCS
- In this pilot setting, there is no behavioral improvement following tDCS applied at specific vigilance levels
- Delta and theta connectivity might represent an appropriate marker for tDCS-related behavioral improvement
- Larger clinical trials are warranted to assess potential beneficial effects of brain-state dependent tDCS in patients with MCS

RESULTS

1) Behavioral changes (CRS-R total score)



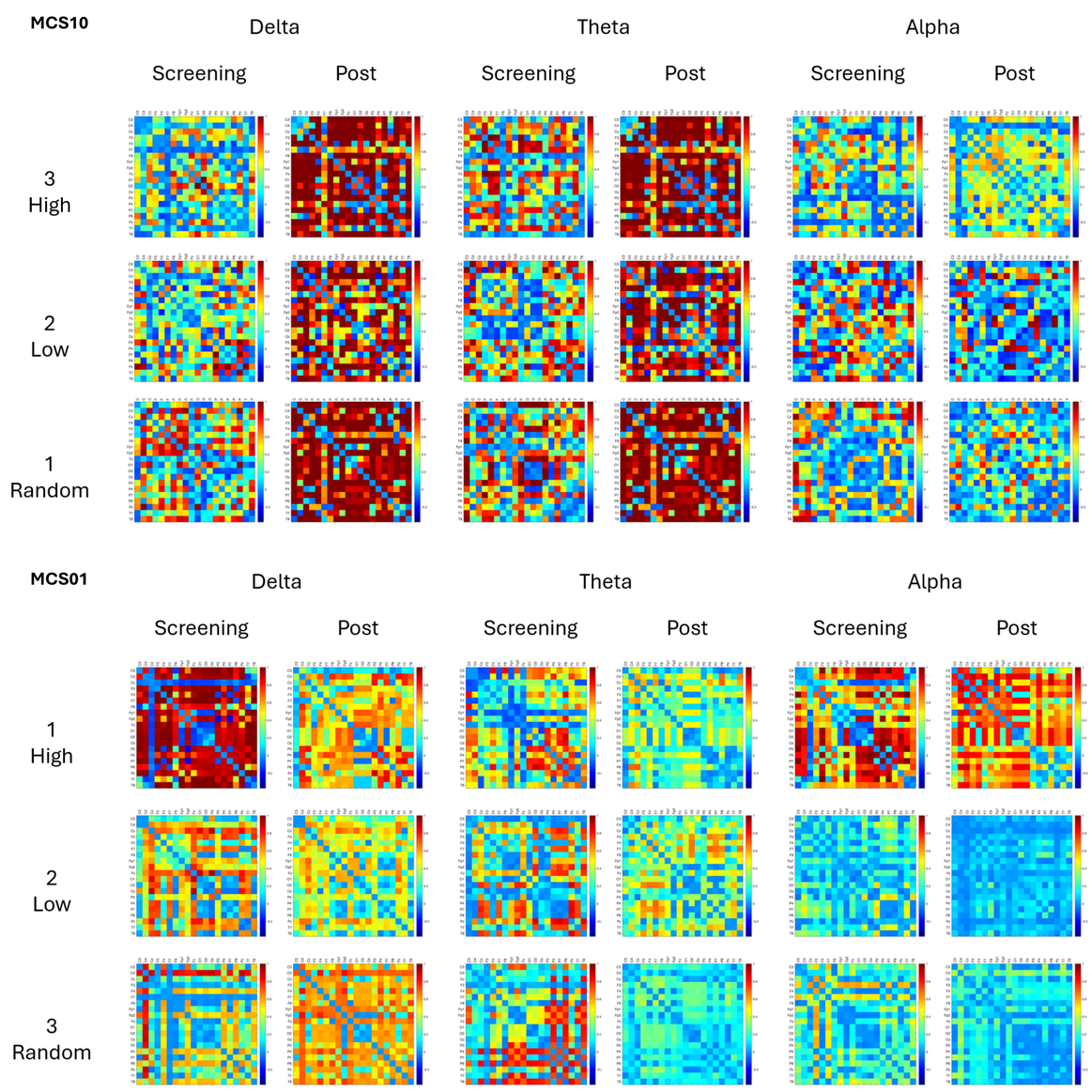
The median CRS-R score remained identical in the high and low conditions and decreased in the random one, with no statistically significant differences between the three conditions

2) Clinically relevant changes: identification of individual tDCS responders

New CRS-R signs of consciousness observed for **4** patients

Patient	CRS-R sign of consciousness	Condition
MCS06	Reproducible command following + object recognition	Random
MCS06	Functional communication	High
MCS10	Visual pursuit	High
MCS12	Reproducible command following	High
MCS12	Reproducible command following	Low

3) EEG connectivity changes (dwPLI)



Delta and theta connectivity increased in the post condition for one behavioral responder, especially at high vigilance, while an overall decrease is observed in one non-responder

References

1 Piarulli et al., *Journal of Neurology*, 2016.
2 Martens et al., *Behavioural Brain Research*, 2021

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