

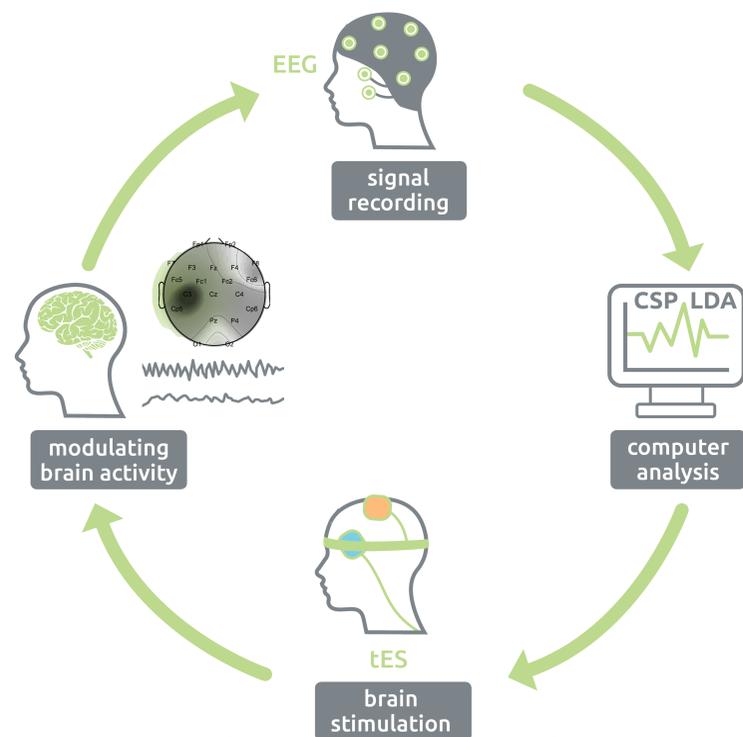
# Closed-loop apparatus for brain state-dependent tES: a proof of principle based on SMR

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## Introduction

Recent research has shown the advantages of combining electroencephalography (EEG) with transcranial magnetic stimulation (TMS) and transcranial electric stimulation (tES) into a closed-loop system and that slow excitability changes [1,2] in the oscillating neuronal network (particularly from the sensorimotor rhythms (SMR)) can explain the response variability to an external stimulation. Moreover, application of TMS pulses during SMR event-related desynchronization (ERD) in the beta range, has shown to significantly increase the corticospinal excitability [3]. Therefore, we reason that a closed-loop system combining tES and EEG during SMR-ERD is a relevant tool to study plasticity-induced tES protocols for motor rehabilitation. In this proof of principle study, we investigated the implementation and online artefact correction algorithms [4, 5] of such closed-loop apparatus by pairing EEG and tES during SMR-ERD.



**Figure 1. Closed-loop stimulation**  
27-channel EEG activity, tACS corrected and uncorrected, was streamed online via TCP/IP to an external computer. There, it was subsampled to 128 Hz, filtered between 6-30 Hz, epoched into 3 seconds (overlapping factor 0.1 sec) and classified using a pre-trained CSP-LDA model. The analog stimulation signal was provided for the stimulator by controlling a digital signal generator via USB. Clock synchronization between the stimulator and the EEG was established. tDCS or 10 Hz tACS stimulation were delivered during motor-imagery and interrupted during rest.

**Highlights:**  
-SMR-ERD during tDCS/tACS  
-CSP-LDA classification >0.80  
-Closed-loop EEG-tES

## Materials and Methods

### Experimental Procedure

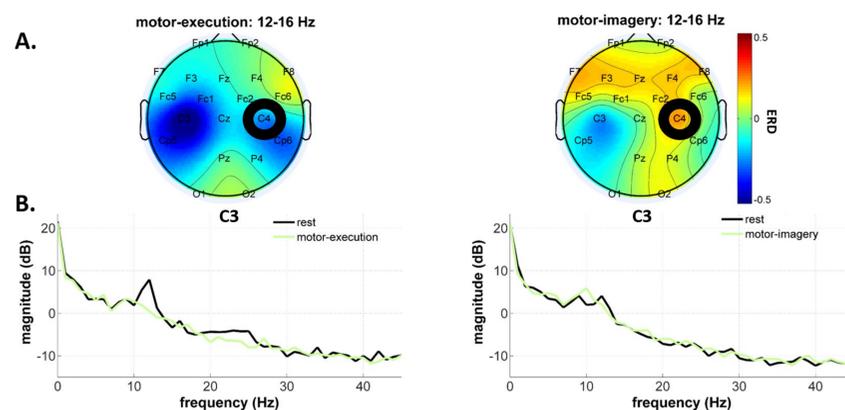
EEG was recorded from two neurological healthy individuals using the NEURO PRAX® TMS/TES (neuroConn GmbH, Germany) in absence and during 100µA tDCS and 100µA 10Hz tACS. tDCS/tACS was delivered by a battery-driven stimulator (neuroConn GmbH, Germany) over C4 (anode) and the right deltoids (cathode).

Participants were asked to execute or imagine grasping with their right hand and to rest. 40 trials were recorded for motor-execution and rest, and motor-imagery and rest. This data was used for training a classifier. 20 extra trials were recorded under the same conditions for testing the classifier performance under different stimulations: **no-stimulation, tDCS and 10 Hz tACS**. The data during 10Hz tACS was replayed (in simulation mode) and two built-in online artefact rejection methods from the NEURO PRAX® TMS/TES were applied. The **'sinusoidal' artefact correction**, based on a recursive discrete Fourier transformation at the stimulation frequency, and the **'regression'** approach, based on a dynamic linear regression model. The performance of these rejection methods had been evaluated previously [ 4, 5, 6].

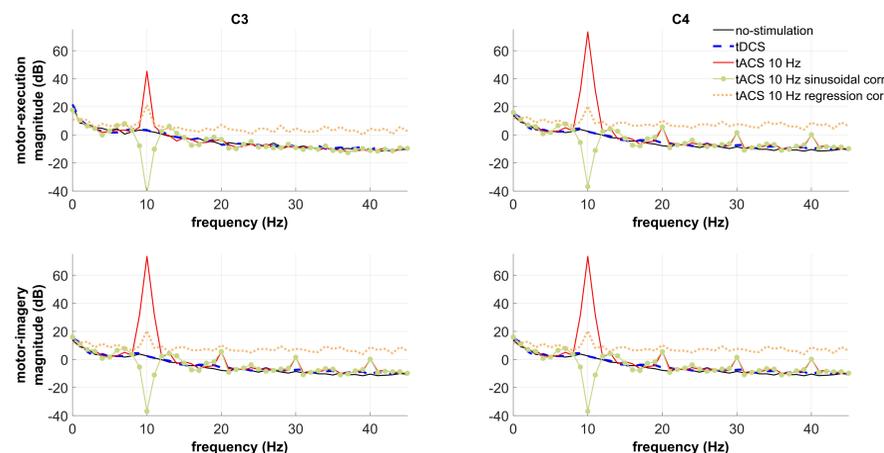
### Feature extraction and classification

Common spatial patterns (CSP) feature extraction was used to extract six different spatial filters to discriminate information between motor-execution/imagery and rest based on the mu and beta rhythms. A Linear Discriminant Analysis (LDA) was applied for classifying task vs. rest.

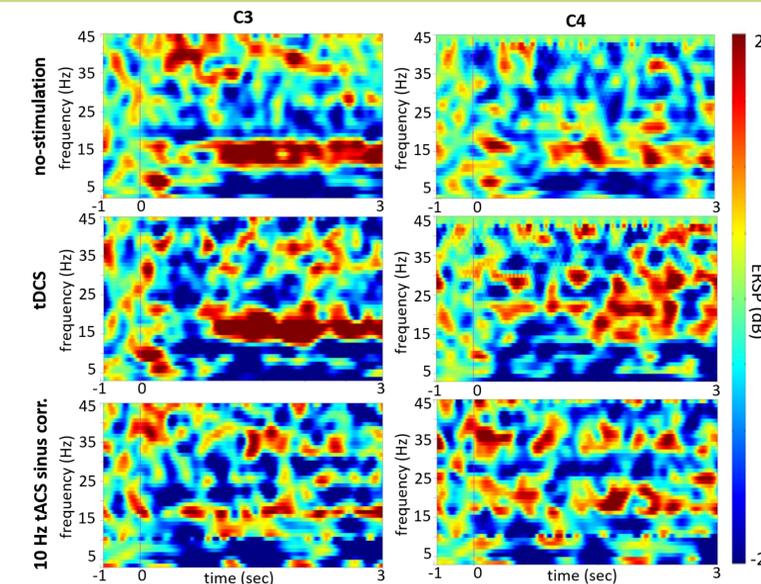
## Results



**Figure 2. A.** Topographic distribution (from one of the participants) of SMR-ERD and **B.** Power spectrum on C3 during motor-execution and imagery in comparison to rest.



**Figure 3.** Power spectrum (from one of the participants) for all stimulation conditions during motor-execution (top) and imagery (bottom): no-stimulation, tDCS, 10Hz tACS uncorrected, 10Hz tACS with



**Figure 4.** ERSP (from one of the participants) for different stimulation condition on C3 (far from the stimulation area) and C4 (on the stimulation area): no-stimulation (top), tDCS (middle), 10Hz tACS with sinusoidal correction (bottom).

	TP	TN	FP	FN	Err
<b>no-stimulation</b>	0,85	0,78	0,23	0,15	0,19
<b>tDCS</b>	0,83	0,83	0,18	0,18	0,18
<b>10 Hz tACS</b>	1,00	0,00	1,00	0,00	0,50
<b>10 Hz tACS sin</b>	0,80	0,90	0,10	0,20	0,15
<b>10 Hz tACS reg</b>	0,53	0,58	0,43	0,48	0,45

**Table 1.** Average classification results for the different stimulation conditions. TP=True Positive, TN=True Negative, FN=False Negatives, FP=False Positives, Err=Error

## References

- [1] Zrenner C, Desideri D, Belardinelli P, Ziemann U. Real-time EEG-defined excitability states determine efficacy of TMS-induced plasticity in human motor cortex. *Brain Stimulation* 2017, 11:374-389. doi.org/10.1016/j.brs.2017.11.016
- [2] Raco V, Bauer R, Tharsan S, Gharabaghi A. Combining TMS and tACS for Closed-Loop Phase-Dependent Modulation of Corticospinal Excitability: A Feasibility Study. *Front Cell Neurosci.* 2016; 10: 143. doi: 10.3389/fncel.2016.00143
- [3] Kraus D, Naros G, Bauer R, Khademi F, Leão MT, Ziemann U., Gharabaghi A. Brain State-Dependent Transcranial Magnetic Closed-Loop Stimulation Controlled by Sensorimotor Desynchronization Induces Robust Increase of Corticospinal Excitability. *Brain Stimulation* (2016). doi: 10.1016/j.brs.2016.02.007.
- [4] Schlegelmilch F, Stein P, Schellhorn K. A method for online correction of artifacts in EEG signals during transcranial electrical stimulation. Poster at the 5<sup>th</sup> International Conference on Non-Invasive Brain Stimulation, Leipzig, Germany, 2013.
- [5] Wunder S, Garcia-Cossio E, Schlegelmilch F. Closed-loop application and artefact correction for tACS-EEG. Sep 2017. Poster presentation: BRAINBOX conference. London. doi.org/10.13140/rg.2.2.14527.82089
- [6] Kohli S, Krachunov S, Casson AJ. Towards closed-loop transcranial electrical stimulation: a comparison of methods for real time tES-EEG artefact removal using a phantom head model. 2nd International Brain Stimulation Conference, Barcelona, Spain, 2017; 467-468.

## Conclusion

Our results (TP-TN>0.80) prove the feasibility of the proposed apparatus to enable **brain state-dependent stimulation** with simultaneous tDCS or tACS during signalization of motor-execution/imagery based on SMR-ERD. Future applications and adaptations of such closed-loop stimulation system could potentially lead to **more effective and better personalized neuromodulation interventions** in the motor rehabilitation field.

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