Brain Stimulation 13 (2020) 815–818

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Probing EEG activity in the targeted cortex after focal transcranial electrical stimulation

Syoichi Tashiro [a, b], Hartwig R. Siebner [a, c, d], Angeliki Charalampaki [a], Cihan Göksu [a], Guilherme B. Saturnino [a, e], Axel Thielscher [a, e], Leo Tomasevic [a, *]

[a] Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital, Hvidovre, Denmark
[b] Department of Rehabilitation Medicine, Keio University School of Medicine, Tokyo, Japan
[c] Department of Neurology, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark
[d] Institute for Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen, Denmark
[e] Department of Health Technology, Technical University of Denmark, Kgs Lyngby, Denmark

ARTICLE INFO

Article history:
Received 26 August 2019
Received in revised form
14 February 2020
Accepted 17 February 2020
Available online 21 February 2020

Keywords:
Transcranial electrical stimulation
Transcranial alternating current stimulation
Electroencephalography
Electrical field simulation

ABSTRACT

Background: Recording electroencephalography (EEG) from the targeted cortex immediately before and after focal transcranial electrical stimulation (TES) remains a challenge.
Methods: We introduce a hybrid stimulation-recording approach where a single EEG electrode is inserted into the inner electrode of a double-ring montage for focal TES. The new combined electrode was placed at the C3 position of the EEG 10–20 system. Neuronal activity was recorded in two volunteers before and after 20 Hz alternating-current TES at peak-to-peak intensities of 1 and 2 mA. TES-induced electric field distributions were simulated with SIMNIBS software.
Results: Using the hybrid stimulation-recording set-up, EEG activity was successfully recorded directly before and after TES. Simulations revealed comparable electrical fields in the stimulated cortex for the pseudomonopolar montage with and without embedded EEG electrode.
Conclusion: The hybrid TES-EEG approach can be used to probe after-effects of focal TES on neuronal activity in the targeted cortex.

Introduction

Transcranial electrical stimulation (TES), delivering alternating or direct currents, is widely used to induce lasting changes of regional activity in the human cortex [[1–4]]. Yet the neuromodulatory effects induced by TES are poorly understood and its aftereffects have been shown to be variable [5]. The combination of TES with neuroimaging techniques may help to gain a deeper understanding of how TES “engages” its cortical target and inform the design of more efficacious and reliable stimulation protocols [6]. Here we focus on the combination of TES and electroencephalography (EEG), the high temporal resolution of which renders it possible to trace changes in regional neuronal activity immediately before and after the stimulation session.

Classic bipolar TES electrode arrangements result in rather non-focal current distributions in the brain and the induced current patterns vary substantially between subjects due to inter-individual anatomical differences [7]. More recently, TES set-ups with one central electrode surrounded either by multiple electrodes or by a ring one have been introduced. These pseudomonopolar electrode set-ups (often called “high-definition” TES) induce more focal and superficial stimulation of the cortex close to the central electrode· [8,9] Yet it remains still challenging to assess the individual neuronal response to focal TES in the targeted cortex, which might differ substantially across subjects. This prompted us to develop a hybrid EEG-TES approach, which enables EEG recordings from the stimulated cortical site immediately before and after TES.

Abbreviations: EEG, Electroencephalography; TACS, transcranial alternating current stimulation; TES, transcranial electrical stimulation; TMS, transcranial magnetic stimulation.

* Corresponding author. Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark.
E-mail address: leot@drcmr.dk (L. Tomasevic).

https://doi.org/10.1016/j.brs.2020.02.015

Material and methods

Participants

Two healthy subjects without any contraindication to TES, after agreeing with written informed consent according to the Declaration of Helsinki, participated in the experiment approved by the Ethics Committee of the Capital Region of Denmark (H15017238). Participants were instructed to look at a fixation point and to minimize eye blinks while sitting in a relaxed position.

Design of the hybrid electrode

For our hybrid EEG-TES approach we used two concentric round rubber stimulation electrodes (Neurocare GmbH, Ilmenau, Germany). The inner, central electrode had a diameter of 34 mm, while the outer electrode had an outer diameter of 100 mm and an inner diameter of 75 mm. A TMS-compatible Ag/AgCl EEG electrode was inserted in a hole (8 mm diameter) cut in the center of the inner electrode (EasyCap GmbH, Herrsching, Germany) (Fig. 1, upper panel).

Pseudo-monopolar transcranial electrical stimulation

Focal TES was applied to the left pericentral cortex positioning the inner (anode) and the outer (cathode) ring electrodes centered at the C3 position according to the 10–20 EEG electrode system (Fig. 2 upper panel) and using an MRI-compatible TES device (DC-STIMULATOR PLUS, neuroConn GmbH, Ilmenau, Germany). A thin layer of Ten20 conductive paste (Weaver and company, Colorado, United States) was applied between the scalp and the inner electrode and Hi-chloride abrasive electrolyte-gel (EasyCap) between the scalp and the external electrode.

The TES protocol consisted of 3 min 20 Hz transcranial alternating current stimulation (TACS) applied at 1.0 and 2.0 mA peak-to-peak amplitude in two different runs, separated by a 10 min interval.

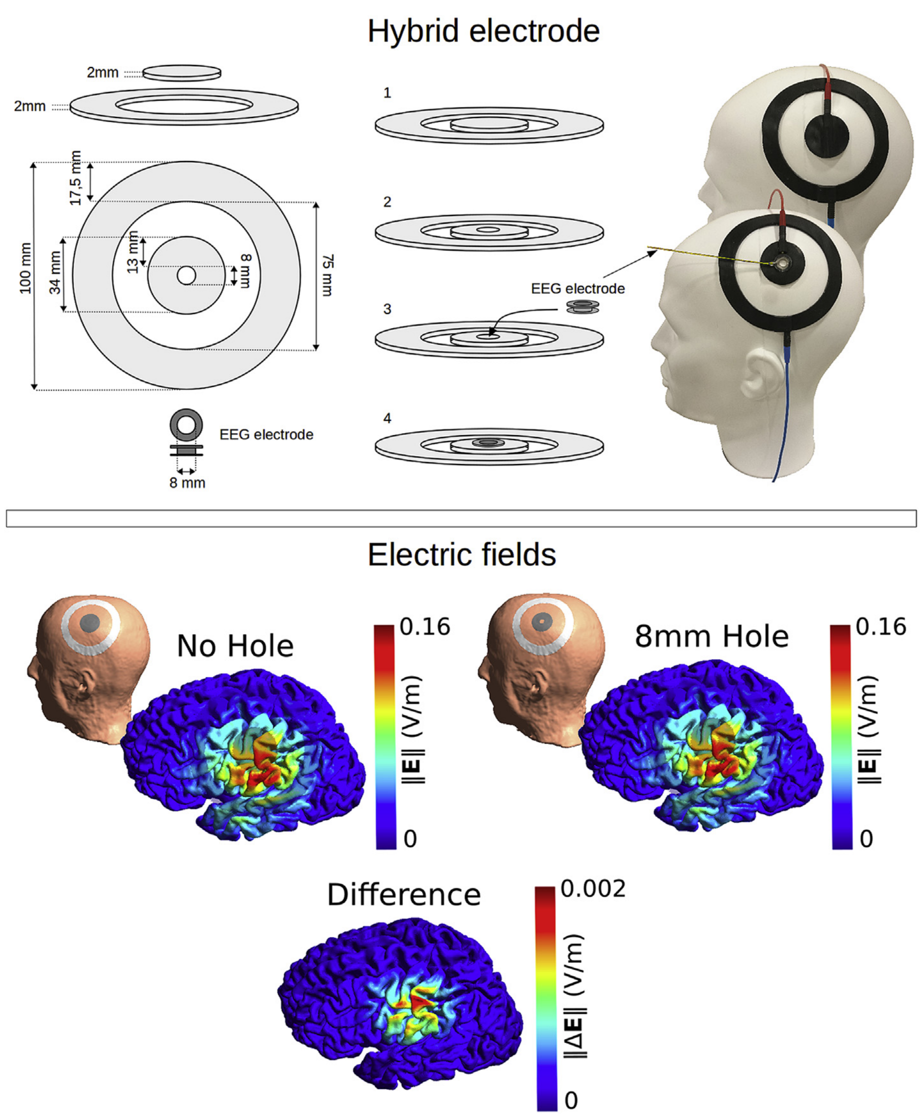

Fig. 1. Hybrid electrode. Upper panel: (Left) Measures of the components used to build the hybrid electrode. (Center) The step by step procedure to build the hybrid electrode. (Right) Photos of the standard and hybrid electrodes. Lower panel: Norm of the electric field produced by the standard pseudo-monopolar ring montage (left). Norm of the electric field produced by electrode with a central hole (8 mm diameter) made for the EEG electrode placement (right). Norm of the electric field difference between the two electric fields (bottom).

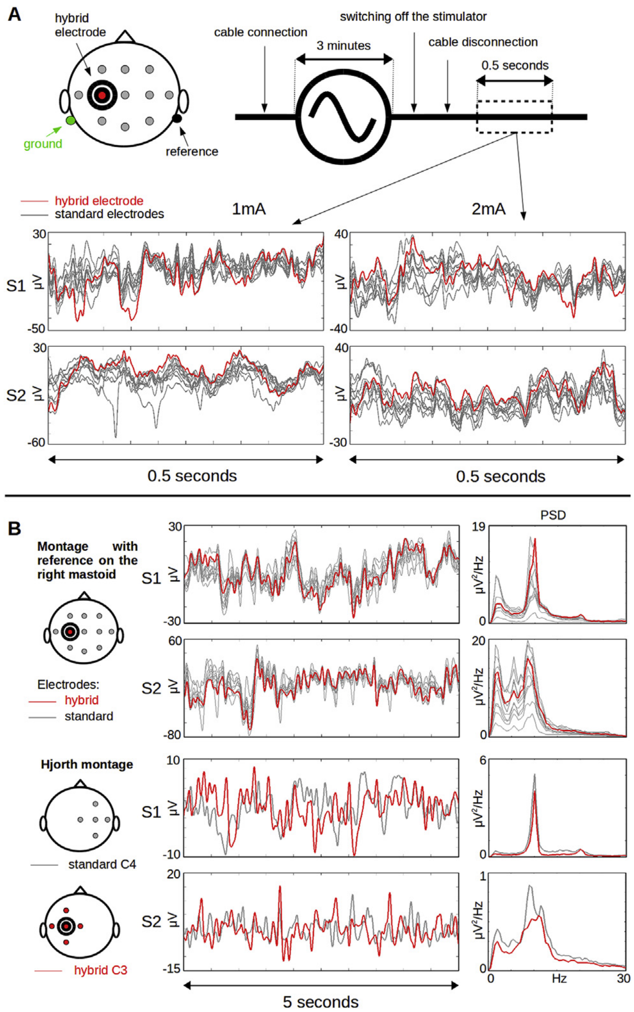

Fig. 2. Validation of the hybrid electrode. **A)** Upper panel: (Left) The distribution of the electrodes on the scalp. (Right) The schematic representation of the protocol. Lower panel: The EEG recordings shortly after TACS (S1-1 mA 5.3 s; S1-2 mA 2.97 s; S2-1 mA 6.5 s; S2-2 mA 8.6 s). The EEG channel C3 which was inserted into the inner ring of the TES electrode at position C3 is highlighted as red trace. Grey traces are the activity recorded from the other EEG channels. EEG activity is plotted separately for the two subjects (S1 and S2) for each stimulus intensity (1 mA vs. 2 mA peak-to-peak TACS). **B)** The first two rows show windows of 5 s of resting state data for both subjects and the power spectral density estimated on 3 min with the acquisition montage (reference on the right mastoid) for standard (grey) and hybrid (red) electrodes. The second two rows show the same as above, but using the Hjorth montage where the average value of the surrounding electrodes has been subtracted from the C4-standard (grey) and C3-hjorth (red) electrodes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

EEG recording

The EEG signal was recorded from 10 TMS compatible Ag/AgCl electrodes (EasyCap) placed at F3, F4, C4, P3, P4, T7, T8, Fz, Cz and POz according to the 10–20 system plus the hybrid electrode at C3 (Fig. 2 upper panel). For all the 11 EEG electrodes, we used Hi-chloride abrasive electrolyte-gel (EasyCap). The impedances were monitored and kept under 5 kΩ throughout the experiment. The reference and the ground electrodes were placed on the right and left mastoid respectively. The signals were recorded with a TMS compatible EEG system (BrainAmp, Brain Products GmbH, Gilching, Germany) at 5 kHz sampling rate in DC mode, 1 kHz low-pass filter, ±327.68 mV operating range and 10 μV resolution.

The experimental timeline is illustrated in Fig. 2, upper panel. EEG was recorded continuously before, during and after TACS, but only the EEG data recorded in the absence of TACS were analyzed. Recordings started and ended 3 min before and after TACS, respectively. The cable connecting the inner TES electrode with the stimulator was manually connected shortly before stimulation block and disconnected after the end of the stimulation block and after switching off the stimulator. This prevented any residual noise from the stimulator to affect the EEG recording in the post-stimulation epoch.

EEG analysis

The extraction of the TES cable after stimulation induced a decay artefact affecting EEG between 8 and 63 ms. Windows of 0.5 s recorded after the end of the decay artefact were band-pass (1–100 Hz) and notch filtered (50 Hz). EEG data recorded from each channel were overlaid for visual comparison, showing the EEG signal recorded from the hybrid EEG electrode at C3 as well as the other standard EEG electrodes (Fig. 2). Even though the TES and EEG electrodes in the hybrid arrangement were physically separated by the plastic case surrounding the EEG electrode, it was impossible to avoid bridging between the EEG and TES electrodes due to the spread of the paste applied between the electrodes and the scalp. Therefore, compared to the standard EEG electrodes, the hybrid electrode acquired electric potentials from a larger area over the scalp, i.e. from the area covered by the EEG electrode and the internal TES electrode.

We used 3 min resting state data in the standard and Hjorth montages [10] to evaluate the ability of the hybrid electrode to record EEG activity in both the time domain, same analysis as above, and the frequency domain, power spectral density (Welch's method with 2 s windows and 50% overlap). Hjorth montages were evaluated over the left (C3 against F3, P3, Cz and T7) and right (C4 against F4, P4, Cz and T8) primary motor areas.

Modelling the electric field distribution in the brain

We performed simulations of the electric field distribution in the brains based on anatomically realistic finite element models (FEM) of the subjects head [11]. We used SimNIBS (version 3.0, www.simnibs.org) for calculating the electric fields in the middle grey matter layer [12]. Calculations were done using the SimNIBS example dataset, whose image acquisition parameters are described in [11].

Results

In all recording conditions, it was possible to reliably record EEG activity from the C3 hybrid electrode overlying the targeted brain region (Fig. 2). Due to manual disconnection of the cable from the inner TES electrode, a few seconds elapsed after the end of TACS until clean EEG data could be recorded, ranging from 2.97 to 8.6 s. In both subjects, the temporal evolution and the spectral content of the EEG traces, recorded with the hybrid electrode (red lines), were within the range and comparable in profile to the signals acquired with the control EEG channels (grey lines). This was the case for both the standard electrode montage (Fig. 2B, upper two panels) and the Hjorth montage (Fig. 2B, lower two panels), at rest and after both stimulation intensities.

Electric field simulations revealed that the TES electrodes of our TES-EEG hybrid set-up induces a normal electric field component similar to that produced by the standard circular electrode without the EEG electrode (Fig. 1, lower panel), with relative difference between the field produced by the two electrode types below 1%.

Discussion

We introduce a novel hybrid TES-EEG approach that allows the recording of the EEG signal from the site of stimulation shortly before and after focal pseudo-monopolar TES. We propose a hybrid electrode, consisting of an EEG recording electrode inserted into the center of a ring electrode for TES (Fig. 1, upper panel).

This hybrid approach can be easily implemented in any laboratory, without requiring ear-marked equipment or additional costs. Our approach renders it possible to record EEG data at rest and immediately after TACS, but the same applies to interventional experiments with transcranial direct current stimulation (TDCS). The hybrid TES-EEG approach can also be applied to other multi-electrode TES montages, if the TES electrode arrangement allows the insertion of an EEG electrode. The importance of EEG assessments of the regional TES effects on cortical activity is not restricted only to the focal ring montage. The only limitation is that only one EEG electrode can be placed in one TES electrode, since any adjunctive EEG electrode would bridge with the stimulation electrode. To avoid bridging even between the stimulation and recording electrode, a previous study tested the feasibility of the concurrent TACS/EEG recordings by placing the EEG electrode within a bigger ring-shaped stimulation electrode [13]. In contrast to our approach, that approach can only be implemented for non-focal montages and it affects the shape of the stimulation electrode, which effects have not been modeled. In our case though, since the hybrid electrode covers a larger surface than standard EEG electrodes, we would suggest not to use it for direct comparison with the activity captured by other EEG electrodes nor for localization procedures. Nevertheless, the aim of the hybrid electrode is to pick up cortical activity from the targeted cortex shortly after stimulation, which makes it suitable to be employed in future for detecting local neuromodulatory effects of interventional TES.

In our study, the onset of EEG recordings after the end of TES was delayed by a few seconds because we had to manually switch off the stimulator and extract the cable of the central stimulation electrode. This delay could be avoided by implementing an automatized procedure, enabling recordings of EEG activity less than 1 s after the end of TES.

While this was not the focus of this report, it is possible to record the EEG signal continuously also during the stimulation blocks with our hybrid TES-EEG approach, but online recordings will be contaminated by stimulation-induced artifacts. Hence, “cleaning” procedures that have been introduced in other studies for online TES-EEG recordings will have to be applied to extract online cortical activity with the hybrid electrode [14].

Conclusions

We introduce a hybrid solution for recording the EEG from the same position where TES electrodes are placed. This approach bears great potential for tracing the local cortical response to TES, and thus can tell us more about short-lasting TES effects on cortical circuit activity. At the individual level, this response profile may be used for personalization of “TES dose” tailoring future neuroscientific and therapeutic applications of TES to the individual patient.

Funding

This work was supported by the Novo Nordisk Foundation Interdisciplinary Synergy Program 2014 [“Biophysically adjusted state informed cortex stimulation (BASICS); NNF14OC0011413]. HRS holds a clinical 5-year professorship in precision medicine at the Institute of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, sponsored by the Lundbeck Foundation (Grant Nr. R186-2015-2138).

Declaration of competing interest

H.R.S. has received honoraria as speaker and consultant from Sanofi Genzyme, Denmark and as senior editor for NeuroImage from Elsevier Publishers, Amsterdam, The Netherlands and as book editor from Springer Publishing, Stuttgart, Germany.

CRediT authorship contribution statement

Syoichi Tashiro: Investigation, Data curation, Writing - original draft, Visualization, Writing - review & editing. **Hartwig R. Siebner:** Resources, Supervision, Project administration, Funding acquisition, Writing - review & editing. **Angeliki Charalampaki:** Investigation, Writing - review & editing. **Cihan Göksu:** Methodology, Writing - review & editing. **Guilherme B. Saturnino:** Formal analysis, Visualization, Writing - review & editing. **Axel Thielscher:** Resources, Methodology, Writing - review & editing. **Leo Tomasevic:** Conceptualization, Formal analysis, Visualization, Writing - original draft, Writing - review & editing.

References

[1] Helfrich RF, Schneider TR, Rach S, Trautmann-Lengsfeld SA, Engel AK, Herrmann CS. Entrainment of brain oscillations by transcranial alternating current stimulation. Curr Biol 2014;24(3):333–9. https://doi.org/10.1016/j.cub.2013.12.041.

[2] Karabanov A, Ziemann U, Hamada M, et al. Consensus paper: probing homeostatic plasticity of human cortex with non-invasive transcranial brain stimulation. Brain Stimul 2015;8(3):442–54. https://doi.org/10.1016/j.brs.2015.01.404.

[3] Ziemann U, Paulus W, Nitsche MA, et al. Consensus: motor cortex plasticity protocols. Brain Stimul 2008;1(3):164–82. https://doi.org/10.1016/j.brs.2008.06.006.

[4] Antal A, Alekseichuk I, Bikson M, et al. Low intensity transcranial electric stimulation: safety, ethical, legal regulatory and application guidelines. Clin Neurophysiol 2017;128(9):1774–809. https://doi.org/10.1016/j.clinph.2017.06.001.

[5] Guerra A, Lopez-Alonso V, Cheeran B, Suppa A. Solutions for managing variability in non-invasive brain stimulation studies. Neurosci Lett 2017. https://doi.org/10.1016/j.neulet.2017.12.060.

[6] Bergmann TO, Karabanov A, Hartwigsen G, Thielscher A, Siebner HR. Combining non-invasive transcranial brain stimulation with neuroimaging and electrophysiology: current approaches and future perspectives. Neuroimage 2016;140:4–19. https://doi.org/10.1016/j.neuroimage.2016.02.012.

[7] Opitz A, Paulus W, Will S, Antunes A, Thielscher A. Determinants of the electric field during transcranial direct current stimulation. Neuroimage 2015;109:140–50. https://doi.org/10.1016/j.neuroimage.2015.01.033.

[8] Minhas P, Bansal V, Patel J, et al. Electrodes for high-definition transcutaneous DC stimulation for applications in drug delivery and electrotherapy, including tDCS. J Neurosci Methods 2010;190(2):188–97. https://doi.org/10.1016/j.jneumeth.2010.05.007.

[9] Heise KF, Kortzorg N, Saturnino GB, et al. Evaluation of a modified high-definition electrode montage for transcranial alternating current stimulation (tACS) of pre-central areas. Brain Stimul 2016;9(5):700–4. https://doi.org/10.1016/j.brs.2016.04.009.

[10] Hjorth B. An on-line transformation of EEG scalp potentials into orthogonal source derivations. Electroencephalogr Clin Neurophysiol 1975;39(5):526–30.

[11] Nielsen JD, Madsen KH, Puonti O, et al. Automatic skull segmentation from MR images for realistic volume conductor models of the head: assessment of the state-of-the-art. Neuroimage 2018;174:587–98. https://doi.org/10.1016/j.neuroimage.2018.03.001.

[12] Thielscher A, Antunes A, Saturnino GB. Field modeling for transcranial magnetic stimulation: a useful tool to understand the physiological effects of TMS? Conf Proc IEEE Eng Med Biol Soc 2015;2015:222–5. https://doi.org/10.1109/EMBC.2015.7318340.

[13] Feher KD, Morishima Y. Concurrent electroencephalography recording during transcranial alternating current stimulation (tACS). JoVE 2016;107:e53527. https://doi.org/10.3791/53527.

[14] Voss U, Holzmann R, Hobson A, et al. Induction of self awareness in dreams through frontal low current stimulation of gamma activity. Nat Neurosci 2014;17(6):810–2. https://doi.org/10.1038/nn.3719.