Lilia Morales
Margarita Báez
Carlos Maragoto
Reinaldo Galvizu
Héctor Vera
Ivette Cabrera
Marilyn Zaldívar
Abel Sánchez
Laboratory of Clinical Neurophysiology, International Center for Neurological Restoration, 25th Ave., No 11805, Playa, 11300 Havana, Cuba

* Corresponding author. Tel.: +53 7 2736923.
E-mail addresses: lazarog@neuro.ciren.cu, azzaro150@gmail.com (L. Gómez)

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The Role of Contact Media at the Skin-electrode Interface During Transcranial Direct Current Stimulation (tDCS)

To the Editor:

tDCS can be considered to be safe with little side-effects when using defined parameters (e.g. current strength, duration of application, frequency of stimulation). However, skin lesions have been reported in single cases after tDCS application with tap water soaked sponges on both cathodal [1,2] and anodal sites [3] in different laboratories. As potential mechanisms, tissue burning by drying-out of sponge electrodes [4], bacterial superinfection, toxic reaction by tap water constituents (e.g. regionally elevated concentration of specific ions) or impurities [2], toxic electrochemical reaction products [5] or pH changes in the skin milieu [6] have been discussed.

Here we report the results of a randomized four-armed crossover study with 15 healthy volunteers (9 male, 6 female, median age 29 ± 6 years) exposed to 20 min/2 mA bifrontal tDCS (anode F7, cathode F8) with sponges (35 cm^2) soaked with condition A: sham tDCS + tap water, condition B: active tDCS + tap water, condition C: active tDCS+ 0.9% NaCl solution, and condition D: active tDCS + conductive rubber electrode + electrode cream (Signacreme, Parker Laboratories Inc., Fairfield, NJ, USA). The skin of participants was classified using the Fitzpatrick Scale [7] to investigate whether the respective skin type has an impact on the dermatological side effects of tDCS. Elasticity of the upper skin layer was measured by mechanic deforming with a Cutometer MPA 580 (Courage and Khazaka Electronic GmbH, Cologne, Germany) on both anodal and cathodal sites before and after each stimulation. The *Comfort Rating Questionnaire* (CRQ), a modified version of the unpublished questionnaire from the Göttingen study group [8] was used to assess the perception of pain, tingling, burning, fatigue, nervousness, disturbed concentration, disturbed visual perception, and headache during stimulation and 24 h after stimulation on a 10-point Likert scale ranging from “not at all” to “extremely” (Supplemental Table 1). Impedance measures displayed by the Eldith DC-stimulator (neuroConn, Ilmenau, Germany) were documented at 0, 5, 10, 30, 60, 120, and 240 s and showed significantly lower mean impedances for condition C compared to condition B ($P = 0.005$; Wilcoxon test, 2-tailed asympt. significance), whereas condition A showed elevated impedances during sham current flow in the impedance checking mode (Fig. 1). In the active + tap water condition (B), round, blister-like, whitened, atrophic lesions on erythematous skin with a diameter of 0.5–1 cm occurred in 5 of 10 participants (3 cathodal, 2 anodal). Therefore this condition was terminated after 10 participants. In the active + electrode

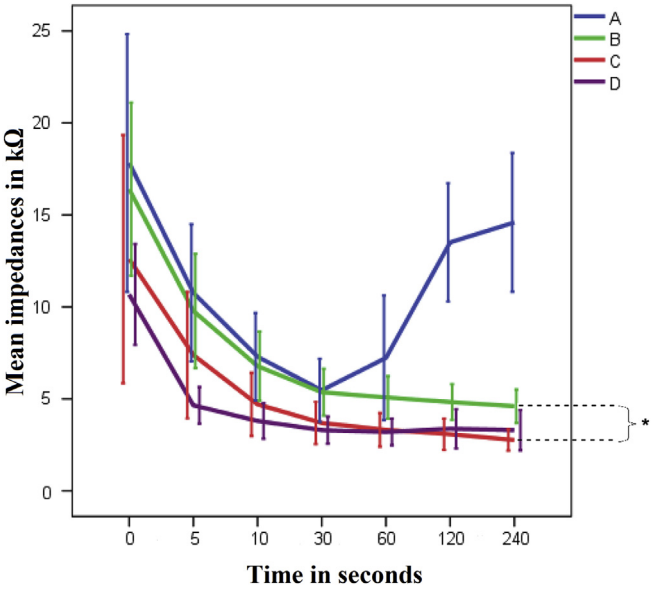

Figure 1. Impedances of conditions A–D (mean ± standard deviation, kΩ) over the time course. Conditions: A: sham + tap water; B: active + tap water; C: active + NaCl; D: active + electrode cream. * indicates significant difference between B and C (Wilcoxon test; $P = 0.005$).

cream condition (D), brown and crusty ulcerations framed by a white rim with a diameter of 0.5–1 cm (2 cathodal, 1 anodal) developed in 3 of 4 participants, resulting in termination of this arm after the forth participant. We also observed that electrode cream had turned into a white, water-soluble powder after tDCS. All skin lesions occurred predominantly underneath the center of electrodes in non-hairy areas (Supplemental Figures 1, 2). Skin lesions occurred independently from skin type (Fitzpatrick type I: $n = 1$; type II: $n = 6$; type III: $n = 0$; type IV: $n = 1$) and were not correlated to impedance measures in conditions B and D ($P = 0.771$ resp. $P = 0.686$; Pearson's correlation coefficient, 2-tailed). Mean sum score of the CRQ Likert scales in condition B (49.2 ± 7.9) was higher than in the other conditions and showed a trend to significant effects compared to conditions A (39.1 ± 7.1; $P = 0.066$), C (40.6 ± 8.2; $P = 0.074$), and D (39.5 ± 5.0; $P = 0.109$) (Wilcoxon test, two-tailed asympt. significance). Although condition D was associated with skin lesions, discomfort did not show significant differences to sham stimulation ($P = 1.0$) and occurrence of skin lesions was not correlated to any CRQ item. Friedman test showed no overall difference in gross skin elasticity, viscoelasticity, and elasticity ratio before and after stimulation for all conditions ($P = 0.127–0.326$).

In this methodological study, we observed an occurrence of small skin lesions with distinct tDCS contact media similar to those which had been previously reported [2,3]. The skin lesions were not related to site (left, right; cathode, anode), skin type, and subjective comfort rating. Sham stimulation was associated with similar discomfort as active conditions, and there were no significant alterations of skin elasticity after any treatment condition. Occurrence of skin lesions in conditions B and D was not correlated to impedance measures in the initial phase of tDCS; however we cannot exclude a further impedance rise during the course of stimulation as impedance was only measured for the first 240 s of stimulation. Further methodological limitations were the small sample size and lacking temperature measurement under the electrodes.

A possible explanation for skin lesions occurring with tap water soaked sponges may be a toxic chemical reaction related to regionally relatively high calcium carbonate concentration in tap water [Munich: 2.93 mmol/l; Regensburg 3.04 mmol/l] [2,3] which could have a noxious action on skin tissue [9] and lead to chemical skin damage by alkaline hydrolysis. This may explain why skin lesions occurred only when using tap water, but not when using saline solution and why this phenomenon has only been observed by single groups [1–3]. Chemical changes of electrode gel to black paste or white powder have already been reported, e.g. by Lagopoulos and Degabriele [10]. This is rather surprising because electrode gels usually are highly conductive (e.g. Signagel 40.000 micromhos/cm) and reciprocally have lower resistivity compared to Signacreme (conductivity: 3500 micromhos/cm). However, in our cases, the cream layer (1 mm) might have been to thin to guarantee sufficient skin protection. Moreover, the use of large electrodes could have led to inhomogeneous current distribution. Our results show that skin lesions were not necessarily reflected by elevated pain or discomfort rating, an observation with important implications for the use tDCS. tDCS application using NaCl-soaked sponges or electrode cream/gel has been performed in labs worldwide over the past years and is generally deemed safe. Tap water is not suggested for soaking sponges. When using cream/gel, particular attention should be paid to the selection/testing of media and an adequate layer thickness.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.brs.2014.06.006.

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Ulrich Palm*
Department of Psychiatry, Psychotherapy and Psychosomatics, Ludwig-Maximilian University, Munich 80336, Germany

Katrina B. Feichtner
Department of Psychiatry, Psychotherapy and Psychosomatics, Ludwig-Maximilian University, Munich, Germany

Department of Dermatology and Venerology, Ludwig-Maximilian University, Munich, Germany

Alkomiet Hasan
Department of Psychiatry, Psychotherapy and Psychosomatics, Ludwig-Maximilian University, Munich, Germany

Gerd Gauglitz
Department of Dermatology and Venerology, Ludwig-Maximilian University, Munich, Germany

Berthold Langguth
Department of Psychiatry and Psychotherapy at Bezirksklinikum, University of Regensburg, Germany

Michael A. Nitsche
Department of Clinical Neurophysiology, Georg-August-University, Göttingen, Germany

Daniel Keeser
Department of Psychiatry, Psychotherapy and Psychosomatics, Ludwig-Maximilian University, Munich, Germany

Institute for Clinical Radiology, Ludwig-Maximilian University, Munich, Germany

Frank Padberg
Department of Psychiatry, Psychotherapy and Psychosomatics, Ludwig-Maximilian University, Munich, Germany

* Corresponding author. Tel.: +49 89 4400 55511; fax: +49 89 4400 54749.
E-mail address: ulrich.palm@med.uni-muenchen.de

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Integration of Cortical Brain Stimulation and Exposure and Response Prevention for Obsessive-compulsive Disorder (OCD)

Dear Editor:

Individuals diagnosed with obsessive-compulsive disorder (OCD) reliably evidence deficits in cognitive control [1] and recent findings suggest hyperactivity of the pre-supplementary motor area (pre-SMA) mediates deficits in cognitive control in OCD [2]. Six studies have attempted to treat OCD with low frequency repetitive transcranial magnetic stimulation (LF-rTMS) of the pre-SMA [3,4]. Much like the psychosocial treatment of choice, exposure and response prevention (ERP) [5], however, many OCD patients do not respond to TMS and symptom remission is rare [3,4]. While LF-rTMS of the pre-SMA is effective for symptoms related to incompleteness (e.g., symmetry) it has limited effectiveness for symptoms related to harm avoidance (e.g., responsibility/checking) [6]. Integration of rTMS and ERP may mitigate shortcomings of each individual treatment and improve treatment efficacy.

Here we present the effects of integrated LF-rTMS and ERP for a patient who showed minimal response to psychopharmacology.

AC was a 52-year-old, middle-class, Caucasian, male. After providing written informed consent, AC completed a pre-treatment Mini International Neuropsychiatric Interview, which revealed that he met DSM-IV-TR criteria for OCD, Recurrent MDD, and Social Anxiety Disorder. AC reported that his OCD began in childhood and became clinically significant during early adulthood. At the time of intake he reported that he spent an average of 1–3 h obsessing and 3–8 h ritualizing per day. AC reported that his OCD interfered with personal relationships and, while he was able to maintain full time employment, his OCD interfered with his professional life.

Upon presenting for treatment, AC was prescribed fluvoxamine, quetiapine, temazepam, and clonazepam. AC reported minimal response to medications. AC discontinued clonazepam at the end of the first week of treatment. AC remained on stable doses of all remaining medications for the duration of the study. AC had no history of evidence-based psychotherapy.

AC was enrolled in the active TMS arm of a non-randomized pilot intervention study. AC received active rTMS but was blinded to the TMS treatment; meaning, he was told that he may receive real or sham (placebo) TMS as part of the study. LF-rTMS treatment strategies mimicked previously reported methods [7,8]. LF-rTMS was delivered to the pre-SMA along the sagittal midline (50% of the distance between the Fz and FCz). 1 Hz pulses were delivered to the pre-SMA using a figure-8 coil for 20 min per session (1200 total pulses) at 110% of resting motor threshold. LF-rTMS was delivered immediately prior to ERP for the duration of the 3-week integrated TMS and ERP period for a total of 15 rTMS treatments (weeks 2–4).

ERP strategies mimicked those described by Foa and colleagues [9]. Psychoeducation and hierarchy development were completed one week prior to TMS and ERP. During the integrated TMS and ERP period, 90–120 min therapist assisted exposure sessions were conducted each weekday [15 sessions (weeks 2–4)]. Finally, 8, weekly, 45 min, ERP-only maintenance sessions were completed (weeks 5–12). An emphasis was placed on *in vivo* exposure, but imaginal exposures were also included. Complete response prevention was encouraged and homework was assigned daily.

AC's pre-treatment (week 1) Yale-Brown Obsessive-Compulsive Scale (YBOCS) score was 25, suggesting severe OCD. AC's YBOCS increased following education and planning (week 2 YBOCS = 28). AC's YBOCS decreased after the first week of TMS + ERP (week 3 YBOCS = 22) but drastically decreased after 2 weeks of TMS + ERP (week 4 YBOCS = 13). After the final week of TMS + ERP, AC's YBOCS reflected a 54% reduction from pre-treatment (week 5 YBOCS = 11) (Fig. 1). YBOCS reductions were maintained through the 8-week ERP maintenance phase and AC's final YBOCS reflected a 64% decrease in obsessions and compulsions (week 12 YBOCS = 9).

Consistent with clinician-rated YBOCS scores, AC's pre-treatment self-reported OCD was severe [Dimensional Obsessive-Compulsive Scale (week 1 DOCS-total = 36)]. Pre-treatment DOCS scores suggested symmetry obsessions and compulsions were AC's primary symptoms (DOCS-symmetry = 13). AC also reported significant contamination/washing (DOCS-contamination = 8) and responsibility/checking (DOCS-responsibility = 10) symptoms. DOCS scores followed patterns of change that were similar to those seen for YBOCS scores. At the end of the TMS + ERP phase, AC's self-reported OCD severity was reduced by 50% (week 5 DOCS-total = 18) and reductions were maintained through the ERP maintenance phase (week 12 DOCS-total = 19). Importantly, AC reported roughly equivalent reductions across all symptom dimensions (week 12 DOCS-symmetry = 6, DOCS-contamination = 4, DOCS-responsibility = 5).

AC's pre-treatment General Anxiety Disorder Scale (GAD-7) and Patient Health Questionnaire (PHQ-9) scores were above clinical cut-offs and were suggestive of severe anxiety (week 1 GAD-7 = 20) and moderately-severe depression (week 1 PHQ-9 = 18). AC's GAD-7 and PHQ-9 scores were below clinical cut-offs following the TMS + ERP phase (week 5 GAD-7 = 8 and PHQ-9 = 7). Reductions in anxiety and depression were maintained through the ERP maintenance phase (week 12 GAD-7 = 7 and PHQ-9 = 5).

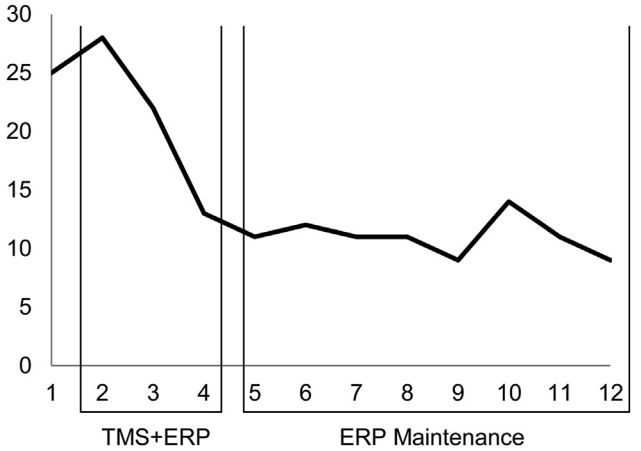

Figure 1. Change in Yale-Brown Obsessive-Compulsive Scale (YBOCS) scores over the course of treatment. YBOCS was completed at the beginning of each week. As such, scores at any given week reflect the effects of previous weeks.