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# A comparative analysis of technical data: At-home vs. in-clinic application of transcranial direct current stimulation in depression



BRAIN

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#### ABSTRACT

*Objective:* The application of transcranial direct current stimulation (tDCS) at home for the treatment of depression and other neuropsychiatric disorders presents both significant opportunities and inherent challenges. Ensuring safety and maintaining high-quality stimulation are paramount for the efficacy and safety of at-home tDCS. This study investigates tDCS quality based on its technical parameters as well as safety of at-home and in-clinic tDCS applications comparing the data from two randomized controlled trials in patients with major depressive disorder.

*Methods:* We analyzed 229 active stimulation sessions from the HomeDC study (at-home tDCS) and 835 sessions from the DepressionDC study (in-clinic tDCS). Notably, five adverse events (skin lesions) were reported exclusively in the at-home cohort, highlighting the critical need for enhanced safety protocols in unsupervised environments. *Results:* The analysis revealed a significant difference in the average variability of impedances between at-home and in-clinic applications (F1,46 = 4.96, p = .031,  $\eta^2$  = .097). The at-home tDCS sessions exhibited higher impedance variability (M = 837, SD = 328) compared to in-clinic sessions (M = 579, SD = 309). Furthermore, at-home tDCS sessions resulting in adverse events (AEs) were associated with significantly higher average impedances than sessions without such issues.

*Conclusion:* The study demonstrates that monitoring the technical parameters of at-home DCS used in this study is essential. However, it may be not sufficient for ensuring safety and promptly detecting or preventing adverse events. Quality control protocols including digital training and monitoring techniques should be systematically developed and tested for a reliable and safe application of at-home tDCS therapies.

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#### 1. Introduction

Non-invasive brain stimulation (NIBS) techniques allow a well tolerable stimulation of the human brain with few side effects for treating and diagnosing neuropsychiatric syndromes [1-4]. In the psychiatric field, NIBS techniques have shown positive effects, especially in the treatment of major depressive disorder (MDD) [5-7]. Therefore, the use of NIBS techniques in clinical trials on the treatment of MDD has increased steadily in recent years. However, the application of NIBS also faces many challenges: high staffing cost, limited capacity, and requirement of multiple treatment sessions for MDD. It often means a high burden for patients to come to the clinic for daily treatments due to time- and cost-intensive commute, on-site employment, childcare responsibilities, physical disabilities, or a combination thereof. Therefore, the idea of a home treatment application is a reasonable option. Compared to repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS) and other transcranial electrical stimulation (tES) modalities can be administered using a small, portable device, making its application at home possible.

Although rTMS has a broader evidence base for MDD treatment, the advantage of at-home tDCS administration has led to increased research on this method in recent years. In line with the current demands of modern psychiatry, which emphasize treating patients in their home environment whenever possible [8] to prevent hospitalization, numerous studies have been published on the feasibility and safety of at-home tDCS treatment [9–12], most prominently in the neurological field [13–16] and recently also for psychiatric disorders [17–20].

The advantages of tES at-home application in terms of enhancing effectiveness include the simpler feasibility of multiple applications, which can address the potential issue of underdosing. In terms of trial methodology, the unspecific effect of clinical care is reduced, which may equally add to the efficacy of active and control arms in randomized controlled clinical trials and could potentially mask a possible difference between active tES and control conditions. Finally, at home (e.g., in a quiet room), tES could be more easily and effectively combined with an ideally synergistic behavioural task or activity [21,22], both to control and harmonize the brain state and to maximize the tDCS effect.

Two large randomized controlled trials (RCTs) [23,24] investigating at-home tDCS in major depressive disorder (MDD) have demonstrated sound feasibility of this approach. Whereas one RCT did not find a significant difference between active and sham tDCS arms [24], the other trial showed superior efficacy of active tDCS [23]. Regarding safety, all studies reported good tolerability with only a few adverse events (AEs). A detailed examination of the AE reports frequently describes skin lesions following tDCS. In the RCT by Woodham [23], 7 AEs related to skin irritations were reported in 6 subjects (only in the active group with n = 87 subjects), with one AE classified as severe. Skin irritations (such as redness, heat, and burning sensations) were also reported in the RCT by Borrione et al. [24], occurring more frequently in the double active and tDCS only groups compared to the double sham group. AEs were classified as mild. Local redness was reported in 55 patients in the double active and tDCS only groups (40 %), and in 11 patients in the double sham group (15 %). Heat or burning sensations were reported by 25 patients in the double active and tDCS only groups (18 %), and by 11 patients in the double sham group (15 %). In addition, one study discontinuation due to a skin lesion under the anode occurred in the double active group.

In the *HomeDC* study, which also investigated the feasibility and safety of at-home tDCS [25], a significant accumulation of AEs in the form of skin lesions led to the premature termination of the study [26]. This accumulation was not observed in the *DepressionDC* study, which used a similar protocol but applied tDCS in an in-clinic setting with a different electrode fixation technique [27].

To investigate tDCS quality which is relevant for both safety and efficacy of at-home tDCS treatment, we compared the technical data from the stimulation sessions of the Munich cohort in the *DepressionDC* 

study (in-clinic application) [27] with those from the *HomeDC* study (at-home application) [25]. Since no established procedures have been described so far for controlling technical parameters in home-based treatment, we utilized impedance variability and exact current measures as potential proxies for stimulation quality, which may also indicate a higher risk for the development of skin lesions, building on our previous work [28].

# 2. Methods

#### 2.1. Data inclusion

We compared technical parameters (impedance and current) from two independent tDCS clinical trials using the same protocol but differing in terms of application: In the *HomeDC* trial (Trial Registration: NCT05172505), patients self-administered tDCS at home, and in the *DepressionDC* trial (Trial Registration: NCT0253016), trained study personnel performed tDCS in the clinic.

The *HomeDC* trial investigated the feasibility, effectiveness, and safety of prefrontal tDCS as a treatment at home for MDD in a placebocontrolled, double-blinded, randomized design. Patients with the primary diagnosis of MDD applied prefrontal tDCS daily in a home treatment setting. Only the very first session was conducted in the clinic for training reasons, but also by the patients themselves with explanation, assistance and supervision by study staff. The *DepressionDC* study is a multicentre, double-blinded, randomized, placebo-controlled trial that investigated the efficacy and tolerability of prefrontal in-clinic tDCS as treatment for MDD [27,29]. Technical data of a blind selection of active stimulations from different centers in the *DepressionDC* trial has been previously reported [28].

Here, we used only the technical data of 835 active tDCS sessions from the Munich study site within the *DepressionDC* trial, to allow comparability with the 229 active tDCS sessions from the *HomeDC* trial which was conducted as monocentric study in Munich. Technical data from sham stimulation sessions were not included. Importantly, while the clinical analysis presented in Kumpf et al. [26] was based on the five *HomeDC* patients who completed active stimulation according to the trial protocol, the present technical analysis includes active stimulation data from a broader set of nine patients of the *HomeDC* trial. This was done to increase the number of analyzable sessions and also comprises datasets from pilot participants who completed full active at-home tDCS as well as from patients who were offered active at-home tDCS in a second treatment phase following nonresponse to the initial blinded phase.

## 2.2. Stimulation procedure and transfer of technical data

In the *HomeDC* trial, tDCS was conducted with identical stimulation parameters as in the *DepressionDC* trial [29], with the exception that the total number of stimulations was increased from 24 to 30 sessions to achieve longer lasting effects, resulting in the application of five tDCS sessions per week (Monday to Friday) for six weeks. Electrode montage was bifrontal with the anode over F3 and the cathode over F4 (international 10–20 EEG system). Stimulation was at 2 mA in the active condition for 30 min each, plus ramp-in (15 s) and ramp-out (30 s). The control group received sham treatment with identical parameters. However, direct current was only active for 15 s during ramp-in and for 30 s during ramp-out periods.

The *HomeDC* study used the same equipment as the *DepressionDC* trial, except for the caps, which were specially designed for home-based treatment [25]. To ease handling of electrode positioning, a custom-made stimulation cap (neuroConn GmbH, Ilmenau, Germany) was used with the electrodes already integrated [30]. The use of the mobile equipment, as well as all necessary application steps — with particular attention to moistening the electrodes with saline solution — was explained during an initial training session and practiced together

with the patient. The patient was instructed to apply approximately 20 ml of saline solution per side using a provided syringe. Instructions for moistening the electrodes together with safety recommendations and caveats against frequently occurring mistakes (e.g. moistening very dry electrode sponges too quickly) were discussed and provided on an information sheet (please see supplementary material). In both trials, the same portable, CE-certified stimulators (DC-Stimulator mobile, neuro-Conn GmbH, Ilmenau, Germany) were used, with implemented stimulation code system to ensure blinding of operators and participants.

## 2.3. Monitoring of technical data

Technical parameters were stored during stimulations on a storage device, which could be connected to a laptop after treatment sessions to export the data to the purpose-built "DCStimulator mobile" software (neuroConn GmbH, Ilmenau, Germany). Within this software, stimulation parameters (sham or active) and technical data were uploaded to a cloud-based database, after the investigator had inserted a stimulation-ID code for the respective patient.

Technical data (impedance, voltage, current) were measured and stored during stimulation every second. Data was transferred to the cloud every time, the saving tool was connected to the study laptop. After each stimulation session patients of the *DepressionDC* trial and of the *HomeDC* trial filled in the Comfort Rating Questionnaire (CRQ) to assess potential side effects of the treatment [31].

# 2.4. Statistical analysis

The stimulator records the route mean square values of stimulation current and electrode voltage averaged over 1 s, resulting in one sample per second. The reported impedance values are calculated values from the stored values of stimulation current and electrode voltage. For the analyses, all respective measured data of the performed active stimulations were used, excluding the measured values of the ramp-in (15 s) and ramp-out (30 s) phases, since these are naturally characterized by a high variability of the technical parameters due to the increase and decrease of the current.

The data (impedance and current) were evaluated using the opensource software "R 4.2" [32]. In order to analyse the variability across measurements, we estimated the similarity between all sequences of measures within each participant using dynamic time warping (DTW) as implemented in the "dtw" package [33]. This algorithm estimates the similarity of two sequences by calculating the optimal match between them based on certain restrictions and rules (for more information on DTW, see Ref. [33]). The resulting scores indicated the variability across trials clustered in participants, days, and study centers. Scores had a minimum of zero indicating no variability across trials whereas higher scores indicated higher variability.

After an increased incidence of adverse events, specifically skin lesions, occurred during the *HomeDC* study, the corresponding sessions that led to such skin lesions were subjected to detailed analysis. In terms of impedance, the means between the "AE-sessions" and the sessions that proceeded without adverse events were compared.

**Steady state calculations:** In addition, we investigated how long it took to reach a steady state of the technical parameters. For this purpose, we used a moving window function to estimate the standard deviation for each consecutive set of three observations. A steady state was assumed for the point after which the standard deviation for a certain window did not differ significantly from the standard deviation of the previous window.

# 3. Results

The *HomeDC* trial was terminated prematurely due to five AEs in four patients. Therefore, regarding the technical data, only 229 stimulation sessions from the *HomeDC* study could be evaluated and compared with

the technical data of 835 stimulation sessions of the *DepressionDC* trial. All five AEs were skin lesions (Fig. 4).

3.1. Comparison of impedance variability between in-clinic and homebased tDCS applications

As a first step, impedance patterns of the stimulations were analyzed independently of the AEs and the variability of the impedances between the at-home tDCS application, and the in-clinic application was compared. Fig. 1 shows the estimated variability for all stimulation sessions and all participants. In line with our hypothesis, there was a significant ( $F_{1,46} = 4.96$ , p = .031,  $\eta^2 = .097$ ) difference in the average variability of impedances between the in-clinic application (mean[M] = 579, standard deviation [SD] = 309) and the home-treatment application (M = 837, SD = 328).

The stimulation device featured a safety mechanism that automatically stops the session if impedance exceeds 55 k $\Omega$ . Throughout the entire study, no stimulation was interrupted due to this mechanism, indicating that absolute impedance levels remained below the threshold in all sessions.

#### 3.2. Comparison of current across settings

Current during active stimulations (without ramp in and ramp out phase) varied between 1996  $\mu$ A and 2012  $\mu$ A depending on impedance and voltage. The average current of the conducted tDCS sessions (without ramp in and ramp out) was compared between participants and the two settings (at-home tDCS vs. in-clinic tDCS, Fig. 2). We found no significant difference (F<sub>1,46</sub> = 0.34, p = .561,  $\eta^2$  = .007) in average currents between the *DepressionDC* (M = 2000, SD = 2.95) and *HomeDC* (M = 1999, SD = 2.72) samples.

#### 3.3. Steady states of impedance and current

A steady state was assumed for the point after which the standard deviation for a certain window did not differ significantly from the standard deviation of the previous window. For the impedance, this point was reached after 11 to 25 observations (i.e., seconds). For the current after 11 to 45 observations (after ramp-in) (Table 1). Based on these analyses, we recommend using the most conservative estimates, the 95 % confidence interval (i.e., 30 and 55 s), for all analyses.

#### 3.4. Adverse events and impedance

We also compared the impedances of stimulation sessions in the *HomeDC* trial, when skin lesions occurred to sessions without such events. Average impedance values were significantly ( $F_{1,90} = 3.98$ , p = .047,  $\eta^2 = .017$ ) higher for sessions in which AEs occurred (M = 2.69, SD = 0.31) than in sessions without any AE (M = 2.12, SD = 0.63) as shown in Fig. 3.

Skin lesions were occurring only underneath the cathode after at least 8 stimulations each (patient 1: after 8 tDCS sessions and after a break after another 12 tDCS sessions, patient 2: after 17 tDCS sessions, patient 3 after 15 tDCS sessions and patient 4 after 23 tDCS sessions). Patient 4 did not adhere to the trial protocol and applied 36 tDCS sessions. This was possible because the saving tools were loaded after each study visit for more stimulation sessions (usually loaded with 14 sessions) than needed (usually 10 sessions within 2 weeks to the next study visit), to prevent the situation that patients are unable to restart after interrupting a session due to technical issues.

Other AEs were not observed based on the CRQ. None of the four patients reported clearly elevated values in the CRQ in association with the occurrence of the skin lesion. Only one patient reported 4/10 for pain and 5/10 for burning after a stimulation that had caused a skin lesion, which was somewhat elevated in the interindividual comparison, but the patient had already reported values between 4 and 5 in the scales



Fig. 1. Variability of impedances in active stimulation sessions. Scores have a minimum of zero indicating no variability across sessions whereas higher scores indicate higher variability.



Fig. 2. Average current during stimulation sessions (without ramp in and ramp out phase) of at-home tDCS (HomeDC) vs. in-clinic tDCS (DepressionDC).

for burning and pain during previous stimulations that had not resulted in a skin lesion. None of the patients affected by a skin lesion manually stopped the respective stimulation, although all patients were informed of this possibility during the instruction phase and also stated afterwards that they were aware of this, but that the stimulation itself, which had led to the skin lesion, had not been particularly painful. This is in line with the available reports about occurrence of skin lesions [34]. Retrospectively, three of the four patients reported a somewhat

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#### Table 1

Steady state times (s).

	HomeDC		DepressionDC	
	Impedance	Current	Impedance	Current
Earliest stabilization	11	11	11	11
Mean stabilization	11.97	13.27	12.63	12.34
Latest stabilization	20	61	25	73
Earliest destabilization	1501	1501	1501	1501
Mean destabilization	1582.07	1501.89	1610.64	1502.22
Latest destabilization	1754	1519	1745	1519

increased burning sensation during the corresponding stimulation.

#### 4. Discussion

This study compared the technical data of tDCS sessions in relation to relevant information on safety from two trial cohorts, namely an inclinic tDCS cohort from the *DepressionDC* trial [27] and an at-home tDCS cohort from the *HomeDC* trial. The objective of the analyses was to investigate differences in stimulation quality between self-administered at-home tDCS and in-clinic tDCS administered by trained technicians. In the *HomeDC* trial, the occurrence of skin lesions

consequently led to a premature termination of the study [26], but provided an opportunity to examine technical parameters in relation to the lesion occurrence. As expected, we observed greater variability in impedance during at-home applications; however, this variability did not exceed the preset safety threshold (i.e. 55 kOhm) and was not associated with premature session termination. Clinically, impedance is also relevant: at-home tDCS sessions that resulted in AEs were associated with significantly higher average impedances compared to sessions without such AEs. This raises the question of whether the preset impedance threshold might have been too high. Given that the same impedance threshold was used in both studies, but skin lesions only occurred in the home-based setting, it appears more likely that factors such as humidification and chemical reactions under the cap contributed to lesion development, rather than absolute impedance values alone. Moreover, our approach provided an online recording of technical parameters, but no real-time transfer of the data or immediate feedback. This means that both adherence and critical technical information regarding tDCS session's events were only noticed when the data were read out at the next study visit. Technical data were extracted via the storage module that patients returned during visits and were subsequently transferred directly to the cloud. The technical data were then manually analyzed for outliers and irregularities, sometimes few days



Fig. 3. Average impedance of tDCS sessions without versus with adverse events (only at-home tDCS sessions).



Fig. 4. Skin lesions after cathodal tDCS. Patient 1 (left) with two AEs, patient 2, 3 and 4.

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Descargado para Lucia Angulo (lu.maru26@gmail.com) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en julio 10, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados. later. In case of such irregularities, feedback was given to the study team. For early detection and potentially preventing AEs, continuous online monitoring with real-time transfer of parameters and immediate feedback would be necessary. For example, brief automated warning message could be generated when significant impedance fluctuations or elevated voltage are detected. Furthermore, increased impedance variability or abrupt impedance shifts is only one of several potential causes [35] of skin lesions. Although impedance variability was higher in the at-home application (*HomeDC*), this did not result in significant group differences in average current. This was expected, as the stimulation device operated in a current-controlled mode, adjusting voltage dynamically to maintain the target current. Moreover, impedance variability, as used in our analysis, does not directly reflect average or absolute impedance levels and therefore would not be expected to correlate with current intensity measures.

Understanding electrochemical processes during tDCS is essential for identifying the underlying causes of AEs. During the current ramp-up phase, electro-osmosis has not yet begun. Initially, the current flows preferentially through paths with lower resistance, notably the sweat glands, potentially resulting in localized heating and potential lesion formation near the anode [36]. As electro-osmosis stabilizes, temperature changes primarily in response to changes in impedance or current. Temperature elevation at the skin-electrode interface correlates with impedance and the square of the current [35,36]. Insufficient skin-electrode contact may contribute to skin lesions by reducing the effective contact area and increasing impedance, which in turn increases heat generation [36]. Additionally, the confined heat is distributed over a smaller area, reducing the ability to dissipate heat. Factors such as inadequate contact medium or the presence of hair and skin irregularities can cause localized disruption of skin-electrode contact [31,35]. A fast ramp-in (suggesting that ramp durations of 10-20 s may be preferable) may also contribute to the development of skin lesions by initiating electro-osmosis and transferring heat from the stimulation site to surrounding tissues.

Both the *HomeDC* and *DepressionDC* trials implemented a 15-s rampin period. Furthermore, the rectangular sponge electrodes used in these studies may lead to uneven current distribution, with peak current concentration at the corners compared to round electrodes [37].

In the HomeDC study, the fact that all skin lesions occurred under the cathode led our consulting dermatologists to hypothesize a thermochemical reaction. This suggests that, beyond thermal effects, the electrode current may induce a chemical reaction that shifts the skin pH to alkaline levels. Based on physiological saline (pH 5-7), the pH value under the anode stabilizes or decreases, which does not represent a major change for the skin's physiological acidic environment. Conversely, at the cathode, a higher pH value is established within the alkaline range, resulting in a discernible pH gradient when compared to the skin. This pH gradient has been demonstrated to contribute to electrochemical skin reactions, predominantly occurring under the cathode [38,39]. According to previous studies, tDCS-induced temperature changes in the skin play a relatively minor role [40,41]. Although the electrode corners were beveled at 45°, the edge effect of rectangular electrodes was not completely eliminated in the applications of this study, potentially leading to current density hotspots near to the electrode edges. Consequently, an increase of current density at the electrode edges likely contributed to the skin lesions [42].

In addition, microscopic analysis of used electrodes performed at the manufacturer's facilities revealed that the silver coating had been partially dissolved, leading to inhomogeneity in the electrical contact distribution. It was also observed that the knitted silver filaments of the sewn-in electrodes darkened over time, and the zinc-coated snap fasteners used to attach the cables to the sponges showed similar discolorations. These findings suggest that galvanization processes may have caused degradation of the silver and zinc components, leading to uneven conductivity within the electrode material. This uneven conductivity may have caused localized impedance peaks that are not reflected in the average impedance value provided by the device, as it reports only a single combined impedance value for both electrodes. As a solution to this issue, the use of a sentinel electrode has been suggested, which would allow for separate monitoring of each electrode's resistance [43].

Table 2 shows a summary of published skin lesions after tDCS [31,34, 44–49].

An important direction for future research will be to identify participant-specific factors that may influence impedance variability and the risk of adverse events. Although the present analysis focused on overall technical performance, we did not collect standardized information on individual characteristics such as skin type (e.g., Fitzpatrick classification), or dermatologically relevant concurrent medication use. Regarding medication, it should be noted that in the DepressionDC trial, patients were treated with a stable dose of a selective serotonin reuptake inhibitor (SSRI) according to the ATHF (Antidepressant Treatment History Form) criteria, with stability required for at least four weeks prior to study initiation and maintained throughout the study period, as detailed in the published study protocol [29]. In contrast, in the HomeDC study, inclusion criteria were less strict: combination pharmacotherapies were allowed, and medication stability was required for only two weeks before study entry and during the trial. Therefore, a case-by-case analysis of participants who developed skin lesions was conducted. However, due to the small sample size resulting from early study termination, no meaningful statistical analysis could be performed. Supplementary Table 1 presents medication profiles for participants with skin lesions. Among participants with skin lesions, two out of four had received bupropion, two had received venlafaxine, and one had received lithium. Analyses examining a potential association between age and impedance variability revealed no significant correlation (r = .03; p = .642). Variables like medication and skin type may plausibly affect the skin-electrode interface and should be considered in future studies to support the development of more individualized safety protocols. These safety considerations should also be contextualized within the broader literature. Large-scale at-home tDCS programs at NYU and the University of Florida have reported more than 14,000 sessions in over 750 patients without any serious adverse events or sustained skin lesions [50,51]. These studies used standardized sponge-based electrodes, stable headset systems, structured training procedures, and daily remote check-ins with study staff, allowing for early detection and management of technical issues. In contrast, our findings suggest that increased impedance variability, although remaining within the device's safety limits, may reflect unstable stimulation conditions and could contribute to adverse skin reactions. Material-related factors, including possible degradation of embedded electrode filaments or uneven current distribution, may also have played a role. These observations underscore the importance of not only monitoring impedance, but also ensuring robust electrode design, consistent application procedures, and appropriate follow-up mechanisms. Strengthening patient training, optimizing ramp-in durations, and implementing brief daily remote contact may be essential for improving the safety of future at-home tDCS applications.

To explore whether impedance variability changed with repeated use of the tDCS setup, we analyzed the standard deviation of impedance values across sessions for each participant. To improve comparability between the two cohorts, we limited the analysis to the first 24 sessions, as the *DepressionDC* protocol included a maximum of 24 sessions. We observed that impedance variability, as measured by session-wise standard deviation, decreased over time. In the *HomeDC* cohort, this may reflect growing familiarity with the procedure and more stable behavior during stimulation (e.g., reduced movement, less tension on the cables). Interestingly, this finding appears to contradict the observation that skin lesions occurred predominantly after multiple sessions rather than at the beginning of treatment. This may suggest that other factors beyond impedance variability contribute to lesion development, or that the delayed occurrence reflects cumulative effects. However, the observed decrease in impedance variability over time was small and

#### Table 2

Summary of reported skin lesions after tDCS.

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Author, year	Contact medium	Protocol	Location, timepoint	Explanation
Lagopoulos and Degrabiele 2008	NaCl 0,05M conductive gel	1 mA, 20min, 10 s ramp-in	Anode. Single session, single person	Partly absence of gel underanode $\rightarrow$ smaller electrode–skin interface $\rightarrow$ increase of impedance $\rightarrow$ increase of heat
Palm et al., 2008	Tap water	1 mA, 2 mA, 20min, 15sec ramp-in and -out	1 case 1 mA, 5 cases 2 mA after 4. or 5. session, all cathodal at the right supraorbital region	High impedance because of the use of tap water. Mild burn through heat $\rightarrow$ superinfection
Frank et al., 2010	Tap water	1.5 mA, 30min, 8sec ramp-in and –out	Anode F3. After 4. tDCS session in 3 cases.	"Substances" that are in small concentrations of tap water could have accumulated over time in the sponges and could have contributed to skin-damaging reactions
Rodriguez et al., 2014	Saline (0.9 % NaCl)	2 mA, 20min, 15sec ramp-in and -out	Cathode (supraorbital area), 3 cases after 2. 8. and 10. session	Properties of the skin unclear – maybe already "problematic skin"
Palm et al., 2014	Tap water Saline Electrode cream	Sham and active: 2 mA, 20min	Anode F7, cathode F8. Single session. 5 cases in active + tap water; (3 cathodal, 2 anodal); 3 cases in active + electrode cream (1 anodal)	Cream layer (1 mm) might have been too thin to guarantee sufficient skin protection. Tap water: toxic chemical reaction related to regionally relatively high calcium carbonate concentration $\rightarrow$ chemical skin damage by alkaline hydrolysis.
Wang et al., 2015	Saline solution (46 mmol)	2 mA, 26 min, 30 s ramp-in and –out	Single session, 1 case under cathode FP2	Reduced conducting area and uneven distribution of current, with higher current under the middle of the electrode over the forehead; high total electric charge
Kortteenniemi et al., 2019	Saline	1.5 mA, 15min, 16sec ramp-in and -out	Cathode. Left wrist. 2 cases, single session tDCS, skin lesion occurred two days after tDCS	Insufficiently moistened electrodes, non- uniform pressure and individual skin properties have been suggested as potential causes. Causes for

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Table 2 (continued)

Author, year	Contact medium	Protocol	Location, timepoint	Explanation
Lu and Lam 2019	10-20 conductive paste	2 mA, 20min, 20 s ramp-in and –out	Cathode. Right upper limb, 3 cases. After 4. or 5. tDCS session	delayed reactions remain open Increased impedance (55 kOhm) in all subjects, melting of conductive paste, thickness of paste caused inhomogeneous electric field, skin condition of older patients and patients with T2DM
Palm and Feichtner 2020	Saline	2 mA, 20min	2 cases, both lesions under cathode right orbit, after 5. and 8. tDCS session	Saline soaked sponge dried out, rubber electrode was not fully covered with saline soaked sponge

likely not clinically meaningful. In *DepressionDC*, for example, only 20 of the 24 sessions were mandatory according to the protocol. A graphical overview of the trend in impedance variability is provided in Supplementary Fig. 1. While preliminary, the results showed a statistically significant decline in variability when including only the first 20 sessions (b = -7.15, p = .010), and a stronger effect when all available sessions were included (b = -12.88, p < .001). Further study is needed to evaluate the potential for adaptation over time, which may have implications for the design of user training and real-time feedback in home-based tDCS.

Our study has significant limitations. The sample sizes are not large, partially due to the premature termination of the HomeDC trial. This particularly limits the reliability of the analyzed stimulus current, with a permissible measurement deviation of approximately 5 % (due to offset, noise, RMS value formation and 12-bit quantization). The calculated impedance values also carry an uncertainty of up to 10 % (due to error propagation). Furthermore, the comparability of the two studies was limited by the, albeit marginally different, equipment (i.e. electrode material), although the same protocol was used. Thus, differences in technical parameters and safety outcomes cannot be attributed to the study setting alone, as was initially assumed. Moreover, impedance and current variability are not the only way to assess stimulation quality. Other important factors (e.g. intra- and interindividual variations of tDCS electrode positioning, day time of stimulation, concurrent activity) are general challenges in tDCS, and in particular in at-home application, need to be included in order to obtain correctly performed tDCS sessions at home, including maintaining a quiet environment and regulating activity before, during, and after stimulation to control for brain state effects. The results of the impedance variability analyses suggest that conventional impedance thresholds may not be sufficient to prevent potential AEs, while artificial intelligence (AI)-based algorithms could facilitate faster and more effective real time analysis of technical parameters, enabling quicker detection of issues. Despite these insights, the mechanisms underlying skin lesion development during tDCS remain incompletely understood. While impedance variability is one possible contributor, it is likely that multiple interacting factors, including cumulative effects over time, microstructural skin properties, or subtle electrode displacement, play a role. Given the limited number of adverse events and participants, our analysis cannot establish causality. Therefore, future studies with larger samples, systematic dermatological assessments, and real-time monitoring should further explore these questions to improve the safety of home-based tDCS

Descargado para Lucia Angulo (lu.maru26@gmail.com) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en julio 10, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados. protocols. Our study provides a methodological foundation to guide such efforts.

# 5. Conclusion

In sum, this study compared two sets of technical tDCS data from independent RCTs, i.e. a trial with tDCS self-administered at-home and a trial where tDCS was applied by trained operators in the clinic. Continuous monitoring of tDCS technical parameters (i.e. current and impedance) was valuable in both studies using a technical cloud based approach, but could be further improved by real-time recording and feed-back to tDCS applicants in future applications. In general, safety may be more critical in applications at-home. Our findings show that in addition to impedances and their intra-individual variability during tDCS, also other factors may be associated with local electrochemical skin reactions underneath the electrodes. In the HomeDC study, these reactions were related to inferior electrode material and its degradation by frequent use, but also insufficient humidification may have contributed to these phenomena. Thus, technical monitoring may be a useful approach for controlling tDCS quality and adherence, but electrode material should be thoroughly tested under manifold conditions, and instructions for application, training and supervision are mandatory for a safe application of at-home tDCS. Future research should investigate and establish equipment as well as general safety precautions for tDCS including long-term and frequent use (e.g. as in 'spaced' or 'accelerated' tDCS protocols [52]).

#### CRediT authorship contribution statement

Ulrike Vogelmann: Writing - review & editing, Writing - original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Matthias Stadler: Visualization, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. Aldo Soldini: Writing - review & editing, Investigation. Kai-Yen Chang: Writing - review & editing. Miaoxi Chen: Writing review & editing, Investigation. Lucia Bulubas: Writing - review & editing. Esther Dechantsreiter: Writing - review & editing, Investigation. Christian Plewnia: Writing - review & editing, Investigation. Andreas Fallgatter: Writing – review & editing. Berthold Langguth: Writing - review & editing. Claus Normann: Writing - review & editing. Lukas Frase: Writing - review & editing. Peter Zwanzger: Writing review & editing. Thomas Kammer: Writing - review & editing. Carlos Schönfeldt-Lecuona: Writing - review & editing. Daniel Kamp: Writing - review & editing. Malek Bajbouj: Writing - review & editing. Alexander Hunold: Writing - review & editing, Software, Methodology, Data curation. Severin Schramm: Writing - review & editing. Josef Priller: Writing - review & editing. Ulrich Palm: Writing - review & editing. Leigh Charvet: Writing - review & editing. Daniel Keeser: Writing - review & editing. Gerrit Burkhardt: Writing - review & editing, Supervision, Investigation, Data curation, Conceptualization. Frank Padberg: Writing - review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

#### Data availability statement

The de-identified individual patient data in this paper will be made accessible after its publication for non-commercial academic projects that have a legitimate research topic and a clearly stated hypothesis. In the event that the application is accepted, researchers will be asked to get the study approved by their institution's ethics board. The authors will subsequently provide the de-identified data sets via a safe data transfer system.

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#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Frank Padberg reports financial support was provided by German Federal Ministry of Education and Research (BMBF). Ulrike Vogelmann reports financial support was provided by LMU Munich Faculty of Medicine. Frank Padberg reports a relationship with Brainsway Inc. (Jerusalem, Israel) that includes: board membership, consulting or advisory, and speaking and lecture fees. Frank Padberg reports a relationship with Sooma medical (Helsinki, Finland) that includes: board membership and consulting or advisory. Frank Padberg reports a relationship with Mag & More GmbH (Munich, Germany) that includes: speaking and lecture fees. Frank Padberg reports a relationship with neuroCare Group GmbH that includes: speaking and lecture fees. Leigh Charvet reports a relationship with Soterix Medical Inc that includes: speaking and lecture fees. Leigh Charvet reports a relationship with Neuroelectrics Corp that includes: consulting or advisory. Peter Zwanzger reports a relationship with MagVenture Inc that includes: consulting or advisory and speaking and lecture fees. Alexander Hunold reports a relationship with neuroConn GmbH that includes: employment. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2025.05.103.

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