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Transcranial Magnetic Stimulation Induces Current Pulses in Transcranial Direct Current Stimulation Electrodes

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Abstract— **Transcranial direct current stimulation (tDCS) is a noninvasive neuromodulation technique where weak direct current is administered through electrodes placed on the subject's head. Transcranial magnetic stimulation (TMS) is a noninvasive method for focal brain stimulation where small intracranial currents are induced by a pulsed magnetic field. TMS can be applied simultaneously with tDCS to probe brain excitability or to effect synergistic neuromodulation. Delivering TMS simultaneously with tDCS can induce electric current pulses in the tDCS electrodes even when the tDCS device is turned off or is set to 0 mA output, as long as the electrodes are connected to the tDCS current source. The output impedance of commercial tDCS devices is in the range of 2–5 kΩ which can allow substantial currents to be induced by TMS. In a rat TMS-tDCS setup, the induced currents are comparable to the tDCS current magnitude. To mitigate the induced currents, the area of the loop formed by the tDCS electrode leads should be minimized and the impedance of the tDCS circuit at TMS pulses frequencies (1–10 kHz) should be maximized.**

I. Introduction

TRANSCRANIAL direct current stimulation (tDCS) is a noninvasive neuromodulation technique that involves the administration of low (1-2 mA) direct current through electrodes placed on the subject's head [1]. It is used as a research tool and is a promising therapeutic intervention for neurological and psychiatric disorders.

The neural excitability changes resulting from tDCS can be characterized by probing the brain with transcranial magnetic stimulation (TMS) before, during, and after a tDCS session [1]–[3]. TMS involves the delivery of brief, high-intensity magnetic pulses to the brain to induce an electric field that activates neurons. The magnetic field is generated by a coil placed on the head and supplied with a pulse of high current [4]. In addition to its use as a probe of brain excitability, TMS also is a neuromodulation intervention and is an approved treatment for depression and an investigational treatment for other psychiatric and neurological disorders.

Thus, TMS can be applied simultaneously with tDCS either as an excitability probe or as a synergistic neuromodulation paradigm. However, the potential for interactions between the TMS and tDCS devices that could alter the induced electric fields in the brain has not been considered. Specifically, since TMS generates a strong, rapidly changing magnetic field, it could induce transient electric currents in the tDCS stimulator. The resulting altered strength and distribution of the electric field could affect both the neuromodulation and excitability probing aspects of TMS-tDCS. Nevertheless, the latest TMS safety guidelines do not address such interaction with tDCS equipment [5].

We previously addressed the problem of TMS-induced currents in deep brain stimulation (DBS) devices [6]. That work indicated that TMS can induce substantial voltages and currents in DBS electrodes via electromagnetic coupling to the electrode leads and the conductive path through the subject's head. The magnitude of the TMS-induced currents depends on the coupling between the TMS magnetic field and the DBS circuit as well as on the DBS circuit impedance. The problem of electromagnetic coupling between TMS and tDCS is similar to that of the coupling between TMS and DBS. Like DBS, the tDCS system consist of a battery-operated stimulus current generator that is connected through wires (leads) to electrodes placed on the subject's head. Unlike DBS, the tDCS system is not implanted, but that does not change fundamentally the mechanisms of electromagnetic coupling to TMS.

In this paper, we perform an initial evaluation of the electromagnetic coupling between TMS and tDCS. We characterize the response of two commercial tDCS devices to TMS-induced voltage pulses injected at their output. We also measure the induced currents in a rat receiving simultaneous TMS and tDCS. Further, we estimate the size of induced currents in human TMS-tDCS. Finally, we provide recommendations for mitigating the TMS-induced currents in tDCS systems.

II. Methods

A. tDCS device characterization

The objective was to determine how tDCS devices behave electrically when a pulse is induced in the tDCS circuit by TMS. The behavior of the tDCS device will contribute to how much electric current is induced in the tDCS electrodes as a result of the TMS pulse.

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TMS was delivered with a Magstim Rapid device with a figure-8 coil (outside diameter = 66 mm; inside diameter = 15 mm; P/N = Eng. Spc. 8458; Magstim Co., Whitland, Carmarthenshire, Wales, UK). A search coil that generates voltage proportional to the induced electric field was placed under the TMS coil and connected to the tDCS stimulator output via a series 4.7 kΩ resistor modeling the subject's inter-electrode impedance, Z_{subj}, and a 100 Ω resistor for current sensing. To estimate the tDCS device output impedance, Z_{o}, the voltage at the tDCS stimulator output, V_{o}, and the voltage across the 100 Ω current sensing resistor were recorded with probes connected to an oscilloscope. The oscilloscope was AC coupled to remove the constant current and voltage generated by the tDCS device. The TMS induced voltage, V_{o}, and current, I_{ind}, pulses were recorded and their root-mean-square (rms) values were calculated. The tDCS device output impedance, Z_{o}, was estimated by least-squares fitting of the measured data pairs (V_{o}, I_{ind}) to the model equation

$$I_{\mathrm{ind}} = \begin{cases} 0 & \text{for} \quad V_{\mathrm{d}} > V_{\mathrm{o}} \geq 0 \\ \dfrac{V_{\mathrm{o}} - V_{\mathrm{d}}}{Z_{\mathrm{o}}} & \text{for} \quad V_{\mathrm{o}} \geq V_{\mathrm{d}} \end{cases} \tag{1}$$

where V_{d} is a deadband voltage below which no induced current flows. The deadband voltage parameter was included in the model since we observed this behavior in DBS devices [6].

TMS was applied with pulse amplitudes A_{TMS} = 30, 45, 60, 75, 90, and 100% of maximum amplitude (MA). We measured the induced voltage and current for both polarities of the induced pulse. We tested three commercial tDCS devices: models 1224-B and ALX-1.0/0.1 from Soterix Medical, Inc. (New York, NY, USA) and Phoresor II Auto from IOMED (Salt Lake City, UT, USA).

B. Rat TMS-tDCS

Simultaneous tDCS and TMS was administered to a single adult male Long-Evans rat (weight = 255 g). The study procedures followed the guidelines of the Animal Care and Use Committee at Children's Hospital (Boston, MA) and the National Institutes of Health Guide for the Care and Use of Laboratory Animals and was approved by the Children's Hospital. The animal was anesthetized with sodium pentobarbital (65 mg/kg i.p.) and placed into a stereotaxic frame (see Fig. 1). The points of contact between the metal frame and the rat were electrically insulated with paraffin film to prevent electric current shunting [7]. A 10 mm × 7 mm disposable electrode (Carefusion, WI, USA) was prepared with conductive paste and secured to the scalp. The second, "reference" electrode was a 30 mm × 30 mm saline-saturated sponge secured to the ventral torso. The TMS device and induced voltage and current measurement methods were as described in Section II-A. The voltage and current were also measured with the leads open- and short-circuited, respectively, in order to calculate the subject's impedance, Z_{subj}. The TMS coil was held in the stereotaxic frame and positioned on the midline at the interocular line over the dorsal scalp. To explore the effect of the loop formed by the tDCS electrode leads, the scalp electrode lead was routed via three different paths shown in Fig. 1. TMS pulses were delivered at A_{TMS} = 30, 60, and 90% MA.

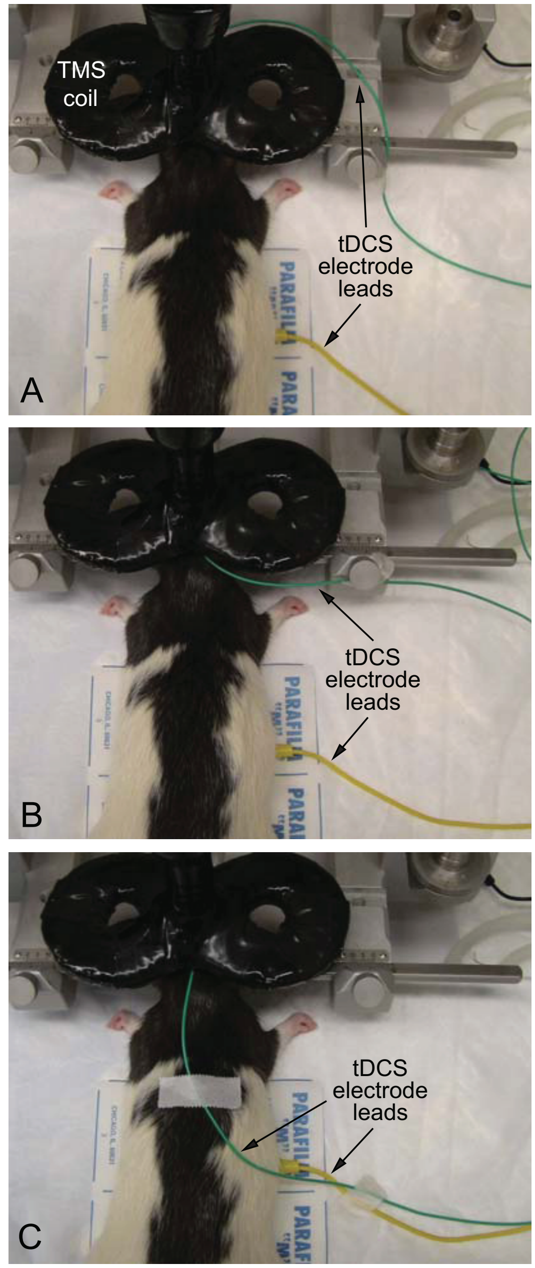

Fig. 1. Setup for simultaneous TMS-tDCS in rat with three different tDCS electrode lead paths. The green and yellow wires are the scalp and torso electrode leads, respectively. A: large loop encircling one wing of the TMS coil; B: intermediate loop excluding the TMS coil; C: minimal loop.

III. Results

The tDCS device generates direct current, I_{o}, in the electrodes (typically set to 1–2 mA in humans and 0.1–1 mA in rats). If a TMS coil is discharged near the tDCS subject's head and/or the tDCS electrode leads, a voltage V_{ind} will be induced in series with the tDCS circuit loop, as shown in Fig. 2. The tDCS device output impedance, Z_{o}, in series with the subject's impedance, Z_{subj}, and the deadband

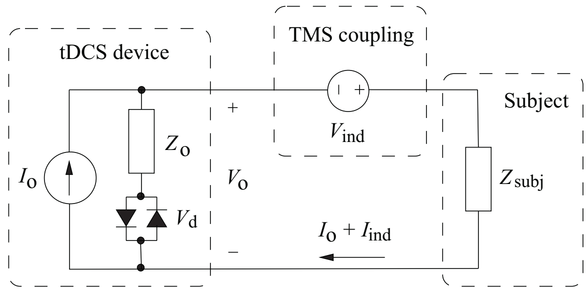

Fig. 2. Circuit model of the coupling of a TMS pulse to a tDCS system. The TMS pulse induces voltage V_{ind} in series with the tDCS stimulator as a result of changing magnetic flux around the tDCS electrode leads and in the subject's body. The tDCS device is modeled as a current source I_o with output impedance Z_o incorporating a deadband voltage V_d. The subject's impedance seen between the tDCS electrodes is Z_{subj}.

voltage, V_d, determine the current induced in the electrodes during the TMS pulse

$$I_{ind} = \begin{cases} 0 & \text{for} \quad V_d > V_{ind} \geq 0 \\ \dfrac{V_{ind} - V_d}{Z_o + Z_{subj}} & \text{for} \quad V_{ind} \geq V_d. \end{cases} \quad (2)$$

In the model, the DC component of Z_o is assumed to be very large since the tDCS device tightly regulates the DC current. The deadband voltage is represented as a pair of antiparallel diodes with forward voltage V_d.

The parameters of the model in Fig. 2 were calculated from the measurements. The estimates of Z_o and V_d, averaged across the two TMS pulse polarities, for the three tested devices are summarized in Fig. 3. Fig. 4 shows the induced voltage amplitude, V_{ind}, per TMS pulse amplitude, A_{TMS}, for the three electrode lead paths. Finally, the subject impedance as a function of the electrode current is plotted in Fig. 5.

Based on these data, the current induced in the tDCS electrodes by TMS, I_{ind}, can be calculated for various system conditions by using equation 2. For example, for representative parameters Z_o = 2.5 kΩ, V_d = 0.1 V, Z_{subj} = 21 kΩ, and A_{TMS} = 100% MA, the induced current is I_{ind} = 1.00, 0.35, and 0.17 mA for lead paths A, B, and C, respectively. Thus, the TMS induced current magnitude is close to the rat tDCS current magnitude of ~ 0.1–1 mA, but can be reduced by as much as 83% by minimizing the electrode lead loop, as shown in Fig. 1C.

IV. Discussion

Delivering TMS simultaneously with tDCS can induce electric current pulses in the tDCS electrodes. TMS can induce current pulses in the tDCS electrodes even when the tDCS device is turned off or is set to 0 mA output, as long as the electrodes are electrically connected to the tDCS current source. The output impedance of commercial tDCS devices at TMS pulse frequencies (~ 3 kHz) is in the range of 2−5 kΩ, which is comparable or lower than the typical human subject's impedance of ~ 5 kΩ and substantially lower than the rat impedance of ~ 25 kΩ. Furthermore, the effective tDCS output deadband voltage V_d is also low and therefore does not offer significant blocking of the induced pulses

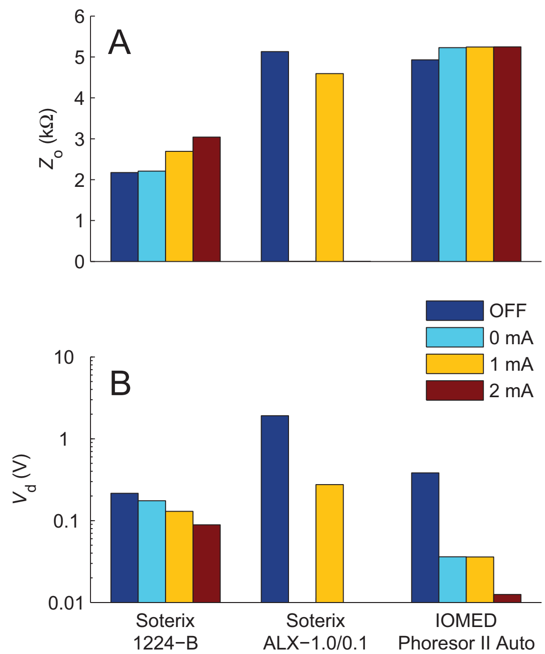

Fig. 3. tDCS device output impedance, Z_o, (A) and deadband, V_d, (B) measured at TMS pulse frequencies for various tDCS current I_o settings.

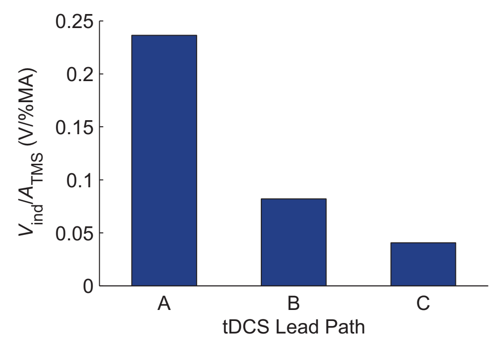

Fig. 4. Induced voltage in tDCS electrode leads, V_{ind}, as a function of the TMS pulse amplitude A_{TMS} for the three lead paths shown in Fig. 1.

either. Thus, tDCS devices do not add substantial protective impedance to the stimulation loop for TMS induced pulses.

In rat, the TMS-induced current magnitude is comparable to the tDCS current magnitude of 0.1–1 mA. The biological effect of current pulses at this amplitude is uncertain, but they could alter the TMS-induced electric field magnitude and distribution. By routing the electrode leads close to each other and away from the coil (see Fig. 1C), the induced current can be reduced by as much as 83%.

We did not present measurements in human subjects, but the general considerations apply for human simultaneous TMS-tDCS as well. Since the human head is larger than the rat, there could be more substantial electromagnetic coupling between TMS and the tDCS circuit in humans, resulting in potentially higher V_{ind}. Furthermore, the lower impedance in human tDCS, Z_{subj} ~ 5 kΩ, may result in stronger induced

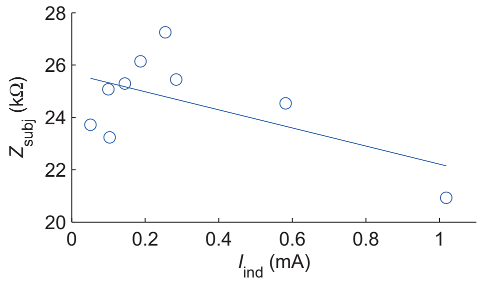

Fig. 5. Subject impedance between the tDCS electrodes, Z_{subj}, as a function of TMS induced current, I_{ind}. There is an expected trend for lower impedance at higher currents (R^2 = 0.34, p = 0.097).

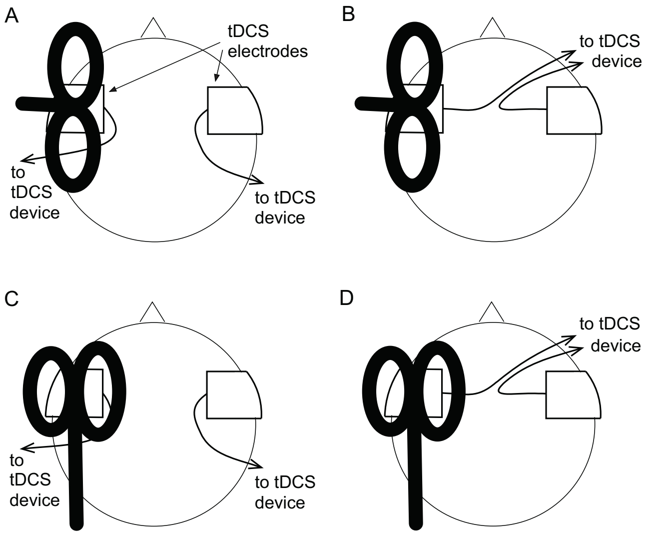

Fig. 6. Example TMS coil orientations and tDCS lead configurations in a human subject. The left column (A, C) illustrates tDCS electrode lead placement that could lead to substantial TMS-induced voltage and current flowing through the electrodes. The right column (B, D) shows how the leads can be routed to reduce the induced currents.

current as well. Thus, the current induced by TMS in tDCS in humans may be higher than in rat. Some example TMS-tDCS configurations in humans are diagrammed in Fig. 6. It is expected that, like in the rat, bringing the two electrode leads together by the shortest path (Fig. 6B,D) would reduce the TMS induced voltage. This hypothesis should be tested experimentally in the future.

A. Recommendations

The currents induced by TMS in the tDCS electrodes can be eliminated completely if the electrode leads are unplugged from the tDCS device. This, however, prevents simultaneous TMS and tDCS. There are two practical strategies for reducing the induced electrode current during simultaneous TMS-tDCS: (1) reduce the TMS-induced voltage and/or (2) increase the tDCS device output impedance. We discuss briefly these strategies below.

The induced voltage depends on the TMS coil current, configuration, and placement relative to the tDCS leads, electrodes, and the subject's head. Of these factors, only the placement of the tDCS electrode leads is not constrained by the design of the TMS-tDCS experiment. Therefore, the tDCS electrode leads are the only element that can be adjusted to reduce the TMS-induced voltage. The general rule is that the tDCS electrode leads should be placed so as to minimize coupling of the magnetic flux. Note that the conductive path of the tDCS stimulation current includes not only the tDCS leads but also the electrodes and the subject's head. The best strategy is to lay the tDCS leads on the head starting from the respective electrode they are connected to and moving toward each other by the shortest path between the two electrodes, as illustrated in Fig. 1C and Fig. 6B,D. After the electrode leads meet, they can be twisted or tied together and routed off the subject's body toward the tDCS stimulator.

In addition to the TMS-induced voltage, the tDCS electrode current depends on the tDCS device impedance. Therefore, tDCS devices intended for simultaneous application of TMS should be designed to have a high impedance in the frequency range of TMS pulses (~ 1−10 kHz). This could be achieved by designing faster current regulation feedback in the tDCS device or by adding passive filtering, e.g. an inductor, in series with the electrode leads.

Finally, the current pulses induced in the tDCS electrodes by simultaneous application of TMS in a specific setup can be easily measured: A small resistor (e.g., 100 Ω) is connected in series with the electrode leads (away from the TMS coil). The voltage across the resistor is measured with an AC-coupled oscilloscope probe; the current is the measured voltage divided by the sense resistance. Thus, all factors involved in the specific setup will be taken into account by the measurement.

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