Published in final edited form as:
*Brain Stimul*. 2019 ; 12(1): 41–43. doi:10.1016/j.brs.2018.09.011.

# Combined transcranial direct current stimulation with virtual reality exposure for posttraumatic stress disorder: Feasibility and pilot results

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## Abstract

**Background:** Facilitating neural activity using non-invasive brain stimulation may improve extinction-based treatments for posttraumatic stress disorder (PTSD).

**Objective/hypothesis:** Here, we examined the feasibility of simultaneous transcranial direct current stimulation (tDCS) application during virtual reality (VR) to reduce psychophysiological arousal and symptoms in Veterans with PTSD.

**Methods:** Twelve Veterans with PTSD received six combat-related VR exposure sessions during sham-controlled tDCS targeting ventromedial prefrontal cortex. Primary outcome measures were changes in skin conductance-based arousal and self-reported PTSD symptom severity.

**Results:** tDCS + VR components were combined without technical difficulty. We observed a significant interaction between reduction in arousal across sessions and tDCS group ($p = .03$), indicating that the decrease in physiological arousal was greater in the tDCS + VR versus sham group. We additionally observed a clinically meaningful reduction in PTSD symptom severity.

**Conclusions:** This study demonstrates feasibility of applying tDCS during VR. Preliminary data suggest a reduction in psychophysiological arousal and PTSD symptomatology, supporting future studies.

### Keywords

Virtual reality; Posttraumatic stress disorder; Brain stimulation; Transcranial direct current stimulation; Treatment; Therapy

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## Introduction

Posttraumatic stress disorder (PTSD) is a chronic and disabling condition [1]. Unfortunately, up to half of patients who receive evidence-based PTSD psychotherapy have significant residual symptoms [2] with even poorer efficacy in military Veterans [3]. At its core, PTSD reflects a persistent maladaptive fear response, with failure of the prefrontal cortex, particularly ventromedial prefrontal cortex (VMPFC), to modulate fear signals from the amygdala and dorsal anterior cingulate [4–8]. Since trauma processing has been associated with reduced neural activity in medial prefrontal cortex, among other areas, in individuals with PTSD [9], facilitating endogenous VMPFC activity – in the context of feared stimuli – using non-invasive brain stimulation represents a novel and conceptually valid way to improve treatment efficacy.

Initial studies in laboratory models support using VMPFC-targeted stimulation to reduce maladaptive fear responses during extinction of conditioned fear [10–12]. Therefore, the next critical step requires testing brain stimulation plus exposure to a trauma-relevant context. Because *in vivo* exposure is often not possible (or ethical), virtual reality (VR) can provide an immersive, contextually relevant environment [13–15] to also allow concurrent psychophysiological monitoring. This is important because reductions in PTSD-related arousal are associated with therapeutic response [16,17], and may provide an objective measure of efficacy.

To this end, we piloted VMPFC-targeted transcranial direct current stimulation (tDCS) during exposure to warzone-related VR (tDCS + VR) in Veterans with warzone-related PTSD. tDCS modulates neuronal resting membrane potentials using a weak (subthreshold) constant current [18,19], and therefore may facilitate learning and memory [20]. Since PTSD is a disorder of learning and memory, stimulation during PTSD-relevant habituation may be particularly effective [21,22]. We hypothesized that, compared to sham, tDCS + VR would result in a more rapid decline in psychophysiological arousal and be associated with clinically meaningful effects.

## Methods

Twelve male Veterans with warzone-related PTSD (mean age 40.5 years, SD 8.8, range 30–53 years) who served in Iraq and/or Afghanistan completed six VR sessions (Bravemind; Virtually Better Inc.) over two weeks (study design informed by Rothbaum et al. [15]). Participants were randomized to receive 25 min of 2 mA active or sham tDCS delivered using a neuroConn DC Stimulator Plus (neuroCare Group GmbH) in a single-blind design with anode over AF3 and cathode over PO8. Electrode configuration was informed by prior work [10,11] with stimulation designed to target the VMPFC (Fig. 1A). Outcome measures included psychophysiological arousal (skin conductance reactivity [SCR]) during each VR session, and self-reported PTSD symptoms (PTSD checklist for DSM-5; PCL-5) [23] obtained at baseline, after all VR sessions, and one month later. Other treatments (i.e., medications/psychotherapy) were stable for ≥6 weeks prior to participation and remained unchanged throughout. Each VR session included three 8-min driving scenarios with standardized presentation of 12 warzone events (IEDs, ambushes, vehicle accidents, etc.) in

each drive. VR included a head-mounted display with integrated head tracking and stereo earphones presenting combat-related multisensory information, including visual (e.g., landscape), auditory (e.g., explosions), olfactory (e.g., weapon fire), and haptic (e.g. driving vibrations) input (Fig. 1B). tDCS was started simultaneously with VR.

Biopac systems (v.4.3, Goleta, CA) were used for data acquisition and preprocessing. We recorded 2 min of baseline SCR before VR for use as a covariate in analyses. SCR to VR events was calculated following procedures used in conditioning [10,24–26]. We used linear mixed models to test the effects of repeated VR sessions, with two-tailed t-tests to compare changes in PCL-5 scores over time, performed in SPSS (v21, Armonk, NY). Stimulation side effects were assessed using a questionnaire based on recommendations by Brunoni et al. [27]. All procedures were approved by the Providence VA Institutional Review Board.

## Results

We observed a significant main effect of VR session on SCR for both the active and sham groups combined ($F(5,2390.9) = 13.20$, $p < .001$), and a significant VR session by tDCS group interaction ($F(5,2391.4) = 2.46$, $p = .03$), favoring active over sham tDCS; SCRs to VR events diminished more quickly over sessions when combined with active tDCS. Although follow up testing revealed that VR led to a decrease in physiological responding across sessions in both groups (all $p < .001$), the above significant interaction indicates that this decrease was greater in the tDCS + VR group (Fig. 1C). Participants who received active stimulation exhibited a statistical trend towards larger SCRs ($F(1,11.1) = 3.24$, $p = .099$). There were no significant SCR changes within VR sessions (all $p > .1$).

Additional exploratory analyses modeled changes in psychophysiological response to individual VR events. This was informed by observations that SCRs were stronger for certain events (e.g., explosions vs. helicopter flyover). Results were similar, revealing significant main effects of specific events ($F(35,1991.1) = 15.44$, $p < .001$) and a significant group by event interaction ($F(35,1991.1) = 1.85$, $p = .002$), favoring active tDCS + VR over sham.

Both groups demonstrated clinically meaningful reduction in PTSD symptoms (active: baseline PCL-5 41.83 ± 10.6, endpoint 32.5 ± 16.3; sham: baseline 44.33 ± 15.5, endpoint 35.8 ± 16.2; $p = .048$ for within-subjects’ comparisons, $p > .1$ for group contrasts). Participants who received tDCS + VR appeared to continue improving during the 1-month follow-up (active: 29.0 ± 13.4; sham: 35.3 ± 19.6; Cohen’s $d = 0.37$, active > sham (Fig. 1D)).

Stimulation side effects were mild and consistent with prior reports of tDCS use in psychiatry [28]. Participants could not accurately guess group assignment ($\chi^2(2) = 1.67$, $p > .1$). tDCS did not obstruct head movements during VR; tDCS impedance and electrode location remained stable throughout VR.

## Discussion

These preliminary results demonstrate the technical feasibility of tDCS + VR and its potential to improve psychophysiological arousal and clinical symptoms of PTSD. While we approach this pilot data with caution [29], the direction of effects on all measured variables was in the hypothesized direction. Observed reductions in arousal *between* sessions is consistent with mechanistic models of PTSD treatment [30], and suggests that VMPFC-targeted tDCS might enhance habituation/extinction-based processes underlying exposure to reduce PTSD symptoms. Future work should include measures of state anxiety, and establish whether the observed trend for increased arousal during active stimulation is related to tDCS, or a feature of our sample size.

To our knowledge this is the first use of simultaneous VR and non-invasive brain stimulation for any psychiatric disorder. If replicated, this represents a path for novel treatment development, combining lessons learned from non-invasive brain stimulation, exposure-based psychotherapy, and VR.

## Acknowledgments

We thank Causey Dunlap BS for her assistance with data collection. This work was supported in part by a Career Development Award (IK2 CX000724) from the U.S. Department of Veterans Affairs (Clinical Sciences Research and Development), and the Center for Neurorestoration and Neurotechnology (Rehabilitation Research and Development, N9228-C; N2864-C) at the Providence VA Medical Center. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs. The authors report no conflict of interest. We thank all the participants.

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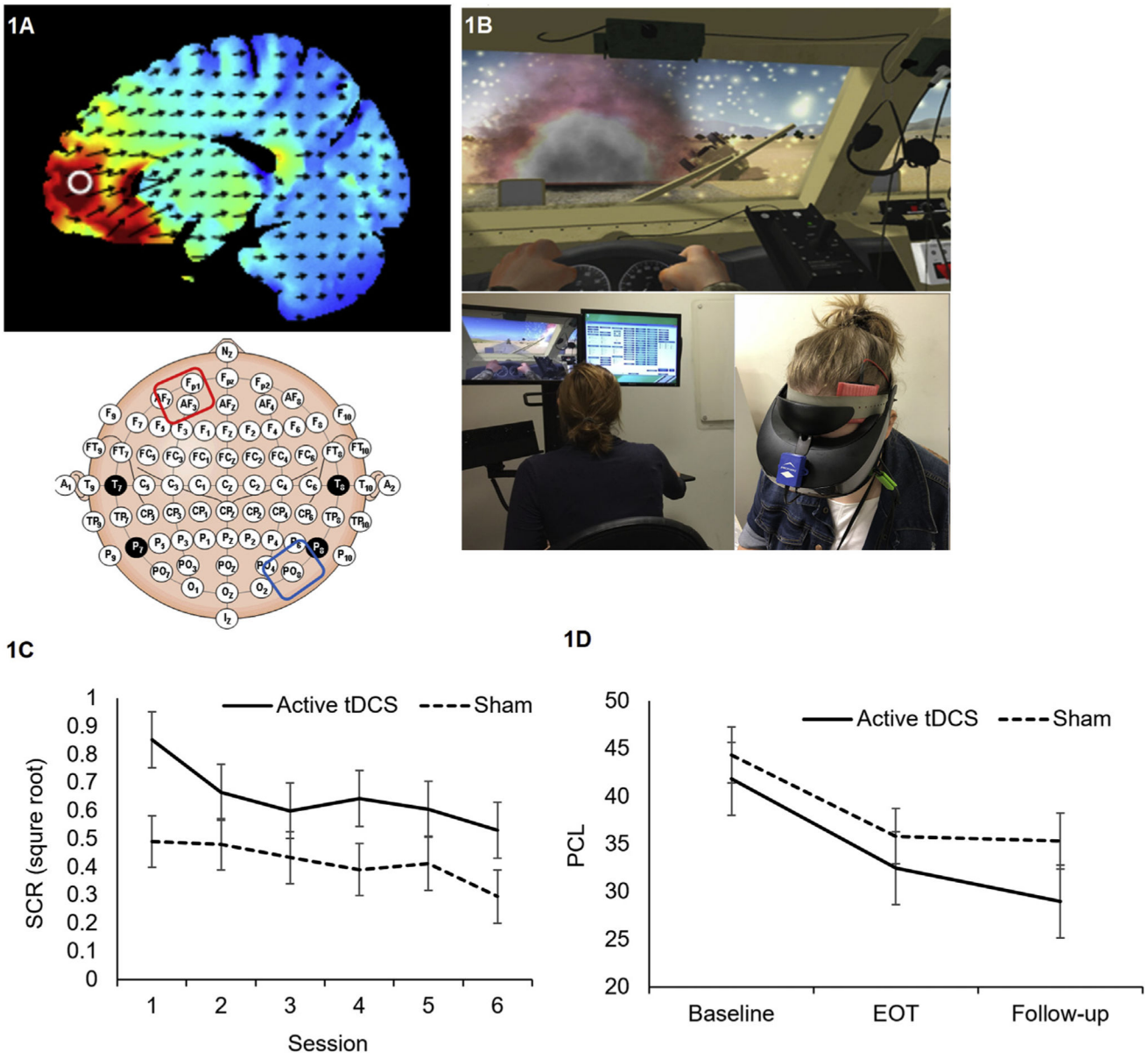


**Fig. 1.**

Electrical field modeling of tDCS electrode montage (1A). Example of VR stimulus in driving scenario and tDCS set-up (1B). Average skin conductance reactivity across VR stimuli during each session separated by group (1C). Average self-reported PTSD symptom severity during baseline, end of treatment (EOT), and at one-month follow-up (1D). Bars represent standard error.