Received: 24 May 2022 | Revised: 7 December 2022 | Accepted: 7 December 2022

DOI: 10.1002/cpp.2812

RESEARCH ARTICLE

WILEY

Augmenting the unified protocol with transcranial direct current stimulation: Effects on emotion regulation and executive dysfunction

Farzad Nasiri[1,3] | Kristen K. Ellard[2] | Ali Mashhadi[3] | Imanollah Bigdeli[3] | Ali Ghanaei-Chamanabad[3]

[1]Department of psychology, Faculty of Humanities and Social Sciences, University of Kurdistan, Sanandaj, Iran

[2]Department of Psychiatry, Massachusetts General Hospital/Harvard Medical School, Boston, Massachusetts, USA

[3]Department of Psychology, Faculty of Educational Sciences and Psychology, Ferdowsi University of Mashhad, Mashhad, Iran

Correspondence
Ali Mashhadi, Department of Psychology, Ferdowsi University of Mashhad, Mashhad, Iran.
Email: mashhadi@um.ac.ir

Abstract

The aim of the current study was to compare the unified protocol for transdiagnostic treatment of emotional disorders (UP) with and without transcranial direct current stimulation (tDCS) for the treatment of emotion regulation and executive control dysfunction in individuals diagnosed with generalized anxiety disorder (GAD) and comorbid major depressive disorder (MDD). A total of 43 individuals with GAD and co-morbid MDD were randomly assigned to three groups including UP with tDCS (UP+tDCS; $n = 15$), UP alone (UP; $n = 13$) or wait-list control ($n = 15$). Difficulties in emotion regulation, reappraisal, suppression, inhibition and working memory were assessed at baseline, post-treatment and 3-month follow-up. Treatment with both UP+tDCS and UP alone resulted in significant improvements in difficulties in emotion regulation, cognitive reappraisal, and working memory, and significant reductions in suppression and inhibition relative to wait-list controls at post-treatment and 3-month follow-up. Relative to UP alone, UP+tDCS showed significantly greater improvements in difficulties in emotion regulation, cognitive reappraisal, inhibition, and working memory at post-treatment and 3-month follow-up. These results suggest combination of UP treatment with tDCS may be an efficacious intervention to improve emotion regulation and executive function in GAD with co-morbid MDD. Trial registration reference is IRCT20140929019334N1 (see https://irct.ir/trial/27988).

KEYWORDS
depression, emotion regulation, executive functions, generalized anxiety disorder, transcranial direct current stimulation, unified protocol

1 | INTRODUCTION

Generalized anxiety disorder (GAD) and major depressive disorder (MDD) are two of the most common forms of psychological disorders and often co-occur. In the absence of DSM rule-out criteria, GAD and MDD show co-morbidity rates as high as 40%–98% (Brown et al., 1995; Newman et al., 2010; Sanderson et al., 1990; Sunderland et al., 2010). The high co-morbidity rates of these disorders indicates a shared underlying vulnerability that represents common transdiagnostic features relevant to both disorders (Kelly & Mezuk, 2017). Thus, interventions that specifically target these shared core deficits in GAD and MDD may offer a parsimonious and efficacious approach to treatment.

Both GAD and MDD are characterized by deficits in emotion regulation, further exacerbated by the co-occurrence of both disorders (Zhou et al., 2017). In addition, individuals with GAD and MDD show deficits in key aspects of executive functioning that are relevant to

emotion regulation, including attention regulation, response inhibition, and working memory, all functions necessary for the ability to maintain goal directed behaviour in the context of irrelevant or context inappropriate emotion-related responses. For example, the ability to remember information in mind when performing complex tasks, the ability to apply past experiences to use in the present situation, and to use problem-solving for the future are all important functions associated with working memory and integral to successful emotion regulation (Baddeley, 2012). The ability to flexibly focus attention on relevant stimuli, and to inhibit inappropriate or maladaptive responses in service of goal directed behaviour are also key executive functions at the centre of successful emotion regulation (Goldstein & Naglieri, 2014). Further, evidence suggests individuals who experience frequent and severe negative emotions develop cognitive impairments, including concentration and memory problems, and have difficulties processing information, suggesting bi-directional effects between executive function and emotion processing (Figueira et al., 2017).

Individuals with GAD have been shown to experience abnormal emotion processing and emotion regulation relative to healthy controls, including experiencing emotions as more intense and intolerable, having difficulty detecting, describing, and explaining emotional experiences, holding more catastrophic beliefs about the consequences of positive and negative emotions, and finding it difficult to manage strong emotions (Mennin et al., 2005). Individuals with GAD also exhibit poorer performance on working memory tasks relative to healthy controls (Tallon et al., 2016), and these performance deficits have been shown to be associated with worry, the hallmark feature of GAD (Vytal et al., 2016). Working memory impairments in turn are associated with a decreased ability to inhibit worry-inducing thoughts (Bomyea & Amir, 2011). Previous studies have shown a negative relationship between inhibition and worry in adults with GAD, in which decreased ability to inhibit responses is associated with an increased tendency towards worry (Hallion et al., 2014).

Similarly, individuals suffering from MDD have also demonstrated increased frequency of negative emotional experiences and decreased ability to regulate these emotions. Individuals with MDD show low awareness of their emotions, difficulty tolerating negative emotions, and use more maladaptive emotion regulation strategies (Joormann & Gotlib, 2010). In addition, individuals with MDD show deficits in executive function relevant to successful emotion regulation (LeMoult & Gotlib, 2019; Rock et al., 2014). For example, in a systematic review and meta-analysis of working memory performance in MDD, individuals with MDD consistently demonstrated increased errors in n-back tasks for 1-, 2- and 3-back tasks compared to control group (Nikolin et al., 2021). Individuals with MDD additionally show impairment in cognitive inhibition (Gohier et al., 2009), attention regulation and cognitive flexibility (see Keller et al., 2019 for recent review).

1.1 | Targeting Emotion Regulation and Executive Functions with the Unified Protocol

Given the high co-occurrence of GAD and MDD and the demonstrated deficits in both emotion regulation and executive control

Key Practitioner Message

- Treatment with the UP resulted in significant improvements in emotion regulation and executive control dysfunction.
- Treatment with the UP+tDCS resulted in significant improvements in emotion regulation and executive control dysfunction.
- UP+tDCS resulted in significantly greater improvements in emotion regulation and executive control dysfunction.
- Improvement of UP+tDCS outcomes remained at 3-month follow-up

across both disorders, developing interventions that directly target these processes transdiagnostically is an important goal for treatment development efforts. The unified protocol for transdiagnostic treatment of emotional disorders (UP), was developed to target common, core underlying deficits in emotion processing across mood and anxiety disorders. The principles of the UP are derived from cognitive behavioural therapy and emotion regulation research (Barlow, Farchione, Sauer-Zavala, et al., 2017). The UP focuses on teaching patients about the adaptive function of emotions, increasing present-focused awareness of the components of emotion experiences (thoughts, physiological sensations, and behaviours), identifying and modifying maladaptive associations between thoughts, physiological sensations and behaviours, increasing cognitive flexibility, countering avoidance behaviours, and increasing tolerance of the physiological sensations associated with emotions. Using emotion regulation strategies acquired through the course of treatment, new associations between thoughts, physiological sensations and behaviours are learned and consolidated through emotion exposures. Thus, the UP teaches patients to cope with unpleasant or uncomfortable emotions and to use their emotion experiences to help them respond in an adaptive manner. The focus on increasing emotion regulation skills through increased cognitive flexibility, attentional control, and inhibition of prepotent responses in favour of goal-directed behaviour suggest the UP also targets core executive processes that serve to support adaptive emotion regulation.

1.2 | Evidence for Efficacy of the UP

Several studies have now examined the efficacy of the UP in the treatment of anxiety (Barlow, Farchione, Bullis, et al., 2017), unipolar depression (Sauer-Zavala et al., 2020), bipolar depression (Ellard et al., 2017), and co-morbid GAD and MDD (Nasiri et al., 2019). In a study conducted by Southward and Sauer-Zavala (2022), within-person use of UP skills decreased anxiety and depression (Southward & Sauer-Zavala, 2022). Also, Ito et al. (2022) examined the effectiveness of UP for improving people suffering from depression and/or anxiety-related disorders. Their findings showed that UP

is effective for depression and anxiety and the improvement maintained at 43 weeks (Ito et al., 2022). In a case study about effectiveness of UP on a patient with co-morbid health anxiety and depression, the results showed reduction in number of health checking episodes, time spent health checking and in depression (Gaskell et al., 2021). Some other studies have consistently shown treatment-related reductions in mood and anxiety symptoms and improvement in emotion regulation, with modest effect sizes. For example, Ellard et al. (2017) examined the UP plus pharmacotherapy treatment as usual compared to pharmacotherapy alone in a sample of bipolar patients with co-morbid anxiety. The addition of the UP to pharmacotherapy resulted in greater decreases in both depressive and anxious symptoms. Further, for those treated with the UP, greater treatment-related increases in emotion regulation skills predicted greater improvements in anxiety related symptoms (Ellard et al., 2017). In a study of adolescents with chronic pain and co-morbid anxiety and depression, Allen et al. (2012) found significant improvements in emotion regulation skills following treatment with the UP (Allen et al., 2012). Bullis et al. (2015) administered UP in group format and showed significant improvement in emotion regulation skills in individuals with anxiety and co-morbid depression relative to a wait-list control (Bullis et al., 2015). Alivand et al. (2018) administered 14 weekly individual sessions of the UP in a sample of patients with insomnia and showed reduced behavioural inhibition, or avoidance of unpleasant experiences, from pre- to post-treatment (Alivand et al., 2018). Similarly, significantly decreased behavioural inhibition and avoidance was found following treatment with the UP in a study of 32 female students with social anxiety disorder (Arshadi et al., 2018).

Whereas collectively these results are promising, it is important to note that not everyone treated with the UP has shown improvement in these studies. Response rates for patients with co-morbid anxiety and depression across studies remain modest, suggesting there is still room for improvement. Thus, continuing to improve upon the efficacy of the UP remains an important goal.

1.3 | Enhancing the Efficacy of the UP with tDCS

One possible barrier to improvement with the UP may lie in pre-existing executive control deficits. Effective emotion regulation relies to a large extent upon the effective recruitment of executive resources. Indeed, individuals suffering from both GAD and MDD have demonstrated deficits in prefrontal regions implicated in adaptive emotion regulation and executive control. Both GAD and MDD are associated with impairments in the right ventrolateral (VLPFC) and dorsolateral prefrontal cortex (DLPFC), key regions implicated in the cognitive control of emotion processing (Madonna et al., 2019; Rogers et al., 2004), as well as impairments in DLPFC functional connectivity to distributed regions implicated in emotion regulation (Mochcovitch et al., 2014; Park et al., 2019). Deficits in DLPFC activation have been associated with impaired inhibition and regulatory mechanisms in MDD (Wang et al., 2015). Similarly, studies show that people suffering from anxiety show less working memory load-related activation in the DLPFC (Balderston et al., 2017). Metabolic dysfunctions in the prefrontal-limbic network, including the DLPFC and hippocampus have also been found in both GAD and MDD (Delvecchio et al., 2017; Palazidou, 2012). The DLPFC in particular plays an important role in regulating and directing targeted behaviours and emotions (Etkin et al., 2015; Goldstein & Naglieri, 2014), and decreasing right DLPFC activation has been shown to improve inhibitory control of emotion (Cho et al., 2010). Collectively, these results suggest normalizing DLPFC functioning in GAD and MDD may be an important target of intervention towards improving emotion regulation and overall treatment outcomes.

The presence of pre-existing deficits in the neurocircuitry supporting executive control may impede the ability to benefit fully from a behavioural intervention such as the UP, and it is an open question whether enhancing executive control through other means such as neuromodulation might increase the therapeutic impact of the UP, specifically with regard to learning and consolidating adaptive emotion regulation skills. Therefore, the current study seeks to examine whether intervening directly upon the neurocircuitry supporting executive control using neuromodulation of the DLPFC with transcranial direct current stimulation (tDCS) adjunctive to treatment with the UP will improve treatment related outcomes, specifically executive function and emotion regulation skills.

1.4 | Targeting executive functions with tDCS

Transcranial Direct-Current Stimulation (tDCS) as a brain stimulation technique is used to facilitate or inhibit spontaneous neuronal activity. It's a method to help people with brain injuries or psychiatric conditions. Two electrodes including anode and cathode are used to deliver a low electric current between 1 and 2 mA on the surface of the skull. Anodal stimulation facilitates behaviours and cathodal stimulation inhibits behaviours (Wagner et al., 2007).

Evidence suggests that tDCS can be a powerful, effective, and cost-effective neuromodulatory approach to improving executive and high-level cognitive functions (Priori et al., 2009; Schaal et al., 2017; Smirni et al., 2015; Wang et al., 2018). To date there is no study on improving executive functions of individuals with GAD, but several studies have targeted working memory and inhibition using tDCS in healthy populations and yielded positive results (Oldrati et al., 2016; Smirni et al., 2015; Wang et al., 2018; Zmigrod et al., 2014). Weidacker et al. (2016) showed inhibitory performance on a go-no go test improved significantly during cathodal stimulation of the right DLPFC (Weidacker et al., 2016). Zmigrod et al. (2014) showed that stimulation of the right DLPFC, but not left DLPFC, improved cognitive control in healthy individuals (Zmigrod et al., 2014). Beeli et al. (2008) showed that cathodal tDCS of the right DLPFC reduced impulsivity in undergraduate participants (Beeli et al., 2008). Loftus et al. (2015) showed that inhibition of the right DLPFC improved inhibitory control in young adults (Loftus et al., 2015). TDCS has also demonstrated positive effects on working memory. Meiron and Lavidor

(2014) demonstrated improvements in working memory (verbal n-back task) following anodal tDCS to DLPFC (Meiron & Lavidor, 2014). Hunter et al. (2018) found the combination of tDCS and mindfulness-based training resulted in higher improvement of working memory and attention in healthy individuals compared to mindfulness training alone (Hunter et al., 2018).

TDCS has also demonstrated positive effects on emotion regulation in healthy and patient samples (Chrysikou et al., 2019; Kelley et al., 2018). For example, Chrysikou et al. (2019) applied simultaneous anodal (excitatory) tDCS to left DLPFC and cathodal (inhibitory) tDCS to right DLPFC in MDD patients during reappraisal of negative stimuli. This resulted in upregulated ventromedial prefrontal cortex (vmPFC) activity, corresponding to decreased ratings of negative affect during reappraisal (Chrysikou et al., 2019). To our knowledge, no published studies have investigated the efficacy of tDCS on the emotion regulation of GAD patients. However, in a study of 25 individuals suffering from GAD, improvements in emotion regulation following low-frequency (inhibitory) repetitive transcranial magnetic stimulation (rTMS) to the right DLPFC were found both post-treatment and at 3-month follow-up (Diefenbach et al., 2016). The authors suggest the mechanism by which rTMS improved emotion regulation was potentially through enhancement of the cognitive mechanisms necessary to support adaptive emotion regulation (Diefenbach et al., 2016).

Few studies have examined the efficacy of the combination of tDCS with psychological treatments for GAD and MDD. D'Urso et al. (2013) showed the effects of combined tDCS+CBT were stronger than either treatment alone in a case study of a patient with MDD (D'Urso et al., 2013). Nord et al. (2019) administered eight weekly sessions of anodal (excitatory) stimulation to left DLPFC prior to treatment with CBT. The addition of tDCS showed modest but insignificant effects over and above the effects of CBT. However, this effect was moderated by baseline activation of left DLPFC as measured by task-based functional magnetic resonance imaging (fMRI), such that greater pre-treatment activation resulted in greater augmentation effects of tDCS. The authors suggest the low frequency of tDCS sessions (weekly rather than daily) may also have contributed to the modest effects (Nord et al., 2019). We recently conducted a randomized controlled trial of the UP with and without tDCS in individuals with GAD and co-morbid MDD (Nasiri et al., 2019). Patients underwent 10 daily sessions of the tDCS, consisting of 30 min stimulation with 2 mA direct current in the last 2 weeks of the UP. Results showed UP+tDCS resulted in significantly greater reductions in anxiety, worry, and anxiety sensitivity relative to UP alone at post-treatment and 3-month follow-up (Nasiri et al., 2019). However, the mechanism for this improvement remains unknown.

The current study seeks to further understand the outcomes reported in Nasiri et al. (2019) by examining the effect of combined tDCS+UP on emotion regulation and executive function, in an attempt to better understand potential mechanisms of treatment response. We hypothesized that concurrent use of tDCS with UP may result in greater improvement in emotion regulation and executive control indices than UP alone in individuals suffering from GAD and co-morbid MDD. Specifically, due to the high activity of the right DLPFC of people with GAD and MDD, and due to previous findings of improved executive function following right DLPFC stimulation, we hypothesized that cathodal (inhibitory) tDCS of the right DLPFC adjunctive to treatment with the UP will lead to greater improvement in emotion regulation and executive control.

2 | METHODS

2.1 | Design

This study reports secondary analyses from the RCT conducted by Nasiri et al. (2019). The study was a double-blind, randomized controlled trial (therapists and participants). Participants were randomly assigned to UP alone ($n = 15$), UP+tDCS ($n = 13$), or wait-list ($n = 15$) and assessed using questionnaires and neuropsychological tasks (see Section 2.3) at pre-treatment, post-treatment, and after a 3-month follow-up. The research was approved and registered in Iranian Registry of Clinical Trials (see https://irct.ir/trial/27988 with the registry code of IRCT20140929019334N1). Additional details of screening, consenting and randomization procedures can be found in the Supplement.

2.2 | Participants

Participants were referred from the Counselling Centre of Ferdowsi University of Mashhad by mental health professionals. Inclusion criteria were (1) DSM-V criteria for GAD as the primary diagnosis and MDD as a co-morbid disorder; (2) not receiving medication; (3) age range 18–40 years; (4) ability to speak and read Persian fluently; (5) have the physical health to perform computerized tasks; and (6) the ability and willingness to participate in all assessment and treatment sessions. Exclusion criteria were (1) history of receiving more than eight sessions of a CBT-based intervention within the past 5 years; (2) diagnosis of any psychological or mental disorder other than GAD and MDD; (3) substance abuse or dependence; and (4) serious suicidal thoughts. Patients were discontinued from the study if they expressed opposition to participate at any phase of research, or were in need of immediate medical attention or other interventions.

Of the 74 individuals recruited for assessment sessions, 47 were qualified to participate in the study. Participants were randomly assigned to three groups including UP alone ($n = 15$), UP+tDCS ($n = 15$), and wait-list ($n = 17$). Of these, 43 individuals completed the study. Figure 1 indicates the details of participant enrolment and study flow.

The mean age of the participants was 20.79 ($SD = 3.01$). The majority were single (90.7%) and undergraduate students (83.7%). Mean age of the participants in the UP+tDCS group was 20.23 ($SD = 2.89$) and in the UP group was 21.53 ($SD = 3.56$). Mean age of the participants in the wait-list group was 20.53 ($SD = 2.53$). Table 1 shows details of participants' demographic data.

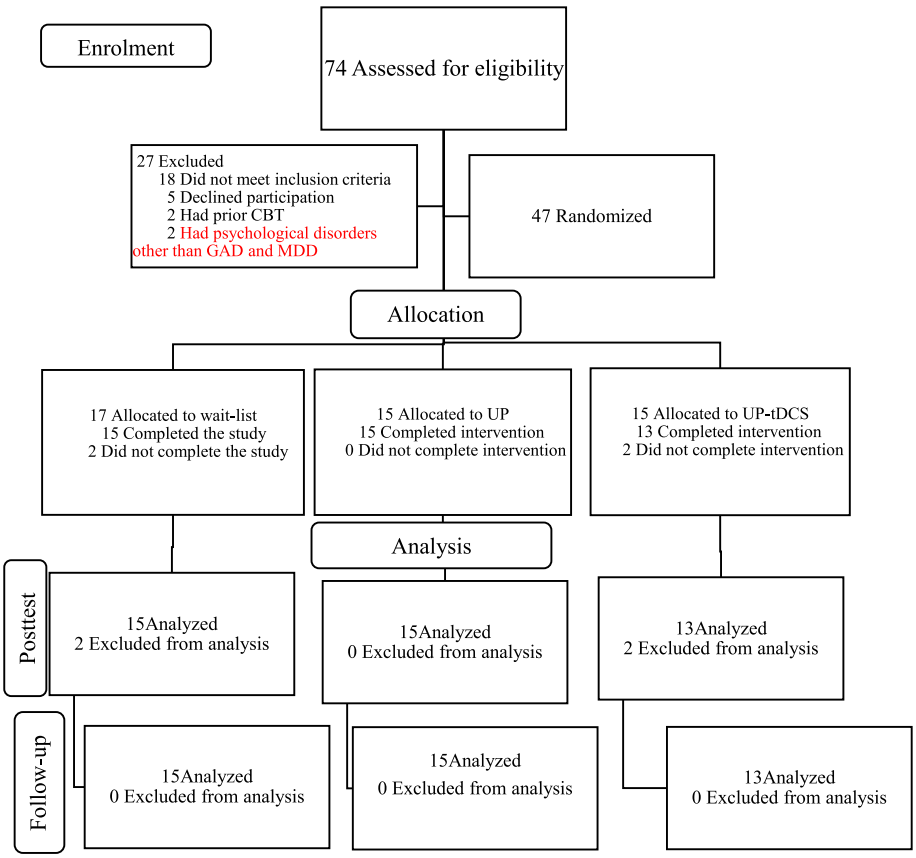

FIGURE 1 Diagram illustrating participant flow during the study. Participants were tracked during enrolment, allocation, and analysis. [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Demographic data across conditions

Demographic	Wait-list ($n = 15$)	UP ($n = 15$)	UP+tDCS ($n = 13$)
Gender (female), *n* (%)	11 (73.3%)	11 (73.3%)	10 (76.9%)
Age, years, mean (*SD*)	20.53 (2.53)	21.53 (3.56)	20.23 (2.89)
Marital status (single), *n* (%)	14 (93.3%)	13 (86.7%)	12 (92.3%)
Education			
Bachelor, *n* (%)	14 (93.3%)	11 (73.3%)	11 (84.6%)
Master, *n* (%)	1 (6.7%)	3 (20%)	2 (15.4%)
PhD, *n* (%)	0	1 (6.7%)	0

Abbreviations: UP, unified protocol for transdiagnostic treatment of emotional disorders; tDCS, transcranial direct current stimulation.

2.3 | Measures

2.3.1 | Diagnostic screening measure

Anxiety disorders interview schedule for DSM-5 (ADIS-5)

This is a semi-structured interview to diagnosis of anxiety, mood, somatoform disorders and previous mental health history. The ADIS-5 also screens the psychotic symptoms and alcohol or substance abuse. Reliability of this interview has been acceptable for the anxiety and mood disorders. In the current study, the Persian version of ADIS-5 was administered (Brown & Barlow, 2014).

2.3.2 | Outcome measures

Difficulties in emotion regulation scale (DERS)

This is a 36-item scale that has six sub-scales including lack of emotional awareness; lack of emotional clarity; difficulty regulating behaviour; difficulty engaging in goal-directed cognition and behaviour; unwillingness to accept certain emotional responses; and lack of access to strategies for feeling better. Gratz and Roemer (2004) have reported Cronbach's alpha coefficient of .93 and the test–retest reliability coefficient of .85 during the 5-week period (Gratz & Roemer, 2004). In the Persian version of this scale the internal consistency and split–half reliability of .86 and .80 were reported respectively (Asgari et al., 2009).

Emotion regulation questionnaire (ERQ)

It has 10 items and two subscales, reappraisal and suppression. The items are answered on a five-point scale. Alpha coefficients of .79 and .73 have been reported respectively for reappraisal and suppression. ERQ has demonstrated test–retest reliability of .69 during a 3-month period (Gross & John, 2003). In a preliminary study of the Persian version of the ERQ conducted by Mohammadi et al. (2014) on 41 students with a mean age of 22.8, internal consistency of .76 and .71 have been reported respectively for reappraisal and suppression. One-month test–retest reliability of .67 and .64 have been obtained respectively for reappraisal and suppression (Mohammadi et al., 2014).

Go/no go task

The go/no go task is a computerized test widely used to assess inhibitory control, consisting of two stimuli: a Go stimulus and a No-go stimulus. In this task, the stimuli for a period of 500 ms are shown in the middle of a 16-inches computer screen at a distance of 60 cm from the subject. Individuals are instructed to press a button rapidly in response to presentation of Go stimuli only and inhibit responding to No-go stimuli. Several practice rounds are administered to ensure the subject fully understands the task and the answer key placement. Subsequently, 100 trials appear, of which 70 are GO stimuli. The greater number of GO trials primes automatic responding, which the subject must inhibit to correctly perform No-go trials. All responses and reaction times of the subjects are recorded. In a study conducted in Iranian culture, the reliability of this task was reported to be .87 (Mirdoraghi et al., 2012).

N-back task

The *n*-back task as a widely used task for the assessment of working memory function. It involves a variety of stimuli (e.g., a shape and a number). The participants are instructed to decide whenever the current stimulus is the same as the one displayed *n* trials ago. For example, in 2-back task, participants must press the button in response to two trials earlier. Participants must press a button in response to the relevant or targets and to avoid responses to distractor or non-targets stimuli. In the current study, a 1-back version was used. Validity coefficients of this task has been reported in the range of .54 to .84. The reliability of this task as a measure for assessment of working memory performance is highly accepted (Kane et al., 2007).

2.4 | Procedures

All participants were assessed at baseline using a battery of questionnaires and neuropsychological tasks (see below). Participants assigned to UP or UP+tDCS were given 12-weekly one-hour sessions of the UP. Participants in the UP+tDCS group additionally received 10 daily sessions (except weekends) of tDCS during the last 2 weeks of UP treatment, corresponding to the relapse prevention module. At the end of treatment (12 weeks post baseline) and after 3-month follow-up, all participants were re-evaluated using the same baseline instruments.

2.5 | Treatment

2.5.1 | Unified protocol for transdiagnostic of emotional disorders (UP)

UP treatment was administered in 12, 60-min weekly individual sessions. The translated workbook of the UP treatment was provided to the participants (Barlow et al., 2011/2018). After each treatment session, relevant topics were identified for between-session home practice to consolidate skills. For more details of the treatment protocol, please refer to (Barlow, Farchione, Sauer-Zavala, et al., 2017).

2.5.2 | Transcranial direct current stimulation (tDCS)

Ten daily sessions (except weekends) of tDCS was administered at a fixed hour of the day. Following procedures used previously in similar studies, the cathode was placed on the right DLPFC (inhibitory stimulation) and the anode was placed on the left arm. Electrodes' size was 25 cm^2. A direct current of 2 mA and a duration of 30 min stimulation were applied. The time of ramp up and ramp down was also set to 30 s.

2.5.3 | Therapists and treatment integrity

The present study was performed by two expert and trained therapists. The therapists were officially licensed for professional practice and had more than 7 years of therapeutic experience. In addition, both therapists were under the supervision of professional supervisors and underwent the necessary courses to perform the UP treatment and the tDCS intervention. The UP supervisor is a specialist in CBT and mindfulness and has conducted numerous courses on the topics to students and therapists. The tDCS supervisor is an expert in neuropsychological interventions, and particularly tDCS. To assure the competence in mastering the UP and tDCS, the therapists treated several patients before beginning the main research study. Based on various criteria including patient satisfaction (report of significant reduction of symptoms), frequency of improved patients (two of three patients) improvement rate (at least 30% decrease in OASIS and ODSIS scales after treatment) and evaluations of the supervisor, the therapists' ability was certified. After the beginning of the study, all sessions and treatment process were monitored by the supervisors. Therapists also spent 16 h familiarizing and working with neuropsychological tasks. Prior to conducting the research, these tasks were administered experimentally on several pilot subjects.

2.6 | Statistical analyses

A 3 (treatment group) × 3 (time point) repeated measures multivariate analyses of covariance (MANCOVA) was run separately on emotion regulation and executive function measures to assess the effectiveness of the treatments. *Box's M* and Levene's test were used prior to running MANCOVAs to test model assumptions. Results of assumption testing were not significant for any of the emotion regulation variables (*Box's* $M = 53.54$, $F = 0.99$, $p = .49$) and executive functions (*BOX's* $M = 117.37$, $F = 1.14$, $p = .19$), and the homogeneity of variance/covariance matrices was correctly observed. The Levene's test was non-significant for all variables, suggesting equality of inter-group variances for all variables (Table 2). Statistical analyses were subsequently performed and Bonferroni correction was used to control error caused by multiple comparisons. The adjusted *p*-value was set after this correction for emotion regulation variables (.016) and executive functions (.012). Reported *p*-values are two-sided. Analyses were conducted using SPSS software version 25.0.

3 | RESULTS

Chi-square and analysis of variance (ANOVA) tests were conducted to detect differences in demographic variables between treatment groups. No significant differences were found between groups in any demographic category, including age ($F_{(2,\ 40)} = 0.73$, $p = .49$), gender ($\chi^2 = .06$, $p = .97$), marital status ($\chi^2 = .45$, $p = .80$), and education ($\chi^2 = 3.21$, $p = .52$).

TABLE 2 Levene's test of equality of error variances

Variables		$F_{(2,\ 40)}$	*p*
DERS	Post-treatment	2.81	.07
	Follow-up	3.04	.06
Reappraisal	Post-treatment	0.98	.38
	Follow-up	1.44	.25
Suppression	Post-treatment	2.47	.10
	Follow-up	0.77	.47
Inhibition	Post-treatment	0.40	.67
	Follow-up	1.84	.17
Inhibition's RT	Post-treatment	2.54	.09
	Follow-up	3.03	.06
Working memory	Post-treatment	0.32	.73
	Follow-up	0.66	.52
Working memory's RT	Post-treatment	0.60	.55
	Follow-up	2.30	.11

Abbreviations: DERS, difficulties in emotion regulation scale; RT, reaction time.

3.1 | Efficacy of UP and UP+tDCS at the post-treatment

The results of the MANCOVA detected a significant difference between treatment groups on at least at one of the emotion regulation variables (Wilk's lambda = .03, $F = 24.26$, $\eta^2 = .82$, $p < .001$) and executive functions (Wilk's lambda = .07, $F = 10.06$, $\eta^2 = .73$, $p < .001$) at the post- treatment or follow-up. The results showed significant main effects of difficulties in emotion regulation ($F_{(2,\ 37)} = 275.48$, $\eta^2 = .94$, $p < .001$), suppression ($F_{(2,\ 37)} = 10.37$, $\eta^2 = .36$, $p < .001$), reappraisal ($F_{(2,\ 37)} = 48.21$, $\eta^2 = .72$, $p < .001$), inhibition accuracy as measured by go/no go task ($F_{(2,\ 36)} = 21.52$, $\eta^2 = .54$, $p < .001$), inhibition reaction time as measured by go/no go task ($F_{(2,\ 36)} = 78.30$, $\eta^2 = .81$, $p < .001$), working memory accuracy as measured by n-back task ($F_{(2,\ 36)} = 42.05$, $\eta^2 = .70$, $p < .001$), working memory reaction time as measured by n-back task ($F_{(2,\ 36)} = 82.86$, $\eta^2 = .82$, $p < .001$) after controlling for the effects of pre-treatment scores. The effect of treatment groups was high on all variables. This showed that a high percentage of the variance in the scores of the variables was explained by the effects of the treatments. The mean and standard deviation of the variables in the pre-treatment, post-treatment, and follow-up are shown in Table 3.

Bonferroni post hoc comparisons of the UP group with the wait-list group showed that UP alone significantly improved difficulties in emotion regulation ($MD = -42.11$, $SE = 2.44$, $p < .001$), suppression ($MD = -4.25$, $SE = 1.41$, $p = .014$), and reappraisal strategies ($MD = 6.90$, $SE = 1.19$, $p < .001$) relative to wait-list controls. Significantly improved inhibition reaction time ($MD = -35.10$, $SE = 3.96$, $p < .001$), inhibition accuracy ($MD = 2.59$, $SE = .47$, $p < .001$), working memory reaction time ($MD = -22.61$, $SE = 2.44$, $p < .001$), and working memory accuracy ($MD = 3.47$, $SE = .72$, $p < .001$) were also found relative to wait-list.

Post hoc comparisons of UP+tDCS and wait-list group showed that UP+tDCS significantly improved difficulties in emotion regulation ($MD = -59.55$, $SE = 2.64$, $p < .001$), suppression ($MD = -6.85$, $SE = 1.53$, $p < .001$), and reappraisal strategies ($MD = 12.55$, $SE = 1.28$, $p < .001$) relative to wait-list controls. Significant improvements in inhibition reaction time ($MD = -51.22$, $SE = 4.31$, $p < .001$), inhibition accuracy ($MD = 2.97$, $SE = .52$, $p < .001$), working memory reaction time ($MD = -32.27$, $SE = 2.65$, $p < .001$) and working memory accuracy ($MD = 7.14$, $SE = .78$, $p < .001$) were also found relative to wait-list.

3.2 | Comparison of UP and UP+tDCS at post-treatment

Pairwise comparisons of the two treatments showed that UP+tDCS relative to UP alone resulted in significantly increased improvements in difficulties in emotion regulation ($MD = -17.44$, $SE = 2.50$, $p < .001$) and reappraisal strategies ($MD = 5.65$, $SE = 1.21$, $p < .001$), as well as improved inhibition reaction time ($MD = -16.12$, $SE = 4.36$,

TABLE 3 Means and standard deviations for measures

Measures	Wait-list ($n = 15$)			UP ($n = 15$)			UP+tDCS ($n = 13$)		
	Pre-treatment Means (*SD*)	Post-treatment Means (*SD*)	Follow-up Means (*SD*)	Pre-treatment Means (*SD*)	Post-treatment Means (*SD*)	Follow-up Means (*SD*)	Pre-treatment Means (*SD*)	Post-treatment Means (*SD*)	Follow-up Means (*SD*)
DERS	117.40 (15.88)	121.73 (12.41)	123.40 (10.36)	120.13 (12.81)	81.86 (10.40)	78.33 (9.62)	123.61 (16.75)	66.92 (10.87)	63.69 (8.69)
Reappraisal	20.67 (5.20)	19.87 (4.47)	18.87 (3.94)	18.87 (5.69)	25.47 (4.67)	26.93 (5.16)	16.85 (6.74)	29.92 (3.80)	32.31 (3.84)
Suppression	16.27 (5.96)	18.20 (5.44)	18.53 (4.19)	18.93 (4.57)	15.80 (5.67)	15.87 (4.01)	20.23 (4.46)	14.38 (4.03)	15.77 (3.61)
Inhibition	35.27 (2.58)	35.27 (2.02)	35.00 (2.36)	35.27 (1.33)	37.87 (1.35)	37.73 (1.10)	34.08 (1.89)	37.85 (0.80)	37.69 (1.31)
Inhibition's RT	387.67 (12.34)	380.80 (11.93)	379.93 (13.92)	389.93 (19.92)	345.87 (12.68)	347.60 (14.47)	385.54 (17.03)	327.31 (13.76)	326.08 (12.87)
Working memory	110.67 (2.58)	110.53 (2.42)	110.27 (2.25)	110.13 (2.82)	113.73 (2.40)	113.40 (2.58)	110.38 (3.15)	117.61 (1.44)	117.23 (1.30)
Working memory's RT	681.27 (11.46)	680.67 (9.11)	680.07 (8.56)	680.40 (9.45)	657.53 (6.65)	658.00 (7.09)	686.46 (9.41)	650.46 (4.68)	652.08 (6.68)

Abbreviations: DERS, difficulties in emotion regulation scale; RT, reaction time; UP, unified protocol for transdiagnostic treatment of emotional disorders; tDCS, transcranial direct current stimulation.

$p = .002$) and working memory accuracy ($MD = 3.67$, $SE = .79$, $p < .001$).

3.3 | Efficacy of UP and UP+tDCS at follow-UP

At follow-up, significant improvements in difficulties in emotion regulation ($F_{(2,\ 37)} = 374.01$, $\eta^2 = .95$, $p < .001$), suppression ($F_{(2,\ 37)} = 9.40$, $\eta^2 = .34$, $p = .001$), reappraisal ($F_{(2,\ 37)} = 62.09$, $\eta^2 = .77$, $p < .001$), inhibition accuracy ($F_{(2,\ 36)} = 17.94$, $\eta^2 = .50$, $p < .001$), inhibition reaction time ($F_{(2,\ 36)} = 55.67$, $\eta^2 = .76$, $p < .001$), working memory accuracy ($F_{(2,\ 36)} = 37.31$, $\eta^2 = .67$, $p < .001$) and working memory reaction time ($F_{(2,\ 36)} = 76.62$, $\eta^2 = .81$, $p < .001$) were present after controlling the effect of pre-treatment scores. The effect of treatment groups was high on all variables. This showed that a high percentage of the variance in the scores of the variables was explained by the effects of the treatments.

Post hoc comparisons of the UP alone and wait-list groups showed sustained improvements at follow-up in difficulties in emotion regulation ($MD = -46.28$, $SE = 2.23$, $p < .001$), suppression ($MD = -3.97$, $SE = 1.13$, $p = .003$), reappraisal strategies ($MD = 9.19$, $SE = 1.31$, $p < .001$), inhibition reaction time ($MD = -32.47$, $SE = 4.37$, $p < .001$), inhibition accuracy ($MD = 2.75$, $SE = .55$, $p < .001$), working memory reaction time ($MD = -21.76$, $SE = 2.42$, $p < .001$) and working memory accuracy ($MD = 3.37$, $SE = .71$, $p < .001$) in the UP alone group relative to wait-list controls.

Post hoc comparisons of UP+tDCS and wait-list groups showed sustained improvements in difficulties in emotion regulation ($MD = -62.64$, $SE = 2.41$, $p < .001$), suppression ($MD = -4.84$, $SE = 1.21$, $p = .001$), reappraisal strategies ($MD = 15.64$, $SE = 1.42$, $p < .001$), inhibition reaction time ($MD = -51.48$, $SE = 5.05$, $p < .001$), inhibition accuracy ($MD = 3.07$, $SE = .59$, $p < .001$), working memory reaction time ($MD = -30.73$, $SE = 2.64$, $p < .001$), and working memory accuracy ($MD = 6.67$, $SE = .78$, $p < .001$) in the UP+tDCS group relative to wait-list controls.

3.4 | Comparison of UP and UP+tDCS at follow-UP

At follow-up, UP+tDCS demonstrated significantly greater improvements in difficulties in emotion regulation ($MD = -16.35$, $SE = 2.28$, $p < .001$), reappraisal strategies ($MD = 6.44$, $SE = 1.34$, $p < .001$), inhibition reaction time ($MD = -19.02$, $SE = 5.10$, $p = .002$) and working memory accuracy ($MD = 3.30$, $SE = .78$, $p < .001$) relative to UP alone.

4 | DISCUSSION

To our knowledge, this is the first study comparing the effects of transdiagnostic treatment with the UP alone versus the UP augmented with tDCS on emotion regulation and executive control

(working memory, response inhibition) in individuals suffering from GAD co-morbid with MDD. Compared to a wait-list control group, treatment with both the UP alone and UP plus tDCS significantly improved indices of general emotion regulation skills, suppression and cognitive reappraisal. Further, treatment with both the UP alone and UP plus tDCS resulted in improvements in indices of executive function, including decreased reaction time and improved accuracy on behavioural tasks of response inhibition and working memory. These results are consistent with previous studies demonstrating the UP's effectiveness at improving emotion regulation skills of individuals suffering from anxiety and depressive disorders (Allen et al., 2012; Bullis et al., 2015; Ellard et al., 2017) and studies showing the UP's effectiveness in improving executive functions (Alivand et al., 2018; Arshadi et al., 2018). Further, augmenting the UP with the addition of tDCS resulted in greater treatment gains relative to the UP alone, leading to significantly greater improvements in general emotion regulation skills, the use of reappraisal strategies, working memory accuracy and inhibitory response times. These effects were found at post-treatment and were sustained at 3-month follow-up. This suggests augmenting the UP with tDCS may be a viable strategy to improve treatment outcomes by further increasing emotion regulation capacity through improved indices of executive control.

Our findings are consistent with previous studies showing positive effects of tDCS on cognitive functions and regulation of emotion (Wolkenstein & Plewnia, 2013), inhibition (Weidacker et al., 2016) and non-verbal recognition memory performance (Smirni et al., 2015). In the current study, tDCS adjunctive to the UP may improve outcomes through reinforcing the capacity for cognitive control, potentially enhancing the ability to engage emotion regulation skills such as cognitive reappraisal, mindful awareness, and inhibition of avoidance behaviour that are the focus of the UP (Feeser et al., 2014). We used cathodal tDCS to inhibit activity of right DLPFC, but it may also impact on other cortical and subcortical regions through functional connectivity between the DLPFC and a broader network of regions supporting emotion regulation, including the VLPFC (Braver et al., 2003; Nord et al., 2019; Tracy et al., 2014). Results of the current study are also consistent with previous studies showing that a combination of psychological and neuropsychological interventions is more effective than either treatment alone, both at the end of treatment and at follow-up (D'Urso et al., 2013; Hunter et al., 2018; Nasiri et al., 2019). Additionally, previous studies have shown these effects increase by simultaneous cognitive training during tDCS (Segrave et al., 2014), an area for further research.

One of the primary goals of UP is to improve and enhance the emotion regulation skills of individuals, and most techniques of the UP are designed for this purpose. Some techniques, including cognitive reappraisal, mindfulness and modifying emotion-driven behaviours rely upon executive control processes such as working memory, attentional control and response inhibition. The UP may exert a positive effect on emotion processing by improving cognitive skills that support adaptive emotion regulation, through improvements in working memory and inhibitory control. The results of the current study suggest augmenting the UP with tDCS strengthen these effects and may be a viable strategy to augment therapy when treatment with the UP alone does not lead to clinically significant improvement.

4.1 | Study limitations and future directions

Despite the strengths of the present study, there were some limitations. First, because of the low sample size, the generalizability of the findings may be limited. In future studies, larger sample sizes are recommended to replicate the results of the current study. The follow-up timeframe was relative short-term (3 months). In future studies, it is recommended to use 6- and 12-month follow-up to better evaluate the durability of treatment effects found here. We did not use tDCS alone or sham tDCS. Therefore, it cannot be ruled out that results in the UP+tDCS group may have represented a placebo or Hawthorne effect. Future studies including both sham tDCS and tDCS alone are needed to clarify the effects found in the current study. The current study delivered tDCS in the last 2 weeks of treatment with the UP. Future studies are needed to determine the relative effects of early versus late augmentation. The tDCS montage used in the current study involved inhibitory modulation of the right DLPFC. It remains to be seen if enhancing left DLPFC using tDCS would demonstrate equivalent, superior or inferior effects. Future studies are needed to clarify which tDCS montage is the most effective for improving emotion regulation and executive control in patients with co-morbid anxiety and depression. Finally, future studies are needed to clarify optimal augmentation strategies, such as simultaneous UP-tDCS sessions, sequential strategies (e.g. tDCS preceding or following treatment with the UP), or the strategic combination of tDCS with the delivery of specific UP modules (e.g. tDCS and present-focused awareness; tDCS and reappraisal; tDCS and emotion exposures). Although the results of the current study are promising, future studies clarifying optimal augmentation strategies may confer even greater benefit.

5 | CONCLUSION

The potential for simultaneous or combined psychological and neuropsychological interventions to improve treatment outcomes for individuals who do not respond to stand-alone behavioural therapy is a promising area for research. Paying attention to both the psychological and biological basis of disorders and the simultaneous use of psychological and neurological interventions has the potential to lead to greater treatment effectiveness or accelerated improvements for patients. Depending on the problem and taking into account various factors, we should use suitable and proportionate treatment solutions and if necessary, use these interventions in a synchronous and complementary manner so that the treatment results are maximized in the most efficacious way. The results found in the current study, if repeated, offers evidence to encourage therapists to pay more attention to the simultaneous use of psychological and neurological interventions.

The augmentation of psychological treatments with neuroscience-based interventions such as tDCS allows for more direct targeting of neurocircuit dysfunction underlying symptoms and impairment, and may result in better and longer improvement for non-responders to behavioural interventions alone. In the present study, combining tDCS with the UP resulted in significantly greater improvement in emotion regulation, inhibitory control and working memory compared to UP alone at post-treatment and 3-month follow-up. Therefore, combining these two interventions may be a promising strategy to improve emotion regulation and executive function in patients with GAD and co-morbid depression. To lend credence to the results of the current study, future studies are needed to replicate and expand upon the results reported here.

ACKNOWLEDGEMENTS

We would like to acknowledge the commitment of individuals who participated in the study. We gratefully acknowledge the staff of consulting centre of university who enabled the administration and continuation of this research.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ETHICS STATEMENT

The present study was evaluated and approved by the Ethics Committee in Bioresearch of Ferdowsi University of Mashhad (Ethical code: IR MUM FUM REC.1397.047). All procedures conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration. In this study, in order to comply with ethical considerations, necessary explanations were provided prior to the study and the duration of the study, potential benefits of receiving treatment, and information about each of the therapeutic interventions were explained to the participants, and informed consent form was provided. All participants were told to participate freely in order to observe the study freely. Participants were also told that information would be provided in such a way as not to identify the participants. They were also assured that the information collected would be purely for the purpose of scientific research. All participants were explained that participation in the research is optional. It was reminded to them that information would be provided in such a way as not to identify the participants. They were also assured that the collected data would be used only for the purpose of scientific research.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Ali Mashhadi https://orcid.org/0000-0002-6212-1372

REFERENCES

Alivand, H. D., Gharraee, B., Farid, A.-A. A., Bandi, M. F. G., & Habibi, M. (2018). Investigating the effects of the unified protocol on common and specific factors in a comorbid insomniac sample: A single-case experimental design. *Iranian Journal of Psychiatry and Behavioral Sciences*. https://doi.org/10.5812/ijpbs.14452 In Press

Allen, L. B., Tsao, J. C. I., Seidman, L. C., Ehrenreich-May, J., & Zeltzer, L. K. (2012). A unified, transdiagnostic treatment for adolescents with chronic pain and comorbid anxiety and depression. *Cognitive and Behavioral Practice*, *19*(1), 56–67. https://doi.org/10.1016/j.cbpra.2011.04.007

Arshadi, N., Mehrabizadeh Honarmand, M., & Fakhri, A. (2018). The effectiveness of unified Transdiagnostic treatment on brain-behavioral systems and anxiety sensitivity in female students with social anxiety symptoms. *International Journal of Psychology (IPA)*, *12*(2), 46–72. https://doi.org/10.24200/ijpb.2018.60313

Asgari, P., Pasha, G. H. R., & Aminiyan, M. (2009). Relationship between emotion regulation, mental stresses and body image with eating disorders of women. *Journal of Clinical Psychology Andishe Va Raftar (Applied Psychology)*, *4*(13), 65–78.

Baddeley, A. (2012). Working memory: Theories, models, and controversies. *Annual Review of Psychology*, *63*, 1–29. https://doi.org/10.1146/annurev-psych-120710-100422

Balderston, N. L., Vytal, K. E., O'Connell, K., Torrisi, S., Letkiewicz, A., Ernst, M., & Grillon, C. (2017). Anxiety patients show reduced working memory related dlPFC activation during safety and threat. *Depression and Anxiety*, *34*(1), 25–36. https://doi.org/10.1002/da.22518

Barlow, D. H., Ellard, K. K., Fairholme, C. P., Farchione, T. J., Boisseau, C. L., Allen, L. B., & Ehrenreich-May, J. (2011). *The unified protocol for transdiagnostic treatment of emotional disorders: Client workbook*. Oxford University Press.

Barlow, D. H., Farchione, T. J., Bullis, J. R., Gallagher, M. W., Murray-Latin, H., Sauer-Zavala, S., Bentley, K. H., Thompson-Hollands, J., Conklin, L. R., & Boswell, J. F. (2017). The unified protocol for transdiagnostic treatment of emotional disorders compared with diagnosis-specific protocols for anxiety disorders: A randomized clinical trial. *JAMA Psychiatry*, *74*(9), 875–884. https://doi.org/10.1001/jamapsychiatry.2017.2164

Barlow, D. H., Farchione, T. J., Sauer-Zavala, S., Latin, H. M., Ellard, K. K., Bullis, J. R., Bentley, K. H., Boettcher, H. T., & Cassiello-Robbins, C. (2017). *Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide*. Oxford University Press.

Beeli, G., Casutt, G., Baumgartner, T., & Jäncke, L. (2008). Modulating presence and impulsiveness by external stimulation of the brain. *Behavioral and Brain Functions*, *4*(4), 33–37. https://doi.org/10.1186/1744-9081-4-33

Bomyea, J., & Amir, N. (2011). The effect of an executive functioning training program on working memory capacity and intrusive thoughts. *Cognitive Therapy and Research*, *35*(6), 529–535. https://doi.org/10.1007/s10608-011-9369-8

Braver, T. S., Reynolds, J. R., & Donaldson, D. I. (2003). Neural mechanisms of transient and sustained cognitive control during task switching. *Neuron*, *39*(4), 713–726. https://doi.org/10.1016/S0896-6273(03)00466-5

Brown, T. A., & Barlow, D. H. (2014). *Anxiety and related disorders interview schedule for DSM-5 (ADIS-5)-adult and lifetime version: Clinician manual*. Oxford University Press.

Brown, T. A., Marten, P. A., & Barlow, D. H. (1995). Discriminant validity of the symptoms constituting the DSM-III-R and DSM-IV associated symptom criterion of generalized anxiety disorder. *Journal of Anxiety Disorders*, *9*(4), 317–328. https://doi.org/10.1016/0887-6185(95)00012-D

Bullis, J. R., Sauer-Zavala, S., Bentley, K. H., Thompson-Hollands, J., Carl, J. R., & Barlow, D. H. (2015). The unified protocol for transdiagnostic treatment of emotional disorders: Preliminary exploration of

effectiveness for group delivery. *Behavior Modification*, *39*(2), 295–321. https://doi.org/10.1177/0145445514553094

Cho, S. S., Ko, J. H., Pellecchia, G., Van Eimeren, T., Cilia, R., & Strafella, A. P. (2010). Continuous theta burst stimulation of right dorsolateral prefrontal cortex induces changes in impulsivity level. *Brain Stimulation*, *3*(3), 170–176. https://doi.org/10.1016/j.brs.2009.10.002

Chrysikou, E. G., Wing, E. K., & van Dam, W. O. (2019). Transcranial direct current stimulation over the prefrontal cortex in depression modulates cortical excitability in emotion regulation regions as measured by concurrent functional magnetic resonance imaging: An exploratory study. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *7*, 85–94. https://doi.org/10.1016/j.bpsc.2019.12.004

Delvecchio, G., Stanley, J. A., Altamura, A. C., & Brambilla, P. (2017). Metabolic alterations in generalised anxiety disorder: A review of proton magnetic resonance spectroscopic studies. *Epidemiology and Psychiatric Sciences*, *26*(6), 587–595. https://doi.org/10.1017/S2045796017000361

Diefenbach, G. J., Assaf, M., Goethe, J. W., Gueorguieva, R., & Tolin, D. F. (2016). Improvements in emotion regulation following repetitive transcranial magnetic stimulation for generalized anxiety disorder. *Journal of Anxiety Disorders*, *43*, 1–7. https://doi.org/10.1016/j.janxdis.2016.07.002

D'Urso, G., Mantovani, A., Micillo, M., Priori, A., & Muscettola, G. (2013). Transcranial direct current stimulation and cognitive-behavioral therapy: Evidence of a synergistic effect in treatment-resistant depression. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *6*(3), 465–467. https://doi.org/10.1016/j.brs.2012.09.003

Ellard, K. K., Bernstein, E. E., Hearing, C., Baek, J. H., Sylvia, L. G., Nierenberg, A. A., Barlow, D. H., & Deckersbach, T. (2017). Transdiagnostic treatment of bipolar disorder and comorbid anxiety using the unified protocol for emotional disorders: A pilot feasibility and acceptability trial. *Journal of Affective Disorders*, *219*, 209–221. https://doi.org/10.1016/j.jad.2017.05.011

Etkin, A., Büchel, C., & Gross, J. J. (2015). The neural bases of emotion regulation. *Nature Reviews Neuroscience*, *16*(11), 693–700. https://doi.org/10.1038/nrn4044

Feeser, M., Prehn, K., Kazzer, P., Mungee, A., & Bajbouj, M. (2014). Transcranial direct current stimulation enhances cognitive control during emotion regulation. *Brain Stimulation*, *7*(1), 105–112. https://doi.org/10.1016/j.brs.2013.08.006

Figueira, J. S. B., Oliveira, L., Pereira, M. G., Pacheco, L. B., Lobo, I., Motta-Ribeiro, G. C., & David, I. A. (2017). An unpleasant emotional state reduces working memory capacity: Electrophysiological evidence. *Social Cognitive and Affective Neuroscience*, *12*(6), 984–992. https://doi.org/10.1093/scan/nsx030

Gaskell, C., Hague, B., & Kellett, S. (2021). Effectiveness of the unified protocol for treating co-morbid health anxiety and depression: An empirical case study. *Behavioural and Cognitive Psychotherapy*, *49*(6), 673–683. https://doi.org/10.1017/S1352465821000205

Gohier, B., Ferracci, L., Surguladze, S. A., Lawrence, E., El Hage, W., Kefi, M. Z., Allain, P., Garre, J.-B., & Le Gall, D. (2009). Cognitive inhibition and working memory in unipolar depression. *Journal of Affective Disorders*, *116*(1–2), 100–105. https://doi.org/10.1016/j.jad.2008.10.028

Goldstein, S., & Naglieri, J. A. (2014). Executive functioning. A. Goldstein, Sam. https://doi.org/10.1007/978-1-4614-8106-5

Gratz, K. L., & Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *Journal of Psychopathology and Behavioral Assessment*, *26*(1), 41–54. https://doi.org/10.1023/B:JOBA.0000007455.08539.94

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology*, *85*(2), 348–362. https://doi.org/10.1037/0022-3514.85.2.348

Hallion, L. S., Ruscio, A. M., & Jha, A. P. (2014). Fractionating the role of executive control in control over worry: A preliminary investigation. *Behaviour Research and Therapy*, *54*, 1–6. https://doi.org/10.1016/j.brat.2013.12.002

Hunter, M. A., Lieberman, G., Coffman, B. A., Trumbo, M. C., Armenta, M. L., Robinson, C. S. H., Bezdek, M. A., O'Sickey, A. J., Jones, A. P., & Romero, V. (2018). Mindfulness-based training with transcranial direct current stimulation modulates neuronal resource allocation in working memory: A randomized pilot study with a nonequivalent control group. *Heliyon*, *4*(7), e00685. https://doi.org/10.1016/j.heliyon.2018.e00685

Ito, M., Horikoshi, M., Kato, N., Oe, Y., Fujisato, H., Yamaguchi, K., Nakajima, S., Miyamae, M., Toyota, A., & Okumura, Y. (2022). Efficacy of the unified protocol for transdiagnostic cognitive-behavioral treatment for depressive and anxiety disorders: A randomized controlled trial. *Psychological Medicine*, 1–12. https://doi.org/10.1017/S0033291721005067

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition and Emotion*, *24*(2), 281–298. https://doi.org/10.1080/02699930903407948

Kane, M. J., Conway, A. R. A., Miura, T. K., & Colflesh, G. J. H. (2007). Working memory, attention control, and the N-back task: A question of construct validity. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *33*(3), 615–622. https://doi.org/10.1037/0278-7393.33.3.615

Keller, A. S., Leikauf, J. E., Holt-Gosselin, B., Staveland, B. R., & Williams, L. M. (2019). Paying attention to attention in depression. *Translational Psychiatry*, *9*(1), 1–12. https://doi.org/10.1038/s41398-019-0616-1

Kelley, N. J., Gallucci, A., Riva, P., Lauro, L. J. R., & Schmeichel, B. J. (2018). Stimulating self-regulation: A review of non-invasive brain stimulation studies of goal-directed behavior. *Frontiers in Behavioral Neuroscience*, *12*, 337. https://doi.org/10.3389/fnbeh.2018.00337

Kelly, K. M., & Mezuk, B. (2017). Predictors of remission from generalized anxiety disorder and major depressive disorder. *Journal of Affective Disorders*, *208*, 467–474. https://doi.org/10.1016/j.jad.2016.10.042

LeMoult, J., & Gotlib, I. H. (2019). Depression: A cognitive perspective. *Clinical Psychology Review*, *69*, 51–66. https://doi.org/10.1016/j.cpr.2018.06.008

Loftus, A. M., Yalcin, O., Baughman, F. D., Vanman, E. J., & Hagger, M. S. (2015). The impact of transcranial direct current stimulation on inhibitory control in young adults. *Brain and Behavior*, *5*(5), e00332. https://doi.org/10.1002/brb3.332

Madonna, D., Delvecchio, G., Soares, J. C., & Brambilla, P. (2019). Structural and functional neuroimaging studies in generalized anxiety disorder: A systematic review. *Brazilian Journal of Psychiatry*, *41*(4), 336–362. https://doi.org/10.1590/1516-4446-2018-0108

Meiron, O., & Lavidor, M. (2014). Prefrontal oscillatory stimulation modulates access to cognitive control references in retrospective metacognitive commentary. *Clinical Neurophysiology*, *125*(1), 77–82. https://doi.org/10.1016/j.clinph.2013.06.013

Mennin, D. S., Heimberg, R. G., Turk, C. L., & Fresco, D. M. (2005). Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. *Behaviour Research and Therapy*, *43*(10), 1281–1310. https://doi.org/10.1016/j.brat.2004.08.008

Mirdoraghi, F., Hashemabady, G., & Mashhadi, A. (2012). Cognitive and behavioral inhibition in veterans with- and without post traumatic stress disorder. *Journal-mil-Med*, *14*(1), 41–47.

Mochcovitch, M. D., da Rocha Freire, R. C., Garcia, R. F., & Nardi, A. E. (2014). A systematic review of fMRI studies in generalized anxiety disorder: Evaluating its neural and cognitive basis. *Journal of Affective Disorders*, *167*, 336–342. https://doi.org/10.1016/j.jad.2014.06.041

Mohammadi, A., Birashk, B., & Gharraee, B. (2014). Comparison of the effect of group Transdiagnostic treatment and group cognitive therapy on emotion regulation. *Ijpcp*, *19*(3), 187–194.

Nasiri, F., Mashhadi, A., Bigdeli, I., Chamanabad, A. G., & Ellard, K. K. (2019). Augmenting the unified protocol for Transdiagnostic treatment of emotional disorders with transcranial direct current stimulation in individuals with generalized anxiety disorder and comorbid depression: A randomized controlled trial. *Journal of Affective Disorders*, *262*, 405–413. https://doi.org/10.1016/j.jad.2019.11.064

Newman, M. G., Przeworski, A., Fisher, A. J., & Borkovec, T. D. (2010). Diagnostic comorbidity in adults with generalized anxiety disorder: Impact of comorbidity on psychotherapy outcome and impact of psychotherapy on comorbid diagnoses. *Behavior Therapy*, *41*(1), 59–72. https://doi.org/10.1016/j.beth.2008.12.005

Nikolin, S., Tan, Y. Y., Schwaab, A., Moffa, A., Loo, C. K., & Martin, D. (2021). An investigation of working memory deficits in depression using the n-back task: A systematic review and meta-analysis. *Journal of Affective Disorders*, *284*, 1–8. https://doi.org/10.1016/j.jad.2021.01.084

Nord, C. L., Halahakoon, D. C., Limbachya, T., Charpentier, C., Lally, N., Walsh, V., Leibowitz, J., Pilling, S., & Roiser, J. P. (2019). Neural predictors of treatment response to brain stimulation and psychological therapy in depression: A double-blind randomized controlled trial. *Neuropsychopharmacology*, *44*(9), 1613–1622. https://doi.org/10.1038/s41386-019-0401-0

Oldrati, V., Patricelli, J., Colombo, B., & Antonietti, A. (2016). The role of dorsolateral prefrontal cortex in inhibition mechanism: A study on cognitive reflection test and similar tasks through neuromodulation. *Neuropsychologia*, *91*, 499–508. https://doi.org/10.1016/j.neuropsychologia.2016.09.010

Palazidou, E. (2012). The neurobiology of depression. *British Medical Bulletin*, *101*(1), 127–145. https://doi.org/10.1093/bmb/lds004

Park, C., Rosenblat, J. D., Lee, Y., Pan, Z., Cao, B., Iacobucci, M., & McIntyre, R. S. (2019). The neural systems of emotion regulation and abnormalities in major depressive disorder. *Behavioural Brain Research*, *367*, 181–188. https://doi.org/10.1016/j.bbr.2019.04.002

Priori, A., Hallett, M., & Rothwell, J. C. (2009). Repetitive transcranial magnetic stimulation or transcranial direct current stimulation? *Brain Stimulation*, *2*(4), 241–245. https://doi.org/10.1016/j.brs.2009.02.004

Rock, P. L., Roiser, J. P., Riedel, W. J., & Blackwell, A. D. (2014). Cognitive impairment in depression: A systematic review and meta-analysis. *Psychological Medicine*, *44*(10), 2029–2040. https://doi.org/10.1017/S0033291713002535

Rogers, M. A., Kasai, K., Koji, M., Fukuda, R., Iwanami, A., Nakagome, K., Fukuda, M., & Kato, N. (2004). Executive and prefrontal dysfunction in unipolar depression: A review of neuropsychological and imaging evidence. *Neuroscience Research*, *50*(1), 1–11. https://doi.org/10.1016/j.neures.2004.05.003

Sanderson, W. C., DiNardo, P. A., Rapee, R. M., & Barlow, D. H. (1990). Syndrome comorbidity in patients diagnosed with a DSM-III–R anxiety disorder. *Journal of Abnormal Psychology*, *99*(3), 308–312. https://doi.org/10.1037/0021-843X.99.3.308

Sauer-Zavala, S., Bentley, K. H., Steele, S. J., Tirpak, J. W., Ametaj, A. A., Nauphal, M., Cardona, N., Wang, M., Farchione, T. J., & Barlow, D. H. (2020). Treating depressive disorders with the unified protocol: A preliminary randomized evaluation. *Journal of Affective Disorders*, *264*, 438–445. https://doi.org/10.1016/j.jad.2019.11.072

Schaal, N. K., Kretschmer, M., Keitel, A., Krause, V., Pfeifer, J., & Pollok, B. (2017). The significance of the right dorsolateral prefrontal cortex for pitch memory in non-musicians depends on baseline pitch memory abilities. *Frontiers in Neuroscience*, *11*, 677. https://doi.org/10.3389/fnins.2017.00677

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation*, *7*(2), 325–331. https://doi.org/10.1016/j.brs.2013.12.008

Smirni, D., Turriziani, P., Mangano, G. R., Cipolotti, L., & Oliveri, M. (2015). Modulating memory performance in healthy subjects with transcranial direct current stimulation over the right dorsolateral prefrontal cortex. *PLoS ONE*, *10*(12), e0144838. https://doi.org/10.1371/journal.pone.0144838

Southward, M. W., & Sauer-Zavala, S. (2022). Dimensions of skill use in the unified protocol: Exploring unique effects on anxiety and depression. *Journal of Consulting and Clinical Psychology*, *90*(3), 246–257. https://doi.org/10.1037/ccp0000701

Sunderland, M., Mewton, L., Slade, T., & Baillie, A. J. (2010). Investigating differential symptom profiles in major depressive episode with and without generalized anxiety disorder: True co-morbidity or symptom similarity? *Psychological Medicine*, *40*(7), 1113–1123. https://doi.org/10.1017/S0033291709991590

Tallon, K., Koerner, N., & Yang, L. (2016). Working memory in generalized anxiety disorder: Effects of verbal and image-based worry and relation to cognitive and emotional processes. *Journal of Experimental Psychopathology*, *7*(1), 72–94. https://doi.org/10.5127/jep.045714

Tracy, D. K., de Sousa de Abreu, M., Nalesnik, N., Mao, L., Lage, C., & Shergill, S. S. (2014). Neuroimaging effects of 1 Hz right temporoparietal rTMS on normal auditory processing: Implications for clinical hallucination treatment paradigms. *Journal of Clinical Neurophysiology*, *31*(6), 541–546. https://doi.org/10.1097/WNP.0000000000000098

Vytal, K. E., Arkin, N. E., Overstreet, C., Lieberman, L., & Grillon, C. (2016). Induced-anxiety differentially disrupts working memory in generalized anxiety disorder. *BMC Psychiatry*, *16*(1), 62. https://doi.org/10.1186/s12888-016-0748-2

Wagner, T., Valero-Cabre, A., & Pascual-Leone, A. (2007). Noninvasive human brain stimulation. *Annual Review of Biomedical Engineering*, *9*, 527–565. https://doi.org/10.1146/annurev.bioeng.9.061206.133100

Wang, J., Tian, J., Hao, R., Tian, L., & Liu, Q. (2018). Transcranial direct current stimulation over the right DLPFC selectively modulates subprocesses in working memory. *PeerJ*, *6*, e4906. https://doi.org/10.7717/peerj.4906/supp-1

Wang, K., Wei, D., Yang, J., Xie, P., Hao, X., & Qiu, J. (2015). Individual differences in rumination in healthy and depressive samples: Association with brain structure, functional connectivity and depression. *Psychological Medicine*, *45*(14), 2999–3008. https://doi.org/10.1017/S0033291715000938

Weidacker, K., Weidemann, C. T., Boy, F., & Johnston, S. J. (2016). Cathodal tDCS improves task performance in participants high in Coldheartedness. *Clinical Neurophysiology*, *127*(9), 3102–3109. https://doi.org/10.1016/j.clinph.2016.05.274

Wolkenstein, L., & Plewnia, C. (2013). Amelioration of cognitive control in depression by transcranial direct current stimulation. *Biological Psychiatry*, *73*(7), 646–651. https://doi.org/10.1016/j.biopsych.2012.10.010

Zhou, Y., Cao, Z., Yang, M., Xi, X., Guo, Y., Fang, M., Cheng, L., & Du, Y. (2017). Comorbid generalized anxiety disorder and its association with quality of life in patients with major depressive disorder. *Scientific Reports*, *7*, 40511. https://doi.org/10.1038/srep40511

Zmigrod, S., Colzato, L. S., & Hommel, B. (2014). Evidence for a role of the right dorsolateral prefrontal cortex in controlling stimulus-response integration: A transcranial direct current stimulation (tDCS) study. *Brain Stimulation*, *7*(4), 516–520. https://doi.org/10.1016/j.brs.2014.03.004

How to cite this article: Nasiri, F., Ellard, K. K., Mashhadi, A., Bigdeli, I., & Ghanaei-Chamanabad, A. (2022). Augmenting the unified protocol with transcranial direct current stimulation: Effects on emotion regulation and executive dysfunction. *Clinical Psychology & Psychotherapy*, 1–12. https://doi.org/10.1002/cpp.2812