



Effects of transdiagnostic cognitive-behavioral therapy and transcranial electrical stimulation on depression symptoms in patients with panic disorder

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Original Article

Abstract

BACKGROUND: Characterized by recurrent panic attacks and a high risk of comorbid anxiety disorders, panic disorder is a chronic and debilitating condition. Despite available treatments, many individuals experience limited response or relapse. This study investigated the potential of transdiagnostic cognitive-behavioral therapy (tCBT) and transcranial electrical stimulation (tES) to reduce depressive symptoms in patients with panic disorder.

METHODS: This quasi-experimental study with pretest-posttest and control group investigated patients diagnosed with panic disorder seeking treatment at psychological centers in Ahvaz City, Iran, in 2023. Using convenience sampling, 60 eligible participants were randomly assigned to one of the three groups (n = 20 each): a tCBT group (ten 60-minute sessions), a tES group (ten 20-minute sessions), and a no-intervention control group. The Beck Depression Inventory (BDI) was used for data collection, and analysis of covariance (ANCOVA) was performed using SPSS software.

RESULTS: Both tCBT and tES significantly reduced depression symptoms ($P < 0.01$). However, no statistically significant difference was observed between the tCBT and tES groups in terms of their effectiveness in alleviating depression symptoms in patients with panic disorder.

CONCLUSION: This study suggests that both tCBT and tES may be viable treatments for reducing depressive symptoms in individuals with panic disorder. Future research with larger, more diverse samples is warranted to establish the long-term efficacy of these interventions and explore their potential for mitigating cognitive-behavioral comorbidities.

KEYWORDS: Cognitive Behavioral Therapy; Transcranial Direct Current Stimulation; Depression; Panic Disorder

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Introduction

Panic disorder involves recurrent panic attacks-episodes of intense fear/discomfort with rapidly escalating physical and psychological symptoms, peaking within minutes.¹ Unlike situational anxiety, panic

attack fear is unrealistic and disproportionate. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines a panic attack as a sudden surge of intense fear/discomfort peaking within minutes.² Attacks can occur unexpectedly, disrupting daily activities. Though affecting all ages, it is more prevalent in women (5%) than men (2%).³ Core symptoms are cognitive, emotional, and physical, often causing significant functional impairment and

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prompting medical attention. Specific situations like crowds, public transport, or queues can trigger attacks.⁴

Individuals with panic disorder often exhibit negative, catastrophizing cognitive biases, potentially contributing to symptom persistence. Panic disorder and depression are significantly comorbid, with depression a major risk factor.⁵ Depressive symptoms (e.g., hopelessness, worthlessness) can exacerbate negative thoughts and rumination in panic disorder.⁶ Depression, characterized by persistent low mood and anhedonia, is a complex disorder with biological, psychological, and social factors. Studies consistently show a strong link between depression and panic disorder, with many patients with panic disorder also experiencing depression.⁷ Despair, characterized by hopelessness and helplessness, may contribute to panic disorder development and maintenance.⁸

Panic disorder significantly impairs quality of life and often co-occurs with other health conditions. While pharmacological and psychological interventions offer positive short-term outcomes, long-term recovery varies.⁹ Transdiagnostic cognitive-behavioral therapy (tCBT) is a promising approach focusing on modifying negative thoughts, promoting emotional regulation and self-efficacy, cultivating positive self-talk, and developing coping mechanisms.¹⁰ Studies show that tCBT reduces panic attack frequency and improves treatment adherence.¹¹ tCBT builds on traditional CBT, which has demonstrated efficacy across diverse populations and conditions.^{12,13}

Beyond psychological interventions, transcranial electrical stimulation (tES) is being explored for various disorders. Functional magnetic resonance imaging (fMRI) studies highlight the crucial role of dorsolateral prefrontal cortex (DLPFC) in attentional cognitive function.¹⁴ Depression research links depressive symptoms to prefrontal cortex (PFC) function, with negative mood potentially

impacting it.¹⁵ Reduced DLPFC activity is also reported in depression. tES delivers low-intensity electrical current (≈ 2 mA) to target neural tissues, modulating excitability and offering promising neuromodulation for enhancing behavioral and cognitive function.¹⁶ Studies suggest tES potential for depression treatment. Oh *et al.* suggest that self-administered tES may improve subjective depressive symptoms.¹⁷ Vizcaino *et al.* proposed cranial electrotherapy stimulation (CES), a tES form, as valuable for major depressive disorder (MDD), alone or combined with other interventions.¹⁸ Wang *et al.* report tES as promising for post-stroke depression.¹⁹

While the etiology of panic attacks is unclear, contributing factors include biological (e.g., neurotransmitter imbalances, genetic predisposition) and environmental (e.g., mood disorders, stress, physical illness) factors. Substance use/withdrawal, medication side effects, and trauma may also contribute. Higher prevalence in those with a family/personal trauma history suggests gene-environment interaction. Given the panic disorder's impact and comorbidity with other mental health conditions, effective treatments are crucial. Although dysfunctional beliefs are a common factor in anxiety disorders, treatment approaches vary. Despite the influence of dysfunctional thoughts on panic attack severity, limited research has compared tCBT and tES effectiveness in this population. This study investigated tCBT and tES effects on depressive symptoms in patients with panic disorder.

Methods

This quasi-experimental study with pretest-posttest and control group investigated tCBT and tES effectiveness on depressive symptoms in patients with panic disorder seeking treatment in Ahvaz City, Iran (April-July 2023). Using convenience sampling, 60 eligible patients were randomly assigned to two

experimental and one control group (n = 20 each) (Figure 1). Inclusion criteria were: clinician-confirmed panic disorder, consent, middle school education, age of 18-45 years, above-mean Beck Depression Inventory (BDI) score, substance abstinence, and no concurrent treatments. Exclusion criteria were: concurrent psychological treatments, psychiatric medication, recent severe stress (past 3 months), or missing > 2 sessions. A power analysis (G*Power, effect size = 0.80, $\alpha = 0.05$, power = 0.90) indicated n = 20 per group. Quasi-experimental designs remain susceptible to confounding factors despite sufficient sample size.

All participants completed the BDI at pre-test. Experimental groups received tCBT or tES; the control group received no intervention. Post-intervention, all participants completed a post-test BDI. The study adhered to ethical

principles, and intensive interventions were offered to the control group post-assessment. Ethical approval was obtained from Bushehr University of Medical Sciences, Bushehr, Iran (IR.BPUMS.REC.1402.197).

Tools

The 13-item BDI assesses depressive symptom severity using a 4-point Likert scale (0-3), yielding scores from 0 to 39 (higher scores indicate greater severity). Common interpretations are: 0-13 (minimal), 14-19 (mild), 20-28 (moderate), and 29-39 (severe). Scores > 13 suggest potential symptoms, requiring clinical interpretation for diagnosis/treatment.²⁰

High internal consistency was reported by Luty and O’Gara²¹ ($\alpha = 0.88$) and Ghassemzadeh *et al.*²² ($\alpha = 0.87$). High content validity index (CVI) and content validity ratio (CVR) scores support content validity. In this study, the Cronbach’s α of BDI was 0.84.²²

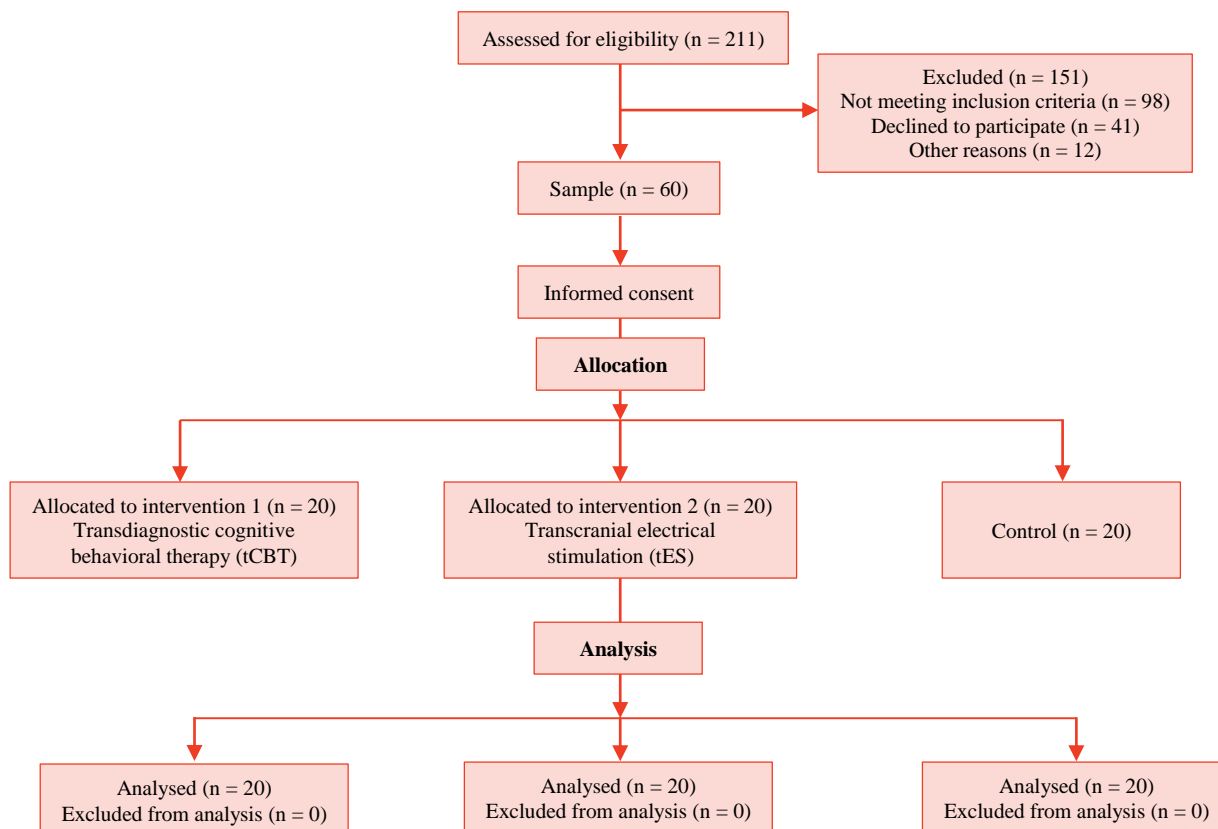


Figure 1. The Consolidated Standards of Reporting Trials (CONSORT) chart of the selection and evaluation process of the participants

Interventions

tCBT consisted of ten 60-minute sessions, delivered twice weekly over ten weeks, adhering to Barlow et al.'s guidelines.²³ The first author, trained in tCBT, conducted all sessions (Table 1).

Transcranial direct-current stimulation (tDCS):

The second experimental group received ten 20-minute tDCS sessions using a Neurostim device (Medina Tab Gostar Company and Sina Institute of Cognitive Sciences, Iran). This device offers flexible stimulation parameters. Cloud electrodes (3.5 cm² × 5.3 cm²) were positioned over the motor cortex with saline solution used for conductivity. A trained psychotherapist administered the intervention.

Data analysis: Analysis of covariance (ANCOVA) was employed to analyze the data. Statistical analyses were conducted using SPSS software (version 27, IBM Corporation, Armonk, NY, USA).

Results

The study sample comprised 60 participants diagnosed with panic disorder, with a mean age of 29.38 ± 6.39 years. The demographic characteristics of the participants

are presented in table 2. Results indicated no significant differences between the experimental and control groups regarding demographic variables.

Table 3 shows means and standard deviations (SD) of pre- and post-test depression symptom scores for each group. Prior to ANCOVA, normality (non-significant Shapiro-Wilk test) and homogeneity of variance (Levene's test) were confirmed.

ANCOVA results showed a significant difference in depression symptoms among groups [$F = 127.91$, sum of squares (SS) = 3925.81, degree of freedom (df) = 2, mean square (MS) = 1962.91, $\eta^2 = 0.82$, power = 0.73, $P < 0.001$], indicating that at least one intervention group differed from control; post-hoc analyses were needed to determine specific group differences.

Bonferroni-corrected post-hoc comparisons (Table 4) revealed significant differences in depression symptom scores between both tCBT and control ($P < 0.001$) and tES and control ($P < 0.001$), indicating that both interventions effectively reduced symptoms. However, no significant difference was found between tCBT and tES.

Table 1. Summary of transdiagnostic cognitive-behavioral therapy (tCBT) sessions

Sessions	Content
1	Introduction to therapy, goal setting (short-term and long-term), and homework assignment of a worksheet on therapy goals
2	Addressing emotions, introducing the three-part model of emotional experience (thoughts, behaviors, and physiological sensations), and assigning a worksheet on these components
3	Identifying negative emotion triggers, considering consequences of emotional responses, and assigning an emotion monitoring worksheet
4	Introducing mindfulness-based awareness, practicing emotion awareness exercises, and assigning homework using mindfulness techniques and worksheets
5	Educating about cognitive appraisal, identifying cognitive traps, implementing cognitive reappraisal, and assigning worksheets on self/future evaluation and the downward arrow technique
6	Reviewing emotional avoidance and its role in negative behavior, addressing emotion-driven behaviors, and assigning an avoidance strategies worksheet
7	Explaining emotion-driven behaviors, assisting in identification and replacement of these behaviors, and assigning a behavior change form
8	Familiarizing with physiological sensations and their role in behavior, exposing the client to unpleasant sensations, and assigning a symptom induction worksheet
9	Introducing and practicing exposure techniques to unpleasant emotions, emphasizing repetition over avoidance, and assigning an emotional exposure worksheet
10	Reviewing emotion coping skills, assessing progress, and learning strategies for maintaining gains and preventing future episodes

Table 2. Demographic characteristics of the participants

Groups	tCBT	tES	Control	P	
Age (year) (mean \pm SD)	27.30 \pm 5.62	29.45 \pm 6.17	31.40 \pm 7.37	0.552	
Education [n (%)]					
	High school	13 (65)	14 (70)	11 (55)	0.605
	College education	7 (35)	6 (30)	9 (45)	
Gender [n (%)]					
	Women	9 (45)	7 (35)	10 (50)	0.622
	Men	11 (55)	13 (65)	10 (50)	
Panic severity [n (%)]					
	Mild	4 (20)	3 (15)	5 (25)	0.916
	Moderate	8 (40)	7 (35)	8 (40)	
	Severe	5 (25)	7 (35)	5 (25)	
	Extreme	3 (15)	2 (15)	2 (10)	

tCBT: Transdiagnostic cognitive-behavioral therapy; tES: Transcranial electrical stimulation; SD: Standard deviation

Discussion

This study investigated the efficacy of tDCS and tCBT in reducing depressive symptoms in individuals with panic disorder. Both interventions significantly alleviated symptoms compared to the control group, but no significant difference was found between tDCS and tCBT.

Our findings support the effectiveness of tCBT in alleviating depressive symptoms in patients with panic disorder, aligning with previous research.^{24,25} The efficacy of tCBT likely stems from its targeting of cognitive and behavioral patterns associated with both panic disorder and depression.²⁵ These results further corroborate the broader literature on CBT effectiveness in reducing depression; for example, Nuraeni *et al.*²⁵ demonstrated CBT efficacy in reducing depression, particularly in short-term follow-up for patients with coronary heart disease. Cognitive restructuring, which helps patients identify and challenge negative thought patterns, is a potential mechanism underlying tCBT therapeutic effects.¹² The behavioral component of tCBT equips patients with coping skills to manage

anxiety and avoidance, key features of panic disorder, potentially alleviating depressive symptoms by reducing overall stress and promoting positive emotions.¹³

This study supports the growing evidence for tES effectiveness in mitigating depressive symptoms in patients with panic disorder, aligning with Vizcaino *et al.*¹⁸ tES is a non-invasive neuromodulation technique using weak electrical currents, unlike transcranial magnetic stimulation (TMS), which uses magnetic fields. While the exact mechanisms of tES antidepressant effects are still under investigation, a proposed mechanism is its influence on brain regions implicated in both depression and panic disorder, such as the DLPFC.¹⁶ Stimulating this region may promote neuroplasticity and enhance cognitive control over emotional regulation and mood.¹⁹

The precise mechanisms by which tES exerts its antidepressant effects remain under investigation. However, various hypotheses have been proposed. One possibility is that tES modulates the activity of specific brain regions implicated in both depression and panic disorder, such as the PFC, amygdala, and hippocampus.²³

Table 3. Mean \pm standard deviation (SD) of depression symptoms in research groups during the pre-test and post-test stages

Variable	Groups	Pre-test	Post-test	P
		Mean \pm SD		
Depression symptoms	tCBT	39.15 \pm 3.87	19.50 \pm 3.98	< 0.001
	tES	39.60 \pm 2.99	20.80 \pm 4.26	< 0.001
	Control	41.00 \pm 0.61	38.35 \pm 4.10	0.062

tCBT: Transdiagnostic cognitive-behavioral therapy; tES: Transcranial electrical stimulation; SD: Standard deviation

Table 4. Bonferroni post-hoc test for paired comparison of depression symptoms

Variable	Groups	Mean difference	SE	P
Depression symptoms	tCBT-control	20.20	1.29	< 0.001
	tES-control	19.83	1.28	< 0.001
	tCBT-tES	0.37	1.26	0.772

tCBT: Transdiagnostic cognitive-behavioral therapy; tES: Transcranial electrical stimulation; SE: Standard error

By stimulating or inhibiting these areas, tES may promote neuroplasticity, potentially leading to improved emotional regulation and mood. Furthermore, tES may influence neurotransmitter systems, particularly those involved in mood regulation, such as serotonin and norepinephrine.²⁵ By influencing these pathways, tES could contribute to a reduction in depressive symptoms. Additionally, research suggests that tES may enhance the effectiveness of existing treatments for depression, such as psychotherapy. As a non-invasive intervention, tES offers several potential advantages over traditional treatment methods for depression. Unlike medication, tES typically has minimal side effects, making it a suitable option for patients who may be hesitant about medication use. In addition, tES offers a more targeted approach compared to medications, potentially leading to faster symptom relief.

While the precise mechanisms of tES antidepressant effects are under investigation, hypotheses include modulation of brain regions implicated in depression and panic disorder (e.g., PFC, amygdala, hippocampus), potentially promoting neuroplasticity and improving emotional regulation/mood. tES may also influence mood-regulating neurotransmitter systems like serotonin and norepinephrine, thus reducing depressive symptoms.¹⁸

This study has limitations. The pretest-posttest design assessed outcomes only immediately post-intervention. Depression severity was measured solely using the BDI. The design did not control for potential confounding factors like age, gender, and socioeconomic status, which could have influenced outcomes.

Conclusion

The findings revealed that both interventions resulted in significant reductions in depression symptoms compared to the control group. Notably, no statistically significant difference was found between the tDCS and tCBT groups regarding their impact on these symptoms. These results suggest that both tDCS and tCBT may be viable treatment options for reducing depression in patients with panic disorder. The comparable efficacy observed between the interventions underscores the need for further research to elucidate the specific mechanisms of action and optimal treatment protocols for each modality within this population.

Conflict of Interests

Authors have no conflict of interests.

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