Research article

Transcranial direct current stimulation based on qEEG combining positive psychotherapy for major depression

Zahra Khayyer[1,*], Leonard Ngaosuvan[2], Sverker Sikström[3], Amir Hossein Ghaderi[4]

[1] *Educational Sciences & Psychology Department, University of Isfahan, Isfahan, Iran*
[2] *Department of Health and Work Science, University of Gävle, Gävle, Sweden*
[3] *Department of Psychology, Cognitive Division, Lund University, Sweden*
[4] *University of Tabriz, Tabriz, Iran*

***Correspondence**: Kayyer.Psyche@edu.ui.ac.ir (Zahra Khayyer)

https://doi.org/10.31083/JIN-170045

Abstract

Frontal cortex activity is reduced in the left hemisphere during depression. Transcranial direct current stimulation is a non-invasive neuromodulation technique that can increase frontal cortex activity. Therapy based on transcranial Direct Current Stimulation and positive psychology therapy was applied for improving patients' quality of life. The present study compared three conditions of subjects with clinical depression; (a) transcranial Direct Current Stimulation therapy, (b) positive psychotherapy, and (c) combined treatment. Hamilton Depression Rating Scale, Adult State Hope Scale and Optimism/Pessimism Scale was used at baseline, 2-week, 4-week, and 3-month follow-up. Combined condition participants showed greater reduction in depressed mood, improved hope and optimism after 4-week as well as during 3-month follow-up than the other conditions. Results are discussed in terms of additive or synergistic relation between transcranial direct current stimulation and positive psychology treatment.

Keywords

Frontal cortex activity; case study; major depression; transcranial direct current stimulation; quantitative electroencephalogram; positive psychotherapy

Submitted: April 21, 2017; **Accepted:** August 10, 2017

1. Introduction

Historically, mood disorders have been present among people. Recent surveys have shown that major depressive disorder is among the most prevalent (5 to 17 percent) psychiatric disorder [1]. Depressive disorders are characterized by sadness, irritability, psychomotoric retardation, and in severe cases, suicidal ideation. According to DSM-5, distinct episodes of depression separated by at least two months with no significant symptoms are included in the definition of depression.

1.1. Depression as a multifactorial disorder

Depression has been linked to dysfunctional brain activity. Quantitative electroencephalography (qEEG) studies have found relative hypoactivation in the left prefrontal cortex (PFC) among depressed people [2]. In addition, asymmetry in the prefrontal cortex is associated with mood and depression, where activity of the left prefrontal cortex improved mood, and activation of the right prefrontal cortex is linked to depression [1]. Functional neuroimaging studies have documented that left prefrontal hypoperfusion during depressive states normalized after successful treatment of the depression [1]. Positron emission tomography (PET) studies of depression have shown decrease in anterior brain metabolism, which is generally more pronounced on the left side. Regarding correlations between mood disorders and emotional dysregulations, the left hemisphere may well be responsible for analyzing positive emotions [1]. Increased alpha waves in the frontal lobe are associated with depression and dysthymia [3]. Feige *et al.* [4] found that alpha rhythm negatively correlated with the fMRI BOLD (Blood Oxygenation Level Dependent) parameter. BOLD is used as a marker of cortical activity. Thus, alpha waves have an inversed relationship with brain metabolism, where increased alpha waves are associated with decreased brain activity. See for a lengthier discussion [5]. This neurological marker could provide a framework for intervention by brain stimulation in depression [1].

From a neurobiological perspective, glucocorticoids are produced by stress and may decrease hippocampal volumes in depression [6]. For instance, brain imaging studies and autopsy examinations showed decrease of neurons of cortico-limbic regions in bipolar disorder and major depression patients [1]. Hyperactivity of the HPA (Hypothalamic Pituitary Adrenal) axis in depressed subjects is one of the most consistent results in the field of biological psychiatry.

1.2. Depression treatments

An alternative treatment method to improve symptoms of depression is transcranial direct current stimulation (tDCS). This method is a non-invasive focal brain stimulation in which a weak, direct current (1–2 mA) is conducted though the scalp using a pair of rubber carbon pads (10.5 cm^2). Nitsche and Paulus [7] argued that prolonged

tDCS could produce lasting and polarity specific changes in cortical excitability. The main effect of tDCS is to modify the excitability of the prefrontal cortex where anodal stimulation increases cortical activity and cathodal stimulation decreases cortical activity [8]. The primary mechanism of DC stimulation on the cerebral cortex is a sub-threshold modulation of neuronal resting membrane potentials. A systematic review from six randomized sham-controlled trials, enrolling 289 patients found that active tDCS showed improvement, relative to sham, on response and remission rate (decrease in scores on depression scales) and depression symptoms (β coefficient 0.35, 95% CI 0.12–0.57). The efficacy of tDCS intervention was consistent with those reported for transcranial magnetic stimulation (TMS) and antidepressant drug intervention in clinical settings [9].

Blumberger *et al.* [8] showed no effect of anodal stimulation on the left DLPFC and cathodal stimulation on the right DLPFC in depressed subjects. However, Dell'Osso *et al.* [10] found an effect of tDCS in mild to severely depressed subjects, as well as in subjects with treatment-resistant depression. Simultaneous anodal stimulation of left DLPFC and cathodal stimulation of right DLPFC (bipolar balanced montage) demonstrated reduced watchfulness for dangerous stimuli compared to sham stimulation providing support for an underlying cognitive mechanism that may improve treatment outcomes in depressedsubjects [11]. Depression is commonly treated with psychotherapy. Among different types of psychotherapy, the positive school is increasingly attracting attention. Positive psychotherapy (PP) is focused on developing positive emotions, buffering positive mental strength, Nikhi principle (in this case building optimism rather than focusing on dysfunctions) against psychological problems, and increasing life satisfaction and mental health [12]. Hope, optimism, and future-mindedness are positive personal views toward upcoming events. This view consisted of expecting good events, trying hard to experience more happiness, enjoying each moment of life, and continually moving toward life's goals [13]. From a positivity perspective, three main factors may cause a depressed mood; poor generation of possible futures, poor evaluation of possible futures, and negative beliefs about the future. Fredrickson and Losada [14] found that PP creates barriers against stressful events through decreasing the autonomic arousal of negative emotions and increasing cognitive flexibility by trying problem solving techniques. PP have demonstrated that short-term interventions, based on buffering mental strength exercises (signature strengths), increase happiness, satisfaction, and fulfilment [15]. Furthermore, Efklides and Moraitou [16] demonstrated that signature strengths-based approaches to change are superior to those that focus on the remediation of deficiencies. Khodabakhsh *et al.* [17] showed that PP decreased 35 percent of depression symptoms and increased 40 percent of meaning in life among subjects with cancer. Peterson and Park [18] found that subjects writing about three good events every day, and using their strengths and virtues daily, experienced more happiness and less depression up to six months after intervention. Group-based positive therapy has shown decreased Beck Depression scores one year after treatment [19]. Depressed mood and poor cognitive functioning may create vicious cycles that maintain faulty prospects of the future. Future-oriented treatment strategies, drawn from cognitive-behavioral therapy, may ameliorate poor prospections [20]. Ko and Hyun [21] showed that a PP program decreased depression and improved self esteem and hope in patients with major depressive disorders. Cross-sectional analyses revealed moderate correlations among sleep quality, depressive mood, and optimism [22]. They also found that cross-lagged analyses show bidirectional relations between optimism and sleep. On the other hand, path analyses demonstrated that depressive mood is a mediator variable between optimism and quality of sleep. Cross-sectional and longitudinal studies have shown positive correlations between children's levels of hopeful thinking and their global life satisfaction (LS), Valle *et al.* [23] have shown that hope can be a buffer against stressful life events on adolescents. Snyder *et al.* [24] distinguished hope from other common motivation-related constructs; when optimism (as conceptualized by Scheier and Carver [25]) and generalized expectancies of good future outcomes are described, hope is more focused on identifying specific pathways around obstacles to reach goals. There are a very limited number of interventions based simultaneously on PP and tDCS (based on qEEG). Most commonly, single-approach interventions are used to treat patients. Despite the progress made in the field of therapy, a large proportion of MDD patients do not respond well to current interventions. The aim of this study was to explore the efficiency of a combined treatment consisting of PP and tDCS for patients with major depressive disorder. Furthermore, in this study electrodes were individually placed using a qEEG device.

2. Method

It took one month to recruit nine females (mean age 45) with resistant major depression disorder based on DSM-5 criteria. Pre-trial interviews showed that no subject had received past or present medication treatment for clinical depression. In Iran, a medical records system is a work in progress, but for the purposes of the present study, there are no medical records to objectively verify subject's statements. All subjects completed consent forms.

2.1. *Design and procedure*

The study comprised a three (Group; tDCS therapy vs. positive therapy vs. combined therapy) and four (Sessions; Baseline vs. 2 weeks vs. 4 weeks vs. 3 months) mixed design, with Group as between-subject variable and Sessions as within-subject variable. The procedure was as follows; (a) neurological baseline data collection (see EEG acquisition and signal processing below), (b) behavioral baseline data collection (see instruments below), (c) randomization into therapy program, (d) treatment with continuous data collection and (e) follow-up data collection. Three subjects were randomly assigned to each of the three condition programs; tDCS therapy, PP, and tDCS combined with positive therapy (combined). Subsequently, subjects received treatment in a therapy program with behavioral data collected after 2 weeks, 4 weeks and 3 months.

qEEG was measured for all three groups. This was done before and after the end of twelve intervention sessions. In all groups (only one patient from each group had EEG recorded), qEEG was measured before and after the intervention sessions. Nineteen active and two reference EEG channels were recorded using Ag/AgCl electrodes in linked-ear montage. Two hundred and fifty samples per minute were acquired and a band-pass filter between 0.1 and 35 Hz was applied to minimise any aliasing effect. A 10–20 electrode arrangement was used and electrode impedance was kept under 5 kΩ. EEG recording was done for 5 minutes in both eye open and eye closed conditions. All recordings were visually inspected for artefacts and at least 90 seconds of artefact-free signal was processed. EEG signal processing was done offline with MATLAB 7.11.0 soft-

ware and the EEG coherences of five frequency bands were obtained: Delta (1–4 Hz), Theta (4.5–7 Hz), Alpha (7.5–12 Hz), Beta (12.5–24.5 Hz), and High Beta (25–30 Hz) between all electrode pairs (totally 171 pairs $\times$ 5 bands).

tDCS was delivered by a pair of rubber carbon pads (10.5 cm^2). Through 12 sessions of tDCS treatment (three times a week), anodal stimulation (1.5 mA, 15 min) was performed at F4 or F3 (where increased alpha was detected based on qEEG Brain Mapping). The localization of the electrodes was fine-tuned using LORETA source localization based on the EEG. The cathodal stimulation was directed over Fz or was extra cephalic. Both anodal and cathodal stimulation were delivered by an electrical stimulator (Active dose II). Safety guidelines specified by Nitsche *et al.* [26] were followed.

2.2. *Positive psychotherapy and combined therapy*

Three certified psychotherapists worked with participants in the PP condition for 30 minutes each session, three times a week for a total of 12 sessions. The twelve therapy sessions followed the program outlined in Table 1. Subjects in the combined condition received tDCS treatment followed by PP therapy. In both cases, the procedures were identical for subjects in either condition.

2.3. *Instruments*

Hamilton Depression Rating Scale (HDRS): The HDRS was developed in the early 1960s to monitor the severity of major depression, with a focus on somatic symptomatology. Reliability was good to excellent, particularly when the structured interview version was used. Validity appeared good based on correlation with other depression symptom measures [27].

Adult State Hope Scale (ASHS): Defining hope as a cognitive set comprising agency (belief in one's capacity to initiate and sustain actions) and pathways (belief in one's capacity to generate routes) to reach goals, the Hope Scale was developed and validated previously as a dispositional selfreport measure of hope [24, 28].

Optimism/Pessimism Scale (OPS): The OPS consists of 18 items measuring optimism, 18 items measuring pessimism, and 20 filler items [29]. Individuals respond to a four-point Likert scale from strongly agree to strongly disagree. The scale has been shown to be reliable, with alpha coefficients of 0.84 and 0.86 for optimism and pessimism. Test-retest reliability over a two week period were r = 0.75 for optimism and r = 0.84 for pessimism [29, 30].

3. Results

3.1. *Neurological data*

qEEG signals were measured (with closed eyes) before and after the end of twelve sessions of intervention just for three participants, one from each group. The qEEG data were processed with Fast Fourier Transformation analysis (time series analysis method). The alpha band power for pre- and post-treatment (three months) data in F3, F4 and Fz are presented in Fig. 1. The results showed decreased alpha band power (8–12 Hz) following treatment when compared with before treatment. As can be verified, the decrease for the combined treatment subject was larger than for the other two subjects combined for all three brain areas. Alpha (8–13 Hz) responses to tDCS intervention (six grouped leads representing 8 to 13 Hz i.e., alpha band power) are presented in Fig. 2. Electrode placement was based on identification of qEEG-bases. Anodal stimulation was used on F3 and cathodal stimulation on Fz for the first patient, anodal stimulation on F3 and cathodal stimulation on the right shoulder for the second patient, and anodal stimulation on F4 and cathodal stimulation on right the shoulder for the third patient.

3.2. *Clinical data*

All participants showed decreased levels of depression symptoms according to the HDRS (Table 2). However, as can be seen for the combined PP condition (Fig. 3), subjects showed improvements of depressive symptoms over time. As can be seen in Table 3, PP condition subjects improved from 32.33 at baseline to 20.00 at the three-month follow-up. The combined condition subjects showed ameliorated depression from 25.00 to 15.7, while the tDCS condition subjects showed only marginal improvement from 24.67 to 20.3. The larger improvement under the PP condition might also be an effect of dissimilar base-line depression levels, as those of the PP condition subjects were higher. From a clinical perspective, the combined condition subjects improved from very severe depression to mild depression, while the other conditions improved from very severe to severe depression [31]. Results from the OPS showed (Fig. 4) dramatic improvement in the combined condition, mean score increased from 21.33 at baseline to 50.7 at follow-up. This pattern was not found for either the tDCS condition (20.33 to 24.7) or the PP condition (17.00 to 27.3). Consistent with neurological and

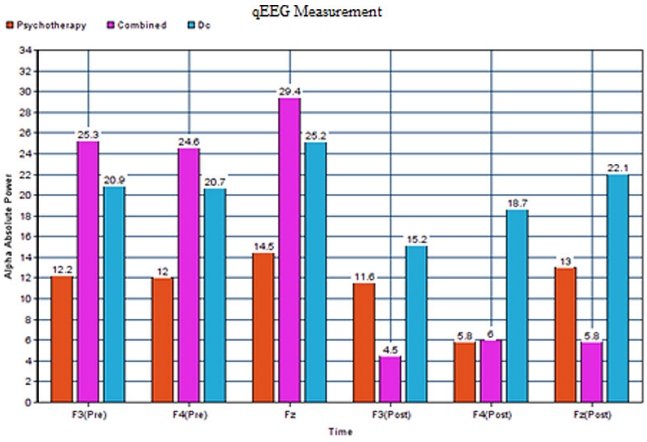

Fig. 1. Alpha absolute power before and after treatments.

depression data, the combined treatment appeared to be more efficient in improving optimism. Concordant with results for depression and optimism, the effect on hope was more pronounced in the combined treatment condition. The combined condition participants' sense of hope (Fig. 5) was improved from 15.33 at baseline to 41.00 at follow-up, whereas the tDCS condition subjects barely increased from 18.00 to 20.3. The PP condition subjects' sense of hope increased from 13.67 to 25.3.

4. Discussion

To the author's knowledge, in the present study, the combined effects of PP and tDCS in a major depressive disorder was explored for the first time. Results were promising, as the combined treatment condition subjects showed greater improvements in both neurological and clinical measurements than did tDCS and PP condition subjects.

Table 1. Positive psychotherapy program

Positive character	Session 1 & 2	Session 3 & 4	Session 5 & 6	Session 7 & 8	Session 9 & 10	Session 11 & 12
Hope	Positive introducing, encouragement	Explicitizing, envisioning, empowering, evolving	Positive stories, savoring, positive emotions, local newspaper	Gratitude jars, helping others, being in the zone	Listing the best activities, making an internal movie	Narrating hopeful stories, focusing on past successes, reviewing
Optimism	Reviewing important persons' strength, sharing positive events	Loving kindness meditation, mindful self-compassion	SBCDE method, focusing on an external/specific/ unstable causes	Identifying pessimistic thinking errors, satisfying exercise	Practicing one door closes, another door opens, exercising active constructive response	Establishing personal goals of tracking progress, writing the future diary

4.1. Neurological data

Previously, stimulation locations were based on protocols [9] rather than the more specific and sensitive qEEG measurements used in the present study. Using qEEG as a functional mapping of the brain has recently been recommended for early diagnosis or prediction of disease status [32]. Previous studies [33] have attempted to find novel and reliable qEEG based methods for the objective and differential diagnosis of depression and for assessing treatment outcomes. The present study used a combination of tDCS and the subjects' brain map to provide a more specific and individual placement of electrodes. In the current study, alpha band power response patterns to tDCS differed in magnitude and duration of affect between subjects. Also, current literature shows conflicting results regarding treatment responses to electrical stimulation [9]. These differences may be explained by variations in depression or co-morbidity with other psychological and physiological disorders. fMRI and EEG studies show reduced neural activity in left frontal regions among depressed patients and activation in this brain region may improve mood [1]. Other studies have demonstrated hippocampal atrophy and altered activity of anterior cingulate cortex (ACC) [34]. In addition to alpha band increase, several studies have highlighted increased slow band or beta activity as indicators of some types of depression [36]. To overcome this challenge, some approaches have been proposed such as LORETA, which determines intra-cortical EEG sources [38]. The alpha band power of the patient in the combined treatment condition, when compared to the other patients, may be due to different personal factors known to influence electrical stimulation, such as; age, gender, skull thickness, and psychological characteristics. Changes in left frontal (F3) alpha band absolute activity were stronger than those in the right frontal are (F4) for tDCS condition subjects. These findings suggest a type of left PFC hypo-activity [2]. In contrast with this, changes in F4 alpha band absolute power were descriptively bigger than F3 in the psychotherapy condition. This can be explained by the active role of right brain functions in early attachment processes, emotional communications within the therapeutic alliance, mutual therapeutic enactments, and therapeutic change processes [39]. This is indirectly related to reduce vigilance against threatening stimuli which help in relieving the symptoms of depression [11]. Furthermore, psychological characteristics such as high self-esteem, the ability of looking at the positive aspects of incidents, as well as an optimistic belief in a bright future are associated with physiological activity in the left-hemisphere (LH) [40], which is hypoactive in depressed patients.

4.2. Clinical data

Positive psychotherapy can help restore activity in parts of the brain and promote quality of life in people suffering from major depression. Optimism scores increased quickly, after just two weeks of treatment, and were maintained at the three-month follow-up, which is consistent with a study reported by Ying Lau *et al.* [22]. Results reported here are also consistent with Khodabakhsh *et al.* [17], who showed that PP decreased 35 percent of depression symptom measurements and increased by 40 percent meaning in life among patients who had breast cancer. Also, the current study showed a trend for decreased optimism in the tDCS condition three months after treatment. A possible interpretation is that, to induce effects beyond tDCS, which are desirable, especially to achieve therapeutic effects in clinical studies, the repetition of both stimulation sessions and optimism therapy is necessary [41]. It was observed that tDCS plus PP and PP conditions showed better mean scores in optimism and hope at a 3-month follow up, and a lower score in depression, compared with the tDCS condition. Subjects showed more optimism and hope following treatment in all three conditions but those who received PP could keep their intervention effects until the three month follow-up. This may be because the therapy helped develop positive emotions and a buffering strength to replace the depressed mood [12]. Furthermore, PP forms a barrier against stressful events by decreasing the autonomic arousal of negative emotions and increasing the cognitive flexibility needed for problem solving techniques [14]. It is clear that measures of hope generally reflect some level of individual responsibility in bringing about a desired state, as well as the assessment of feelings of self-efficacy or motivational states [42]. Lack of self-confidence and self-efficacy are behavioral symptoms among depressed people, thus practicing hopeful mental states might decrease symptoms of MDD. ASHS mean scores increase after positive training which is inconsistent with Valle *et al.* [23]. In the case of satisfaction with treatment, psychotherapy tries to find new ways of interaction with different aspects of intrapersonal skills while simultaneously improving interpersonal abilities; adding a bio-neurological approach such as electrical stimulation may facilitate reaching this goal.

4.3. Relation between tDCS and PP

Given the results of the present study, analysis of the relation between tDCS and PP is possible. Assuming that both treatments are helpful against major depression, tDCS and treatment interact in an overlapping, additive or synergistic manner. If tDCS and PP overlapped, then there would no added improvement from combining the treatments. In theory, this might mean that the two types of treatment could have the same effect but with different strategies.

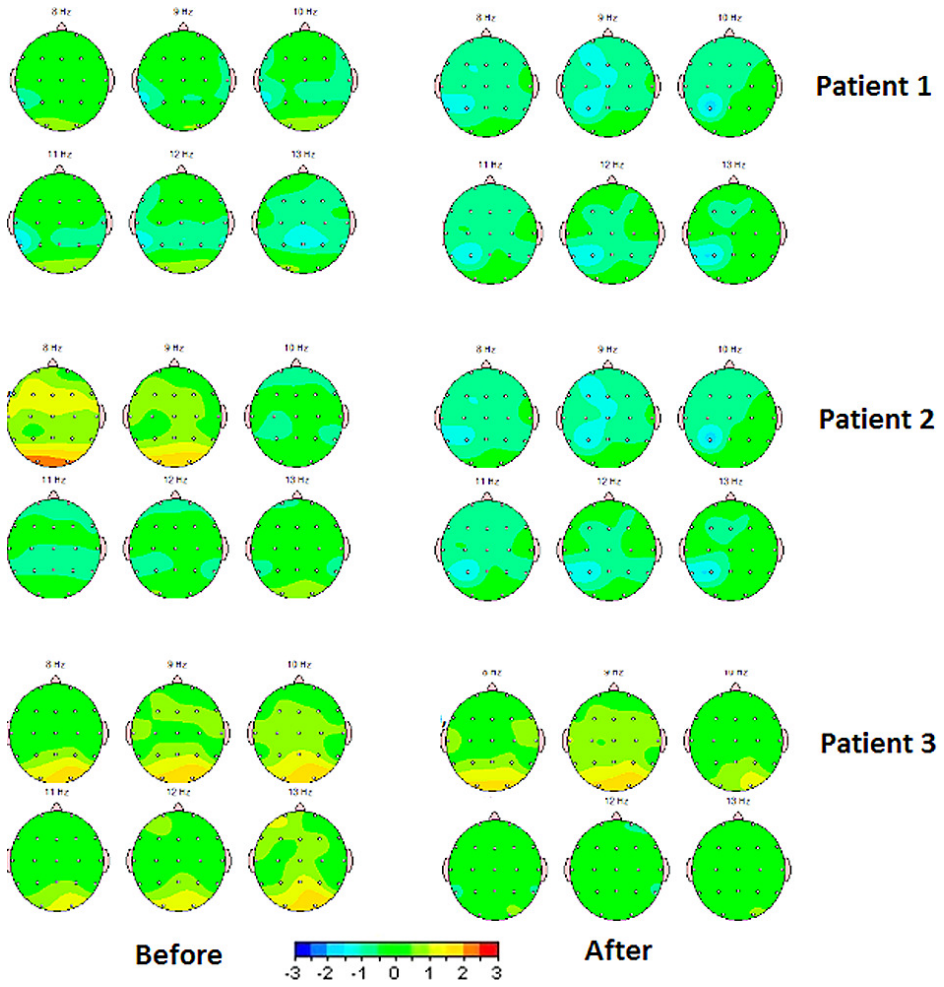

Fig. 2. Alpha absolute power (8–13 Hz) of the patients, before and after the end of twelve sessions of intervention just for three participants, one from each group.

Table 2. Clinical evaluation

Treatment	Baseline			2 weeks			4 weeks			Follow-up		
	HDRS	OPS	ASHS	HDRS	OPS	ASHS	HDRS	OPS	ASHS	HDRS	OPS	ASHS
Combined												
Participant 1	24	19	15	18	35	27	16	37	49	16	52	38
Participant 2	23	28	17	16	39	31	13	55	52	12	60	52
Participant 3	28	17	14	22	28	30	20	39	33	19	40	33
tDCS												
Participant 1	23	18	14	20	23	20	19	25	25	20	21	23
Participant 2	21	26	15	17	31	25	15	31	26	15	28	20
Participant 3	30	18	10	25	24	18	25	26	18	26	25	18
PP												
Participant 1	35	16	13	25	25	19	23	26	22	21	27	25
Participant 2	25	20	19	20	28	27	18	30	27	17	30	27
Participant 3	37	15	9	29	21	18	25	23	20	22	25	24

The results of the present study suggest that tDCS and PP were not overlapping because the improvement in both neurological and clinical data for the combined condition was greater than in the single treatments. Thus, the overlapping hypothesis is less likely. The additive hypothesis would assume that both tDCS and PP treatment are efficient in different aspects of MDD, but that they do not affect each other in any way. That is, tDCS treatments ameliorate X percent and PP treatments Y percent, and the combined treatment improvement efficiency would be $Y + X$ percent. However, the results from this study show that improvement for combined treatment condi-

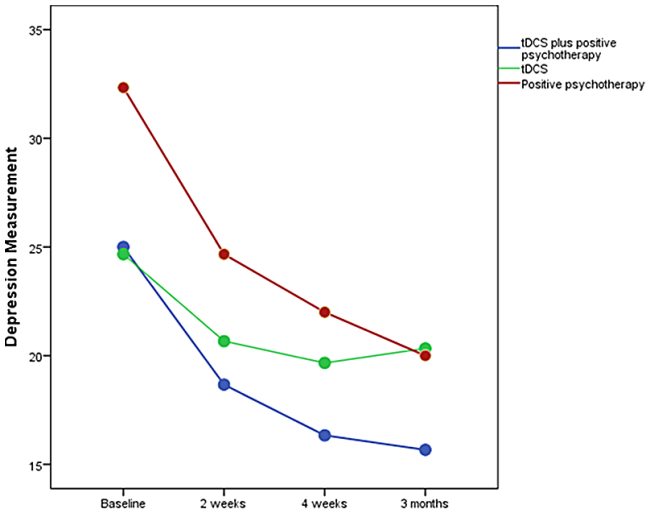

Fig. 3. Mean Scores of Depression over time.

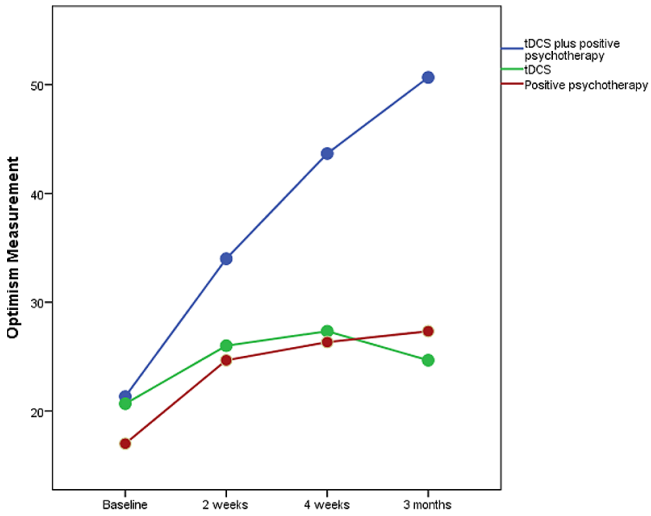

Fig. 4. Mean Scores of Optimism over time.

Table 3. Descriptive statistics

Group	Mean (SD)			*N*
	2 weeks	4 weeks	3 months	
HDRS				
tDCS plus PP	18.7 (3.0)	16.3 (3.5)	**15.7 (3.5)**	3
tDCS	20.7 (4.0)	19.7 (5.1)	**20.3 (5.5)**	3
PP	24.7 (4.5)	22.0 (3.6)	**20.0 (2.6)**	3
Total	21.3 (4.3)	19.3 (4.3)	18.7 (4.2)	9
OPS				
tDCS plus PP	34.0 (5.5)	43.7 (9.8)	**50.7 (10.1)**	3
tDCS	26.0 (4.3)	27.3 (3.2)	**24.7 (3.5)**	3
PP	24.7 (3.5)	26.3 (3.5)	**27.3 (2.5)**	3
Total	28.2 (5.9)	32.4 (10.0)	34.2 (13.5)	9
ASHS				
tDCS plus PP	29.3 (2.1)	44.7 (10.2)	**41.0 (9.8)**	3
tDCS	21.0 (3.6)	23.0 (4.3)	**20.3 (2.5)**	3
PP	21.3 (4.9)	23.0 (3.6)	**25.3 (1.5)**	3
Total	23.9 (5.2)	30.2 (12.3)	28.9 (10.6)	9

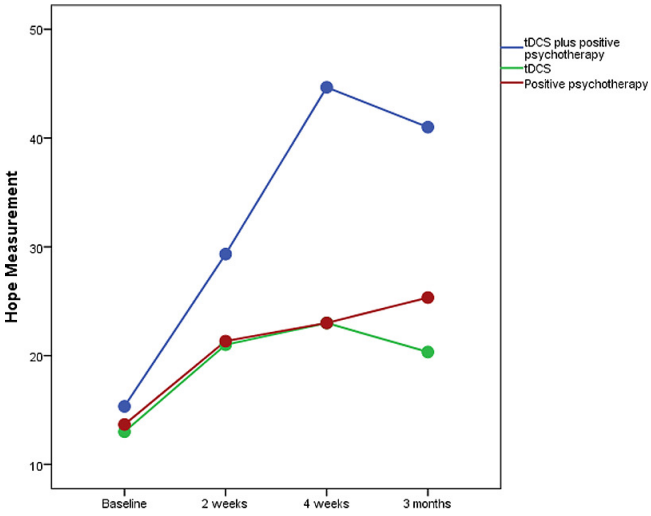

Fig. 5. Mean Scores of Hope over time.

tion subjects was greater than the added improvement for the other two condition subjects, where all subjects improved in neurological measurements, depression, optimism and sense of hope. In other words, the improvement in the combined treatment was greater than the simple addition of improvement in tDCS and PP, respectively. Thus, the dramatic improvement in the combined group suggests that the relation between tDCS and PP may be synergistic, rather than additive. Over the last decade, multimodal association approaches combining more than one method to establish more targeted treatment techniques have increased [9]. Using transcranial electrical stimulation to alter cortical activity and affect underlying regions such as the ACC through some depression related neural network (fronto-cingulo-striatal) is one modality of intervention. Empowering positive psychology concepts such as optimism and hope can reduce poor functioning and promote behavioral adaptation. Results reported here are in line with Schwartz and Santarsieri [43] who reported that combining antidepressant treatment and psychotherapy (psycho-pharmaco-psychotherapy or PPPT) created potentially observable neurofunctional changes. They suggested that the sum of these effects in PPPT may produce more sustained symptom relief. Regarding the important role of Left Pre-Frontal lobe in experiencing mood disorders, severe depression symptoms were more prevalent in stroke patients with left hemisphere lesion [44]. Furthermore, several open-label studies have suggested that left DLPFC cathodal and right DLPFC anodal tDCS may be an effective treatment configuration in more severely depressed subjects [45], as we employed in the present study for the third participant in the tDCS condition.

4.4. Limitations

Primarily, issues such as larger sample size, inclusion of control conditions, double-blind designs and objective control of previous or ongoing therapy would be desirable for the present study. However, in practice, these issues are not so easy to satisfy. Recruiting for one month resulted in nine subjects. Extrapolating from this, it would take about four months to find a minimal number of subjects for each condition. During such recruitment, the first voluntary subjects may drop out while waiting for the others, seek help elsewhere, or even

worse commit suicide while waiting for treatment. In addition, the heterogeneity among participants is increased if some subjects seek help and wait four months, where others seek help two days prior to treatment. Given the difficulty in recruiting participants, there may not be a sufficient number of voluntary subjects at any given time in the area where trials can reasonably begin. Possibly, other research groups in regions with larger populations and access to more resources may be able to replicate this study with sufficient sample-sizes. For ethical reasons, the study contained neither placebo nor no-treatment control conditions. Although a significant limitation, subjects were also patients in need of immediate treatment. Given the seriousness of the conditions of subjects, it is morally questionable problematic to simply leave them on a waiting list. Additionally, double or single blind control condition subjects could remove another limitation of studies such as this one. Some dependent measures about symptoms and subject/client emotional connection might have been affected by treatment knowledge. Although participants have no particular reason to lie about drugs or previous therapy, they might forget or find it shameful to admit. The welfare system in Iran does not provide objective control for previous or ongoing therapy, so the present study simply has to accept subject honesty at face value.

4.5. Future studies

Previous studies have found that subject heterogeneity may affect different dimensions of depression selectively. For example, participants susceptible to mood disorders scored highly in the cognitive and somatic dimensions of the BDI-II [46]. Additionally, Entsuah et al. [47] demonstrated that sub-scales are more sensitive to change than total scores. Thus, a possibly important technique in future studies is the application of BDI, tracking changes in specific feelings such as hopelessness, pessimism, irritability, guilt or feelings of being punished. They may benefit greatly from using such designs. Furthermore, transcranial Direct Current Stimulation combined with PP decreased depressive mood symptoms according to mean scores and the effect was maintained at a three-month follow-up compared with two other conditions. This provides hope for tDCS as a new method to attenuate MDD disorders. Further studies may focus on qEEG based treatment instead of protocol based treatment. Combining different treatments might improve prognosis, lower side effects, and decrease subject relapse in such a recurrent and chronic disorder. Finally, it is suggested that there is a need for review and reeducation of the concepts of positive psychology, especially hope, during shorter time intervals. This study was the first to combine tDCS and PP; more studies with larger sample size and controlling intervening variables are needed to replicate these findings.

Acknowledgments

We thank all participants and anonymous reviewers for invaluable assistance with the manuscript.

Conflict of Interest

No author declared any conflicts of interest.

References

[1] Sadock BJ, Sadock VA, Ruiz P, Kaplan HI (2015) *Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry*. Philadelphia, Pa, Wolters Kluwer.

[2] Johnstone T, van Reekum CM, Urry HL, Kalin NH, Davidson RJ (2007) Failure to regulate: counterproductive recruitment of top-down prefrontal-subcortical circuitry in major depression. *Journal of Neuroscience* **27(33)**, 8877-8884.

[3] Goldstein BL, Shankman SA, Kujawa A, Torpey-Newman DC, Olino TM, Klein DN (2016) Developmental changes in electroencephalographic frontal asymmetry in young children at risk for depression. *Journal of Child Psychology and Psychiatry* **57(9)**, 1075-1082.

[4] Feige B, Scheffler K, Esposito F, Di Salle F, Hennig J, Seifritz E (2005) Cortical and subcortical correlates of electroencephalographic alpha rhythm modulation. *Journal of Neurophysiology* **93(5)**, 2864-2872.

[5] Kropotov JD (2016) *Functional neuromarkers for psychiatry: Applications for diagnosis and treatment*. Amsterdam, Academic Press.

[6] Eisch AJ, Petrik D (2012) Depression and hippocampal neurogenesis: a road to remission? *Science* **338(6103)**, 72-75.

[7] Nitsche MA, Paulus W (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology* **527(3)**, 633-639.

[8] Blumberger D, Tran L, Fitzgerald P, Hoy KB, Daskalakis ZJ (2012) A randomized double-blind sham-controlled study of transcranial direct current stimulation for treatment-resistant major depression. *Frontiers in Psychiatry* **3**, 74.

[9] Brunoni AR, Moffa AH, Fregni F, Palm U, Padberg F, Blumberger DM, Daskalakis ZJ, Bennabi D, Haffen E, Alonzo A (2016) Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. *The British Journal of Psychiatry* **208(6)**, 522-531.

[10] Dell'Osso B, Zanoni S, Ferrucci R, Vergari M, Castellano F, D'Urso N, Dobrea C, Benatti B, Arici C, Priori A (2012) Transcranial direct current stimulation for the outpatient treatment of poor-responder depressed patients. *European Psychiatry* **27(7)**, 513-517.

[11] Ironside M, O'Shea J, Cowen PJ, Harmer CJ (2016) Frontal cortex stimulation reduces vigilance to threat: implications for the treatment of depression and anxiety. *Biological Psychiatry* **79(10)**, 823-830.

[12] McCullough ME, Witvliet CV (2002) The psychology of forgiveness. *Handbook of Positive Psychology* **2**, 446-455.

[13] Seligman ME (2012) *Flourish: A visionary new understanding of happiness and well-being*. New York, Simon and Schuster Audio.

[14] Fredrickson BL, Losada MF (2005) Positive affect and the complex dynamics of human flourishing. *American Psychologist* **60(7)**, 678-686.

[15] Proyer RT, Gander F, Wellenzohn S, Ruch W (2015) Strengths-based positive psychology interventions: a randomized placebo-controlled online trial on long-term effects for a signature strengths-vs. a lesser strengths-intervention. *Frontiers in Psychology* **6**, 456.

[16] Efklides A, Moraitou D (2012) *A positive psychology perspective on quality of life*. Dordrecht, Springer Science & Business Media.

[17] Khodabakhsh R, Khosravi Z, Shahangian S (2014) The effects of positive therapy on decreasing depression symptoms and improving character strengths in cancer patients. *Positive Psychology Research* **1(1)**, 35-50.

[18] Peterson C, Park N (2004) Classification and measurement of character strengths: Implications for practice. In, Linley PA & Joseph S (Eds.), *Positive psychology in practice* (pp. 433-446). Hoboken, NJ, US: John Wiley & Sons Inc.

[19] Seligman ME (2004) *Authentic happiness: Using the new positive psychology to realize your potential for lasting fulfillment*. New York, Simon and Schuster Audio.

[20] Miloyan B, Pachana NA, Suddendorf T (2014) The future is here: A review of foresight systems in anxiety and depression. *Cognition & Emotion* **28(5)**, 795-810.

[21] Ko YS, Hyun MY (2015) Effects of a positive psychotherapy program on depression, self-esteem, and hope in patients with major depressive disorders. *Journal of Korean Academy of Psychiatric and Mental Health Nursing* **24(4)**, 246-256.

[22] Lau EYY, Hui CH, Cheung SF, Lam J (2015) Bidirectional relationship between sleep and optimism with depressive mood as a mediator: A longitudinal study of Chinese working adults. *Journal of Psychosomatic Research* **79(5)**, 428-434.

[23] Valle MF, Huebner ES, Suldo SM (2004) Further evaluation of the Children's Hope Scale. *Journal of Psychoeducational Assessment* **22(4)**, 320-337.

[24] Snyder CR (2000) The past and possible futures of hope. *Journal of Social and Clinical Psychology* **19(1)**, 11-28.

[25] Scheier MF, Carver CS (1985) Optimism, coping, and health: assessment and implications of generalized outcome expectancies. *Health Psychology* **4(3)**, 219-247.

[26] Nitsche MA, Liebetanz D, Lang N, Antal A, Tergau F, Paulus W (2003) Safety criteria for transcranial direct current stimulation (tDCS) in humans. *Clinical Neurophysiology* **114(11)**, 2220-2222.

[27] Leentjens AF, Dujardin K, Marsh L, Richard IH, Starkstein SE, Martinez-Martin P (2011) Anxiety rating scales in Parkinson's disease: a validation study of the Hamilton anxiety rating scale, the Beck anxiety inventory, and the hospital anxiety and depression scale. *Movement Disorders* **26(3)**, 407-415.

[28] Snyder CR (1996) To hope, to lose, and to hope again. *Journal of Loss & Trauma* **1(1)**, 1-16.

[29] Dember WN, Martin SH, Hummer MK, Howe SR, Melton RS (1989) The measurement of optimism and pessimism. *Current Psychology* **8(2)**, 102-119.

[30] Burke KL, Joyner AB, Czech DR, Wilson MJ (2000) An investigation of concurrent validity between two optimism/pessimism questionnaires: The life orientation test-revised and the optimism/pessimism scale. *Current Psychology* **19(2)**, 129-136.

[31] Hamilton M (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry* **23(1)**, 56.

[32] Yadollahpour A, Nasrollahi H (2016) Quantitative electroencephalography for objective and differential diagnosis of depression: a comprehensive review. *Global Journal of Health Science* **8(11)**, 249.

[33] Hunter AM, Muthénb BO, Cook IA, Leuchter AF (2010) Antidepressant response trajectories and quantitative electroencephalography (QEEG) biomarkers in major depressive disorder. *Journal of Psychiatric Research* **44(2)**, 90-98.

[34] Frodl T, Schaub A, Banac S, Charypar M, Jäger M, Kümmler P, Bottlender R, Zetzsche T, Born C, Leinsinger G (2006) Reduced hippocampal volume correlates with executive dysfunctioning in major depression. *Journal of Psychiatry and Neuroscience* **31(5)**, 316-323.

[35] Johansen-Berg H, Gutman D, Behrens T, Matthews P, Rushworth M, Katz E, Lozano A, Mayberg H (2007) Anatomical connectivity of the subgenual cingulate region targeted with deep brain stimulation for treatment-resistant depression. *Cerebral Cortex* **18(6)**, 1374-1383.

[36] Knott V, Mahoney C, Kennedy S, Evans K (2001) EEG power, frequency, asymmetry and coherence in male depression. *Psychiatry Research: Neuroimaging* **106(2)**, 123-140.

[37] Lieber AL, Prichep LS (1988) Diagnosis and subtyping of depressive disorders by quantitative electroencephalography: I. Discriminant analysis of selected variables in untreated depressives. *Hillside Journal of Clinical Psychiatry* **10(1)**, 71-83.

[38] Jaworska N, Blier P, Fusee W, Knott V (2012) Alpha power, alpha asymmetry and anterior cingulate cortex activity in depressed males and females. *Journal of Psychiatric Research* **46(11)**, 1483-1491.

[39] Schore AN (2014) The right brain is dominant in psychotherapy. *Psychotherapy* **51(3)**, 388-397.

[40] Hecht D (2013) The neural basis of optimism and pessimism. *Experimental Neurobiology* **22(3)**, 173-199.

[41] Knotkova H, Rasche D (2016) *Textbook of Neuromodulation*. New York, Springer-Verlag.

[42] Boyle GJ, Saklofske DH, Matthews G (2014) *Measures of personality and social psychological constructs*, Amsterdam, Academic Press.

[43] Schwartz TL, Santarsieri D (2016) Neural implications of psychotherapy, pharmacotherapy, and combined treatment in major depressive disorder. *Mens Sana Monographs* **14(1)**, 30-45.

[44] Ahn DH, Lee YJ, Jeong JH, Kim YR, Park JB (2015) The effect of post-stroke depression on rehabilitation outcome and the impact of caregiver type as a factor of post-stroke depression.*Annals of Rehabilitation Medicine* **39(1)**, 74-80.

[45] Ferrucci R, Bortolomasi M, Vergari M, Tadini L, Salvoro B, Giacopuzzi M, Barbieri S, Priori A (2009) Transcranial direct current stimulation in severe, drug-resistant major depression. *Journal of Affective Disorders* **118(1-3)**, 215-219.

[46] Mackinger HF, Svaldi JJ (2004) Autobiographical memory predicts cognitive but not somatic change in sleep apnea patients vulnerable for affective disorder. *Journal of Affective Disorders* **81(1)**, 17-22.

[47] Entsuah R, Shaffer M, Zhang J (2002) A critical examination of the sensitivity of unidimensional subscales derived from the Hamilton Depression Rating Scale to antidepressant drug effects. *Journal of Psychiatric Research* **36(6)**, 437-448.