

Home-Based Transcranial Direct Current Stimulation (tDCS) for Bipolar Depression: Effects on Quality of Life and Functioning: an open-label study

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Abstract

Purpose

Individuals with bipolar disorder often experience reduced quality of life (QoL). Transcranial direct current stimulation (tDCS) is a promising non-invasive treatment for bipolar depression that is portable, safe, and suitable for use at home. We developed a home-based tDCS protocol with real-time remote supervision and examined its effect on QoL in bipolar depression.

Methods

In an open-label design, 44 participants (31 women) with bipolar depression of at least a moderate severity received 21 sessions of home-based tDCS (2 mA, 30 min, F3 anode/F4 cathode) over 6 weeks, with a follow up visit conducted 5 months from baseline. QoL was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire at baseline, week 2, end of treatment, and follow up session. Baseline and post treatment scores were compared with healthy control participants (28 adults; 17 women).

Results

At baseline and at the end of treatment, bipolar participants showed a significantly lower Q-LES-Q score than healthy controls ($p < .001$). Within the bipolar group, there was a significant improvement in total Q-LES-Q scores ($p < .001$) and across multiple domains by week 6 and remained elevated at follow-up. Changes in Q-LES-Q were no longer significant after adjustment for depressive symptoms.

Conclusion

A 6-week course of supervised home-based tDCS was associated with significant QoL improvements in bipolar depression, which appeared to be closely linked to reduction in depressive symptoms. Randomized, sham-controlled trials are warranted to clarify the specific contribution of tDCS to improve QoL in bipolar depression.

Introduction

Bipolar disorder is a mood disorder characterized by recurrent episodes of (hypo-) mania and depression. Episodes of depression are more frequent and longer lasting than (hypo-) manic episodes [1]. Bipolar depression is often associated with an increased risk of suicidal behaviour [2], profound fatigue, reduced concentration, and diminished motivation, leading to disability and functional impairment across multiple domains, including work or academic responsibilities, household tasks, and interpersonal relationships [3, 4]. Depressive symptoms often have a greater impact on functional

impairment than hypo(manic) symptoms [5]. The severity of depressive symptoms is strongly associated with both functional impairment and a poor quality of life (QoL)[6, 7]. However, symptom remission does not necessarily restore QoL[8] and even in euthymic states, patients with bipolar disorder showed reduced QoL compared to healthy controls [9, 10]. Depressive symptoms have been identified as key predictors of QoL in bipolar disorder, and effective management of these symptoms may contribute to significant improvements in patients' well-being [11].

While traditional clinical assessments often focus on symptom severity or psychosocial disability in areas like work or family roles, QoL offers a broader, patient-centered perspective. QoL is now seen as a crucial treatment outcome in bipolar disorder, often holding more personal significance for patients than symptom relief [12]. It captures an individual's subjective experience of satisfaction and enjoyment across various life areas, including physical, emotional, social, occupational, and even spiritual well-being that is not simply a reflection of their symptoms or medical condition [12, 13]. Importantly, QoL assessments allow patients to identify and prioritize life domains that matter most to them, rather than focusing solely on symptom control [14].

Pharmacological treatments have demonstrated varying degrees of effectiveness in improving QoL among individuals with bipolar disorder. Mood stabilizers like lithium can improve QoL through symptoms stabilization during remission [15] and when paired with psychoeducation [16], but offer no additional benefit when added to optimized personalized treatment [17] and may be less effective than combination therapy [18]. Lamotrigine, especially as adjunctive therapy, improved QoL over 12 weeks [19], while divalproex showed no added benefit [20]. Among atypical antipsychotics, several agents such as quetiapine, olanzapine, lurasidone, and aripiprazole have demonstrated significant improvements in QoL in bipolar depression [18, 21–25], whereas others, including risperidone and ziprasidone, showed only short-term or modest effects [26, 27]. The olanzapine/fluoxetine combination also led to QoL improvements in paediatric bipolar depression, though scores remained lower than in healthy controls [28]. However, these medications raise treatment challenges due to their association with side effects (e.g., antipsychotic-induced weight gain or sedation), high rates of nonadherence, and the risk of manic switching with antidepressant use [29, 30].

In addition to medications, psychosocial interventions can enhance QoL in bipolar disorder. Psychoeducation improves general health and social functioning [16], while CBT has demonstrated benefits in vitality and emotional role functioning [14]. Family-focused therapy in adolescents improves physical health and relationships [31] and qualitative findings emphasize the value of routine, identity, and support [32]. Physical activity, at least 150 minutes per week, has also been linked to significantly higher QoL [33]. Digital tools, such as smartphone-based interventions, show promise for improving biological rhythm regulation and well-being, especially in youth [34, 35]. These therapies are most effective when used alongside medication, though many individuals with bipolar disorder continue to experience residual symptoms or incomplete recovery despite treatment [36, 37]

In recent years, non-invasive brain stimulation techniques, particularly repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS), have been increasingly explored for their potential to improve clinical outcomes, functioning, and QoL in individuals with mood disorders [38]. Studies in major depressive disorder have demonstrated significant improvements in QoL following rTMS, as measured by EQ-5D and Q-LES-Q-SF [39–41]. A tele-supervised study of nine sessions of home-based tDCS in MDD increased QoL assessed by Q-LES-Q short form by 33% from baseline to the follow up assessment [42]. In our fully remote, double-blind, placebo-controlled randomized controlled trial of 10-week home-based tDCS in major depressive disorder, QoL, as measured by the EQ-5D-3L, significantly improved over time in both active and sham groups, although no significant between-group differences were observed [43].

In bipolar disorder, 20 sessions of rTMS have been associated with significant improvements in QoL, as measured by the GQOLI-74 [44] and GAF [45, 46], particularly after 2 weeks of treatment [46] and at week 4 [44, 45] compared to sham group. A sham-controlled trial of cranial electrotherapy stimulation (CES) in bipolar depression reported a significant post-treatment increase in QoL in the active group [47]. Similarly, 15 sessions of continuous theta-burst stimulation (cTBS) resulted in within-group improvements in QoL, particularly in physical and psychological domains, although differences between the active and sham groups were not statistically significant [48].

Transcranial direct current stimulation (tDCS) is a novel non-invasive brain stimulation technique that delivers a low-intensity electrical current (typically 1–2 mA) through electrodes placed on the scalp. This current modulates cortical excitability and neuronal activity, with potential antidepressant effects [49, 50]. In bipolar depression, tDCS has emerged as a promising therapeutic modality, particularly given the limited efficacy and tolerability of existing pharmacological treatments [51]. Meta-analyses and randomized controlled trials suggest that longer treatment durations and specific protocols, such as anodal stimulation over F3 and cathodal over F4, may enhance clinical outcomes by reducing depressive symptoms [50].

In terms of QoL outcomes, significant improvements in the physical and psychological domains of the WHOQOL-BREF have been reported following 10 sessions of tDCS compared to sham in bipolar disorder [52]. In contrast, a large randomized controlled trial including both unipolar and bipolar depression found no added benefit from active tDCS, although QoL improved significantly over time regardless of group, measured by Q-LES-Q-SF [53]. A six-week trial of home-based tDCS in bipolar depression reported no significant changes in either mood or QoL, despite high tolerability [54].

As tDCS typically requires repeated sessions over several weeks, in-clinic protocols can raise logistical and accessibility challenges [55]. However, because the technique is well tolerated and has a strong safety profile [56], it can be safely adapted for home use, enabling patients to receive consistent treatment without the burden of frequent clinic visits, while remaining user-friendly, safe, and cost-effective [57]. In the current study, we examined the effect of home-based tDCS on QoL in individuals with bipolar depression using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)

[58]. The clinical outcomes of this trial showed significant improvement in depressive symptoms [59]. The present analysis focuses specifically on QoL as a key patient-centered outcome.

Materials and methods

2.1. Study design and tDCS protocol

The study was an open-label, single-arm acceptability and feasibility trial of home-based tDCS for bipolar depression (ClinicalTrials.gov: NCT05436613 registered on 23 June 2022

<https://www.clinicaltrials.gov/study/NCT05436613>), approved by the London Fulham Research Ethics Committee (21/LO/0910) and conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). All participants provided electronic informed consent after receiving detailed explanations of the study procedures and having the opportunity to ask questions. Assessments were conducted via videoconference, though participants had the option to attend in person, which none chose to do.

After completing a thorough clinical evaluation, the tDCS equipment was mailed directly to each participant enrolled in the study. A member of the research team provided real-time guidance on device setup and usage through a video call. The stimulation protocol involved active tDCS sessions lasting 30 minutes each, using a bifrontal electrode configuration. Specifically, the anodal electrode was positioned over the left dorsolateral prefrontal cortex (DLPFC) at F3, and the cathodal electrode was placed at F4, targeting the right DLPFC, following the international 10–20 EEG system. Stimulation intensity was set at 2 mA, with a gradual increase over the first 120 seconds and a ramp-down phase of 15 seconds at the end. The schedule included five sessions per week over three weeks, followed by two sessions per week for an additional three weeks, resulting in a total of 21 sessions. Participants needed to complete at least 15 sessions to be considered as having completed the intervention.

Each session was remotely monitored by a research team member, who kept their camera on to maintain a passive presence. Participants had both their camera and microphone activated to enable communication if support was needed, but interaction was kept minimal unless assistance was requested. During stimulation, participants could engage in quiet activities such as reading or using electronic devices, or they could simply rest.

2.2. Study population

Participants were recruited through online advertisements (77.3%), general practitioner (GP) clinics in primary care (15.9%), and secondary care community mental health teams (6.8%). Eligible participants were adults aged 18 years or older, with diagnosis of bipolar disorder as per the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [60], confirmed through structured clinical interviews using the Mini-International Neuropsychiatric Interview (MINI; Version 7.0.2) [61]. They had moderate or greater depressive symptom severity indicated by a Montgomery-Åsberg Depression Rating Scale (MADRS) [62] score of 18 or higher, and were either on a stable mood-stabilizing medication

regimen for at least two weeks prior to enrolment or were medication-free for a minimum duration of two weeks. Exclusion criteria included any concurrent psychiatric disorder, including obsessive compulsive disorder, substantial risk of suicide as evaluated through the MINI suicidality module, MADRS, and 17-item Hamilton Depression Rating Scale (HDRS-17) [63], or presence of manic or hypomanic symptoms, defined as scoring above 8 on the Young Mania Rating Scale (YMRS) [64]. Exclusion criteria for tDCS, included having a scalp or skin conditions, metallic implants, a personal history of epilepsy or seizures involving loss of consciousness, or neurological disorders or migraine history.

The healthy control group were recruited through online ads (57.1%) or local outreach (42.9%). Healthy control participants were required to be adults aged 18 or older. Exclusion criteria for this group included a personal or familial psychiatric history, significant suicide risk, or manic or hypomanic symptomatology as indicated by YMRS scores greater than 8. Psychiatric assessments were conducted using the Mini-International Neuropsychiatric Interview. The healthy control participants underwent all baseline assessments but did not receive any tDCS sessions or follow-up.

2.3. Clinical assessments

Clinical measures and assessment protocols were described comprehensively in our prior publication [59]. In brief, bipolar depression participants underwent assessments at baseline, week 2, week 6 and at the 18-week follow-up. The healthy control group completed assessments at baseline only. Clinician-rated measures included MADRS and HDRS-17 for depression severity, Hamilton Anxiety Rating Scale (HAMA) [65] for anxiety severity, YMRS for manic symptoms, self-report measure of disability and impairment: Sheehan Disability Scale (SDS) [66] and self-report measures Patient Health Questionnaire-9 (PHQ-9) [67] for depressive symptoms. Clinical response was defined by a $\geq 50\%$ improvement in MADRS or HDRS-17 scores from baseline, while remission criteria required scores below 10 (MADRS) and 8 (HDRS-17).

2.4 Quality of Life Assessment

The Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) [58] is a 93-item self-report measure designed to assess QoL from the participant's perspective across eight broad domains: physical/health activities, feelings, leisure time activities, social relations, and general activities, which were scored for all participants. Three domains of work, household duties, school/coursework were scored only for participants to whom these domains applied. Items were rated using a 5-point Likert scale (1 = Very poor, 2 = Poor, 3 = Fair, 4 = Good, 5 = Very good), with higher scores reflecting greater enjoyment and satisfaction. Q-LES-Q assessments were conducted at baseline, week 2, week 6, with a follow-up assessment at week 18 after the initial tDCS session. The questionnaire was shared on the research team's screen, and participants were asked to read each item independently and report their chosen response. The selected number was then highlighted by the researcher. If assistance was requested, the questions were read aloud, this occurred for only one participant.

These raw item scores were summed within each domain and also as an overall total score to generate summary scores. These were then converted into maximum possible score percentage (MPS%) ranging

from 0 to 100 to account for differences in the number of items and the number of items completed across domains. Score closer to 0 indicates very poor QoL, while those closer to 100 reflect excellent QoL.

2.5 Statistical analysis

The Q-LES-Q scores were calculated as the percentage maximum possible score achieved by each participant across four timepoints: baseline (t0), week 2 (t1), week 6, end of treatment period (t2), and week 18, follow-up session (t3).

A linear mixed model (LMM) was used to examine changes in Q-LES-Q MPS% scores over time. Timepoint was modeled as a categorical variable with four levels (baseline, week 2, week 6, and week 18) to account for unequal spacing between assessments. Timepoint was included as a fixed effect and participant was specified as a random effect to account for within-subject variability. An unstructured covariance matrix was used to model correlations between repeated measures. Fixed effects were assessed using Type III F-tests, and pairwise comparisons were performed on estimated marginal means. Analyses were conducted first without covariates and then repeated with percentage change in MADRS scores included as a covariate to control for changes in depressive symptoms.

Comparisons of demographic variables between the bipolar depression group and the healthy control group were conducted using independent samples t-tests for continuous variables (age, years of education, and IQ), and a Chi-square test for the categorical variable (gender). To evaluate differences in Q-LES-Q scores between participants with bipolar depression and healthy controls, independent samples t-tests were performed.

All statistical procedures were carried out using IBM SPSS Statistics for Mac, version 29.0. Analyses were two-tailed, with statistical significance set at $p = 0.05$.

Result

3.1. Participants

A total of 44 participants with bipolar depression (31 women) were enrolled, with a mean age of 47.27 ± 12.94 (mean \pm standard deviation) years and a mean duration of illness of 18.98 ± 12.47 years (Table 1). 41 participants (93.2%) (mean age 47.93 ± 13.15 years) completed the full 6-week course of treatment. 38 participants (86.3%) were taking mood-stabilizing medication, including Lamotrigine, Lithium, Quetiapine, Olanzapine, and Aripiprazole; 1 participant (2.3%) was taking antidepressant medication without mood-stabilizing medication, and 5 participants (11.4%) were not taking any pharmacological treatment. Additionally, 27.3% ($n = 12$) were engaged in psychotherapy (either CBT or psychodynamic psychotherapy) in combination with their medication. During the follow-up period, 24 participants continued to use the tDCS device for at least some portion of that time, with 16 participants still using the device at the 5-month visit.

Table 1
Baseline demographic and clinical data

	BD group	HC group
	Mean \pm SD	Mean \pm SD
Total number (Female)	44 (31)	28 (17)
Mean Age (years)	47.27 \pm 12.9	44.68 \pm 14.45
Age range (years)	24–76	21–72
Years of education	16.30 \pm 2.46	16.89 \pm 2.11
IQ	100.66 \pm 9.3	103.39 \pm 8.77
Clinical rating		
MADRS	24.59 \pm 2.64	0.75 \pm 1.07
HDRS-17	19.98 \pm 2.62	0.82 \pm 1.44
HAMA	16.55 \pm 5.26	0.25 \pm 0.51
PHQ-9	16.80 \pm 4.94	1.36 \pm 1.54
SDS	20.77 \pm 5.87	0.46 \pm 0.92
Duration of illness (years)	18.98 \pm 12.47	
Duration current depressive episode (weeks) (range)	49.55 \pm 100.4	
Previous number of episodes	18.16 \pm 16.13	
Treatments during trial		
Taking mood stabilizer and other medications (%)	38 (86)	
Taking antidepressant medication only (%)	1 (2)	
Taking no medication (%)	5 (11)	
Engaged in psychotherapy (%)	12 (27)	
Categorical variables are presented as number of participants with percentage in parentheses for treatment during trial. Mean values are presented with \pm standard deviation; BD, bipolar depression; HC, healthy control; Montgomery-Åsberg Depression Rating Scale; HDRS-17, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale; PHQ-9, Patient Health Questionnaire-9; SDS, Sheehan Disability Scale		

Healthy controls participants consisted of 28 adults (17 women) with a mean age of 44.68 \pm 14.45 years. The bipolar depression and healthy control groups were comparable in demographic characteristics, with similar distributions in age (47.27 \pm 12.9 vs. 44.68 \pm 14.45 years), education (16.30 \pm 2.46 vs. 16.89 \pm 2.11 years), and IQ (100.66 \pm 9.3 vs. 103.39 \pm 8.77). As expected, healthy controls had significantly lower MADRS scores (0.75 \pm 1.07; p < 0.001).

3.2. Clinical outcomes

Clinical outcomes are available in full details in our prior publication [59]. In summary, depressive symptoms, as measured by MADRS, showed marked reduction by week 6 ($M = 8.91$, $SD = 5.56$), with 77.3% of participants meeting criteria for clinical response and 47.7% achieving remission. Significant improvements from baseline were also observed in HDRS-17, HAMA, YMRS, PHQ-9, and SDS scores.

3.3. Quality of life

At baseline, participants with bipolar depression reported significantly lower QoL across all Q-LES-Q domains compared to healthy controls (all $p < .001$; Fig. 1), with total Q-LES-Q scores substantially lower in the bipolar group ($M = 38.46$, $SD = 14.42$) compared to controls ($M = 83.86$, $SD = 8.64$; $t_{(66.05)} = -16.32$, $p < .001$; Table 2).

Table 2
Comparison of baseline Q-LES-Q scores between participants with bipolar depression and healthy controls

	BD (n)	BD Mean (SD)	HC (n)	HC Mean (SD)	t	P-value	d
Total score	41	38.46 ± 14.42	28	83.86 ± 8.64	-10.52	< .001***	-3.49
physical/health activities	41	41.15 ± 16.15	28	80.00 ± 13.31	-15.14	< .001***	-2.58
feelings	41	39.41 ± 15.60	28	86.29 ± 10.09	-15.14	< .001***	-3.43
leisure activities	40	39.60 ± 22.20	28	87.00 ± 14.20	-10.85	< .001***	-2.45
social relations	41	39.59 ± 16.95	28	84.96 ± 11.52	-12.34	< .001***	-3.02
general activities	41	47.98 ± 17.20	28	80.57 ± 10.49	-12.33	< .001***	-2.19
work	21	51.43 ± 16.59	20	87.55 ± 11.90	-9.78	< .001***	-2.49
household duties	37	44.16 ± 20.29	24	85.33 ± 11.19	-10.45	< .001***	-2.38
school/coursework	9	34.22 ± 7.46	6	84.83 ± 11.72	-7.72	< .001***	-5.43
Mean values are presented with '±' standard deviation. P-value represent two-sided t-test. BD, bipolar depression; HC, healthy control. * $p < .05$, ** $p < .01$, *** $p < .001$							

In the bipolar depression group, the results showed a significant effect of timepoint on Q-LES-Q total scores, $F_{(3, 37.26)} = 21.99$, $p < .001$, indicating that total scores changed significantly over the course of

the treatment (Fig. 2). Estimated marginal means showed that total scores increased from 38.46 (SE = 2.25) at baseline to 46.95 (SE = 2.61) at week 2, and peaking at end of treatment 59.85 (SE = 2.98), and remaining relatively stable at follow-up 56.96 (SE = 3.32). Pairwise comparisons revealed that all changes from baseline to later timepoints were statistically significant (all $p < .001$), except between final treatment session and the follow up ($p = 1.000$). After controlling for depressive symptom severity (percentage changes in MADRS scores), the effect was no longer statistically significant, $F_{(3, 35.58)} = 1.740$, $p = .176$, suggesting that improvements in QoL were at least partially attributable to reductions in depressive symptoms.

Significant improvements were observed across most Q-LES-Q domains from baseline to follow-up (Table 3). Physical/health activities domain showed a substantial increase in scores, rising from 41.14 (SE = 2.52) to 48.58 to 57.73 (SE = 3.22) at the end of treatment. Feeling domain also improved from 39.41 (SE = 2.43) at baseline to 60.85 (SE = 3.21) at week 6, ($F_{(3,40)} = 20.17$, $p < .001$). A similar trend was found in leisure time activities, which rose from 38.63 (SE = 3.5) to 60.53 (SE = 3.30) by end of treatment ($F_{(3,40)} = 12.13$, $p < .001$). Social relations also improved significantly over time ($F_{(3,40)} = 15.31$, $p < .001$), increasing from 39.58 (SE = 2.64) to 62.63 (SE = 3.27). Likewise, the general activities domain increased from 39.39 (SE = 2.40) at baseline to 60.87 (SE = 2.93) at week 6 ($F_{(3,40)} = 18.66$, $p < .001$).

Table 3

Mean change for Q-LES-Q percentage maximum scores from baseline to follow up session

Q-LES-Q domain	Mean change	F-value	p-value	Significant after controlling for MADRS
total score	38.46 ± 2.25 → 46.95 ± 2.61 → 59.85 ± 2.98 → 56.96 ± 3.32	21.99	< .001***	No
physical/health activities	41.14 ± 2.52 → 48.58 ± 3.05 → 57.73 ± 3.22 → 55.00 ± 3.19	17.44	< .001***	No
feelings	39.41 ± 2.43 → 47.09 ± 2.90 → 60.85 ± 3.21 → 57.95 ± 3.12	20.17	< .001***	No
leisure time activities	38.63 ± 3.55 → 45.26 ± 3.61 → 60.53 ± 3.30 → 59.92 ± 3.91	12.13	< .001***	No
social relations	39.58 ± 2.64 → 51.97 ± 2.62 → 62.07 ± 2.97 → 62.63 ± 3.27	15.31	< .001***	No
general activities	39.39 ± 2.40 → 48.29 ± 3.11 → 60.87 ± 2.93 → 56.36 ± 3.11	18.66	< .001***	No
work	31.97 ± 4.62 → 43.04 ± 5.31 → 54.24 ± 5.31 → 50.45 ± 5.29	0.92	< .001***	No
household duties	43.70 ± 3.29 → 51.14 ± 3.04 → 62.48 ± 3.40 → 64.78 ± 3.41	12.68	< .001***	No
school/coursework	31.47 ± 4.03 → 34.83 ± 4.80 → 36.93 ± 3.97 → 35.03 ± 5.34	0.45	.720	No
Mean values are presented with '±' standard error, * $p < .05$, ** $p < .01$, *** $p < .001$				

Three domains of work, household duties, school/coursework were scored only for participants to whom these domains applied. The work domain showed significant improvement over time ($F_{(3,39)} = 10.92$, $p < .001$), increasing from 31.97 (SE = 4.62) at baseline to 54.24 (SE = 5.31) at week 6. Household duties showed steady improvement across all timepoints, from 43.70 (SE = 3.29) to 62.48 (SE = 3.40) at end of treatment ($F_{(3,40)} = 12.68$, $p < .001$). School/coursework domain did not change significantly ($F_{(3,12)} = 0.45$, $p = .720$), with means of 31.47 (SE = 4.03) to 36.93 (SE = 3.97) by end of treatment. After controlling for percentage changes in MADRS scores, the effect of time was no longer significant for any of the Q-LES-Q domains.

At the end of treatment, Q-LES-Q scores in participants with bipolar depression remained significantly lower than healthy controls across all domains (Fig. 3). Post-treatment total Q-LES-Q score was significantly lower in the bipolar group ($M = 59.85$, $SD = 19.09$) than controls ($M = 83.86$, $SD = 8.64$, $t_{(59.63)} = -7.06$, $p < .001$; Table 4). However, after controlling for change in MADRS score, the group difference in Q-LES-Q total score became non-significant ($F_{(1.65)} = .88$, $p = .351$).

Table 4

Comparison of post-treatment Q-LES-Q scores between participants with bipolar depression and healthy controls

	BD (n)	BD Mean (SD)	HC (n)	HC Mean (SD)	t	P-value	d
Total score	41	59.85 ± 19.09	28	83.86 ± 8.64	-7.06	< .001***	-1.53
physical/health activities	41	57.73 ± 20.62	28	80.00 ± 13.31	-5.45	< .001***	-1.24
feelings	41	60.85 ± 20.56	28	86.29 ± 10.10	-6.81	< .001***	-1.48
leisure activities	41	60.54 ± 21.13	28	87.00 ± 14.21	-5.79	< .001***	-1.42
social relations	41	62.07 ± 19.05	28	84.96 ± 11.52	-6.21	< .001***	-1.39
general activities	41	60.88 ± 18.81	28	80.57 ± 10.49	-5.56	< .001***	-1.23
work	32	57.56 ± 34.08	20	87.55 ± 11.91	-4.55	< .001***	-1.06
household duties	38	63.92 ± 21.91	24	85.33 ± 11.19	-5.07	< .001***	-1.14
school/coursework	10	45.90 ± 27.32	6	84.83 ± 11.72	-3.55	.063	-0.85
Mean values are presented with '±' standard deviation. P-value represent two-sided t-test. BD, bipolar depression; HC, healthy control. * $p < .05$, ** $p < .01$, *** $p < .001$							

Discussion

Individuals with bipolar disorder consistently report reduced QoL across multiple domains, including social relationships, work productivity, and emotional well-being, even during euthymic phases[9] and in the early stage of illness [68]. Depression severity is shown to be strongly associated with lower QoL [7]. In contrast to symptom-based assessments, QoL measures can also reflect aspects of daily life that may be overlooked in clinical evaluations [14].

In this study, we examined the impact of home-based tDCS on QoL among individuals with bipolar depression, using both total and domain-level Q-LES-Q scores. A 6-week course of home-based tDCS with real-time supervision was associated with significant improvements across multiple domains of QoL by the end of treatment. Notably, several of these improvements were maintained at the follow-up, indicating sustained benefits. The effect of time on QoL were no longer statistically significant after controlling for change in depressive symptoms, suggesting that improvements in QoL are closely linked to reductions in depressive symptoms [69, 70]. This pattern is consistent with a wide range of literature across different intervention types including pharmacological treatment [19, 23, 24], psychoeducational interventions [14, 16], and in NIBS such as TMS[44–46] and tDCS [52]. These studies highlight the role of depressive symptom severity in QoL outcomes, and report strong associations between improvements in mood and enhanced perceived QoL [6, 70, 71].

Improvement in symptoms does not always translate into proportional improvements in QoL [8]. This has been observed in pharmacological studies, where mood stabilizers or antipsychotics improved symptoms without corresponding QoL gains [17, 20]. Our RCT of home based tDCS in MDD showed significant improvement in depressive symptoms compared to sham stimulation but there were no significant differences between groups on QoL scale [43].

When we compared QoL in bipolar depression with the healthy control group, consistent with previous literature [14, 71, 72], our results indicated that individuals with bipolar disorder had significantly lower QoL compared to healthy controls at baseline and after end of treatment, despite significant clinical improvement in depressive symptoms within the bipolar depression group.

While our findings suggest that improvements in QoL were largely influenced by reductions in depressive symptoms, previous research indicates that symptom relief alone may not be sufficient for full functional recovery and are not limited to symptomatic phases. A meta-analysis comparing QoL in euthymic bipolar patients with healthy controls mentioned that QoL in euthymic bipolar disorder patients remains impaired even in the absence of mood symptoms, suggesting a trait-like component [73]. In our study, although depressive symptom reduction statistically accounted for improvement in QoL, the bipolar depression group continued to report lower QoL than controls at the end of the treatment, suggesting residual deficits that may not be solely attributable to mood state. This was observed despite significant clinical gains following tDCS intervention [59]. These findings highlight that while symptom relief is important, it may not be sufficient to fully restore overall functioning.

Limitations of the study include the absence of a sham control group, which restricts the ability to distinguish the specific effects of active tDCS from sham condition. The relatively small sample size, combined with a predominantly white and female participant pool, limits the generalizability of the findings to more diverse populations. Another potential limitation is the influence of therapeutic contact, which may have contributed to the high response and remission rates. Our thematic analyses of participants' views on home-based tDCS in both bipolar [74] and unipolar depression [75] have suggested that the consistent presence of the same researcher at each visit, built a sense of safety and

connection, which may have enhanced treatment engagement and symptom improvement [76]. Furthermore, the study did not control for concurrent psychotherapy or the types of medications participants were taking. Although participants were required to either maintain a stable dosage of mood-stabilizing medication for at least two weeks or abstain entirely, the lack of control over pharmacotherapy introduces potential confounds.

Conclusion

In conclusion, home-based tDCS with real-time remote supervision was associated with improvement in QoL in bipolar depression, with benefits sustained beyond the treatment period. Our findings contribute to the growing body of evidence showing that improvements in QoL are closely associated with reductions in depressive symptoms, while also raising the possibility that tDCS may contribute to QoL through mechanisms not entirely explained by mood improvement. These findings suggest potential benefits of tDCS for improvement of QoL in bipolar depression and should be further investigated in a randomized, sham-controlled design.

Abbreviations

BD: Bipolar Depression

CBT: Cognitive behavioural therapy

CES: Cranial Electrotherapy Stimulation

cTBS: Continuous Theta-Burst Stimulation

DSM-5: Diagnostic Statistic Manual of Mental Disorders, Fifth Edition

EQ-5D-3L: European Quality of Life 5 Dimensions Questionnaire 3 Level version

GAF: Global Assessment of Functioning

GQOLI-74: General Quality of Life Inventory-74

HC: Healthy Control

HAMA: Hamilton Anxiety Rating Scale

HDRS-17: 17-item Hamilton Depression Rating Scale

mA: milliAmpere

MADRS: Montgomery-Åsberg Depression Rating Scale

MDD: Major Depressive Disorder

MINI: Mini-International Neuropsychiatric Interview

MPS%: Maximum Possible Score percentage

rTMS: Repetitive Transcranial Magnetic Stimulation

SDS: Sheehan Disability Scale

tDCS: Transcranial Direct Current Stimulation

PHQ-9: Patient Health Questionnaire-9

QoL: Quality of Life

Q-LES-Q: Quality of Life Enjoyment and Satisfaction Questionnaire

Q-LES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire- Short Form

WHOQOL-BREF: World Health Organization Quality of Life

YMRS: Young Mania Rating Scale

Declarations

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Competing interests

Authors AG, RW, HR, PR, EB and MB do not report any declarations of interest. Author CF acknowledges support from National Institute of Mental Health (R01MH134236), Milken Institute Baszucki Brain Research (BD00029), Rosetrees Trust (CF20212104), International Psychoanalytical Association (IPA158102845), and research grant funding from Flow Neuroscience. tDCS devices were provided by Flow Neuroscience. Author AY reports the following declaration of interests: Paid lectures and advisory boards for the following companies with drugs used in affective and related disorders: Flow Neuroscience, Novartis, Roche, Janssen, Takeda, Noema pharma, Compass, Astrazenaca, Boehringer Ingelheim, Eli Lilly, LivaNova, Lundbeck, Sunovion, Servier, Livanova, Janssen, Allegan, Bionomics, Sumitomo Dainippon Pharma, Sage, Neurocentrx. Principal Investigator for the following studies: (1) the

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Authors' contributions

C.F. was the chief investigator of the study, formulated the conception of the work, led its conduct, led the interpretation of data. H.R. was involved in preparation of data, analysis, interpretation, and presentation of data as well as the drafting of the original manuscript. C.F., H.R., R.W., A.G., E.B., M.B., P.R., A.Y., made substantial contributions to the design of study. H.R., R.W. and A.G. contributed to the data acquisition. P.R., C.F. reviewed the analysis and provided critical feedback on the manuscript. All authors have critically appraised the work for intellectual content and approved the submission of the manuscript for publication.

Ethics approval and consent to participate

The study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the London Fulham Research Ethics Committee (21/LO/0910). All participants provided written informed consent for their participation. The privacy and rights of human subjects was observed at all times.

Consent to publish

Not applicable.

Availability of data and material

The anonymised datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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128. Statements & Declarations

Figures

Fig. 1 Q-LES-Q scores: bipolar depression vs. healthy controls

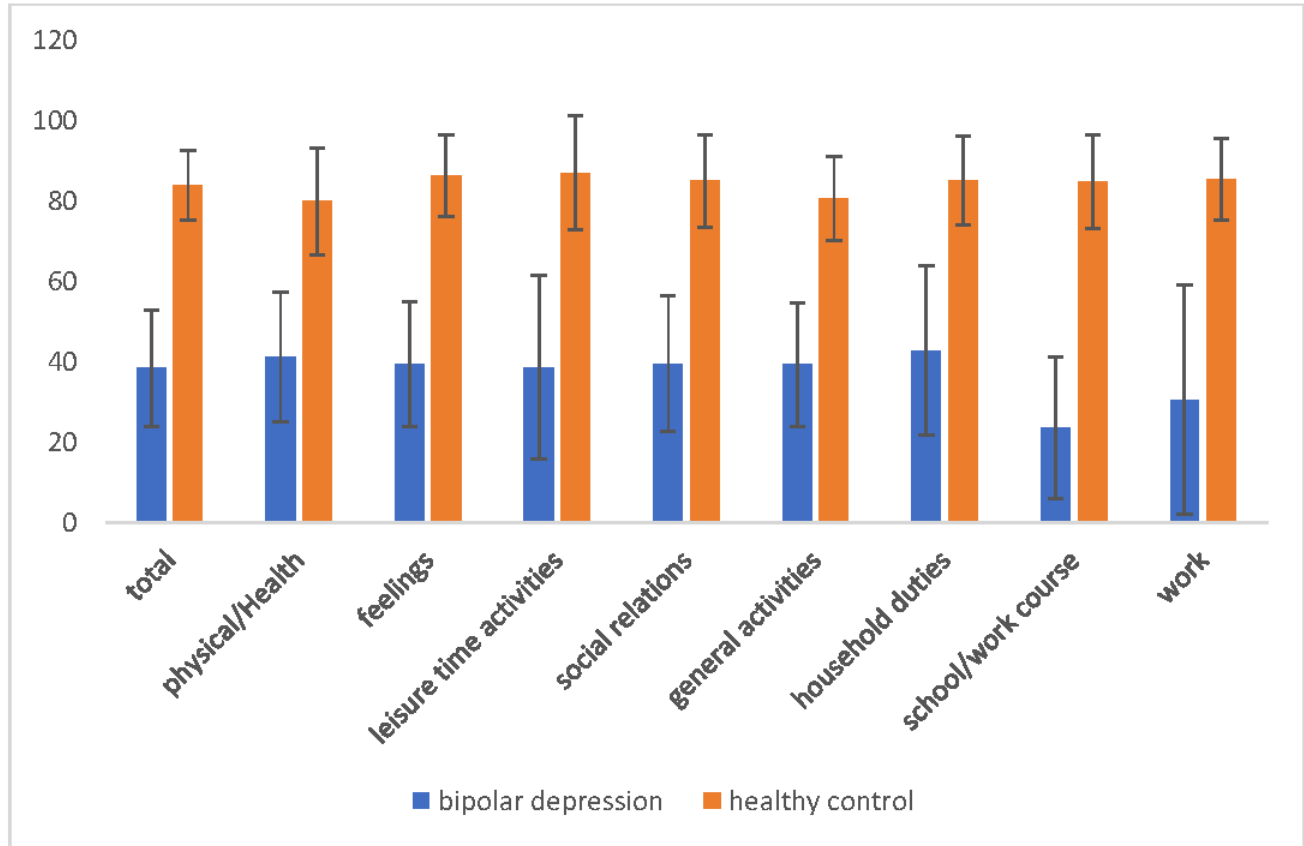


Figure 1

Comparison of Q-LES-Q domain scores between participants with bipolar depression and healthy controls at baseline. Mean scores across all domains were significantly lower in the bipolar group compared to healthy controls, $p < .001$.

Fig. 2 Change in mean Q-LES-Q scores over time

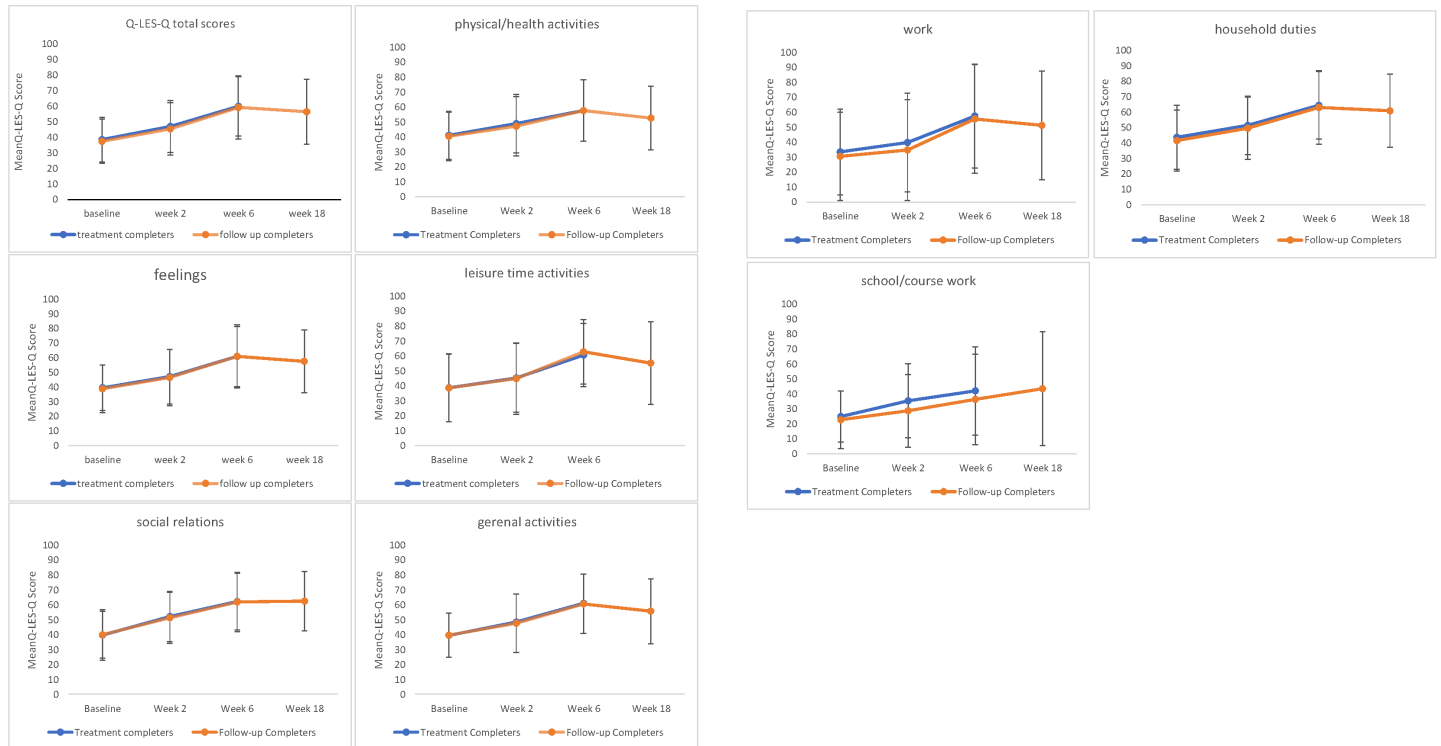


Figure 2

Change in Q-LES-Q scores across four timepoints. Error bars represent standard deviations. Q-LES-Q percentage maximum scores range from 0 to 100, with higher values indicating greater QoL.

Fig. 3 Post-treatment Q-LES-Q scores in bipolar depression vs. healthy controls baseline

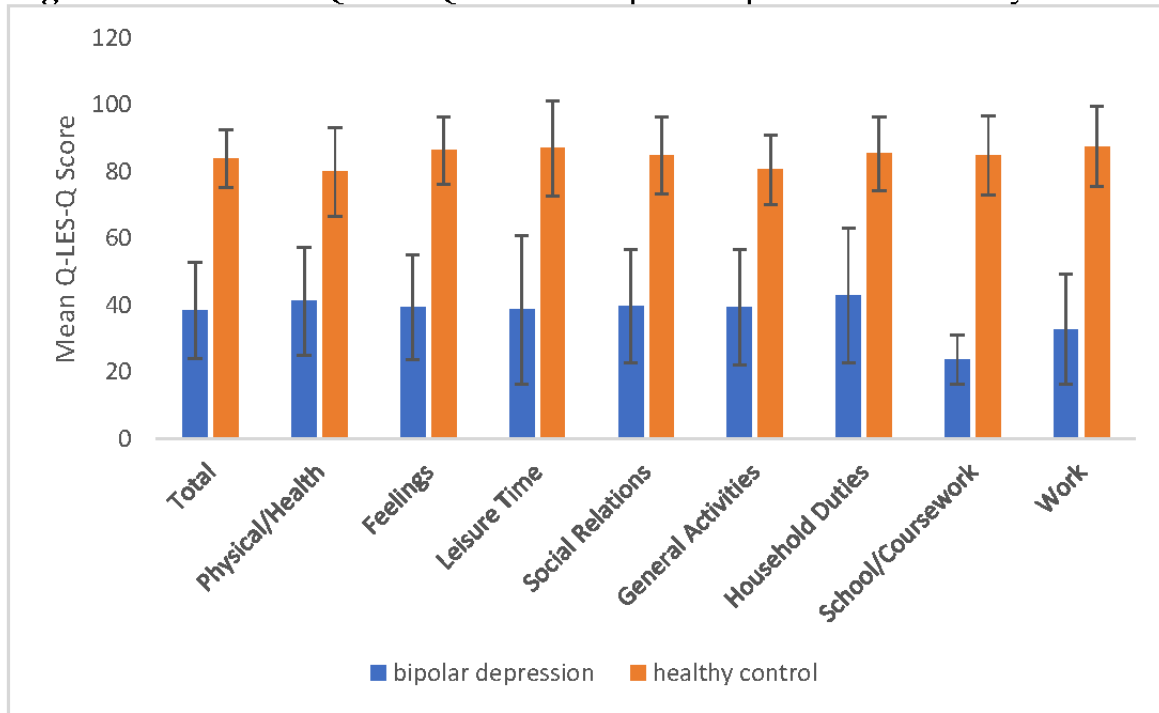


Figure 3

Comparison of Q-LES-Q domain scores between participants with bipolar depression and healthy controls at end of treatment. Mean scores across all domains were significantly lower in the bipolar group compared to healthy controls, $p < .001$.