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Home-based transcranial direct current stimulation for major depressive disorder: 6-month follow-up from randomised sham-controlled trial and open-label treatment phases

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ABSTRACT

Transcranial direct current stimulation (tDCS) is a potential home-based treatment for major depressive disorder (MDD). In our double-blind randomised controlled trial (RCT) (n = 174; UK and USA), a 10-week course of home-based tDCS demonstrated clinical efficacy (clinical response: 58.3 % active treatment arm and 37.8 % sham ($p = 0.017$). tDCS was delivered in a bifrontal montage, with anode over left dorsolateral prefrontal cortex (DLPFC) and cathode over right DLPFC. Each session was 30 min, with active stimulation at 2 mA and sham at 0 mA, incorporating brief ramp-up and ramp-down phased. Following the 10-week RCT, all participants were offered active tDCS in a 10-week open-label treatment phase, with 111 participants completing this phase. UK cohort (n = 77 MDD) were invited for additional 3-month and 6-month follow-ups, extending the total study period to 11 months post-randomisation. Participants were able to continue using the tDCS device during follow-up. At least one follow-up visit was attended by 42 MDD participants (27 women). Device usage rates were 59 % at 3-month follow-up and 55 % at 6-month follow-up. Clinical response rate was 64 % at 3-month follow-up and 76 % at 6-month follow-up. Among participants who had shown a clinical response after the open-label phase, 90 % maintained their response at the 6-month follow-up. In summary, long-term follow-up showed high and sustained clinical response rates regardless of continued tDCS device use.

1. Introduction

Major depressive disorder (MDD) is a leading cause of disability worldwide (World Health Organization, 2017) and is characterized by a prolonged low mood or an inability to experience feelings of pleasure that is associated with impairments in cognition, psychomotor functioning and disturbances with sleep, appetite and energy levels. Current first line treatments are antidepressant medications and psychological therapies. However, over a third of people do not achieve clinical remission despite full treatment trials (Cuijpers et al., 2014; Rush et al., 2006).

A potential novel treatment for MDD is transcranial direct current stimulation (tDCS), a non-invasive brain stimulation method which modulates cortical tissue excitability by applying a weak (0.5–2 mA) direct current via electrodes (Woodham et al., 2021). tDCS does not directly trigger action potentials in neuronal cells, in contrast to repetitive transcranial magnetic stimulation (rTMS) but modifies neuronal membrane polarity and, thus, their threshold for action potential generation (Nitsche and Paulus, 2000). In MDD, the anode electrode is typically placed over the left dorsolateral prefrontal cortex (DLPFC) and

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cathode over the right DLPFC, suborbital or frontotemporal region (Mutz et al., 2019). tDCS is safe, portable, and can be provided in a clinic or self-administered by patients at home (Rimmer et al., 2024).

Meta-analyses have reported clinical benefits of active as compared to sham tDCS in MDD (Moffa et al., 2020; Mutz et al., 2019), with less effective outcomes for treatment resistant depression (Brunoni et al., 2016; Meron et al., 2015; Mutz et al., 2018, 2019). An individual patient meta-analysis indicates longer treatment durations up to 10 weeks demonstrate clinical efficacy (Nikolin et al., 2023). Recent randomized controlled trials (RCT) of home-based, self-administration include a 6-week, single-blind RCT of adjunctive active tDCS to an antidepressant medication as compared to sham tDCS with antidepressant medication in a small sample (n = 58) which found no significant effects but was underpowered (Oh et al., 2022); 6-week, double-blind RCT with a small sample size (n = 11) which ended early due to several participants having skin burns at the electrode site and similarly underpowered (Kumpf et al., 2023); 6-week, double-blind RCT with the largest sample size (n = 210), which observed no significant differences between three treatment arms: active tDCS, active tDCS combined with a digital psychological intervention; and sham tDCS combined with internet browsing (Borrione et al., 2024), and our 10-week double-blind RCT (n = 174) which demonstrated significant efficacy (Woodham et al., 2024).

Understanding the effects of tDCS beyond the acute course of treatment is necessary when considering its benefits as a potential first line treatment. Long term follow-up assessments at 6 months report relapse rates from 26 to 53 % in MDD and bipolar depression following a course of tDCS, ranging from 3 to 6 weeks and ongoing treatment sessions over 6 months (Aparicio et al., 2019; Martin et al., 2013; Valiengo et al., 2013), with the lowest relapse rate observed in the protocol with a higher frequency of stimulations during the follow-up period (Aparicio et al., 2019). Razza et al. (2021) meta-analysis reported a moderate to large improvement of tDCS treatments effects in the 6-month follow-up period as compared to the end of trial measure in interventional studies. In our home-based, double-blind RCT of MDD participants (n = 174), we observed a significantly greater improvement in clinician-rated depressive symptoms, self-reported depressive symptoms, clinical response and remission rates in the active as compared to sham group at 10 weeks. Following unblinding, all participants were given the option to receive active tDCS for a further 10-week open-label phase (Woodham et al., 2024). However, whether the effects are maintained in a longer term is unclear.

The present study investigated long-term clinical outcomes, safety and acceptability of home-based self-administered tDCS treatment in a 6-month observational follow-up of participants who had completed a 10-week double-blind RCT and a 10-week open-label treatment phase (Woodham et al., 2024) for a total follow-up period of 11 months post-randomisation.

2. Material and methods

2.1. Trial design

Ethical approval was provided by the South Central-Hampshire B Research Ethics Committee, UK (ref. 22/SC/0023) and WIRB-Copernicus Group International Review Board, USA (ref. 1324775). All participants provided written informed consent to participate in the clinical trial and follow-up study. The double-blind, placebo-controlled, randomized, superiority trial of home-based tDCS in MDD (ClinicalTrials.gov NCT05202119) was conducted in England and Wales, UK, and Texas, USA, at University of East London and University of Texas Health Science Center at Houston, respectively. The long-term follow-up was conducted at the UK study site as the trial duration required extended observation, ethics approval had been obtained in the UK site and participants were able to keep the tDCS device.

All study visits were via Microsoft Teams videoconference. The trial consisted of a 10-week blinded treatment phase, where participants were randomly assigned (1:1 ratio) to receive active or sham tDCS, using block randomisation with permuted block sizes of four and six, performed independently in the UK and USA. An optional 10-week open-label treatment phase was offered to participants in both groups who had completed the blinded phase. Participants self-administered the tDCS at home using the Flow Neuroscience FL-100 device for the duration of the trial, with study team supervision by video conference for the initial session. The device was a headset with two pre-positioned conductive rubber electrodes, each 23 cm^2. Active stimulation was 2 mA direct current stimulation (current density = 0.09 mA/cm^2) for 30 min with ramp up over 120 s at the start and 15 s ramp down at the end of each session. Sham stimulation had initial ramp up from 0 to 1 mA over 30 s then ramp down to 0 mA over 15 s, repeated at the end of session. Anode and cathode were over left and right dorsolateral prefrontal cortices, respectively. The blinded phase included 5 tDCS sessions per week for 3 weeks followed by 3 sessions per week for 7 weeks (36 in total). Participants and researchers were blind to group allocation. A second independent research team member, who was blind to treatment allocation, joined clinical reviews for independent ratings.

The 10-week open-label phase consisted of active tDCS sessions for all participants who had been in either the 10-week RCT active or sham treatment arm. Participants in the initial active tDCS treatment arm could complete 3 active sessions per week for 10 weeks (30 in total), and participants who had been in initial sham tDCS treatment arm were offered the active tDCS stimulation schedule, 5 active sessions per week for 3 weeks then 3 active sessions per week for 7 weeks (36 in total). Participants who had been in the active treatment arm were not given any expectation of additional improvements in the open-label phase, and participants who had been in the sham treatment arm were informed that the active treatment might be associated with some improvements in depressive symptoms. A full description of trial design and results has been published elsewhere (Woodham et al., 2024).

Participants at the UK site who had completed the 10-week RCT and 10-week open-label treatment phases were invited to participate in follow-up visits at 3-months and 6-months after (8 months and 11 months post-randomisation). During the follow-up period, participants were not under any instruction regarding device use or other antidepressant treatments and were told that changes to antidepressant treatment or device use would not affect their continuation into the follow-up phase. If they wanted to continue with stimulation, participants needed to use the tDCS device app, which limits the number of tDCS sessions to 5 sessions per week for 3 weeks and then 2 sessions per week (stimulation schedule can be reset after 6-weeks of maintenance), with only one session permitted per day. The final follow-up was conducted on January 26, 2024.

2.2. Participants

174 participants were enrolled (mean age 37.63 ± 11.00 years, 120 women), with MDD in current depressive episode based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria (American Psychiatric Association, 2013) by structured clinical assessment, Mini-International Neuropsychiatric Interview (MINI; Version 7.0.2) (Sheehan et al., 1998), having at least a moderate severity of depressive symptoms, as measured by score 16 or more on 17-item Hamilton Rating Scale for Depression (HDRS) (Hamilton, 1960). All participants were under GP care and could be treatment-free, or taking stable antidepressant medication or in psychotherapy for at least 6 weeks prior to enrolment and agreeable to maintaining the same treatment throughout the blinded and open-label trial phases. Exclusion criteria included: having treatment resistant depression, defined as inadequate clinical response to two or more trials of antidepressant medication at an adequate dose and duration; significant suicide risk based on Columbia Suicide Severity Rating Scale (C-SSRS) Triage and Risk Identification Screener (Posner et al., 2011); comorbid psychiatric disorder; taking medications that affect cortical excitability (e.g.,

benzodiazepines); and contraindications to tDCS. Following the 10-week RCT, 141 participants continued in the 10-week open-label phase (100 UK, 41 USA).

2.3. Assessments and outcomes

Follow-up assessments were performed at 3-months and 6-months following the 20-week end of the open-label treatment phase (8- and 11-months post-randomisation). Depressive severity was measured by clinician-rated scales, HDRS, Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Åsberg, 1979), suicide ideation with Columbia-Suicide Severity Rating Scale (C-SSRS) (Posner et al., 2011); mania symptoms with Young Mania Rating Scale (YMRS) (Young et al., 1978); anxiety symptoms with Hamilton Anxiety Rating Scale (HAMA) (Hamilton, 1959), and quality of life with EQ-5D-3L (Brooks, 1996; Rabin and de Charro, 2001), which has five dimensions: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression, and three severity levels. Adverse events were assessed using the tDCS Adverse Events Questionnaire (AEQ) (Brunoni et al., 2011). Treatment acceptability was assessed by our treatment acceptability questionnaire (TAQ) (Rimmer et al., 2024; Woodham et al., 2022). Clinical response was assessed by a HDRS score reduction of at least 50 % relative to the baseline HDRS score, and clinical remission was HDRS score of 7 or less.

2.4. Statistical analysis

An intention to treat analysis was completed, using a Worst Observation Carried Forward (WOCF) for missing data on clinical assessments from week 10 to 6-month follow-up. Four mixed ANOVAs were conducted; original treatment arm was the between-subjects variable, HDRS, MADRS, HAMA and EQ-5D-3L total scores were the dependant variables and assessment time-point was the within-subjects factor, with four levels including end of week-10 RCT ($t1$), end of open-label phase ($t2$), 3-month follow-up ($t3$) and 6-month follow-up ($t4$). Completers analyses including participants with observed data from the four time points was conducted using the same statistical methods.

Two mixed ANOVAS were completed using data from participants who had attended each of the two follow-ups to explore any interaction between continued tDCS use during the follow-up period and depressive symptoms. Both ANOVAs included tDCS use during that follow-up period as the between-subjects variable, HDRS total score was the dependant variable, and assessment time point was the within-subjects factor with two levels. For the first ANOVA these were the end of open-label treatment period ($t1$) and the 3-month follow-up ($t2$), and for the second ANOVA they were and the 3-month follow-up ($t1$) and the 6-month follow-up ($t2$).

Statistical analyses were conducted using IBM SPSS Statistics (version 29.0.1.0). All analyses were two tailed and significance value of $p = 0.05$ was set. Greenhouse-Geisser correction was applied if Mauchley's assumption of sphericity was violated. Post hoc pairwise comparisons with Bonferroni corrections were conducted.

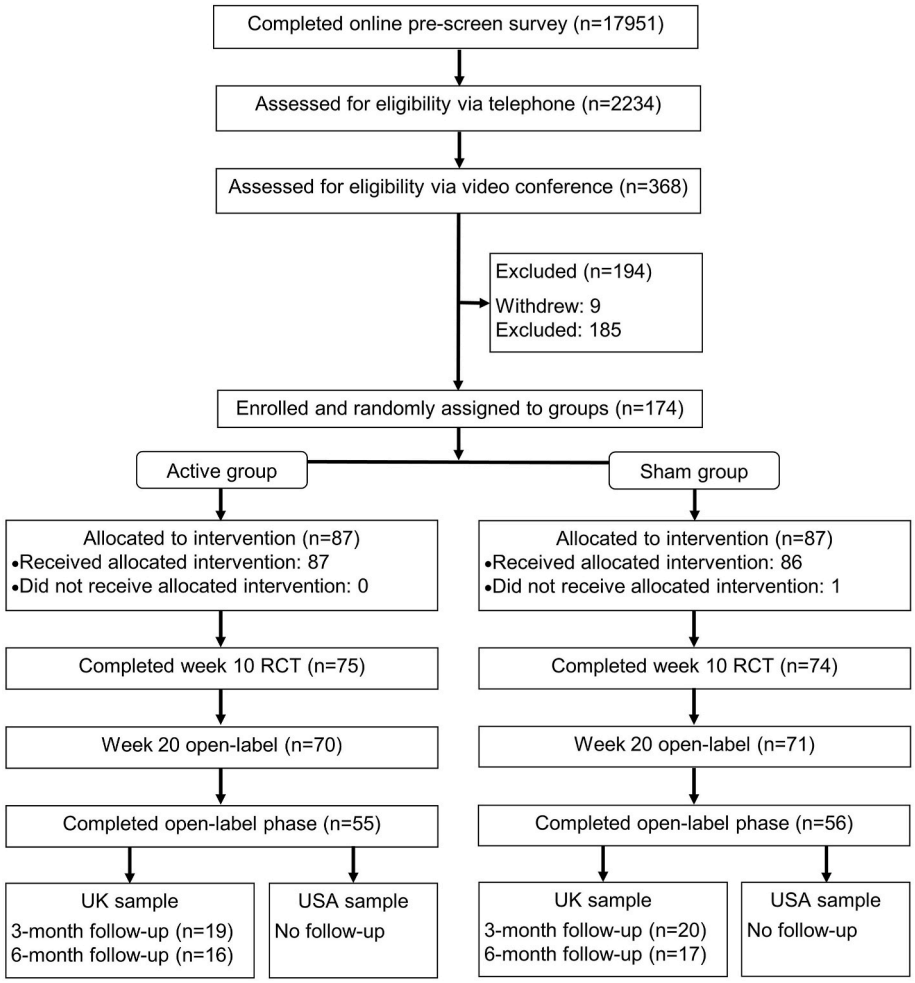

Fig. 1. Flow chart of the blinded phase, open-label phase and follow-up visits of the tDCS for major depression at home study (Empower study).

3. Results

3.1. Clinical assessments

174 MDD participants were enrolled and randomised to active (n = 87) or sham tDCS (n = 87) treatment arms. In the active group, decrease in HDRS score (HDRS = 9.41 points, SD = 6.25) and HDRS clinical response rate (58.3 %) were significantly greater than in the sham group (decrease in HDRS = 7.14, SD = 6.02, response rate = 37.8 %) at 10-weeks. From the 10-week RCT phase, 149 MDD participants completed the week 10 end-of-treatment assessment. From the next 10-week open-label treatment phase, 111 MDD participants completed the week 20 assessment (77 UK, 34 USA) (Fig. 1) and 64 % of participants showed a clinical response at week 20 (Woodham et al., 2024). Table 1

In the UK sample, 77 participants had completed the combined 20-week RCT and open-label phase (Supplementary Table 1)

Baseline characteristics and reasons for not participating in phases of the trial are presented in the Supplementary Materials (Tables 2–5).

Additional follow-up visits were conducted after 3- and 6-months (at 8- and 11-months following randomisation). 42 MDD participants (27 women) (54.5 % from week 20 in UK site) attended at least one follow-up visit (mean age 38.07 ± 10.93 years; mean baseline HDRS 18.21 ± 2.28) (Table 1). Concurrent treatments at baseline were: antidepressant medication (n = 27), combination of antidepressant medication and psychotherapy (n = 4) (antidepressant medication duration: range 6 weeks–30 years, psychotherapy duration: range 13–100 weeks), and being treatment-free (n = 15). Treatment arm allocation had been active tDCS (19 participants; 11 showed a clinical response at week 10) and sham tDCS (23 participants; 10 showed clinical response at week 10).

At 3-month follow-up, participants completing follow-up (n = 39), consisting of participants maintaining tDCS sessions (n = 23), number of sessions: 9–33 in 3 months, and participants who discontinued sessions (n = 16). Concurrent treatments were: antidepressant medication (n = 25), standalone psychotherapy (n = 1), combination medication and psychotherapy (n = 1), and being treatment-free (n = 13) (Table 2). Based on HDRS ratings, mean was 7.83 ± 4.79, and clinical outcomes were: treatment response (n = 25; 64 %), remission (n = 22; 56 %). Based on MADRS ratings, mean was 10.43 ± 6.87, and clinical outcomes were: treatment response (n = 26; 67 %), remission (n = 24; 62 %), HAMA mean 7.76 ± 5.07, and EQ-5D-3L mean 0.83 ± 0.17.

At 6-month follow-up, participants completing follow-up (n = 33), consisting of participants maintaining tDCS sessions (n = 18), number of sessions: 12–28 in 3 months, and participants who discontinued sessions (n = 15). Concurrent treatments were: antidepressant medication (n = 20), standalone psychotherapy (n = 3), combination medication and psychotherapy (n = 1), and being treatment-free (n = 10) (Table 2). Based on HDRS ratings, mean was 7.50 ± 5.09, and clinical outcomes were: treatment response (n = 25; 76 %), clinical remission (n = 21; 64 %). Based on MADRS ratings, mean was 10.38 ± 7.05, and clinical outcomes were: treatment response (n = 25; 76 %), clinical remission (n = 24; 73 %), HAMA mean 8.17 ± 5.35, and EQ-5D-3L mean 0.83 ± 0.17.

In the intention to treat analyses there was a significant main effect of time in HDRS score ($F(2.22, 88.69) = 9.27$, $p < 0.001$), MADRS score ($F(2.32, 92.96) = 7.06$, $p < 0.001$) and HAMA score ($F(3, 120) = 3.99$, $p = 0.009$). Pairwise comparisons showed significant improvements in HDRS and MADRS from week 10 to all other time points, and in HAMA from week 10 to week 20 (Supplementary Table 6) There were no interaction effects between time and original treatment arm in HDRS score ($F(2.22, 88.69) = 1.57$, $p = 0.22$) (Table 3, Fig. 2), MADRS score ($F(2.33, 92.96) = 0.95$, $p = 0.41$) (Table 3, Fig. 3) or (HAMA score $F(3, 120) = 0.77$, $p = 0.51$) (Table 3, Fig. 4). In EQ-5D-3L there was no main effect of time ($p = 0.95$), but a time by group interaction effect was observed ($F(3, 120) = 2.78$, ($p = 0.044$) (Table 3, Fig. 5). The assumption of normality was violated for EQ-5D-3L, increasing the likelihood of a type 1 error. Completers analyses followed a similar pattern of results (Supplementary Table 7).

Analyses to compare participants who had continued tDCS during the follow-up period with those who had not continued did not show any significant interaction effect between tDCS use during the follow-up period and time on HDRS scores, at 3-month follow-up ($F(1, 37) = 0.15$, $p = 0.71$) nor at 6-month follow-up ($F(1, 28) = 0.89$, $p = 0.35$).

Table 1
Baseline demographic and clinical characteristics of participants at the start of the trial and week 20 outcomes.

Characteristic	Total (N = 42)	Active (N = 19)	Sham (N = 23)
Age	38.07 ± 10.93	36.68 ± 11.96	39.22 ± 10.12
Gender			
Female	27 (64)	11 (58)	16 (70)
Race			
Asian	3 (7)	2 (11)	1 (4)
Black or African American	1 (2)	0 (0)	1 (4)
White	37 (88)	16 (84)	21 (91)
Other	1 (2)	1 (5)	0 (0)
Educational Level			
College	15 (36)	5 (26)	10 (44)
Bachelor's or Professional Degree	14 (33)	7 (37)	7 (30)
Master's or Doctoral Degree	13 (31)	7 (37)	6 (26)
Age of onset of MDD	22.93 ± 9.70	19.74 ± 7.34	25.57 ± 10.70
Previous number of episodes	2.5 (0, 5)	1 (0, 4.5)	4 (0.5, 5)
Previous number of suicide attempts	0 (0, 0)	0 (0, 0)	0 (0, 0)
First episode MDD	14 (33)	8 (42)	6 (26)
Clinical ratings			
HDRS baseline	18.21 ± 2.28	18.16 ± 1.92	18.26 ± 2.58
HDRS week 20 response	28 (67)	13 (68)	15 (65)
HDRS week 20 remission	23 (55)	12 (63)	11 (49)
MADRS baseline	24.17 ± 4.25	24.05 ± 3.36	24.26 ± 4.94
HAMA baseline	14.81 ± 4.59	14.74 ± 4.04	14.87 ± 5.08
YMRS baseline	2.43 ± 1.74	2.37 ± 2.01	2.48 ± 1.53
EQ-5D-3L baseline	0.73 ± 0.18	0.71 ± 0.18	0.75 ± 0.18
Total number of active tDCS sessions completed	39 ± 14.56	49 ± 14.46	30 ± 8.02
Range of active tDCS sessions completed	9–66	23–66	9–39
Antidepressant medication during trial	27 (64)	14 (74)	13 (57)
Selective serotonin reuptake inhibitor	22 (52)	13 (68)	9 (39)
Non-selective monoamine reuptake inhibitor	1 (2)	0 (0)	1 (4)
Other antidepressant medications	5 (12)	2 (11)	3 (13)
Combination psychotherapy and antidepressant medication	4 (10)	1 (5)	3 (13)
No antidepressant medication or psychotherapy during trial	15 (36)	5 (26)	10 (44)

Characteristics are presented for participants who attended at least one of the two follow-up visits at 3-month or 6-month follow-up. Categorical variables are presented as number of participants with percentage in parentheses for gender, race, educational level, first episode MDD, antidepressant medication and individual medications, individual psychotherapy during trial and No antidepressant or psychotherapy during trial. Mean values are presented with '±' standard deviation values. Previous number of episodes and previous number of suicide attempts are presented as median with interquartile range in parenthesis. HDRS, Hamilton Rating Scale for Depression; MADRS, Montgomery-Åsberg Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale; EQ-5D-3L, quality of life measure (https://euroqol.org). One participant in the active group was taking a combination of one other antidepressant medication and one selective serotonin reuptake inhibitor.

3.2. Outcomes for participants who showed a clinical response at week 20

From participants who showed clinical response at week 20 (n = 28)

Table 2
Depression treatments at 3- and 6-month follow-up assessments.

3-month follow-up	Total (N = 39)	Week 20 responders (n = 26)
Antidepressant medication	25 (64)	14 (54)
Selective serotonin reuptake inhibitor	18 (46)	10 (38)
Non-selective monoamine reuptake inhibitor	1 (3)	0 (0)
Other antidepressant medications	6 (15)	4 (15)
Standalone individual psychotherapy	1 (3)	1 (4)
Combination psychotherapy and antidepressant medication	1 (3)	1 (4)
Treatment free	13 (33)	11 (42)
Continued regular tDCS	23 (59)	18 (69)
Once per week	3 (8)	3 (12)
Twice per week	14 (36)	10 (38)
Once or twice per week	2 (5)	2 (8)
Reset stimulation to 5 times per week	4 (10)	3 (12)
6-month follow-up	**Total (N = 33)**	**Week 20 responders (n = 21)**
Antidepressant medication	20 (61)	10 (48)
Selective serotonin reuptake inhibitor	14 (42)	6 (29)
Non-selective monoamine reuptake inhibitor	1 (3)	0 (0)
Other antidepressant medications	5 (16)	4 (19)
Standalone individual psychotherapy	3 (8)	3 (12)
Combination psychotherapy and antidepressant medication	1 (3)	1 (5)
Treatment free	10 (30)	8 (38)
Continued regular tDCS	18 (55)	14 (67)
Once per week	1 (3)	1 (5)
Twice per week	13 (40)	10 (48)
Once or twice per week	2 (6)	2 (10)
Reset stimulation to 5 times per week	2 (6)	1 (5)

tDCS, transcranial direct current stimulation. Categorical variables are presented as number of participants with percentage in parentheses. At 3-month follow-up one participant had started taking antidepressant medication, 22 participants were taking the same antidepressant medication as before, one had changed antidepressant medication, two participants had stopped their antidepressant medications and one participant had stopped one of their medications. One participant had continued psychotherapy and one had started psychotherapy during the 3- month follow-up period. At 6-month follow-up, one participant was taking the same antidepressant medication as during the clinical trial, 19 participants were taking the same antidepressant medication as they were at 3-month follow-up, one participant had stopped taking antidepressant medication and one participant had a mood stabiliser added as a combination medication. No participants had started antidepressant medication that were not taking it previously. Two participants had continued psychotherapy and two had started during the follow-up period. One participant in the sham group was taking a combination of a non-selective monoamine reuptake inhibitor and a mood stabiliser at 6-month follow-up. During the initial 3-month follow-up period, 5 participants were not stimulating for the full 12 weeks (range 3–8 weeks). During the follow-up to 6-month follow-up 7 participants were not stimulating for the full 12 weeks (range 1.5 weeks–10 weeks).

as measured by HDRS ratings, at the 3-month follow-up, participants completing follow-up (n = 26) showed the following clinical outcomes: clinical response (n = 22; 84 %), remission (n = 21, 81 %), and none had a depressive relapse. At the 6-month follow-up, of the participants completing follow-up (n = 21), (n = 19) participants showed clinical outcomes of both clinical response and remission (90 %), one participant did not show a clinical response (5 %) and one participant had a depressive relapse (5 %) as measured by HDRS score of at least 14 (Supplementary Fig. 1). tDCS device use patterns were: regular use over 6-month period (n = 10), use in first 3-month period only (n = 3), intermittent use over 6-month period (n = 5), and discontinued use (n = 3).

3.3. Safety and tolerability

Most common side effects were tingling, skin redness, itching and burning sensation, with less common reports of headache, scalp pain, acute mood change and sleepiness (Table 4). The severity was rated at mild: 85 %, moderate: 13 %, and severe: 2 %, which were one report each for skin redness and acute mood change. There were no episodes of hypomania or mania as measured by YMRS and no suicide attempts as measured by C-SSRS.

At both the 3- and 6-month follow-ups, acceptability was endorsed as being "very acceptable", ethicality remained high at "very ethical", effort required remained consistent at "the same amount of effort as usual", impact of side effects was rated as "quite unaffected", and participants "would strongly recommend" tDCS treatment to others. Ratings for perceived effectiveness were "quite helpful" at the 3-month follow-up and "very helpful" at the 6-month follow-up (Table 5).

Table 4
Adverse events at months 8 and 11 as measured by the tDCS Adverse Events Questionnaire (Brunoni et al., 2011).

Adverse event	3-month follow-up (N = 22)	6-month follow-up (N = 18)
Headache	4 (18.2 %)	1 (5.6)
Neck Pain	0 (0.0 %)	0 (0.0)
Scalp Pain	2 (9.1 %)	4 (22.2)
Tingling	15 (68.2 %)	15 (83.3)
Itching	10 (45.5 %)	6 (33.3)
Burning Sensation	3 (13.6 %)	8 (44.4)
Skin Redness	14 (63.6 %)	11 (61.1)
Sleepiness	0 (0.0 %)	1 (5.6)
Trouble Concentrating	0 (0.0 %)	0 (0.0)
Acute Mood Change	3 (13.6 %)	0 (0.0)
Dry skin	1 (4.5 %)	1 (5.6 %)
Skin irritation	1 (4.5 %)	1 (5.6 %)
Flash of light	1 (4.5 %)	1 (5.6 %)

AEQ was completed for participants who had continued tDCS use during the follow-up-period. Values are number of participants with percentage in parentheses. An adverse event was present if the participant rated that it was at least remotely possible that it was associated with the intervention. Participants rated the severity of the adverse events as mild, moderate, or severe. One participant who had continued tDCS during some of the 3-month follow-up period did not complete the AEQ.

Table 3
Clinical rating scale scores during the trial period and at follow-up, intention to treat analysis.

Clinical ratings	Week 10		Week 20		3-month follow-up		6-month follow-up	
	Active	Sham	Active	Sham	Active	Sham	Active	Sham
HDRS	9.16 ± 5.41	11.48 ± 4.57	7.53 ± 5.43	8.57 ± 5.64	7.79 ± 5.23	7.87 ± 4.50	7.42 ± 5.00	7.57 ± 5.30
MADRS	12.21 ± 8.48	15.57 ± 7.48	9.68 ± 7.72	11.74 ± 8.26	10.00 ± 7.32	10.78 ± 6.61	10.00 ± 6.83	10.70 ± 7.37
HAMA	8.95 ± 5.80	10.57 ± 5.08	6.58 ± 5.63	8.74 ± 5.30	7.58 ± 5.35	7.91 ± 4.95	7.84 ± 4.91	8.43 ± 5.76
YMRS	1.37 ± 1.30	2.17 ± 1.83	1.05 ± 1.31	1.61 ± 1.41	1.11 ± 1.05	1.39 ± 1.70	1.11 ± 1.10	1.30 ± 1.70
EQ-5D-3L	0.83 ± 0.20	0.82 ± 0.16	0.84 ± 0.14	0.84 ± 0.19	0.78 ± 0.21	0.88 ± 0.10	0.85 ± 0.17	0.80 ± 0.17

Mean values are presented with '±' standard deviation values. HDRS, Hamilton Rating Scale for Depression; MADRS, Montgomery-Åsberg Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale; EQ-5D-3L, quality of life measure (https://euroqol.org). Active (n = 19), Sham (n = 23).

Table 5
Acceptability questionnaire and responses at month 8 and month 11 follow-up.

Question	Median (IQR)	Likert Ratings						
		1	2	3	4	5	6	7
How acceptable did you find the tDCS sessions?		**Very unacceptable**	**Quite unacceptable**	**Unacceptable**	**Neither**	**Acceptable**	**Quite acceptable**	**Very acceptable**
3-month follow-up	7 (7, 7)	0 (0 %)	0 (0 %)	1 (3 %)	0 (0 %)	0 (0 %)	8 (21 %)	29 (76 %)
6-month follow-up	7 (6, 7)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	9 (27 %)	24 (73 %)
How helpful do you think the tDCS sessions were for improving your depressive symptoms?		**Very unhelpful**	**Quite unhelpful**	**Bit unhelpful**	**Neither**	**Bit helpful**	**Quite helpful**	**Very helpful**
3-month follow-up	6 (6, 7)	0 (0 %)	2 (5 %)	0 (0 %)	2 (5 %)	4 (11 %)	14 (37 %)	16 (42 %)
6-month follow-up	7 (6, 7)	0 (0 %)	1 (3 %)	0 (0 %)	3 (9 %)	1 (3 %)	11 (33 %)	17 (52 %)
How were you bothered by any negative side effects from the tDCS sessions?		**Very much unaffected**	**Quite unaffected**	**Bit unaffected**	**Neither**	**Bit affected**	**Quite affected**	**Very affected**
3-month follow-up	2 (1, 5)	17 (45 %)	6 (16 %)	1 (3 %)	3 (8 %)	10 (26 %)	1 (3 %)	0 (0 %)
6-month follow-up	2 (1, 4)	14 (43 %)	8 (24 %)	1 (3 %)	2 (6 %)	8 (24 %)	0 (0 %)	0 (0 %)
How ethical do you think the tDCS sessions are?		**Very unethical**	**Quite unethical**	**Bit unethical**	**Neither**	**Bit ethical**	**Quite ethical**	**Very ethical**
3-month follow-up	7 (7, 7)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	1 (3 %)	4 (11 %)	33 (87 %)
6-month follow-up	7 (7, 7)	0 (0 %)	0 (0 %)	0 (0 %)	1 (3 %)	0 (0 %)	6 (9 %)	29 (88 %)
How much effort did you need to put in for the tDCS sessions?		**Very much more than usual**	**Some more than usual**	**Little bit more than usual**	**Same as usual**	**Little bit less than usual**	**Some less than usual**	**Very much less than usual**
3-month follow-up	4 (3,5)	0 (0 %)	4 (10 %)	13 (34 %)	10 (26 %)	3 (8 %)	3 (8 %)	5 (13 %)
6-month follow-up	4 (3,6)	0 (0 %)	3 (9 %)	8 (24 %)	8 (24 %)	4 (12 %)	5 (15 %)	5 (15 %)
Would you recommend the tDCS sessions to others?		**Would very strongly not recommend**	**Would strongly not recommend**	**Would not recommend**	**Would not for or against**	**Would recommend**	**Would strongly recommend**	**Would very strongly recommend**
3-month follow-up	6 (6, 7)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	5 (13 %)	15 (40 %)	18 (47 %)
6-month follow-up	6 (6, 7)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	5 (15 %)	10 (30 %)	18 (55 %)

IQR, inter quartile range; tDCS, transcranial direct current stimulation. 3-month follow-up, n = 38 (one participant did not complete the questionnaire); 6-month follow-up, n = 33.

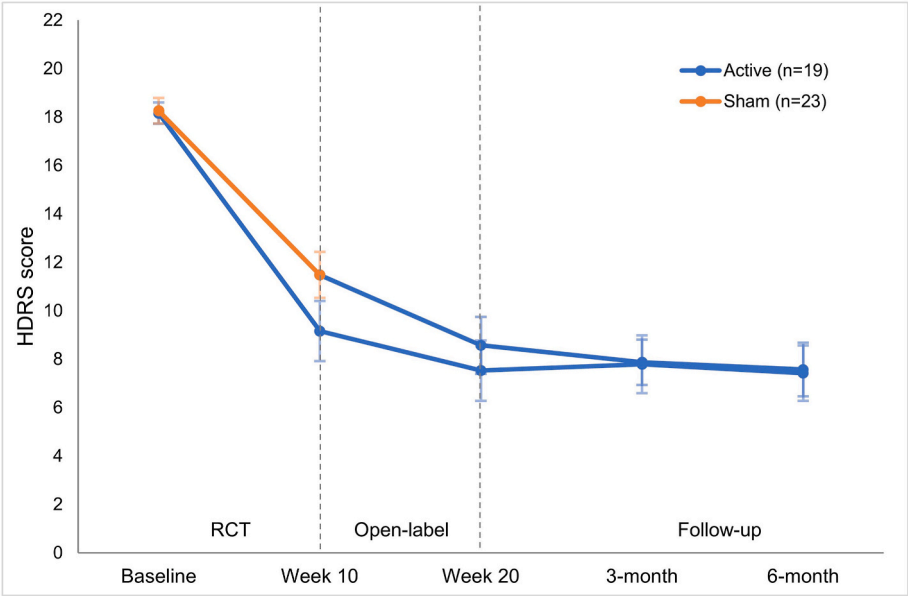

Fig. 2. Mean Hamilton Rating Scale for Depression (HDRS) total scores for patients that attended a follow-up visit, who were allocated to the active or sham treatment group at each assessment time point from the end of the blinded phase of the trial to the 6-month follow-up. Error bars represent standard error. Number of participants in the original active group (n = 19) and in sham group (n = 23).

4. Discussion

Long term follow-up assessments in participants from a phase 2 randomised controlled trial of home-based tDCS treatment of MDD demonstrated significant maintenance of treatment effects. All participants had engaged in the open-label phase of the trial and had received active tDCS (Woodham et al., 2024). Maintenance of treatment effects were observed at the 3- and 6-month follow-up (8- and 11-months post-randomisation), which was evident in high response and remission rates. In particular, participants who had shown a clinical response at the end of the week 20 open-label phase, 90 % maintained remission at the 6-month follow-ups.

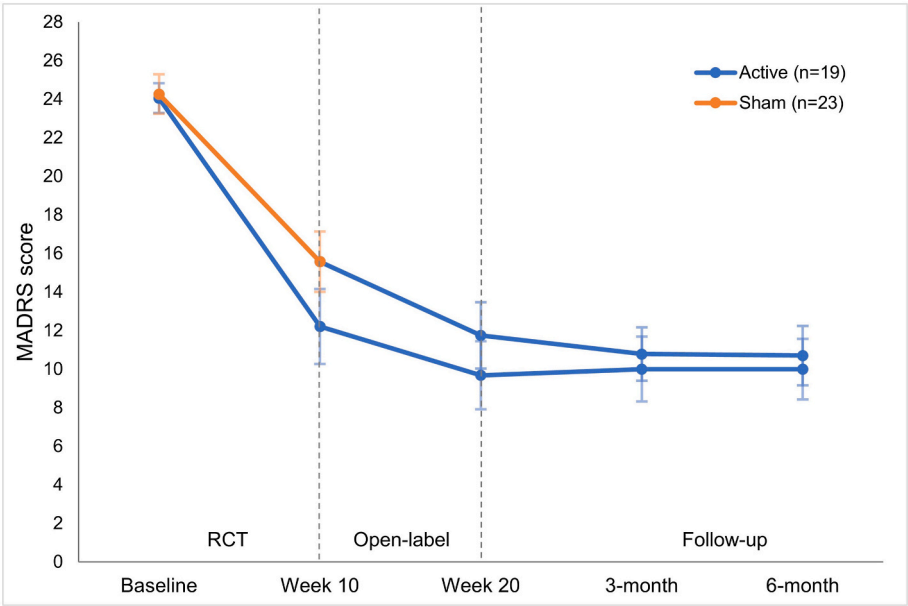

Fig. 3. Montgomery-Åsberg Depression Rating Scale (MADRS) total scores for patients that attended a follow-up visit, who were allocated to the active or sham treatment group at each assessment time point from the end of the blinded phase of the trial to the 6-month follow-up. Error bars represent standard error. Number of participants in the original active group (n = 19) and in sham group (n = 23).

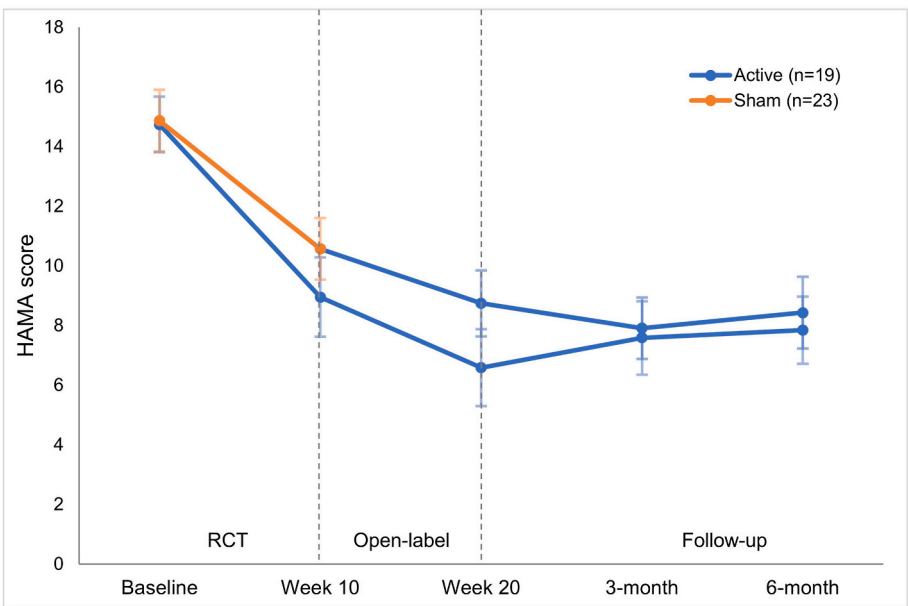

Fig. 4. Mean Hamilton Anxiety Rating Scale (HAMA) total scores for patients that attended a follow-up visit, who were allocated to the active or sham treatment group at each assessment time point from the end of the blinded phase of the trial to the 6-month follow-up. Error bars represent standard error. Number of participants in the original active group (n = 19) and in sham group (n = 23).

Treatment outcomes remained stable for both depression (HDRS and MADRS) and for anxiety symptoms (HAMA). At the 10-week RCT end of treatment, there were no differences between treatment groups in change score for the quality-of-life measure and scores on this measure did not change significantly over time in the present analyses. The scores on the quality-of-life measure were relatively high at baseline for a sample of patients with moderate to severe depression (Sobocki et al., 2007) and although there were some improvements that were maintained during follow-up, these changes were not significant. The time by group interaction indicated an increase in quality of life in the original sham treatment arm over the first 3-month follow-up period, and a decrease in the original active group, which could reflect an increase for the sham group following the 10-week open-label treatment phase. Future trials looking at effectiveness should aim to include multiple quality-of-life measures.

Over half of participants continued to use the tDCS device in the follow-up period. A significant linear correlation was found between the number of active tDCS sessions completed and decrease in HDRS score at week 20 (Supplementary Fig. 2), however, no significant differences were found in depressive symptom scores between those who had continued and those who had not continued with tDCS use during the follow-up phase of the trial. Open-label studies of home-based tDCS treatment have observed continued high response and remission rates at 6 months (Alonzo et al., 2019; Woodham et al., 2022). Razza et al.

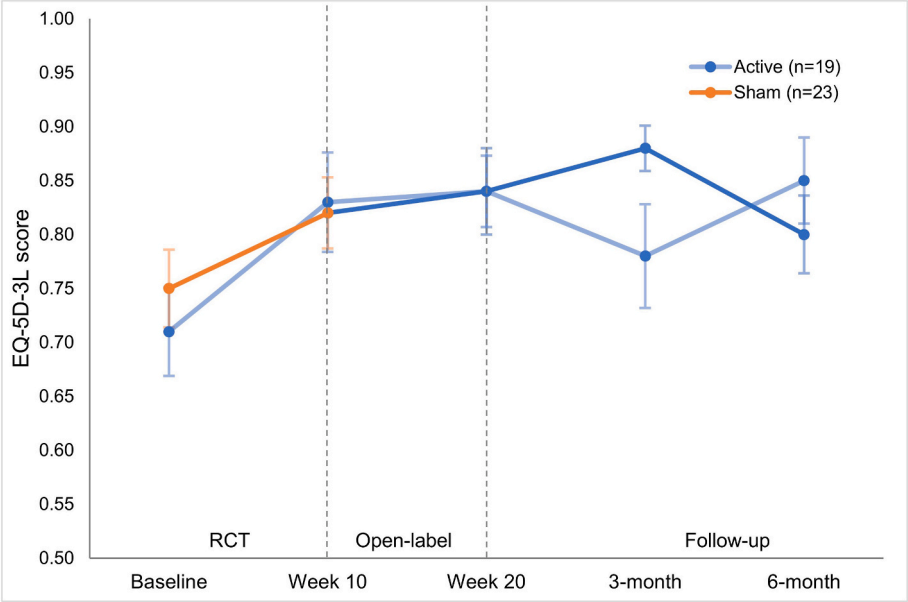

Fig. 5. Mean EQ-5D-3L total scores for patients that attended a follow-up visit, who were allocated to the active or sham treatment group at each assessment time point from the end of the blinded phase of the trial to the 6-month follow-up. Error bars represent standard error. Number of participants in the original active group (n = 19) and in sham group (n = 23).

(2021) meta-analysis identified that interventional follow-up periods may lead to the continuation of improvements beyond the acute phase of treatment. In clinic-based studies, Aparicio et al. (2019) found relapse rates to be lower in an interventional study of participants who had responded to active tDCS, with a maintenance stimulation schedule of 2 times per week over 6-months compared to two interventional studies with less intensive maintenance stimulation schedules (Martin et al., 2013; Valiengo et al., 2013), indicating that more frequent schedules might be more beneficial.

Although our follow-up study was not interventional, many participants had chosen to continue with stimulation, allowing some assessment of its effects. When only considering the sub-sample of participants who had responded to tDCS at the end of the 20-week open-label phase, response rates at the 3- and 6-month follow-ups were 84 % and 90 % respectively, which was higher than for the full follow-up sample, which were 64 % and 76 % respectively. Most participants who had maintained clinical response from the end of the 20-week open-label phase to the 6-month follow-up had continued with tDCS use. In addition to exploring the frequency of follow-up maintenance stimulation, future studies with interventional follow-up periods might aim to compare continued maintenance stimulation and no stimulation to better understand if relapse rates are comparable.

The continued use of tDCS by participants in long term follow-up further demonstrates the acceptability and feasibility of home-based self-administered tDCS over a longer time period. Although tDCS use was not being monitored by the study team, acceptability reports remained high, no serious adverse events occurred, and no participants developed mania or hypomania.

Relapse following rTMS treatment is more likely in the absence of maintenance treatment. Interventional maintenance periods are effective for continued clinical response beyond the acute treatment phase and in preventing relapse (Chen et al., 2023; Matsuda et al., 2023). However, continued treatment requires regular visits to clinics. rTMS and tDCS are comparable in their ability to reduce electrophysiological complexity in MDD (Čukić, 2019). Future research could explore the effectiveness of home-based tDCS as a more accessible maintenance treatment for rTMS and other treatments. A clinical question of significance is whether continued maintenance tDCS sessions beyond the acute treatment phase is necessary or beneficial for preventing future relapse. Given its portability and low cost, maintenance treatment could be feasible, as is typically the case with antidepressant medication which is maintained in order to prevent a relapse.

Limitations of the present study include being a sub-sample of the original RCT sample, which limited power to detect group differences. The observational design of the study did not control for frequency of tDCS use, nor adherence to a specific schedule, therefore analyses comparing those who had continued stimulation with those who had not, have limited clinical implications. Not all participants continued in the long-term follow-up and 66 % of those who did not had unknown non-participation reasons, preventing an assessment of discontinuation reasons. The discontinuation rate was 21 % at the 6-month follow-up is comparable to long term tDCS follow-up studies (Aparicio et al., 2019; Martin et al., 2013; Valiengo et al., 2013). The sample included participants who had shown a treatment response (67 %) and those who had not (33 %) at the end of the 20-week open-label treatment phase, therefore, samples comparing groups likely include participants for whom tDCS is not effective. Future interventional studies with control groups are necessary to better understand the role of maintenance tDCS in the year following acute treatment and to determine the most effective schedules of maintenance treatment. Generalisability of findings may be limited as participants were predominantly of white ethnicity, and treatment resistant depression and history of hospital admissions were exclusion criteria.

5. Conclusion

In conclusion, long term response and remission rates were maintained at the 3- and 6-month follow-up (8- and 11-month post randomisation) following a 10-week RCT and 10-week open-label treatment. In particular, participants who had shown a clinical response at the end of the 20-week open-label phase, the majority maintained a clinical response and remission. No significant differences were found in depressive symptoms between those who had continued tDCS with those who had not in the long term. Over half of participants chose to continue with tDCS in the long term, indicating that long-term home-based tDCS is acceptable and feasible.

CRediT authorship contribution statement

Rachel D. Woodham: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Sudhakar Selvaraj:** Writing – review & editing, Project administration. **Nahed Lajmi:** Writing – review & editing, Investigation. **Harriet Hobday:** Writing – review & editing, Investigation. **Gabrielle Sheehan:** Writing – review & editing, Investigation. **Ali-Reza Ghazi-Noori:** Writing – review & editing, Investigation. **Peter J. Lagerberg:** Writing – review & editing, Investigation. **Rodrigo Machado-Vieira:** Writing – review & editing, Project administration. **Jair C. Soares:** Writing – review & editing, Methodology. **Allan H. Young:** Writing – review & editing, Methodology. **Cynthia H.Y. Fu:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization.

Ethics statement

All procedures involving human subjects/patients were approved by research ethics boards of the University of East London and by South Central-Hampshire B Research Ethics Committee, UK (ref. 22/SC/0023). Study procedures were explained to participants prior to signing informed consent. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Data statement

Anonymised data will be made available on request.

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Funding for the follow-up study was provided by the Rosetrees Trust (CF20212104). Funding for the original randomized control trial was provided by Flow Neuroscience. The funders had no role in data analysis, interpretation of data, decision to publish, or manuscript preparation.

Declaration of competing interest

Author C.F. reports the following declaration of interests: Research grant funding on behalf of the University of East London from Flow Neuroscience (R102696); research grant funding: NIMH (R01MH134236), Baszucki Brain Research Fund Milken Institute (BD0000009), Rosetrees Trust (CF20212104), International Psychoanalytic Society (158102845), MRC (G0802594), NARSAD, Wellcome Trust. Associate Editor of Psychoradiology, Section Editor of Brain Research Bulletin.

Author A.Y. reports the following declaration of interests: Paid lectures and advisory boards for the following companies with therapies 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, Novartis, Neurocentrx. Principal Investigator for the following studies: 1. the Restore-Life VNS registry study funded by LivaNova; 2. ESKETINTRD3004: "An Open-label, Long-term, Safety and Efficacy Study of Intranasal Esketamine in Treatment-resistant Depression"; 3. The Effects of Psilocybin on Cognitive Function in Healthy Participants; 4. The Safety and Efficacy of Psilocybin in Participants with Treatment-Resistant Depression (P-TRD); 5. A Double-Blind, Randomized, Parallel-Group Study with Quetiapine Extended Release as Comparator to Evaluate the Efficacy and Safety of Seltorexant 20 mg as Adjunctive Therapy to Antidepressants in Adult and Elderly Patients with Major Depressive Disorder with Insomnia Symptoms Who Have Responded Inadequately to Antidepressant Therapy. (Janssen); 6. An Open-label, Long-term, Safety and Efficacy Study of Aticaprant as Adjunctive Therapy in Adult and Elderly Participants with Major Depressive Disorder (MDD). (Janssen); 7. A Randomized, Double-blind, Multicentre, Parallel-group, Placebo-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of Aticaprant 10 mg as Adjunctive Therapy in Adult Participants with Major Depressive Disorder (MDD) with Moderate-to-severe Anhedonia and Inadequate Response to Current Antidepressant Therapy; 8. A Study of Disease Characteristics and Real-life Standard of Care Effectiveness in Patients with Major Depressive Disorder (MDD) With Anhedonia and Inadequate Response to Current Antidepressant Therapy Including an SSRI or SNR. (Janssen). UK Chief Investigator for the following studies: 1. Novartis MDD study MIJ821A12201; 2. Compass; COMP006 & COMP007 studies. Grant funding (past and present): NIMH (USA); CIHR (Canada); NARSAD (USA); Stanley Medical Research Institute (USA); MRC (UK); Wellcome Trust (UK); Royal College of Physicians (Edin); BMA (UK); UBC-VGH Foundation (Canada); WEDC (Canada); CCS Depression Research Fund (Canada); MSFHR (Canada); NIHR (UK). Janssen (UK) EU Horizon 2020. Editor of Journal of Psychopharmacology and Deputy Editor, BJPsych Open. No shareholdings in pharmaceutical companies.

Author S.S. reports the following declaration of interests: S.S. is a fulltime employee of Intra-Cellular Therapies, Inc. Research grant funding on behalf of the University of Texas Health Science Center at Houston from Flow Neuroscience. Paid advisory boards for the following companies: Worldwide Clinical Trials and Inversago; Vicore pharma. He has received grants/research support from NIMH, United States (1R21MH119441-01A1), NIMH (1R21MH129888-01A1), NICHD 1R21HD106779-01A1, SAMHSA (6H79FG000470-01M003) and Fizer foundation. He has received research funding as a Principal investigator or study/sub-investigator from and/or participated as consultant/speaker for Flow Neuroscience, COMPASS Pathways, LivaNova, Janssen, Relmada, and Psychiatry education forum. Intra-Cellular Therapies (ITI) or NIH or SAMHSA or any other organizations had no role in the study's design and conduct; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. This study's content is solely the responsibility of the authors and does not necessarily represent the official views of the ITI or NIH or SAMHSA.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2025.03.047.

References

Alonzo, A., Fong, J., Ball, N., Martin, D., Chand, N., Loo, C., 2019. Pilot trial of home-administered transcranial direct current stimulation for the treatment of depression. J. Affect. Disord. 252, 475–483. https://doi.org/10.1016/j.jad.2019.04.041.

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, (DSM-5®), Fifth. American Psychiatric Association.

Aparicio, L.V.M., Rosa, V., Razza, L.M., Sampaio-Junior, B., Borrione, L., Valiengo, L., Lotufo, P.A., Benseñor, I.M., Fraguas, R., Moffa, A.H., Gattaz, W.F., Brunoni, A.R., 2019. Transcranial direct current stimulation (tDCS) for preventing major depressive disorder relapse: results of a 6-month follow-up. Depress. Anxiety 36, 262–268. https://doi.org/10.1002/da.22878.

Borrione, L., Cavendish, B.A., Aparicio, L.V.M., Luethi, M.S., Goerigk, S., Carneiro, A.M., Valiengo, L., Moura, D.O., de Souza, J.P., Baptista, M., Aparecida da Silva, V., Klein, I., Suen, P., Gallucci-Neto, J., Padberg, F., Razza, L.B., Vanderhasselt, M.-A., Lotufo, P.A., Bensenor, I.M., Fregni, F., Brunoni, A.R., 2024. Home-use transcranial direct current stimulation for the treatment of a major depressive episode: a randomized clinical trial. JAMA Psychiatry 81, 329–337. https://doi.org/10.1001/jamapsychiatry.2023.4948.

Brian Chen, Y.-C., Chou, P.-H., Tu, Y.-K., Brunoni, A.R., Su, K.-P., Tseng, P.-T., Liang, C.-S., Lin, P.-Y., Carvalho, A.F., Hung, K.-C., Hsu, C.-W., Li, C.-T., 2023. Trajectory of changes in depressive symptoms after acute repetitive transcranial magnetic stimulation: a meta-analysis of follow-up effects. Asian J. Psychiatry 88, 103717. https://doi.org/10.1016/j.ajp.2023.103717.

Brooks, R., 1996. EuroQol: the current state of play. Health Policy 37, 53–72. https://doi.org/10.1016/0168-8510(96)00822-6.

Brunoni, A.R., Amadera, J., Berbel, B., Volz, M.S., Rizzerio, B.G., Fregni, F., 2011. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. Int. J. Neuropsychopharmacol. 14, 1133–1145. https://doi.org/10.1017/S1461145710001690.

Brunoni, A.R., Moffa, A.H., Fregni, F., Palm, U., Padberg, F., Blumberger, D.M., Daskalakis, Z.J., Bennabi, D., Haffen, E., Alonzo, A., Loo, C.K., 2016. Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. Br. J. Psychiatry 208, 522–531. https://doi.org/10.1192/bjp.bp.115.164715.

Cuijpers, P., Karyotaki, E., Weitz, E., Andersson, G., Hollon, S.D., van Straten, A., 2014. The effects of psychotherapies for major depression in adults on remission, recovery and improvement: a meta-analysis. J. Affect. Disord. 159, 118–126. https://doi.org/10.1016/j.jad.2014.02.026.

Čukić, M., 2019. The reason why rTMS and tDCS are efficient in treatments of depression. Front. Psychol. 10. https://doi.org/10.3389/fpsyg.2019.02923.

Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62. https://doi.org/10.1136/jnnp.23.1.56.

Hamilton, M., 1959. The assessment of anxiety states by rating. Br. J. Med. Psychol. 32, 50–55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x.

Kumpf, U., Palm, U., Eder, J., Ezim, H., Stadler, M., Burkhardt, G., Dechantsreiter, E., Padberg, F., 2023. TDCS at home for depressive disorders: an updated systematic review and lessons learned from a prematurely terminated randomized controlled pilot study. Eur. Arch. Psychiatr. Clin. Neurosci. 273, 1403–1420. https://doi.org/10.1007/s00406-023-01620-y.

Martin, D.M., Alonzo, A., Ho, K.-A., Player, M., Mitchell, P.B., Sachdev, P., Loo, C.K., 2013. Continuation transcranial direct current stimulation for the prevention of relapse in major depression. J. Affect. Disord. 144, 274–278. https://doi.org/10.1016/j.jad.2012.10.012.

Matsuda, Y., Sakuma, K., Kishi, T., Esaki, K., Kito, S., Shigeta, M., Iwata, N., 2023. Repetitive transcranial magnetic stimulation for preventing relapse in antidepressant treatment-resistant depression: a systematic review and meta-analysis of randomized controlled trials. Brain Stimul. Basic Transl. Clin. Res. Neuromodulation 16, 458–461. https://doi.org/10.1016/j.brs.2023.01.1680.

Meron, D., Hedger, N., Garner, M., Baldwin, D.S., 2015. Transcranial direct current stimulation (tDCS) in the treatment of depression: systematic review and meta-analysis of efficacy and tolerability. Neurosci. Biobehav. Rev. 57, 46–62. https://doi.org/10.1016/j.neubiorev.2015.07.012.

Moffa, A.H., Martin, D., Alonzo, A., Bennabi, D., Blumberger, D.M., Benseñor, I.M., Daskalakis, Z., Fregni, F., Haffen, E., Lisanby, S.H., Padberg, F., Palm, U., Razza, L.B., Sampaio-Jr, B., Loo, C., Brunoni, A.R., 2020. Efficacy and acceptability of transcranial direct current stimulation (tDCS) for major depressive disorder: an individual patient data meta-analysis. Prog. Neuropsychopharmacol. Biol. Psychiatry 99, 109836. https://doi.org/10.1016/j.pnpbp.2019.109836.

Montgomery, S.A., Åsberg, M., 1979. A new depression scale designed to be sensitive to change. Br. J. Psychiatry J. Ment. Sci. 134, 382–389. https://doi.org/10.1192/bjp.134.4.382.

Mutz, J., Edgcumbe, D.R., Brunoni, A.R., Fu, C.H.Y., 2018. Efficacy and acceptability of non-invasive brain stimulation for the treatment of adult unipolar and bipolar depression: a systematic review and meta-analysis of randomised sham-controlled trials. Neurosci. Biobehav. Rev. 92, 291–303. https://doi.org/10.1016/j.neubiorev.2018.05.015.

Mutz, J., Vipulananthan, V., Carter, B., Hurlemann, R., Fu, C.H.Y., Young, A.H., 2019. Comparative efficacy and acceptability of non-surgical brain stimulation for the acute treatment of major depressive episodes in adults: systematic review and network meta-analysis. BMJ 364, 1079. https://doi.org/10.1136/bmj.l1079.

Nikolin, S., Moffa, A., Razza, L., Martin, D., Brunoni, A., Palm, U., Padberg, F., Bennabi, D., Haffen, E., Blumberger, D.M., Salehinejad, M.A., Loo, C.K., 2023. Time-course of the tDCS antidepressant effect: an individual participant data meta-analysis. Prog. Neuropsychopharmacol. Biol. Psychiatry 125, 110752. https://doi.org/10.1016/j.pnpbp.2023.110752.

Nitsche, M.A., Paulus, W., 2000. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J. Physiol. 527, 633–639. https://doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x.

Oh, J., Jang, K.-I., Jeon, S., Chae, J.-H., 2022. Effect of self-administered transcranial direct stimulation in patients with major depressive disorder: a randomized, single-blinded clinical trial. Clin. Psychopharmacol. Neurosci. Off. Sci. J. Korean Coll. Neuropsychopharmacol 20, 87–96. https://doi.org/10.9758/cpn.2022.20.1.87.

Posner, K., Brown, G.K., Stanley, B., Brent, D.A., Yershova, K.V., Oquendo, M.A., Currier, G.W., Melvin, G.A., Greenhill, L., Shen, S., Mann, J.J., 2011. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am. J. Psychiatr. 168, 1266–1277. https://doi.org/10.1176/appi.ajp.2011.10111704.

Rabin, R., de Charro, F., 2001. EQ-5D: a measure of health status from the EuroQol Group. Ann. Med. 33, 337–343. https://doi.org/10.3109/07853890109002087.

Razza, L.B., De Smet, S., Moffa, A., Sudbrack-Oliveira, P., Vanderhasselt, M.-A., Brunoni, A.R., 2021. Follow-up effects of transcranial direct current stimulation (tDCS) for the major depressive episode: a systematic review and meta-analysis. Psychiatry Res. 302, 114024. https://doi.org/10.1016/j.psychres.2021.114024.

Rimmer, R.M., Woodham, R.D., Cahill, S., Fu, C.H.Y., 2024. Acceptability of home-based transcranial direct current stimulation (tDCS) in major depression: a qualitative analysis of individual experiences. Ment. Health Rev. 29, 79–91. https://doi.org/10.1108/MHRJ-07-2022-0050.

Rush, A.J., Trivedi, M.H., Wisniewski, S.R., Nierenberg, A.A., Stewart, J.W., Warden, D., Niederehe, G., Thase, M.E., Lavori, P.W., Lebowitz, B.D., McGrath, P.J., Rosenbaum, J.F., Sackeim, H.A., Kupfer, D.J., Luther, J., Fava, M., 2006. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am. J. Psychiatr. 163, 1905–1917. https://doi.org/10.1176/ajp.2006.163.11.1905.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl. 20), 22–33 quiz 34-57.

Sobocki, P., Ekman, M., Agren, H., Krakau, I., Runeson, B., Mårtensson, B., Jönsson, B., 2007. Health-related quality of life measured with EQ-5D in patients treated for depression in primary care. Value Health J. Int. Soc. Pharmacoeconomics Outcomes Res. 10, 153–160. https://doi.org/10.1111/j.1524-4733.2006.00162.x.

Valiengo, L., Benseñor, I.M., Goulart, A.C., de Oliveira, J.F., Zanao, T.A., Boggio, P.S., Lotufo, P.A., Fregni, F., Brunoni, A.R., 2013. The sertraline versus electrical current Therapy for treating depression clinical study (SELECT-TDCS): results of the crossover and follow-up phases: research article: phases II and III of SELECT-TDCS. Depress. Anxiety 30, 646–653. https://doi.org/10.1002/da.22079.

Woodham, R., Rimmer, R.M., Mutz, J., Fu, C.H.Y., 2021. Is tDCS a potential first line treatment for major depression? Int. Rev. Psychiatr. 33, 250–265. https://doi.org/10.1080/09540261.2021.1879030.

Woodham, R., Rimmer, R.M., Young, A.H., Fu, C.H.Y., 2022. Adjunctive home-based transcranial direct current stimulation treatment for major depression with real-time remote supervision: an open-label, single-arm feasibility study with long term outcomes. J. Psychiatr. Res. 153, 197–205. https://doi.org/10.1016/j.jpsychires.2022.07.026.

Woodham, R.D., Selvaraj, S., Lajmi, N., Hobday, H., Sheehan, G., Ghazi-Noori, A.-R., Lagerberg, P.J., Rizvi, M., Kwon, S.S., Orhii, P., Maislin, D., Hernandez, L., Machado-Vieira, R., Soares, J.C., Young, A.H., Fu, C.H.Y., 2024. Home-based transcranial direct current stimulation treatment for major depressive disorder: a fully remote phase 2 randomized sham-controlled trial. Nat. Med. 1–9. https://doi.org/10.1038/s41591-024-03305-y.

World Health Organization, 2017. Depression and Other Common Mental Disorders: Global Health Estimates (No.WHO/MSD/MER/2017.2).

Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A., 1978. A rating scale for mania: reliability, validity and sensitivity. Br. J. Psychiatry 133, 429–435. https://doi.org/10.1192/bjp.133.5.429.