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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

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ABSTRACT

Current treatments for major depressive disorder (MDD) have limited effectiveness and acceptability. Transcranial direct current stimulation (tDCS) is a novel non-invasive brain stimulation method that has demonstrated treatment efficacy in MDD. tDCS requires daily sessions, however clinical trials have been conducted in research centers requiring repeated visits. As tDCS is portable and safe, it could be provided at home. We developed a home-based protocol with real-time supervision, and we examined the clinical outcomes, acceptability and feasibility. Participants were 26 MDD (19 women), mean age 40.9 ± 14.2 years, in current depressive episode of moderate to severe severity (mean 17-item Hamilton Rating Scale for Depression (HAMD) score 19.12 ± 2.12). tDCS was provided in a bilateral frontal montage, F3 anode, F4 cathode, 2 mA, each session 30 min, in a 6-week trial, for a total 21 sessions. Participants maintained their current treatment (antidepressant medication, psychotherapy, or were enrolled in online CBT). Two tDCS device brands were used, and a research team member was present in person or by real-time video call at each session. 92.3% MDD participants (n = 24) completed the 6-week treatment. Attrition rate was 7.7%. There was a significant improvement in depressive symptoms following treatment (mean HAMD 5.33 ± 2.33), which was maintained at 6 months (mean HAMD 5.43 ± 2.73). Acceptability was endorsed as "very acceptable" or "quite acceptable" by all participants. Due to the open-label feasibility design, efficacy findings are preliminary. In summary, home-based tDCS with real-time supervision was associated with significant clinical improvements and high acceptability which were maintained in the long term.

1. Introduction

Major depressive disorder (MDD) is a leading cause of disability worldwide and is the most significant precursor in suicide (James et al., 2018). MDD is characterised by low mood or loss of enjoyment for a prolonged period that is associated with impairments in sleep, appetite, and cognition, as well as low energy and often feelings of guilt. MDD is often expressed in impaired interpersonal, school or workplace functioning (Wittchen et al., 2011), with a socioeconomic cost of over $326 million in the USA (Greenberg et al., 2021) and £9 billion in the UK (Thomas and Morris, 2003).

The most common treatments for MDD are pharmacological and psychological therapies. However, the clinical response to a full course of either treatment is usually achieved in less than 50% of patients (Cuijpers et al., 2014; Rush et al., 2006). Even after multiple treatment trials, over a third of patients do not achieve remission (Rush et al., 2006). Residual symptoms increase the risk of another episode and, in turn, repeated episodes, resulting in cycles of more frequent recurrences (Kessing et al., 2004). Moreover, up to 40% of patients are not accessing treatment, despite having severe depressive symptoms (McManus et al., 2016), and patient preference is an important determinant of engagement and clinical outcomes (Windle et al., 2020).

Transcranial direct current stimulation (tDCS) is a non-invasive form of brain stimulation, which is a potential novel treatment for depression (Woodham et al., 2021). tDCS delivers a weak direct current (0.5–2.5 mA), in which electrode placement is typically with the anode over the

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left dorsolateral prefrontal cortex (DLPFC) and cathode over either the right DLPFC, suborbital or frontotemporal region (Brunoni et al., 2016b; Fregni et al., 2021). The current changes neuronal membrane potential and facilitates discharge. In contrast to rTMS and ECT, tDCS does not directly trigger an action potential. The most common side effects are tingling, itching, burning sensation, skin redness or headache, with no differences reported in active relative to sham tDCS (Brunoni et al., 2011).

A course of active tDCS treatment is associated with significant improvements in depressive symptoms, clinical response and remission relative to placebo sham stimulation (Brunoni et al., 2016b; Fregni et al., 2021). Meta-analyses of randomised sham-controlled trials show that a course of tDCS treatment is associated with a fourfold increased rate of clinical response and a threefold increased rate of clinical remission (Mutz et al., 2018, 2019). Moreover, the onset of improvement might be seen in the first 2 weeks of treatment (Brunoni et al., 2016b; Meron et al., 2015), and the strongest efficacy has been observed in first episode and recurrent MDD (Mutz et al., 2018, 2019).

However, tDCS requires daily sessions for several weeks, which are time consuming and potentially costly for travel requirements. As tDCS devices are low cost and portable, providing the treatment at home could improve availability and engagement. In an open label 4-week trial, Alonzo et al. (2018) found a response rate of 38% in 33 MDD patients, and in an open label 6-week trial, Borrione et al. (2021) found a response rate of 80% in 5 MDD using a tDCS protocol combined with app-based psychological intervention. While treatment effects seem to be evident, long term clinical outcomes have not been investigated. We sought to investigate the long term effects, acceptability and feasibility of a home-based protocol with clinical assessments at 3 and 6 months.

2. Materials and methods

2.1. Study design and tDCS protocol

Ethical approval was provided by the London Fulham Research Ethics Committee. All participants provided informed written consent. The study was an open-label acceptability and feasibility trial of home-based tDCS treatment for MDD (ClinicalTrials.gov ID: NCT03632434). The protocol consisted of a 6-week treatment period of active tDCS, consisting of 5 sessions per week for 3 weeks and then 2 sessions a week for 3 weeks, for a total of 21 sessions. A minimum of 15 sessions was required for study completion. Given the novelty of the treatment, ethical approval required that all participants receive active tDCS in addition to their current treatment e.g. antidepressant medication, psychotherapy, or an online course of cognitive behaviour therapy (CBT), Living Life to The Full (www.llttf.com). Long term clinical assessments were conducted at 3 and 6 months by telephone or video call.

The anode was positioned over the left dorsolateral prefrontal cortex (DLPFC) (position F3 on the international 10/20 EEG system) and cathode over the right DLPFC (position F4). Conductive rubber electrodes covered by saline soaked sponges were 35 cm^2 in diameter. Stimulation was 2 mA for 30 min with a gradual ramp up and ramp down of 10 s. A research team member was present at each session. In person, the research member provided a discreet presence, remaining in the same room as the participant. By Microsoft Teams video call, the research member would have their camera on and the participant would have their camera and microphone on, so they could easily communicate with the researcher. The researcher would ensure that the participant was visible at the side of the screen. The participant and team member did not interact unless the participant required support.

Two tDCS devices were used: Neuroelectrics Starstim 8 system (3 participants) and Flow Neuroscience tDCS device (23 participants). The Neuroelectrics tDCS device was initially used, which required in person administration as electrodes are placed within a neoprene cap. During the Covid-19 pandemic, the Flow tDCS device was used which in a fully remote protocol with real-time remote supervision. The participant would put on the tDCS device with a research team member present by video call. All additional study activities were conducted by video call. Written informed consent was provided electronically. Neuropsychological assessments were mailed to participants and necessary sections were completed by pen and paper. A screenshot of the completed assessment was taken by the researcher following completion.

2.2. Inclusion and exclusion criteria

Participants were recruited from online advertisements and GP referrals. Inclusion criteria: (1) adults aged 18 or older; (2) current major depressive episode, without psychotic features, defined by Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (American Psychiatric Association, 2013), determined by a structured assessment using the Mini-International Neuropsychiatric Interview (MINI; Version 7.0.2) (Sheehan et al., 1998); (3) having at least a moderate severity of depressive symptoms, as measured by a minimum score of 16 on the 17-item Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960); and (4) taking antidepressant medication or engaging in psychological therapy, including online CBT. Exclusion criteria: (1) treatment resistant depression as defined by poor clinical response to 2 or more antidepressant trials; (2) any concurrent DSM-5 comorbid Axis I or II disorder within the previous 6 months; (3) history of bipolar disorder, obsessive compulsive disorder, or primary psychotic disorder; (4) significant risk of suicide or self-harm; (5) pregnant women or women who were breastfeeding; (6) history of ECT, TMS or VNS; (7) any exclusion criteria for receiving tDCS, including having a scalp or skin condition (e.g. psoriasis or eczema), contact with the scalp is not possible, having metallic implants, including intracranial electrodes or a pacemaker, history of epilepsy or seizure resulting in loss of consciousness, neurological disorder or history of migraine.

2.3. Clinical assessments

Clinical assessments were conducted at baseline and at weeks 1, 2, 3, 4, 5, 6, 18 and 30, following initiation of tDCS sessions. The following rating scales were used: 17-item Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960), Hamilton Anxiety Rating Scale (HAMA) (Hamilton, 1959), Sheehan Disability Scale (SDS) (Sheehan, 1893), Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001) and Young Mania Rating Scale (YMRS) (Young et al., 1978). Clinical response was defined as an improvement of 50% or greater in HAMD, and clinical remission was defined as a HAMD score of less than 8. Each participant was rated by the same researcher throughout the study with clinical supervision.

2.4. Safety, tolerability and acceptability

Safety and tolerability were assessed with monitoring of any adverse events before and after each treatment session at the same timepoints, using the tDCS Adverse Events Questionnaire (AEQ) (Brunoni et al., 2011). We devised an acceptability questionnaire based on Sekhon et al. (2017) framework model, consisting of five questions: (1) general acceptability: 'How acceptable do you consider the tDCS sessions to be?'; (2) perceived effectiveness: 'How helpful do you think the tDCS sessions may be for improving your depressive symptoms?'; (3) side effects: 'How likely do you think that there will be negative side effects from the tDCS sessions?'; (4) ethicality: 'How ethical do you think the tDCS sessions are?'; (5) burden: How much effort do you think you need to put in for the tDCS sessions?'. Responses were rated on a 7-point anchored Likert scale, ranging from e.g. "very acceptable" to "very unacceptable", with the opportunity for open-ended responses (Table 1). Responses were acquired at baseline, 6-week end of treatment and at the 6-month follow up.

At the end of treatment and at follow up, the acceptability questionnaire consisted of the same questions written in the past tense, with

Table 1
Acceptability questionnaire and responses at baseline (n = 26), at the end of treatment (n = 24) and at 6-month follow up (n = 18). Italics represent post-treatment phrasing.

Question	Median (IQR)	Likert Ratings						
		1	2	3	4	5	6	7
How acceptable do *(did)* you consider the tDCS sessions to be?		Very unacceptable	Quite unacceptable	Unacceptable	Neither	Acceptable	Quite acceptable	Very acceptable
Baseline	7 (1)	1 (3.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	11 (42.3%)	14 (53.8%)
After 6 weeks treatment	7 (1)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (25%)	18 (75%)
6 months follow up	7 (1)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (27.8%)	12 (66.7%)
How helpful do you think the tDCS sessions may be *(were)* for improving your depressive symptoms?		Very unhelpful	Quite unhelpful	Bit unhelpful	Neither	Bit helpful	Quite helpful	**Very helpful**
Baseline	6 (1)	0 (0%)	0 (0%)	1 (3.8%)	1 (3.8%)	6 (23.1%)	14 (53.8%)	4 (15.4%)
After 6 weeks treatment	6 (2)	0 (0%)	0 (0%)	0 (0%)	2 (8.3%)	6 (25%)	7 (29.2%)	9 (37.5%)
6 months follow up	6.5 (1)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (16.7%)	6 (33.3%)	9 (50%)
How likely do you think that there will be negative side effects from the tDCS sessions?*/How were you bothered by any negative side effects from the tDCS sessions?*		Very unlikely/ Very much unaffected	Quite unlikely/ Quite unaffected	Bit unlikely/Bit unaffected	Neither	Bit likely/ Bit affected	Quite likely/ Quite affected	**Very likely/ Very *affected***
Baseline	3 (2)	2 (7.7%)	7 (26.9%)	6 (23.1%)	5 (19.2%)	6 (23.1%)	0 (0%)	0 (0%)
After 6 weeks treatment	2 (4)	7 (29.2%)	6 (25%)	0 (0%)	2 (8.3%)	7 (29.2%)	1 (4.2%)	1 (4.2%)
6 months follow up	1.5 (4)	9 (50%)	4 (22.2%)	0 (0%)	0 (0%)	5 (27.8%)	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**
Baseline	7 (1)	0 (0%)	0 (0%)	0 (0%)	3 (11.5%)	1 (3.8%)	7 (26.9)	15 (57.7)
After 6 weeks treatment	7 (1)	0 (0%)	0 (0%)	0 (0%)	3 (12.5%)	1(4.2%)	4(16.7%)	16 (66.7%)
6 months follow up	7 (2)	0 (0%)	0 (0%)	0 (0%)	4 (22.2%)	0 (0%)	2 (11.1%)	12 (66.7%)
How much effort do you think you need *(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**
Baseline	3 (2)	2 (7.7%)	9 (34.6%)	4 (15.4%)	7 (26.9%)	1 (3.8%)	2 (7.7%)	1 (3.8%)
After 6 weeks treatment	3 (3)	1 (4.2%)	5 (20.8%)	7 (29.2%)	5 (20.8%)	0 (0%)	2 (8.3%)	4 (16.7%)
6 months follow up	3 (1)	0 (0%)	3 (16.7%)	7 (38.9%)	4 (22.2%)	1 (5.6%)	1 (5.6%)	2 (11.1%)
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**
After 6 weeks treatment	6 (1)	0 (0%)	0 (0%)	0 (0%)	1 (4.2%)	9 (37.5%)	9 (37.5%)	5 (20.8%)
6 months follow up	7 (1)	0 (0%)	0 (0%)	0 (0%)	1 (5.6%)	1 (5.6%)	6 (33.3%)	10 (55.6%)

the addition of a sixth question: (6) affective attitude: 'Would you recommend the tDCS sessions to others?', and questions related to the study design: (7) 'Please explain, in your view, what were the most successful parts of the study?'; (8) 'Please explain in your view what were the least successful parts of the study?'; (9) 'Are there any ways in which the study can be improved?'; (10) 'Do you have any other comments?' Participants completed the questionnaires in writing or in a video recorded semi-structured interview conducted via Microsoft Teams.

2.5. Neuropsychological assessments

IQ was evaluated with Weschler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) in person or Ammons Quick Test (Ammons and Ammons, 1962) by video call. Neuropsychological functioning was assessed at baseline and after sessions 1, 10 and 21, using the Symbol Digit Modalities Test (SDMT) (Smith, 1991), to assess psychomotor processing speed and visuospatial attention, and the Rey Auditory Veral Learning Test (RAVLT) (Rey, 1964) to assess memory and verbal learning. Different versions of each test were used at each session and the administration order was counterbalanced.

2.6. Statistical analysis

An intention to treat analysis was completed, using a last observation carried forward (LOCF) method for missing data on clinical assessments. Four within-subject ANOVAS were conducted, with HAMD, HAMA, PHQ-9 and SDS total scores were the dependant variables and assessment time-point was the within-subjects factor, with four levels including baseline ($t0$), end of treatment period ($t1$), 3-month follow-up ($t2$) and 6-month follow-up ($t3$). Statistical analyses were conducted using IBM SPSS Statistics for MacOS, version 26.0. All analyses were two tailed and a significance value of $p = 0.05$ was set. Greenhouse-Geisser correction was applied if Mauchley's assumption of sphericity was violated. An analysis was also conducted for participants who completed the course of treatment and both follow up sessions. Post hoc pairwise comparisons with Bonferroni corrections were conducted. Neuropsychological test scores were analysed with within-subject ANCOVA,

examining a main effect of time with baseline HAMD scores as a covariate. For the acceptability questionnaire, median and interquartile range were calculated at each time point for each response. Nonparametric Friedman's ANOVA was performed to assess the repeated measures for each response for participants with data at all three timepoints (n = 18), and nonparametric Wilcoxon signed-rank test was used to assess significance given the Likert scale, uncertain differences between anchors, and small range of response choices.

3. Results

3.1. Participants

26 MDD participants were enrolled (19 women), mean age 40.9 ± 14.2 years, mean HAMD 19.12 ± 2.12 (Table 2). Mean duration of the current episode was 17.0 ± 11.4 weeks. 12 participants were taking antidepressant medication, range 1 week–10 years prior to starting the study. 13 participants had online CBT (Living Life to the Full), and 1 participant had telephone CBT. 92.8% participants (n = 24) completed the 6-week course of treatment, mean number of tDCS sessions 19.8 ± 1.6 (range 15–21). One participant declined the follow-up sessions and was not included in the completers analysis. In person sessions using the Neuroelectrics device was stopped for 2 participants due to the Covid-19 pandemic, and remote sessions could not continue for one participant due to a broken device, but all participants had completed at least 15 sessions. One participant discontinued after 3 sessions due to physical health and one participant after 12 sessions for personal reasons. Five participants continued with tDCS treatment on their own during the 6-month follow up period, 4 continuing twice weekly sessions and 1 reporting occasional use.

3.2. Clinical assessments

For all four time points (weeks 0, 6, and months 3, 6), 88.5% of participants (n = 23) completed clinical assessments at all time points in the completers analysis. Data was missing for 7.7% of participants (n = 2) at the end of treatment (week 6) and 11.5% (n = 3) at 3- and 6- month follow up.

At week 6, mean HAMD score was 5.33 ± 2.33, in which 22 participants (91.7%) show a clinical response and 21 participants (87.5%) achieved clinical remission. At the 3-month follow up, mean HAMD score was 5.65 ± 3.02, clinical response was 20 out of 23 participants (87.0%) and clinical remission was 18 out of 23 participants (78.2%). At the 6-month follow up, mean HAMD score was 5.43 ± 2.73, clinical response was 21 out of 23 participants (91.3%) and remission was 17 out of 23 participants (73.9%) (Fig. 2). Four participants (16.7%) showed an early response following 2 weeks of treatment (10 tDCS sessions); 3 participants were in remission (12.5%). Significant clinical improvements from baseline were maintained at the 6-month follow up in the intention to treat analysis (Table 3) as well as completers analysis (Table 4).

HAMA, PHQ-9 and SDS scores showed significant improvements from baseline which were maintained from the end of the trial to the 6-month follow up (Table 3, Table 4). Mean HAMA score at baseline was 15.13 + 1.70 (range = 12–19), reflecting mild to moderate severity of anxiety. Following treatment, the mean score was 6.17 ± 2.86 which was maintained at 6 months (Fig. 3). Mean PHQ-9 score at baseline was 16.04 + 3.81, which improved following treatment (mean 9.00 + 4.28) and was maintained at 6 months (mean 7.8 + 4.17) follow up (Fig. 4). SDS ratings of functional impairment were high at baseline (mean 19.09 + 5.57), in which the maximum score is 30. Functional impairment was significantly improved at the end of treatment (mean 9.57 + 6.86) and maintained at 6 months (mean 11.85 + 8.15) (Fig. 5).

Table 2
Mean baseline demographic and clinical characteristics of MDD participants.

Total number (female)	26 (19)
Age (years)	40.85 (14.16)
Age range (years)	19–73
Age of onset (years)	22.3 (8.8)
Years of education	15.38 (2.33)
IQ	101.04 (8.43)
Duration of illness (years)	19.36 (12.47)
Duration of current episode (weeks) (range)	28.87 (32.96) (8–156)
Previous number of episodes	8 (8.45)
HAMD	19.12 (2.12)
HAMA	15.19 (1.7)
PHQ-9	16.19 (4.08)

Mean values are presented with standard deviation in parenthesis.

3.3. Safety, tolerability and acceptability

The most common side effects were skin redness, tingling, itching or mild burning sensation and headache (Supplementary Materials Table 1). 84.9% of reports were rated as mild, 14.5% were rated as moderate, and 0.6% were rated as severe, which were for sleepiness (2 reports) and for a positive change in mood (1 report). There were no episodes of hypomania or mania as measured by the YMRS.

Acceptability was endorsed as being "very acceptable" at each timepoint with no significant changes over time (t1 Mdn = 7, IQR = 1; t2 Mdn = 7, IQR = 1; t3 Mdn = 7, IQR = 1) (X^2_F (2) = 2.0, p = 0.368). Ethicality remained high at "very ethical" with no significant changes over time (t1 Mdn = 7, IQR = 1, t2 Mdn = 7, IQR = 1, t3 Mdn = 7, IQR = 2) (X^2_F (2) = 071, p = 0.965). The effort required remained consistent at "little bit more than usual" with no significant changes over time (t1 Mdn = 3, IQR = 2, t2 Mdn = 3, IQR = 3, t3 Mdn = 3, IQR = 1) (X^2_F (2) = 3.796, p = 0.150).

There was a significant increase in endorsements from "would recommend" tDCS at the end of treatment to "would strongly recommend" at follow up (t2 Mdn = 6, IQR = 1; t3 Mdn = 7, IQR = 1; T = 4.5, $p < 0.01$) with a moderate effect size (r = −0.44). 20.8% of participants chose "would very strongly recommend" tDCS which increased to 55.6% at follow up (Fig. 1). Ratings for perceived effectiveness showed an increase from "quite helpful" at baseline to "quite helpful"/"very helpful" at follow up, which approached significance (t1: Mdn = 6, IQR = 1, t2; Mdn = 6, IQR = 2, t3; Mdn = 6.5, IQR = 1) (X^2_F (2) = 5.42, p = 0.067). The impact of side effects showed a decrease from being "a bit unlikely" at baseline to being "very much unaffected"/"quite unaffected" at follow up, which approached significance (t1; Mdn = 3., IQR = 2, t2; Mdn = 2, IQR = 4, t3; Mdn = 1.5, IQR = 4) (X^2_F (2) = 5.48, p = 0.065).

3.4. Neuropsychological assessments

No significant changes in performance were observed in SDMT or AVLT following the initial tDCS session, at 10 sessions, or at the end of treatment (Supplementary Material Table 2). Data from one participant was not included in the SDMT analysis as they were unable to follow the task instructions.

4. Discussion

Home-based tDCS with real-time remote supervision was associated with significant clinical improvements, which were maintained over a 6-month follow up. There was high participant retention, high acceptability for the treatment, and adverse effects were transient and mild. Significant improvements were also observed in anxiety, self-reported depressive symptoms and in interpersonal, social and work functioning. The high rates of remission were maintained at 6 months, reflecting the long term effects of the treatment, and participants reported a noticeable impact in their lives. While the present is a home-based study, participants had been experiencing a depressive episode of at least a moderate severity for an average of 5 months and the

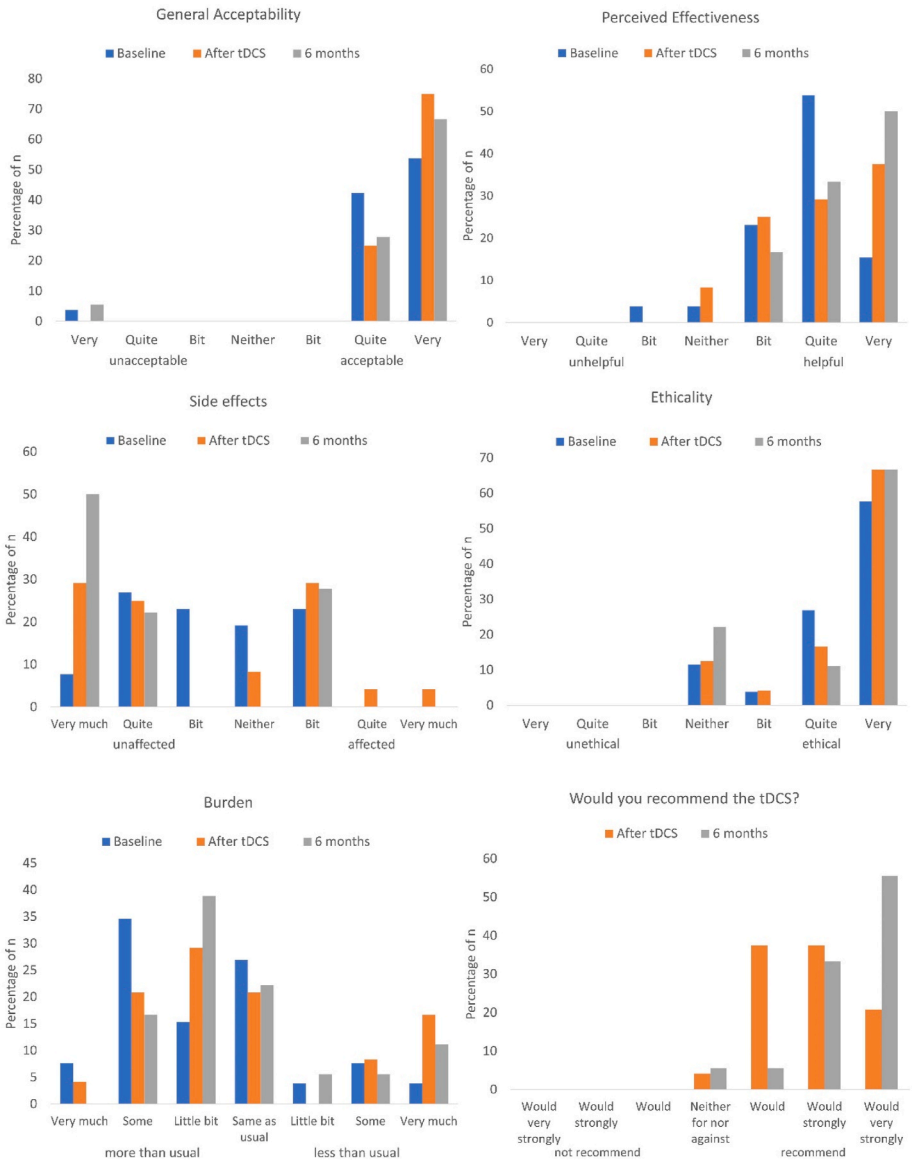

Fig. 1. Percentage of participants who endorsed each response in the acceptability questionnaire.

majority had a history of multiple previous episodes.

tDCS parameters were based on meta-analyses which demonstrated that treatment effects are most evident at 2 mA current of 30 min stimulus duration for at least 20 sessions in recurrent MDD (Brunoni et al., 2016b; Meron et al., 2015; Mutz et al., 2018). While there is no firm consensus on the optimal tDCS dosage, meta-analyses indicate that increased session numbers may be associated with improved clinical outcomes (Brunoni et al., 2016b; Moffa et al., 2020; Shiozawa et al., 2014). tDCS and rTMS have demonstrated efficacy in treating anxiety disorders (Matza et al., 2010; Vergallito et al., 2021), and we observed a further long term maintenance of the improvements in the present study.

In the present study, participants had a concurrent treatment, which included online CBT, while larger treatment effects have been observed for tDCS as a stand-alone treatment (Brunoni et al., 2016b; Meron et al., 2015).

A significant benefit of a home-based protocol is the flexibility to have regular treatment sessions at a suitable time. In the present study, a research team member was present, and participants were asked to sit quietly during each session. The presence of an observer is a unique experience which could have provided additional treatment effects, which may have contributed to the high rates of symptom improvement (Papoutsi and Fu, 2021).

The rate of attrition was 7.7%, which appears to be lower than clinic-based studies with rates of 10.1% (Brunoni et al., 2016b) and 14.7% (Moffa et al., 2020) and lower than rates for pharmacological and psychological therapies, which range from 11 to 15% within 8 weeks (Amick et al., 2015; DeRubeis et al., 2005). Most participants had experienced skin redness after tDCS at some point during the treatment period, although they were generally rated as being mild. Having a research team member present allowed for detailed safety monitoring and clinical assessments at each session. Patients may have difficulty in managing side effects adequately without regular supervision, which could result in worsening adverse effects and in turn discontinuation. Monitoring of daily side effects through completion of an online entry though might be sufficient (Alonzo et al., 2019).

Overall acceptability was high prior to the start of treatment and remained high at the end of treatment and at the 6-month follow up, indicating that anticipated beliefs about the treatment were experienced. The low attrition rate seemed also to reflect the high overall acceptability. Perceived effectiveness was anticipated to be “quite helpful” and was then experienced to be “quite helpful” immediately

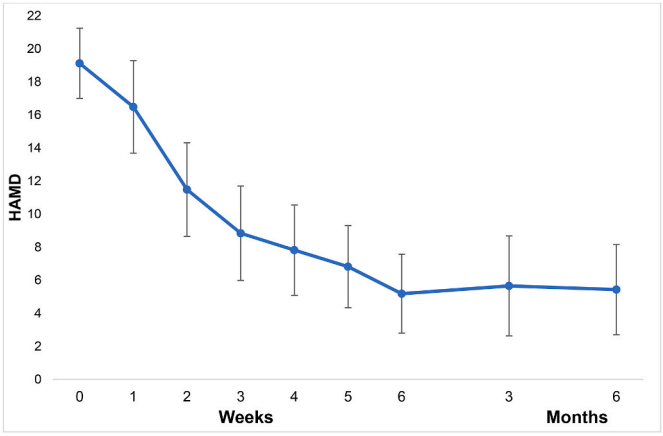

Fig. 2. Mean Hamilton Depression Rating Scale (HAMD) total scores in patients at every assessment time point from baseline to 6-month follow up, not including missing data. Error bars represent standard deviation. Number of participants, n = 26 at week 0, n = 25 at weeks 1–3, n = 22 at weeks 4–6, n = 23 at months 3 and 6.

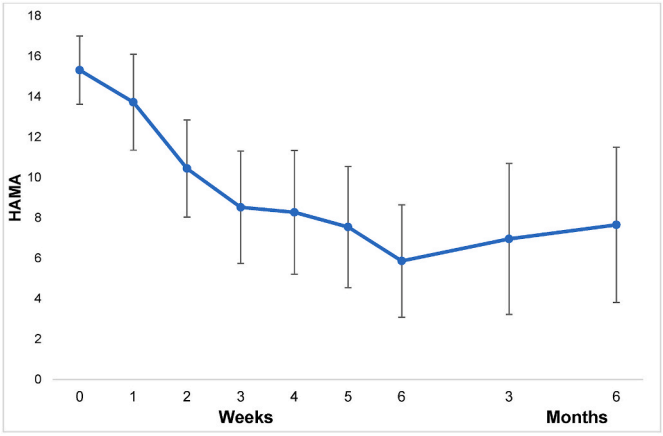

Fig. 3. Mean Hamilton Anxiety Rating Scale (HAMA) total scores in patients at every assessment time point from baseline to 6-month follow up, not including missing data. Error bars represent standard deviation. Number of participants, n = 26 at week 0, n = 25 at weeks 1–3, n = 22 at weeks 4–6, n = 23 at months 3 and 6.

Table 3
Clinical rating scale scores over course of treatment and at follow up, intention to treat analysis.

	Baseline	6 weeks	3 months	6 months	P-value
HAMD	19.12 (2.12)	5.92 (3.37)	6.12 (3.80)	5.92 (3.62)	*<0.001*
HAMA	15.31 (1.69)	6.81 (3.71)	7.50 (4.25)	8.12 (4.26)	*<0.001*
PHQ-9	16.12 (4.10)	9.35 (4.98)	8.15 (5.60)	8.48 (4.92)	*<0.001*
SDS	18.73 (5.42)	9.69 (6.75)	9.38 (6.30)	12.33 (7.79)	*<0.001*

Based on an intention to treat analysis, using last observation carried forward (n = 26). HAMD, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; PHQ-9, Patient Health Questionnaire-9; SDS, Sheehan Disability Scale. Parentheses represent standard deviation.

Table 4
Clinical rating scale scores over course of treatment and at follow up, completers analysis.

	Baseline	6 weeks	3 months	6 months	P-value
HAMD	19.3 (2.14)	5.44 (2.33)	5.65 (3.02)	5.43 (2.73)	*<0.001*
HAMA	15.13 (1.7)	6.17 (2.86)	6.96 (3.73)	7.65 (3.85)	*<0.001*
PHQ-9	16.04 (3.81)	9.00 (4.28)	7.65 (4.95)	7.80 (4.17)	*<0.001*
SDS	19.09 (5.57)	9.57 (6.86)	8.78 (6.35)	11.85 (8.15)	*<0.001*

Data from participants who completed treatment and follow up (n = 23). HAMD, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; PHQ-9, Patient Health Questionnaire-9; SDS, Sheehan Disability Scale. Parentheses represent standard deviation.

following the course of treatment, increasing to "very helpful" at follow up. High perceived effectiveness paralleled the high response and remission rates in the present study. Expecting that a treatment will be beneficial can enhance treatment effects (Bystad et al., 2015; Krell et al., 2004). Furthermore, the increase in perceived effectiveness ratings at the 6-month follow up reflected greater certainty in beliefs about effectiveness, likely due to the long term sustained improvements. Moreover, there was a significant increase in personal endorsement from "would strongly recommend" at the end of the treatment to "would very strongly recommend" at follow up.

There was a wide range of ratings for side effects, with equal numbers endorsing being "unaffected" and being "affected". Acceptability has usually been measured by tolerability and adverse effect attrition (Brunoni et al., 2016a), yet being affected by expected side effects did not appear to impact on acceptability ratings. The full range of responses were selected to the question about effort, ranging from

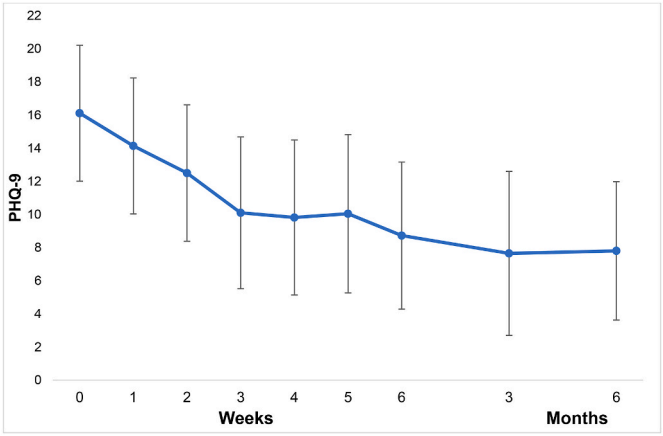

Fig. 4. Mean Patient Health Questionnaire-9 (PHQ-9) total scores in patients at every assessment time point from baseline to 6-month follow up, not including missing data. Error bars represent standard deviation. Number of participants, n = 26 at week 0, n = 25 at weeks 1–3, n = 22 at weeks 4–6, n = 23 at months 3 and 6.

"very much more [effort] than usual" to "very much less [effort] than usual". Alongside patient beliefs about a treatment, self-efficacy and ease of administration can reduce the likelihood of nonadherence to treatment (Bandura, 1978; Horne et al., 2013) and should be considered for future community-based tDCS protocols. Ratings for ethicality remained high, ranging from "neither ethical or unethical" to "very ethical" with the majority of participants rating the tDCS treatment as "very ethical", perhaps reflecting participants' informed consent to take part in the study and might suggest that the information they had received about treatment was a good representation of the treatment.

In the present study, pregnant and breastfeeding women had not been included, although rTMS in both pregnant women and breastfeeding women has not shown any additional side effects or harm compared to other adult populations (Al-Shamali et al., 2022; Cole et al., 2019). In fact, non-invasive brain stimulation, including tDCS could potentially be an important alternative treatment in peripartum depression (Cole et al., 2019; Pacheco et al., 2021). Future studies should consider researching tDCS within these populations and carefully consider if these exclusion criteria are necessary.

Limitations of the present study include the lack of a sham tDCS treatment arm as all participants received active tDCS treatment in an

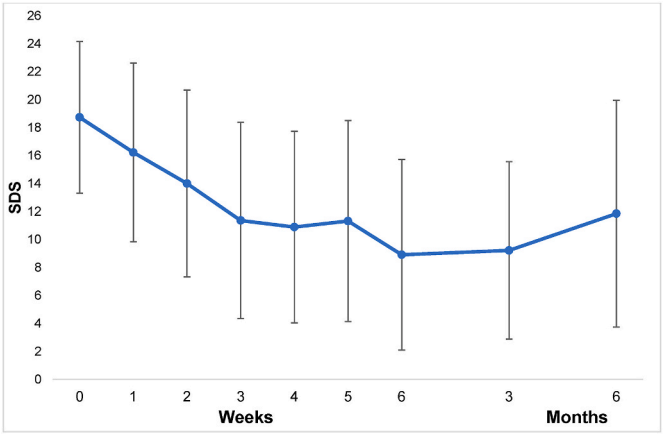

Fig. 5. Mean Sheehan Disability Scale (SDS) total scores in patients at every assessment time point from baseline to 6-month follow up, not including missing data. Error bars represent standard deviation. Number of participants, n = 26 at week 0, n = 25 at weeks 1–3, n = 22 at weeks 4–6, n = 23 at months 3 and 6.

open-label design. Moreover, having real-time supervision for each session likely contributed to symptom improvement. As the protocol was not designed to establish efficacy, the findings should be considered as preliminary, and a placebo sham treatment control group is required to investigate efficacy. The acceptability questionnaire that we developed was based on Sekhon et al. (2017) framework to assess participant views but there we had not measured validity or reliability prior to using the questionnaire, which is required in the early stages of a technology intervention cycle (International Test Commission (ITC), 2014). Further feasibility assessment should include access to the technology required for app-based devices as lower socioeconomic status is associated with higher rates of depression and reduced life expectancy, but internet non-usage is higher amongst people who are economically inactive or on a low income (Lorant et al., 2003; Strategic Review of Health Inequalities in England post-2010, 2010; Stringhini et al., 2017). It is important to consider potential barriers when assessing access to treatment.

In summary, home-based tDCS with real-time remote supervision was associated with significant improvements in depressive symptoms in moderate to severe severity of MDD, which were maintained at the long term follow up. The treatment showed high acceptability, tolerability and safety. Home-based tDCS is a potential novel treatment in first-episode MDD. As all participants had received active tDCS with real-time supervision, large-scale randomised sham-controlled trials are required to investigate efficacy.

CRediT author statement

Rachel Woodham: Data Curation, Investigation, Formal Analysis, Writing- Original draft preparation, Writing- Reviewing and Editing; **Rachael Rimmer:** Data Curation, Investigation, Writing- Reviewing and Editing; **Allan Young:** Methodology, Writing- Reviewing and Editing. **Cynthia Fu:** Conceptualization, Methodology, Funding Acquisition, Project Administration, Supervision, Writing- Original draft preparation, Writing- Reviewing and Editing.

Data statement

Anonymised data will be made available on request.

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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.2022.07.026.

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