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# Self-Administered "Flow" Transcranial Direct Current Stimulation (tDCS) Depression Treatment in a Crisis Resolution & Home Treatment (CRT) Service: Functioning, and Health-Related Quality of Life Outcomes

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## Abstract

Background: Transcranial direct current stimulation (tDCS) has research evidence that it can reduce symptoms of depression. Flow FL-100 is a transcranial direct current stimulation (tDCS) device self-administered by a patient at home in combination with a software application that delivers wellbeing behaviour therapy training. Purpose/aim: The purpose of this study was to investigate if Flow can be introduced to a Crisis Resolution & Home Treatment (CRT) service and the impact of Flow in treating depression. The study addresses the questions: 1) "what are the depression reliable improvement and remission rates?" and 2) "can Flow significantly reduce depressive symptoms and improve real world functioning (every-day, social and occupational functioning) and health-related quality of life?". Methods: An open-label patient cohort design with no control group. Pre-intervention and 6-week follow-up intervention assessments using the participant self-report measures: Patient Health Questionnaire (PHQ-9), Work and Social Adjustment Scale (WSAS), and EuroQol five-dimension (EQ-5D-5L). Participants were 49 CRT patients, 19 males and 30 females, with an age range of 20 to 66 years, and average age of 42 years. Results: PHQ-9 reliable improvement and remission rates were 57.1% and 14.3%. PHQ-9 scores significantly improved, from 23.1 (*SD* 3.44) to 14.8 (*SD* 6.82) at 6 weeks, with a large effect size. PHQ-9 suicide/self-harm related question significantly improved from 2.51 (*SD* 0.77) to 1.08 (*SD* 1.17), with a large effect size. WSAS scores significantly improved, from 33.6 (*SD* 5.22) to 21.9 (*SD* 10.82) at 6 weeks, with a large effect size. EQ-5D-5L results

showed significant improvements in the health index score, global assessment of health EQ-VAS from 34.2 (22.26) to 51.6 (24.95), and three EQ-5D-5L dimensions ("self-care", "usual activity", and "anxiety/depression"). Conclusion: A CRT service effectively integrated Flow tDCS treatment. Flow was beneficial in terms of improving functioning and quality of life and reducing depression symptoms and thoughts of suicide/self-harm. Flow FL100 tDCS and wellbeing behaviour therapy training could be offered through all CRT services to treat depression, reduce thoughts of suicide/self-harm, enable better functioning, and improve quality of life.

## Keywords

Depression, Quality of Life, Functioning, Transcranial Direct Current Stimulation (tDCS)

## 1. Introduction

Globally depression causes 7.5% of all years lived with disability, the largest contributor to disability and is defined as experiencing a low mood and loss of pleasure or interest in activities, and can include symptoms such as poor concentration, feelings of low self-worth, hopelessness, suicidality, disrupted sleep, and fatigue [1]. In Great Britain (GB) around one in six (16%) of the general population experience depression [2]. Depression symptoms can have a severe negative impact on everyday functioning and quality of life [1] [3] and depression is the most common mental illness factor determinant of death by suicide [4]. The mortality risk for suicide among patients with major depression has been calculated to be 20 times that where major depression is not present [5]. Severe mental illnesses (SMI) are psychological problems causing severe functional and occupational impairment, and the prevalence of depression in people experiencing SMI is higher than in the general population [6].

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation by weak electrical currents (0.5 - 2.5 mA) and has been used in addressing various mental illnesses [7]. Electrode placement for treating depression typically involves the anode over the left dorsolateral prefrontal cortex (DLPFC) (F3) and cathode over the right DLPFC (F4) [8]. tDCS mechanisms of action include significant gray matter increases in brain regions functionally connected with the stimulation target, including the bilateral DLPFC, bilateral posterior cingulate cortex, subgenual anterior cingulate cortex, the right hippocampus, thalamus and left caudate brain regions; tDCS leads to neurostructural changes at predetermined brain targets in depression, and plasticity effects may propagate over brain networks [9].

Meta-analyses of the results of randomised sham-controlled trials show tDCS can significantly improve depressive symptoms and clinical response, with remission being significantly better than placebo sham stimulation [10]-[13]. tDCS is

effective as a standalone treatment or in combination with other anti-depression treatments [13]. tDCS is safe [13] and generally reported by patients as acceptable and well-tolerated, with mild and transient physical sensations that usually do not prevent use: burning sensations (16.2%), skin redness (12.3%), scalp pain (10.1%), itching (6.7%), and tingling (6.3%) [7] [14].

Treatment resistant depression (TRD) can be defined as no response to at least two consecutive courses of antidepressant medication [15]. A systematic review of evidence of tDCS for TRD found favourable evidence that tDCS is clinically effective as measured by response, symptom improvement and remission in comparison to sham treatment [16].

"Flow" combines tDCS (delivered by Flow FL-100 device) and software application wellbeing behaviour training (physical exercise, nutrition, mindfulness, sleep, and choosing actions). A randomised sham-controlled trial of Flow FL-100 in major depressive disorder (MDD) found significant improvement in depression symptoms following 10 weeks of treatment, with a clinical response of 58.3% and a remission rate of 44.9% [17]. A "real world" health service open-label primary care patient study of Flow found depression reliable improvement and remission rates of 58.1% and 32.3%, and significant improvement in depression, everyday functioning, and quality of life [18] [19]. Qualitative studies undertaken on experience of Flow found most patients reported that Flow improved depression symptoms, was acceptable, and that they would recommend it to others [20]-[22].

This open-label patient cohort study investigates if Flow FL-100 tDCS and behaviour change wellbeing training can be successfully introduced to the treatments offered by a Crisis Resolution & Home Treatment (CRT) service. It assesses the impact of Flow in treating depression for people with SMI. The study addresses the questions: "what are the depression reliable improvement and remission rates?" and "can Flow significantly reduce depressive symptoms and improve real world functioning (every-day, social and occupational functioning) and health-related quality of life?"

## 2. Methods

### 2.1. Design

Open-label patient cohort design with no control group.

### 2.2. Approval

The project was undertaken from January 2024 to September 2024. This was approved by the WeImproveQ working group and ratified by the NHS Trust's Clinical Reference Group. Reference name "Flow-CRT". The study was undertaken in accordance with the Declaration of Helsinki.

### 2.3. Setting

The sample was recruited from people using a Crisis Resolution & Home Treatment (CRT) service within the United Kingdom's (UK) National Health Service (NHS).

The service is for adults aged 18 and over who, without this service, would require hospital admission to an acute mental health ward due to a mental health crisis which impacts on the person's ability to cope with day-to-day activities. CRT accepts all mental health diagnoses with the exception of where drug and alcohol abuse or dementia is the primary diagnosis. CRT also facilitates hospital transfer back into the community to enhance recovery and reduce the length of hospital admissions. CRT provides care co-ordination to enable recovery, appropriate management of acute relapse, short-term interventions, signposting to other appropriate services, and decisions on in-patient admission. A patient has access to a consultant psychiatrist and a named key worker. flow Neuroscience AB (manufacturer of Flow) provided CRT staff with training.

## 2.4. Intervention

Flow FL-100 is a Conformite Europeene Européenne (CE) marked Class IIa medical device for the treatment of major depressive disorder (MDD) and has United States (US) Food and Drug Administration (FDA) "Breakthrough Device" designation, indicating its potential to provide effective treatment. Flow can be purchased directly by anyone via the manufacturer's website in the European Union and other European countries. Flow has been used by >15,000 users in UK/EU and is offered by >70 private healthcare institutions.

In the treatment protocol, patients remain awake and self-administers at home five sessions per week for the first three weeks and then three sessions per week for the following three weeks: 24 sessions, with a maximum of one 30-minute session per day. After the initial six-week period, patients can choose to self-administer up to 3 sessions per week for as long as they choose.

Flow treatment was concurrent with any current treatment, e.g., antidepressant medication, face-to-face psychotherapy, or any online psychotherapy. The anode was positioned over the left dorsolateral prefrontal cortex (DLPFC) (F3 on the international 10/20 EEG system) and the cathode over the right DLPFC (F4); stimulation is 2 mA for 30 min. On the Flow mobile phone software app, seven brief (around 20 minutes, pace of completion chosen by user) healthy lifestyle behaviour therapy training sessions are available for users to optionally engage with. These provide information about the links between behaviour and wellbeing and how to take actions to improve wellbeing and reduce depressive symptoms. They are titled: "the basics", "choosing your actions", "mindfulness meditation", "exercise for your brain", "the anti-depression diet", "therapeutic sleep", and "looking back and planning ahead".

The Flow mobile phone software app is used to control the Bluetooth-connected Flow FL-100 tDCS headset via the user's smartphone. Flow also provides depression symptom level tracking that enables users to monitor their progress/symptoms. This is done by the completion of the nine-question Montgomery–Åsberg Depression Rating Scale Self-report (MADRS-S) [23] via the user's smartphone prior to a tDCS session. Flow also provides an integrated platform for

the patient's healthcare provider, with the ability to monitor patients, and customise protocols remotely. A patient can decide whether or not to allow their healthcare provider access to this information.

### 2.5. Inclusion/exclusion criteria

The inclusion criterion was age 18 or over, and PHQ score of 14 or higher (an exception was having a score above 5 but below 14 if CRT considered that a patient could benefit from Flow).

Exclusion criteria:

- Defect in the neurocranium and/or implant in the skull.
- Active implanted medical device, e.g., a pacemaker, implanted hearing aids, any implanted metallic or electronic device.
- History of manic/hypomanic episodes.
- History of a serious neurological condition, e.g., stroke, epilepsy, seizures, or severe migraine.
- Being pregnant.

### 2.6. Procedure

Patients were selected if they met the inclusion/exclusion criteria and were provided with information about the treatment and evaluation. Participants stayed on the same medication and continued any current psychological interventions they were undertaking. Informed consent was obtained by their mental health practitioner prior to beginning treatment. Following informed consent, demographic, treatment, and health information was extracted from clinical records containing routinely collected data. Participants could withdraw consent or stop treatment at any point without the need to provide a reason. Following informed consent, participants were given the Flow device and instructions, and completed three self-report measures. Participants were informed about Flow Neuroscience AB's website which provides information, training on use, and email support. Between weeks one and two, patients received a phone call from a mental health practitioner to check on usage and any concerns. Follow-up self-report measures were collected after six weeks of treatment. Protocol compliance was monitored using the clinical portal web-based dashboard, which included the patient's daily use of Flow and the change in depression scores.

### 2.7. Measures

The Work and Social Adjustment Scale (WSAS) is a self-report measure of functional impairment attributable to an identified problem (e.g., depression) [24]. The five questions on impairment to work, home management, social leisure, private leisure, and close social relationships each scored zero (not at all) to eight (very severely). The WSAS is a reliable, valid, and sensitive to change outcome measure [25]. Severe functional impairment is 20 and over and scores below 10 are associated with subclinical populations; a score of 9 or below is the clinical

(recovery) cut off [26].

Patient Health Questionnaire-9 (PHQ-9) is a self-report measure of depression; it has good sensitivity and specificity for major depression as well as good internal consistency; scores for depression severity are: 0 - 4 none, 5 - 9 mild, 10 - 14 moderate, 15 - 19 moderately severe, and 20 - 27 severe [27]. Remission is defined as a score of 9 or less, and reliable improvement is a drop of 6 points [28]. A score of 9 or below is the clinical remission cut off. Question nine states: "Thoughts that you would be better off dead, or of hurting yourself?"

European Quality of Life Five Dimension (EQ-5D-5L) [29] [30] is a 5-item question and visual analogue scale (VAS) self-rated measure of health-related quality of life and overall health status developed by EuroQol group to provide a simple, standardised measure for a clinical appraisal [29]. It comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each of which is measured within five levels (no problems, slight problems, moderate problems, severe problems, and extreme problems). The digits from the five dimensions are combined to create a five-digit number measuring holistic health state. Each health state can be assigned an index score based on societal preference weights for the health state. Health state index scores 1 = the value of full health, with higher scores indicating higher health utility. The EQ VAS is a subjective measure of a participant's current health, ranging from 0 (worst health imaginable) to 100 (best health imaginable). The EQ-5D-5L has good construct validity and is sensitive to change in patients with depression and anxiety [31]. The EQ-5D-5L is a validated measure of health status widely used in national health surveys worldwide and in clinical trials of health interventions [32] [33], and EQ-5D is recommended by the UK's National Institute for Health and Care Excellence (NICE) to estimate health state utility weights for quality-adjusted life year (QALYs) [34].

### 2.8. Analysis

Data were analysed using the statistical software package SPSS Statistics 26.

## 3. Results

### 3.1. Participant Characteristics

Forty-nine participants completed a six-week Flow treatment. Their average age was 41.84 years (age range from 20 to 66 years). 30 (61.22%) were females and 19 (38.78%) were males. Participants' mean baseline scores were in the highest "severe" range for depression. Baseline EQ-5D-5L crosswalk data values indicated participants had a low average holistic health index and EQ VAS score compared to the general population. Numbers currently prescribed antidepressants was 45 (91.84%). Forty-five participants had information on self-harm, out of these 29 (64.44%) did not self-harm and 16 (35.56%) self-harmed, the majority of these reported cutting themselves (62.5%). See **Table 1** and **Table 2**.

**Table 1.** Baseline characteristics (n = 39).

| Variable | Mean (SD) |
|---|---|
| PHQ-9 | 23.10 (3.44) |
| WSAS | 33.61 (5.22) |
| EQ Health Index | .25 (.25) |
| EQ VAS | 34.23 (22.26) |

**Table 2.** Numbers for each type of antidepressant.

| Antidepressant | Number of participants prescribed this antidepressant |
|---|---|
| Citalopram | 1 (2.22%) |
| Clomipramine | 2 (4.44%) |
| Duloxetine | 8 (17.78%) |
| Escitalopram | 2 (4.44%) |
| Fluoxetine | 4 (8.89%) |
| Mirtazapine | 15 (33.33%) |
| Olanzapine | 1 (2.22%) |
| Paroxetine | 2 (4.44%) |
| Sertraline | 5 (11.11%) |
| Trazadone | 1 (2.22%) |
| Venlafaxine | 9 (20%) |
| Vortioxetine | 8 (17.78%) |

### 3.2. PHQ-9

PHQ-9 scores significantly improved from 23.1 (*SD* 3.44) to 14.8 (*SD* 6.82) (decrease in PHQ-9 score of 8.33) at 6 weeks, $p < 0.001$, with large effect sizes (Cohen's d = 1.08). At follow-up seven participants (14.29%) experienced remission (a PHQ-9 score of 5 or less at post-intervention follow-up) and 28 participants (57.14%) reliable improvement (a reduction of 6 points or more on the PHQ-9 from baseline). PHQ-9 suicide/self-harm related questions significantly improved from 2.51 (SD 0.77) to 1.08 (SD 1.17), with a large effect size (1.38).

### 3.3. WSAS

WSAS scores significantly improved, from 33.6 (*SD* 5.22) to 21.9 (*SD* 10.82) (decrease in WSAS score of 11.73) at 6 weeks, with medium effect size (Cohen's d = 0.7).

### 3.4. EQ-5D-5L

There was a significant increase in the EQ VAS score of 17.33 ($p < 0.001$) from baseline to post-intervention follow-up. Table 3 contains data for each of the five dimensions, the mean health index and VAS at baseline and after the six-week

intervention. From baseline to week six, quality of life increased with an improvement of 0.26. Measured across ten years, this intervention adds 2.6 QALYs.

**Table 3.** Means and standard deviations within each dimension across time with corresponding mean variation, significance, and effect size.

| EQ-5D-5L Dimension | Baseline | Week 6 | *t* | *p* | *d* |
|---|---|---|---|---|---|
| | *M (SD)* | *M (SD)* | | | |
| Mobility | 1.67 (1.01) | 1.57 (1.04) | .962 | .341 | .137 |
| Self-care | 2.37 (1.20) | 1.76 (1.05) | 4.054 | < .001* | .579 |
| Usual activity | 3.37 (.99) | 2.59 (1.22) | 4.140 | < .001* | .591 |
| Pain/discomfort | 2.08 (1.34) | 2.08 (1.41) | 0.000 | 1.000 | .000 |
| Anxiety/depression | 4.61 (.73) | 3.35 (1.20) | 7.822 | < .001* | 1.12 |
| Health index score | .25 (.25) | .51 (.34) | -6.397 | < .001* | -.914 |
| EQ-VAS score | 34.22 (22.26) | 51.55 (25.00) | -4.244 | <0.001 | -0.606 |

*Significant at $p < 0.05$ level.

Data screening permitted the use of a paired-sample t-test to determine whether there was a statistically significant difference in participants' EQ dimensions, as well as their health index score and VAS at the 6-week data point. The improvement was statistically significant for three EQ dimensions ("usual activity", "self-care", and "anxiety/depression"), and for the overall health index score, with medium effect sizes.

## 4. Discussion

Flow delivered tDCS can be provided to patients by a CRT service, and when offered patients will choose to use Flow. Flow reduced impaired functioning, depression symptoms, and thoughts of suicide/self-harm, and increased health related quality of life in CRT patients with symptoms of depression. This supports the evidence of effectiveness of tDCS in reducing depression symptoms [10]-[13] [17].

The statistically significant improvements in the "ability to perform usual activity" and "self-care" dimensions were measured by the EQ-5D-5L, and impaired functioning was measured by the WSAS. This indicates the positive impact of Flow on self-management, mental health recovery, and real-world functioning, which are factors highly valued by people in their everyday lives. They can also increase resilience, sense of meaningfulness, and purpose in life [35].

A high average PHQ-9 baseline score (depression in the highest "severe" range) was seen in this study's participants, indicating the potential value of Flow for those with severe depression. Many of the participants in this study would meet the definition of TRD, this study's results add evidence to the potential value of tDCS in treating TRD [16]. In this study, tDCS was delivered to patients, most of whom were on antidepressants, and this combination can possibly enhance overall outcomes [13].

The participants in this study had high rates of self-harm, which is typical of people with SMI [36]. People who self-harm have high rates of depression [37] [38]. Depression is a predicting factor in suicide attempts in those with histories of self-harm [39]. Treating depression is particularly important for those self-harming, as self-harm increases the risk of suicide [40]. A systematic review and meta-analysis examining the efficacy of suicide and self-harm psychosocial interventions found interventions were no more effective than in control groups in reducing self-harm, suicidality, depression, hopelessness, or suicide attempts [41]. Meta-analyses of RCTs found that psychotropic medications to treat and prevent self-injurious thoughts and behaviours produce only small treatment effects [42], and there is no treatment effect on repetition of self-harm for newer generation antidepressants [43]. These findings highlight the need for effective self-harm treatment. tDCS at the right inferior frontal gyrus may have a positive influence on emotional regulation, *i.e.*, lower impulsiveness agitation and, by doing so, has the potential to decrease non-suicidal self-injury frequency [44]. The potential for tDCS to reduce depression and specifically suicidal and self-harm thoughts seen in this study indicates the potential value of using tDCS.

In this study, there was a relatively quick (six-week) improvement in depression symptoms, and another study showed Flow provided good rates of depression remission at three weeks [19]. Serotonin and norepinephrine reuptake inhibitors (SNRIs) and selective serotonin re-uptake inhibitors (SSRIs) antidepressants time course of response around 2 to 4 weeks to achieve significant benefits; but it may take longer to achieve most of the improvement [45]. Therefore, Flow might be considered as a treatment where a relatively quick relief of depression symptoms is required, of particular value in CRT patients to address or prevent a mental crisis which may lead to suicide attempt, self-harm, or acute mental health ward admission.

A systematic review and meta-analysis showed that tDCS plus SSRI antidepressant medication provided significant improvement in depression and achieved a significantly higher response rate than sham intervention, and that this was more effective than tDCS treatment alone [46]. This finding is important for clinical practice, as it indicates that patients should continue their existing prescribed SSRI antidepressant use during tDCS treatment, and that patients can start using both tDCS and SSRIs at the same time (Wang et al., 2021) [46]. The majority of patients in this current study were prescribed antidepressants.

For those who have failed to respond to antidepressant medication or psychotherapy or who find medication side effects intolerable, or factors related to psychotherapy unacceptable (e.g., waiting times, travel costs, time required, other commitments preventing attendance), Flow tDCS can be an alternative treatment option. The NHS "Mental Health and Wellbeing Plan" states: "We know there are limitations to the current treatment offer. More needs to be done… to diversify the range of treatments available" [47]. CRT service is well-placed to deliver Flow tDCS treatment as they provide patients with a named keyworker, access to a psychiatrist, and seeks to understand a patient's individual circumstances and provide

individualised support and treatment.

Not all participants experience remission or reliable change following the use of Flow. In a CRT patients are told they may need to try a number of antidepressant treatment options and a combination of treatments. A CRT service's active engagement with its patients enables it to prepare them for non-treatment response and ensure that they receive ongoing support, and access to other antidepressant treatments.

## 5. Limitations

There were several limitations of the study. There was no control group, a relatively small sample size, and the treatment with Flow tDCS was open-label and adjunct to any existing depression or other treatments or therapies. The sample was over-represented by females, and so the results are less generalisable to males. This study collected outcome measures after six weeks of treatment, with no later follow-up data collection; it is recommended that future studies employ additional follow-up data collection points: 12, 24 and 36 weeks. The participants were from a single UK county reducing generalisability; however, this county has the most ethnically diverse population in the UK outside of London.

## 6. Conclusions

Flow tDCS can be fully and effectively integrated into CRT depression treatment. CRTs are willing to offer, and their patients will choose to use Flow, providing evidence of the acceptability of and demand for Flow FL-100 delivered tDCS and software app behaviour change wellbeing training. Flow tDCS can be effective against depression symptoms when offered through a CRT for patients with depression symptoms. Treating depression symptoms, thoughts of self-harm and suicide, improving functioning and quality of life using tDCS in a CRT service may prevent mental health in-patient admission, reduce A&E attendance, and prevent the need for more costly transcranial magnetic stimulation (TMS) or electroconvulsive therapy (ECT) depression treatment; and, therefore, may reduce healthcare costs. Patient delivered antidepressant treatment at their home reduces burden on patients attending outpatient depression treatment options such as TMS or ECT.

There is a need to offer patients a wide choice of effective depression treatment options. This study's results support the use of Flow tDCS as a treatment option for people in a CRT service with symptoms of depression. More evidence is required on the long-term effectiveness of tDCS and the potential need for ongoing maintenance sessions to sustain benefits. Future studies could also look into the patient-experience of Flow tDCS for patients in CRT services through qualitative interviews.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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