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THE USABILITY OF ADD-ON TRANSCRANIAL DIRECT CURRENT STIMULATION IN MAINTENANCE NEUROMODULATION TREATMENTS – A CASE SERIES

ABSTRACT

***Background**: Electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS) are commonly used to treat treatment-resistant depression (TRD). Due to the large risk for relapses after acute treatment, maintenance ECT and rTMS are often needed. Their numbers are increasing, consuming the resources and possibly leading to increased waiting times for acute treatment. Therefore, it is important to study possible interventions to decrease the need for maintenance ECT and rTMS in depression. Add-on transcranial direct current stimulation (tDCS) is one option for this, but there are no previous studies on combining tDCS to maintenance ECT or rTMS treatment. **Objectives:** In this clinical case series, we describe a clinical development project aimed to investigate the usability and effects of add-on tDCS for depression patients receiving or fulfilling the indication for maintenance ECT or rTMS. **Methods:** Patients (n=12) with unipolar depression, without current acute suicidality or psychosis being treated with or fulfilling the indication for maintenance ECT or rTMS, were offered the possibility of tDCS in addition to or instead of the ongoing maintenance treatment. tDCS started with a 6 week (w) acute treatment, with control visits/phone calls at 1w, 3w and 6w from the start. The patients took 5-7 tDCS treatments per week at home. At 6w, tDCS was stopped or continued, with control visits/phone calls every 6w. We collected data from the medical records from baseline, 3w, 6w and 6-month check-ups. We analysed patients' adherence (whether they used tDCS), subjective view of the treatment, adverse effects, and if adding tDCS improved the clinical status, reduced the severity of symptoms and affected the frequency of rTMS or ECT maintenance treatment sessions. Due to small sample, no tests on statistical significance were done. **Results:** During the 6w acute tDCS treatment, mean BDI and GAD-7 scores decreased, and the majority of the patients benefitted from the treatment. There were minor side effects. During the 6-month follow-up, the number of both ECT and rTMS maintenance treatments decreased compared to the 6-month period before the intervention (ECT –1.8 sessions and rTMS –8 sessions). **Conclusions:** tDCS may be a potential treatment for decreasing the need for maintenance ECT or rTMS for TRD patients. More studies of longer duration, larger study population and with placebo control are needed to verify this. Furthermore, the cost-effectiveness of add-on tDCS needs to be studied.*

KEYWORDS: ECT, RTMS, TDCS, NEUROMODULATION, ADD-ON, ADJUNCTIVE TREATMENT, DEPRESSION, TREATMENT-RESISTANT DEPRESSION, TRD, TREATMENT, MAINTENANCE, RELAPSE

INTRODUCTION

Major depressive disorder, MDD, is the leading cause of disability and burden of disease in developed countries, with about 280 million people in the world suffering from depressive disorders (1). In Finland, the prevalence of depression (including MDD and dysthymia) is 5-7% (2). Pharmacological and psychosocial treatments are the first-line treatments for depression, but they have limited effectiveness, with even two-thirds of patients not experiencing sufficient benefit from antidepressant (AD) medication (3,4) The definition of treatment-resistant depression (TRD) varies but is most often described as failing two adequate antidepressant medication treatment courses (5). Numerous other ways to define TRD

have been suggested, such as the Maudsley staging method, where the treatment-resistance is staged based on three factors: the severity of the illness, the duration of the episode and the treatment(s) use. According to the Maudsley staging method, only one antidepressant medication trial can be sufficient to reach TRD (6). It has been estimated that over 100 million people worldwide and 6-55% of depression patients meet at least one definition for TRD (7). According to a Finnish cohort study conducted in 2004-2016, about 11% of patients with depression have TRD (8).

TRD leads to increased use of services, costs and suffering. Compared to non-treatment-resistant depression (non-TRD) the healthcare costs of TRD patients are nearly double (9), with outpatient service use 1.5-fold, inpatient service use 3-fold and loss of working days 2-fold (10). Furthermore, self-harming behaviour is over four times more common and mortality 17% to 23% higher (10,11). Clinical treatment-practice of depression in Finland is not adequate, as changes to treatment protocols are made slowly in clinical practice, with approximately eight months of treatment to reach the third treatment trial, thus, meeting the criteria for TRD. In addition, AD monotherapy is still the most common treatment even at the fifth line of treatment (8).

The strongest evidence for treating TRD is for ketamine, esketamine, adjunctive psychotherapy, electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS) (7). ECT requires anaesthesia and has possible side effects, such as transient memory deficits, headache and myalgia. rTMS does not require anaesthesia, has fewer side effects compared to ECT, but needs to be administered daily for three to six weeks in the clinic. In clinical use, a relatively recent neuromodulation method is transcranial direct current stimulation (tDCS), which is easy to use even at home with a portable device and is currently under active research. These treatments and their implementation in practice are described in *Table 1* (References (12–17)).

Table 1. Indication, mode of action, practical implementation, side effects, maintenance protocols and the evidence base of neuromodulation treatments in the treatment of depression.

	ECT	rTMS	tDCS
Indication	Severe MDE Psychotic depression In some cases, can be used also to moderate severity TRD with several treatment failures	TRD	Mild to moderate depression
Mode of action	Generalized epileptic seizure caused by electric current	Activation of cortical neurons caused by a changing magnetic field, which causes long-term potentiation of neurons and changes in deeper brain areas	Moderation of the neuronal threshold for action potential, 0.5-2mA direct current via scalp electrodes, anode excitatory and cathode inhibitory
Practical implementation	Treatment with anaesthesia and muscle-relaxation. Follow-up in recovery room. Usually requires post-ECT monitoring by an adult until next morning.	Treatment given awake. No need for any special monitoring. Can be given navigated (based on head MRI) or non-navigated.	Treatment given awake. No need for any special monitoring. Can be taken at home with a hand-held device.
Duration of one treatment session	60-90min including preparations and recovery time	10-60min[a]	30min
Frequency of treatment sessions	2-3x/week	5x/week[b]	5-7/week
Duration of acute treatment series	6-15x / 2-8 weeks	15-30x / 3-6 weeks	3-6(10) weeks
Side-effects	Muscle pains, headache, nausea, fatigue, antero- and retrograde memory problems	Headache, movement in the facial area, seizures, fatigue	Headache, skin irritation, fatigue

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	ECT	rTMS	tDCS
Maintenance treatment protocols	Various protocols, usually tapering schedule starting after the acute series, starting from 1 treatment/week to one treatment every 4-8 weeks	Various protocols 1. Tapering schedule starting after the acute series, usually from 1-3 treatments/week to 1 treatment /month 2. Tapering schedule starting after the acute series, usually from 1-3 treatments/week to 1 treatment /month	Few studies, no established procedures
Evidence-base, based on the Finnish Current Care Guideline of Depression	A (strong evidence) in severe and/or psychotic depression C (weak evidence) for moderate severity, treatment-resistant depression	A in TRD	B (moderate evidence) for acute episode of depression. Based on Council for Choices in Health Care in Finland, no evidence in the treatment of TRD.
Price of a treatment session[c]	610e	487e	975e[d]
Price of an average acute treatment series[c]	7320e (12 treatment sessions/4 weeks)	10227e (one appointment for preparations and 20 treatment sessions/4 weeks)	3900e (30 treatment sessions/6 weeks)[e]

[a] Duration depends on the treatment protocol and the parameters used. Usually 3-38min per treatment for unilateral and 20-60min for bilateral treatments.
[b] In traditional treatment protocols. Experimental protocols with accelerated protocols (2-20x daily for 1-5 days)
[c] Prices and average durations from Oulu University Hospital neuromodulation unit
[d] Price of one appointment in the clinic or phone call check-up. Acute treatment protocol consists of four appointments or phone call check-ups during the six-week treatment period, three by a nurse and one by a doctor. Patients take the treatment at home. The price includes the costs of the tDCS device and the tDCS medical supplies.
[e] Price calculated for four appointments or phone call check-ups during the six-week treatment period. Patients take the treatment at home.

References: Isometsä et al. 2025, Lam et al. 2024, Lefaucheur et al. 2020, Wilson et al. 2022, Woodham et al. 2024, Aparicio 2019
Abbreviations: ECT = electroconvulsive therapy; MDE = major depressive episode; MRI = magnetic resonance imaging; rTMS = repetitive transcranial magnetic stimulation; tDCS = transcranial direct current stimulation; TRD = treatment resistant depression

ECT efficacy has been well shown. For example, ECT is even 4 times more effective than antidepressant drugs (18). Response is usually defined as a 50% decrease in depression rating scores (19). Response rates for ECT in patients with TRD are approximately 50-75% (19) and in psychotic depression, even higher (20). In comparison, the response to medication switch after two or more failed pharmacological trials is between 10% and 20% (4). Response rates in the treatment of depression with rTMS vary between 30-60% (13,14). For TRD, the response rate has been shown to be about 46-54% in retrospective observational studies (21,22). Newer accelerated protocols with more than one treatment per day have shown higher efficacy, with a 69% response rate at four weeks post-intervention for TRD patients, with the TRD diagnosis based on the Maudsley staging method, but more studies are needed to verify the results (23).

tDCS has been shown to be effective in the treatment of mild to moderate depression, but studies are heterogeneous and inconsistent and do not support its use in TRD (13,24,25). In a recent pooled analysis of two RCT studies of tDCS for MDD, tDCS was found to be effective in decreasing depression symptoms scores more than sham, but there was no statistically significant difference to sham in response rates (27). The other study included patients with zero to over two failed antidepressant courses and in the other, TRD was considered a contraindication (27). In earlier studies the treatment protocols included fewer sessions, such as 15 treatments during three weeks, which may have affected the results (24), and it may be that six weeks of treatment are needed, and the effects may increase up to ten weeks of treatment (28). According to recent treatment guidelines for TRD by the Council for Choices in Health Care in Finland, COHERE (Palveluvalikoimaneuvosto, Palko), tDCS is not included in the range of public health

services for treating TRD in adults, due to lack of evidence supporting its efficacy for this patient group (29). The advantages of tDCS include ease of use, minor side effects, suitability for home-based treatment and lower costs (30). However, more studies on tDCS are needed to determine the optimal treatment duration and appropriate patient selection.

The indications for different neuromodulation treatments vary somewhat (*Table 1*), but usually ECT is used to treat patients with the most severe and treatment-resistant forms of depression, such as those experiencing severe depressive episodes unresponsive to antidepressant medication and augmentation strategies. In addition, it is used to treat acute depression patients with suicidality, psychotic symptoms or catatonia —even as a first-line treatment— due to its efficacy and rapid onset of action in this usually hospitalized patient group (12,13). For rTMS, the indication is usually TRD, as it is in the recent Finnish recommendation from COHERE (29). In the Canadian treatment guidelines for depression, rTMS is recommended after two different antidepressants or if the augmentation of the first antidepressant has not been effective (13). Based on current knowledge, tDCS can be used for treating mild to moderate, non-TRD (13). Before the guidelines from COHERE, tDCS had been used for treating patients with TRD in some units in Finland, due to its ease of use and as an alternative for the other neuromodulation treatments, and also during the waiting period for other treatments.

Patients with MDD have high relapse rates. Both ECT- and rTMS-treated patients have a similar relapse risk of approximately 50% within the first year following a successful treatment series (31,32). Continuation ECT treatment is aimed at preventing the recurrence of symptoms of the same episode and is usually defined as six months additional therapy after the acute phase. Maintenance ECT treatment is used to prevent the onset of a new depressive episode and defined as treatment beyond continuation treatment (33). In clinical practice, the term maintenance treatment is often used to describe both continuation and maintenance phases. For depression patients who respond well to ECT, maintenance therapy combining ECT and pharmacotherapy has been shown to prevent relapse and hospitalization rates more than pharmacotherapy alone (34). Maintenance rTMS has demonstrated potential efficacy in reducing relapse risk, but the results are mixed, possibly due to varying criteria, protocols and parameters used (15,35,36). For rTMS, continuation and maintenance treatments have not been defined. More studies are needed on the optimal way to perform maintenance ECT and rTMS, including treatment protocols and patient-selection (15,35–38). Nevertheless, these treatments are frequently used in clinical practice (39,40), due to the limited availability of other effective options and the established safety profiles of maintenance ECT and rTMS (36,41).

tDCS has been studied very little in the context of maintenance protocols, highlighting the need for further research in this area. One study on continuation tDCS for 24 weeks included patients from two earlier RCT tDCS studies(17). One compared tDCS (n=94), escitalopram (n=91) and placebo (n=60) in the treatment of MDD, and the response rates were 40%, 47% and 23%, respectively (42). The other compared tDCS (n=30) to placebo (n=29), and the response rates were 67.6% and 30.4%, respectively (43). In a following crossover study (n=48) of these two RCTs (42,43), 15 tDCS sessions over three weeks was offered to all non-responders who had not received active tDCS previously. Continuation tDCS was offered to all patients who had responded to tDCS either during the original RCTs or the open-label phase, and 24 patients continued to the continuation phase (16 patients with unipolar and 8 with bipolar depression). tDCS was continued with 2 weekly sessions over 24 weeks, and 18 patients completed the follow-up, and the relapse rate was 22% at 12 weeks and 26.5% at 24 weeks (17). This relapse rate is less than the 48.9% relapse rate at 6-month follow-up in an earlier study (n=24) with continuation tDCS administered weekly for three months and every two weeks for three months (44), and less than the 53% relapse rate in a different trial (n=42) with continuation tDCS administered every two weeks for three months and monthly for three months (45).

The problem is that many patients require very long-term maintenance treatment with ECT or rTMS, due to the sometimes chronic nature of depression. Often, when the maintenance treatment interval is extended or the treatment is stopped, the patients relapse. Therefore, many patients require maintenance neuromodulation treatments for extended periods—sometimes even years—and the treatment interval may need to remain short, requiring substantial resources. If maintenance treatments continue for years, and more treatments are initiated than finished, the treatment numbers in neuromodulation units increase, potentially limiting access to acute care. This has happened at the neuromodulation unit at Oulu University Hospital, with increasing numbers of maintenance treatments, patients receiving maintenance treatment and number of maintenance treatments per patient, while the number of acute treatments has plateaued, for both ECT and rTMS (46,47). Furthermore, maintenance treatments may have only a partial effect in preventing relapse (36,41), and ways to improve their effectiveness are needed.

Therefore, it is important to study other treatments that can be used to maintain remission and prevent relapse after acute ECT and rTMS. Some retrospective and controlled studies

have been published on using add-on treatments or changing the treatment for maintaining the response after acute ECT. In most of these studies, maintenance ECT plus medication has been shown more effective than maintenance ECT alone (48,49). Switching from maintenance ECT to maintenance rTMS has been shown promising in two small retrospective case series (50,51). There is a small case series (n=4) of maintenance tDCS after response to acute ECT or rTMS, with 75% of patients maintaining the response or improving during the 30-120-week follow-up (52). This is quite high, compared to the usual 50% relapse risk after acute ECT or rTMS, if no maintenance treatment was used (31,32). More detailed information about studies on any add-on or switching treatments after acute ECT or rTMS can be seen in *Table 2* (48–58). To our knowledge there are no large controlled studies with a long follow-up on add-on treatments or changing the treatment for maintaining the response after acute rTMS, nor any studies on how to decrease the need for and frequency of maintenance rTMS and ECT.

Table 2. Studies on add-on treatments or switching treatments after acute electroconvulsive (ECT) or repetitive transcranial magnetic stimulation (rTMS) treatment or during maintenance ECT to maintain the treatment response or to decrease the need for maintenance treatments.

Reference	Study design and sample	Description of intervention to prevent relapse or decrease the need of maintenance ECT or rTMS	Maintenance neuromodulation treatment protocol	Results
M-rTMS after ECT				
Cristancho et al. 2013	Case series, n=6 Mean age 64 years 5/6 female 5/5 recurrent depression, 1/6 bipolar depression 4/6 comorbid GAD Follow-up 7-23 months	M-ECT replaced by M-rTMS, due to side effects or patient preference. Patients in full remission (1) or with a clinical response to ECT (5)	M-rTMS started at ratio 1:2 relative to frequency of previous ECT. –for 5 patients there was a transition period of 2-3 months, during which there were 1 ECT session and two rTMS sessions per month) -One patients switched directly from 1 ECT per month to 2 rTMS sessions per month At the end, mean frequency of rTMS was one treatment per 3.5 weeks (range 1-8 weeks)	At 3 and 6 months of M-rTMS treatment, all patients maintained or improved their clinical status At last observation time point, 4/6 maintained or improved clinical status reached with ECT 2/6 relapsed, both reached remission with acute rTMS
Noda et al. 2013	Case series, n=6 4/6 female 4/6 unipolar depression 2/6 bipolar depression all TRD and recurrent With a response to acute ECT and 5/6 had continued to C-ECT Follow-up 6-13 months	C-ECT replaced by M-rTMS or M-rTMS started after acute ECT due to side effects or poor tolerability	M-rTMS at the frequency of 1-2 treatments per week depending on symptom severity and patients' compliance	5/6 patients maintained response status at the time of the last observation rTMS well-tolerated
M-tDCS after acute ECT or rTMS				
Le et al. 2022	Case series, n=1 post-response to acute ECT, Female, age 20 years, illness duration >24 months, unipolar depression n=3 post-response to acute rTMS Female, ages 20, 21 and 59 years, illness duration 12- >24 months, unipolar depression	M-tDCS combined to ongoing treatment with pharmaceuticals and / or psychological therapy after acute treatment with ECT or rTMS	M-tDCS usually 7 times per week, post-ECT 4 times per week. Weekly evaluation. If there was clinical improvement at week 4, the treatment frequency was gradually tapered or treatment discontinued if no benefit by week 6	Mean number of tDCS sessions 305, and mean number of weeks of treatment 75 1 patient post-ECT entered remission during M-tDCS 2 patients post-rTMS stayed in remission during M-tDCS 1 patient post-rTMS discontinued M-tDCS because of relapse at 38 weeks

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Reference	Study design and sample	Description of intervention to prevent relapse or decrease the need of maintenance ECT or rTMS	Maintenance neuromodulation treatment protocol	Results
Medication vs placebo after acute ECT				
Sackeim 2001	RCT, patients (n=84) who remitted after acute ECT Follow-up 6 months	Patients randomized to three groups: -placebo (n=29) -Nortriptyline (n=27, target level 75-125ng/mL) -Combination of nortriptyline and lithium (n=28, target level of nortriptyline 75-125ng/mL, target-level of lithium 0.5-0.9mEg/L)	No ECT	Relapse rate nortriptyline-lithium / nortriptyline / placebo: 39% / 60% / 84% 13/14 of the relapsed patients in the lithium group relapsed within 5 weeks Medication-resistant patients, female patients and those with more severe depressive symptoms had more rapid relapse
Prudic 2013	RCT Phase 1: RCT (n=319), with unipolar or bipolar MDD and a pretreatment HAM-D (24) score or ≥21. Randomized to moderate dose BL ECT vs. High-dose RUL ECT AND to concurrent treatment with placebo, nortriptyline (100-120ng/mL) or venlafaxine (225mg dose). 181 patients met remission criteria post-ECT (60% reduction in HAM-D scores and maximum 10p at 2 days post-ECT and reassessment 4-8d after ECT. The remission rate was higher with RUL than with BL ECT. 122 patients continued to the Phase 2: -mean age 48.9 years -female 64.75% Follow-up until relapse or 6 months	Phase 2: patients (n=122) earlier randomized to nortriptyline or venlafaxine continued the treatment, whereas patients randomized to placebo were randomized to nortriptyline or venlafaxine and lithium was added for all patients. Target doses / blood levels: -nortriptyline blood level 100-120ng/ML, -venlafaxine targeted at 300mg dose -lithium blood level 0.5-0.7mEq/L	No C-ECT	No indication that the beginning of AD medication at the start of the ECT affected relapse rate relative to starting placebo No difference in starting nortriptyline-lithium vs. Venlafaxine-lithium 50% of patients relapsed within 6-month follow-up Older age was associated with a lower relapse risk
Medication + M-/C-ECT vs only C-/M-ECT after acute ECT				
Vothknecht 2003	Prospective, controlled study Patients (n=24) who responded to acute ECT MDD n 16 Bipolar depression n=2 Schizoaffective n=2 Depressive NOS n=1 Mean age 57 Follow-up M-ECT 1.5 years and M-pharm 1 year	Maintenance treatment modality after the acute ECT was chosen by the clinician and the patient Arguments for continuing ECT were incomplete remission, early signs of relapse and a preference of the patient for M-ECT -M-ECT (n=11) -M-Pharm (n=13, ADs, mood-stabilizers, APs, BZDs) Neuropsychological testing 1 week before and 6 weeks after acute ECT and at 6-month intervals during M-ECT	M-ECT one per week, tapered every 3 treatments when stable to ≤1 per month -Mean 1 treatment per every 2.2 weeks (0.9.4.4) -Average duration 65 weeks	Relapse rate for M-ECT vs. M-pharm was 9.1% vs 30.8% Cognitive functioning remained stable during maintenance ECT and there were no differences between the groups

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Reference	Study design and sample	Description of intervention to prevent relapse or decrease the need of maintenance ECT or rTMS	Maintenance neuromodulation treatment protocol	Results
Kellner et al. 2006	RCT Patients (n=201) who remitted after acute ECT (given 3 treatment sessions/week bilaterally until remission) Mean age 57y Follow-up 6 months	Patients randomized to two groups and followed for 6 months: -C-ECT (n=98) -C-Pharm (Lithium + nortriptyline, n=103), flexible dosing, targeting levels of 125ng/mL of nortriptyline and 0.7mEq/L of lithium	C-ECT 10x -1 treatment sessions per week for 4 weeks -1 treatment sessions per 2 weeks for 8 weeks -1 treatment monthly for 2 months	No significant difference between C-ECT and C-Pharm in relapse or remission Relapse in C-ECT/C-Pharm 37.1/ 31.6% Mean time to relapse 9.1/6.7w Remission 46.1/46.3% Dropouts 16.8/22.1%
Nordenskjold 2013	RCT (n=56), patients with unipolar or bipolar depression and a response to acute ECT, follow-up 1y	-C-ECT/pharm (n=28, two switched to pharm alone) -Pharm (n=28) Pharmachotherapy was individualized, with venlafaxine the first choice and lithium augmentantion offered to all patients AD 98% lithium 56% (mean concentration 0.56mmol/L in Pharm and 0.60mmol/L in C-ECT/pharm, antipsychotics 30%	29 ECT treatments; weekly for 6w, then every second week	Relapse rate for C-ECT/pharm vs pharm 32% vs 61% Cox proportional hazard ratio 2.32 (1.3-5.22) Cognitive functioning and memory measures stable for patients without relapse in both groups One suspected suicide and 3 suicide attempts in the pharm group
Kellner 2016	RCT, phase 2 of a two-phase multiside study. Phase 1, patients ≥60 years old with MDD received acute ECT + venlafaxine (n=240) Phase 2: remitted patients (n=120) Follow-up 6 months	-C-ECT/pharm (n=61) -Pharm (n=59) Both groups started lithium with a target blood level of 0.4-0.6mEq/L	C-ECT with an initial fixed and tapered schedule with four treatments in 1 month, and then on weeks 5-24 an algorithm was used, where 0-2 ECT treatments per week were given depending on HAM-D scores. 34.4% of patients received at least one ECT during weeks 5-24.	Mean HAM-D score for C-ECT/pharm vs Pharm was 5.5 vs 9.4, and C-ECT/pharm group had a sharper decline in HAM-D scores Relapse rate for C-ECT/pharm vs Pharm was 13.1 vs 20.3%, with the odds of relapsing 1.7x higher in the pharm group
Psychotherapy after acute ECT				
Brakemeier 2013	RCT (n=90), inpatients with MDD received acute ECT. 70% responded, 47% remitted.	Responders (n=63, of which 60 underwent randomization) continued AD medication (MED) and were randomized to add-on cognitive behavioural therapy (CBT) or C-ECT or no add-on (MED). After 6mo of continuation treatment, follow-up of 6mo.	C-ECT	CBT / ECT / MED sustained response at 6mo: 77% / 40% / 44% at 1y: 65% / 28% / 33%
Carstens 2021	Non-controlled pilot trial after inpatient ECT, n=14 8 ECT responders and 6 ECT non-responders	15 weekly sessions of group CBT with cognitive behavioural analysis system of psychotherapy (CBASP) elements offered to all patients regardless of response status to ECT. Patients continued other treatments, such as pharmacological treatments, psychotherapy, C-ECT	Medication intake, number of C-ECT sessions and individual psychotherapy were documented	Post-ECT symptom reduction sustained 6mo after the end of the group, regardless of the response status after ECT Aspects of quality of life and emotion regulation improved during group CBT and were maintained 6 mo after the end of the group

Abbreviations: ECT = electroconvulsive therapy; MDE = major depressive episode; GAD = generalized anxiety disorder; rTMS = repetitive transcranial magnetic stimulation; TRD = treatment resistant depression; BL = bilateral ECT; RUL = right unilateral ECT; M-ECT = maintenance ECT; C-ECT = continuation ECT; M-rTMS= maintenance rTMS; RCT = randomized controlled trial; MPharm = maintenance pharmacotherapy; AD = antidepressant; BZD = benzodiazepine; AP = antipsychotic; HAM-D = Hamilton Depression Rating Scale

Compared to tDCS, ECT and rTMS require more resources from the healthcare system and involve frequent hospital visits causing the need for travel for the patient. In addition, ECT may have more adverse effects for the patients and requires monitoring after the treatment. For these reasons, it is necessary to research and develop ways to decrease or replace maintenance ECT and rTMS. Despite its lack of efficacy in the acute treatment of TRD, tDCS could be one solution for decreasing the need for maintenance ECT and rTMS, as these are patients whose depressive symptoms are not as severe as they were in the beginning of the acute ECT or rTMS. Replacing or decreasing the need for maintenance ECT and rTMS with tDCS could increase the accessibility of ECT and rTMS to other patients. To our knowledge, no previous studies have examined the usability or efficacy of add-on tDCS in combination with maintenance ECT or rTMS for preventing the worsening of depressive symptoms or reducing the frequency of maintenance ECT or rTMS sessions.

AIMS

This register-based clinical case series describes a clinical development project of add-on tDCS treatment to MDD patients with ongoing or in need of ECT or rTMS maintenance treatment. For a small group, tDCS was started without previous ECT or rTMS maintenance treatment, directly after acute treatment. The aim was to investigate the usability of add-on tDCS for either improving patients' clinical wellbeing or enabling the increase in ECT or rTMS maintenance treatment interval or switching to only tDCS. The aim was to evaluate whether patients can adhere to the tDCS treatment as planned, identify any potential adverse effects and gather patients' subjective views on the treatment. We also aimed to analyse if adding tDCS improves the clinical status, reduces the severity of symptoms and affects the frequency of rTMS or ECT maintenance treatment sessions. Most of the patients in the neuromodulation unit are TRD patients.

METHODS

SAMPLE AND SETTING

The study sample consisted of patients (n=12) being treated with or fulfilling the indication for maintenance ECT or rTMS at the psychiatric neuromodulation unit at Oulu University Hospital. The unit provides ECT, rTMS, tDCS and ketamine infusions. The majority of the patients of the Oulu University Neuromodulation unit (Nemo unit) have a medication-resistant disorder, e.g. TRD where the person has used at least 2 different antidepressants with adequate dose and duration, without effectiveness. The diagnoses of the patients are based on the diagnosis made by the physicians (psychiatric or psychiatric trainee) at the appointment before starting the ECT or rTMS, and the diagnoses are not changed during the treatment. For ECT, the catchment area of the unit is Northern Ostrobothnia, with a population of 417,000 in 2022, and Kainuu, with a population of 70,521(59). For rTMS, the catchment area of the neuromodulation unit includes the wellbeing services counties of Lapland and Central Ostrobothnia in addition to Northern Ostrobothnia and Kainuu, with a total population of about 731,000 in 2022 (59). rTMS service was started in Lapland at the beginning of 2025. While tDCS is not included in the service offering for TRD patients, the unit has some devices available for home treatment.

This case series is based on a clinical development project aimed at improving the operations of the neuromodulation unit. It was implemented in daily clinical practice, with data collection being part of the routine clinical evaluation, which is why ethical approval was not required. The clinical development project started by pilot cases in 2019 and 2020, was launched comprehensively in 2021 and is still ongoing. The research permit from Northern Ostrobothnia Hospital District (145/2022) was granted on August 17, 2022, and its amendment was granted on September 15th, 2025. The design of the study is a retrospective case series. In this paper, we describe the results of the 6-month period after adding tDCS to maintenance ECT or rTMS.

TREATMENT PRACTICES IN THE OULU UNIVERSITY NEUROMODULATION UNIT

In the Oulu University Neuromodulation unit (Nemo unit), both acute and maintenance ECT and rTMS treatments are administered. Until May 2024, ECT was delivered with Somatics Thymatron® System IV device using 2x dose stimulus program, with a maximum of 1008mC energy. Pulse width and frequency are automatically adjusted to obtain the longest duration possible for any given per cent energy dial setting. Half-age method is used to calculate the initial dose (½x the approximated patient's age in per cent energy dial setting) and adjusted throughout the course depending on the seizure duration and quality. From May 2024 onwards, ECT has been delivered with Sigmastim Σigma device using Near Ultra Brief (NUB) and Brief Pulse (BP) programs. NUB with a 0.5ms pulse width is used with frontoparietal and BP with a 1.0ms

pulse width with bitemporal electrode placement. The initial stimulus frequency and duration are chosen based on the device manual's age- and sex-based table and then adjusted. The used electrode placement is usually frontoparietal (FP), to reduce side effects. FP is given only to right side. FP is the first option for depressed patients, and bilateral electrode placement (BL) for patients suffering from psychosis needing higher effectiveness. If there is no sufficient response from FP ECT during the first 6-8 treatment sessions, the electrode placement can be changed to BL based on evaluation done by the physician responsible for administering ECT. No specific measure for response has been used, but the non-response is defined as no improvement of symptoms during the course of ECT. This is the normal ECT treatment protocol in the Nemo unit, that the sample of this case series also followed.

rTMS is given with two Nexstim ® neuronavigated rTMS. In 2016-2019, depression treatment was given at the left dorsolateral prefrontal cortex (DLPFC) with a 10Hz 3000 pulse protocol. From 2019 onwards, the rTMS protocol in our unit has been intermittent theta burst stimulation (iTBS) 600 pulse protocol. If the patient had comorbid anxiety or obsessive-compulsive disorder, a 1Hz 1800 pulse protocol at the right DLPFC can be given instead of iTBS.

In our unit, maintenance treatment is started when a patient previously responsive to acute ECT or rTMS relapses within a year from the acute treatment, and additionally when re-treatment as an acute treatment series is also effective. In selected cases, if the patient relapses quickly after the acute treatment and his/her symptoms haven't reached the level prior to the initial acute treatment, maintenance treatment can be started directly without a new acute treatment, to enable faster access to treatment and to avoid worsening of the symptoms. In maintenance ECT, until the year 2023, the maintenance ECT protocol included weekly treatments for 4 weeks and then gradually increasing the treatment interval to 4-6 weeks. In 2023, the protocol was changed to one weekly treatment, two treatments with a two-week interval and then gradually the interval is increased to 4-6 weeks. For some patients the interval cannot be increased without a decline in psychiatric wellbeing and thus, it is possible to offer maintenance treatments more frequently if needed. In our unit, maintenance treatment is intended to end when low frequency (4-6 weeks) is obtained and remission has lasted for a year. Maintenance rTMS criteria and timeline are somewhat similar to that of ECT, with the difference of weekly frequency for 2-3 months and then gradually increasing the treatment interval, if possible, to 3-4 weeks. When remission has lasted for one year, maintenance rTMS is usually stopped. For some patients, it has not been possible to increase the treatment interval or to stop maintenance treatment, and some patients have received treatment for several years.

PATIENT SELECTION

From patients receiving maintenance ECT or rTMS in the Nemo unit, 12 were selected to add tDCS treatment to the ongoing maintenance ECT or rTMS or to replace these with tDCS. Selection was done by chief psychiatrist (SK). Selection was based on: 1) the need for frequent ECT or rTMS, i.e. maintenance treatment every one to three weeks, 2) the capability to perform treatment at home, and 3) clinician (SK) evaluation that either there is a need and it would be possible to improve patients' mental health from the level achieved with the current maintenance treatment, or it would be possible to decrease the frequency of maintenance ECT/rTMS treatments without a decline in mental health, or it would be possible to replace ECT/rTMS maintenance therapy with tDCS. For some patients, long distance to the hospital was an additional reason for adding tDCS. Only unipolar depression patients (ICD-10 diagnoses F32-F33) were chosen, and contraindications were acute psychosis or suicidality.

INTERVENTION

Intervention of this study was combining tDCS to maintenance ECT or rTMS, or tDCS replacing ECT and rTMS maintenance therapy. Intervention started for selected patients in intervals between spring 2019 and spring 2024. tDCS treatment was initiated as 6-week (w) period containing 5-7 treatments per week. Treatments were performed at home, with a Sooma® tDCS device, and patients got the device and equipment from the Nemo unit at the start and at check-ups. The tDCS treatment included anodal left DLPFC stimulation, with the cathode over the right DLPFC at 2 mA intensity. Each treatment session lasted for 30 minutes.

The patients were given the first tDCS session, the tDCS home device and instructions on its use during the visit to the Nemo unit. During the initial 6-w period the follow-up schedule was the following: a nurse's check-up after 1w by a phone call, a nurse's check-up at 3w by a phone call and then a psychiatrist's check-up at 6w, when the decision was made to either stop or continue tDCS, and the frequency of tDCS was planned. After the initial 6-week treatment period, the frequency of tDCS treatments was planned to be 3-7 treatments per week, depending on the tolerability of the treatment and the symptoms, and could be adjusted during the check-ups. The need for maintenance ECT or rTMS was also evaluated at

the 6-week follow-up based on clinical assessment of patients' symptoms and wellbeing, also using the symptom scale scores (described below in "Outcomes – symptom scales"), and the frequency of the maintenance treatments was planned. Then nurse's check-ups continued at 6-week intervals, with every second being a visit and every second a phone call. tDCS was planned to be stopped if there were adverse effects or response to treatment was not sufficient. Decision on stopping tDCS was done by the Nemo unit's chief physician (SK).

DATA COLLECTION AND MEASURES OF BACKGROUND FACTORS AND OUTCOMES

Background Variables

Gender, age of the patient, all psychiatric diagnoses and the medications used at the beginning of tDCS treatment were collected for each patient from their medical records. Psychiatric medications were categorized as antidepressants, antipsychotics, benzodiazepines or sedatives and mood stabilizers, based on WHO ATC classification (WHO Anatomical Therapeutic Chemical classification system) (60), except for not considering Lithium as an antipsychotic (as in ATC classification) but instead as mood stabilizer as done in clinical practice. Medication and neuromodulation treatment history before the acute ECT or rTMS preceding the start of tDCS were also collected from the medical records, to determine treatment resistance.

Outcomes – Symptom Scales

Symptom questionnaires Beck's depression inventory (BDI, (61)) and Generalized anxiety disorder 7-item scale (GAD-7, (62)) were filled by the patient at the start of tDCS and at check-ups, either 0-7 days before the check-up, during the check-up or as soon as possible after the check-up, if not done before. The check-ups were at 3 and 6 weeks from the start of the tDCS treatment and then if tDCS treatment continued, every 6 weeks. For this study, we collected BDI and GAD-7 data only from the 3-week, 6-week and 6-month check-ups. GAD-7 measure is included in the questionnaire battery of the Nemo unit for all the patients treated in the unit, since ECT, and especially rTMS, based on our experience and previous studies (63) may also alleviate anxiety symptoms of the patients.

Outcomes – Experience of the Patient, Adherence and Treatment Frequency

tDCS treatment frequency, as number of treatments per week since the start of tDCS until 6 months, adherence (i.e. if the patient continued the use of tDCS), patients' subjective experience on benefits and side effects of the tDCS treatment, as well as the patients' wellbeing and effectiveness of the treatment recorded by the nurse or the doctor during the follow-up were collected from medical records at 3-week, 6-week and 6-month check-ups. Information on patients' experience on benefits and side effects of the tDCS treatment was based on routine clinical assessment done in check-ups, and there were no specific questionnaires or structured interviews in use. The frequency of maintenance ECT or rTMS 6 months prior tDCS and during the 6-month follow-up period, the duration of maintenance ECT/rTMS, and the reason for adding tDCS were collected.

DATA ANALYSIS

Data were analysed using descriptive statistics and frequencies, and no tests for statistical significance were made. Proportions are presented for categorical variables, while means with standard deviations are reported for continuous variables. Because our sample size is small, results and characteristics of the sample with values equal to or less than 3 are blurred for data protection.

RESULTS

CHARACTERISTICS OF THE SAMPLE

The sample consisted of 12 participants, most of them being females (≥9) (Table 3). All participants were diagnosed with depression, and most of them (≥9) with TRD (i.e. having used at least 2 different antidepressants) before the start of the acute ECT or rTMS. Half of the participants had three or more previous AD courses, and four participants had previous antipsychotic augmentation. Of the sample, the majority (≥9) had severe non-psychotic depression. Five participants had single-episode depressive disorder and 7 had recurrent depressive disorder. The diagnoses were set at the time of the acute ECT or rTMS series and had not been changed even though the acute treatment may have decreased the symptom level. Majority (≥9) of participants were prescribed antidepressants, 7 participants were using antipsychotics, 6 were using benzodiazepines or sedatives and ≤3 of the participants were using mood stabilizers.

The reasons for adding tDCS were to enhance the treatment effects/decrease the symptoms (9/12), decrease the frequency of maintenance ECT or rTMS treatment sessions (5/12), to decrease the need for frequent visits to the Nemo unit due to long distance (≤3/12), adverse effects of maintenance ECT

or rTMS (≤3/12) and/or practical reasons/schedules of the patient (≤3/12).

Before starting tDCS, 6 participants had received ECT, and 6 participants had received rTMS. Three or less of the patients received 0-2 maintenance treatment sessions before starting tDCS, and the rest of the sample had been on maintenance ECT or rTMS longer (*Table 3*). The mean duration of the previous maintenance treatment was 20 months. The mean age of the participants was 48.8 years (SD=9.7).

Table 3. Background variables and characteristics of study subjects.

	N
Gender female	≥9
Severity of depression severe, non-psychotic	≥9
Recurrent depression	7
Use of medication	
Antidepressant	≥9
Antipsychotics	7
Benzodiazepines or sedatives	6
Mood stabilizers	≤3
Treatment resistance at the start of maintenance treatment	
≥2 antidepressant trials	≥9
≥3 antidepressant trials	6
Antipsychotic augmentation	4
Previous / ongoing psychotherapy at the start of maintenance ECT or rTMS	7
Neuromodulation treatment received before tDCS	
ECT	6
rTMS	6
Patients with more than one previous acute treatment series (ECT or rTMS)	6
Patients with both ECT and rTMS previously	≤3
Time of starting tDCS	
After 0-2 maintenance ECT or rTMS treatments, i.e. no or at most two maintenance rTMS or ECT treatment sessions	≤3
After receiving several sessions of maintenance ECT or rTMS	≥9

ECT = electroconvulsive therapy; rTMS = repetitive transcranial magnetic stimulation;
tDCS = transcranial direct current stimulation

USE OF TDCS DURING THE STUDY PERIOD

A total of 11 participants continued using tDCS until the end of the 6-month follow-up period. One discontinuation of tDCS happened after 24 weeks. At 6 weeks (n=12), 10 patients took at least 5 treatments per week. At 6 months (n=11), 6 patients took at least 5 treatments per week.

CHANGE OF SYMPTOMS

At baseline, the mean score for depression (BDI) was 26.7 (SD=11.8) (Table 4). After three weeks of treatment, the mean BDI score decreased slightly to 25.9 (SD=12.5), and by six weeks, to a mean of 21.8 (SD=10.1). At the six-month follow-up, the mean BDI score was 24.3 (SD=13.1), with 7 participants having completed the six-month assessment. In the six-month follow-up, all 7 participants reported either a stable or somewhat worsened score compared to their six-week follow-up, but the score still remained lower than at baseline. Regarding anxiety, the mean score of GAD at baseline was 9.3 (SD=5.5), at three weeks 6.1 (SD=2.9) and at six weeks 10.4 (SD=6.2) (*Table 4*). At the six-month follow-up, the mean GAD score was 5.7 (SD=4.2), with scores remaining stable or improving in most participants compared to baseline and the six-week measurement.

PATIENT EXPERIENCES AND CLINICIANS' OBSERVATIONS

Regarding the patients' experience of tDCS benefits at 6-week or 6-month assessment, five participants reported an increased capacity to perform daily activities like picking berries, shopping and socializing. Three or less participants

Table 4. Depression and anxiety symptoms at baseline, 3 and 6 weeks and 6 months.

	Participants with questionnaire data (n)	Mean score (SD)
Depression symptoms, BDI total score		
Baseline	10	26,7 (11,82)
3 weeks	9	25,9 (12,47)
6 weeks	9	21,8 (10,12)
6 months	7	24,3 (13,07)
Anxiety symptoms, GAD-7 total score		
Baseline	9	9,3 (5,52)
3 weeks	8	6,1 (2,85)
6 weeks	9	10,4 (6,20)
6 months	6	5,7 (4,20)

BDI = Beck Depression Inventory; GAD-7 = Generalized Anxiety Disorder scale

noted improved sleep, with longer, uninterrupted sleep and easier onset of sleep. Seven participants felt their overall wellbeing, particularly their mood, had improved. Three or less participants experienced worsening of symptoms, while eight participants showed improvement in their symptoms during the 6-month period. For ≤3 participants, there was no evaluation of their clinical status mentioned in their medical record.

During the tDCS treatment, altogether 8/12 participants reported experiencing adverse effects. Of them, six participants had skin irritation, including blisters, redness and a stinging sensation, while ≤3 participants experienced headaches. Additionally, ≤3 participants reported tiredness.

FREQUENCY OF MAINTENANCE ECT OR RTMS

For seven patients, the frequency of maintenance ECT or rTMS decreased after starting tDCS. For ≤3, there was an increase of maintenance ECT or rTMS frequency. Three or less patients had no change in maintenance treatment frequency but reported subjective improvement based on medical records. Three or less continued with tDCS as their only neuromodulation treatment, i.e. tDCS replaced maintenance rTMS or ECT.

Among patients who had received maintenance ECT (n=6), the mean number of maintenance ECT sessions during the 6 months before starting tDCS was 7.5 (range 2-10), and the number of maintenance ECT sessions during the 6 months after starting tDCS decreased on average by 2.3 sessions (range from –5 to 0 sessions). Regarding patients who received maintenance rTMS (n=5), the mean number of maintenance rTMS sessions during the 6 months before starting tDCS was 24.8 (range 11-40), and the number of maintenance rTMS sessions during the 6 months after starting tDCS decreased on average by 8.0 sessions (range –32 to +7 sessions).

DISCUSSION

MAIN RESULTS

Based on this retrospective register-based case series without control group, depression symptom scores did not change during follow-up, which may indicate no extra effect of adding tDCS, but may also indicate that adding tDCS, and at the same time for some patients decreasing the frequency of or switching from maintenance ECT or rTMS to tDCS, did not lead to increasing depression symptoms. For over half of the patients, the number of maintenance ECT or rTMS treatments decreased during the six months after starting tDCS compared to the six months before. Most participants reported benefit from tDCS treatment, for example, an increased ability to perform daily tasks, improved wellbeing and improvement in sleep quality. Eight participants experienced side effects of tDCS. Most patients continued tDCS treatment until the 6-month follow-up.

Although the BDI scores showed a slight improvement over the first 6 weeks of treatment, the results at the 6-month follow-up indicated a slight increase of depressive symptoms for most participants. This may relate to the decreased number of maintenance ECT or rTMS treatment sessions after the initial 6-week start period. Furthermore, participants whose BDI scores had increased between the 6-week and the 6-month check-up visits still reported a decrease in depressive symptoms in the clinical interview at the 6-month clinical check-up. Overall, the mean of the BDI scores was less at the 6-month check-up compared to the start of the intervention.

The findings show the potential of tDCS to reduce the frequency of ECT/rTMS without a major decline in symptom management, although not all participants were able to reduce the frequency of the other maintenance neuromodulation treatment. For 7/12 patients, the number of maintenance ECT or rTMS treatments decreased and for ≤3/12 the number of treatments increased. For ≤3/12 there was no change in the frequency of ECT or rTMS. Three or less of the patients continued with only maintenance tDCS. To summarize, for the majority, the treatment number decreased, even during this relatively short follow-up of 6 months.

The majority of the patients had previously been in ECT or rTMS maintenance treatment. Based on clinical experience, some patients' symptoms increase as the ECT or rTMS maintenance intervals are extended. Research on this topic is very limited. For ECT, in a retrospective cohort study on maintenance ECT, some patients needed reintensification of the maintenance treatments and there was large variability in how fast the treatments could be tapered (64). Further, the lack of access to ECT treatment during the COVID pandemic showed an increase in relapses due to abrupt cessation of maintenance ECT (65). As for rTMS, the findings of a systematic review on maintenance rTMS suggested that there should be over 2 rTMS maintenance treatments per month and that 1-2 treatments per month may not be sufficient (36). In our study, as a group, maintenance treatment sessions were decreased by a mean of 2.3 sessions among those in maintenance ECT, and by a mean of 8.0 sessions among those in maintenance rTMS.

COMPARISON TO EARLIER STUDIES

There are no previous studies on combining tDCS and maintenance rTMS or ECT treatment. According to the recent recommendation from the Finnish Council for Choices in Health Care, COHERE, rTMS should be offered for TRD after two failed antidepressant courses, whereas tDCS is not recommended for TRD, due to lack of evidence (29). Based on current knowledge, tDCS can be used for the treatment of mild to moderate, non-TRD (13,30). tDCS may moderately reduce depression severity in adults with treatment-resistant depression compared to placebo, but the evidence is limited (27). Though there is no evidence of effectiveness of tDCS in TRD, it is possible that it may have benefits as an add-on treatment to maintenance ECT or rTMS among this patient population. In addition, add-on tDCS may decrease the frequency of ECT or rTMS maintenance treatment sessions, which is considerable concerning the significant increase in these maintenance treatment modalities (46,47). Our study gives some preliminary support for add-on tDCS to maintenance ECT or rTMS, but larger studies are needed for better understanding of the effects of this treatment combination.

STUDIES ON EFFECTIVENESS OF COMBINATION OF TDCS AND OTHER NEUROMODULATION TREATMENTS IN ACUTE PHASE TREATMENT OF DEPRESSION

Two studies have been made on the combination of tDCS and other neuromodulation treatments in the treatment of acute phase of depression. In one study (n=16), tDCS was given concomitantly with ECT, with daily tDCS, and on ECT days, tDCS was administered just before ECT. ECT was given only six times for two weeks, so the protocol was shorter than usual. There was no difference in cognitive tests or depression severity from baseline between the tDCS+ECT and placebo+ECT groups (66). In a more recent RCT (n=240, 57.9% females), active and sham tDCS and rTMS were given concomitantly, so that there were four different groups (active tDCS+active rTMS, sham tDCS+active rTMS, active tDCS+sham rTMS and sham tDCS+sham rTMS), with a 2-week treatment protocol, 2mA tDCS given for 20min in 30-60min prior to the rTMS. rTMS was given with a 10Hz 1600 pulse protocol to the left dorsolateral prefrontal cortex. The primary outcome was the reduction in the Hamilton Depression Rating Scale (HAM-D) score at 2 weeks, which was significantly greater in the active tDCS+active rTMS group (-18.33 points), compared to the other groups (sham tDCS+active rTMS -14.86 points, active tDCS+sham rTMS -9.21 points and sham tDCS+sham rTMS -10.77 points). Further, there was no significant difference between active tDCS+sham rTMS and sham TDCS +sham rTMS groups. Thus, active tDCS did not produce a significant extra effect. At 4-week follow-up from the start, the symptoms continued to decrease, with the largest portion of response and remission in the active-active group (92% and 83%), with sham tDCS +active rTMS at 88% and 62%, active tDCS +sham rTMS at 90% and 72% and sham tDCS -sham rTMS at 92% and 55%, respectively, with a very high response and remission rate even for placebo. There were no serious adverse effects (67). These results and our small pilot study support the need of further studies on the potential of combining tDCS to other neuromodulation treatments either in acute or maintenance treatment.

THE COSTS AND ECONOMIC IMPACT OF DIFFERENT MAINTENANCE TREATMENT METHODS

The prices of ECT, rTMS and tDCS at our unit are presented in Table 1. In our unit, acute treatment with tDCS includes four visits or phone call visits during the 6-week acute treatment period and then monitoring visits every 6 weeks (visit or a phone call), i.e. a total of 11 visits during the first year. After the first year, follow-up visits decrease to 4-8 visits annually. Since the treatment is taken at home, there are no treatment visits to the clinic.

During maintenance rTMS, doctor's follow-up visits or phone calls are every 3-12 months, and for maintenance ECT, every 12 months. Weekly maintenance treatment with rTMS involves 52 sessions and visits to the clinic per year. When rTMS is administered every three weeks, the number of sessions decreases to approximately 17 per year. ECT administered every week results in 52 sessions annually. ECT given every two weeks corresponds to 26 sessions per year.

In addition to the direct treatment costs, there are additional costs associated with treatment given in the clinic (i.e. ECT and rTMS), such as travel costs, accommodation and sick leave. ECT requires more monitoring than rTMS, until the next morning, and the patients cannot drive themselves. Thus, they often use a taxi for travelling to treatments. The longest distance to treatment in our unit inside the wellbeing services area is from Kuusamo, where taxi can cost 960 € for a two-way travel (https://www.otaxi.fi/hinnasto/#hintalaskuri), making a total of 49 920 € costs for the society for yearly weekly visits. In addition, some patients need a hospital bed for monitoring after ECT treatment. Furthermore, patients usually have to take sick leave for the treatment days, especially for ECT, and also for rTMS if they live further from the hospital. If ECT

or rTMS maintenance visits can be decreased and replaced by tDCS taken at home at any time, not requiring any follow-up or travelling, these other costs can also be decreased.

Adding tDCS to maintenance rTMS or ECT may decrease the total costs, especially when the frequency of maintenance rTMS or ECT is high (e.g. weekly or biweekly), and if add-on tDCS allows to decrease of frequency. However, studies on cost effectiveness of add-on tDCS to ECT or rTMS are needed.

CLINICAL AND PRACTICAL IMPLICATIONS

From a clinical standpoint, this study gives some preliminary support for the idea that tDCS could be a valuable option for depression patients who require frequent maintenance ECT or rTMS. The ability to administer tDCS at home with minimal supervision is a significant advantage, particularly for patients who live far from treatment centres or have difficulty adhering to regular in-person appointments. tDCS could serve as a long-term solution for maintenance therapy, potentially reducing the burden on hospital resources and improving patient convenience, though studies are needed on the acute and long-term effects of add-on tDCS.

Patient preference is also considered when choosing treatments. Some patients prefer tDCS over other neuromodulation treatments for its ease of use, portability and fewer adverse effects.

Some patients (≤3/12) in our sample were even able to discontinue other neuromodulation treatments entirely, suggesting that tDCS may serve as an effective alternative or complementary approach for some depression patients needing maintenance neuromodulation treatments. Based on earlier studies, tDCS is only recommended for mild or moderate depression (30). Our study also included patients with severe depression. However, due to small sample size, we were not able to analyse the effect of add-on tDCS in severe compared to moderate depression.

Other strategies for reducing the need for rTMS and ECT maintenance therapy could include pharmacological optimization, psychotherapy and lifestyle changes. However, their effectiveness in directly replacing or reducing neuromodulation treatments remains uncertain and requires further investigation (68). More studies have been conducted on the prevention of relapses after acute ECT than rTMS, and lithium has shown the best benefit, with a meta-analysis presenting the number needed to treat (NNT) 7 and weighted odds ratio (OR) 0.55 with lithium compared to post-ECT prophylaxis without lithium. The quality of evidence was, however, very low due to most studies being observational, there being substantial heterogeneity and indications for publication bias (69). Lithium has potentially severe side effects and needs regular laboratory monitoring. Acute ECT is used for more severely ill patients, and therefore the addition of lithium is more justifiable than for patients treated with rTMS, with moderate to severe TRD. Furthermore, lithium is not suitable for all patients and still has limited efficacy. No studies on any medications to prevent relapses after successful rTMS have been made, to our knowledge.

STRENGTHS AND LIMITATIONS

This is the first study about adding tDCS to maintenance ECT or rTMS to increase the effectiveness of treatments and to decrease the need for ECT or rTMS maintenance treatments. The increasing need for maintenance ECT and rTMS is an important clinical challenge due to limited resources and lack of other efficient treatments for this patient population. The inclusion of both subjective patient experiences and objective clinician evaluations provides a comprehensive understanding of tDCS's potential benefits and side effects. Use of multiple follow-up points allows for an assessment of both short-term and medium-term outcomes. The real-world setting and the evaluation of tDCS in a clinical context is both a strength and a limitation. The sample was heterogeneous in terms of depression severity, medication use and prior neuromodulation treatments, which may have contributed to the variability in treatment responses. However, at the same time the heterogeneity is representative of clinical reality.

The largest limitation of this study was small sample size and the lack of a placebo control or a control group without tDCS. The addition of a different treatment modality and the increased frequency of follow-up visits or phone calls compared to usual clinical protocols may have affected the results. It may be the increased contact that may have beneficial effects. The sample size was small, which limits the generalizability of the results. The sample included mainly females. The length of follow-up was relatively short (6 months), and longer follow-up would have allowed more detailed analysis of potential of add-on tDCS in decreasing the frequency of maintenance ECT or rTMS. Further studies with a larger sample size, including more males and clinically/diagnostically more homogeneous samples, a placebo-control group and a longer follow-up are needed to confirm these findings and explore the long-term efficacy of tDCS in combination with ECT or rTMS as a maintenance therapy. Originally, this pilot study was designed and conducted as a clinical development initiative aimed at improving the operations of the neuromodulation unit. The study was implemented in clinical practice, with data collection being part of the clinical

evaluation. This resulted in limitations in data availability, e.g. symptoms scales were lacking for some patients, and the collection of clinical status was not systematic for all patients. The diagnoses of the patients are based on the clinical diagnosis made by the physicians (psychiatric or psychiatric trainee) at the appointment before starting the ECT or rTMS, and the diagnoses are not changed during the treatment nor evaluated using structured interviews.

However, despite these limitations, this study is important in being the first ever to report on the effects and feasibility of add-on tDCS in combination with maintenance ECT or rTMS.

CONCLUSIONS

Based on this small case series, tDCS shows promise as an adjunct to traditional neuromodulation maintenance treatments ECT and rTMS for patients with TRD. While it may not fully replace these treatments, it offers potentially a more accessible and for some patients, more achievable option for long-term treatment. Larger studies with placebo control are needed to better understand the long-term effects and optimal protocols.

Declarations of interest

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