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The efficacy of transcranial direct current stimulation (tDCS) in the treatment of depression and brain functional changes compared to venlafaxine

Submission date
23/09/2015

Recruitment status
No longer recruiting

Registration date
02/10/2015

Overall study status
Completed

Last Edited
10/10/2022

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Major depressive disorder (MDD), often referred to as depression, is one of the most common mental health conditions in the world. The symptoms of MDD can vary greatly from person to person, but they generally include low mood, problems with sleeping and/or eating, and a general loss of interest in life. Treatment often relies heavily on antidepressant medications, which work by increasing the activity and levels of a group of chemicals in the brain (neurotransmitters). Venlafaxine is considered to be one of the most effective antidepressant medications on the market, and is regularly prescribed in cases of severe depression. Although many people benefit from antidepressant treatment, it does not work for everyone and so other treatment options are essential. Transcranial direct current stimulation (tDCS) is a treatment which involves using very mild electrical current to trigger activity the brain. When receiving tDCS treatment, sticky pads which conduct electricity (electrodes) are placed on the scalp which stimulates specific parts of the brain. The aim of this study is to compare the effects of venlafaxine and tDCS on brain activity and the treatment of depression.

Who can participate?
Right handed adults suffering from major depressive disorder who have not responded to previous treatment.

What does the study involve?
In part one of the study, participants are randomly allocated into one of two groups. After one week of not having receiving any treatment for depression, participants are started on a four week treatment plan. Those in group one are treated with venlafaxine and those in group two are treated with tDCS. All participants have their brain activity measured at the start and end of the four week treatment period using brain scanning techniques. After the four week treatment period, participants who have responded to their treatment move onto part two of the study. In

part two of the study, participants continue the treatment plan that they were started on in part one of the study for a further eight weeks. These participants then have their brain activity measured again at the end of the eight week period.

What are the possible benefits and risks of participating?
A possible benefit of participant in the study is the improvement of depressive symptoms. There is no substantial risk of participating, other than the possibility of medication side effects or side effects of tDCS. tDCS is generally well tolerated, the main side effects are itching, tingling, headache or burning sensation.

Where is the study run from?
National Institute of Mental Health (Czech Republic)

When is the study starting and how long is it expected to run for?
October 2015 to April 2019 (updated 09/10/2019, previously: December 2019)

Who is funding the study?
Ministry of Health (Czech Republic)

Who is the main contact?
Dr Martin Bares

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-001639-19

Protocol serial number
AZV CR 15-29900A

Study information

Scientific Title
The efficacy of transcranial direct current stimulation (tDCS) in the treatment of depression and brain functional changes compared to venlafaxine: A four week, double-blind, parallel, randomized study with an eight week, open-label, follow-up study

Study objectives
1. To compare efficacy and tolerability of transcranial direct current stimulation (tDCS) and venlafaxine in the acute treatment of depressive disorder and relapse prevention
2. To identify predictors of response to both interventions and map functional brain changes during the treatment (fMRI, QEEG cordance, LORETA)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethic Committee of the National Institute of Mental Health (Czech Republic), 17/06/2015, ref: 62 /15

Study design
1. Single-centre double-blind randomised parallel trial
2. Open-label follow-up study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Depression

Interventions
Part one: Single-centre double-blind randomised parallel trial
Following an initial wash-out period (5-7 days), eligible subjects will receive 4-week treatment. They will be randomly allocated according to permuted block design with a fixed block size 4, in a 1:1 ratio (no stratification) to either tDCS + placebo group or venlafaxine + placebo stimulation group. Both groups will also receive hydroxyzine (maximum 100 mg/day) for anxiety and zolpidem for insomnia during the study. The continuation of benzodiazepine medication will be allowed in unchanged dosage in patients who used them before the study. Participants who do not respond to treatment in the acute phase of study will be treated as usual according to their psychiatrists.

Group 1: Venlafaxine extended release (ER) + placebo stimulation
Patients assigned to venlafaxine treatment will take 75mg of venlafaxine ER for the first 5 days of the study period. From day 6 onward, the dose could be increased every 5 days by 75 mg to maximal dose (375mg/day) according to the clinical judgment of the attending physician. Patients who will not tolerate at least 150mg of venlafaxine ER/day will be excluded from the study. The placebo stimulation will be delivered in the same anatomical location with identical stimulation parameters as real stimulation but the device will be turned-off after 1 minute of active stimulation.

Group 2: Transcranial direct current stimulation (tDCS) + placebo medication
The tDCS montage will comprise placement of the anode over the F3 area and cathode over the F4 area (corresponding to the left and right DLPFC according to 10-20 EEG system). Rubber electrodes will be inserted in 25-cm2 saline and gel soaked sponge and fixed with a headband to

stimulation area. Each week day (altogether 20 sessions), subjects will receive a direct current of 2mA (current density 0.08 mA/m2 for 30 min/ day). Placebo capsules will be administered at the same schedule as Venlafaxine ER.

Part two: Open label follow-up study
Participants who finish the acute phase of the study and achieve response to tDCS or venlafaxine are enrolled into the follow up study, lasting for a period of 8 weeks. There is no change in allowed concomitant treatment with exception of possibility to reduce benzodiazepines. At the end of the study period, participants are subsequently treated according to clinical judgment of the attending psychiatrist.

Group 1: Venlafaxine group
Participants continue the venlafaxine treatment in unchanged daily dose.

Group 2: TDCS group
Participants receive stimulated once a week with the same parameters of stimulation (current, duration of stimulation etc.) as in the acute phase study.

For both groups, EEG data (10 minutes in duration) will be recorded at baseline and after first and fourth week of acute treatment and at the end of follow up phase of study (week 12) under the standard condition (semi-recumbent position, eyes closed) with 21 surface electrodes placed according to the international 10/20 system. fMRI measurements will be performed on a 3 Tesla scanner before the start of study and at the end of acute study (week 4).

Intervention Type
Mixed

Primary outcome(s)
Double-blind study:
1. Response to treatment with both interventions measured as ≥50% reduction of MADRS (Montgomery and Åsberg Rating Scale) score at the end of the study (week 4)
2. The number of participants who drop-out from the study for any reason in either study group during the duration of the study
3.The ratio of occurrence of a priory defined predictor (reduction of prefrontal cordance value) in responders and non-responders to both interventions measured after the first week of treatment

Open-label, follow-up study:
The number of patients suffering from relapse of depression defined as the score ≥20 points in the MADRS in combination with score 4 or more points in the CGI at the time of follow-up visits or need of change of antidepressant treatment due to substantial worsening of clinical status during the duration of the open-label follow-up study (8 weeks)

Key secondary outcome(s))
Double-blind study:
1. Remission rate for both interventions measured as MADRS score ≤10 points at the end of the study (week 4)
2.The distribution of current density and its change measured by sLORETA (low resolution electromagnetic tomography) and the analysis of functional connectivity measured by eLORETA (exact low resolution brain electromagnetic tomography) in responders and non-responders to both interventions at baseline, week 1 and the end of the study (week 4)

3. Functional connectivity in rsfMRI in responders and non-responders to both interventions (tDCS, venlafaxine) and its change measured at baseline and week 4 of the study

Open-label, follow-up study:
1. The distribution of current density measured by sLORETA (low resolution electromagnetic tomography) and the analysis of functional connectivity measured by eLORETA (exact low resolution brain electromagnetic tomography) in participants of the open-label, follow-up study (responders in the double-blind study) treated with both interventions at the beginning and the end of the study

Completion date
24/04/2019

Eligibility

Key inclusion criteria
1. Patients suffering from major depressive disorder (recurrent or single episode) diagnosed according to Diagnostic and Statistical Manual of the American Psychiatric Association-IV. revision criteria, confirmed using The Mini-International Neuropsychiatric Interview - M.I.N.I., Czech version 5.0.0
2. Patients fulfilling at least Stage I criteria for resistant depression according to Thase and Rush (≥1 previous, unsuccessful, adequate, antidepressant treatment)
3. The mental ability to understand and sign Informed Consent Form
4. The score in the Montgomery and Åsberg Rating Scale (MADRS) ≥25 and the score in Clinical Global Impression ≥4
5. Inpatients in the double-blind phase of treatment
6. Age between 18 and 65 years
7. Right handedness

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
57

Key exclusion criteria
1. Psychiatric comorbidity on axis I and II according to DSM IV in the 6 months before enrollment to the study

2. Psychotic, bipolar disorder or dementia in the history
3. Contraindications of venlafaxine treatment according to SPC
4. Contraindications of MRI (metallic plates in the head, applied pacemaker or other electronic stimulation devices, etc.)
5. Contraindications of tDCS (skin disease, superficial injury and fracture or infraction of skull in the stimulation area, epilepsy, metallic plates in the head)
6. Pregnancy or breast-feeding
7. Patients with severe somatic disorders (cardiovascular disease, neoplasms, endocrinology disorders etc.) that could be associated with depression due to somatic diseases
8. Patients treated with electroconvulsive therapy less than 3 months before enrollment or suffering
from neurologic disorder (e.g., epilepsy, head trauma with loss of consciousness) and patients using any treatment which can strongly affect EEG
9. Application of other concomitant medication that is not allowed in protocol (e.g. antipsychotics,
mood stabilizers etc.)
10. Unsuccessful treatment with venlafaxine or tDCS in the current episode of depressive disorder
11. Fluoxetine treatment before the enrollment to the study

Date of first enrolment
01/04/2019

Date of final enrolment
01/09/2019

Locations

Countries of recruitment
Czech Republic

Study participating centre
National Institute of Mental Health
Topolova 748
Klecany
Czech Republic
250 67

Sponsor information

Organisation
Ministry of Health, Czech Republic

ROR
https://ror.org/00y6khe77

Funder(s)

Funder type
Government

Funder Name
Ministry of Health, Czech Republic

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	23/10/2019	02/04/2020	Yes	No
Protocol file			10/10/2022	No	No