BiOmarkers tO perSonalise Treatment of depression (BOOST depression)

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Ethical review	Approved WMO
Status	Pending
Health condition type	Mood disorders and disturbances NEC
Study type	Observational non invasive

Summary

ID

NL-OMON57365

Source
ToetsingOnline

Brief title
Biomarkers for treatment of depression

Condition

- Mood disorders and disturbances NEC

Synonym
clinical depression, major depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: NWO,Biogen,BitBrain,Philips

Intervention

Keyword: Artificial Intelligence, Biomarkers, Depression, Treatment

Outcome measures

Primary outcome

The main study parameter for our primary objective is the machine learning performance of classifying antidepressive treatment responders and non-responders across five different treatments with the use of various biomarkers.

Secondary outcome

Main study parameters for our secondary objective are differential changes in epigenetic and neuroimaging (MRI, EEG) markers after treatment between outcome/diagnostic groups.

Study description

Background summary

Major depressive disorder (MDD) is a severely debilitating psychiatric disorder affecting 550.000 individuals in the Netherlands each year and is the leading cause of disability worldwide. Treatment options (including pharmacological treatment with a selective serotonin reuptake inhibitor (SSRI), cognitive behavioural therapy (CBT), repetitive transcranial magnetic stimulation (rTMS), intranasal esketamine, and electroconvulsive therapy (ECT) only result in 30-50% of patients achieving clinical response. Each subsequent treatment attempt can become less successful, which increases the risk for chronic depression and suicidality.
Uncovering biomarkers predictive of treatment outcome would help us circumvent current trial and error care based on a one-size fits- all stepped care protocols. While previous re-search has shown that various behavioral/clinical and biological factors at baseline are related to eventual treatment response across the five treatments mentioned above, these studies are performed on small samples and/or not validated with independent methods, limit-ing the reliability of the associations and preventing utilization in clinical care.

This study aims to discover and validate biological (MRI, EEG, (epi)genetics) and clinical markers (questionnaires) (together henceforth called biomarkers) obtained from patients with MDD that are related to treatment outcome. We will develop a machine learning model that can perform differential predictions of treatment outcome with these biomarkers for possible use in future care. This could replace current trial-and-error treatment practice, which would have an enormous benefit for patients and society, could reduce the number of ineffective treatments and suffering of unneeded side-effects, and could improve our understanding of the biological and clinical factors underlying effective treatments in depression.

Study objective

Our primary objective in this study is to predict treatment outcome for SSRI, CBT, rTMS, esketamine, and ECT in patients with MDD with the use of biomarkers and machine learning using data obtained before a new or follow-up treatment. Our secondary objective is to identify the neurobiological mechanisms underlying treatment response using data obtained before and after treatment.

Study design

We will use a longitudinal parallel group design. Patients with a verified diagnosis of MDD will receive one of the five investigated new or follow-up treatments as usual in accordance with national guidelines. We will acquire biological and clinical data from each participant before and after treatment. In order to control for test-retest effects in the longitudinal analysis of neuroimaging data, we will additionally recruit a group of matched healthy controls who will also be investigated twice at a comparable interval.

Study burden and risks

As this is a prospective non-interventional study, the burden for participants is limited to time investment, which includes filling in questionnaires (40 minutes at baseline, 5 minutes every two weeks, ~0.5 hours at 3-month follow-up, 5 minutes at 6-month follow-up) and obtaining a saliva sample at home, and an on-site visit for additional questionnaires, physical measurements, and neuroimaging (~2/2.5 hours at baseline and ~2 hours at 3-month follow-up).
In addition, participants can voluntarily decide if they want to invest additional time (approximately 40 minutes) through opt-in procedures for the ecological momentary assessment (EMA; 8 times a day for 6 days, 1 minute per administration at home).
We have attempted to reduce the time burden where possible, and most of the study procedures can be performed at home at the participant*s own pace. Study procedures and associated time burden have been constructed and approved by representatives from our consortium partner De Depressievereniging serving the

interest of patients with depression.
The study entails no physical risk, as the MRI scan will be performed by trained personnel in hospitals/research institutions. There is no (clinical) benefit for participation, but the data acquired from the study may greatly improve personalized treatments for future patients.

Study procedures and the expected time burden are as follows:
• Questionnaires:
Participants will be asked to complete several standardised questionnaires regarding participation eligibility, demographic measures, and clinical measures of symptom occurrence and severity one week prior to the start of their treatment. It is expected to take a total of 1.5 hours to fill out these questionnaires (40 minutes at home, 50 minutes on site), of which 7 out of 12 questionnaires can be filled out at home in the participant*s own time, spread out over the 7 days prior to treatment. The MINI-S, HDRS-17, HAM-A DM-TRD and C-SSRS need to be assessed by a trained and qualified employee during the first site visit. The biweekly repeated online questionnaire QIDS-SR for three-month follow-up takes approximately 5 minutes. A final QIDS-SR will be assessed after 6 month for long term efficacy assessment.
• Neuroimaging:
Neuroimaging data will be obtained by trained personnel with the use of EEG and MRI. Acquisition of neuroimaging data including preparation time and instructions is expected to take approximately one hour and fifteen minutes.
• Saliva sampling
Participants will be asked to spit in a sample tube for the collection of genetic material. This will be done at home in the morning on an empty stomach for accurate epigenetic measurement.
• Physical measurements
We will measure the participant*s height, weight, heart rate, and blood pressure.

Opt-in study procedures:
• EMA:
The EMA measures daily affective fluctuations and will be performed with the online smartphone app M-path (https://m-path.io/) installed on the participant*s mobile phone. Participants will receive a notification to complete a 10-Item PANAS short-form questionnaire at random timepoints 8 times a day for 6 days. Affective dynamics have previously been associated with depressive symptoms and treatment response in similar EMA designs [17, 18]. While the number of assessments per day may be a time burden for the participants, the time it takes to complete the 10 items in each assessment is short (approximately 1 minute).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients:
• Diagnosis of major depressive disorder (MDD) classified according to the DSM-5 with a moderate to severe depression as assessed by an HDRS-17 score of >=14
• 18-75 years of age
• Willingness and ability to give written informed consent and willingness and ability to understand, to participate, and to comply with the study requirements
• Starting treatment for the depressive episode with CBT, sertraline, rTMS, ECT, or intranasal esketamine

Healthy controls:
• 18-75 years of age

• Willingness and ability to give written informed consent and willingness and ability to understand, to participate, and to comply with the study requirements

Exclusion criteria

Patients:
• Diagnosis of bipolar disorder or psychotic disorder assessed by the MINI-S. Other comorbid disorders will not be excluded to ensure representativeness of the sample.
• For MRI: contraindication such as metal implants, claustrophobia, and pregnancy
• Major head trauma or neurological disease, current or in history

Healthy controls:
• A current or past psychiatric diagnosis, assessed by the MINI-S
• Major head trauma or neurological disease, current or in history
• For MRI: contraindications such as metal implants, claustrophobia, and pregnancy

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025
Enrollment:	900
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	05-03-2025
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL87593.018.24