New Exploratory Tools, Technologies and Biomarkers to characterize Depression

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To assess utility and accuracy of an electroencephalography (EEG) -based brain network analysis platform as potential diagnostic tool for MDD, to correlate digital biomarkers and *gold standard* psychometric questionnaires such as MADRS in MDD and...

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

Summary

ID

NL-OMON48699

Source
ToetsingOnline

Brief title
New methods to characterize depression

Condition

- Mood disorders and disturbances NEC

Synonym
Depression

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: depression, Major depressive disorder, mood disorder

Outcome measures

Primary outcome

Mini International Neuropsychiatric Interview (MINI)

Structured Interview for the Hamilton Rating Scale for Depression (SIGHD-IDS)

Montgomery-Åsberg Depression Rating Scale Structured Interview Guide

(MADRS-SIGMA)

Quick Inventory of Depressive Symptomatology (QIDS-SR) self-reportversion

Columbia Suicide Severity Rating Scale (C-SSRS).

Depression Stress Scales (DASS)

WHO Disability Assessment Schedule 2.0 (WHODAS 2.0)

ElMindA Cognitive Tests (Brain Network Activation)

Cambridge Cognition, CognitionKit (cognition and mood assessments)

Sonde Health (voice sampling procedure, vocal analytics)

NeuroCart (Neuropsychological Test Battery)

BeHapp (social interactions)

Neurotrack (eye movement)

Emotional Bias Task (EBT)

F1l

Secondary outcome

Exploratory (fluid) Biomarkers :

Metabolic, inflammatory, and disease state markers including but not limited to

the following: BDNF, D-serine, IL-6, CRP, TNF-alpha, IFN-gamma, IL- 1beta,

IL-1Ra, IL-4, IL-13 and Tryptophan/kynurenine pathway metabolites. Exploratory genetic markers including but not limited to polymorphisms associated with disease may also be examined.

Study description

Background summary

Since the introduction of antidepressants to psychiatry in the 1960s, the Hamilton Depression Rating Scale (HAMD) and the Montgomery & Äsberg Depression Rating Scale (MADRS) have been the most frequently used rating scales to assess patient outcome in major depressive disorder (MDD). As a result, they are considered the *clinical gold standard* to assess pharmacodynamic effects in MDD drug trials. However, both scales are associated with methodological limitations such as unintended therapeutic effects when administered by researchers, over-predicting therapeutic effects in research settings compared to naturalistic settings and concerns about sensitivity to the effects of novel nonmonoaminergic
compounds. The development of novel and potentially more effective antidepressant drugs is therefore hampered by the lack of reliable objective biomarkers and the excessive reliance on clinic-based psychometric questionnaires to quantify drug effects. Taken together, there is a need to identify, validate and implement more sophisticated and methodologically sound technologies to quantify pharmacodynamic effects of novel CNS penetrating compounds in patients with MDD.

Study objective

To assess utility and accuracy of an electroencephalography (EEG) -based brain network analysis platform as potential diagnostic tool for MDD, to correlate digital biomarkers and *gold standard* psychometric questionnaires such as MADRS in MDD and to identify digital biomarkers that are potentially predictive of MDD diagnosis.

Furthermore, we will explore whether there are any differences between healthy volunteers and MDD patients with regard to exploratory soluble biomarkers including but not limited to inflammatory, metabolic, and disease state markers and will conduct exploratory genetic analyses including but not limited to polymorphisms associated with MDD disease state.

Study design

The study will be a cross-sectional, non-interventional study.

Study burden and risks

There is no benefit expected for subjects participating in this study and no or minimal risk (blood withdrawals) is anticipated. MDD patients will be carefully evaluated to assess whether it would be desirable and safe for them for participate. Hopefully this study will help develop new objective methods to test novel and potentially more effective antidepressant drugs which are now being hampered by the lack of reliable objective biomarkers and the excessive reliance on clinic-based psychometric questionnaires to quantify drug effects.

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:
1. Written informed consent must be obtained before any assessment is performed.
2. Males and females, age 18 to 65 years (inclusive).
3. Subjects must be diagnosed by the attending general practitioner, psychiatrist or clinical psychologist with, and meet the diagnostic criteria for at least one of the following disorders as confirmed with the Mini International Neuropsychiatric Interview (MINI):
4. Current major depressive disorder (MDD) without psychotic features according to DSM-5 (296.22, 296.23, 296.32, 296.33).
5. Current persistent depressive disorder (PDD) or dysthymia according to the DSM-5 (300.4).
6. Total HAMD-17 total score of >16 at Screening.
7. Use of mono-aminergic antidepressant drug (SSRI, SNRI, mirtazapine, TCA, MAO-I) at a stable dose for at least 4 weeks (6 weeks for fluoxetine).
8. Must read and speak both Dutch and English as a first or second language.
9. Subjects must own and use a personal computer (desktop or laptop) using the Windows operating system
10. Able to comply with the study procedures, prohibitions and restrictions (drug and alcohol use) as specified in the protocol.
11. Android-based smartphone , Healty volunteers :
1. Written informed consent must be obtained before any assessment is performed.
2. Male or female subjects, 18 to 65 years (inclusive)
3. Body mass index (BMI) between 18 and 30 kg/m2.
4. Must read and speak both Dutch and English as a first or second language.
5.Subjects must own and use a personal computer (desktop or laptop) using the Windows
operating system.
6. Able to comply with the study procedures, prohibitions and restrictions (drug and alcohol use) as specified in the protocol.
7. Android-based smartphone

Exclusion criteria

Patients:
1. Current primary DSM-5 diagnosis of general anxiety disorder (GAD), panic disorder, obsessive compulsive disorder (OCD), posttraumatic stress disorder (PTSD), anorexia nervosa, bulimia nervosa or cluster C personality disorder (e.g. avoidant, dependent, obsessive-compulsive personality disorders). Subjects for whom the diagnosed mood disorder (MDD, PDD or dysthymia) is considered the primary diagnosis are not excluded.
2. Current or previously diagnosed psychotic disorder, mood disorder with psychotic features, bipolar disorder, mental retardation, cluster B personality

disorder (e.g., borderline, antisocial, narcissistic personality disorders).
3. Current or recent history of clinically significant suicidal thoughts or ideation within the past 12 months or any suicidal behavior within the past 6 months as demonstrated with the C-SSRS should be carefully screened and only included at the discretion of the investigator.
4. Positive urine test for drugs of abuse at Screening or on study days or a current diagnosis of substance use disorder (including alcohol but excluding nicotine), or previous substance use disorder (including alcohol but excluding nicotine) within the past 12 months according to DSM-5.
5. Evidence of renal, hepatic, cardiovascular or metabolic dysfunction or any active or chronic disease or condition that could interfere with the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the investigator to have no clinical relevance.
6. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during Screening may be repeated before randomization to confirm eligibility or to assist in evaluating clinical relevance.
7. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during Screening may be repeated to confirm eligibility or to assist in evaluating clinical relevance.
8. Positive urine *-human chorionic gonadotropin (*-hCG) pregnancy test at Screening in women of childbearing potential.
9. Current enrollment in an interventional study., Healthy volunteers:
1. Current or previous clinically relevant history or family history of psychiatric disorders, neurological disorders or neurosurgery.
2. Positive urine test for drugs of abuse at Screening or on study days or a current diagnosis of substance use disorder (including alcohol but excluding nicotine) or previous substance use disorder (including alcohol but excluding nicotine) within the past 12 months according to DSM-5.
3. Evidence of renal, hepatic, cardiovascular or metabolic dysfunction or any active or chronic disease or condition that could interfere with the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the investigator to have no clinical relevance.
4. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood

count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during Screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
5. Use of any medications (prescription or over-the-counter [OTC]), within 14 days of Visit 1, or less than 5 half-lives (whichever is longer). An exception is paracetamol (up to 2 g/day). Other exceptions will only be made if the rationale is clearly documented by the investigator.
6. Positive urine *-human chorionic gonadotropin (*-hCG) pregnancy test at Screening in women of childbearing potential.
7. Current enrollment in an interventional study

Study design

Design

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

Primary purpose: Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-07-2018
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	05-07-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	28-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL64192.056.18

Study results

Date completed:	29-08-2019
Results posted:	20-08-2020

First publication
03-07-2020