The effects of antipsychotic maintenance therapy on brain volume: randomized (dis)continuation after remission of a first psychotic episode.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Schizophrenia and other psychotic disorders
Study type	Observational non invasive

Summary

ID

NL-OMON52454

Source
ToetsingOnline

Brief title
HAMLETT MRI

Condition

- Schizophrenia and other psychotic disorders

Synonym
Psychotic disorder / Schizophrenia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: ZONMW / NARSAD

Intervention

Keyword: Antipsychotics, First Episode of Psychosis, Magnetic Resonance Imaging, Maintenance treatment

Outcome measures

Primary outcome

The main study parameter concerns brain volume measured with anatomical magnetic resonance imaging (MRI), at two time points: at baseline and at 12 months follow-up. MRI scans will be acquired on a standard 3 Tesla Siemens clinical scanner located at the Radiology Department of the University Medical Center Groningen.

Secondary outcome

A secundary study parameter is retinal nerve fiber layer (RNFL) thickness, as measured by optical coherence tomography (OCT). The measurement takes 10 minutes and is non-invasive. Results will be correlated to whole brain volume and total grey volume assessed with MRI. The RNFL of FEP patients will be compared with the RNFL of healthy controls.

Other secundary study parameters are assessed during and as part of the HAMLETT core study and include: Physical health, movement disorders, language, symptom severity, cognition, global functioning, social functioning, medication use and adverse events.

Study description

Background summary

Previous research has reported a negative association between cumulative dose of antipsychotic medication and brain volume in patients with schizophrenia. A problem with these studies is that patients with severe symptoms tend to need a higher dose than patients with mild symptoms, i.e. it is impossible to disentangle whether smaller brain volumes are caused by more medication use or higher symptom severity.

Study objective

The aim of the proposed study is to investigate the effects of antipsychotic medication on total brain volume and specific brain structures known to be affected in schizophrenia, such as hippocampus, thalamus, caudate, parietal and prefrontal cortex, as measured with magnetic resonance imaging (MRI).

We will also investigate effects of sex and type of antipsychotic medication on brain volumes. Furthermore, we will associate brain volume loss between the two scans (12 months follow-up) with short and long-term clinical outcome of the patients, as assessed by the HAMLETT core study and we will associate retinal nerve fiber layer (RNFL) thickness, as measured by optical coherence tomography (OCT) with brain volume as measured by MRI. RNFL will be compared between FEP patients and healthy controls.

Study design

The HAMLETT study is a large Dutch clinical trial that randomizes patients after remission of a first psychotic episode, to continue or reduce/discontinue their antipsychotic medication. It is performed in the UMC Utrecht and UMC Groningen (Handling Antipsychotic Medication: Long-term Evaluation of Targeted Treatment; Protocol number: [62202.042.17]/80-84800-98-41015) and funded by the Dutch research organization (ZonMW; grant number 8480411003). The study is currently including 512 participants over the course of three years. The current add-on study aims to add MRI measurements for participants of the HAMLETT study at baseline and at a 12 months follow-up, using an observational design.

Study burden and risks

Subjects of this study will undergo two MRI scans. Each MRI scan will last 45 minutes and will pose minimal risk. Participants will be exposed to a field-strength of 3 Tesla and scanner noise. Thus far, there is no evidence to suggest that exposing humans to a magnetic field of this strength has a

negative influence on their health. With regard to the noise, earplugs and headphones will be provided. The small space of the MRI scanner may cause anxiety to those with claustrophobia. The potential benefit to society in the future is considerable if the findings lead to more insight in effects of antipsychotic medication on brain volume. There is no individual benefit to the participants.

Healthy controls undergo a single OCT scan, which is noninvasive, lasts for only 10 minutes, and poses minimal risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Inclusion criteria for FEP patients:
1. The participant has had a first episode of psychosis and uses antipsychotic

medication.
2. Psychotic symptoms are in remission for 3-6 months with an antipsychotic.
3. Age 18-60 years.
4. The participant understands the study and is able to provide written informed consent.
5. HAMLETT is the only medical-scientific medication study in which the patient participates.
6. Sufficient command of the Dutch language.

Inclusion criteria for healthy controls for OCT:
1. Age 18-60 years.
2. The participant understands the study and is able to provide written informed consent.

Exclusion criteria

Exclusion criteria for FEP patients:
1. Dangerous or harmful behaviour occurred during the psychosis
2. Coercive treatment (based on judicial ruling)
3. The refusal to be informed of structural brain abnormalities that could be detected during the experiment
4. MRI contra-indications, e.g. Ferrous objects in or around the body, or claustrophobia
5. Pregnancy

Exclusion criteria for healthy controls for the OCT-scan:
1. (History of) diagnosed psychiatric disorders
2. (History of) psychotropic medication use
3. (History of) neurological diseases that may affect the brain
4. (History of) substance abuse
5. (History of) ophthalmological disorders, as determined with the questionnaire on eye health ('Vragenlijst ooggezondheid*)
6. (History of) systemic and autoimmune diseases that may affect the eye or optic nerve, e.g. diabetes, glaucoma or refractory arterial hypertension
7. First-degree family member with glaucoma

Study design

Design

Study type:	Observational non invasive

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-02-2019
Enrollment:	225
Type:	Actual

Ethics review

Approved WMO Date:	31-08-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-06-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL66377.042.18