Treatment Response in Non-Affective Psychosis

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON28864

Source
Nationaal Trial Register

Brief title
TRIP

Health condition

Schizophrenia, Schizofrenie, psychosis, psychose

Sponsors and support

Primary sponsor: GGZ Leiden, Rivierduinen; Department of Radiology and Nuclear Medicine, Amsterdam University Medical Centre.
Source(s) of monetary or material Support: GGZ Rivierduinen Leiden, Rivierduinen, Department of Radiology and Nuclear Medicine, Amsterdam University Medical Centre & Stichting J.M.C. Kapteinfonds

Intervention

Outcome measures

Primary outcome

- [18F]-DOPA influx (Ki) values in the whole striatum and its associative, limbic, and sensorimotor subregions (assessed in subgroup).

- Glutamate/Creatine and Glx/Creatine ratios on 1H-MRS in the ACC.
- GABA concentration on 1H-MRS in the ACC.
- Degree of change of positive symptoms on the CGI-SCH at the first and second follow-up compared to the start of non-clozapine antipsychotic treatment.
- AEA and 2-AG plasma concentrations at the day of the MRI/PET scans.

Secondary outcome

- Percentage change in positive symptom score on the PANSS following 4-6 weeks of non-clozapine treatment at adequate dose (first follow-up) and 6 months after the start of antipsychotic medication (second follow-up).
- Percentage change of total PANSS score between the baseline assessment and the first and second follow-up.
- Neuromelanin contrast ratio on NM-MRI.

Study description

Background summary

Approximately 30% of patients with non-affective psychotic disorder show insufficient response to non-clozapine antipsychotic treatment. Therefore, it is desirable to identify these patients early on by use of a clinical algorithm. This algorithm is likely to be based on a number of biomarkers. Potential biomarkers are striatal dopamine synthesis capacity (sDSC), glutamate and gamma aminobutyric acid (GABA) concentrations in the anterior cingulate cortex (ACC).
Interestingly, cannabis use is associated with an increased risk of psychosis. The main constituent of cannabis, delta-9-tetrahydrocannabinol (THC), exerts its psychotropic effect by binding to receptors of the endocannabinoid system (ECS), and influences dopamine release. The evidence in support of sensitisation of the mesolimbic dopamine system in the pathogenesis of first episode non-affective psychotic disorder is large. However, the relationships between sDSC and blood levels of the endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) have never been examined. Understanding the relationships between the activity of various neurotransmitter systems and treatment response is an important step in the development of personalized treatment.

Study objective

Primary hypotheses:
- Responders (CGI-SCH degree of positive symptom change rating of 1 or 2) have significantly higher [18F]-DOPA influx (Ki) values in the whole striatum and its associative and sensorimotor subregions compared to non-responders (CGI-SCH degree of positive symptom change rating of ≥3) and healthy controls. This dopaminergic dysfunction is expected to be the greatest in the associative region. There are no significant differences in the limbic subdivision or between non-responders and healthy controls.

- AEA and 2-AG plasma levels are negatively correlated with [18F]-DOPA influx (Ki) values in the whole striatum and its subregions.

Secondary hypotheses:
- [18F]-DOPA influx (Ki) values in the whole striatum and its associative and sensorimotor subregions are positively correlated with the percentage decrease of positive symptoms at first- and second follow-up.
- Glutamate levels in the ACC are negatively correlated with the percentage decrease of positive symptoms at first- and second follow-up.
- AEA plasma concentration is positively correlated with percentage decrease of positive symptoms at first- and second follow-up.
- AEA and 2-AG plasma levels are significantly elevated in psychotic patients compared to controls.
- Neuromelanin contrast ratios in the substantia nigra (SN) are positively correlated with the percentage decrease of positive symptoms at first- and second follow-up.
- Striatal [18F]-DOPA influx (Ki) values in the whole striatum are positively correlated with neuromelanin contrast ratios in the SN.

Study design

Procedures: 43 patients will be assessed on four separate occasions:
- Baseline assessment (before or within 4 weeks after the start of non-clozapine antipsychotic medication): informed consent, screening, urine drug test, and assessment of symptoms;
- Test day (before or within 9 weeks after the start of non-clozapine antipsychotic medication): MRI scan, urine drug test, determination of fatty acid pattern, AEA, 2-AG, and antipsychotic plasma concentrations, and assessment of depressive symptoms and factors that may influence AEA and 2-AG. In a subgroup of 26 FEP patients, an additional [18F]-DOPA PET scan will be acquired;
- First follow-up (after 4-6 weeks of non-clozapine antipsychotic treatment at adequate dose): diagnostic interview and assessment of symptoms and determination of antipsychotic plasma concentrations;
- Second follow-up (6 months after the start of non-clozapine antipsychotic treatment): assessment of symptoms and substance use.
If applicable, treatment compliance will be evaluated together with the patient during each occasion.

Twenty healthy controls will be assessed on two separate occasions: (T1) informed consent, screening, psychiatric interview, urine drug test, and assessment of symptoms and medication use; (T2) PET and MRI scans, urine drug test, evaluation of depressive symptoms and blood sampling.

Intervention

None

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Eligibility criteria

Inclusion criteria

1) First or later episode of psychosis, provided that the patient has not used antipsychotics for at least one year and that lifetime use of antipsychotics does not exceed 6 months (Patients only).
2) A rating of at least 5, corresponding to moderate severe, on two or more items of the positive symptom subscale of the PANSS at the moment that the patient enters the mental health services (Patients only).
3) Age: 18-35 years.
4) Within the first 5 years after onset of the first psychotic episode (Patients only).

Exclusion criteria

1) Antipsychotic use longer than 9 weeks at the moment of the PET scan (Patients only).
2) Current neurological disorder or history of neurological disorder (e.g. epilepsy) or history of severe head trauma (contusio cerebri).
3) Current psychotic disorder or history of any psychotic disorder (Controls only).
4) First-degree relative with schizophrenia spectrum disorder (Controls only).
5) Incompetence (Dutch: wilsonbekwaamheid) according to the responsible physician or researcher. Participants should be able to understand the purpose of the study (understanding what happens in the brain and the development of a tool to select the best medication for a particular individual), the associated benefit (none for them), burden (hours of time) and risk (minimal, but not zero).
6) Patients who resist or oppose antipsychotic medication (Patients only).
7) Primary diagnosis of bipolar disorder with psychotic features or major depressive disorder with psychotic features at the moment that the patient enters the mental health services

(Patients only).
8) Psychotic disorder due to another medical condition or substance/medication-induced psychotic disorder (Patients only).

Exclusion criteria related to alcohol, soft/hard-drugs, and medicinal drugs:
1) Lifetime history of DSM-5 diagnosis of any Substance Use Disorder (SUD; except tobacco use disorder and alcohol use disorder, mild) or substance use which would have met the DSM-5 criteria for SUD.
2) Current use of substances other than tobacco or alcohol, such as XTC, cannabis, cocaine, amphetamine, opioids or GHB. A) Use of cocaine, amphetamine, GHB or opioids in the past is allowed, if last use occurred at least three months before the study and if the substance was used only once in the past year. B) Use of XTC in the past is allowed, if last use occurred at least three months before the study and if substance was used on no more than five occasions in the past year. C) Use of cannabis in the past is allowed, if last use occurred at least one month before the study and if there was no disorder in the use of cannabis in the past.
3) Positive urine drug screen at the baseline assessment. Participants will be tested on cannabis, amphetamine, XTC, cocaine, and opiates.
4) Positive urine drug screen at the test day (Controls only). Participants will be tested on cannabis, amphetamine, XTC, cocaine, and opiates.
5) Current or recent (less than 3 months ago) use of other psychotropic drugs that may influence the dopamine system (e.g. sodium valproate, lithium or methylphenidate). The use of benzodiazepines, hypnotics and antidepressants in amounts within the therapeutic range is allowed.

Exclusion criteria directly related to MRI and PET/CT scanning:
1) Smoking during the period of three hours prior to the PET/CT scan and eating or using caffeinated drinks during the period of six hours prior to the PET/CT-scan.
2) Participation in a scientific examination where radiation was used, in the last year.
3) In women: positive pregnancy test on the day of the MRI and/or PET/CT scans and lactation.
4) Metal objects in or around the body (e.g. pacemaker and ferromagnetic implants) or claustrophobia.

Study design

Design

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

Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2020
Enrollment:	63
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 54876
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8338
CCMO	NL72218.058.20
OMON	NL-OMON54876

Study results

Summary results
N/A