Effect of different antipsychotic medications on craving and craving related brain activity in patients with schizophrenia and cannabis abuse or dependence: a randomized controlled study comparing clozapine and risperidone.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21257

Source
Nationaal Trial Register

Brief title
fmri.clo.ris.can

Health condition

Schizophrenia, cannabis, risperidone, clozapine, fMRI

Schizofrenie, cannabis, risperidon, clozapine, fMRI

Sponsors and support

Primary sponsor: L. de Haan
Source(s) of monetary or material Support: ZonMW

Intervention

Outcome measures

Primary outcome

Differences between the treatment conditions in pre-post treatment changes in craving related brain activity are the primary outcome measure.

Secondary outcome

Differences between the treatment conditions in pre-post treatment changes in questionaires on craving and schizophrenia.

Study description

Background summary

Cannabis abuse and dependence in patients with schizophrenia occurs frequently and is associated with adverse outcomes. Craving is regarded as a central phenomenon that contributes to the continuation of cannabis use and to relapse after a period of abstinence. Antipsychotic medications with high affinity for the dopamine D2 receptor have been found to increase craving. Clozapine, with its low affinity for the dopamine D2 receptor, is associated with reduced substance use. However, firm evidence for clozapine’s superiority is lacking.

Objective:
To test the hypothesis that clozapine treatment compared to risperidone treatment is associated with differences in functional craving and the associated brain activity patterns related to reduction in subjective craving.

Study design:
A randomized controlled trial comparing the effect of clozapine and risperidone on cannabis craving in cannabis abusing or dependent patients with schizophrenia. Specific cognitive tasks will be used to test craving pathways and associated brain activities are assessed with functional MRI.

Study population:
Eligible for the study are male in- and outpatients age 18 to 30, meeting DSM-IV criteria for schizophrenia, schizoaffective - or schizophreniform disorder and cannabis abuse or dependence based on the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (SCID-P).

Intervention:
Patients will be randomly allocated to receive clozapine or risperidone.

Main study parameters/endpoints:
Differences in pre-post treatment changes in brain activation are the primary outcome measure. [At baseline, before the first dose of the study medication and after 4 weeks treatment, craving related brain activity will be assessed using specific fMRI craving paradigms.]

Study objective

That clozapine treatment compared to risperidone treatment is associated with a significant reduction in subjective craving and in a lower activity of the different functional craving pathways and their associated brain activity patterns.

Study design

Baseline and after 4 weeks of medication.

Intervention

Patients will be randomly allocated to receive clozapine or risperidone. One extra session is needed to inform patients on the study design and procedure. Two extra sessions are needed to assess baseline and outcome data. Two fMRI scanning sessions are needed during which specific tests will be administered. Duration of first fMRI scanning session is 38 minutes. Duration of second fMRI session is 32 minutes. Task difficulty of these tests will be set such that each participant will succeed on approximately 66% of his or her target responses. Scanning procedures may induce some burden because participants need to refrain from movements. To diminish the burden from the noise from the scanner, earplugs are used. Use of cannabis is prohibited in the three days before scanning. Three hours before scanning participants are not allowed to smoke cigarettes. One cup of coffee is allowed in the morning before scanning. Urine drug screen will be taken. Before the second fMRI scan blood level of risperidone or clozapine will be taken. Risk: There is a risk on adverse effects related to the treatment with clozapine or risperidone. Careful clinical procedures will be performed to detect adverse effects and respond to them as needed. There are no known risks related to fMRI scanning.

Contacts

Public
Adolescentenkliniek AMC,
Meibergdreef 5,
M.W.J. Machielsen
Amsterdam 1105 AZ

The Netherlands
+31 (0)208913674
Scientific
Adolescentenkliniek AMC,
Meibergdreef 5,
M.W.J. Machielsen
Amsterdam 1105 AZ
The Netherlands
+31 (0)208913674

Eligibility criteria

Inclusion criteria

1. Diverse ethnicity;

2. Meeting DSM-IV criteria for schizophrenia, schizoaffective - or schizophreniform disorder and cannabis abuse or dependence based on the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (SCID-P);

3. Women will not be included because co-morbid cannabis abuse or dependence occurs more frequent in men and the expected number of included subjects, therefore, would not allow separate analysis;

4. We will also include schizophrenia patients without cannabis abuse or dependence and compare their outcomes with those of patients with co-occurring cannabis abuse or dependence;

5. A group of healthy, matched controls will be included to get information on brain activation patterns associated with specific cognitive tasks in antipsychotic-naïve healthy controls. These controls are included to make a comparison with patients with schizophrenia who have been treated with antipsychotics for 4 weeks;

6. All patients need to be abstinent for cannabis use minimally three days before assessment of functional craving pathways.

Exclusion criteria

1. Known hypersensitivity to any ingredient of clozapine or risperidone;

2. Concomitant use of any antipsychotic drug other than clozapine or risperidone;

3. Use of depot antipsychotics in the three months prior to inclusion;

4. Use of psychotropic medications other than oxazepam or biperiden;

5. Narrow angle glaucoma;

6. Known neurological or endocrine disease;

7. Presence of non-removable metal objects;

8. Myeloproliferative disorders;

9. Unstable epilepsy;

10. Agranulocytosis or leucopenia in the past;

11. Current leukocyte level is lower than 3.5 x 109/l, current neutrophilic granulocyte level is lower than 2.0x 109/l.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-04-2009
Enrollment:	50
Type:	Anticipated

Ethics review

Positive opinion

Date:	16-04-2009
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 32193
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL1662
NTR-old	NTR1761
CCMO	NL22828.018.08
ISRCTN	ISRCTN wordt niet meer aangevraagd
OMON	NL-OMON32193

Study results

Summary results
N/A