Phenomics & Genomics of Clozapine Pharmacotherapy: To a better understanding of the backgrounds of clozapine use

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To assess whether the genetic architecture of this severe therapy-resistant SCZ phenotype differs from the broad DSM-based SCZ phenotype.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON20386

Source
NTR

Brief title
CLOZIN Current

Health condition

Genetics of clozapine use because of schizophrenia, schizo-affective disorder, schizophreniform disorder

Sponsors and support

Primary sponsor: Dr. J. Luykx
Source(s) of monetary or material Support: Research funds dr. Luykx

Intervention

Outcome measures

Primary outcome

First, in a discovery cohort a case-control genome-wide association study (GWAS) will be performed on 2000 CLZ using subjects (cases) and >30,000 already available SCZ patients (controls, drawn from the most recent Psychiatric Genomics Consortium analysis, . We hereby aim to reveal potential differences in the genetic architecture between the severe CLZ-SCZ phenotype and the broad SCZ phenotype.

Secondary outcome

Second, a replication cohort of the same size as the discovery cohort (N=2,000 CLZ using subjects and the same number of controls) will be used to replicate any positive associations for each of the two GWAS analyses. Should funding allow and if replication cohorts are available elsewhere and possibly for the purpose of participation in large-scale consortia, GWAS and NGS may be performed on >2,000 CLZ users, e.g. the entire study population. In addition, we use the data with our other protocol (NTR 5257) to create a prediction model for clozapine response and side effects.

Study description

Background summary

Clozapine (CLZ) is generally prescribed if at least two trials of antipsychotic agents have not led to satisfactory clinical improvement, thereby implying that patients on CLZ generally suffer from more severe and/or persistent symptoms than patients suffering from schizophrenia spectrum disorders (SCZ) on other antipsychotic agents. Unraveling the (functional) genetic variation underlying this severe SCZ phenotype therefore has the potential to deepen our understanding of the biological underpinnings of SCZ beyond the boundaries of DSM-based consensus criteria. Such knowledge in turn has the potential to shape future pharmacotherapeutic research. We here hypothesize that targeting this phenotype in genome-wide association studies and next-generation sequencing studies will signal genetic risk loci implicated in this severe SCZ phenotype. In the future, this may lead to early detection of severe SCZ, which in turn will enable tailoring of pharmacotherapeutic strategies to such SCZ subtypes.

In addition, we use the data with our other protocol (NTR 5257) to create a prediction model for clozapine response and side effects.

Study objective

To assess whether the genetic architecture of this severe therapy-resistant SCZ phenotype

differs from the broad DSM-based SCZ phenotype.

Study design

One visit

Intervention

None

Contacts

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Eligibility criteria

Inclusion criteria

-he/she currently uses CLZ
-he/she has received a diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder or psychosis not otherwise specified
-his/her age must be ≥18 years old
-he/she must be able to speak and read the Dutch language
-he/she must be mentally competent and have decisional capacity with regard to a decision

to participate in the current study

Exclusion criteria

- admission to a psychiatric unit involuntarily in the context of an ‘inbewaringstelling’ (IBS)
- a history of Parkinson’s disease

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2015
Enrollment:	2500
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	11-06-2015
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 50518
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5116
NTR-old	NTR5248
CCMO	NL52726.041.15
OMON	NL-OMON50518

Study results

Summary results
None yet