Schizophrenia and MUscarinic Receptor Functioning

No registrations found.

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

Summary

ID

NL-OMON28658

Source
NTR

Brief title
SMURF

Health condition

Psychosis
Cognition

Sponsors and support

Primary sponsor: Academic Medical Center (AMC)
Source(s) of monetary or material Support: ZoNmW

Intervention

Outcome measures

Primary outcome

-M1 receptor binding: ROI’s will be the hippocampus, striatum, anterior cingulate cortex and the dorsolateral prefrontal cortex.

Secondary outcome

-BOLD signal activation during cognitive tasks (PAL, visual learning and memory) and ERT (social cognition) under colinergic challenge and in placebo. (ROI's DLPFC and the hippocampus).

-Neuropsychological tests: CANTAB battery for schizophrenia.

-DTI

-RSfMRI

-MRS

-genetics

Study description

Background summary

Schizophrenia is a serious chronic disorder, usually starting in adolescence. Currently available treatments show no therapeutic effects on cognitive dysfunction, one of the most disabling characteristics of the disease. Cognitive impairment is a predictor of functional outcome and thus pertinent to successful treatment paradigms. Post mortem studies have found evidence of changes in acetylcholine neurotransmission at the muscarinic (M1) receptor, both in the frontal cortex and hippocampal regions of the brain, associated with cognitive functioning in both healthy control subjects and schizophrenia. Results from a hallmark post-mortem study identified a subgroup of patients among schizophrenia with "muscarinic receptor-deficit schizophrenia (MRDS)" with up to 75% loss of muscarinic receptors. It is not known whether MRDS patients present schizophrenia-associated cognitive deficits. This study will test the hypothesis that MRDS can be identified in-vivo and that clincal and neurobiological characteresation of this group of patients will help identifying the neurobiological basis of cognitive impairments in schizophrenia.

The main objective of the study is to investigate the muscarinic cholinergic system as a biological substrate for cognitive dysfunction in first episode psychosis patients, i.e. at onset of illness. We seek to assess whether deficits in M1 cholinergic neurotransmission exist at onset psychosis and if there is dissociation between MRDS patients, with significantly lower M1 binding, and non–MRDS patients. Furthermore, M1 bindingpotential in these regions will be related to cognitive functioning. The modulatory role of acetylcholine at M1 and differentiation in functional activation patterns will be assessed in comparison to healthy control subjects in verbal learning and memory and social cognition.

The study is a single-blind, cross-sectional placebo-controlled study. Only the first episode psychosis patients will receive SPECT imaging using 123I-IDEX on one occasion to assess brain M1 receptor binding. All Participants will then undergo two MRI scanning sessions with cognitive tasks- once under a cholinergic challenge with biperiden, and once after receiving a placebo.

45 first episode psychosis patients 18 years of age and older will be recruited and these will be matched with 45 healthy control subjects. All participants will be mentally competent to assess participation. Only the patients will undergo SPECT imaging.

Study objective

It is hypothesized that:

-there will be a subgroup of patients with first episode psychosis with reduced Muscarinic M1 receptor binding.

-The patients with reduced M1 receptor binding will perform significanlty worse on a cognitive test battery (CANTAB) than the patients without reduced M1 binding

-The patients with reduced M1 receptor binding will have decreased hippocampal and prefrontal activation response to the cholinergic challenge biperiden during a fMRI visual learning & memory ans a social cognition task than the patients without reduced M1 receptor binding and healthy controls.

Study design

All Participants will undergo two MRI scanning sessions with cognitive tasks- once under a cholinergic challenge with biperiden, and once after receiving a placebo. Time-inteval between testdays will be at least one week.

Intervention

On two occasions non- invasive 3.0 Tesla MRI recordings will be conducted following a single dose of 4 mg biperiden or placebo, administered orally. For the SPECT study a registered, well- validated radioligand 123I-IDEX will be administered intravenously.

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Eligibility criteria

Inclusion criteria

-Patients with first-episode psychosis as defined by the standardised criteria of the CASH

-Medication free

-Duration of untreated psychosis no more than 1 year.
-18 years and older

Exclusion criteria

-Use of antipsychotics and anticholinergics

-Contraindications for MRI

-Severe neurological, endocrine or psychiatric disorders

-Pregnancy

-Current use of recreational drugs; participants must be abstinent of recreational drugs such as cannabis at least 4 weaks prior to participation.

-Tardive dyskinesia

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non-randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-02-2015
Enrollment:	90
Type:	Anticipated

Ethics review

Positive opinion

Date:	11-03-2015
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 41528
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL4972

Register	ID
NTR-old	NTR5094
CCMO	NL44908.018.13
OMON	NL-OMON41528

Study results