Schizophrenia and MUscarinic Receptor Functioning

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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…

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28658

Bron
NTR

Verkorte titel
SMURF

Aandoening

Psychosis
Cognition

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC)
Overige ondersteuning: ZoNmW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

the dorsolateral prefrontal cortex.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

-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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

-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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Niet-gerandomiseerd
Blindering:	Enkelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	04-02-2015
Aantal proefpersonen:	90
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	11-03-2015
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 41528
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4972
NTR-old	NTR5094
CCMO	NL44908.018.13
OMON	NL-OMON41528

Resultaten