The Brain Mechanisms Underlying Apathy in Patients with Schizophrenia – a PET study

No registrations found.

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

Summary

ID

NL-OMON21681

Source
NTR

Brief title
Apathy-PET

Health condition

schizophrenia
apathy

Sponsors and support

Primary sponsor: UMCG
Source(s) of monetary or material Support: ERC

Intervention

Outcome measures

Primary outcome

Binding potential for [11C]-raclopride.

Secondary outcome

endpoint

MRI-scan

PET-scan

AES-C

MINI-plus

CDSS

SANS

AES-S

SHAPS

TEPS

TCI

FT

N-back

Study description

Background summary

Rationale: Apathy is a quantitative reduction of self-generated voluntary and purposeful behavior. It is a common symptom in several neuropathological disorders, like schizophrenia. Apathy is very bothersome for the patients and is a strong predictor of poor outcome. Clinically, a distinction has been made between a cognitive (CA) and a social-emotional (SEA) form of apathy. These forms both result in reduced behavioral activation. However, CA and SEA might reflect different cognitive deficits with different underlying neural substrates. It has been suggested that CA is due to a lack of self-initiated action and cognitive control, whereas reduced salience signaling of positive events lies at the core of SEA. The neurochemical systems underlying these two forms of apathy are hypothesised to be predominantly glutamatergic and cortical in case of CA and dopaminergic and subcortical in case of SEA. These circuits might be altered in apathetic patients with schizophrenia. A recent study showed a positive association between tracer binding and negative symptoms

(Pogarell, 2012). However, this has never been directly investigated for apathy. In this study, the presence of dopaminergic abnormalities in relation to CA and SEA are examined in patients with schizophrenia.

Hypothesis: Binding of [11C]-raclopride is lower in patients with schizophrenia than in healthy controls, and this correlates with SEA scores, but not with CA scores.

Objective: The primary objective of the proposed study is to examine the neural substrates of CA and SEA in patients with schizophrenia. Second, we intend to explore the relation between the dopamine system and CA, SEA , and apathy in general.
Study design: The proposed study has an experimental design. Subjects will be scanned with a PET-scanner under resting conditions. Furthermore six interviews will be administered concerning apathy, depression, and other symptoms of schizophrenia. Two questionnaires will be filled out by all participants, in order to assess the experience of pleasure.

Study population: The study population will consist of 20 patients with a diagnosis of schizophrenia and 10 healthy control subjects. The healthy controls will be matched to the patient groups on age, sex, handedness, body mass, and level of education. Ten of the patients will be selected on high levels of cognitive apathy and ten will be selected on high levels of social-emotional apathy.

Main study parameters/endpoints: The main study parameter will be binding potential of [11C]-raclopride in a voxel-wise manner.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Possible participants will first be selected from a sister study (METC 2013.086 ABR 43372, this procedure has been approved by METc UMCG) on the basis of their levels of apathy. The rest of the study will consist of interviews and questionnaires with a maximum total duration of 90 minutes. The PET-scan will have a maximum total duration of 60 minutes and will use a low risk dose (2.75 mSv) of radioactivity according to ICRP 62. There are no direct benefits for subjects to participate. General benefit will be the better understanding of the involvement of the dopamine system in apathy. When SEA scores are indeed correlated with [11C]-raclopride binding, this could aid the development of treatment strategies targeting this dysfunction.

Study objective

A failure to signal the salience, and especially the anticipation of positive events, is thought to be at the core of social-emotional apathy (SEA) in patients with schizophrenia. This salience system is highly dependent on dopamine from the mesencephalon. In order to further investigate this, we will use PET-scanning with [11C]-raclopride. In patients, we expect a significant correlation between binding and SEA scores.

Study design

Single

Intervention

None.

Contacts

Public
A. Aleman
Groningen
The Netherlands
+31 (0)50 363 8798
Scientific
A. Aleman
Groningen
The Netherlands
+31 (0)50 363 8798

Eligibility criteria

Inclusion criteria

Patients with schizophrenia (N=20):

- At least 18 years of age

- DSM-IV diagnosis of schizophrenia or schizoaffective disorder

- Patient groups will be matched on age, sex, education, levels of depressive symptoms, medication and handedness

- Written Informed Consent

Healthy controls (N=10):
- At least 18 years of age

- Matched to patients on age, sex, education, levels of depressive symptoms and handedness
Absence or low levels of apathy

- Written Informed Consent

Exclusion criteria

Patients with schizophrenia (N=20):

Use of medication that can influence task results (e.g. beta-blockers, insulin) with the exception of antipsychotics

Healthy controls (N=10):

- Use of medication that can influence task results (e.g. beta-blockers, insulin)

- High level of apathy

- Presence of a psychiatric disorder, in present or past.

All subjects (N=30):

- Presence of a neurological or substance dependence disorder

- Visual or hearing problems that cannot be corrected

- Insufficient knowledge of the Dutch language

- Inability to undergo cognitive testing

Additional criteria, due to the use of neuroimaging (all subjects):

- (Suspected) pregnancy

- Claustrophobia

- The refusal to be informed (by notifying the participant's physician) of structural brain abnormalities that could be detected during the experiment

- MR incompatible implants in the body (such as ear prostheses or other metal implants)

- Risk of having metal particles in the eyes

- Tattoos containing red pigments that form a safety risk

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2014
Enrollment:	30
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
NTR-new	NL4636
NTR-old	NTR4805
Other	: METc2014/267

Study results