

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

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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...

<b>Ethische beoordeling</b>	Niet van toepassing
<b>Status</b>	Werving nog niet gestart
<b>Type aandoening</b>	-
<b>Onderzoekstype</b>	Observationeel onderzoek, zonder invasieve metingen

## Samenvatting

### ID

NL-OMON21681

### Bron

NTR

### Verkorte titel

Apathy-PET

### Aandoening

schizophrenia  
apathy

## Ondersteuning

**Primaire sponsor:** UMCG

**Overige ondersteuning:** ERC

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

## Toelichting onderzoek

### Achtergrond van het onderzoek

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.

### **Doel van het onderzoek**

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.

### **Onderzoeksopzet**

Single

### **Onderzoeksproduct en/of interventie**

None.

## **Contactpersonen**

### **Publiek**

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

## Onderzoeksopzet

### Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel

Blinding:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

## Deelname

Nederland	
Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-10-2014
Aantal proefpersonen:	30
Type:	Verwachte startdatum

## Ethische beoordeling

Niet van toepassing	
Soort:	Niet van toepassing

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

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

## Resultaten