The neural substrate of cognitive and social-emotional apathy in patients with schizophrenia

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Observational invasive

Summary

ID

NL-OMON43784

Source
ToetsingOnline

Brief title
The neural substrate of apathy in schizophrenia

Condition

- Schizophrenia and other psychotic disorders

Synonym
apathy, listlessness

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: NWO- VICI-453-11-004

Intervention

Keyword: apathy, neuroimaging, schizophrenia

Outcome measures

Primary outcome

The main study parameter will be brain activation (BOLD-response) measured with functional Magnetic Resonance Imaging (fMRI).

Secondary outcome

Secondary parameters will be metabolic differences using Magnetic Resonance Spectroscopy (MRS) and white matter pathways using Diffusion Tensor Imaging (DTI). Furthermore, we will explore local concentration of grey matter, using Voxel-Based Morphometry (VBM) of a structural MRI scan and fronto-parietal connectivity and perfusion during a resting-state scan.

Study description

Background summary

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. Previous studies have suggested that activation and connectivity in a dorsal frontostriatal circuit, including the parietal cortex, may underlie self-initiation. Furthermore, it has been suggested that activation and connectivity in a ventral frontostriatal network may underlie positive salience signaling. These circuits might be altered in apathetic patients with schizophrenia. However, this has never been directly investigated. In this study, the neural substrates for CA and SEA are examined

in patients with schizophrenia.
Hypotheses: We intend to unravel two possible distinct neural routes for cognitive and social-emotional apathy, namely a dorsal frontostriatal route, including the right parietal cortex, for cognitive apathy and a ventral frontostriatal reward route for social-emotional apathy. In this light we will examine CA- and SEA-related neural activation and connectivity during tasks and rest.

Study objective

The primary objective of the proposed study is to examine the neural substrate of cognitive and social-emotional apathy in patients with schizophrenia. Secondary, we intend to explore the concentration of brain metabolites and structural differences between patients with high CA, high SEA, low apathy and healthy controls.

Study design

The proposed study has an experimental design. Subjects will be presented with four different fMRI tasks which we expect to robustly activate underlying circuits for cognitive or social-emotional apathy. The tasks intend to measure self-initiated realization of intentions, cognitive control, reward anticipation and affective forecasting. Furthermore 6 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 burden and risks

The study will consist of interviews and questionnaires with a maximum total duration of 2 hours and 55 minutes, and Magnetic Resonance scans with a maximum total duration of 2 hours and 10- minutes. Possible participants will first be interviewed in a screening session of 75 minutes, in order to confirm of rule out possible diagnoses and establish the level of apathy. In order to reduce the strain that a long interview and scanning session could entail the remaining interview and scanning procedures will be divided into two sessions with a maximum duration of 2 hours and 10 minutes each. These sessions will preferably take place within one week from each other.
Concerning the MRI scanner, participants will be exposed to a field-strength of 3 Tesla and scanner noise. Thus far, there is no evidence to suggest that exposing humans to a magnetic field of this strength has a negative influence on their health. With regard to the noise, earplugs and headphones will be provided. Subjects will not benefit directly from participating in the study, however the data collected during this study will enhance understanding of the neural basis of apathy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with schizophrenia (N=60)
- At least 18 years of age
- DSM-IV diagnosis of schizophrenia, or schizoaffective disorder
- High levels of cognitive or social-emotional apathy
or
- Absence or low level of apathy
- Patient groups will be matched on age, sex, education, levels of depressive symptoms, levels of D2 dopamine receptor occupancy and handedness
- Written informed consent;Healthy controls (N=20)
- At least 18 years of age
- Matched to patients on age, sex, education, levels of depressive symptoms and handedness

- Written informed consent

Exclusion criteria

Patients with schizophrenia (N=60)
• Presence of a substance dependence disorder
• Presence of a neurological disorder
• Use of medication that can influence task results (e.g. beta-blockers, insulin);Healthy controls (N=20)
• Presence of a neurological or psychiatric disorder, in present or past.
• Use of medication that can influence task results (e.g. psychopharmaca, beta-blockers, insulin)
• High levels of apathy (a score of more than 27 on the AES);All subjects (N=80):
• Visual or hearing problems that cannot be corrected
• Insufficient knowledge of the Dutch language
• Inability to undergo cognitive testing

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-12-2013
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	27-05-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-05-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL43372.042.13