Schizophrenia as a disorder of social cognition: an fMRI study in adolescents

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

Summary

ID

NL-OMON39432

Source
ToetsingOnline

Brief title
Social cognition in adolescents at risk of developing psychosis

Condition

- Schizophrenia and other psychotic disorders

Synonym
schizophrenia; psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: - adolescence, - psychosis, - social cognition, - trust

Outcome measures

Primary outcome

The main study parameter is the hemodynamic response (i.e. change in blood flow) in response to the investment and the repayment phase of the trust game.

Secondary outcome

The secondary study parameters consists of the behavioural data, i.e. the actual amounts invested during the three games. We also want to obtain insight in the relationship of activities, stress and self-appraisal to the occurrence of a psychosis. The social variables like Theory of Mind (Reading the Mind in the Eyes task) and SoMi will be included in the analysis.

Study description

Background summary

Psychosis manifests itself in social interactions. This is most evident in the core symptoms of psychosis, especially paranoid delusions, which are characterised by a fundamental lack of trust in others. Trust is a necessary component of successful human interactions, yet appears too complex to probe experimentally. However, the contemporary development of *neuroeconomics* has shown that complex social interactions, such as trust, can be operationalised in economic exchange games. Recent studies in healthy individuals measuring cortical responses during such games have shown that being engaged in a real interaction involves motivational and emotional processes, that are crucial to the development of trust between interacting subjects (King-Casas et al., 2005). This approach has highlighted activation in brain areas linking sensory representations with their motivational significance (e.g., striatum, amygdala, orbitofrontal cortex) (King-Casas et al., 2005; Rilling et al., 2002; Singer et al., 2004), in addition to the set of brain regions traditionally associated with social cognitive tasks (i.e., the posterior superior temporal sulcus, the temporal poles, the inferior frontal cortex, and the medial prefrontal cortex)

(Gallagher & Frith, 2003; Frith & Frith, 2003; Gallese, Keysers & Rizzolatti, 2004). This points to a possible mechanism underlying disturbed social interactions in psychosis, bringing into play contemporary theories of dopamine (DA) function. Mesolimbic DA has a central role in reward, learning and motivation (Schultz, 2002), and is also thought to be crucial to the pathophysiology of psychotic symptoms (Davis, Kahn, Ko, & Davidson, 1991; Seeman & Kapur, 2000). Through linking recent insights in the mechanisms underlying social interactions, with contemporary theories on the role of DA in psychosis (Kapur, 2003), it is possible to develop the hypothesis that an aberrant reward processing mechanism underlies disturbed social interactions which in turn may lead to the formation of paranoid delusions.
Paranoid delusions and hallucinations can also be triggered by the mental state of the person and his interaction with his environment. To elucidate this proces, we added the Experience sampling method. This method alows us to register fluctuations in daily activity, emotions, mental states and stress. Correlations with other tasks will be investigated.
Recently, studies investigating psychosis include induviduals with high risk of psychosis. Siblings and relatives are one group, by their shared genetic vulnerability. Another group is the *Ultra High Risk* (UHR) group, individuals who show some characteristics of psychosis, but are not (yet) psychotic. These individuals are usually medication-free, this means that there is one confounding factor less. This makes outcomes more reliable. By including a Ultra High Risk group, the difference between consequences of the disorder and precursors/markers of it, can be distinguished: If the UHR group shows the same characteristics as the patients, these characteristics will be markers of psychosis; characteristics only found in the patient group will be due to the disorder, and consequences of it.
For research in the field of psychosis, especially the early detection and intervention, discovering markers is vital.

Study objective

The aim of this project is to elucidate the mechanisms underlying one of the most incapacitating psychiatric disorders, psychosis. Despite antipsychotic treatment, up to a third of patients with psychotic illness continue to experience significant distressing and disabling psychotic symptoms. Acquiring an understanding of the cognitive and emotional mechanisms that have led to the psychotic beliefs is crucial. The current project applies novel approaches derived from behavioural game theory to further understanding of the mechanisms underlying symptom formation. These approaches allow the study of the symptoms as they are expressed in social interactions.

Study design

This is an experimental study which consists of two separate sessions: During the first session, participants will be screened, assessed on the

questionnaires and trained on the trust game task. The second session consists of a one hour fMRI-scan, during which participants will perform three trust games (i.e. each with a different partner).
The task in this study represents a slightly modified version of the multiround game implemented by King-Casas et al. (2005). Participants in the study play the role of the investor throughout the whole game, and thus always make the first move. Both investor and trustee start with the same amount of money (10¤). The investor decides which part of this amount, i.e. between 1¤ and 10¤, he wants to share. Shared money will be tripled. The partner, i.e. the trustee, can either repay part of the received money back to the investor or keep all the money. Functional MRI data will be obtained throughout the entire game session. Participants will play against the computer, but are told they are playing against two different human partners and a computer with a random repayment strategy. Specifically, they will be informed that their human partners are tested in a different location and they play together via the internet. The computer algorithm will consist of two versions, reflecting a cooperative and a deceptive style of playing, all programmed in a probabilistic way. Each experiment starts with a few practice trials in order to ensure that participants fully understand the instructions. The entire experiment consists of 3 games with 40 trials that include 20 control trials per game.
Besides the trust game, in the scanner the Social Mindfulness task (SoMi) will be performed. In this paradigm, choices are made in favour of oneself or keeping in mind the interest of another person. 4 Identical (but for one detail as colour or shape) items are shown, food and non-food. The items are shown in a ratio 2:2 (2 red and 2 green apples) or 3:1 (3 blue pencils and 1 green pencil). The 2:2 ratio is the controlcondition, the choice does not influence the options the second (virtual) player has. In the ratio 3:1 the choice does influence the options for the second player: if the subject chooses the single item, the second player has no choice; does he choose one of 3, the second player still has the choice between 2 different items. In short: does the subject choose for himself (unmindful) or does he consider the options of the other and mae a mindful choice?
Every item is presented in the choice (3:1) and in the control (2:2) condition, making analysis possible as to what he really likes and if he chooses that option in the choice-condition or not (mindful). Thus we can control for personal preferences (Van Doesum & Van Lange, submitted).

In the week prior to the testing/scanning, participants receive an IPod touch from the VU University. This device contains a questionnaire that participants are requested to fill in 10 times a day, for 7 consecutive days, at randomly chosen moments between 7.30 and 22.30. The IPod will beep (give a short alarm) and participants are to fill in the questionnaire directly after that.
Questions are asked about activities, environment, mood, stress and consumption (including drugs and alcohol). Psychosis-related symptoms will also be assessed.

Study burden and risks

The burden and risks associated with participation in this study are minimal. Subjects will be exposed to a high static magnetic field of 3 Tesla. Ample experience with such field strengths yields no indication of adverse effects on humans. In order to protect the subjects* hearing, protective headphones will be provided.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- adolescents-between 16-21 years of age and UHR + controls (16-31 years)
- Dutch speaking
- For patients: only atypical medication

Exclusion criteria

- intellectual impairment (i.e., IQ < 80)
- contraindications to fMRI
- drugs or alcohol use 48 hours prior to scanning
- For controls: history of psychosis and use of medication

Study design

Design

Study type:	Observational non 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):	15-02-2013
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	15-12-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	26-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL37604.029.11