An fMRI study of self-related cognitive-emotional processing in adolescents with psychometric schizotypy

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Observational non invasive

Summary

ID

NL-OMON33968

Source
ToetsingOnline

Brief title
Neural basis of cognitive-emotional processing in schizotypy

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
psychosis proneness, Schizotypy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: EURYI Grant from the European Science Foundation (NWO nr. 044035001) to prof.dr. A. Aleman

Intervention

Keyword: Emotion regulation, Schizotypy, Self-evaluation

Outcome measures

Primary outcome

The main study parameters will be the differences in brain activation between high an low psychosis prone adolescents while engaging in cognitive-emotional functions involved in insight into symptoms.

In the present study, by using fMRI, we would like to investigate the activation of distinct brain areas engaged during self-evaluation, emotion regulation, affective and cognitive mentalizing, and reality monitoring, all being crucial cognitive-emotional processes involved in insight. fMRI has the best spatial resolution amongst the other non-invasive techniques which allow one to have the closest look at the neuronal activity available with imaging. Furthermore, current studies which have been investigating cognitive processes related to self-awareness and emotion regulation are mostly behavioral. Additionally, the few available studies on the use of fMRI paradigms has been indeed promising toward an effective delineation of the neural correlates subserving these functions by this technique. In light of this, the proposed study would be an innovative research that, besides elucidating the cognitive and neural basis of subclinical psychotic symptoms, will also inform our future studies of self-processing in relation to poor insight (illness awareness) in psychosis.

Secondary outcome

not applicable

Study description

Background summary

Psychometric schizotypy (or psychosis proneness) refers to the presence of psychosis-like experiences that do not reach a clinical threshold of pathology. Psychosis proneness can be considered as a dimensional trait, which may be detected in the non-clinical population ranging from *normality* to clinical cases of psychosis. In psychotic disorders, lack of insight is a common and clinically relevant feature, and may be already present to some degree in individuals with subclinical psychotic features (e.g., not recognizing symptoms as abnormal). However, the cognitive and neural bases of insight are still unknown, as cognitive factors do not seem to be a sufficient explanation. Furthermore, late adolescence is regarded as a critical period for the expression of psychosis, thus the presence of high psychosis proneness during this period may have a role in the neurobiology of psychosis.

Study objective

The aim of the proposed research is to test, by the use of functional magnetic resonance imaging, the hypothesis that psychometric schizotypy (referring to, e.g., subclinical hallucinations in healthy people) is associated with reduced activation of brain circuits subserving self-evaluation and emotion regulation. Hence, our study will be focused on the neural substrates of subclinical psychotic features in healthy, non-medicated adolescents, from a community-based approach.

Study design

In this study, right-handed subjects will undertake four fMRI tasks, to be completed in one session. By the use of fMRI, we would like to investigate the activation of distinct brain areas engaged during self-evaluation, emotion regulation, affective and cognitive mentalizing, and reality monitoring, all being crucial cognitive-emotional processes involved in insight.
In order to assess emotion regulation, subjects will be presented with a set of pictures containing either a neutral or a negative emotional valence (International Affective Picture System, IAPS; Lang et al 1997). In one condition, they will be required to let themselves experience naturally the emotional experience that the picture elicits in them (Attend condition),

whereas in the other they will have to reinterpret the content of the photograph so that it no longer elicits a negative state (Reappraise condition). For the reality monitoring task, participants will have to recollect whether information had previously been perceived or imagined by themselves of by the experimenter. Subjects will be presented with a set of common word-pairs (i.e., rock and roll, bacon and eggs) and it will comprise a learning phase and then a test phase, in which they will have to recall either if the information was self-generated or perceived (internal vs external source), or whether they did this themselves or another person.

To assess the ability to perform a conscious reflection on one's sense of self, we will adapt a task applied by Johnson et al. (2002) as a functional MRI paradigm. Participants will be asked to make decisions about themselves on specific statements requiring self-evaluation in the domains of mood, social interactions, cognitive and physical abilities (Self-reflection condition). In the control condition (used to control for visual processing, attention, language comprehension, decision making, the motor response and memory retrieval), participants will be instructed to make decisions about statements of semantic knowledge. For the present study, a third condition will be added, in which participants will be asked to reflect about a familiar person, that is, a good acquaintance of the subject (Familiar other-reflection condition).

In order to investigate differential patters of ToM functioning between high and low psychosis prone subjects, we will implement a task designed by Castelli et al. (2000, 2002), already used in fMRI settings as also with adolescent samples (Moriguchi et al. 2007). In those studies, animations of geometrical figures depicting a social scene were used. Also a control condition was applied, in which the figures performed random movement sequences. Before each fMRI experiment, subjects were told to watch the animations and think about what the triangles were doing and thinking during the scanning. After scanning, subjects saw again the stimuli on a computer screen outside the scanner and were asked to recall what they had thought during the fMRI scan that the triangles were doing.

The Stroop task (Stroop 1935) has been widely used for the study of cognitive control. People with schizophrenia exhibit impaired performance on cognitive control tasks (Cohen and Servan-Schreiber 1992), an ability that is supported by a distributed neural network that includes the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex. As differences in brain activation with fMRI paradigms have been found also in healthy relatives of schizophrenia patients (Becker et al. 2008), as well as in adolescents with depressed mood (Killgore et al. 2007) and conduct problems (Banich et al. 2007), we expect to find differences in activation in these areas supporting cognitive control in our sample, with greater activation associated to better cognitive control for those with low psychosis proneness.
Stimuli consist of one of three words (RED, GREEN, BLUE) printed in one of the three colors. Trials are either congruent (eg, the word *BLUE* written in blue

ink) or incongruent (eg, the word *BLUE* written in red ink). For all trials, participants are instructed to respond to the color of the stimulus and to ignore the word, as quick as possible.
The Stroop task, which involves high response conflict and strongly activates ACC in controls (both for response conflict and for errors), as is related to the cognitive impairment in set-shifting found as related to impaired insight in psychosis (Aleman et al. 2006).

For the tasks, we will use a custom-made MRI-compatible device (button box) which will be placed on the lower abdomen of the subject who is lying on the scanner table. The subject can touch the button box with both hands and, through a mirror, see the box and his/her own fingers to ensure pressing the desired button.
Aside from the fMRI experiments, a behavioral assessment battery will be administered to complement and extend the data obtained through scanning, with instruments that have been proved to be effective in the detection of deficits in those brain regions of interest that will also be tested through fMRI. Therefore, subjects will be tested for selective attention, automatic-response inhibition and perspective taking abilities.

Study burden and risks

Subjects will be exposed to a magnetic field of 3 Tesla and rapidly alternating magnet gradients and radio frequency fields. This field strength is used on a routinely basis in fMRI and MRI research. So far, no side effects have been described. On rare occasions, a peripheral nerve (abdomen) is stimulated by the changing magnet gradients. This will cause an itching feeling, but it is not harmful

Contacts

Public
Universitair Medisch Centrum Groningen

P.O. Box 196
9700 AD
Nederland
Scientific
Universitair Medisch Centrum Groningen

P.O. Box 196
9700 AD
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Psychosis proneness
Participants will be selected from a random selection within the upper extreme of the distribution according to the CAPE scores (above the 75th percentile, high schizotypy group), and a random selection within 0.5 SD around the mean (control group).

Exclusion criteria

Subjects with history of psychiatric or relevant neurologic disease will be excluded from the study.
Further exclusion criteria will be based on the presence of MRI incompatible implants. For safety reasons we will also exclude female participants who may be pregnant. Subjects with claustrophobia, alcohol and/or drug abuse, or insufficient grasp of the Dutch language will also be excluded. To make sure subjects are only prone to psychosis and not clinically psychotic, the following questions will be asked to them: (1) Are you in treatment for a psychiatric disorder?, (2) Do you have any psychiatric problems? Should they answer positively to either one of these questions, they will be excluded from the study.

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:	Will not start
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL22438.042.08