An fMRI investigation of Pavlovian Instrumental Transfer and Avoidance Learning with Primary Reinforcement in Psychopathy

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Personality disorders and disturbances in behaviour
Study type	Observational non invasive

Summary

ID

NL-OMON32649

Source
ToetsingOnline

Brief title
An fMRI study of PIT in psychopathy.

Condition

- Personality disorders and disturbances in behaviour

Synonym
Psychopathy, sociopathy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: NWO vidi

Intervention

Keyword: Agression, Learning, Pavlovian instrumental transfer, Psychopathy

Outcome measures

Primary outcome

During the performance of the tasks we will collect behavioural,

psychophysiological (heart rate and eye tracking) data and functional imaging

data.

Secondary outcome

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Study description

Background summary

Unlike many other neuropsychiatric disorders, psychopathy is characterized by instrumental or proactive aggression. Previous research on psychopathy has focused on impairments in various learning tasks and aversive processing, and associated abnormalities in the ventromedial prefrontal cortex (vmPFC) and amygdala respectively. This will be the first study to assess interactions between aversive (Pavlovian) processes and instrumental decision making by making use of a Pavlovian Instrumental Transfer (PIT) paradigm and a reinforcement learning paradigm. In addition, we will assess not only neural activity in the vmPFC and the amygdala, but critically also connectivity between the amygdala and the vmPFC.
PIT refers to the phenomenon that Pavlovian cues (that predict reward or punishment) influence instrumental responding. For instance, aversive cues (that predict punishment) inhibit appetitive instrumental behaviours (such as approach), while potentiating aversive instrumental behaviours (such as active withdrawal and passive avoidance). The paradigm enables us to assess a new hypothesis on the pathophysiology of psychopathy in the context of alternative leading hypotheses on psychopathy: the violence inhibition model in the integrated emotion system, the somatic marker theory, and the response set modulation hypothesis.
Specifically, we hypothesise that psychopathy is characterized not just by a

failure of aversive processing per se, nor by impaired instrumental decision making per se, but rather by a failure to adjust instrumental (goal-directed) decision making based on aversive, but not appetitive Pavlovian cues (i.e. stimuli that predict reward or punishment). Thus PPs are expected to exhibit disinhibited approach, but impaired withdrawal and avoidance, only in the context of aversive Pavlovian cues. Performance of PPs will be compared with that of healthy controls, as well as people with antisocial personality disorder (ASPD) without psychopathy (ASPD-P). In contrast to PPs, the latter group is mostly characterized by reactive aggression, and not proactive aggression and are predicted to exhibit exaggerated rather than disrupted modulation of instrumental behaviour by Pavlovian cues.
Complementarily we will employ an integrated reinforcement learning and Go/NoGo paradigm, enabling us to assess influences of reward and punishment cues on a different dimension of responding, i.e. inhibition vs. activation. We hypothesize that psychopathy does not modulate the processing of appetitive or aversive cues per se, nor the activation or inhibition of responding by itself, but rather will influence the interaction between affective processing and response activation. Accordingly we expect that psychopathy will be accompanied by disruption of passive punishment avoidance while not affecting the other conditions. Finally, we expect that the fMRI experiments will localize these neuromodulatory effects to activity changes in subcortical brain regions associated with appetitive and aversive processing and in cortical brain regions that regulate descending behavioral control mechanisms. Specifically, changes in activity are predicted to occur in the striatum, amygdala, lateral/medial (orbito)frontal cortex and their connectivity.

Study objective

The main objective is to elucidate the role of Pavlovian cues in instrumental behaviour in PPs and PASPD-Ps and its neural underpinnings. To this end we will acquire fMRI data from PPs, PASPD-Ps, and healthy controls during the performance of two tasks. Based on prior literature, we predict that abnormal task performance in PPs and PASPD-Ps is accompanied by, respectively, reduced and enhanced connectivity between the amygdala, the ventromedial prefrontal cortex (vmPFC), and/or the striatum.

Study design

A cross-sectional design will be employed with a healthy control group matched to the patient groups (PPs and PBPDs) on age, sex and intelligence. We will use liquid outcomes - sucrose and citric acid for reward, and magnesium sulfate for punishment. Prior to each fMRI session, a short calibration (simple choice) task to titrate the magnesium sulfate concentration. During scanning, subjects will complete two tasks. The first task enables the assessment of reward and punishment predictive cues on active approach versus active withdrawal. The second task enables the assessment of such cues on active

approach versus passive avoidance. Heart rate and pupil dilation (eyetracking) measurements will be obtained to assess autonomic responsiveness to the cues. Pre- and post-scanning different questionnaires and neuropsychological tests will be filled out and performed to control a.o. for attentional deficits.

Study burden and risks

Participants will get two appointments: during and before the first appointment participants will receive information and have to fill out some questionnaires and will participate in diagnostic interviews. During a second appointment, participants will participate in several experimental tasks during which functional imaging data will be collected. Collection of data will be done at the Donders Centre for Cognitive Neuroimaging. This does not involve any special risks (see also Appendix C).

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

• Age 18-55 years.
• Men.
• Group 1: Patient, meeting the DSM-IV criteria for ASPD and scoring * 26 on the PCL-R.
• Group 2: Patient, meeting the DSM-IV criteria for ASPD; and showing low levels of psychopathy (PCL-R< 26).
• Group 3: Controls, matched for age, education and intelligence, not meeting DSM-IV criteria for ASPD or psychopathy.
Group 4: Healthy young subjects (for pilot study) without psychiatric morbidities.

Exclusion criteria

General exclusion criteria for fMRI: Metal implants or splinters, surgical clips, protheses, artificial heart valves, claustrophobia, electronic equipment in body (such as a pacemaker), pregnancy, epilepsy. ;Psychiatric:
• Recurrent Major Depressive disorder or Single Major Depressive disorder within five years.
• Bipolar disorder
• Schizophrenia, delusional disorder, schizoaffective disorder, schizopheniform disorder or other psychotic disorders
• Schizoid or schizotypical personality disorder
• (Current) alcohol- or substance intoxication
• Anti-social personality disorder/Psychopathy co-morbidity in healthy volunteers
• ADHD
• First degree relatives with DSM IV axis I schizophrenia, or schizophreniform disorder
• Mental retardation;Somatic
• Visual and auditory disorders
• Neurological disorders
• First degree relatives with any relevant neurological disorders;Pre-testing use of drugs and substances
• Use of alcohol within 24 hours before measurement.
• Use of cannabis or other illicit drugs within the week before measurement.
• Use of any psychotropic medication, other than benzodiazepines, during the 5 days before measurement.
• Use of benzodiazepines within 3 times T¬1/2 before measurement.
• Smoking within 3 hours before measurement.

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:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-05-2010
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	07-01-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL30545.091.09