An fMRI investigation of Pavlovian-to-instrumental transfer with primary reinforcement in borderline personality disorder before and after dialectical behavioural therapy.

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1. Advance knowledge of the cognitive and neural mechanisms underlying emotional dysregulation in borderline personality disorder. 2. Advance knowledge on the cognitive and neural mechanisms of dialectical behaviour therapy in borderline personality…

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

Summary

ID

NL-OMON35910

Source
ToetsingOnline

Brief title
PIT in BPD voor en na DBT

Condition

- Personality disorders and disturbances in behaviour

Synonym
borderline, borderline personality disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,MWO (AGIKO beurs)

Intervention

Keyword: borderline personality disorder, dialectical behavioral therapy, emotion, Pavlovian to instrumental transfer

Outcome measures

Primary outcome

During the performance of the tasks we will collect behavioural, psychophysiological (skin conductance and eye tracking) data and functional imaging data. We also collect measures of treatment success (by means of two questionnaires: Outcome Questionnaire and borderline personality disorder severity index).

Secondary outcome

Results will be related not only to measures of severity of BPD, but also to self report measurements of reward and punishment sensitivity, of trait and state anger and anxiety, of impulsivity and of delay discounting. All these measures are thought to have influence either on the instrumental learning phase, Pavlovian conditioning or the PIT phase.

Study description

Background summary

Impulsive and aggressive disorders have a major impact on society as well as on the individual. For example, borderline personality disorder, associated with both impulsiveness and aggression, is a devastating psychiatric condition, affecting 1%-2% of the population. The functional impairment in patients is

severe. This contributes to the high suicide rate of almost 10%[1, 2]. Moreover these patients constitute a disproportionately large subset of psychiatric in and outpatient populations, who consume considerably more (mental) healthcare resources than other psychiatric patients[3].

A cognitive neuropsychiatric approach is paramount for understanding, developing and optimizing treatments for these complex neuropsychiatric disorders. In line with recent advances in this area (e.g. [4]), we anticipate that individual variability in treatment efficacy can be quantified, as well as predicted by objective indices of cognitive-affective deficits and their neural mechanisms. Emotion dysregulatioin is thought to be the core psychological process in borderline personality disorder. From this perspective we developed an fMRI-suitable Pavlovian-to-instrumental transfer (PIT) task addressing emotional/affective regulation of goal-directed instrumental behaviour in a basic neurocognitive manner.

PIT refers to the phenomenon that Pavlovian cues (which predict reward or punishment) influence instrumental responding. For instance, aversive cues (which predict punishment) inhibit appetitive instrumental behaviours (such as approach), while potentiating aversive instrumental behaviours (such as active withdrawal and passive avoidance). The Pavlovian conditioned stimuli are interpreted as emotional stimuli, because they influence the assessment of the value of (other) stimuli; this assessment of positive and negative value is a key aspect of emotions. This will be the first study in BPD to assess interactions between experimentally controlled aversive and appetitive processes and instrumental decision making by making use of a PIT paradigm before and after treatment.

The PIT paradigm enables us to assess a neurocognitive hypothesis about the pathophysiology of borderline personality disorder, but also about the neurocognitive working of dialectical behaviour therapy. It is important to evaluate this particular treatment strategy, because it is one of the world-wide most used and successful psychotherapies in the treatment of borderline personality disorder. Critically, our paradigm targeted at emotion regulation sorts with this therapy as the normalisation of emotion dysregulation lies at the heart of this therapy.

Neuroimaging studies on borderline personality disorder indicate a dysfunctioning fronto-limbic inhibition system. This system consists of among others ventromedial and orbitofrontal cortex, amygdala and striatum. These structures along with the nucleus accumbens are also indicated in animal research as essential for PIT.

Specifically, we hypothesize that borderline personality disorder 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 patients with borderline personality disorder are expected to exhibit exaggerated inhibition of approach and exaggerated promotion of avoidance, only in the context of aversive Pavlovian cues. We expect this to be accompanied by differential responses of amygdala and vmPFC/OFC and a compromised fronto-limbic connectivity. Furthermore we expect that dialectical behavioural therapy will improve this fronto-limbic connectivity by imposing more frontal control. In line with thes predictions we will explore if fronto-limbic dysfunction is prognostic for treatment success.

Study objective

1. Advance knowledge of the cognitive and neural mechanisms underlying emotional dysregulation in borderline personality disorder.
2. Advance knowledge on the cognitive and neural mechanisms of dialectical behaviour therapy in borderline personality disorder. This objective is twofold: (i) exploring the specific neural mechanisms underlying the treatment success of dialectical behaviour therapy and (ii) discovering individually tailored prognostic functional neurocognitive markers.

Study design

An explorative observational study (including a non-experimental initiated treatment intervention) with age, sex and intelligence matched control subjects will be employed using functional magnetic resonance imaging (fMRI) for neural measurements. We will use liquid outcomes for reward and punishment. There will be two fMRI scanning sessions: one before the start of dialectical behaviour therapy and one afterwards. Both sessions have the same procedure. The main task enables the assessment of reward and punishment predictive cues on active approach versus active withdrawal. Skin conductance and pupil dilation 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, for instance, for attentional deficits.

Study burden and risks

Participants will get three appointments. During and before the first appointment participants will receive information and fill out some questionnaires, they participate in a diagnostic interviews, and a structural MRI scan will be made. In this session they will also receive training on the experimental task they will perform during the scan session. During the second appointment, participants participate in the experimental task during which functional imaging data will be collected. The third appoint will be the same as the second appointment but scheduled after dialectical behaviour group therapy (approximately 9 months) is finished. In these last two sessions

participants will also be asked to fill out questionnaires regarding psychological dimensions that might well be expected to change during therapy/over time (9 months). Collection of data will be carried out at the Donders Centre for Cognitive Neuroimaging. This does not involve any special risks.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Kapittelweg 29
6525 EN Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Kapittelweg 29
6525 EN Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Age over 18.
• Group 1: Patients meeting the DSM-IV criteria for BPD and who are enrolled in the pretreatment group for dialectical behaviour group therapy at the Psychiatry Dept of the RUNMC.
• Group 2: Controls, matched for age, gender, and intelligence, not meeting DSM-IV criteria

for BPD.

Exclusion criteria

Patients:
we do not exclude patient suffering from several *comorbidities*, for instance mood- or eating disorders, because these are more a rule than an exception in BPD . Most important reasons for this are: (i) that the subgroup of patients with BPD formed by excluding the majority of them is not representative for the clinical population; (ii) we are primarily interested in the effectiveness of the therapy over the whole BPD population rather than the efficacy in a certain small subset. Acceptance of this approach in leading literature on BPD can, for example, be seen in the following publication of Silbersweig and colleagues [16].
;Healthy controls:
Psychiatric:
• Recurrent Major Depressive disorder or Single Major Depressive disorder within five years.
• Other mood- (e.g. bipolar disorder), anxiety- (e.g. social phobic), psychotic- (e.g. delusional disorder, schizophrenia), pervasive devolpmental- (e.g. autistic disorder), attention-deficit- (e.g. ADHD), eating- (e.g. anorexia nervosa) or personality disorders.
• (Current) substance abuse or dependence
• First degree relatives with DSM IV axis I schizophrenia, or schizophreniform disorder or with bipolar depression, ADHD or BPD.
• Mental retardation;Both patients and healthy controls:
General exclusion criteria for fMRI:
unable to give informed consent, metal implants or splinters, surgical clips, prostheses, artificial heart valves, claustrophobia, electronic equipment in body (such as a pacemaker), pregnancy, and epilepsy.;Psychiatric:
• Bipolar disorder, dementia, schizophrenia, delusional disorder, schizophreniform, schizoaffective disorder, shared psychotic disorder, pervasive devolpmental- (e.g. autistic disorder).
• Current substance dependence.
• First degree relatives with DSM IV axis I schizophrenia, or schizophreniform disorder.
• Mental retardation.

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:	Recruitment stopped
Start date (anticipated):	29-02-2012
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO

Date:	12-01-2012
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	NL36001.091.11