PROSPER - Prediction and Outcome Study in PTSD and Personality disorders

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Ethical review	Approved WMO
Status	Pending
Health condition type	Personality disorders and disturbances in behaviour
Study type	Interventional

Summary

ID

NL-OMON50353

Source
ToetsingOnline

Brief title
PROSPER

Condition

- Personality disorders and disturbances in behaviour

Synonym
borderline personality disorder (BPD) and cluster C personality disorder (CPD), post-traumatic stress disorder (PTSD)

Research involving
Human

Sponsors and support

Primary sponsor: Arkin (Amsterdam)
Source(s) of monetary or material Support: Stichting Steunfonds Joodse Geestelijke Gezondheidszorg (SSF JGG). Dhr. S. Glaser;voorzitter. Postbus 2063;1180 EB Amstelveen;020-5457275.

Intervention

Keyword: personality disorder, post-traumatic stress disorder (PTSD), prediction, treatment outcome

Outcome measures

Primary outcome

Primary outcome measure is PTSD symptom response rate after 12 months.

Secondary outcome

Secondary outcome measures are PTSD symptom effect size and PD symptom effect size and response rate after 12 months.

At baseline (T0) and after 6 (T2) and 12 months (T4) clinical interviews (CAPS-5, SCID-II dimensional score) and self-rating scales (PCL-5) will be used. After 3 months (T1) and 9 months (T3), and at follow-up (18 months), questionnaires only will be used. Other outcome measures are quality of life and health costs.

At baseline, candidate predictors and mediators will be measured including cognitive (educational level/IQ, working memory, emotion regulation), affective (anger, sleep, dissociation), relational factors (therapeutic alliance, attachment, social support) and hormonal en epi-genetic factors (cortisol/FKBP-5 methylation, oxytocin/OXTR-gene, serotonin/ 5HTTLPR-gene). In a subgroup, hair cortisol, BDNF and FKBP-5 will be measured again. In a second subgroup, structural and functional MR, with resting-state, face recognition and Stop task will be performed.

Study description

Background summary

Evidence-based treatments for posttraumatic stress disorder (PTSD), such as Eye Movement Desensitization and Reprocessing (EMDR) and Imagination and Rescripting Therapy (ImRs), are highly effective treatments in the majority of the PTSD patients. PTSD is highly comorbid with personality disorders (PD), especially borderline personality disorder (BPD), and cluster C - avoidant, dependent, or obsessive-compulsive - personality disorders (CPD). It is not clear yet what treatment is most effective for those who suffer from both PTSD and PD.
There is growing motivation in clinicians to offer PTSD treatments to PTSD with comorbid PD, because these treatments are highly effective, relatively short (weekly sessions, 3-6 months) and there is some evidence that with PTSD treatment, comorbid PD symptoms might resolve as well. PTSD are less time-consuming than PD treatments and - at least in the short term - financially attractive. However, at least 30-44% PTSD patients do not sufficiently respond to these treatments. Moreover, a high number of PTSD patients are excluded from these therapies because of suicidality, self-destructive behaviour or other personality problems. Therefore, it might be more efficient to add a PD treatment at the same time. Evidence-based treatments for personality disorders (PD), such as dialectical behaviour treatment (DBT) for BPD, and schema-focused treatment (SFT) for CPD are well established. These treatments are more intensive (twice a week for at least one year) than PTSD treatments. There is some evidence that integrated PTSD-PD treatment is twice as effective on reducing PTSD symptoms than PD treatment alone, but integrated PTSD-PD treatment is not yet directly compared to PTSD treatment alone. This study will address this knowledge gap, including secondary outcome measures on functioning, quality of life and cost-effectiveness.
The result of this study might be that one or the other treatment works better, depending on the personal profile of the patient. So far, some psychological factors have been found to be associated with worse outcome of PTSD treatment. These are cognitive (educational level, working memory emotion regulation), affective (anger, sleep problems, dissociation), and relational factors (therapeutic alliance, attachment, social support). In addition, neurobiological factors are found to predict PTSD treatment outcome, such as increased activity connectivity of the limbic network and decreased activity and connectivity of the cognitive control networks, and disturbed hormonal levels and epigenetic factors (5-HTTLPR, BDNF, cortisol/FKBP5-methylation, oxytocin/OXTR) and possibly mediate treatment outcome (BDNF, cortisol and FKBP5). Because these candidate predictors and mediators are found on a group level (in non-responders vs. responders), they cannot directly be used on an individual level. By using machine-learning techniques we might use these candidate predictors and mediators on an individual level to guide treatment

choices and thereby personalise psychiatry.

Study objective

In the current project, we will firstly study effectiveness of PTSD-treatment compared to integrated PTSD-PD-treatment in treatment-seeking, adult patients with comorbid PTSD and PD in a wide range of severity (minimally 4 criteria of a personality disorder). Secondly, we will investigate psychological (cognitive, affective, and relational) and neurobiological candidate predictors and mediators of treatment outcome, and use them in a machine-learning paradigm to predict and explain which treatment works best for which specific individual, thereby presonalizing psychiatry.

Study design

Two parallel RCTs will be conducted with predictor analyses.

Intervention

In patients with PTSD and BPD: EMDR (6 months plus 6 months treatment pause) compared to integrated DBT-EMDR-treatment (12 months);
in patients with PTSD and CPD: ImRs (6 months plus 6 months treatment pause) compared to integrated ImRs-SFT treatment (12 months).

Study burden and risks

The burden and risks associated with participation in this study is reasonable. All patients will receive psychotherapy, which is considered to be the most effective treatment for PTSD and/or PD. There is evidence that both interventions are therapeutic in patients with PTSD and PD. There is no evidence yet what treatment (PTSD or integrated PTSD-PD) is more effective. Suicidality or self-injurious behaviour is very common in the study population included for this study. It is also known that starting a new treatment, such as EMDR or DBT could increase symptoms in the beginning, which can develop into suicidal behavior. To monitor the possible increased symptoms, patients have to fill in a questionnaire on self-injury at the assessments every three months. In between the assessments the therapists will monitor SAE*s and take appropriate action.
Total time of the clinical interviews/questionnaires is approximately 12.5 hour in 1.5 year per patient with three visits to the Sinai Center and online filling in of questionnaires. If the respondent also participates in the blood/hair and/or MRI study, resp. 30 min (visit to the local hospital) and 180 min (2 visits to VUmc for MRI) is added. Questionnaires, which are partly part of the routine outcome measurements (ROM), can be filled in online at home. The burden and risks - fatigue - are acceptable while the benefits are expected to be considerable. On the one hand, extended clinical interviews and self-rating

scales can be felt as disturbing because taken time and emotional burden. On the other hand, patients may feel well recognized by the time taken by specialized clinicians for an extensive assessment. Assessors will be well-trained with close connection with the clinicians and treatment teams. For the identification of predictors and mediators of the treatment response, biological and genetic measures are integrated in the study. These measurements include physical examination, blood samples and hair samples. The burden and risk associated with the baseline blood sample and hair sample is reasonable. For the subgroup of MRI research, participants will have a 60-minutes MRI session during which they will recall traumatic events, and perform some cognitive-affective tasks during scanning. Functional MRI is a commonly used technique that is considered to be safe if you follow the safety instructions (e.g. no metal objects in the MRI room) and contraindications (e.g. no metal implants, no pregnant, no seriously claustrophobia). Lying in the scanner and/or performing affective-laden tasks in the scanner can occasionally give patients uncomfortable feelings of anxiety and distress by reliving of their traumatic experiences. During and after the scan procedure a debriefing will be held to cover this by the executor of the scan protocol. The principal investigators of this study have long experience with symptom provocation in the scanner (Thomaes: early traumatized PTSD patients with comorbid personality disorders: only 1 in 33 patients had a panic attack; OA van den Heuvel in patients with panic disorder, PTSD, OCD, Tourette, Parkinson, hypochondriasis: panic attacks were rare and not more frequently than healthy controls). In all, we consider the risk and burden associated with participation to be low. Benefits for PTSD patients as a whole are that this study will provide important information about best treatment choice in patients with both PTSD and personality problems. It will help profiling patients and predict response or non-response on an individual basis, to know what works for whom and be able to provide personalize mental health care that can be as short as possible and at the main time most effective. It will help to understand why (working mechanisms) what treatment works best for whom.

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

See Page 22 of the research protocol:
In order to be eligible for study participation, a subject must meet all of following criteria at T0:
- Diagnosed with PTSD (309.81)
- Diagnosed with a personality disorder (301.81 borderline, 301.4 obsessive-compulsive, 301.6 dependent, 301.82 avoidant), or at least 4 PD symptoms of those PDs (301.9 PD otherwise specified).
- Age between 18 and 65 years
- Written informed consent is obtained
- Speak / understand Dutch sufficiently

Exclusion criteria

See page 22 of the research protocol:
A patient who meets any of following criteria will be excluded from participation in this study:
- Current psychosis
- Comorbidity interfering with treatment or randomisation (severe outward aggression, antisocial PD, treatment interfering addiction or eating disorders, somatic problems)
- Primary diagnosis of paranoid, schizoid, schizotypal, narcissistic, histrionic or antisocial PD
- Mental retardation
For the subgroup that also undergo MRI examination more exclusion criteria are:

- Pregnancy
- Metal implants (such as pacemakers, etc.)
- Somatic disorders interfering with brain functioning
- Claustrophobia
- High dosis benzodiazepines

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2017
Enrollment:	292
Type:	Anticipated

Ethics review

Approved WMO Date:	04-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	29-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-08-2023
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	NL61495.029.17