ISRCTN29668369 https://doi.org/10.1186/ISRCTN29668369

Improving anxiety treatment by modifying emotional memories before real-life exposure

Submission date
24/05/2022

Recruitment status
No longer recruiting

Registration date
27/06/2022

Overall study status
Completed

Last Edited
03/09/2025

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Many people suffer from an anxiety-related disorder. They typically suffer from excessive fear in anticipation or the presence of feared (innocuous) stimuli and avoidance of disorder-related situations. For instance, patients with panic disorder suffer from an intense fear of certain bodily sensations (e.g., heart palpitations) and situations that provoke them (e.g., drinking coffee, exercise). During exposure therapy, patients are systematically confronted with feared disorder-related stimuli and situations. This way, they can learn that the anticipated feared outcome does not occur (e.g., having a heart attack), which reduces their anxiety. Exposure-based therapy is one of the most effective treatments for anxiety disorders, but many patients do not benefit sufficiently from it. Distressing images of threat, related to the content of the anxiety disorder (e.g. having a heart attack), may maintain anxiety symptoms or reduce exposure therapy effectiveness. A treatment that targets these distressing images is eye movement desensitization and reprocessing (EMDR) therapy. The main goal of this study is to examine whether EMDR therapy with exposure therapy (ET), compared to supportive counseling with exposure therapy, improves treatment efficacy, tolerability, and adherence in patients with panic disorder.

Who can participate?

Patients aged 18 years and over with panic disorder

What does the study involve?

Participants are allocated (at random) to one of two groups. Those in the first group receive four 90-minute sessions of EMDR followed by eight 90-minute sessions of ET. Those in the second group receive four 90-minute sessions of SC and eight 90-minute sessions of ET. Both groups will receive manualized treatment by trained and supervised staff. Researcher assistants or graduate students blind to group allocation will conduct assessments before treatment (T1), between treatments (T2) and after treatments (T3). Panic-related symptoms are measured to assess how well EMDR works. The researchers further assess whether EMDR also works to improve the tolerability of exposure therapy (less initial avoidance, more willingness to start exposure therapy, less considered drop-out; less no-show and drop-out) and reduce functional impairment as well as related psychiatric symptoms (e.g. generalized anxiety, depression).

What are the possible benefits and risks of participating?
The benefit of participating is that people will receive a well-controlled treatment for panic disorder and possibly gain more benefits from our new treatment approach. To the researchers' knowledge, there are no additional risks or negative effects compared to treatment as usual. Due to assessments, study participation will take more time compared to treatment as usual.

Where is the study run from?
The study is run from two mental healthcare institutions in the Netherlands: Altrecht (i.e., Altrecht Academic Anxiety Center) and Mondriaan/PsyQ (i.e., Academic Anxiety Center).

When is the study starting and how long is it expected to run for?
January 2020 to September 2025

Who is funding the study?
Netherlands Organization of Scientific Research (NWO) (Netherlands)

Who is the main contact?
Prof. Iris M. Engelhard
i.m.engelhard@uu.nl

Contact information

Type(s)
Principal investigator

Contact name
Prof I.M. Engelhard

Contact details
Heidelberglaan 1
Utrecht
Netherlands
3584 CS
+31 (0)634103344
i.m.engelhard@uu.nl

Type(s)
Scientific

Contact name
Mr B. Endhoven

ORCID ID
https://orcid.org/0000-0002-4425-514X

Contact details
Heidelberglaan 1
Utrecht
Netherlands

3584 CS
+31 (0)613257610
b.endhoven@uu.nl

Type(s)
Public

Contact name
Mr B. Endhoven

Contact details
Heidelberglaan 1
Utrecht
Netherlands
3584 CS
+31 (0)613257610
b.endhoven@uu.nl

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
MREC Utrecht: Source ID: NL73918.041

Study information

Scientific Title
Reducing panic-related symptoms through eye movement desensitization and reprocessing therapy or supportive counseling before exposure therapy in patients with panic disorder: a randomized controlled trial

Acronym
IMPROVE

Study objectives
The first goal of this research is to investigate whether eye movement desensitization and reprocessing (EMDR) therapy, compared to supportive counseling (SC), prior to exposure therapy (ET) improves treatment efficacy, tolerability, and adherence in patients with panic disorder.

It is hypothesized that:
1. EMDR therapy is more effective in reducing panic-related symptoms, compared to SC from baseline (T1) to between-treatment (T2)
2. EMDR + ET is more effective in reducing panic-related symptoms, compared to SC+ET at post-treatment (T3)

3. EMDR therapy results in higher tolerability of exposure therapy (less initial avoidance, more willingness to start exposure therapy, less considered drop-out; less no-show and actual drop-out) compared to SC

It is further hypothesized that:
4. EMDR therapy is more effective in reducing related symptomatology (generalized anxiety, depression) and functional impairment, compared to SC from baseline (T1) to between-treatments (T2)
5. EMDR + ET is more effective in reducing related symptomatology (generalized anxiety, depression) and functional impairment, compared to SC+ET at post-treatment (T3)

Hypotheses concerning the following goals will be preregistered at the Open Science Framework (OSF; osf.ip). The second goal is to unravel predictors of optimal treatment allocation (EMDR+ET > SC+ET). These include theory-driven variables (reduced extinction learning, less experienced life events, low intolerance of uncertainty, anxiety sensitivity, low worrying, enhanced imagery ability), patient variables (e.g. greater treatment credibility, better working alliance) and therapist factors (e.g. enhanced trait anxiety, better working alliance, greater treatment expectancy). The third goal is to elucidate mechanisms of change (most notably mental threat imagery, encapsulated threat beliefs) of this novel approach (EMDR+ET). Finally, the researchers will assess the cost-effectiveness of the new approach (EMDR+ET).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/08/2020, amendment approved 08/02/2023, Medical Research Ethics Committee UMC Utrecht (MREC NedMec, PO Box 85500, 3508 GA Utrecht, Netherlands; +31 (0)88 7556376; info@metcutrecht.nl), ref: NL73918.041

Study design
Multicenter interventional single-blind randomized controlled trial with a two-arm mixed factorial design

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Panic disorder

Interventions
Patients will be randomized (by computer) to one of two conditions: (1) four EMDR sessions followed by eight ET sessions or (2) four SC sessions followed by eight ET sessions. Sessions will take 90 min (once weekly) and will be provided face to face or online by videoconferencing.

The total treatment duration is 16 weeks (week 1: baseline measurement T1, week 2: case conceptualization, week 3-6: treatment phase 1; EMDR or SC, week 7: between-treatments measurement T2, week 8-15: treatment phase 2; ET, week 16: post-treatment T3). Follow up 1 (FU1) and follow up 2 (FU2) will be conducted 1 month and 6 months post-treatment (T3).

Intervention Type
Behavioural

Primary outcome(s)
Panic-related symptoms:
1. Panic disorder severity (self-report) is measured with a questionnaire: Panic Disorder Severity Scale (PDSS-SR), total severity score at T1, T2, T3, FU1, FU2 and once weekly during the intervention phase
2. Panic disorder severity is measured using an interview: Panic Agoraphobia Scale (PAS), total severity score and panic attack frequency at T1, T2, T3 and FU1

Key secondary outcome(s))
Other anxiety symptomatology (avoidance, safety behavior, panic disorder cognitions, diagnosis):
1. Avoidance is measured with the Fear Questionnaire-Agoraphobia (FQ-A), total severity score at T1, T2, T3, FU1, FU2
2. Safety behavior is measured with the Subtle Avoidance Frequency Examination-Agoraphobia (SAFE-A) questionnaire, total severity score at T1, T2, T3, FU1, FU2
3. Panic disorder cognitions are measured with the Bodily Sensation Questionnaire (BSQ), total severity score at T1, T2, T3, FU1, FU2
4. Panic disorder diagnosis is measured with an interview: Mini-International Neuropsychiatric Interview Simplified (MINI-S-DSM-V), diagnosis yes/no at T1 and FU1

Treatment tolerability:
1. Behavioral avoidance is measured with a standardized interoceptive exposure task: total avoidance score at ET session 1 and ET session 8
2. Exposure willingness is measured with a single item, total score during intervention 1 (EMDR or SC), intervention 2 (ET), FU1 and FU2
3. Intention to stop treatment is measured with a questionnaire, total score at T2 and T3
4. Client satisfaction is measured with the Client Satisfaction Questionnaire (CSQ-8) and Net Promotor Score (NPS), total score at T2 and T3.

Adherence:
1. Session attendance rate is measured as drop out and no-show rates during intervention 2 (ET)

Related symptomatology, functional impairment and quality of life:
1. General anxiety is measured with the General Anxiety Disorder 7 (GAD 7) questionnaire, total severity score at T1, T2, T3, FU1, FU2 and once weekly during the intervention phase
2. Depression is measured with the Patient Health Questionnaire (PHQ-9), total severity score at T1, T2, T3, FU1, FU2 and once weekly during the intervention phase.
3. Quality of life is measured with the EuroQol (EQ-5D), total score at T1, T2, T3, FU1, FU2
4. Adjustment is measured with the Work and Social Adjustment Scale (WSAS), total score at T1, T2, T3, FU1, FU2

Completion date
01/09/2025

Eligibility

Key inclusion criteria

1. Patients ≥18 years of age
2. Sufficient mastery of the Dutch language and ability to complete questionnaires and understand informed consent information
3. Meeting Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for (primary) panic disorder (with or without agoraphobia)
4. Stable medication for at least 6 weeks and willingness of the patient and physician to keep medication stable during the study period (until follow up 1). The use of sedating medication (e. g., benzodiazepines) is not a contraindication, but participants are discouraged to use sedating medication before or after treatment sessions and subsequent days. Use of sedating medication will be registered.
5. The self-reported ability to refrain from alcohol or drugs 24 hours before and after each session. General use of alcohol or drugs will be discouraged.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Self-reported neurological disorder
2. Acute or recent history of suicide attempts according to the M.I.N.I. section C
3. Self-reported visual or auditory impairments that could hinder treatment
4. Self-reported epilepsy, pregnancy, or heart disease (only for the fear-conditioning task)
5. Self-reported current psychological treatment for other DSM-5 disorder
6. Not willing or able to fill in (online) questionnaires

Date of first enrolment
01/02/2022

Date of final enrolment
01/02/2025

Locations

Countries of recruitment
Netherlands

Study participating centre

Altrecht Academic Anxiety Center
Nieuwe Houtenseweg 12
Utrecht
Netherlands
3524 SH

Study participating centre
Mondriaan/PsyQ Academic Anxiety Center
Oranjeplein 10
Maastricht
Netherlands
6624 KD

Sponsor information

Organisation
Dutch Research Council

ROR
https://ror.org/04jsz6e67

Funder(s)

Funder type
Research council

Funder Name
Nederlandse Organisatie voor Wetenschappelijk Onderzoek: VICI Innovational Research grant (453-15-005) awarded to Prof. I. M. Engelhard.

Alternative Name(s)
Netherlands Organisation for Scientific Research, Dutch National Scientific Foundation, Dutch National Science Foundation, Dutch Research Council (Nederlandse Organisatie voor Wetenschappelijk Onderzoek), NWO:Nederlandse Organisatie voor Wetenschappelijk Onderzoek, Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO), Dutch Research Council, The Dutch Research Council (NWO), Dutch Research Council, Netherlands, NWO

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Iris M. Engelhard (i.m.engelhard@uu.nl). Requests can be submitted by researchers with an appropriate research question and statistical analysis plan, with guarantees of privacy regulations and not interfering with publication plans of the study board.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		14/03/2023	16/03/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes