

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

Submission date 24/05/2022	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 27/06/2022	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 28/08/2024	Condition category Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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 December 2024

Who is funding the study?

Netherlands Organization of Scientific Research (NWO) (Netherlands)

Who is the main contact?

Prof. Iris M. Engelhard

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Study website

<https://www.uu.nl/onderzoek/improve/behandelingen>

Contact information

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

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

Secondary study design

Randomised controlled trial

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

Not available in web format

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 measure

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

Secondary outcome measures

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

Overall study start date

01/01/2020

Completion date

31/12/2025

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

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

50

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

01/12/2025

Locations

Countries of recruitment

Netherlands

Study participating centre**Altrecht Academic Anxiety Center**

Nieuwe Houtenseweg 12

Utrecht

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Study participating centre**Mondriaan/PsyQ Academic Anxiety Center**

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Sponsor information

Organisation

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Research council

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Funder(s)

Funder type

Research council

Funder Name

Nederlandse Organisatie voor Wetenschappelijk Onderzoek: VICI Innovative 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, Dutch Research Council, Netherlands, NWO

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Netherlands

Results and Publications

Publication and dissemination plan

The papers will be submitted for publication to (inter)national peer-reviewed scientific journals, regardless of the results, and will be made available through open access. The sponsor (NWO) requires that all publications emerging from research it funds are made available in open access immediately upon publication. Furthermore, results will be shared at national and international conferences, and be used for education and training purposes. NWO will have no influence on the publication of the results and promotes knowledge utilization.

Intention to publish date

31/12/2025

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