# Resolving distress overnight: the role of noradrenaline during sleep

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We aim to lay the fundament of novel interventions by gaining an in-depth comprehensive understanding of individual differences in the overnight adaptation of emotional memory and malleability thereof by noradrenergic modulation.

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON56727

**Source**
ToetsingOnline

**Brief title**
RESOLVING DISTRESS OVERNIGHT

### Condition

- Other condition
- Anxiety disorders and symptoms

**Synonym**
anxiety disorder, insomnia

**Health condition**

insomnia

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Nederlands Herseninstituut
**Source(s) of monetary or material Support:** ZonMW grant

## Intervention

**Keyword:** anxiety, insomnia, sleep

## Outcome measures

### Primary outcome

The primary study parameter is the overnight resolution of recent emotional distress (the karaoke task) as measured by a subjective question (how embarrassed do you feel by this fragment), as well as by heart rate derived from electrocardiography.

### Secondary outcome

We will include the other autonomic responses on the karaoke task: galvanic skin responses, blushing response and facial electromyography, as well as subjective ratings of valence and arousal.
The overnight resolution of long-lived distress (autobiographical memory task) will also be used as secondary study parameter, including the same autonomic and subjective indices as the karaoke task. The assessments will quantify distress elicited by repeated exposure to a relived embarrassing shameful experience from the distant past, as successfully used by us and others.
Lastly, we will exploratively create an individualized stress response, defined by the strongest objective stress response during the karaoke-task in the evening (i.e. the physiology measurement with the largest change between the karaoke-task and the baseline per participant). With this approach we can

account for the possibility that shame will be expressed in a different

physical manner for different participants.

Other study parameters are autonomic resting state features (electrocardiogram,

galvanic skin responses, blushing response and facial expressions) and features

derived from the nightly electroencephalography (EEG) recording, specifically

regarding REM sleep.

# Study description

### Background summary

The most prevalent and costly mental disorders are Anxiety & Stress Related Disorders (ASRD) and Insomnia Disorders (ID). The current transdiagnostic project aims to find answers on why anxious and distressing experiences or restless nights perpetuate into chronicity of ASRD and ID and to provide means for better treatment and prevention.

### Study objective

We aim to lay the fundament of novel interventions by gaining an in-depth comprehensive understanding of individual differences in the overnight adaptation of emotional memory and malleability thereof by noradrenergic modulation.

### Study design

A double-blind placebo controlled intervention study.

### Intervention

Participants will be administered a one-time dose of Atomoxetine (40 mg), Nebivolol (5 mg), Daridorexant (25 mg), Clonidine (50 mcg), and placebo on separate nights.

### Study burden and risks

Participants receive a one-time dose of Atomoxetine (40 mg), Nebivolol (5 mg), Daridorexant (25 mg), Clonidine (50 mcg), and placebo throughout the course of the study. Previous studies have shown that a single dose of 40 mg Atomoxetine, 5 mg Nebivolol, 50 mcg Clonidine, and 25 mg of Daridorexant are well tolerated in healthy adults with very little side effects. Considering the extensive exclusion criteria, screening procedure and constant monitoring of the subjects, no serious side effects are expected.

## 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

In order to be eligible to participate in this study, a volunteer must meet the two inclusion criteria of an age of 18 years or older and the capability of completing online questionnaires and diaries in the Dutch language.

To include the severity of insomnia and anxiety as covariates in our analysis, we will assess the Insomnia Severity Index (ISI; Morin et al., 2011) and the Generalized Anxiety Disorder Questionnaire (GAD-7; Williams, 2014) scores of interested volunteers. These scores will not affect potential inclusion. Volunteers will undergo formal diagnostic procedures according to the DSM-5 (M.I.N.I.; Sheehan et al., 1998) for descriptive purposes only. Meeting the criteria of a diagnosis is not an inclusion criterion.

### Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• other relevant treatment for ASRD or ID at the time of study - either pharmacologically or with cognitive behavioral therapy (CBT)
• diagnosis of mental disorders other than ASRD or ID (co-occurring depression is allowed).
• use of psychotropic medication
• history of cardiovascular diseases
• heart problems among first-degree relatives
• HR < 60 or HR > 120 (bpm)
• BP < 90/60 or BP > 170/100 (systolic/diastolic mmHg)
• diabetes
• liver or kidney diseases
• hyperactive production of thyroid hormones
• epilepsy
• any medication contra-indicative of the use of Atomexatine, Nebivolol, Clonidine, or Daridorexant (as described in the Summary of Product Characteristics)
• pregnancy
• breastfeeding

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |

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| Primary purpose: | Other |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 16-12-2024 |
| Enrollment: | 59 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 26-04-2024 |
| Application type: | First submission |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 22-08-2024 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 09-10-2024 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |

## 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 | NL84049.100.23 |