# Revealing individual neural underpinnings of anxiety in healthy subjects

Published: 30-10-2017
Last updated: 12-04-2024

In this proof-of-concept study, we aim to characterize healthy individuals with regard to their individually predominant neural mechanism. Thereby, we aim to divide a sample of healthy individuals into three clusters based on their individual...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Anxiety disorders and symptoms |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON44325

**Source**
ToetsingOnline

**Brief title**
neural phenotype of anxiety

### Condition

- Anxiety disorders and symptoms

**Synonym**
anxiety

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Radboud Universiteit Nijmegen
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** anxiety, fMRI, neuronal networks, proof-of-concept study

## Outcome measures

### Primary outcome

In the fMR session three paradigms will be tested to determine the neural

phenotype:

- prefrontal regulation task

- salience processing task

- face processing task

### Secondary outcome

questionnaires:

- HADS (Hospitality Anxiety and Depression Scale, Zigmond & Snaith, 1983)

- FEEL-E (Emotional Adjustment Questionnaire for Adults, Grob & Horowitz, 2014)

- BDI (Becks Depression Inventory, Beck, Steer, & Brown, 1996)

Biological markers for stress:

- heart rate

- skin conductance

# Study description

### Background summary

Symptoms of anxiety are based on amygdala responsiveness, which can be evoked by the activation of multiple different brain circuits. We aim to characterize the following neural mechanisms that might cause amygdala hyper-responsiveness; high locus coeruleus drive, low prefrontal control or increased amygdala

sensitivity. We hypothesize that variation in local sensitivity and variation in specific control mechanisms may explain why certain individuals are more fearful than others. The same phenotype may result from different neural mechanisms.

## Study objective

In this proof-of-concept study, we aim to characterize healthy individuals with regard to their individually predominant neural mechanism. Thereby, we aim to divide a sample of healthy individuals into three clusters based on their individual anxiety related circuit activation. Selection of high trait anxious individuals will most probably increase the chance to identify anxiety related neural mechanisms, which might not be detectable in a randomly drawn sample of healthy participants. Furthermore, a comparison to a low anxious group secures specificity of these mechanisms. We will validate our stratification procedure by assessing different neural and behavioral measures.

## Study design

The online link to our questionnaire on www.soscisurvey.de will be distributed by flyers on campus and the study will be advertised during university lectures. Participants are informed about the rationale of the study and the potential possibility to take part in an fMRI investigation before filling out an online questionnaire. Participants are asked to create an online-account on soscisurvey.de and anonymously fill in the HADS questionnaire. After completion of the questionnaire the participant*s score is calculated by the online platform*s software and each participant receives a personal code. Participants that reach a score of eight or higher are immediately after the questionnaire informed by an on-screen message about the possibility to take part in an fMRI investigation in our institute. In case they are interested, they are asked to indicate their interest by button press. This will trigger an anonymous message to our experimenter account on soscisurvey.de. Soscisurvey allows to participate in the survey and indicate interest an fMRI investigation without the chance on behalf of the experimenter to link questionnaire results to a participant. Via soscisurvey, the experimenter can contact potential participants anonymously and based on their score in the questionnaire. This happens without any knowledge on and access to the personal or questionnaire data of the potential participant. For selection of participants that score according to our design, a corresponding algorithm is implemented in the survey software. Hence, despite communicating with a participant based on their score, the examiner does not have access to their personal data and the participant*s individual answers on the questionnaire as long as these do not provide their code and have signed the consent form. An appointment for the fMRI examination will be arranged and participants will be asked to bring their code. At the institute, participants will be fully informed about the rationale and procedure of the fMRI investigation. They are asked to give their consent and

after signing the informed consent form to provide their code. This enables the experimenter to retrieve the participant*s score from the soscisurvey database. During the fMRI investigation, three tasks will be applied to probe the three amygdala-centered networks. A pre-frontal regulation task will be applied to monitor activity in the prefrontal cortex. Amygdala reactivity will be monitored by applying an emotional face processing task. Salience processing will be used to monitor activity in the locus coeruleus. Stimulus materials for visual stimulation are taken from standardized stimulus sets. Tactile stimulation is applied using stimulation by electrodermal stimulation. After the fMRI session, participants are asked to complete the emotional adjustment questionnaire (FEEL-E, Grob & Horowitz, 2014). This questionnaire evaluates adaptive and maladaptive emotion regulation strategies.

### Study burden and risks

MRI is a non-inversive imaging technique. Only occasionally (< 0,5%) subjects report vertigo-like sensations and/ or slight nausea symptoms due to movement in the static field of the scanner. Sensitivity to these effects varies considerably between individuals. In rare cases, minimal muscle contractions due to nerve stimulation abating when the scanning procedure stops. Acoustic noise from the MRI scanner can be reduced wearing shielded earphones during the scanning procedures.
Burdens and risks are very minimal to negligible. The HADS is a 14-item online questionnaire that evaluates symptoms of anxiety and depression. The HADS is a screening tool to evaluate trait anxiety in healthy and clinical populations, without specification of certain affective disorder. Participation in the questionnaire takes approximately two to six minutes. Administration of the HADS in an unsupervised manner does not cause any known risks. The FEEL-E questionnaire evaluates adaptive and maladaptive emotion regulation strategies and takes approximately 30 minutes. The FEEL-E will be filled out in the institute under supervision of the investigator. Hence, no risks for the participants relating to the questionnaire procedures are expected.
Participants that reach a score of clincal relevance on the HADS (>10) are advised to consult their GP or psychologist. Incidental neurological findings during the fMRI session are reported to the participant's GP.

## Contacts

**Public**
Radboud Universiteit Nijmegen

Kapittelweg 29
Nijmegen 6525EN
NL

**Scientific**
Radboud Universiteit Nijmegen

Kapittelweg 29
Nijmegen 6525EN
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

healthy volunteers (18-50 years)
fMRI compartibility

## Exclusion criteria

History of or current neurological or psychiatric treatment
History of or current brain surgery or epilepsy
Pregnancy
Metal parts in the upper body, implants, medical devices or medicinal plasters
Claustrophobia

# 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: | Recruiting |
| Start date (anticipated): | 24-11-2017 |
| Enrollment: | 250 |
| Type: | Actual |

## Ethics review

Approved WMO

| | |
|---|---|
| Date: | 30-10-2017 |
| 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 | NL61806.091.17 |