

# Studying the impact of Doxycycline on fear memory in healthy individuals

<b>Submission date</b> 05/06/2015	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 23/06/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/07/2023	<b>Condition category</b> Other	<input checked="" type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Anxiety disorders and phobias are thought to result from pathological learning. The erasing of fear memory could therefore have a therapeutic effect. Memory is transformed from an unstable into a stable form during consolidation (the strengthening of memory) in a process that depends on protein synthesis (i.e. the production of protein). Re-activation of an existing memory can make that memory unstable, in particular if new information is being added to the old memory that is being recalled. This suggests that memory can be erased by first re-activating an old memory, and then blocking the synthesis of proteins necessary for the strengthening of that memory by giving a drug (i.e. stopping the proteins that are needed to strengthen the memory). The antibiotic Doxycyclin blocks the activity and the synthesis of specific proteins, and has been shown to weaken memory of general knowledge. Here, we are testing the effect of Doxycycline on the strengthening of human fear memory (phase 1). If phase 1 is successful, then in phase 2 we will test its effect on re-activation of old fear memories. Phase 1 will prove the potential of the drug to weaken fear memory, and phase 2 its potential as a therapy for erasing already strengthened fear memory. Phase 2 will only take place if phase 1 is successful. We will study the impact of Doxycyclin by giving Doxycyclin, or placebo, to healthy individuals and testing their memory.

### Who can participate?

Healthy adults between 18-40 years of age.

### What does the study involve?

The study is conducted in two separate phases. For both phases, participants are physically examined, and give blood and urine samples. Participants who pass the medical examination are invited for study visit 2. Participants from phase one fill in four questionnaires and randomly (by chance) receive a single dose of either Doxycycline (an antibiotic) or placebo (dummy). Participants from phase two skip this step and instead do it during study visit 3. Next, electrodes for measuring ECG (heart activity), EMG (muscle activity), skin conductance, and also breathing, are placed on the participants from both phases. Participants then perform a computer task during which they will learn the association between a neutral stimulus (a geometric shape on a screen) and a fearful stimulus (mild electric stimulation) and as a result, will form a fear memory. For the second phase study, participants additionally come in for study visit 3. The same

procedures as for study visit 2 is repeated, and the fear memory that was learned during the previous study visit is re-activated. Participants from both study phases attend study visit 4. The same procedures as for study visit 2, with the exception of drug administration, is repeated. The previously formed fear memory is then recalled.

What are the possible benefits and risks of participating?

Doxycycline is an approved drug with rare serious side effects. It may cause abdominal or stomach tenderness, in severe cases allergic reactions. Participants have no direct benefit from taking the study medication. This study will potentially benefit patients with anxiety disorders.

Where is the study run from?

The study will be conducted at the Psychiatric University Hospital Zürich (PUK ZH)

When is study starting and how long is it expected to run for?

July 2015 to July 2018

Who is funding the study?

The University of Zürich (UZH)

Who is the main contact?

Professor Dominik R. Bach

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## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Dominik Bach

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**Contact details**

Comparative Emotion Group

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8032

## Additional identifiers

**Protocol serial number**

DoxMem

## Study information

**Scientific Title**

A randomised, double-blind, placebo-controlled, two-phase study on the impact of Doxycycline on fear memory in healthy individuals

**Study objectives**

Null hypothesis: Doxycyclin and placebo groups do not differ in fear recall

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Kantonale Ethikkommission Zürich, 23/04/2015, ref: KEK-ZH-Nr.2014-0669

**Study design**

Randomised placebo-controlled double-blind trial

**Primary study design**

Interventional

**Study type(s)**

Other

**Health condition(s) or problem(s) studied**

Fear memory

**Interventions**

A single dose 200 mg of Doxycycline or placebo

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Doxycycline

**Primary outcome(s)**

Current primary outcome measures as of 25/08/2016:

The difference in fear memory recall between a fear-conditioned CS+ and a safety-conditioned CS-, as estimated from startle eye blink EMG (The initially registered primary outcome, skin conductance responses, is not measured during the memory recall phase, due to a change in study design before inclusion of the first participant)

Previous primary outcome measures:

The difference in fear memory between a fear-conditioned CS+ and a safety-conditioned CS-, as estimated from skin conductance responses.

**Key secondary outcome(s)**

Current secondary outcome measures as of 25/08/2016:

Fear memory indices derived from skin conductance responses and heart rate during fear acquisition and re-learning

Previous secondary outcome measures:

A fear memory index derived from heart rate, pupil size, and startle response quantified via EMG of the M. orbicularis oculi

**Completion date**

27/07/2018

## **Eligibility**

**Key inclusion criteria**

1. Informed consent as documented by signature
2. Age 18 – 40 years

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

160

**Key exclusion criteria**

1. Allergy to Doxycycline or to any other ingredient in the named drug
2. Use of any drugs in the 2 weeks prior to the study with the exception of contraceptive drugs and incidental use of NSARs or paracetamol
3. Women who are pregnant or breast feeding
4. Intention to become pregnant during the course of the study
5. Lack of safe contraception, defined as: Female participants of childbearing potential, not using and not willing to continue using a medically reliable method of contraception for the entire study duration, such as oral, injectable, or implantable contraceptives, or intrauterine contraceptive devices, combined with a mechanical contraceptive (condom, diaphragm)
6. Other clinically significant concomitant disease states (e.g., renal failure, hepatic dysfunction, cardiovascular disease, etc.)
7. Any history of psychiatric, neurological, dependence or systemic/rheumatic disease
8. Known or suspected non-compliance, drug or alcohol abuse
9. Inability to follow the procedures of the study, e.g. due to language problems

- 10. Participation in another study with investigational drug within the 30 days preceding and during the present study
- 11. Previous enrolment into the current study
- 12. Members of the study team and their family members and dependants

**Date of first enrolment**

01/11/2015

**Date of final enrolment**

27/03/2018

## Locations

**Countries of recruitment**

Switzerland

**Study participating centre**

**Zürich Psychiatric University Hospital (Psychiatrische Universitätsklinik) Zürich (PUK ZH)**

Psychiatrische Universitätsklinik Zürich

Lenggstrasse 31

Postfach 1931

Zürich

Switzerland

8032

## Sponsor information

**Organisation**

Psychiatric University Hospital (Psychiatrische Universitätsklinik) Zürich (PUK ZH)

**ROR**

<https://ror.org/01462r250>

## Funder(s)

**Funder type**

University/education

**Funder Name**

Universität Zürich

**Alternative Name(s)**

University of Zurich, Switzerland, University of Zurich, UZH

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Universities (academic only)

**Location**

Switzerland

**Results and Publications**

**Individual participant data (IPD) sharing plan**

After final publication of the results, anonymised participant-level data will be made publicly available on zenodo.org, following the procedures mandated by Swiss Human Research Law.

**IPD sharing plan summary**

Stored in repository

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/07/2018	09/07/2019	Yes	No
<a href="#">Results article</a>		15/10/2019	10/07/2023	Yes	No
<a href="#">Dataset</a>		18/09/2019	10/07/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes