ISRCTN66987216 https://doi.org/10.1186/ISRCTN66987216

Studying the impact of Doxycycline on fear memory in healthy individuals

Submission date 05/06/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [X] Individual participant data
Registration date 23/06/2015	**Overall study status** Completed	
Last Edited 10/07/2023	**Condition category** Other	

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 Doxycyline 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
dominik.bach@uzh.ch

Contact information

Type(s)
Scientific

Contact name
Dr Dominik Bach

ORCID ID
http://orcid.org/0000-0003-3717-2036

Contact details
Comparative Emotion Group
Prof. Dr. Dominik R Bach
Psychiatric Hospital, University of Zurich
Lenggstrasse 31
Zurich
Switzerland
8032

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

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 measure
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.

Secondary outcome measures
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

Overall study start date
27/03/2015

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
160

Total final enrolment

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)

Sponsor details
c/o Prof. Dominik R. Bach
Psychiatric University Hospital (Psychiatrische Universitätsklinik)
Lenggstrasse 31
Postfach 1931
Zürich
Switzerland
8032

Sponsor type
University/education

Website
http://www.pukzh.ch/

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

Publication and dissemination plan
The trialists intend to publish the results of the study in a peer-reviewed journal within 2 years following data collection. Anonymity of participants shall be guaranteed.

Intention to publish date
27/07/2020

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?
Results article	results	01/07/2018	09/07/2019	Yes	No
Dataset		18/09/2019	10/07/2023	No	No
Results article		15/10/2019	10/07/2023	Yes	No