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Studying the impact of Lorazepam on approach /avoidance behaviour in healthy individuals

Submission date
26/11/2014

Recruitment status
No longer recruiting

Registration date
08/12/2014

Overall study status
Completed

Last Edited
23/01/2019

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Everyone feels anxious at some point in their life, for example, when they are worried about an examination or a job interview. Feeling anxious in these situations is perfectly normal. However, some people find it hard to control their fears of anxiety. They can feel anxious constantly and their feelings can have a significant effect on their day-to-day life. Anxiety is a common symptom of a number of psychiatric disorders. Better treatment is therefore needed to treat this condition. Approach avoidance conflicts refer to situations or events that have both a positive and a negative side to them. One positive aspect (approach) of marriage, for example, might be companionship, while a negative aspect (avoidance) may be arguments. Current medicines for treating anxiety have been developed by studying mouse behavior in situations of approach-avoidance conflict. However, it is unknown if rodent anxiety-like behaviour truly models (reflects) human anxiety. We have designed a study that allows us to compare human and mouse anxiety-like behaviour in a similar paradigm (situation). The findings of this study will help in the development of new anxiety reducing drugs.

Who can participate?
Healthy adults between 18-40 years of age.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given a single dose of lorazepam, a drug that reduces anxiety. Those in group 2 are given a single dose of a placebo (dummy) pill. They then play an approach/avoidance computer game and their behaviour is recorded. During approach-avoidance conflict, an animal or person is motivated to approach and to avoid a situation at the same time, for example, because in the same situation both reward and punishment are possible. If lorazepam causes a similar change of behaviour in approach-avoidance conflict in humans and in rodents, then we will be able to confirm that human and rodent anxiety-like behaviour is the same and drugs can be developed to reflect this.

What are the possible benefits and risks of participating?
Lorazepam is an approved drug with rare serious side effects at single doses. It may, however,

cause muscle weakness or drowsiness and in severe cases allergic reactions. Participants will not get any direct benefit from taking the study medication but will potentially benefit patients with anxiety disorders.

Where is the study run from?
The Psychiatric University Hospital Zürich (PUK ZH) (Switzerland)

When is study starting and how long is it expected to run for?
December 2014 to September 2017

Who is funding the study?
The University of Zürich (UZH) (Switzerland)

Who is the main contact?
Professor Dominik R. Bach
dominik.bach@uzh.ch

Contact information

Type(s)
Scientific

Contact name
Prof Dominik Bach

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

Contact details
Psychiatric University Hospital (Psychiatrische Universitätsklinik)
Lenggstrasse 31, Postfach 1931
Zürich
Switzerland
8032

Additional identifiers

Protocol serial number
AAAX

Study information

Scientific Title
A randomised, double-blind, placebo-controlled study on the impact of Lorazepam on approach /avoidance behaviour in healthy individuals

Study objectives
Null hypothesis: Lorazepam and placebo do not differ in their impact on approach/avoidance behaviour.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Kantonale Ethikkommission Zürich (Cantonal Ethics Committee Zürich), 17/11/2014, ref. 2014-0196

Study design
Randomised, placebo-controlled, double-blind, interventional, single-centre study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Validation of a human version of the rodent approach/avoidance conflict model

Interventions
A single dose 1 mg of lorazepam or placebo

Approach/avoidance behaviour task:
We have developed a human approach-avoidance task that emulates rodent anxiety paradigms such as operant conflict tests, the elevated plus maze (EPM), and the open field test (OT). In this task, presented over successive epochs in the form of a computer game, collection of monetary tokens on a grid provides approach motivation. The possibility that a virtual predator might wake up and remove all tokens harvested during the epoch provides a potential threat, and thus avoidance motivation. In each epoch, one of three predators representing different levels of threat (corresponding either to chase speed or wake-up probability, in different versions of the task) are present but inactive in a corner of the grid. The grid corner opposite to that of the predator represents a safe place where the predator cannot catch the participant. Participants start either in the same corner as the predator (‘‘active’’ epoch) or from the safe place (‘‘passive’’ epoch).

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Primary outcome is the overall probability of being in the safe quadrant in the computer game. Probability of being in the safe quadrant will be assessed over all rounds of the experiment and analysed in a time x task x threat level factorial design. Probability of being in the safe quadrant is a surrogate marker for passive avoidance, and was highly sensitive in distinguishing between patients with hippocampal lesions and healthy controls in a previous study.

Measured during the entire computer game (average behaviour in the computer game).

Key secondary outcome(s))
Secondary outcomes are distance from threat, distance from walls, probability of being in the threat quadrant, probability of being in the safe place, rate of token collection and speed when on grid, in the computer game. All secondary outcomes will be assessed over all rounds of the experiment and analyzed in a time x task x threat level factorial design.

Measured during the entire computer game (average behaviour in the computer game).

Completion date
01/08/2015

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

Key exclusion criteria
1. Contraindications to benzodiazepines: dependence or former dependence, history of allergic reactions, history of hypotonia associated with benzodiazepines
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, or who are not using any other method considered sufficiently reliable by the investigator in individual cases
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 dependents

Date of first enrolment
01/12/2014

Date of final enrolment
01/08/2015

Locations

Countries of recruitment
Switzerland

Study participating centre
Psychiatric University Hospital (Psychiatrische Universitätsklinik) Zürich (PUK ZH)
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
University of Zürich (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2017	23/01/2019	Yes	No