Enhancing extinction of conditioned sexual response by a partial NMDA receptors agonist.

Published: 29-09-2014
Last updated: 21-04-2024

The aim of the study is: to investigate the effect of DCS on the physiological and subjective correlates reflecting conditioned sexual response and subsequent extinction thereof. Hypothesis: We hypothesize that administration of DCS after an...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON41206

Source
ToetsingOnline

Brief title
Enhancing extinction of conditioned sexual response

Condition

- Other condition

Synonym
Hypersexuality, Hyposexuality, Sexual Motivation Disorders

Health condition

Seksuele aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: DCS, Extinction, NMDA-agonism, Sexual Reward

Outcome measures

Primary outcome

1) measures of vaginal pulse amplitude (VPA) assessed by a vaginal

photoplethysmograph; 2) Subjective ratings of US expectancy, affective valence

and sexual arousal

Secondary outcome

nvt

Study description

Background summary

Many sexual disorders are thought to involve a learned component. For example, in hypersexuality or sex addiction, sex-associated cues are thought to elicit sexual arousal and craving for sex. Clinical interventions to reduce the impact of cues in eliciting these maladaptive conditioned responses are likely to be beneficial. Extinction is a method of lessening conditioned responses and involves repeated exposures to a cue in the absence of the event it once predicted. Glutamate is the brain's main excitatory neurotransmitter, and also the precursor for GABA, the brain's main inhibitory neurotransmitter. Glutamate receptors are responsible for the glutamate-mediated postsynaptic excitation of neural cells, and are important for neural communication, memory formation, learning, and regulation. Research on the role of glutamate in extinction has led to the development of pharmacotherapeutics to enhance the efficacy of extinction-based protocols in clinical populations with anxiety disorders. Despite it hypothesized relevance, studies on pharmacological interventions in sexual learning and extinction in humans are lacking in the literature. This knowledge may help in the treatment of sexual motivation disorders such as too little or excessive sexual desire.

In the present study, the effect of D-Cycloserine (DCS; a partial glutamatergic N-methyl-D-aspartate (NMDA) receptor agonist) on enhanced conditioning and extinction memory consolidation of conditioned sexual responses will be investigated. The study will be conducted in healthy sexually functional women. To investigate the effects of DCS on extinction memory, genital and subjective sexual arousal will be studied in women (N=2X34) in a differential conditioning experiment.

Study objective

The aim of the study is: to investigate the effect of DCS on the physiological and subjective correlates reflecting conditioned sexual response and subsequent extinction thereof.

Hypothesis: We hypothesize that administration of DCS after an extinction procedure will enhance extinction of conditioned sexual responses. Compared to the placebo-condition, for the DCS- condition a decrease in sexual conditioned responses elicited by reward-conditioned cues will be seen in the extinction context, on a test phase 24hrs later. The DCS condition will show weaker conditioned genital and subjective responding in the extinction context, compared to the placebo condition.

Study design

Design: Double-blind randomized placebo controlled between-subjects design. Participants will be randomly assigned to the groups receiving either DCS or placebo after extinction on day 1.

Day 1: Discrimination Learning and Drug Administration
The experimental design involves conditioning with one stimulus (the CS+) being followed by the sexual appetitive US during the acquisition phase, whereas another stimulus (the CS-) never is followed by the US. Which CS is paired with the sexual appetitive stimulus is counterbalanced among subjects. Participants view repeated presentations of a male abdomen (CS+ and CS-) projected on a white screen, with the colour of the depicted picture (Blue or Yellow) the only difference (CS+ and CS-). Which stimulus serves as CS+ and CS- is counterbalanced across participants. The CSs are presented for 9 s, followed by inter-trial intervals that vary between 20 and 30 s. The unconditioned stimulus (US) is the vibrotactile stimulation for 2 s. Subjects are first habituated to the CSs and contexts by presenting each CS 4 times (in random order) in each context prior to the actual experiment. During this preconditioning phase the CS+ is not followed by the US.
Subjects then learn to discriminate the 2 CSs on the basis of how they predict genital vibrostimulation to follow each CS. In acquisition phase A1, the CS+ and the CS- are each presented 10 times in a randomized order in the centre of the monitor. Presentation of a perfectly predicted reward does not

generate a prediction error and fails to support new learning (Rescorla & Wagner, 1972;Schultz, Dayan & Montague (1997), therefore we chose a CS+ reinforcement ratio of 80% (8 out of 10 CS+ presentations are followed by genital vibrostimulation). By introducing this reward prediction uncertainty we will make conditioning somewhat more extinction resistant and therefore increase the likelihood of recall of sexual reward memory on day 2. The CS- is never followed by vibrostimulation.
In the following extinction phase B1, which is different from the preceding acquisition phase in terms of lighting colour of the experimental room (see stimulus materials), conditioned sexual responses are extinguished by presenting the CS+ and CS-each 10 times in a randomized order in the same fashion but the CS+ is no longer followed by vibrostimulation. At the beginning of each block, the context is present without any CS for 10 s. This phase is followed by another acquisition phase (A2) and extinction phase (B2) in its corresponding context. This design allows subjects to learn to discriminate between 2 different contexts on the basis of whether the CS+ is (conditioning context) or is not (extinction context) associated with the US. Immediately after the experiment participants receive DCS or placebo.

Day 2: Test Phase 24 h Later
Subjects again complete an experimental procedure. Each context is presented 18 times in an alternating order (ABABAB etc). In half of the participants, the experiment will start with the conditioning context (ABABAB etc.) and in half of the participants, it will start with the extinction context (BABABA etc). In these blocks of A and B each, 1 CS+ and 1 CS- are presented in random order for a duration of 9 s each, followed by inter-trial intervals that vary between 20 and 30 s. In the A blocks, subjects receive genital vibrostimulation 3 s after the start of the block. Associating context A with vibrostimulation during recall theoretically promotes reinstatement, thus facilitating recall of the CS-associated sexual arousal memory in this context.

Study burden and risks

There will be no benefits nor great risks for the participants. The single dose of DCS may result in mild side effects like drowsiness, headache, and dysarthria. If these effects appear, these will usually disappear within several hours.

Contacts

Public
Leids Universitair Medisch Centrum

Postbus 9600 Rijnsburgerweg 10

Leiden 2300RC
NL
Scientific
Leids Universitair Medisch Centrum

Postbus 9600 Rijnsburgerweg 10
Leiden 2300RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age < 18 or > 45 years
- Heterosexual orientation

Exclusion criteria

- Pregnancy or lactation
- Colour blindness
- A diagnosis of affective, psychotic or substance related disorder according to DSM 5.
- Current or recurrent use (less than 4 weeks before participation) of medication that may affect sexual response. To determine possible sexual side-effects the *Farmacotherapeutisch kompas* 2014 will be used.
- Current or previous disorders of the genitals or treatments for such disorders that may influence the sexual response or the measurement of the response.
- Other medical disorders that may influence the sexual response or the measurement of the response.
- Current or recurrent use (less than 4 weeks before participation) of medication that may affect or interact with the effects of DCS. To determine possible contra-indications, instructions for use as supplied by *King Pharmaceuticals* will be used (see Appendix).

- Current or previous disorders (like severe anxiety or psychosis, liver disease or severe renal insufficiency, epilepsy) that increase the possibility of side effects of DCS and for which usage of DCS is contra-indicated.
- Alcohol or drug use on the night and day before participation, as well as alcohol and drug use between test moments (day 1 and day 2).

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-10-2014
Enrollment:	68
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cycloserine
Generic name:	Cycloserine

Ethics review

Approved WMO

Date:	29-09-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO Date:	10-11-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
EudraCT	EUCTR2014-003228-29-NL
CCMO	NL49644.058.14