Boosting oxytocin after trauma: The effects of intranasal oxytocin administration on emotional and motivational brain processes in PTSD

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anxiety disorders and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON39817

Source
ToetsingOnline

Brief title
The effect of oxytocin in PTSD

Condition

- Anxiety disorders and symptoms

Synonym
posttraumatic stress disorder (PTSD) and stress disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW TOP-subsidie toegekend aan Prof. Dr. M. Olff

Intervention

Keyword: fMRI, oxytocin, PTSD

Outcome measures

Primary outcome

The main outcome measures of this study are the acute effects of intranasal OT administration on emotional- and reward related brain processes in men and women diagnosed with PTSD compared to traumatized healthy controls.

Emotional and reward-related brain processes will be acquired on a 3T Philips Achieva MR system located at the Spinoza Center. To measure the effects of OT administration on neural BOLD response, echo-planar images sensitive to BOLD-contrast will be obtained from each subject during three tasks:

1. Emotional face matching task, in which three faces of the same emotion (either happy, fearful or neutral) are presented and the participant is required to match the gender of the first face with those of the other faces. The face matching condition will be compare with a sensorimotor control condition.

2. Reward task, in which sensitivity to monetary and social reward- and loss anticipation and consumption is measured. This will be compared to a neutral condition in which no reward or loss is anticipated or consumed.

3. Emotion regulation task, in which the participant is asked to either look at pictures of negative and neutral scenes or to reappraise negative scenes. BOLD

contrast images will be calculated for the emotion regulation versus the passive viewing condition.

During task execution, psychobiological measures such as reaction times and accuracy on the face-matching and reward tasks, heart rate and heart rate variability will be assessed.

In addition, a resting-state scan, a high-resolution T1-weighted anatomical scan and Diffusion Tensor Weighted Images (DTI) will be collected.

Secondary outcome

1. Gender differences in the effects of intranasal OT administration on functional (task-specific) brain activation between PTSD patients and traumatized healthy controls will be investigated. Salivary levels of estrogen and testosterone will be measured during both fMRI sessions to assess the role of endogenous steroid hormone levels on the main study outcome.
2. Answers to various questionnaires will be used to examine potential associations between the main study outcome and representations of attachment style, social support and history of (childhood) trauma and life events.
3. (Epi)genetic variation will be assessed to investigate potential associations with the main study outcome. In addition, information on genetic variants of participants will be used in a meta-analysis on genes associated with PTSD, carried out by the Psychiatrics Genetics Consortium. Participants will be asked for additional consent to share the data within this international collaboration.

4. Individual variation in HPA axis functioning (i.e. cortisol levels assessed

in hair) will be assessed to investigate potential associations with the main

study outcome.

Study description

Background summary

About 80% of people experience a traumatic event during their life. Of these 10% develop a posttraumatic stress disorder (PTSD), thus leading to an overall estimated lifetime prevalence of PTSD of 8% in the general population. Because of this high prevalence, but also its excess disability, negative impact on quality of life and somatic consequences, the public health impact of PTSD is enormous. Regarding treatment of PTDS, a substantial part of patients drop out of treatment, remain symptomatic or relapse after initial response to treatment, making novel strategies to boost treatment response necessary.

A promising candidate to improve treatment response in PTSD is the neuropeptide oxytocin (OT). OT is involved in several processes disrupted in PTSD, i.e. the fear response, social interaction and reward. In addition, OT is implicated in the pathophysiology of psychiatric disorders involving disturbed stress regulation as well as disrupted attachment and/or social deficits. Therefore, investigating the role of OT administration on emotional and reward-related processes in the brain may lead to novel strategies to improve treatment for PTSD. OT is a safe drug normally used for lactation deficiency and is easy to administer as a nasal spray.

Study objective

In this functional Magnetic Resonance Imaging (fMRI) study, the primary objective is to examine the acute effects of intranasal OT administration on emotional- and reward-related brain processes in PTSD patients compared to traumatized healthy controls.

In the baseline (placebo) condition, we expect PTSD patients to show higher neural sensitivity to fear-inducing visual stimuli and lower neural sensitivity to (social) reward compared to traumatized healthy controls. In addition, we hypothesize to find increased functional connectivity between the amygdala and brainstem regions after placebo administration in PTSD patients compared to traumatized controls.

We expect that OT administration in PTSD patients and controls will dampen

amygdala responsivity towards threatening stimuli. Furthermore, we expect to find increased reward sensitivity, i.e. increased activity in reward-related brain areas (i.e. nucleus accumbens and subgenual prefrontal cortex) and altered interregional communication within fear-and reward-related neural networks after OT administration in PTSD patients and controls.

We expect to see a group by treatment interaction effect, such that the neural effects of OT treatment will differ in magnitude between PTSD patients and controls.

Study design

In this double-blind randomized controlled within-subjects study, a comparison is made between PTSD patients and traumatized healthy controls. In a double-blinded way, participants will be randomized to medication order. Half of the participants will receive intranasal OT during the first and placebo during the second fMRI session. The other half of the participants will receive placebo during the first and intranasal OT during the second fMRI session.

We will assess the effects of one dose of intranasal OT (40 IU; 5 puffs of 4 IU per nostril) compared to placebo (saline) on emotional -and reward-related brain processes. OT is a safe drug to administer (Macdonald et al., 2011), registered in the Netherlands and commonly used in women who have difficulties breastfeeding. The dose of 40 IU has been used safely in a study with psychiatric patients.

Study burden and risks

Since we will conduct a study in psychiatric patients (i.e. PTSS patients), the risk classification associated with this study is *minimal excess of negligible risk*. OT is a save drug, except during pregnancy. Therefore, female participants with childbearing potential must have a negative pregnancy test before commencing study participation. Functional magnetic resonance imaging (fMRI) is not harmful for the participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Age 18 * 65 years
* Capable to read and comprehend the Dutch language
* Eligibility for MRI (i.e. no metals, pacemakers or claustrophobia)
* Exposed to a potentially traumatic event, according to PTSD A1 criterion in the DSM-IV (minimal 1 month ago), quantified as a score of 1 or higher on the Life Events Checklist (LEC).
PTSD patients:
* Current PTSD diagnosis
* CAPS score * 45
Traumatized healthy controls:
* CAPS-score < 15

Exclusion criteria

* Any severe or chronic systemic disease
* Current psychotic, bipolar, substance-related, severe personality disorder, or mental retardation
* Current severe depressive disorder
* Prominent current suicidal risk or homicidal ideation
* Severe cognitive impairment or a history of organic mental disorder
* History of neurological disorders (e.g., traumatic brain injury, seizure history)
* Reports of ongoing traumatization (e.g., in case of partner violence as index adult trauma)

* Evidence of clinically significant and unstable medical conditions in which OT administration is contra-indicative such as cardiovascular, gastro-intestinal, pulmonary, severe renal, endocrine or hematological disorders, glaucoma, history of epilepsy, or a stroke or myocardial infarction within the past year
* Use of certain medication: prostaglandins, certain anti-migraine medications (ergot alkaloids), ß-adrenergic receptor-blocking agents, systemic glucocorticoids and psychopharmacological medication.
* Sensitivity or allergy for OT or its components (e.g. methylhydroxybenzoate and propylhydroxybenzoate)
* Female participants: pregnancy and breast feeding (NB. Female participants with childbearing potential must have a negative pregnancy test).
Traumatized healthy controls only:
* (lifetime history of) PTSD diagnosis, major depressive disorder.
* Current DSM-IV axis 1 disorder

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-07-2012
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Syntocinon

Generic name:	Oxytocin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-03-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2012-001288-58-NL
CCMO	NL40122.018.12

Study results

Date completed:	01-01-2015
Actual enrolment:	83