Boosting Oxytocin after trauma: Neurobiology and the Development of Stress-related symptoms.

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Primary aim:In recently traumatized individuals (at the latest on day ten post trauma exposure) with a high initial level of distress, we aim to assess the effectiveness of intranasal OT in preventing symptoms of PTSD at one months post intervention…

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

Summary

ID

NL-OMON39401

Source
ToetsingOnline

Brief title
BONDS

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

Intervention

Keyword: early intervention, fMRI, oxytocin, PTSD

Outcome measures

Primary outcome

The main study outcome is the difference in PTSD symptoms severity (CAPS scores) between the two trial arms (i.e. OT versus placebo) at one month post intervention follow-up.

The main study outcomes for the fMRI substudy are differences in amygdala activation to emotional faces and differences in brain functional connectivity after stress induction between the two study conditions.

Secondary outcome

* Differences between intervention groups in depression and general anxiety symptoms, neuroendocrine / psychophysiological measures, perceived social support and psychological functioning between the two groups after one week of OT treatments, and one and a half, three and six months post trauma exposure.
* Differences between intervention groups in PTSD symptoms severity (CAPS scores) between the two trial arms (i.e. OT versus placebo) at three and six months post trauma follow-up.
* Potential associations between the main study outcome and gender, genetic variation, perceived social support, representations of attachment style, coping style, subjective health complaints, quality of life, trauma type, history of (childhood) trauma and life events.

fMRI substudy only:

* Differences in salivary cortisol, DHEAS, and OT reactivity after intranasal OT between the two study groups.

* Differences in the role of endogenous steroid hormone levels (i.e. estrogen, progesterone and testosterone) in the effect of intranasal OT on neural (stress) reactivity between the two groups.

* Potential associations between the main study outcome and gender, genetic variation, perceived social support, representations of attachment style, coping style, subjective health complaints, quality of life, trauma type, history of (childhood) trauma and life events.

Study description

Background summary

Eighty per cent of the general population experiences a traumatic event in their life span, of which 10% will develop post traumatic stress disorder (PTSD). It is widely acknowledged that PTSD has a major influence on the health and economic situation of patients, their relatives, and society in general. However, no effective early interventions in the acute phase after traumatization exist that can decrease the subsequent risk for PTSD development.

Social support is one of the most powerful protective influences against PTSD. However, little is known about the neurobiology behind this mechanism and no proven effective interventions are available that stimulate social support seeking behavior.
An important role in the mechanism behind the positive effects of social support is attributed to the neuropeptide oxytocin (OT), a hormone that is synthesized in the brain and released during positive social interactions and is associated with pair bonding, empathy, and trust. It is believed that OT treatment results in in increased susceptibility for (the positive effects of) experiencing social support.
Furthermore, OT is synthesized and released during stressful events. This consequently promotes stress regulation at the level of both the neuroendocrine and autonomic stress system. Studies using intranasal OT treatments in humans have demonstrated that OT influences brain activity patterns and stress

responses during a (stress) task. This is relevant for PTSD research, in which it is currently believed that inadequate and prolonged stress responses are an underlying mechanism in PTSD development.

Thus, OT treatment could benefit individuals that are at risk of developing PTSD in several ways: by influencing the neuroendocrine and autonomic stress response and by enhancing susceptibility for social support.

fMRI substudy: Animal and human research show that OT administration influences brain areas involved in stress regulation. Handholding has also been shown to reduce neural reactivity to threat.

Study objective

Primary aim:
In recently traumatized individuals (at the latest on day ten post trauma exposure) with a high initial level of distress, we aim to assess the effectiveness of intranasal OT in preventing symptoms of PTSD at one months post intervention follow-up.
In an fMRI-eligible subgroup of the participants, we aim to investigate the acute effects of intranasal OT on brain activation and connectivity patterns.

Secondary aims include to:
* Investigate the effects of OT on depression and general anxiety symptoms, neuroendocrine and psychophysiological measures, perceived social support, and psychological functioning after one week of intranasal treatments, and at one and a half, three and six months post trauma follow-up;
* Investigate the effectiveness of intranasal OT administration in preventing symptoms of PTSD at 3 and 6 months,post trauma follow-up compared to intranasal placebo treatment.
* Examine potential associations between the main study outcome and gender, genetic variation, subjective measures of social support, representations of attachment style, coping style, subjective health complaints, quality of life, trauma type and history of (childhood) trauma and life events.
fMRI substudy only:
* To study the effects of intranasal OT on salivary cortisol, DHEAS, and OT reactivity.
* To assess the role of endogenous steroid hormone levels (i.e. estrogen, progesterone and testosterone) in the effect of OT on neural (stress) reactivity.
* Examine potential associations between the main study outcome and gender, genetic variation, subjective measures of social support, representations of attachment style, coping style, subjective health complaints, quality of life, trauma type and history of (childhood) trauma and life events.

Study design

We propose to conduct a double-blind randomized placebo controlled trial on the effectiveness of oxytocin versus placebo treatments on the development of trauma related psychopathology in recently traumatized individuals at risk for developing PTSD.

At the latest on day ten after trauma exposure participants (after written informed consent) will be blindly randomized to the oxytocin or placebo treatment condition.

This is a cross-sectional double-blind (for OT administration) randomized controlled study to assess the acute effects of our interventions on brain activation.

Intervention

Half of the participants will self-administer a total of 15 doses of intranasal oxytocin (40 IU, 5 sprays per nostril) or placebo (5 sprays per nostril). The first treatment will be at the AMC. 14 treatments will occur on 7 consecutive days in the home environment. The total duration of intranasal treatments is 8 days.
In case a participant only wants to participate in the fMRI study, he/she will only apply a single dose of intranasal treatment.

Study burden and risks

The burdens and risks associated with participation with this study are minimal. Oxytocin is safe to administer to non-pregnant individuals (Females with a child-bearing potential should have a negative pregnancy test). Undergoing an fMRI scan is not harmful.

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

* Presentation at the Trauma Room or Emergency Department after a potential traumatic event, according to PTSD A1 criterion in the DSM-IV (either as a patient or direct witness);
* Trauma Screening Questionnaire (TSQ) <=/> 5 and/or Peritraumatic Distress Inventory (PDI) <=/> 17 preferably between 24 and 72 hours after trauma exposure (in case of contacting difficulties up to 7 days after trauma);
* Age 18 * 65 years;
* Capable to read and comprehend either the Dutch or English language;

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;
* Evidence of PTSD or depression immediately prior to the index trauma;
* 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), bèta-adrenergic receptor-blocking agents, and systemic glucocorticoids;
* Sensitivity or allergy for OT or its components (e.g., methylhydroxybenzoate and propylhydroxybenzoate);

* Impaired consciousness, or amnesia or confusion (due to for example head injury) (objectified by Glasgow Coma Scale lower than 13 at time of inclusion)
* Female participants: pregnancy and breast feeding (NB. Female participants with childbearing potential must have a negative pregnancy test);

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-04-2012
Enrollment:	220
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:	05-09-2011

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-01-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Not approved Date:	12-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2013
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	EUCTR2011-004177-83-NL
CCMO	NL37202.018.11

Study results

Date completed:	09-07-2015
Actual enrolment:	124

Summary results

Trial is onging in other countries