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

Summary

EudraCT number	2012-001288-58
Trial protocol	NL
Global end of trial date	19 May 2014

Results information

Result version number	v1 (current)
This version publication date	12 July 2021
First version publication date	12 July 2021
Summary attachment (see zip file)	OXT amygdala (Final - Koch 2015 - Hariri NPP npp2015299a.pdf) oxytocin amygdala connectivity (Koch 2016 FINAL - npp20161a - Intranasal Oxytocin Normalizes Amygdala Functional Connectivity in Posttraumatic Stress Disorder.pdf) oxytocin distraction (koch 2018 ENP Oxytocin distraction.pdf) oxytocin social reward (FINAL Soc Cogn Affect Neurosci-2016-Nawijn-scan-nsw123.pdf) oxytocin monetary reward (Nawijn 2016 MID PNEC.pdf)

Trial information

Trial identification

Sponsor protocol code	40122

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amsterdam UMC, location Academic Medical Center
Sponsor organisation address	Meibergdreef 9, Amsterdam, Netherlands, 1105 AZ
Public contact	prof. dr. Miranda Olff, Amsterdam UMC, location Academic Medical Center, Academic Medical Center, Department of Psychiatru, +31 (0)208913662, m.olff@amc.uva.nl
Scientific contact	prof. dr. Miranda Olff, Amsterdam UMC, location Academic Medical Center, Department of Psychiatry, +31 (0)208913662, m.olff@amc.uva.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 May 2014
Global end of trial reached?	Yes
Global end of trial date	19 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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. Furthermore, we aim to examine gender differences in the effects of intranasal OT administration on functional (task-specific) brain activation and in structural anatomy (i.e. volume and white matter integrity) between PTSD patients and traumatized healthy controls.

Protection of trial subjects:

All study procedures were carried out in accordance with relevant laws and regulations.
All involved reseachers had received GCP training.
An independent monitor regularly monitored the RCT.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 June 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 83
Worldwide total number of subjects	83
EEA total number of subjects	83

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	83
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

relevant details in terms of medication use:
- Evidence of clinically significant and unstable medical conditions in which OT administration is contra-indicative
- Use of: prostaglandins, anti-migraine medications (ergot alkaloids), ß-adrenergic receptor-blocking agents, systemic glucocorticoids and psychopharmacological medication.

Period 1

Period 1 title	Inclusion/baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	PTSD women

Arm description: -

Arm type	Experimental
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

single adminstration of 40 IU

Arm title	PTSD men

Arm description: -

Arm type	Experimental
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

single adminstration of 40 IU

Arm title	Healthy control women

Arm description: -

Arm type	healthy control
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

single adminstration of 40 IU

Arm title	healthy control men
Arm description: -	
Arm type	healthy control group
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

single adminstration of 40 IU

Number of subjects in period 1[1]	PTSD women	PTSD men	Healthy control women
Started	20	21	20
Completed	20	21	20

Number of subjects in period 1[1]	healthy control men
Started	20
Completed	20

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 2 participants dropped out prior to randomization

Period 2

Period 2 title	2 fMRI sessions
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Medication allocation was concealed using a treatment code, only accessed by an independent researched who performed the randomization, made the randomization list and had no role in data collection . The study was conducted in a double-blinded way, in which both the participants and researchers involved in data collection were blind to treatment allocation. The treatment coding key remained concealed until data collection was completed unless in case of SAEs (NA in this trial).

Arms

Are arms mutually exclusive?	Yes
Arm title	PTSD women
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use
Dosage and administration details: single adminstration of 40 IU	
Arm title	PTSD men
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use
Dosage and administration details: single adminstration of 40 IU	
Arm title	healthy control women
Arm description: -	
Arm type	healthy control group
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use
Dosage and administration details: single adminstration of 40 IU	
Arm title	healthy control men
Arm description: -	
Arm type	healthy control group
Investigational medicinal product name	oxytocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal/oromucosal spray, solution
Routes of administration	Nasal use
Dosage and administration details: single adminstration of 40 IU	

Number of subjects in period 2[2]	PTSD women	PTSD men	healthy control women
Started	19	21	20
Completed	17	21	20
Not completed	2	0	0
Adverse event, non-fatal	2	-	-

Number of subjects in period 2[2]	healthy control men

Started	20
Completed	20
Not completed	0
Adverse event, non-fatal	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 participant dropped out prior to starting the mri sessions because of logistical reasons

Baseline characteristics

Reporting groups	
Reporting group title	Inclusion/baseline

Reporting group description: -

Reporting group values	Inclusion/baseline	Total	
Number of subjects	81	81	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	81	81	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	40		
standard deviation	± 10	-	
Gender categorical Units: Subjects			
Female	40	40	
Male	41	41	

End points

End points reporting groups	
Reporting group title	PTSD women
Reporting group description: -	
Reporting group title	PTSD men
Reporting group description: -	
Reporting group title	Healthy control women
Reporting group description: -	
Reporting group title	healthy control men
Reporting group description: -	
Reporting group title	PTSD women
Reporting group description: -	
Reporting group title	PTSD men
Reporting group description: -	
Reporting group title	healthy control women
Reporting group description: -	
Reporting group title	healthy control men
Reporting group description: -	

Primary: amygdala connectivity	
End point title	amygdala connectivity
End point description:	
End point type	Primary

End point timeframe:

functional brain connectivity at the level of the right amygdala (CEM) with left vmPFC as measured during resting state during each scanning session, comparing activity during oxytocin to activity during placebo

End point values	PTSD women	PTSD men	healthy control women	healthy control men
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	19	19	19
Units: AU contrast oxytocin vs placebo				
arithmetic mean (standard error)	.0542 (± .1010)	-.1355 (± .185)	-.0009 (± .108)	.0606 (± .155)

Statistical analyses

Statistical analysis title	Difference OTvsPL

Statistical analysis description:

see Koch et al 2015 NPP

second-level repeated measures anovas with contrast estimates of positive correlations of ROIs with

amygdala seeds, with between-subject factors PTSD status and SEX, and within subjects factor DRUG (OT vs PL), with drug order and mean framewise displacement added as covariate.

Comparison groups	PTSD women v healthy control women v PTSD men v healthy control men
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)

Notes:

[1] - FWE corrected

Adverse events

Adverse events information	
Timeframe for reporting adverse events: within 90 minutes after administration and one week after administration	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	2021AA

Reporting groups	
Reporting group title	PTSD patients after oxytocin
Reporting group description: -	
Reporting group title	PTSD patients after placebo
Reporting group description: -	
Reporting group title	controls after oxytocin
Reporting group description: -	
Reporting group title	controls after placebo
Reporting group description: -	

Serious adverse events	PTSD patients after oxytocin	PTSD patients after placebo	controls after oxytocin
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	controls after placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	PTSD patients after oxytocin	PTSD patients after placebo	controls after oxytocin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 37 (40.54%)	15 / 39 (38.46%)	16 / 40 (40.00%)
Nervous system disorders			

Headache			
subjects affected / exposed	6 / 37 (16.22%)	8 / 39 (20.51%)	2 / 40 (5.00%)
occurrences (all)	6	8	2
concentration impaired			
subjects affected / exposed	1 / 37 (2.70%)	2 / 39 (5.13%)	6 / 40 (15.00%)
occurrences (all)	1	2	6
lightheadedness	Additional description: lightheadedness or dizziness		
subjects affected / exposed	2 / 37 (5.41%)	2 / 39 (5.13%)	1 / 40 (2.50%)
occurrences (all)	2	2	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 37 (18.92%)	6 / 39 (15.38%)	10 / 40 (25.00%)
occurrences (all)	7	6	10

Non-serious adverse events	controls after placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 40 (25.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
concentration impaired			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
lightheadedness	Additional description: lightheadedness or dizziness		
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2012	added questionnaire on workrelated traumatic events
26 October 2012	collection of hair for cortisol assessment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported