



Clinical trial results: Oxytocin-based pharmacotherapy for Autism Spectrum Disorders: Investigating the neural and behavioral effects of a promising intervention approach Summary

EudraCT number	2014-000586-45
Trial protocol	BE
Global end of trial date	20 December 2019

Results information

Result version number	v1 (current)
This version publication date	03 September 2020
First version publication date	03 September 2020
Summary attachment (see zip file)	Summary (journal abstracts) (Summary _ abstracts of NNP&MolAutism.docx)

Trial information

Trial identification

Sponsor protocol code	S56327
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02940574
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	KU Leuven
Sponsor organisation address	Tervuursevest 101, Leuven, Belgium, 3000
Public contact	Dr. K. Alaerts, KU Leuven, 0032 16376446, kaat.alaerts@kuleuven.be
Scientific contact	Dr. K. Alaerts, KU Leuven, 0032 16376446, kaat.alaerts@kuleuven.be

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
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	20 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2019
Global end of trial reached?	Yes
Global end of trial date	20 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The current trial aims to explore the neural and behavioral effects of oxytocin in autism spectrum disorders (ASD). Initial studies showed that intranasal administration of oxytocin can have a positive effect on social functioning in ASD. However, future studies are necessary to explore whether and how oxytocin effects neural processes in the brain underlying these behavioral improvements. This trial will not only measure behavioral enhancements, but will specifically focus on elucidating the associated neurophysiological changes by guiding the administration of oxytocin with regular neurophysiological assessments.

Protection of trial subjects:

Regular screenings of potential side-effects

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were mainly recruited from the Autism Expertise Centre at the Leuven University Hospital between April 2015 and December 2016.

Pre-assignment

Screening details:

Assessed for eligibility (n= 68)

Excluded (n = 28)

Not meeting inclusion criteria (n= 3)

Not interested to participate (n= 25)

Period 1

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

Blinding implementation details:

Participants were randomly assigned to receive the oxytocin or placebo treatment based on a computer-generated randomized order. Except for the manager of randomization, all research staff conducting the study, participants, parents and partners were blind to treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Syntocinon (Oxytocin, Product Code RVG 03716)

Arm description:

Administration via nasal spray Syntocinon (Oxytocin): Syntocinon nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Arm type	Experimental
Investigational medicinal product name	Syntocinon (oxytocin), nasal spray 40 IE/ml
Investigational medicinal product code	RVG 03716
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Arm title	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))
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Arm description:

Administration via nasal spray

Placebo (Physiological water (solution of sodium chloride (NaCl) in water)): Placebo nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Arm type	Placebo
Investigational medicinal product name	Physiological water(sodium chloride (NaCl) 0.9 % solution)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Placebo (Physiological water (solution of sodium chloride (NaCl) in water))

Placebo nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Number of subjects in period 1	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl))
Started	22	18
Completed	21	18
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	Syntocinon (Oxytocin, Product Code RVG 03716)
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Reporting group description:

Administration via nasal spray Syntocinon (Oxytocin): Syntocinon nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Reporting group title	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))
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Reporting group description:

Administration via nasal spray

Placebo (Physiological water (solution of sodium chloride (NaCl) in water)): Placebo nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Reporting group values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl))	Total
Number of subjects	22	18	40
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	22	18	40
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	25.00	24.00	
standard deviation	± 4.86	± 5.55	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	22	18	40
Total IQ			
6-subtest short-version of the Wechsler Adult Intelligence Scale-IV - Dutch version Block design, Digit span, Similarities, Vocabulary, Symbol search and Visual puzzles			
Units: units on a scale			
arithmetic mean	102.27	104.61	
standard deviation	± 12.45	± 21.59	-

End points

End points reporting groups

Reporting group title	Syntocinon (Oxytocin, Product Code RVG 03716)
Reporting group description: Administration via nasal spray Syntocinon (Oxytocin): Syntocinon nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray	
Reporting group title	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))
Reporting group description: Administration via nasal spray Placebo (Physiological water (solution of sodium chloride (NaCl) in water)): Placebo nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray	

Primary: Change From Baseline in Brain Activity during task (Task-based fMRI) after a single dose of nasal spray

End point title	Change From Baseline in Brain Activity during task (Task-based fMRI) after a single dose of nasal spray ^[1]
End point description: Change From Baseline in Task-related Brain Activity during Biological Motion Recognition Task (Task-based fMRI) After a Single Dose of Nasal Spray	
End point type	Primary
End point timeframe: Value at 30 minutes minus value at baseline	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17 ^[2]		
Units: Change-from-baseline Contrast estimate				
arithmetic mean (standard deviation)				
Brain activity - Superior temporal sulcus	0.11 (± 0.49)	-0.26 (± 0.72)		
Brain activity - Amygdala	-0.15 (± 0.50)	-0.16 (± 0.58)		

Notes:

[2] - n=1 not included, due to unusable data (excessive in-scanner head motion)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain activity during task (task-based fMRI) after 4 weeks of nasal spray

End point title	Change from baseline in brain activity during task (task-based
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End point description:

Change From Baseline in Task-related Brain Activity during Biological Motion Recognition Task (Task-based fMRI) after 4 weeks of nasal spray

End point type Primary

End point timeframe:

Value at 4 weeks minus value at baseline

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17 ^[4]		
Units: Change-from-baseline Contrast estimate				
arithmetic mean (standard deviation)				
Brain activity - Superior temporal sulcus	-0.10 (± 0.59)	-0.29 (± 0.68)		
Brain activity - Amygdala	-0.09 (± 0.46)	0.06 (± 0.45)		

Notes:

[4] - n=1 not included, due to unusable data (excessive in-scanner head motion)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain activity during task (task-based fMRI) after 8 weeks, including 4 weeks without nasal spray

End point title Change from baseline in brain activity during task (task-based fMRI) after 8 weeks, including 4 weeks without nasal spray^[5]

End point description:

Change From Baseline in Task-related Brain Activity during Biological Motion Recognition Task (Task-based fMRI) after 8 weeks, including 4 weeks without nasal spray

End point type Primary

End point timeframe:

Value at 8 weeks minus value at baseline

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17 ^[6]		
Units: Change-from-baseline Contrast estimate				
arithmetic mean (standard deviation)				

Brain activity - Superior temporal sulcus	-0.21 (\pm 0.58)	-0.16 (\pm 0.66)		
Brain activity - Amygdala	-0.18 (\pm 0.52)	0.04 (\pm 0.56)		

Notes:

[6] - n=1 not included, due to unusable data (excessive in-scanner head motion)

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain activity during task (task-based fMRI) after 52 weeks, including 48 weeks without nasal spray

End point title	Change from baseline in brain activity during task (task-based fMRI) after 52 weeks, including 48 weeks without nasal spray ^[7]
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End point description:

Change From Baseline in Task-related Brain Activity during Biological Motion Recognition Task (Task-based fMRI) after 52 weeks, including 48 weeks without nasal spray

End point type	Primary
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End point timeframe:

Value at 52 weeks minus value at baseline

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	14		
Units: Change-from-baseline Contrast estimate				
arithmetic mean (standard deviation)				
Brain activity - Superior temporal sulcus	-0.18 (\pm 0.56)	-0.48 (\pm 0.73)		
Brain activity - Amygdala	-0.21 (\pm 0.51)	0.03 (\pm 0.40)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain connectivity during rest (resting-state fMRI) after a single dose of nasal spray

End point title	Change from baseline in brain connectivity during rest (resting-state fMRI) after a single dose of nasal spray ^[8]
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End point description:

Change From Baseline in Brain Connectivity During Rest (Resting-state fMRI) After a Single Dose of Nasal Spray

Amygdala connectivity (Change-from-baseline z-transformed r-value)

End point type	Primary
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End point timeframe:

Value at 30 minutes minus value at baseline

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17		
Units: Change-from-base z-transformed r-value				
arithmetic mean (standard deviation)	-0.07 (± 0.21)	0.03 (± 0.20)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain connectivity during rest (resting-state fMRI) after 4 weeks of nasal spray

End point title	Change from baseline in brain connectivity during rest (resting-state fMRI) after 4 weeks of nasal spray ^[9]
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End point description:

Change from baseline in brain connectivity during rest (resting-state fMRI) after 4 weeks of nasal spray

Amygdala connectivity (Change-from-baseline z-transformed r-value)

End point type	Primary
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End point timeframe:

Value at 4 weeks minus value at baseline

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	18		
Units: Change-from-base z-transformed r-value				
arithmetic mean (standard deviation)	-0.04 (± 0.22)	0.11 (± 0.21)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain connectivity during rest (resting-state fMRI) after 8 weeks, including 4 weeks without nasal spray

End point title	Change from baseline in brain connectivity during rest (resting-state fMRI) after 8 weeks, including 4 weeks without nasal spray ^[10]
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End point description:

Change from baseline in brain connectivity during rest (resting-state fMRI) after 8 weeks, including 4 weeks without nasal spray

Amygdala connectivity (Change-from-baseline z-transformed r-value)

End point type	Primary
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End point timeframe:

Value at 8 weeks minus value at baseline

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17		
Units: Change-from-base z-transformed r-value				
arithmetic mean (standard deviation)	-0.07 (± 0.17)	0.13 (± 0.18)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in brain connectivity during rest (resting-state fMRI) after 52 weeks, including 48 weeks without nasal spray

End point title	Change from baseline in brain connectivity during rest (resting-state fMRI) after 52 weeks, including 48 weeks without nasal spray ^[11]
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End point description:

Change from baseline in brain connectivity during rest (resting-state fMRI) after 52 weeks, including 48 weeks without nasal spray

Amygdala connectivity (Change-from-baseline z-transformed r-value)

End point type	Primary
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End point timeframe:

Value at 52 weeks minus value at baseline

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See attached chart/documents for results

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	14		
Units: Change-from-base z-transformed r-value				
arithmetic mean (standard deviation)	-0.06 (± 0.20)	0.11 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in performance on the emotion recognition task (accuracy/reaction time) after a single dose of nasal spray

End point title	Change from baseline in performance on the emotion recognition task (accuracy/reaction time) after a single dose of nasal spray
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End point description:

Change from baseline in performance on the emotion recognition task (accuracy/reaction time) after a single dose of nasal spray

Emotion recognition from point-light displays conveying biological motion.

End point type	Secondary
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End point timeframe:

Value at 30 minutes minus value at baseline

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17		
Units: Change from baseline Acc/reaction time				
arithmetic mean (standard deviation)	0.000029 (± 0.000069)	0.000065 (± 0.000071)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 4 weeks of nasal spray

End point title	Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 4 weeks of nasal spray
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End point description:

Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 4 weeks of nasal spray.

Emotion recognition from point-light displays conveying biological motion.

End point type	Secondary
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End point timeframe:

Value at 4 weeks minus value at baseline

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17		
Units: Change from baseline Acc/reaction time				
arithmetic mean (standard deviation)	0.000044 (± 0.000079)	0.000073 (± 0.000071)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 8 weeks (including 4 weeks without nasal spray)

End point title	Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 8 weeks (including 4 weeks without nasal spray)
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End point description:

Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 8 weeks (including 4 weeks without nasal spray).

Emotion recognition from point-light displays conveying biological motion.

End point type	Secondary
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End point timeframe:

Value at 8 weeks minus value at baseline

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17		
Units: Change from baseline Acc/reaction time				
arithmetic mean (standard deviation)	0.000070 (± 0.000084)	0.000088 (± 0.000089)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 52 weeks (including 48 weeks without nasal spray)

End point title	Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 52 weeks (including 48 weeks without nasal spray)
End point description: Change from baseline in performance on the emotion recognition task (accuracy/ reaction time) after 52 weeks (including 48 weeks without nasal spray)	
End point type	Secondary
End point timeframe: Value at 52 weeks minus value at baseline	

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	14		
Units: Change from baseline Acc/reaction time				
arithmetic mean (standard deviation)	0.000071 (\pm 0.000079)	0.000084 (\pm 0.000094)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in informant-based/ self-report scores on questionnaires assessing attachment, social functioning, quality of life and mood after 4 weeks of nasal spray

End point title	Change from baseline in informant-based/ self-report scores on questionnaires assessing attachment, social functioning, quality of life and mood after 4 weeks of nasal spray
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End point description:

The Social Responsiveness Scale (for adults) (SRS-A) uses a four-point Likert-scale. Higher scores indicate lower social responsiveness.

The Repetitive Behavior Scale – Revised (RBS-R) uses a four-point Likert-scale. Higher scores indicate a higher frequency and/or higher severity of restricted and repetitive behaviors.

The State Adult Attachment Measure (SAAM) uses a seven-point Likert-scale. Higher scores indicate lower perceived secure attachment on the attachment avoidance and attachment anxiety subscales, and

higher perceived secure attachment on the attachment security subscale.

Inventory of Parent and Peer Attachment (IPPA) uses a four-point Likert-scale. Higher scores indicate increased feelings of secure attachment towards peers or parents.

World Health Organization Quality of Life – Bref (WHO-QL) uses a five-point Likert scale. Higher scores indicate better quality of life.

Profile of Mood States (POMS). five-point Likert scale.

End point type	Secondary
End point timeframe:	
Value at 4 weeks minus value at baseline	

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[12]	18 ^[13]		
Units: Change from base (units on a scale)				
arithmetic mean (standard deviation)				
SRS-A self-report	-5.55 (± 11.40)	-1.06 (± 10.01)		
SRS-A informant-based	0.0 (± 15.86)	-0.87 (± 12.83)		
RBS-R	-4.77 (± 6.47)	-1.76 (± 4.75)		
SAAM avoidance	-0.40 (± 0.71)	0.06 (± 0.98)		
SAAM security	0.27 (± 0.77)	0.05 (± 0.66)		
SAAM anxiety	-0.14 (± 0.75)	0.28 (± 0.95)		
IPPA Peers	1.45 (± 3.85)	0.56 (± 4.05)		
IPPA Mother	-0.52 (± 2.71)	0.44 (± 3.45)		
IPPA Father	0.43 (± 3.30)	-0.61 (± 3.81)		
WHO-QOL	1.77 (± 8.04)	-1.35 (± 6.74)		
POMS - Tension	-2.00 (± 2.29)	-2.39 (± 3.03)		
POMS - Anger	0.00 (± 4.05)	-0.61 (± 2.73)		
POMS - Depression	-1.14 (± 4.50)	-0.33 (± 2.81)		
POMS - Vigor	-1.00 (± 2.53)	-2.94 (± 3.64)		
POMS - Fatigue	-2.09 (± 3.99)	-1.11 (± 5.12)		

Notes:

[12] - Intention-to-treat

[13] - Intention-to-treat

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in informant-based/ self-report scores on questionnaires assessing attachment, social functioning, quality of life and mood after 8 weeks, including 4 weeks without nasal spray

End point title	Change from baseline in informant-based/ self-report scores on questionnaires assessing attachment, social functioning, quality of life and mood after 8 weeks, including 4 weeks without nasal spray
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End point description:

The Social Responsiveness Scale (for adults) (SRS-A) uses a four-point Likert-scale. Higher scores indicate lower social responsiveness.

The Repetitive Behavior Scale – Revised (RBS-R) uses a four-point Likert-scale. Higher scores indicate a higher frequency and/or higher severity of restricted and repetitive behaviors.

The State Adult Attachment Measure (SAAM) uses a seven-point Likert-scale. Higher scores indicate lower perceived secure attachment on the attachment avoidance and attachment anxiety subscales, and higher perceived secure attachment on the attachment security subscale.

Inventory of Parent and Peer Attachment (IPPA) uses a four-point Likert-scale. Higher scores indicate increased feelings of secure attachment towards peers or parents.

World Health Organization Quality of Life – Bref (WHO-QL) uses a five-point Likert scale. Higher scores indicate better quality of life.

Profile of Mood States (POMS). five-point Likert scale.

End point type	Secondary
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End point timeframe:

Value at 8 weeks minus value at baseline

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[14]	18 ^[15]		
Units: Change from base (units on a scale)				
arithmetic mean (standard deviation)				
SRS-A self-report	-5.64 (± 12.57)	-7.67 (± 12.09)		
SRS-A informant-based	-9.59 (± 10.98)	-1.20 (± 10.73)		
RBS-R	-4.91 (± 6.33)	-2.35 (± 3.43)		
SAAM avoidance	-0.38 (± 0.70)	-0.06 (± 0.76)		
SAAM security	0.04 (± 1.01)	-0.40 (± 0.99)		
SAAM anxiety	0.08 (± 1.05)	0.11 (± 0.87)		
IPPA Peers	1.32 (± 3.71)	0.06 (± 3.70)		
IPPA Mother	-0.38 (± 3.43)	0.06 (± 4.35)		
IPPA Father	0.52 (± 3.59)	-0.33 (± 3.87)		
WHO-QOL	1.14 (± 5.48)	0.35 (± 4.53)		
POMS - Tension	-2.64 (± 2.80)	-2.11 (± 3.22)		
POMS - Anger	0.36 (± 3.68)	-0.39 (± 3.91)		
POMS - Depression	-0.82 (± 2.63)	0.22 (± 3.41)		
POMS - Vigor	0.14 (± 3.58)	-1.44 (± 4.33)		
POMS - Fatigue	-2.69 (± 2.71)	-2.33 (± 4.47)		

Notes:

[14] - Intention-to-Treat

[15] - Intention-to-Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Informant-based/ Self-report scores on questionnaires assessing attachment, social functioning, quality of life and mood

after 52 weeks, including 48 weeks without nasal spray

End point title	Change from baseline in Informant-based/ Self-report scores on questionnaires assessing attachment, social functioning, quality of life and mood after 52 weeks, including 48 weeks without nasal spray
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End point description:

The Social Responsiveness Scale (for adults) (SRS-A) uses a four-point Likert-scale. Higher scores indicate lower social responsiveness.

The Repetitive Behavior Scale – Revised (RBS-R) uses a four-point Likert-scale. Higher scores indicate a higher frequency and/or higher severity of restricted and repetitive behaviors.

The State Adult Attachment Measure (SAAM) uses a seven-point Likert-scale. Higher scores indicate lower perceived secure attachment on the attachment avoidance and attachment anxiety subscales, and higher perceived secure attachment on the attachment security subscale.

Inventory of Parent and Peer Attachment (IPPA) uses a four-point Likert-scale. Higher scores indicate increased feelings of secure attachment towards peers or parents.

World Health Organization Quality of Life – Bref (WHO-QOL) uses a five-point Likert scale. Higher scores indicate better quality of life.

Profile of Mood States (POMS). five-point Likert scale.

End point type	Secondary
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End point timeframe:

Value at 52 weeks minus value at baseline

End point values	Syntocinon (Oxytocin, Product Code RVG 03716)	Placebo (Physiological Water(Sodium Chloride (NaCl) Solution))		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[16]	18 ^[17]		
Units: Change from base (units on a scale)				
arithmetic mean (standard deviation)				
SRS-A self-report	-8.59 (± 20.95)	-6.72 (± 21.01)		
SRS-A informant-based	-7.41 (± 19.26)	-4.13 (± 24.64)		
RBS-R	-4.91 (± 9.46)	-0.41 (± 4.27)		
SAAM avoidance	-0.52 (± 1.18)	0.0 (± 0.75)		
SAAM security	0.20 (± 1.52)	-0.14 (± 0.66)		
SAAM anxiety	0.17 (± 0.94)	0.11 (± 1.21)		
IPPA Peers	0.68 (± 6.26)	1.28 (± 4.17)		
IPPA Mother	0.33 (± 3.91)	1.50 (± 5.44)		
IPPA Father	0.57 (± 4.08)	-0.50 (± 4.53)		
WHO-QOL	1.14 (± 8.37)	0.29 (± 4.21)		
POMS - Tension	-1.86 (± 2.29)	-2.28 (± 3.46)		
POMS - Anger	0.59 (± 3.69)	0.06 (± 3.84)		
POMS - Depression	0.50 (± 2.63)	-0.28 (± 3.51)		
POMS - Vigor	1.14 (± 3.88)	-0.61 (± 3.27)		
POMS - Fatigue	-0.23 (± 6.04)	0.39 (± 4.73)		

Notes:

[16] - Intention-to-Treat

[17] - Intention-to-Treat

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected over a period of (approximately) four weeks.

Adverse event reporting additional description:

Adverse event data were collected via weekly journal entries. Participants were asked to indicate whether or not they had experienced any potential adverse events, when it started, how long it lasted, and the severity of the adverse event (mild, moderate, severe).

Assessment type	Systematic
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Dictionary used

Dictionary name	Self-report
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Dictionary version	2014
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Reporting groups

Reporting group title	Syntocinon (Oxytocin, product code RVG 03716)
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Reporting group description:

Administration via nasal spray

Syntocinon (Oxytocin): Syntocinon nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Reporting group title	Placebo (Physiological water(sodium chloride (NaCl) solution))
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Reporting group description:

Administration via nasal spray

Placebo (Physiological water (solution of sodium chloride (NaCl) in water)): Placebo nasal spray. A single dose (24IU) of nasal spray (3 puffs of 4IU per nostril), followed by 4 weeks of a daily single dose (24IU; 3 puffs of 4IU per nostril) of nasal spray

Serious adverse events	Syntocinon (Oxytocin, product code RVG 03716)	Placebo (Physiological water(sodium chloride (NaCl))	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Syntocinon (Oxytocin, product code RVG 03716)	Placebo (Physiological water(sodium chloride (NaCl))	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)	3 / 18 (16.67%)	
Respiratory, thoracic and mediastinal disorders			

Nasal irritation/ runny nose subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	3 / 18 (16.67%) 3	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32161366>

<http://www.ncbi.nlm.nih.gov/pubmed/31969977>