(Grand)parenting, oxytocin, and the oxytocin receptor gene: an fMRI and observational study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41691

Source
ToetsingOnline

Brief title
(Grand)parenting and oxytocin

Condition

- Other condition
- Age related factors

Synonym
not applicable (the study is concerned with normal behavior)

Health condition

ouderschap, grootouderschap, (groot)ouder-(klein)kind interactie

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: Ministerie van OC&W,NWO

Intervention

Keyword: empathic and protective responses, fMRI, grandparenting, oxytocin

Outcome measures

Primary outcome

The main study parameter is activity in brain areas associated with (hyper)arousal and fearfulness (notably the amygdala), as well as social cognition, attachment, and empathy (e.g., superior temporal cortex, inferior frontal gyrus, fusiform gyrus, insula). We will examine the effects of oxytocin on activity in these areas in both mothers and grandmothers during a priming task designed to elicit protective responses and during a cyberball task designed to elicit empathic responses and behavior. In addition, we will examine whether effects of oxytocin are moderated by the oxytocin receptor genotype. Second, empathic behavior, i.e., compensatory ball throwing to an excluded participant, during the cyberball task, will be measured. We will examine effects of oxytocin on empathic behavior in both grandmothers and mothers, and we will examine the relation between oxytocin*s effects on empathic behavior and its affects on brain activity during the cyberball task. The third parameter is sensitive responsiveness toward the (grand)child. We will examine effects of oxytocin on both mothers* and grandmothers* sensitive responsiveness toward their (grand)child while working at a drawing together with the (grand)child, and we will examine whether effects of oxytocin are

moderated by the oxytocin receptor genotype.

Secondary outcome

Measurements of mothers* and grandmothers* interactive behavior, of children*s empathic behavior and rejection sensitivity, and of salivary oxytocin levels, as well as questionnaire measures of parenting style and empathy will be obtained.

Study description

Background summary

With the proposed study we aim to gain insight into the effects of oxytocin (OT) on both parents* and grandparents* sensitive, empathic, and protective responses to their (grand)children, and in the neural origins of these responses.
In humans, as well as other mammals, OT is profoundly involved in parturition and lactation, mother-infant bonding, the formation of romantic partner relationships, and parental behavior (Bakermans-Kranenburg & Van IJzendoorn, 2008; Campbell, 2008; Carter, 2003; Feldman et al., 2007; Galbally et al., 2011; Insel, 1992; Naber et al., 2010; Parker et al., 2005). Research into the role of OT in human parent-child relationships has remained largely limited to (positive) effects of OT on adequate, empathic and sensitive-responsive parental behaviors (see e.g., Bakermans-Kranenburg & Van IJzendoorn, 2008; Feldman et al., 2007). In addition, the focus of human OT research more generally has been on OT*s capacity to promote prosocial behaviors, such as generosity (e.g., Kosfeld et al., 2005) and charitable donating (e.g., Barraza et al. 2011; Van IJzendoorn et al., 2011). However, there is also some evidence that OT can, under some circumstances, promote aggressive behavior, aimed at protecting one*s offspring (Bosch et al., 2005) or in-group members (De Dreu et al., 2010) from external threat or danger. With the proposed study we intend to study not just empathic and sensitive, but also protective responses of (grand)parents toward their (grand)children.
Given the considerable amount of evidence detailing the involvement of OT in human as well as animal parenting, and considering that many grandparents maintain (close) relationships with their grandchildren (e.g., Mueller et al., 2002), it is surprising that studies focusing on the potential role of OT in grandparent-grandchild relationships are currently lacking. As OT has been shown to be involved in parenting of infants and (young) children, and in bonding throughout life, as well as in human social behavior toward non-kin

(e.g., Heinrichs et al., 2009; Van IJzendoorn & Bakermans-Kranenburg, 2011), it seems highly likely that OT plays a role in facilitating grandparenting and grandparent-grandchild relationships as well. However, various factors limit the generalizability of findings obtained from younger adults to ageing individuals (Huffmeijer et al., 2012c). Studies of older adults, grandparents in this case, comparing their responses to those of younger adults (parents) are thus urgently needed.

Results of a growing number of neuroimaging experiments, investigating the neural origins of OT*s behavioral effects, suggest that oxytocin modulates amygdala activity in response to salient social stimuli, including facial expressions (Domes et al., 2007) an infant cries (Riem et al., 2011), which is relevant with respect to effects of OT on attention, social stress and anxiety (e.g., Baumgartner et al., 2008; Kirsch et al., 2005). In addition, because the amygdala is involved in fear, anger, and aggression (e.g., Derntl et al., 2009), modulation of amygdala activity may be important for (potential) effects of OT on protective responses and protective aggression. Effects of OT on other brain regions involved in social cognition, theory of mind, and empathy (e.g., superior temporal cortex, inferior frontal gyrus, fusiform gyrus; Domes et al., 2010) have also been observed. In the current study, we may thus expect effects of OT on (grand)parents* sensitive, empathic, and protective responses toward their own (grand)children to be related to both modulation of amygdala activity and changes (increases) in activity in areas involved in social cognition and reward processing.

In most neuroimaging studies a direct link between effects of OT on neural activation and those on behavior is missing. In the proposed study we aim to remedy this by combining measures of neural and behavioral effects of OT in a single study, and by recording brain activation during a virtual interaction with the (grand)child. Brain activity will be recorded using fMRI during two tasks: a priming task, designed to elicit protective responses by showing the participants pictures of their own and an unfamiliar (grand)child preceded by a subliminally presented picture with neutral or mildly threatening content, and a cyberball game, a virtual ball tossing game that the participant plays with her own (grand)child and an unfamiliar (grand)mother-(grand)child pair (computerized players in reality) designed to elicit empathic responses and behavior when a child is excluded from the game by the remaining two participants.

Finally, all action of oxytocin is necessarily dependent on the oxytocin receptor (OXTR). In several studies associations have been found between social behavior, including mothers* sensitive responsiveness, and variations in the OXTR genotype that cause variations in OT transmission (e.g., Bakermans-Kranenburg & Van IJzendoorn, 2008). However, in OT administration studies the role of the OXTR has largely been ignored. In the proposed study we aim to investigate the interactive effects of administered oxytocin and the OXTR genotype on (grand)parents neural activity and behavior toward their (grand)children.

Study objective

With the proposed study we aim to gain insight into the effects of oxytocin (OT) on both parents* and grandparents* sensitive, empathic, and protective responses to their (grand)children, and in the neural origins of these responses.

The primary objectives of the proposed study are to investigate effects of oxytocin on mothers* and grandmothers* neural activity (measured using fMRI) related to empathic and protective responding to their (grand)children. We expect that oxytocin will decrease activity in brain areas associated with hyperarousal and fearfulness (notably the amygdala) thereby promoting adaptive (protective) responding, increase activity in brain regions associated with social cognition and empathy (e.g., superior temporal cortex, inferior frontal gyrus, insula, fusiform gyrus), and facilitate empathic responses. In addition we expect changes in brain activity to be related to increases in empathic behavior, with larger changes in brain activity associated with enhanced facilitation of empathic behavior. We will also examine the role of the oxytocin receptor gene in mediating effects of administered oxytocin. We expect effects of oxytocin to be more pronounced in individuals carrying those alleles associated with more efficient oxytocin transmission.
Second, we will examine effects of oxytocin on mothers* and grandmothers* sensitive responsiveness toward their (grand)children and on grandmother-mother interactions. Third, the potential relations between the (grand)child*s rejection sensitivity and both mother*s and grandmother*s empathic responding to the child, and the potential relations between the grandmother*s, mother*s, and child*s level of empathic behavior will be examined.

Study design

We will employ a randomized, double-blind, placebo-controlled design: 50 trios of grandmother, mother, and child will come to the LUMC for two identical experimental sessions, separated by 4 weeks. Both mother and grandmother will receive 24 IU of oxytocin via nasal spray during one session and a nasal spray containing placebo during the other. The order of administration (oxytocin during the first or during the second session) will be counterbalanced across grandmother-mother pairs, but grandmother and mother within each pair will receive the same treatment. Children do not receive nasal spray. The data collection is expected to take approximately 9 months. The study will be conducted at the fMRI facilities at the Leiden University Medical Center.

Intervention

Trios of grandmother, mother, and child will come to the LUMC for two experimental sessions, separated by four weeks. Three types of measurements will be conducted during each session: A) fMRI (mother and grandmother), B)

behavioral observations, and C) a computer task performed by the child. Both mother and grandmother will receive 24 IU of oxytocin via nasal spray during one session and a nasal spray containing placebo during the other. The order of administration (oxytocin during the first or during the second session) will be counterbalanced across grandmother-mother pairs, but grandmother and mother in each pair will receive the same treatment. Children do not receive nasal spray.

Study burden and risks

There are no risks associated with the assessments used in this study. Possible side effects of oxytocin are negligible. No adverse effects have been reported in participants/patients undergoing MRI at the currently available field strengths. The parenting context in which a child is raised is of profound importance for the child*s cognitive and emotional development. Studies focusing on the (neural) processes affecting the way grandparents, parents, and (grand)children interact are thus also important for our understanding of the processes leading to children*s successful or aberrant development. Although oxytocin has been shown to mediate positive parenting behaviors, there are no studies into the role of oxytocin in promoting defensive and protective behaviors in threatening contexts in parents. In addition, the neural mechanisms underlying parental sensitivity, empathy, and protective behaviors are currently poorly understood. Finally, the rapidly growing interest in oxytocin as a method of therapeutic intervention makes it vital to thoroughly examine the full scope of psychological functioning that intranasal oxytocin administration may affect.
Participants will be protected against any procedural risks via a thorough pre-screening process. Structural MRI scans will be inspected by a radiologist, and in case of visible abnormalities the participant, participant*s physician, and researcher will be notified. Participants* data will be handled strictly confidentially, except as required by law. Data will be stored in a confidential manner both through the use of a numbering system (a number will be assigned to the data from a given subject instead of the subject*s name) and through the security of the files and computer systems. There will be no personal identification of participants in scientific communications.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
-Mothers: female adults having a 6-8 year old child and a mother willing to participate.
-Grandmothers: female adults, whose daughter with a 6-8 year old child is willing to participate.
-Children: 6-8 year old boys and girls.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
-Mothers, grandmothers, and children:
o Any known neurological and (uncorrected) visual impairments
o Psychiatric disorders
-Mothers and grandmothers:
o smoking
o alcohol and drug abuse
o pregnancy
o breastfeeding
o use of medication, except oral contraceptives

o MRI contraindications

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-04-2014
Enrollment:	150
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:	20-02-2013
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	21-08-2013

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	22-08-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-03-2015
Application type:	Amendment
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	EUCTR2013-000454-22-NL
CCMO	NL43068.058.13

Study results

Date completed:	12-08-2016
Actual enrolment:	63