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# The Influence of Oxytocin Administration on Responses to Infant Faces and Potential Moderation by OXTR Genotype

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## Abstract

**Rationale—**Oxytocin is a neuropeptide that is associated with increases in social affiliative behaviors, particularly toward infants. However, no previous study has investigated healthy adults' responses to infant faces following oxytocin administration. In addition, given that preliminary evidence suggests that a single nucleotide polymorphism (SNP) of the oxytocin receptor (*OXTR*) gene, *rs53576*, may influence behaviors associated with parental sensitivity, we assessed whether such responses vary according to *OXTR rs53576* genotype.

**Objectives—**The present study assessed the effects of intranasally administered oxytocin and *OXTR* genotype on human adults' preferences for infant faces.

**Methods—**A double-blind, between-groups design was used, with 57 genotyped volunteers randomly assigned to receive intranasally administered oxytocin or placebo. Fifty minutes following the administration of oxytocin or placebo, participants viewed infants' and adults' faces showing neutral expressions and assessed how appealing they found each face.

**Results—**Infants' faces were more strongly preferred following oxytocin inhalation relative to placebo. When participants were separated according to genotype, this effect was only observed for participants homozygous for the *rs53576G* allele. Parallel effects were not seen for adults' faces.

**Conclusions—**The present results are consistent with the hypothesis that acute oxytocin administration increases sensitivity to reward-relevant features of infants and/or reduces sensitivity to their aversive properties. The results also are consistent with suggestions of more efficient oxytocinergic function in *rs53576G* homozygotes.

### Keywords

Oxytocin; OXTR; parental; faces; affiliation

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The authors have full control of all primary data and agree to allow the journal to review their data if requested

## INTRODUCTION

Oxytocin is a neurotransmitter that has wide-ranging effects on mammalian social behaviors, particularly behaviors relevant to care of offspring. Although oxytocin's effects on cognition and behavior vary widely across and within species, the oxytocin system generally promotes nurturing and affiliative behaviors toward infants (Carter 1998; Insel 1992). Only relatively recently have the neurocognitive effects of intranasally administered oxytocin been assessed in humans (Guastella and Kemp 2011). The present study assesses how intranasal oxytocin influences healthy adults' responses to infants' faces. In addition, given that *OXTR* genotype has been linked to sensitive parenting (Bakermans-Kranenburg and van Ijzendoorn 2008) and that the interaction of oxytocin manipulations and *OXTR* genotype has not yet been investigated with regard to any dependent variable, we assessed how response to infant faces following oxytocin administration is moderated by OXTR genotype.

Oxytocin is produced in the hypothalamus and released into the periphery by the pituitary. In mothers, it regulates processes relate to parturition and nursing, including uterine contractions and milk letdown in females (Kendrick 1997). Centrally, oxytocin's effects reflect its role in bearing and caring for offspring by both sexes (Carter 1998; Leng et al. 2008). These functions include promoting affiliative behaviors, particularly species-specific parental behaviors, including nursing, grooming, retrieval of infants, and the inhibition of aggression toward infants (Francis et al. 2000; Kendrick et al. 1987; Pedersen et al. 1992). Care for infants may be disrupted by interventions that impair oxytocin release (Leng et al. 2008). Oxytocin also affects *alloparental* responses, or responses towards infants who are not the adult's own young (Madden and Clutton-Brock 2011). Higher densities of oxytocin receptors in brain regions such as the nucleus accumbens correlate with spontaneous alloparenting (Ross et al. 2009).

In keeping with the effects of oxytocin observed in other mammalian species, correlations between human parenting behaviors and levels of endogenous oxytocin have been observed (Feldman et al. 2007; Strathearn et al. 2009), although the effects of oxytocin administration on behaviors relevant to human parenting have been minimally explored (Fewtrell et al. 2006; Naber et al. 2010; Riem et al. 2011). The administration of oxytocin to people has been demonstrated to increase a variety of other related affiliative responses, such as empathic accuracy (Bartz et al. 2010), trust (Baumgartner et al. 2008; Kosfeld et al. 2005) generosity (Zak et al. 2007), and sensitivity to positive social cues (Marsh et al. 2010). This suggests that oxytocin generally facilitates sensitivity to social-reward-driven stimuli and decreases the experience of social threat (Guastella and Kemp 2011). These properties of oxytocin may help to explain why oxytocin facilitates parental responses: oxytocin may sensitize adults to rewarding properties of infantile stimuli and/or decrease the extent to which novelty or other properties of infant cues are perceived as threatening or aversive (Carter 1998; Fleming et al. 1980; Pedersen et al. 1992; Riem et al. 2011).

The specific effects of oxytocin vary both across and within species due to variations in the regional expression of oxytocin receptors (Francis et al. 2002; Ross et al. 2009; Young et al. 2001). Some variation in affiliative behaviors within species may stem from genetic variants associated with oxytocinergic function, such as the *OXTR* gene (Ebstein et al. 2010; Insel, 2010; Kogan et al. 2011). A particular single nucleotide polymorphism (SNP) of this gene, *rs53576* (*G/A*), has been linked to variation in affiliative behaviors (Kogan et al. 2011; Tost et al. 2010). Recent research suggests that *rs53576A* is associated with reductions in prosocial and affiliative behaviors, including empathy (Rodrigues et al. 2009), sensitivity to social communication (Tops et al. 2011), and sensitive parenting (Bakermans-Kranenburg and van Ijzendoorn 2008). These differences may result from the influence of this SNP on

the structure and function of the amygdala and hypothalamus, regions associated with sensitivity to social reward and threat and with parental care behaviors (Insel 1992; Swain et al. 2008; Tost et al. 2010). Although the specific function of *rs53576* is not known (Tost et al. 2010), evidence that *rs53576A* is associated with reductions in behaviors generally promoted by oxytocin suggest this allele may be associated with less efficient oxytocinergic function (Bakermans-Kranenburg and van Ijzendoorn 2008). However, no previous study has assessed the interaction of *OXTR* genotype and oxytocin administration in influencing human behavior.

In this study, we assessed whether intranasal oxytocin affected preference for infants' faces, and whether responses were moderated by in *rs53576* genotype. We predicted that oxytocin would increase preference for infants' faces relative to adults' faces. We also predicted that this effect would be stronger for *G* homozygotes than *A* carriers.

## MATERIALS AND METHODS

### Participants

Fifty-seven healthy volunteers (39 males, 17 females, M age = 25.9 years, range = 18–41 years) participated in this study. Participants were recruited via fliers distributed throughout the Washington, D.C. metropolitan area. All participants gave informed written consent and were paid for their participation. A physician evaluated physical health by conducting a medical history and physical exam (which included blood, urine, and EKG screening), and a psychologist evaluated participants' psychological health by administering the Standard Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV (SCID). Intelligence was assessed by a researcher using the Wechsler Abbreviated Scale of Intelligence (Wechsler 1999). Participants were excluded in whom screening indicated current use of hormonal contraceptives or psychotropic medications, past major affective disorder, anxiety disorder, psychotic disorder, substance dependence, anorexia nervosa, bulimia, or IQ less than 80. Participants who were pregnant or nursing were also excluded. This research was approved by the Institutional Review Board at the National Institute of Mental Health in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, and all participants' written informed consent was obtained prior to the study's commencement.

A between-groups, double-blind, placebo-controlled design was used to assign participants to receive oxytocin or placebo. Prior to testing, participants were randomly assigned to self-administer an intranasal dose of 24 IU oxytocin or saline solution placebo. Post-hoc tests confirmed that participants' ages and intelligence were not significantly different across conditions, nor were the distributions of participants' racial and ethnic identities (Table 1). All females were tested during the follicular phase of their menstrual cycle (approximately days 6 though 12) (Razzoli et al. 2003). Ovulation testing was conducted beginning the day of testing to confirm that female participants were tested prior to ovulation.

### Oxytocin preparation

The oxytocin spray was formulated by the National Institutes of Health's Clinical Center Pharmacy from the powder version of the drug (Spectrum Pharmaceuticals, Irvine, CA). The solution was prepared by combining 35.2 mg of oxytocin (568 units) with 300 mL of a 0.9% sodium chloride solution and adjusting the pH with 10× diluted acetic acid (final pH = 4.01). The filtered and sterile solution was then distributed in individual vials (1.5 mL each). These vials were frozen, then thawed and refrigerated (4° C) on the day of the study. A clinician prepared the nasal spray by transferring the oxytocin or placebo from the vial into the

nebulizer. The nebulizer was primed and provided to the participants, who self-administered the nasal spray while being monitored by a clinician and an experimenter.

## Genotype analysis

Genomic DNA was isolated from saliva samples using Oragene•DNA kits (DNA Genotek, Ottawa, Ontario, Canada). The *OXTR* SNP rs53576 was obtained as a Taqman Assay-on-Demand (Applied Biosystems, Foster City). Genotyping was performed according to the manufacturers' protocol and genotype determined at end-point using an ABI 7900HT Sequence Detection System. Genotyping accuracy was determined empirically by duplicate genotyping of 25% of the samples selected randomly and no errors were detected. Based on extensive experience with Taqman genotyping of duplicate samples for different loci, the error rate is < 0.005. Of our 57 participants, 54% of genotyped participants were *rs53576A* carriers ($N = 8$ *AA*, 14%, 23 *AG*, 40%) and 46% were *rs53576G* homozygotes ($N = 26$), frequencies that do not deviate from Hardy-Weinberg equilibrium, $\chi^2 = 0.61$, $p = 0.43$. Allele frequencies across racial and ethnic groups in our sample were consistent with previously published estimates (Table 2).

## Procedure

Testing was conducted in private or semi-private rooms in the Clinical Center of the National Institutes of Health. Before testing commenced, participants completed baseline measures of adverse symptoms including abdominal, neurological, dermatological, and cardiac symptoms. They also completed visual analogue scales measuring alertness, anxiety, irritability, boredom, calmness, excitement, happiness, tension, tiredness, sadness, and friendliness.

Subsequently, participants received oxytocin or placebo in a total of four puffs delivered to alternating nostrils at 30–45 second intervals. Fifty minutes following administration of drug or placebo participants completed the face rating task (which followed an emotion recognition task); following the task participants completed additional behavioral tasks that will not be described here. A clinician assessed heart rate and blood pressure before and after behavioral testing and immediately prior to discharge. Prior to discharge participants also completed follow-up measures of adverse symptoms and mood. Prior analyses found no relationship between study condition and mood or other self-assessed symptoms (Marsh et al. 2010).

## Task

We used a novel task generated for the present protocol that required participants to judge the appeal of 40 infant (less than 1 year old) and 40 adult faces (Fig. 1). These faces were drawn from publically available databases and were selected to convey neutral expressions and direct gaze. Half the faces in each group were male and half female. All faces were converted to grayscale and cropped to exclude all features other than the face. Infants' and adults' faces were matched across age group for race as well as for luminosity ($t(78) = 1.59$, $p = 0.12$) and contrast ($t(78) = 1.12$, $p = 0.27$). Faces were presented using the stimulus presentation software E-prime. Faces were presented in random order, each appearing for 3.0 s followed by a 0.5 s fixation cross. During each 3.5 s presentation interval, participants rated each face on a 7-point scale (1 = not at all appealing, 7 = extremely appealing). Forty 3.5 s fixation trials also appeared at random intervals during the task.

## RESULTS AND DISCUSSION

### Face preference ratings

In order to assess the effects of genotype and drug on preference for infants' and adults' faces, we conducted a 2 (drug: oxytocin, placebo) × 2 (genotype: *A* carriers, *G* homozygotes) × 2 (age: adult face, infant faces) × 2 (sex: male faces, female faces) ANOVA using the faces themselves as the units of variance (Marsh et al. 2009) to control for variation in appearance among faces across categories. *AA* and *AG* genotypes were combined (Kogan et al. 2011; Tops et al. 2011) to maintain statistical power.

Our first hypothesis was that oxytocin would increase the perceived appeal of infants' faces more than adults' faces. A significant drug × age effect confirmed an interaction between these variables ($F(1,76) = 32.013$, $p < 0.001$, $\eta^2 = 0.296$). Follow-up t-tests confirmed that preference for infants' faces increased following oxytocin induction ($t(39)= 2.20$, $p < 0.05$) whereas preference for adults' faces dropped following oxytocin induction ($t(39) = 5.053$, $p<0.001$) (Fig 2a).

Our second hypothesis was that oxytocin induction would interact with genotype to influence preference for infants' faces. The results of a drug × genotype × age interaction confirmed this hypothesis ($F(1,76) = 33.173$, $p < 0.001$, $\eta^2=0.304$). This effect was decomposed by conducting separate analyses of variance for each age group. The results indicated a drug × genotype interaction for both infants ($F(1,39) = 19.308$, $p < 0.001$, $\eta^2 = 0.331$) and adults ($F(1,39) = 11.377$, $p < 0.005$, $\eta^2 = 0.226$). Follow-up t tests indicated that preference for infants' faces increased in *G* homozygotes following oxytocin induction relative to placebo ($t(39) = 4.162$, $p < 0.001$). By contrast, preference for infants' faces declined in *A* carriers following oxytocin induction relative to placebo ($t(39) = 2.310$, $p < 0.05$). For adults' faces, *G* homozygotes showed a reduced preference following oxytocin induction ($t(39) = 6.481$, $p < 0.001$). By contrast, *A* carriers showed no significant change in preference for adults' faces following oxytocin induction ($t(39) = 1.888$, ns) (Fig. 2b). For mean scores across conditions, see Table 3.

The only significant interaction between the sex of the face and drug or genotype was a drug × genotype × sex interaction ($F(1,76)=7.564$, $p<0.005$, $\eta^2=0.091$). Decomposition of this result indicated that female faces were always preferred to male faces, but that the strength of this preference varied across conditions. Because this result collapsed across both infant and adult faces, this effect was not easily interpretable and was not further analyzed. (These response patterns remained consistent when the results for only male participants were analyzed.)

### Response times

In order to assess the effects of genotype and drug on response times, we conducted an analysis of variance that paralleled our analysis of response options: a 2 (drug: oxytocin, placebo) × 2 (genotype: *A* carriers, *G* homozygotes) × 2 (age: adult face, infant faces) × 2 (sex: male faces, female faces) ANOVA. The only significant interaction effects observed were a drug × genotype interaction, and a drug × genotype × age interaction. T tests revealed that *A* carriers responded more quickly to all faces following oxytocin induction relative to placebo ($t(79) = 5.425$, $p < 0.001$) whereas the opposite was true for *G* homozygotes, who responded to faces more quickly following placebo ($t(79) = 3.184$, $p < 0.005$). Decomposition of the drug × genotype × age interaction indicated that the drug × genotype interaction described above held up for infants' faces ($F(1,39) = 54.742$, $p < 0.001$, $\eta^2 = 0.584$) but not adults' faces ($F(1,39) = 2.570$, ns. A main effect of age on response times was also observed ($F(1,39) = 27.986$, $p < 0.001$, $\eta^2 = 0.269$) such that infants' faces were responded to more quickly than adults' faces across all conditions (Table 3).

## Discussion

This study found that healthy adults administered oxytocin find infants' faces more appealing than those administered a placebo, whereas adults' faces are viewed as less appealing following oxytocin. This result provides evidence in favor of the hypothesis that oxytocin increases adults' sensitivity to the rewarding properties (and/or reduces sensitivity to aversive properties) of infants (Carter 1998; Guastella and Kemp 2011; Riem et al. 2011). Oxytocin is a neurotransmitter produced only in mammals, and it has long been theorized that it emerged to facilitate specific features of the care of mammalian young (Carter 1998; Insel 1992). Studies in both non-human animals (Kendrick et al. 1987; Pedersen et al. 1982) and humans (Naber et al. 2010) have established that oxytocin sensitizes adults to infant cues and tends to promote approach-related behaviors toward infants. These findings suggest that increased oxytocin may cause adults to perceive infant cues as subjectively more appealing, a suggestion consistent with the present data.

It should be noted that the effect of oxytocin on responses to social stimuli is selective—it does not universally promote social approach behaviors. In non-human animals, oxytocin actually promotes aggression toward intruders (Pedersen, 2004) and in humans it increases negative emotions, like envy and gloating, toward competitors (Shamay-Tsoory et al. 2009) and aggressive behavior toward out-group members (De Dreu, 2012). These facts may help to explain an effect that was not predicted in the present study, which was that oxytocin administration reduced participants' preference for adult faces. In non-human animals, the increased aggressiveness toward unknown adult conspecifics associated with oxytocin is interpreted as increased sensitivity to threat toward objects of attachment (Pedersen, 2004). It is possible that, in the context of our task, adult faces showing neutral expressions were perceived as potential threats by participants who received oxytocin. Another, perhaps more parsimonious, explanation for this finding in the context of our paradigm is that, if oxytocin increases preference for infant faces, faces will be preferred the more infantile they appear. This would leave adult faces relatively less preferred. Whether this is true might be investigated in a follow-up paradigm in which responses to adult faces with paedomorphic (or "babyish") features (Zebrowitz et al. 2009) are assessed following oxytocin inhalation.

We also observed that participants' response times to the stimuli varied in a pattern that mirrored their responses. Response times were generally slower under conditions when faces were rated to be more appealing, for example, following oxytocin induction relative to placebo when responding to infants' faces. This effect has several possible interpretations. The most parsimonious is that participants spent more time looking at faces that they found more appealing. Another possibility is that the emotional salience of faces that participants' found particularly *unappealing* reduced their response times to these faces, as affectively negative stimuli can promote faster response times (Heekeren et al. 2005). Finally, delayed response times may in some circumstances result from the interference generated by response conflict. However, because the present task did not feature explicitly conflicting task demands, this seems an unlikely interpretation of our findings. In general, we interpret response time results with some caution, as no instructions were given regarding the importance of responding quickly.

Some limitations of this study must be considered. First, we did not obtain a sufficient sample of female participants to allow us to compare responses across male and female participants. Due to both safety considerations and the possible interactions between oxytocin and estrogen, female participants were subject to more extensive screening and exclusion criteria than males (e.g., exclusion of females who were pregnant, nursing, or using hormonal contraceptives), which resulted in the enrollment of fewer females than males. However, despite the fact that hormone/peptide interactions have been predicted based on previous animal work (Champagne et al. 2001), we did not predict sex differences

in behavioral responses and found consistent patterns of effects when we analyzed results from only male participants. Recent research in humans has demonstrated that the effects of intranasal oxytocin (Marsh et al. 2010) and *OXTR* genotype (Tost et al. 2010) may sometimes be similar across males and females. That said, it will be important for future studies to consider potential sex differences in the effects of intranasal oxytocin and *OXTR* variants on responses toward infants, given the inherently sexually dimorphic nature of some forms of parental care (e.g., lactation) and the potential for peptide/hormone interactions. It will also be important to explore whether additional interactions occur depending on whether participants are parents, a variable that could not be adequately explored in this sample due to the young average age and the fact that our screening did not ascertain whether participants were parents or had other significant childcare experience.

In addition, the present study used a novel task, which assessed a dependent variable of unknown ecological validity. How variations in preference for infants' versus adults' faces would extend to variations in responses to actual infants (particularly one's own infant) cannot be determined based on our data. However, these data do provide much more specific information than do behavioral observations in a naturalistic setting. That is, variations in parenting behavior at home might stem from a wide variety of environmental and neurocognitive changes. Future studies might assess whether preference for infants' faces is a variable that moderates or mediates adults' behavior towards actual infants.

The observed patterns were qualified by *OXTR* genotype. When participants carrying the *rs53576G* and *A* alleles were examined separately, we found that our main effects were driven primarily by *G* homozygotes. Specifically, preference for infant faces increased following oxytocin only in *G* homozygotes, whereas preference for infant faces decreased in *A* carriers following oxytocin. These data are consistent with the hypothesis that a) the *G* allele promotes efficient functioning of the oxytocin system and enhances the effects of oxytocin administration (Tost et al. 2010), and b) When oxytocin levels are increased, the *OXTR rs53576G* allele promotes sensitive responding to children (Bakermans-Kranenburg and van Ijzendoorn 2008). It is significant that genetic differences were particularly marked in this study following oxytocin administration. In general, events associated with imminent need to provide a child with care, including parturition and lactation (Carter and Altemus 1997; Carter and Altemus 1997; Forsling 1986), or even exposure to infant cues (Grosvenor et al. 1990), increase endogenous oxytocin levels. It is thought that increased oxytocin then precipitates the provision of care. Thus, it is particularly important when considering the influence of *OXTR* genotype on parenting to consider its effects in the presence of increased levels of oxytocin rather than at baseline.

The present results may help to explain why the effects of intranasal oxytocin administration have been observed to vary across groups of participants in recent studies. Oxytocin's effects on a variety of affiliative behaviors have been observed to vary in accordance with a number of individual difference variables, including autistic traits in healthy adults (Bartz et al. 2010), generalized anxiety symptoms (Labuschagne et al. 2010), attachment security (Rockliffe et al. 2011), and diagnosis of borderline personality disorder (Bartz et al. 2011). So, for example, individuals diagnosed with borderline personality disorder show *decreased* trust and cooperative behavior in economic games in laboratory settings following oxytocin administration, particularly among anxiously attached and rejection sensitive participants. Given some indications that *OXTR* variants have been previously associated with individual variation in autistic traits (Wu et al. 2005) but see (Tansey et al. 2010), amygdala functioning (Tost et al. 2010), and attachment security (Chen et al. 2011; Costa et al. 2009), this presents the possibility that some divergences in the effects of intranasal oxytocin may result from genetic variants like OXTR, and supports the need for more nuanced assessments of oxytocin's influence on human behavior.

### Conclusions

In conclusion, the present results are consistent with the hypothesis that acute oxytocin induction increases sensitivity to reward-relevant features of infants (and/or reduces sensitivity to their aversive properties). Future research should explore neural correlates that underlie the effects of the oxytocin system in responses towards infants. Our results are also consistent with suggestions of more efficient oxytocinergic function in *rs53576 G* homozygotes. *OXTR* genotype has been demonstrated to influence both the structure and function of the amygdala and hypothalamus (Tost et al. 2010), which are structures important to the provision of parental care (Francis et al. 2000; Insel 1992; Swain et al. 2008). Given speculation that the neural circuitry that subserves parental care constitutes the basis of empathic and prosocial behavior in humans more generally (de Waal 2008; Eibl-Eibesfeldt 1996; Toth et al. 2007), research in this vein could be important for understanding the basis of a variety of human prosocial behaviors.

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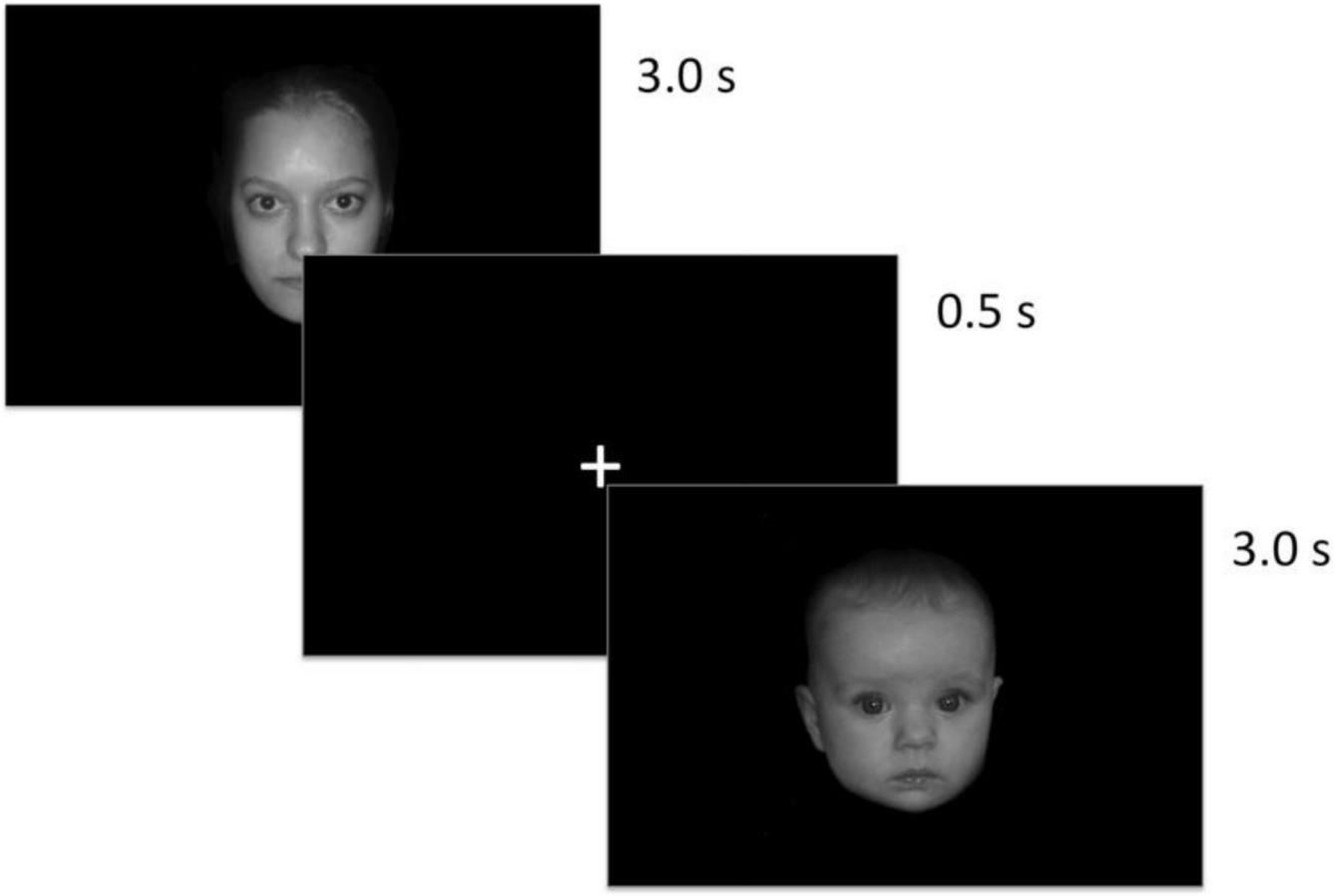


**Fig. 1.**
Sample infant and adult stimuli from the face rating task

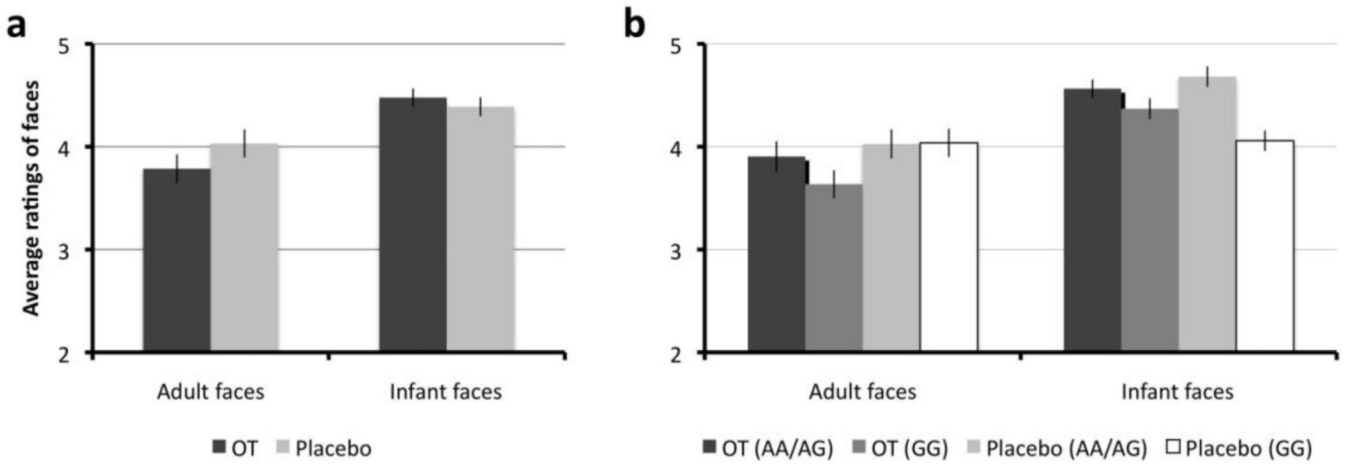


**Fig. 2.**
Responses to infant and adult faces as a function of study condition (a) and study condition plus genotype (b). Bars represent standard errors.

## Table 1

Characteristics of study participants

| Participant characteristics | Oxytocin | Placebo | P |
|---|---|---|---|
| *N* | 31 | 26 | – |
| *Males / Females* | 21 / 10 | 18 / 7 | > 0.10 |
| *A carriers / GG* | 17 / 14 | 14 / 12 | > 0.10 |
| *Age (SD)* | 25.6 (4.9) | 26.6 (5.0) | > 0.10 |
| *IQ (SD)*[a] | 116.2 (11.0) | 116.5 (11.9) | > 0.10 |
| *Race / Ethnicity (N)* | | | |
| *Non-Hispanic* | 27 | 25 | > 0.10 |
| Asian | 7 | 4 | > 0.10 |
| Black | 2 | 3 | > 0.10 |
| Caucasian | 15 | 16 | > 0.10 |
| Native American | 3 | 1 | > 0.10 |
| Pacific Islander | 0 | 1 | > 0.10 |
| *Hispanic* | 4 | 1 | > 0.10 |

[a]IQ data were not available for 4 participants in the placebo group and 5 participants in the oxytocin group

## Table 2

Characteristics of participant demographics by genotype

| Race / Ethnicity (N) | AA | AG | GG |
|---|---|---|---|
| *Non-Hispanic* | | | |
| Asian | 4 | 4 | 3 |
| Black | 0 | 3 | 2 |
| Caucasian | 2 | 13 | 16 |
| Native American | 1 | 1 | 2 |
| Pacific Islander | 0 | 1 | 0 |
| *Hispanic* | 0 | 0 | 3 |

## Table 3

Mean responses and RTs across genotype and study condition

| Condition | Genotype | *Infant faces* | *Adult faces* |
|---|---|---|---|
| | | *Means (SD)* | |
| Oxytocin | AA / AG | 4.564 (0.56) | 3.905 (0.93) |
| | GG | 4.369 (0.64) | 3.635 (0.86) |
| Placebo | AA / AG | 4.681 (0.63) | 4.027 (0.90) |
| | GG | 4.059 (0.63) | 4.037 (0.86) |
| | | *RT (SD)* | |
| Oxytocin | AA / AG | 1624 (95) | 1784 (125) |
| | GG | 1743 (121) | 1790 (156) |
| Placebo | AA / AG | 1795 (152) | 1824 (119) |
| | GG | 1638 (120) | 1759 (170) |