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Sexual dimorphism in oxytocin responses to health perception and disgust, with implications for theories on pathogen detection

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ABSTRACT

In response to a recent hypothesis that the neuropeptide oxytocin might be involved in human pathogen avoidance mechanisms, we report the results of a study in which we investigate the effect of intranasal oxytocin on two behaviors serving as proxies for pathogen detection. Participants received either oxytocin or a placebo and were asked to evaluate (1) the health of Caucasian male computer-generated pictures that varied in facial redness (an indicator of hemoglobin perfusion) and (2) a series of pictures depicting disgusting scenarios. Men, but not women, evaluated all faces, regardless of color, as less healthy when given oxytocin compared to a placebo. Women, on the other hand, expressed decreased disgust when given oxytocin compared to a placebo. These results suggest that intranasal oxytocin administration does not facilitate pathogen detection based on visual cues, but instead reveal clear sex differences in the perception of health and sickness cues.

Introduction

Oxytocin (OT), the hormone involved in mammalian parturition and lactation, has recently attracted much attention with regard to its role in regulating social behavior. As a neurotransmitter in the central nervous system, OT has been shown to mediate a host of socially relevant behaviors, including social perception, social memory, trust, generosity, and cooperation (see reviews in Bos et al., 2012; Campbell, 2008; Meyer-Lindenberg et al., 2011). However, the effect of OT is not straightforward, and may include prosocial as well as anti-social effects depending on the context (Bartz et al., 2011; Declerck et al., 2010; Guastella and McLeod, 2012). Such findings have prompted researchers to identify the conditions that determine when and how OT moderates behavior and thereby impacts the outcome of social interactions.

Because social interactions provide key opportunities for parasitic transmission, humans have evolved a rich repertoire of behavioral responses by which they minimize pathogen exposure (Oaten et al., 2009). In a recent review article Kavaliers and Choleris (2011) put forth the hypothesis that OT may play a role in safeguarding people against pathogen infection by improving the ability to recognize and avoid contaminated others. Their arguments are mostly based on evidence from animal research. In rodents, OT has been specifically associated with detecting and responding to disease-infected conspecifics (Kavaliers et al., 2004). For example, in mate-choice experiments, female mice are able to discriminate between the odors of healthy and infected males. But OT-gene knockout mice, or mice treated with an OT antagonist, lack this ability and show reduced aversion towards infected males. OT-gene knockout mice are furthermore unable to discriminate between the urinary odors of male mice that have been treated with a chemical substance containing elements of bacterial cell-walls, a procedure that is often used to simulate bacterial infections. However, while rodents rely primarily on olfaction, social cognition in humans is dominated by interpreting visual cues (Broad et al., 2006), making it difficult to extrapolate the findings of animal research regarding OT to humans. While rodents have evolved olfactory mechanisms to avoid stimuli that smell like disease, humans show behaviorally more elaborate responses to threatening social stimuli, including in-group favoritism, out-group exclusion, and specific emotions such as trust and schadenfreude, all of which have previously been associated with OT (Kavaliers and Choleris, 2011). For example, exogenous OT tends to promote in-group cooperation and ethnocentrism (reviewed in De Dreu, 2012), increase the perception of fear expression (Fisher-Shofty et al., 2010), decrease trust when people are perceived to be untrustworthy (Mikolajczak et al., 2010) and decrease cooperation with anonymous others (Declerck et al., 2010). Such behaviors are useful to prevent contact with out-groups which may not only be hostile but are also potential carriers of strange parasites and bacteria.

So far, we are not aware of studies that have empirically addressed if OT directly or indirectly facilitates the detection of pathogens in humans. This report is a first step towards filling this gap by presenting the results of an experiment whereby we test if intranasal OT affects sensory perceptions that may have to do with detecting pathogens. First, we tested if OT enhances the perception of health cues by discriminating between pictures of faces that vary in redness. There is evidence

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that facial redness is perceived to reflect physiological health of Caucasians, while pallor, indicating poor blood perfusion, has been associated with infections like malaria (Stephen et al., 2009a). Hence if OT plays a role in pathogen detection, we expect that compared to a placebo, individuals given OT would assign lower health scores to pale individuals. Second, we tested if OT enhances feelings of disgust in response to pictures of repulsive situations that reveal a high pathogen load. In the field of evolutionary psychology, there is abundant literature to substantiate that disgust is an adaptive response to avoid infestation by pathogens (Oaten et al., 2009). If OT facilitates avoiding infection, then we expect that OT will also increase feelings of disgust when exposed to pictures representing foul, bacteria-loaded conditions. Finally, because OT interacts with estrogen in females, making sex differences in OT regulation very probable (Bos et al., 2012; Choleris et al., 2013), we also investigate if the effects of OT on health perception and feelings of disgust are moderated by gender.

Methods

A student population ($N = 106$, 61 females, mean age $= 22 \pm 2.5$) registered by e-mail to participate in exchange for a €10 remuneration fee. The study was described as an experiment that tested the effect of a hormone on evaluative judgments. Exclusion criteria included the use of alcohol and nicotine for 12 h, and any other medication other than anti-conception for 24 h prior to the study, and any diagnosed neurological or psychological disorder, nasal obstruction or colorblindness. To make sure that none of the female participants were pregnant, they took a pregnancy test between 1 and 48 h prior to the experiment. Participants consented to the procedures which were in accordance with the Declaration of Helsinki and approved by the Ethical Commission of the University. Debriefing occurred by sending each participant an e-mail referring to a website where the intent and results of the study were explained. This experiment was part of a larger study in which we investigated the effect of exogenous OT on two dimensions: trustworthiness and health evaluations.[1] Here we report only on the latter.

The experiment was conducted in computer rooms during 17 sessions with no less than 4 and no more than 10 participants in each session. They were instructed to self-administer an intranasal dose of 24 IU OT (Syntocinon, Novartis; three puffs per nostril) or placebo (with only the carrier) following a double-blind random design. Participants then waited 35 min before starting with the experiment. They were instructed to remain quiet and not leave the room. A room supervisor stayed with them the entire time.

The task consisted of evaluating two series of pictures. For the first series (testing the first objective) five artificially generated, male[2] compound faces were selected out of a large database created by Oosterhof and Todorov (2008). The advantage of using artificial faces is that they are perfectly symmetrical and emotionally neutral. In a preliminary task (conducted with the same population) we asked the participants to rate the health of these five neutral faces on a scale from 0 to 9. From this we could deduce that the health of these "neutral standards" were rated higher by males (mean $= 5.8$, S.E. $= .15$) compared to females (mean $= 5.3$, S.E. $= .15$). OT, however, had no effect on the evaluation of neutral faces, neither for men, nor for women. Furthermore, there is no significant interactive effect between sex and OT on the evaluation of neutral faces (see Supplementary materials 1A–C).

For the actual task, each face was manipulated by the authors to vary along a gradient of 7 shades of redness, going from an extremely pale face (given the value of -3) to an exaggerated red face (given the value of $+3$). The neutral variant was given value of 0 and the original pictures were manipulated to ensure equal mean CIELab[3] values for each face before manipulating redness. A total of 35 pictures (5 facial identities in 7 color gradations) were shown one by one on a computer screen, always in combination with a neutral face (the "standard") of the same identity. The neutral face was always shown on the left side of the screen, and the face that varied in redness on the right side of the screen. The participants were asked to give a score ranging from -4 (right face less healthy than the left face) to $+4$ (right face more healthy than the left face),[4] with 0 indicating no difference between the left and the right face. Scoring was self-paced and occurred by left-mouse clicking on a scale displayed at the bottom of the screen.

The second series (testing the second objective) consisted of five pictures depicting disgusting scenes. These included: (1) a diphtheria skin lesion on the leg, (2) a filthy bathroom, (3) a pot of worm-infested soup, (4) a festering arm-wound and (5) rotten teeth. These pictures, obtained from the internet, were chosen because they contain cues that are indicative of an adaptive, pathogen-related disgust response (Tybur et al., 2013). Participants were asked to indicate on a scale of 0 to 9 how disgusted they felt when looking at each picture.

The dependent variables are the health scores (-4 to $+4$) assigned to the stimuli in series 1, and the disgust scores (0–9) in series 2. The independent variables of interest are OT (coded 1, versus placebo, coded 0) and sex (males coded 1).

Results

To test if OT affects health perception on the basis of facial redness (perceived hemoglobin perfusion), we plotted the health score of each face versus the redness gradient (see Fig. 1), separately for men and women. The linear relation between perceived health and redness is consistent with the results of Stephen et al. (2009a) and Stephen et al. (2009b) indicating that people optimize health appearance by increasing facial redness above basal levels. Visual inspection reveals that (1) for both men and women the relation between perceived health and redness is similar across the 5 facial identities, and that (2) for men, but not for women, OT appears to lower health scores for nearly all shades of red. To test the latter finding statistically we averaged the health scores corresponding to each redness grade over the five facial identities and conducted regression analyses on panel data (7 averaged scores per participant).[5] To control for potential differences in the a-priori evaluations of the five neutral faces, the average neutral score obtained from each individual in the preliminary task is added as a factor in the regression models. To control for unobserved heterogeneity between subjects, we use a random effect model that accounts for the clustering of observations per individual. All reported p-values are two-tailed. The analyses of the female participants also include a dummy variable "contraceptive", indicating whether or not the participant was on hormonal contraceptives. From questionnaire data collected on the day of the experiment we knew that 66% of the females were taking hormonal contraceptives, and that one of the naturally cycling women reported an unusually long cycle of 221 days. This person was

[1] Trustworthiness evaluations were assessed with different experimental stimuli than the ones presented here and are highly unlikely to have affected the current results. We do not report these data here because they were collected with the purpose of testing a different hypothesis that was unrelated to the current experiment. The order of presenting the two sets of stimuli was determined randomly. For more information regarding these additional data, please contact the corresponding author.

[2] Using only male faces simplifies the interpretation of the results by eliminating the possibility that perceptions of health depend on the sex of the target. A drawback, however, is that we introduce a bias (same sex evaluations versus opposite sex evaluations for males and females respectively), making an absolute comparison between the evaluations of men and women problematic. This is an additional reason why we analyze the results for men and women separately.

[3] The CIELab color system (L = light–dark; a = red-green, b = yellow-blue) is commonly used in research on visual perception and designed to be perceptually uniform (see Stephen et al., 2009b).

[4] Note that the range of possible answers (-4 to $+4$) was greater than the range of possible color values assigned to each picture (-3 to $+3$) in order to broaden the response variance.

[5] We first tested the effect of OT on perceived health for each face separately and confirmed that the effect of OT did not differ between faces.