

Acting on Anger: Social Anxiety Modulates Approach-Avoidance Tendencies After Oxytocin Administration

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Abstract

Oxytocin attenuates responses to stress and threat (e.g., by fostering social approach in animals), but direct investigations of whether the hormone also facilitates approach-related social behaviors in humans are lacking. To assess approach-avoidance tendencies, we had participants respond to images of happy and angry faces with direct or averted gaze by either pulling a joystick toward themselves (approach) or pushing it away from themselves (avoidance). When given a placebo, participants' action tendencies were typical, with happy faces eliciting approach responses and angry faces eliciting avoidance responses. However, 24 IU of oxytocin moderated these tendencies, with the inclination to approach angry faces with direct gaze being negatively related to social anxiety. The results demonstrate that oxytocin facilitates approach in humans in response to social threat, which verifies its anxiolytic potential. Moreover, they underscore the moderating role of dispositional factors reported in endocrine research and their therapeutic implications.

Keywords

avoidance, emotions, facial expressions, neuroendocrinology, social interaction

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The growing interest in the therapeutic potential of the neuropeptide oxytocin stems from its role in attenuating anxiety (Heinrichs, Baumgartner, Kirschbaum, & Ehler, 2003) and promoting complex prosocial behaviors, such as trust and empathy (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005). However, translation of these findings into therapeutic applications for disorders associated with social impairments, such as social anxiety disorders, warrants further investigation, especially because some recent studies report antisocial rather than prosocial effects (Bartz, Zaki, Bolger, & Ochsner, 2011). Because social deficits often affect social motivational behavior, and many clinical interventions aim to modify behavior, knowledge of the influence of oxytocin on social approach-avoidance tendencies is highly important. Moreover, because in both preclinical and clinical research, oxytocin effects tend to be moderated by dispositional and situational factors (Alvares, Chen, Balleine, Hickie, & Guastella, 2012; Bartz et al., 2011; Bartz et al., 2010; Guastella,

Howard, Dadds, Mitchell, & Carson, 2009), insight into the underlying mechanisms is essential to determine for whom and in which contexts meaningful therapeutic benefits from oxytocin can be anticipated. Accordingly, in the present study, we investigated whether oxytocin influences basic social approach-avoidance tendencies and whether its effects are modulated by individual differences in social anxiety.

Approach and avoidance are the fundamental behavioral responses associated, respectively, with appetitive and aversive motivation (Chen & Bargh, 1999; Roelofs, Minelli, Mars, van Peer, & Toni, 2009); pleasant or positive cues typically trigger approach behavior and threatening or negative stimuli typically trigger avoidant behavior

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(Chen & Bargh, 1999). These automatic action tendencies can be assessed using reaction-time (RT) paradigms such as the approach-avoidance task (AAT; Roelofs et al., 2010; Rotteveel & Phaf, 2004), in which participants react to facial expressions by pulling a joystick toward (approach) or pushing it away from (avoidance) themselves. Participants typically show an approach tendency to happy faces and an avoidance tendency to angry faces.

On the assumption that improved processing of social information will facilitate social approach behavior and interpersonal communication, human oxytocin research has focused on the processing of facial expressions. It is argued that oxytocin intensifies the salience of social stimuli, manifest in an increase in gaze shifts toward the eye region of faces (Guastella, Mitchell, & Dadds, 2008) and in emotion recognition (Domes et al., 2007). The valence specificity of these effects being unresolved (e.g., Fischer-Shofty, Shamay-Tsoory, Harari, & Levkovitz, 2010; Lischke et al., 2011), the question remains whether changes in recognizing facial emotions are rooted in an intensified salience perception or in a stronger motivation to approach social interactions.

Oxytocin fosters social approach behavior in animals (Ross & Young, 2009). Yet, despite the need for experiments to involve “a behavioral measure of approach and avoidance behavior” (Gamer & Büchel, 2012, p. 91), human studies to date have mainly focused on the recognition of facial emotions. To bridge the gap between emotion detection and action, and to determine whether oxytocin increases the salience of social information (Kemp & Guastella, 2010) or the motivation to seek social interactions (enhancing prosocial, approach-related behaviors), we employed the AAT and manipulated the direction of stimuli’s eye gaze—a subtle but highly relevant indicator of social salience in humans (Petrovic, Kalisch, Singer, & Dolan, 2008).

Direct gaze is a strong imperative, signaling the start of an interaction and prompting the recipient to react (Adams & Kleck, 2005), whereas averted gaze does not incorporate such motivational affordances (Roelofs et al., 2010). A general increase in the motivation to seek social interactions would promote approach in response to all facial expressions; however, the social salience hypothesis predicts a differentiation between gaze directions and emotions. Given its anxiolytic properties (Heinrichs et al., 2003), we expected oxytocin to reduce avoidance or possibly even induce approach responses only to salient, threatening social cues (i.e., angry faces with direct gaze). Moreover, as the effects of oxytocin can be moderated by dispositional anxiety (Alvares et al., 2012; Bartz et al., 2010; Guastella et al., 2009), we also investigated whether social anxiety modulated oxytocin-induced effects.

Method

Participants

Twenty-four healthy male students (mean age = 21.46 years; $SD = 1.93$) participated voluntarily and were financially compensated. None reported a current or past neurological or endocrine disease, medication use, or drug or alcohol abuse. Exclusion criteria included being below the age of 18 or above the age of 30, smoking more than five cigarettes a day, participating in another pharmacological study or donating blood within 2 months prior to the study, and having fever, the common cold, or allergic rhinitis (“hay fever”) on test days. Participants abstained from caffeine, alcohol, and nicotine for 24 hr before, and from eating and drinking (except water) for 2 hr before, substance administration.

All participants gave their written informed consent. Procedures were in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of the Radboud University Nijmegen Medical Centre.

Procedure

The study was conducted following a randomized, placebo-controlled, double-blind, within-subjects design and using a standardized procedure (for pharmacological details, see the Supplemental Material available online). Participants were tested in two sessions: Prior to the first session, we administered 24 IU of oxytocin (Syntocinon; Novartis, Basel, Switzerland), and prior to the second session, we administered a saline solution; both were given intranasally. During each session, participants performed several tasks approximately 40 min after substance administration, a time window derived from earlier oxytocin studies (Domes et al., 2007; Gamer & Büchel, 2012; Kosfeld et al., 2005). As the order of the tasks was counterbalanced between subjects, one half started the AAT approximately 45 min after substance administration and the other half approximately 65 min after substance administration (see the Supplemental Material).

AAT. To perform the AAT, participants needed to respond as quickly and as accurately as possible to the emotional expression of face cues by pulling a joystick toward themselves (approach) or pushing it away from themselves (avoidance). The stimuli consisted of three expressions (angry, happy, neutral) with either a direct or averted gaze (for additional information on the stimuli, see the Supplemental Material).

A total of 384 experimental trials were randomly presented in six blocks (3 emotions \times 2 responses). Participants were instructed to respond with approach movements to one emotion and with avoidance movements to the other

(approach happy faces-avoid angry faces, approach happy faces-avoid neutral faces, approach angry faces-avoid neutral faces, approach angry faces-avoid happy faces, approach neutral faces-avoid happy faces, approach neutral faces-avoid angry faces). The order of the blocks was counterbalanced. Each block was preceded by 16 practice trials. RTs were recorded at four different joystick angles (7°, 14°, 21°, and 30°). For all analyses, the time between stimulus onset and the maximum joystick displacement was used.

Liebowitz Social Anxiety Scale. The Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987) was used to assess fear and avoidance in 24 social situations. Respondents rated on a 4-point scale how anxious they would feel in the specified situation and how often they would avoid it.

Statistical analyses

Following a standard procedure (Roelofs et al., 2010), we excluded trials with RTs less than 150 ms and greater than 1,000 ms (5.5% of all trials) from analysis. Median RTs were calculated for correct responses for each level of the four experimental factors: substance (oxytocin, placebo), emotion (angry, happy), gaze (direct, averted), and movement (approach, avoid). As in previous AAT analyses (Roelofs et al., 2009), we contrasted the RTs for angry and happy faces with direct gaze using a repeated measures analysis of variance (ANOVA) with substance, emotion, and movement as within-subjects factors.

To investigate the motivational direction of the effects and to correct for individual velocity differences, we obtained AAT effect scores by subtracting the individual median RTs for joystick pulls from the individual median RTs for joystick pushes; negative values reflected a relative avoidance tendency, and positive values reflected a relative approach tendency (Heuer, Rinck, & Becker, 2007; Roelofs et al., 2010). The effect scores were entered into a repeated measures analysis of covariance (ANCOVA; Substance \times Emotion) with the LSAS score as a covariate to determine the moderating effect of social anxiety.

Results

The repeated measures ANOVA on the RTs for angry and happy faces with direct gaze showed a significant main effect of emotion, $F(1, 23) = 52.10$, $p < .001$, $\eta^2 = .69$, and a significant Substance \times Emotion \times Movement interaction, $F(1, 23) = 6.96$, $p = .015$, $\eta^2 = .23$. None of the other main effects or interactions were significant ($F_s < 1.06$, $p_s > .32$).

The main effect of emotion was due to faster reactions to happy faces ($M = 638.06$ ms, $SD = 72.30$) than to angry faces ($M = 680.27$ ms, $SD = 63.26$). Separate analyses

of joystick pulls and pushes revealed a significant Substance \times Emotion interaction for pulls (approach), $F(1, 23) = 8.23$, $p = .009$, $\eta^2 = .26$, but not for pushes (avoidance), $F(1, 23) = 1.02$, $p = .32$, $\eta^2 = .04$.

The interaction between substance, emotion, and movement was qualified by an Emotion \times Movement interaction in the placebo condition, $F(1, 23) = 4.31$, $p = .049$, $\eta^2 = .16$, which was not significant after oxytocin administration, $F(1, 23) = 1.03$, $p = .32$, $\eta^2 = .04$. The AAT effect scores (Fig. 1) illustrate this expected pattern of approach for happy faces ($M = 12.02$, $SD = 52.01$) and avoidance for angry faces ($M = -17.00$, $SD = 47.88$) in the placebo condition. As predicted, after oxytocin administration, the AAT effect scores for angry and happy faces were not significantly different ($M = 8.15$, $SD = 41.07$, and $M = -4.88$, $SD = 42.94$, respectively).

Social anxiety effects

The repeated measures ANCOVA on AAT effect scores with social anxiety as a covariate showed a main effect of

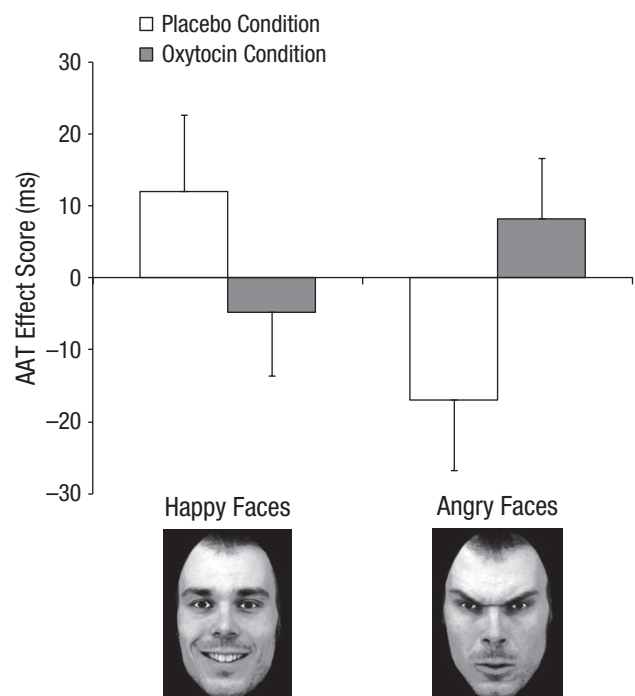


Fig. 1. Mean effect score on the approach-avoidance task (AAT) for direct-gaze stimuli as a function of emotion type and drug condition. Effect scores were obtained by subtracting reaction times for pull movements from reaction times for push movements. Negative effect scores indicate avoidance tendencies, whereas positive effect scores indicate approach tendencies. Error bars represent standard errors. Also shown are sample angry and happy faces obtained from the Karolinska Directed Emotional Faces database (Lundqvist, Flykt, & Öhman, 1998; Identity AM29) and reproduced with permission from the copyright holders.

substance, $F(1, 22) = 6.84$, $p = .016$, $\eta^2 = .24$, and interaction effects for substance and social anxiety, $F(1, 22) = 7.42$, $p = .012$, $\eta^2 = .25$, substance and emotion, $F(1, 22) = 11.20$, $p = .003$, $\eta^2 = .34$, and, most critically, substance, emotion, and social anxiety, $F(1, 22) = 4.84$, $p = .039$, $\eta^2 = .18$. The main effect of social anxiety was not significant ($p = .24$), and neither were the effect of emotion and the Emotion \times Social Anxiety interaction ($F_s < .35$, $p_s > .56$).

The significant interactions were driven by a substance effect in reaction to angry faces, $F(1, 22) = 13.11$, $p = .002$, $\eta^2 = .37$, which was additionally modulated by social anxiety (i.e., a Substance \times Social Anxiety interaction), $F(1, 22) = 9.03$, $p = .007$, $\eta^2 = .29$. Under oxytocin, approach toward angry faces increased, whereas responses to happy faces showed no substance effect, $F(1, 22) = 0.28$, $p = .60$, $\eta^2 = .01$, nor a Substance \times Social Anxiety interaction, $F(1, 22) = 0.30$, $p = .59$, $\eta^2 = .01$.

Social anxiety associations were further explored using correlation analyses between social anxiety and individual AAT effect scores for emotional faces. There was a significant negative correlation for angry faces after oxytocin administration, $r = -.58$, $p = .003$ (Fig. 2), which was absent after placebo administration, $r = .30$, $p = .16$. For happy faces, action tendencies were not associated with social anxiety after either oxytocin administration, $r = -.23$, $p = .28$, or placebo administration, $r = -.10$, $p = .65$. Accordingly, oxytocin increased approach behavior for angry faces with direct gaze specifically in participants scoring low on social anxiety.

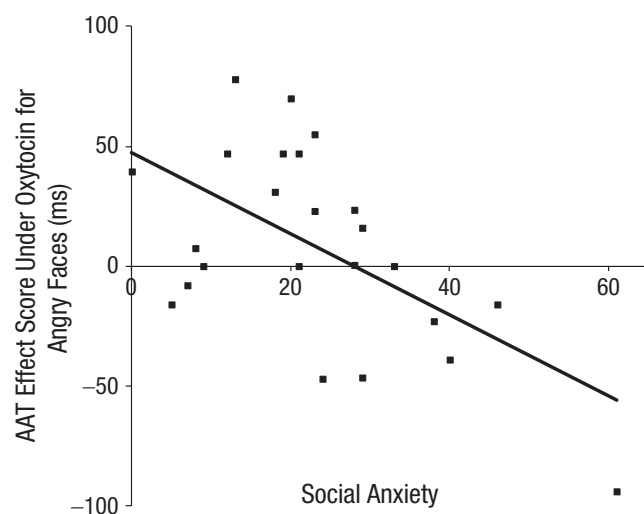


Fig. 2. Scatter plot (with best-fitting regression line) showing effect scores on the approach-avoidance task (AAT) for angry faces with direct gaze after oxytocin administration as a function of social anxiety. Effect scores were obtained by subtracting reaction times for pull movements from reaction times for push movements. Social anxiety was measured using the Liebowitz Social Anxiety Scale (Liebowitz, 1987).

Averted gaze and neutral faces

Averted-gaze stimuli yielded no substance-related effects. Detailed analyses of averted-gaze stimuli and RTs for neutral faces are provided in the Supplemental Material.

Discussion

Our investigations into the influence of oxytocin on social motivational behavior in human subjects yielded three major findings. After placebo administration, participants displayed typical behavior on the AAT—approach tendencies for happy faces and avoidance tendencies for angry faces—replicating previous findings (Roelofs et al., 2010; Rotteveel & Phaf, 2004). Oxytocin altered approach-avoidance behavior for direct-gaze cues, which confirmed our hypothesis. It increased approach toward angry faces with direct gaze in participants with low levels of social anxiety.

Our results corroborate previous studies showing that oxytocin attenuates anxiety and stress (Heinrichs et al., 2003), for example, by decreasing aversion to angry faces (Evans, Shergill, & Averbeck, 2010) and arousal to human threat stimuli (Norman et al., 2010). But do oxytocin's anxiolytic properties foster prosocial, approach-related behaviors or enhance the salience of social information (Kemp & Guastella, 2010)? Our findings favor salience modulation as the underlying mechanism and do not support the prosocial-approach account (universally enhanced approach). They corroborate earlier findings differentiating the salience of social cues (i.e., the direction of eye gaze and valence) but also point to the importance of dispositional factors.

Crucially, the inclination under oxytocin to approach signals of social threat or dominance (i.e., angry faces with direct gaze; Adams & Kleck, 2005; Roelofs et al., 2010; Terburg, Aarts, & van Honk, 2012) was negatively related to social anxiety, which highlights the fundamental role of personal variability in social endocrinology (Mehta & Josephs, 2011; van Honk, Montoya, Bos, van Vugt, & Terburg, 2012; van Peer, Spinhoven, van Dijk, & Roelofs, 2009) and in oxytocin research in particular (Bartz et al., 2011; Guastella & MacLeod, 2012). As to dispositional anxiety, findings are inconsistent, showing more beneficial effects of oxytocin for participants with low rather than high attachment anxiety (Bartz et al., 2010) but also for individuals with high trait anxiety (Alvares et al., 2012) and social anxiety disorder when administered alongside exposure therapy (Guastella et al., 2009). A crucial difference between these seemingly opposing results lies in the social focus of the dependent measures used, namely, features of the attachment bond between subjects and their parents (Bartz et al., 2010) versus cognitive self-perceptions about one's

speech performance (Alvares et al., 2012; Guastella et al., 2009). Whereas the latter is essentially self-centered, the former involves the perception of interaction partners, which renders it more similar to the current study. Consistent with the absence of reductions in anxiety or symptom severity as such (Guastella et al., 2009) in individuals with severe social anxiety, our results showed that oxytocin may not provide sufficient anxiolytic properties to improve their social functioning (Hoge, Pollack, Kaufman, Zak, & Simon, 2008). Similarly, a differential sensitivity to external oxytocin might underlie our findings, as the approach/avoidance-social anxiety association was evident only under oxytocin. It is also debatable whether in individuals with high social anxiety, anxiety reduction would induce approach to social threat. Given that oxytocin effects are most likely dependent on an individual's social repertoire and context, appetitive tendencies might first develop in quiescent, safe environments or when social support is provided as an external stress buffer (Heinrichs et al., 2003). Regarding its therapeutic potential, it is thus essential to establish which personal and situational factors will facilitate or counteract the beneficial effects of oxytocin.

Moreover, it remains to be investigated how far oxytocin-induced perceptual changes of angry faces complement the approach inclination. Recent data on gaze endurance suggests that unconscious, reflexive biological mechanisms trigger testosterone-induced dominance when individuals are confronted with social threat stimuli (Terburg et al., 2012). Eye movements and endocrine assessments could then improve the understanding of automatic reactions, such as interactions of oxytocin and cortisol (Heinrichs et al., 2003), that might underlie anxiety.

In sum, our study is the first to establish that in humans, oxytocin facilitates approach behavior in response to social threat, most likely by reducing anxiety. But what is the affective and adaptive value of approaching social threat? In animals, both affiliative (tend-and-befriend) and aggressive (fight-or-flight) tendencies have been associated with oxytocin (Campbell, 2008; Ross & Young, 2009), which renders it an important regulator of different expressions of social approach behavior. As dispositional characteristics such as anxiety further modulate the neuroendocrine priming of prepotent responses, tuning motivational behavior to intra- and interpersonal dynamics may prove to be important in optimizing flexibility and adaptiveness in social interactions.

Author Contributions

All authors developed the study concept and design. Testing, data collection, and data analysis were performed by S. Radke. Data interpretation was performed by all authors. S. Radke drafted the article, and K. Roelofs and E. R. A. de Bruijn

provided critical comments and suggestions throughout the writing process. All authors approved the final version of the article and its order of author listing for submission.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Supplemental Material

Additional supporting information may be found at <http://pss.sagepub.com/content/by/supplemental-data>

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