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# Attachment Style Moderates the Effects of Oxytocin on Social Behaviors and Cognitions During Social Rejection: Applying a Research Domain Criteria Framework to Social Anxiety

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## Abstract

Whereas the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* categorizes individuals with similar self-reported symptoms, the research domain criteria offers a new approach for classifying mental disorders on the basis of dimensions of observable behaviors and neurobiological measures. The objective of this proof-of-concept study was to adopt this approach by distinguishing individuals on the basis of disorder-related personality traits during an experimental manipulation that targeted a disorder-related biological mechanism. In a double-blind, placebo-controlled study design, we examined whether attachment style moderated the effect of oxytocin administration on social behaviors and cognitions during a social-exclusion test in individuals with social anxiety disorder. Among participants who received oxytocin, as opposed to a placebo, only individuals with low attachment avoidance displayed more social affiliation and cooperation, and only those with high attachment avoidance showed faster detection of disgust and neutral faces. Thus, attachment style moderated oxytocin's effects among individuals who shared the same *DSM* diagnosis. We conclude that neurobiological tests can inform new classification strategies by adopting a research domain criteria framework.

## Keywords

RDoC, oxytocin, social anxiety disorder, social rejection, individual differences

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In 2008, the National Institute of Mental Health launched the research domain criteria (RDoC) initiative with the goal to develop new ways of classifying mental disorders on the basis of dimensions of observable behaviors and neurobiological measures (Insel et al., 2010). An example of such a dimensional construct is social affiliation and social avoidance within the social domain of RDoC. A biological correlate of social affiliation and attachment is oxytocin, a nine-amino-acid neuropeptide, which is produced in the hypothalamus and acts as a neuromodulator or neurotransmitter throughout the brain, including the limbic areas, midbrain, and brainstem (Heinrichs, von Dawans, & Domes, 2009; Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011).

Studies have shown that intranasal delivery of oxytocin enhances social cognition by improving trust and cooperation (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005), attachment perception (Buchheim et al., 2009), and emotion recognition (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007; Guastella et al., 2010). Although the effects of oxytocin on social behaviors and cognitions are relatively strong and robust, these effects

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appear to be specific to certain individuals and under certain conditions (Guastella et al., 2010; Olff et al., 2013). Specifically, individual differences in sex, hormone levels, attachment orientation, and psychiatric status appear to moderate oxytocin's effects (MacDonald, 2013). Furthermore, studies have begun to focus on the genetic mechanisms of inter-individual variation in the oxytocin signaling, providing evidence for variations in specific genes contributing to individual differences in social behavior and cognition (Kumsta & Heinrichs, 2013). These studies have suggested that there are meaningful individual differences in response to oxytocin administration and that these differences might identify subgroups within the same *Diagnostic and Statistical Manual of Mental Disorders (DSM)* category, which is in line with the RDoC initiative.

Our objective was to conduct a proof-of-concept study by adopting the RDoC framework in a clinical sample. Specifically, we examined whether attachment style moderates the effect of oxytocin on social behaviors and cognitions in a sample of individuals with a *DSM-IV* (4th ed.; American Psychiatric Association, 1994) diagnosis of social anxiety disorder. We chose to focus on oxytocin and attachment style in severe social anxiety for a number of reasons. First, social anxiety disorder is a heterogeneous diagnostic category within which individuals differ on a number of dimensions (Hofmann, Heinrichs, & Moscovitch, 2004). One of these dimensions appears to be attachment style which can be measured using dimensional self-report scales. Second, a neurobiological correlate of attachment is oxytocin, which is also implicated in social behaviors and cognitions (Meyer-Lindenberg et al., 2011). For example, studies have shown that individuals with high levels of social anxiety exhibit prominent deficits in social cognitions and behaviors (i.e., maladaptive attentional biases and social-avoidance behaviors), which are in part regulated by oxytocin (Ellenbogen et al., 2012; Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). Third, social behaviors and cognitions associated with social anxiety can be reliably measured and quantified in the laboratory. For example, previous investigators have measured behavioral response to social rejection using the Cyberball game (Williams & Jarvis, 2006) and early cognitive biases to social threat using the modified Posner task (Posner, 1980; Posner, Snyder, & Davidson, 1980).

In this proof-of-concept study, we translated research from clinical science, neuroscience, and social science to shed light on the neurobiological dimension of a common mental-health problem by adopting an RDoC framework. Our hypothesis was that attachment style moderates the effect of oxytocin on social behaviors and cognitions in response to social rejection in individuals with a *DSM-IV* diagnosis of social anxiety disorder.

## Method

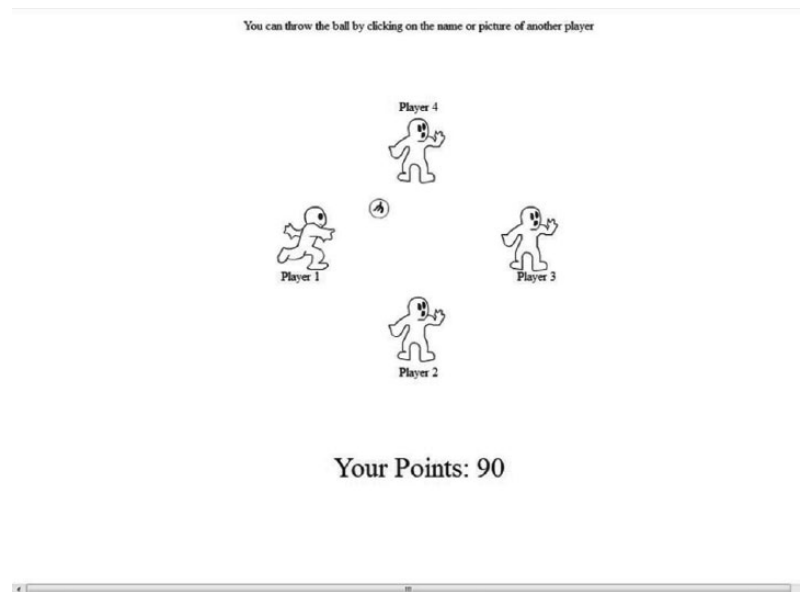
### Participants

Participants were 60 males at least 18 years of age with a principal or coprincipal diagnosis of social anxiety disorder and a current Liebowitz Social Anxiety Scale (Liebowitz, 1987) score of 60 or higher. Females were excluded from the study because of potential fluctuations of oxytocin during menstrual phases. No participants had significant nasal pathology; smoked more than 15 cigarettes per day; had a serious medical illness; had active suicidal or homicidal ideation; had a current diagnosis of schizophrenia, psychotic disorder, bipolar disorder, or substance abuse/dependence; or were concurrently taking psychotropic medications, except for antidepressants taken at a stable dose for at least 2 weeks prior to study entry, as in other published work (Guastella, Howard, Dadds, Mitchell, & Carson, 2009). Participants received \$40 for their participation in the study and additional earnings from the Cyberball task. The study was approved by the Boston University Medical Center Institutional Review Board and registered by the National Institutes of Health ClinicalTrials.gov (Registry NCT01856530).

Six participants were excluded from analyses as a result of ineligibility (3 did not have social anxiety disorder, 2 met criteria for substance dependence, and 1 had a principal diagnosis of posttraumatic stress disorder). The final sample included 54 participants (mean age = 24.39 years, range = 18–45). Two participants did not complete the Cyberball task because of technical difficulties. Chi-square and *t* tests showed no differences between groups in demographic or baseline clinical characteristics (all *ps* > .05). The most common comorbid diagnoses were major depression (18.5%), generalized anxiety disorder (16.7%), and panic disorder with agoraphobia (7.4%).

### Materials

**Cyberball task.** Cyberball (Williams, Cheung, & Choi, 2000; Williams & Jarvis, 2006) appears to the participant as a four-person computerized ball-tossing game, whereas it is played by a single individual and is designed to simulate and manipulate rejection. Participants were led to believe that they were playing with three “others” in real time. The program was modified to create three behavioral profiles for the confederates. For the first 80 trials (play condition), Players 1, 4, and 3, respectively, were programmed to toss on average 70%, 30%, and 10% of their balls to the participant, who was always Player 2. Each trial consisted of a single ball-toss exchange represented by a short animation of one player tossing the ball and another player catching the ball (see Fig. 1 for example screenshot). The participant was instructed to send



**Fig. 1.** Example screenshot from Cyberball task.

the ball to a player when he received it from a previous trial and to obtain as many points as possible to be exchanged for real monetary rewards. After 80 trials, the profiles switched (switch condition), and Player 1 was programmed to toss only 10% of his balls to the participant for the next 80 trials. The decision time for other players was varied from trial to trial to enhance the believability of realistic play behavior. The primary outcome measure was the number of total balls tossed to each player during the play and switch conditions. Ratings of trust, empathy, preference, perceived rejection, and willingness to reengage in another game of Cyberball with each player were also measured on a 7-point Likert scale at the end of the task. The entire task consisted of 160 trials and took approximately 8 min to complete.

**Modified Posner task.** The Posner task (Posner, 1980; Posner et al., 1980) measures attentional engagement toward and disengagement from social threat cues. The stimuli for this task were modified to include a set of disgust, happy, and neutral faces. During each trial, the participant saw a fixation cross displayed for 500 ms. Next, a face (disgust, happy, or neutral) appeared for 500 ms within the top or bottom half of the screen (the other half of the screen remained blank) and then disappeared. Subsequently, a probe (the letter “E” or “F”) appeared within the top or bottom half of the screen. The participant was instructed to indicate the letter as quickly and accurately as possible by clicking the left or right mouse button (left for “E,” right for “F”). For valid trials, the probe appeared in the position previously occupied by

the face stimulus. For invalid trials, the probe appeared in the empty half of the screen. The entire task consisted of 360 trials and took 10 min to complete.

### **Drug information**

The oxytocin and placebo nasal sprays were provided by a local compounding pharmacy under Investigational New Drug Application 113,827. The oxytocin sprays consisted of 24 IU of oxytocin and were dispensed in metered-dose spray bottles to deliver exactly 4 IU per spray; six sprays total were administered to each participant using alternating nostrils. The placebo sprays were identical to the oxytocin nasal sprays except for the active oxytocin ingredient and the addition of 0.65% sodium chloride to minimize nasal irritation to the patient, which was included at the recommendation of the compounding specialist. Assessment of blind revealed that participants could not distinguish between drug conditions. Of the participants, 63% reported no adverse events, and there was no difference between groups in the frequency and nature of reported adverse events. The most common adverse events reported were jitteriness/restlessness (17%), anxiety/nervousness (11%), dry mouth (7%), and sedation/drowsiness (7%).

### **Procedure**

Participants were recruited from community advertisements and an outpatient wait list from an anxiety-disorders clinic. Potential participants were phone screened for basic eligibility requirements and asked to

avoid caffeine, alcohol, and nicotine for 24 hr prior to their appointment.

During the study visit, participants gave written informed consent and were assessed for diagnostic eligibility by the first author using the Mini Adult Diagnostic Interview Schedule for *DSM-IV* (DiNardo, Brown, & Barlow, 1994). The study physician then conducted a medical screen to assess vitals, medical history, and concurrent medications. Next, participants completed a set of self-report questionnaires to assess social-interaction anxiety, using the Social Interaction and Anxiety Scale (SIAS; Mattick & Clarke, 1998); rejection sensitivity, using the Interpersonal Sensitivity Measure (IPSM; Boyce & Parker, 1989; Harb, Heimberg, Fresco, Schneier, & Liebowitz, 2002); attachment style, using the Experience in Close Relationships Inventory (ECR; Brennan, Clark, & Shaver, 1998); and subjective mood, using the Positive and Negative Affect Scales (PANAS; Watson, Clark, & Tellegen, 1988). The ECR yielded two subscales reflecting attachment anxiety (anxiety about rejection or abandonment) and attachment avoidance (discomfort with closeness and intimacy). In the current sample, the two subscales were not significantly correlated,  $r = -.32$ ,  $n = 25$ ,  $p = .12$ . As a result of administrative issues, the ECR was added halfway through data collection, which contributed to sample-size fluctuations between analyses. In the current sample, the test-retest reliability was fair for the SIAS ( $r = .66$ ), PANAS Positive ( $r = .73$ ), and PANAS Negative ( $r = .64$ ). Internal consistency estimates ranged from good to excellent for the IPSM ( $\alpha = .73$ ), SIAS ( $\alpha = .88$ ), ECR Avoidance ( $\alpha = .88$ ), and ECR Anxiety ( $\alpha = .90$ ). No reliability or validity data were available for the Likert scale ratings of trust, empathy, preference, perceived rejection, and willingness to reengage in another game of Cyberball with each player.

Participants were randomly assigned to conditions in which they received a nasal spray containing either oxytocin or placebo. The study was double blind such that neither the study physician nor the experimenter was aware of the participants' assigned drug conditions. Using a standardized protocol, participants self-administered a nasal spray in the presence of the study physician or nurse.

Next, participants were asked to sit alone in a waiting room for 45 min before starting the computer tasks, which reflects a standard wait period after intranasal oxytocin administration, to allow the drug to be absorbed (Heinrichs et al., 2003). After 45 min, the experimenter led the participant and three male confederates individually into a common waiting area, asked each to introduce his first name to the group, and then led them to separate experimental rooms to enhance the credibility of the Cyberball task. The order of the tasks was always Cyberball first followed by the Posner task. The experiment concluded with a debriefing session.

## Data analytic plan

A regression approach was adopted to investigate the main effects of oxytocin and interactions between oxytocin and continuous moderators (attachment anxiety and attachment avoidance) on outcomes during the Cyberball and Posner tasks. Specifically, the primary outcome on the Cyberball task was difference scores in the number of balls tossed to Player 1 during the play and switch conditions. On the Posner task, the primary outcomes were mean response latencies during valid and invalid trials that followed happy, neutral, or disgust facial stimuli. Faster response latencies when detecting validly cued targets that followed disgust faces indicated an attentional "engagement" or bias toward threat-relevant information. Slower response latencies when detecting invalidly cued targets that followed disgust faces indicated difficulty disengaging attention away from threat-relevant information.

We investigated interaction effects by conducting hierarchical regression analyses on all participants to examine the effects of dummy-coded drug group, mean-centered attachment anxiety and attachment avoidance (entered in Step 1), and their two- and three-way interactions (entered as product terms in Steps 2 and 3, respectively) on each outcome. These analyses reflected much smaller sample sizes because the ECR was included in the study midway through data collection. Regression analyses were followed up by generating predicted values based on each regression equation and plotting XY graphs to examine the nature of the interaction. Given that there were no significant differences in age and social anxiety symptom severity between groups, and that inclusion of covariates would significantly reduce test power, we did not control for covariates in the analyses.

## Results

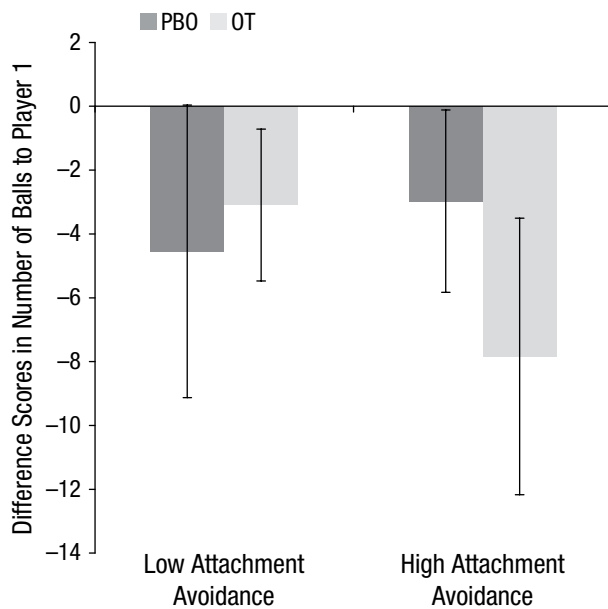
### Cyberball manipulation check

The majority (82.7%) of participants who completed Cyberball reported noticing that Player 1 played the most with them at first, Wilks's Lambda = .66,  $F(2, 44) = 11.15$ ,  $p < .001$ ,  $\eta_p^2 = .34$ , but there was no reported difference in other players' behavior later on during the switch condition of the game, Wilks's Lambda = .95,  $F(2, 44) = 1.28$ ,  $p = .29$ ,  $\eta_p^2 = .06$ .

### Effects on ball-tossing behavior during Cyberball

Regression analyses revealed a significant Group  $\times$  Attachment Avoidance interaction on difference scores in balls tossed to Player 1 during Cyberball,  $\beta = 6.90$ ,  $t(19) = -2.11$ ,  $p = .05$ . The attachment interaction terms explained





**Fig. 2.** Interaction effect of Group (placebo, oxytocin)  $\times$  Avoidant Attachment (low, high) on difference scores in ball tosses to Player 1 between play and switch conditions ( $n = 25$ ). Error bars represent standard errors. PBO = placebo; OT = oxytocin.

an additional 19.9% of the variance in ball tosses,  $\Delta F(2, 19) = 2.72$ ,  $p = .09$ . Among participants with low attachment avoidance, assignment to the oxytocin group, compared with assignment to the placebo group, resulted in smaller difference scores in the number of balls tossed to Player 1 across Cyberball conditions, which suggested increased cooperation with Player 1 (see Fig. 2). Among participants with high attachment avoidance, assignment to the oxytocin group, relative to the placebo group, resulted in larger difference scores, which suggested decreased cooperation with Player 1.

Without considering attachment style, oxytocin did not differ from placebo in ball-tossing behavior as a result of the experimental manipulation. There was no significant Group  $\times$  Time interaction, Wilks's Lambda = 1.00,  $F(1, 50) = 0.02$ ,  $p = .88$ ,  $\eta_p^2 = .00$ . Both groups threw significantly more balls to Player 1 than to the other players, Wilks's Lambda = .47,  $F(2, 49) = 27.32$ ,  $p < .001$ ,  $\eta_p^2 = .53$ , but this did not differ by group,  $F(1, 50) = 0.32$ ,  $p = .57$ ,  $\eta_p^2 = .01$ .

### Effects on attention

Regression analyses showed a significant Group  $\times$  Attachment Avoidance interaction on engagement scores for disgust faces,  $\beta = -106.12$ ,  $t(18) = -2.34$ ,  $p = .03$ , and for neutral faces,  $\beta = -102.47$ ,  $t(18) = -2.07$ ,  $p = .05$ , but not for happy faces,  $\beta = -81.30$ ,  $t(18) = -1.52$ ,  $p = .15$ . When participants were given oxytocin, those with high attachment avoidance responded faster to validly cued

disgust faces and neutral faces, whereas those with low attachment avoidance took longer to respond. For disengagement scores, there was a trend toward a group difference for the Group  $\times$  Attachment Avoidance interaction for all face types—disgust faces:  $\beta = -106.87$ ,  $t(19) = -1.98$ ,  $p = .06$ ; neutral faces:  $\beta = -99.14$ ,  $t(19) = -1.82$ ,  $p = .09$ ; happy faces:  $\beta = -93.32$ ,  $t(19) = -2.03$ ,  $p = .06$ . Among participants given oxytocin, individuals with high attachment avoidance responded faster to invalidly cued disgust, neutral, and happy faces, whereas those with low attachment avoidance took longer to respond.

Without considering attachment style, oxytocin was not associated with facilitated attentional engagement or disengagement scores for any face type, given that there was no significant interaction of Group  $\times$  Cue Type  $\times$  Face Type, Wilks's Lambda = .93,  $F(2, 50) = 0.44$ ,  $p = .65$ . Separate Group  $\times$  Cue Type analyses were conducted for each face type and yielded no significant interactions—disgust faces: Wilks's Lambda = 1.00,  $F(1, 51) = 0.15$ ,  $p = .70$ ; happy faces: Wilks's Lambda = 1.00,  $F(1, 51) = 0.09$ ,  $p = .77$ ; neutral faces: Wilks's Lambda = .99,  $F(1, 51) = 0.70$ ,  $p = .41$ .

### Effects on self-report measures

Individuals who received oxytocin, relative to those who received a placebo, reported lower ratings of overall rejection from all players during Cyberball,  $F(1, 48) = 3.98$ ,  $p = .05$ ,  $\eta_p^2 = .08$ . However, compared with placebo, oxytocin did not significantly affect trust ratings for Player 1 relative to ratings for other players, Wilks's Lambda = .98,  $F(2, 47) = 0.44$ ,  $p = .64$ ,  $\eta_p^2 = .02$ , nor did oxytocin significantly affect perceived rejection ratings from Player 1, Wilks's Lambda = .99,  $F(2, 47) = 0.27$ ,  $p = .77$ ,  $\eta_p^2 = .01$ . Oxytocin also did not significantly reduce negative mood, positive mood, or social-interaction anxiety, given that all of these interaction effects were not significant—negative mood: Wilks's Lambda = 1.00,  $F(1, 50) = 0.23$ ,  $p = .63$ ,  $\eta_p^2 = .01$ ; positive mood: Wilks's Lambda = .99,  $F(1, 51) = 0.57$ ,  $p = .45$ ,  $\eta_p^2 = .01$ ; social-interaction anxiety: Wilks's Lambda = 1.00,  $F(1, 23) = 0.01$ ,  $p = .91$ ,  $\eta_p^2 = .001$ .

### Discussion

Results from our approach demonstrated that individuals with severe social anxiety can be distinguished by attachment styles during an experimental manipulation of social exclusion that implicated oxytocinergic mechanisms. We predicted that attachment style would moderate the effect of oxytocin on social behaviors and cognitions during a Cyberball social-exclusion test in individuals with social anxiety disorder. Consistent with our hypothesis, results showed that oxytocin contributed to ongoing cooperation with a rejecting but initially

cooperative partner only for those participants with low attachment avoidance. Moreover, in line with previous work that has shown that oxytocin promotes flexible attentional shifting (Ellenbogen et al., 2012), our results demonstrated that oxytocin not only facilitated disengagement from all social cues depicting disgust, neutral, and happy faces for these individuals but also sped up the detection of disgust and neutral faces among individuals with high attachment avoidance.

This result is consistent with previous work that has suggested that oxytocin's effects are dependent on individual difference factors (Bartz, Zaki, Bolger, & Ochsner, 2011). More specifically, our results showed that attachment style, which maps onto specific biological systems (Sanislow et al., 2010), moderates the effects of the oxytocin system on social behaviors and cognitions after social rejection. This distinguishes our approach from others that directly compare patients from various diagnostic categories with a comparison group to draw conclusions about diagnostic specificity. Indeed, intranasal delivery of oxytocin has been shown to improve social cognition across the diagnostic and developmental continuum from youth with autism (Guastella et al., 2010) to adults with schizophrenia (Davis et al., 2013). In addition, our findings suggest that oxytocin administration in conjunction with an experimental rejection paradigm can identify meaningful subgroups of individuals that differ in attachment style. This not only has important implications for the nosology of severe social anxiety but also may contribute to the development of personalized and improved treatment strategies for this common mental disorder (Heinrichs, Chen, & Domes, 2012; Meyer-Lindenberg et al., 2011). It might further clarify interindividual variation in responding to oxytocin, which can ultimately inform biomarker validation in later phases of research on biomarker development (Niciu et al., 2013).

To further advance our understanding of the oxytocin-ergic mechanisms underlying psychopathology, we suggest that an important question for future research is whether genetic polymorphisms of the oxytocin receptor gene are linked to attachment style to confer risk for psychopathology. Indeed, genetic findings point to associations among depression and certain genotype groups of two oxytocin receptor single nucleotide polymorphisms (Costa et al., 2009). Of note, researchers have associated the GG genotype of these polymorphisms with higher scores on certain attachment styles, which have been previously associated with depression (Costa et al., 2009). Therefore, it is conceivable that attachment style is an endophenotype for the response to oxytocin during social rejection. It is quite possible that attachment style is not the only or even the best measure of such an endophenotype. Other potential candidates that have been discussed include behavioral inhibition and impulsivity,

both of which have been associated with functional polymorphisms of dopamine-related genes (Congdon, Lesch, & Canli, 2008). Thus, researchers could study these polymorphisms in individuals with mood and anxiety symptoms and examine whether these symptoms are associated with personality styles that predict response to oxytocin during social rejection.

Another important future research question concerns examination of the association between the neuroendocrine responses to social rejection and the onset, course of the illness, and response to treatment in specific subgroups. To date, this research has been primarily focused on cortisol. For example, researchers have shown that high levels of behavioral inhibition and elevated cortisol levels in early childhood are risk factors for the development of social anxiety disorder by adolescence (Essex, Klein, Slattery, Goldsmith, & Kalin, 2010). Moreover, elevated cortisol and temperament appears to be associated in children of mothers with social anxiety disorder, such that behaviorally inhibited children display elevated afternoon cortisol levels in general, and when confronted with a naturalistic stressor, they display elevated nighttime cortisol levels (Russ et al., 2012) and lower cortisol awakening response (Hek et al., 2013). Therefore, we suggest that future research focus on the association between oxytocin and other neuroendocrine measures, especially cortisol, during social rejection in vulnerable individuals, and encourage researchers to explore the role of oxytocin in the onset and development of anxiety problems.

Finally, we suggest that researchers examine oxytocin-relevant brain circuits linked to specific attachment styles to identify individuals who are at risk for developing anxiety problems or social deficits (e.g., deficits in emotion recognition, trust or affiliative behavior). Recent studies have suggested that fearful faces are associated with exaggerated amygdala activity in individuals with social anxiety disorder (relative to control participants), which decreased after oxytocin treatment compared with placebo (Labuschagne et al., 2010). In a follow-up study, Labuschagne et al. (2011) found that when individuals viewed sad faces, participants with social anxiety disorder, compared with control participants, responded with heightened reactivity in the medial prefrontal cortex and the anterior cingulate cortex, and this reactivity decreased after oxytocin treatment. Future studies should focus on whether these brain-activation patterns are linked to specific subgroups identified by attachment style and the aforementioned genetic polymorphisms. These research programs are consistent with the RDoC initiative and would further contribute to the development of a new classification system for mood and anxiety problems on the basis of neurobiological measures.

Our proof-of-concept study shows several limitations. First, we did not include a molecular genetic perspective,

which has been proposed for social behaviors and cognitions in several “distinct” psychopathologies (Meyer-Lindenberg et al., 2011). It remains uncertain how attachment style is associated with genetic variation of the oxytocin system. With regard to the variability in individual responses to oxytocin administration, we advocate the need for pharmacogenetic approaches in order to test how the efficacy of oxytocin administration is modulated by genetic variation of the oxytocin receptor or other genes involved in oxytocin signaling (Kumsta & Heinrichs, 2013). Furthermore, the origin of the attachment style remains unknown (such as childhood abuse or attachment history), and the same events can affect the oxytocin system (Sanislow et al., 2010). Second, given that the ECR was added to the study halfway through data collection, several comparisons have much smaller sample sizes and weak statistical power. Relatedly, no reliability or validity data were available for the Likert scale ratings of trust, empathy, preference, perceived rejection, and willingness to reengage in another game of Cyberball with each player. It should be noted, however, that these ratings possess face validity, and they were not the primary outcome measures. Instead, we included these ratings as secondary measures and subjective correlates of participants’ behaviors as indexed by the number of times participants tossed the ball. Another issue involves the considerable controversy with regard to actual mechanisms of intranasal oxytocin delivery (for a review, see Evans et al., 2013; Meyer-Lindenberg et al., 2011). Notwithstanding these limitations, this study illustrates how neurobiological tests can inform empirically based classification strategies by adopting an RDoC framework.

### Author Contributions

A. Fang and S. G. Hofmann developed the study concept and study design. A. Fang collected and analyzed the data. E. A. Hoge and M. Heinrichs aided in developing the study concept and provided essential direction with study drug procedures and consultation for study procedures. A. Fang and S. G. Hofmann drafted the manuscript with input from E. A. Hoge and M. Heinrichs. All authors contributed to writing the manuscript and approved the final version of the manuscript 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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