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REGULAR RESEARCH ARTICLE

Oxytocin Facilitates Self-Serving Rather Than Altruistic Tendencies in Competitive Social Interactions Via Orbitofrontal Cortex

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Abstract

Background: While the neuropeptide oxytocin can facilitate empathy and altruistic behavior, it may also promote self-serving tendencies in some contexts, and it remains unclear if it would increase altruistic or self-interest behaviors when they compete within a social situation.

Methods: The current between-subject, double-blind, placebo-controlled fMRI study investigated the effect of intranasal oxytocin on empathy for social exclusion using a modified online ball-tossing game that incorporated monetary rewards and the potential to display both altruistic and self-interest behaviors.

Results: Results showed that when subjects in both oxytocin and placebo groups were observing a player being excluded (victim) by other players in the game, there was activation in the mentalizing network. When subjects then played both with the victim and the players who had excluded them, they threw more balls to the victim player, indicative of an altruistic response. However, subjects in the oxytocin group threw more balls to the excluder players indicative of greater self-interest, since the latter would be perceived as more likely to reciprocate to maximize financial gain. This behavioral effect of oxytocin was associated with greater medial orbitofrontal cortex activation when playing with the excluders and negatively correlated with trait-altruism scores.

Conclusions: Overall, our findings suggest that in the context of competing motivations for exhibiting altruistic or self-interest behavior, oxytocin enhanced self-interest and this was associated with greater activation in frontal reward areas.

Keywords: altruism, empathy, oxytocin, orbitofrontal cortex, self-interest

Introduction

Empathy represents a core social function that allows individuals to recognize and understand the emotional states of others and respond to them accordingly (Eisenberg and Eggum, 2009). Empathy has 2 main components: cognitive empathy, which includes cognitive processes of perspective-taking allowing us to infer the mental states of others; and emotional empathy, reflecting a direct affective reaction involving understanding, sharing, and responding appropriately to their feelings (Shamay-Tsoory et al., 2009). Numerous studies have focused specifically on empathy in response to physical pain (Marsh, 2018) and social pain caused by being rejected or excluded (Wesselmann et al., 2009) and established that both share common neural circuits (Eisenberger et al., 2003).

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Significance Statement

The neuropeptide oxytocin can facilitate both altruistic and self-serving behaviors, but it is unclear what effect it has when they compete with each other. In the current study, we examined the effect of intranasal oxytocin treatment on empathy-induced altruistic as opposed to self-serving behaviors using a game-playing paradigm. Oxytocin had no influence on increased empathy for individuals who were observed to be socially excluded in the game. However, when subjects subsequently played with victims of exclusion and players who had excluded them, oxytocin increased their cooperation with the excluders rather than the victims, indicative of increased interest in personal gain since this strategy would potentially earn them more money. Oxytocin also increased orbitofrontal cortex activation when playing with excluders, providing neural support for facilitated reward processing. Overall, our findings demonstrate that when altruistic and self-serving behaviors are in competition, oxytocin only promotes the latter by enhancing their rewarding effect.

Empathy for those in suffering leads to distressed feelings and a motivation for altruistic helping behavior (FeldmanHall et al., 2015). Reciprocal altruism is associated with increased activity in the reward system (Rilling et al., 2002), although altruism is often exhibited in the absence of an expected reciprocity and can occur at the cost of self-interest (de Waal, 2008). Such costly altruistic behaviors and associated activity in reward-related regions are driven by other-oriented empathy rather than personal distress (FeldmanHall et al., 2015).

The neuropeptide oxytocin (OXT) can modulate core pain empathy regions, including the anterior cingulate cortex (ACC) and insula, as well as mentalizing and reward-related striato-frontal circuits (see Wigton et al., 2015). Intranasal OXT administration particularly enhances emotional—rather than cognitive—empathy via the amygdala (Hurlemann et al., 2010; Geng et al., 2018a). On the other hand, insula responses can be either enhanced (Striepens et al., 2012) or decreased in the context of pain empathy (Bos et al., 2015) and embarrassment (Geng et al., 2018b). In line with its emotional empathy-enhancing effects, intranasal OXT has been reported to increase altruistic behavior towards an ostracized individual (Riem et al., 2013). However, in this latter study exhibiting altruistic behavior had no cost to the participants, whereas in real-life situations it often does (Camerer and Fehr, 2006). Although OXT has often been reported to facilitate prosocial behaviors, it can also promote anti-social ones such as self-serving lying and group-serving dishonesty (Shalvi and De Dreu, 2014; Kendrick et al., 2017; Sindermann, 2018). On the other hand, OXT can also increase altruistic behaviors (Hu et al., 2016; Aydogan et al., 2017a). Thus, although OXT can influence empathy, altruistic, and self-serving behaviors, it is unclear what its functional role may be when these motivations are competing.

The current placebo (PLC)-controlled double-blind functional magnetic resonance imaging (fMRI) study therefore aimed at determining the effects of intranasal OXT on competing behavioral tendencies between empathy-motivated altruism and self-interest. A Cyberball paradigm was employed where subjects initially observed a social exclusion situation and subsequently engaged in the game. The Cyberball game is widely used to induce social exclusion leading to painful feelings (Williams, 2009) and can induce social pain empathy when observing others being excluded (Wesselmann et al., 2009) and prosocial behavior towards them (Masten et al., 2011). This paradigm is also effective in capturing effects of OXT on social behaviors, for example, increasing social interactions with a reciprocal player in high-functioning autism spectrum disorders (Andari et al., 2010) and motivation to restore social connections with negative players in men (Xu et al., 2017).

In the current paradigm, participants were scanned while first observing 3 unknown individuals playing the game and where 1 player (victim) was gradually excluded by the other 2 (excluders), thereby gaining more money than the victim. Immediately after the observe session, participants played with the victim and one of the excluders as well as another new player. To create a situation of competing empathy and self-interest, participants were told that any player receiving a ball would receive a small additional monetary reward. In this case, the excluder player was manipulated to be the most attractive cooperator to maximize self-interest, while playing with the victim of exclusion would be rather motivated by empathy-induced altruistic behavior.

Considering convergent evidence for OXT-enhanced emotional empathy, we hypothesized that it would increase empathy for the victim of exclusion. We additionally hypothesized that OXT-facilitated empathy would be accompanied by increased activation in (social) pain (dorsal anterior cingulate cortex [dACC] and anterior insula) and mentalizing networks (medial frontal cortex, posterior superior temporal sulcus [pSTS], posterior cingulate cortex [PCC], and precuneus) (Eisenberger et al., 2003; Masten et al., 2011). In the second stage of the experiment when the subjects played, we hypothesized that if OXT promotes costly altruistic behavior subjects should increase their proportion of throws to the victim and throw less to the excluder, whereas if it promotes increased self-serving behavior then they would throw more to the excluder player, indicating an increased interest in personal financial gain. Given the engagement of striato-orbitofrontal reward-processing circuits in both monetary reward-anticipation (O'Doherty et al., 2001) and altruistic behavior (FeldmanHall et al., 2015) we hypothesized that the OXT-induced behavioral preference for a player would be mirrored by increased activity in this circuit. Since cultural orientation, that is, horizontal independence (HI), has been shown to modulate the effect of OXT following social exclusion (Xu et al., 2017), and higher trait altruism is associated with stronger empathic brain responses (Haas et al., 2015), these traits were additionally assessed. Finally, in view of our previous study demonstrating long-term effects on memory and preference for replaying with specific players (Xu et al., 2017), we also investigated these same factors 1 week later.

Methods

Participants

A total of 82 healthy Chinese male university students (right-handed, age = 18–27 years, mean ± SE = 21.36 ± 0.24 years) were recruited and randomly assigned to receive either PLC (n = 41, age = 18–26 years, mean ± SE = 21.68 ± 0.34 years) or OXT nasal spray (n = 41, age = 18–27 years, mean ± SE = 21.05 ± 0.34 years; PLC vs OXT, $t = 1.31$, $P = .195$) in a double-blind between-subject experiment. The chosen sample size can detect a medium effect size of 0.62 with 80% power (G-power). Subjects reported being free from current or a history of psychiatric or neurological disorders and did not use any medication in the 4 weeks before the experiment and were asked to abstain from caffeine and alcohol in the 24 hours before.

Study procedures were approved by the local ethics committee at the UESTC and adhered to the latest revision of the Declaration of Helsinki. Each participant provided written informed consent before the experiment and received monetary compensation for participation (180 RMB). Study protocols were preregistered at clinical trials.gov (https://www.clinicaltrials.gov/ct2/show/NCT03122067, Trial ID: NCT03122067). For Consort Flow diagram, see Figure 1.

Procedure

To control for potential confounding effects of pretreatment differences in affective state and empathy-related domains, questionnaires to assess mood (Positive and Negative Affect Schedule, PANAS) (Watson and Clark, 1988), anxiety (State-Trait Anxiety Inventory, Barnes et al., 2002; Liebowitz Social Anxiety Scale, Heimberg et al., 1999), depression (Beck Depression Inventory) (Beck et al., 1996), trait autism (Adult Autism Spectrum Quotient) (Baron-Cohen et al., 2001), trait empathy (Interpersonal Reactivity Index-C), and early-life stress (Childhood Trauma Questionnaire) were administered. In line with our previous study on the effects of OXT on social exclusion (Xu et al., 2017), we explored associations with the HI scale of the Individualism and Collectivism Scale. In the context of previously reported associations between trait altruism and empathic brain activity (Haas et al., 2015), we additionally explored associations between the effects of OXT and the level of pretreatment altruistic prosocial behavior using the altruistic subscale of the Prosocial Tendency Measure (PTM), which assesses concerns about individuals in need of help that incurs a cost to the helper (Carlo and Randall, 2002). Mood (PANAS) was additionally assessed after the experiment to control for unspecific effect of treatment on these domains.

After subjects completed the questionnaires, portrait photos with neutral facial expressions were taken of them for use during the subsequent Cyberball game. Finally, subjects were asked to rate portrait photos with neutral facial expressions of their fellow players in the experiment for likeability, trustworthiness, and valence using a visual analogue scale (0–100). Subjects next self-administered 24 IU OXT (Oxytocin-spray,

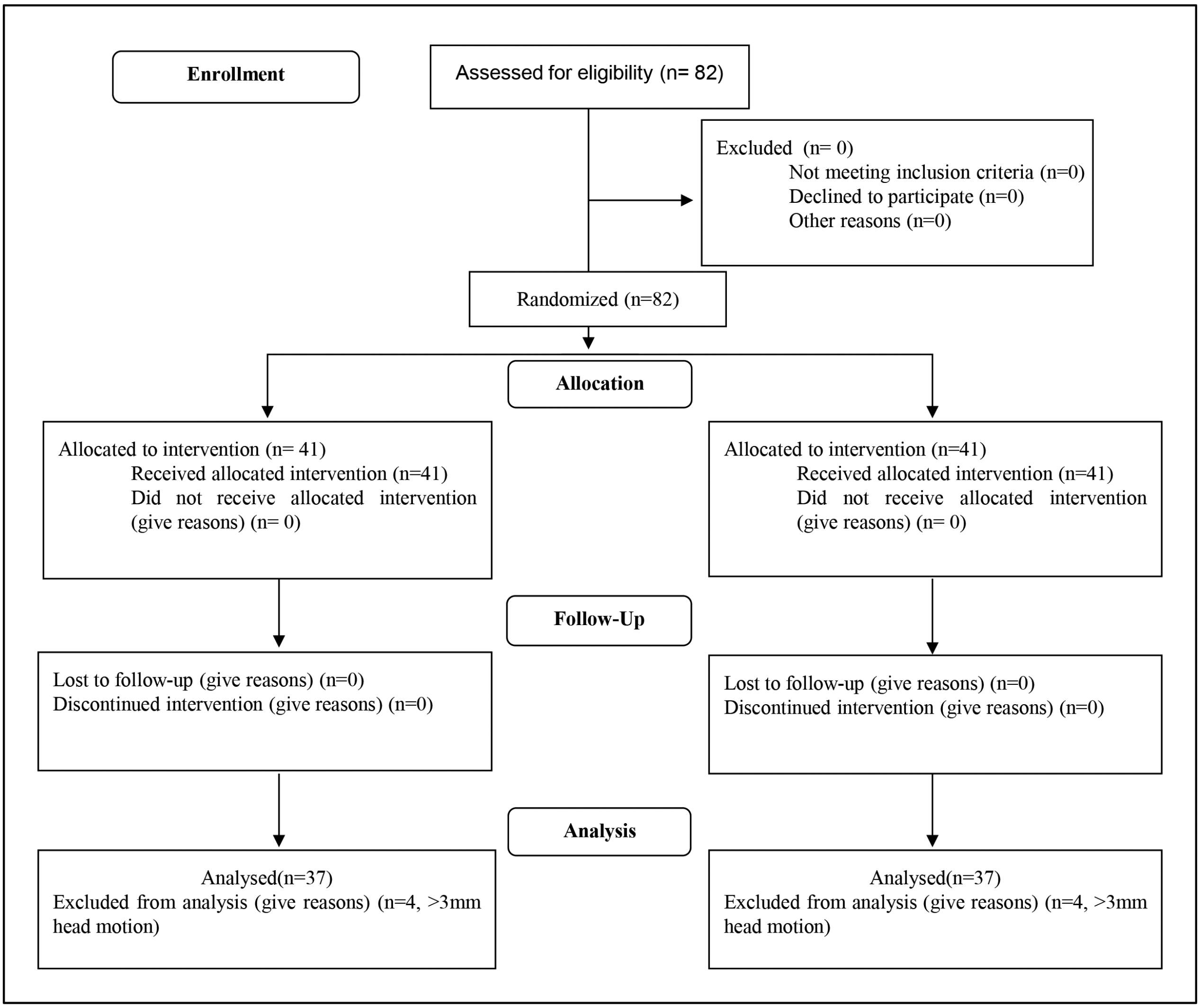

Figure 1. Consort flow diagram for the clinical trial.

Sichuan Meike Pharmaceutical Co., Ltd; 3 puffs of 4 IU per nostril with 30 seconds between each puff) or PLC (identical sprays with the same ingredients other than OXT, i.e., sodium chloride and glycerol) 45 minutes before the start of the experimental paradigm in accordance with a standardized protocol for intranasal OXT administration (Guastella et al., 2013).

Modified Cyberball Paradigm

Participants were told they would first observe and then participate in a ball-tossing game (Cyberball) with 4 other individuals online while they were in the fMRI scanner and that the other players were sitting in separate compartments in a nearby behavioral testing room to avoid direct personal interaction during the entire experiment. However, the 4 other players were in fact fictitious and preprogrammed in the experimental paradigm. The revised Cyberball task included 2 sessions acquired during separate fMRI runs. The first session (OBSERVE condition) aimed to prime the subject's attitude towards each of the players observed (victim or excluder, see Figure 2a) in order to influence their subsequent behavior when they participated in the game during the second session (Play condition, see Figure 2b). During the Observe run, subjects simply observed 3 individuals playing the game and were told that each player would receive 0.3 RMB reward for every ball thrown to them. Subjects were explicitly instructed to observe the game and to consider what each player might be thinking or feeling during it (Masten et al., 2011). The first run (Observe) contained 10 blocks with each block lasting for 30 seconds, starting with 4 "fair" blocks during which the 3 players threw the ball equally often to each other, followed by 2 "transition" blocks during which 1 of the players was gradually excluded, and 4 "exclusion" blocks during which 1 player (victim) was totally excluded by the other 2 players (excluder 1 and excluder 2). After each round, the subject was shown how much money each of the 3 players had gained (displayed for 12 seconds). In this way, the subject observing the game was expected to detect that one of the players (victim) was eventually excluded by the 2 other players (excluders) and that the result of this was the 2 excluders had learned that by throwing only to each other they ended up gaining more money at the expense of the victim who gained less. The actual increased financial gain that subjects could observe the excluder players receive relative to the victim was 11 RMB, which was approximately double (19 vs 8 RMB respectively). The second run (Play) involved the subject and 3 other players, including the victim, 1 excluder (1 or 2) from the first run and a new player, and comprised 6 rounds with a fixed number of 24 ball throws per round. All virtual players were programmed to throw the balls equally to the other 3 players. Subjects were told that during the first 4 rounds they would be informed how much each player would have gained

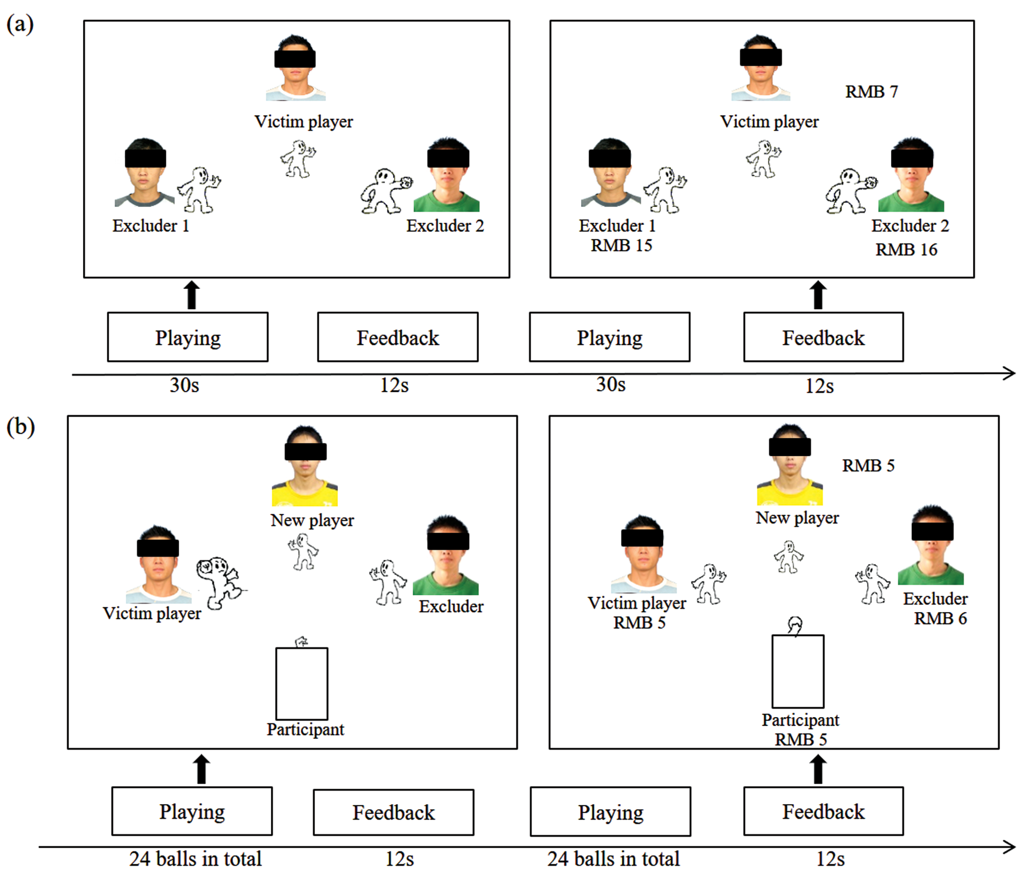

Figure 2. The Cyberball game paradigm employed. (a) Subjects first completed an "Observe" session that included a total of 10 blocks (4 blocks where players threw equally to each other followed by 2 blocks where 2 players [excluders] started to throw more often to each other and finally 4 blocks where the excluders threw exclusively to each other and did not throw to the other player [victim] at all). Blocks lasted for 30 seconds; during a 12-second period between each block the subjects viewed how much money each of the players had won. Subjects were instructed during their observation of the game to consider what the individuals playing it were thinking and feeling. (b) Subjects next completed a "Play" session where they played the game together with the victim and one of the excluders and a novel player. This session was for 6 blocks with 24 ball throws in each block (after each block the subject could see how much money they and the other players had won, and a 2-second maximum was allowed to throw the ball to avoid a monetary deduction).

(0.3 RMB per ball received—amount gained per player was displayed for 12 seconds) but that they would only actually receive the monetary reward from the final 2 rounds. This meant that subjects could effectively only earn a maximum extra amount of 7.2 RMB, although in reality all subjects actually received the same additional sum of 5 RMB. This strategy allowed us to additionally assess whether subjects' responses were influenced by whether their behavior directly gained them a monetary reward. To confirm whether the pattern of throwing was in fact different when a monetary incentive was included, we initially explored potential interaction effects between treatment and the monetary condition (i.e., first 4 vs last 2 blocks). No main effect of monetary condition or interaction effects with treatment were found (see supplementary information), and consequently this factor was not analyzed further.

As a manipulation check, subjects were asked to rate the other players' likeability, trustworthiness, and valence using a visual analogue scale (0–100) before treatment administration and following the OBSERVE and PLAY sessions respectively. Subjects were also asked to report if any specific events had happened during the Observe session (e.g., "Did all 3 players treat each other fairly?", "Was there anyone who was treated unfairly?") and to rate how empathic they felt towards the excluded player (0–100). As an additional control variable, the PANAS questionnaire was administered again to test whether OXT had altered participants' mood after the paradigm.

Long-Term Effects of OXT: Follow-up After One Week

Subjects were asked to return to the laboratory to complete follow-up assessments 1 week after the Cyberball game. The assessment included ratings of the other players with respect to likeability, trustworthiness, and valence. Moreover, a surprise memory test was employed to examine if the previous Cyberball game had an effect on social recognition memory and whether this was influenced by OXT. Subjects were asked if they would play with the previous players again and rated how much they wanted to (on a 1–9 scale). When subjects had completed their ratings they were asked an open question if they had any comments about how they perceived the experiment. Only 3 subjects (2 in the OXT group and 1 PLC) voiced some suspicion as to whether there were actually other players involved, suggesting that overall the majority of subjects were convinced of the reality of the situation. We chose not to exclude data from these 3 subjects from the final analysis, however.

Behavioral Data Analyses

Statistical analyses for the questionnaires and behavioral ratings were performed using SPSS 18.0 software (SPSS Inc., Chicago, IL). Post hoc analyses of interaction effects were performed employing Bonferroni correction for multiple comparisons. Associations between traits, behavior, and neural indices were examined using Pearson correlation and group differences correlations examined using Fisher's Z test with Bonferroni correction.

Image Acquisition

Imaging data were collected using a 3T GE Discovery MR750 system (General Electric, Milwaukee, WI) with the following sequence parameters: repetition time (TR) = 2000 milliseconds; echo time (TE) = 30 milliseconds; flip angle = 90°; number of slices = 43; slice thickness = 3.2 mm; field of view (FOV) = 220 × 220 mm^2; matrix = 64 × 64; slice orientation = axial. High-resolution whole-brain T1-weighted images were additionally acquired using a spoiled gradient echo pulse sequence to improve normalization of the functional data (TR = 6 milliseconds; TE = 2 milliseconds; flip angle = 12°; number of slices = 156; slice thickness = 1 mm; FOV = 256 × 256 mm^2; matrix = 256 × 256).

fMRI Data Analysis

Statistical Parametric Mapping as implemented in SPM12 (http://www.fil.ion.ucl.ac.uk/spm/) was used to preprocess and analyze the neuroimaging data. The first 6 volumes of each functional neuroimaging time-series were removed to allow for T1 equilibration. Preprocessing included slice timing, image realignment to correct for head motion, normalization into the Montreal Neurological Institute space resampled at 3 × 3 × 3 mm voxel size, and spatially smoothed using an 8-mm FWHM Gaussian kernel. Generalized linear models were built to investigate the BOLD signal changes. A 128-second high-pass filter was applied to further control for low-frequency noise artifacts.

The first-level design matrix for the OBSERVE run was modelled using a blocked-design matrix including the first 4 blocks as the inclusion condition and the last 4 blocks as the exclusion condition. The monetary reward feedback and the middle 2 blocks with the transfer between inclusion and exclusion were additionally modelled and the 6 head motion parameters included.

The first-level design matrix for the PLAY run was modelled using an event-related design matrix to specifically examine the throws made by the participant to the other individual players. Ball-tosses towards the excluder, victim, and new player were implemented as experimental conditions and modelled as separate events. To specifically model the expectation phase for a reciprocal action, independent from the decision phase, the time between the other player receiving the ball from the participant and the throw of that player was modelled as experimental event. Monetary feedback, rating periods, and head motion parameters were additionally included in the matrix.

Due to technical issues during the fMRI assessment and excessive motion (>3 mm), data from 8 participants had to be excluded (OXT = 4, PLC = 4), leading to a final sample size for the fMRI analysis of OXT = 37 and PLC = 37. Effects of OXT during the OBSERVE and PLAY sessions were assessed by employing independent *t* tests. In line with the main aim of the study, the contrast (exclusion > inclusion) was used for the OBSERVE condition, and for the PLAY condition player-specific contrasts were examined (excluder, victim, new player). The threshold *P* value level was set at <.05 cluster-level with family wise error (FWE) correction for multiple comparisons and an initial cluster-forming threshold at the voxel-level of $P < .001$, uncorrected (see Eklund et al., 2016; Slotnick, 2017).

Results

No significant differences between subjects in the PLC and OXT groups were found in pretreatment affective state and empathy-related domains (independent *t* tests, Table 1). Importantly, mood as assessed by the PANAS did not differ after the experiment, arguing against unspecific confounding effects of treatment on mood.

Effects of Perceived Social Exclusion and OXT on Player Ratings

A 2 (treatment: OXT/PLC) × 3 (player: excluder/victim/new) mixed ANOVA with subjects' likeability, trustworthiness, and valence

Table 1. Questionnaire scores in PLC and OXT groups before and after treatment

Measurements	Placebo	Oxytocin	t-Value	P value
Before treatment				
Positive and Negative Affect Schedule (PANAS)				
Positive	29.15 ± 1.10	28.93 ± 0.79	0.16	.87
Negative	15.20 ± 0.79	14.29 ± 0.75	0.83	.41
State-Trait Anxiety Inventory (STAI)				
State	37.68 ± 1.44	36.93 ± 1.32	0.39	.70
Trait	37.63 ± 1.20	39.56 ± 1.22	−1.13	.26
Liebowitz Social Anxiety Scale (LSAS)				
Avoid	19.85 ± 1.40	21.56 ± 1.31	−0.89	.38
Fear	22.56 ± 1.53	20.2 ± 1.34	1.16	.25
Beck Depression Inventory (BDI-II)	5.41 ± 1.32	6.10 ± 1.09	−0.40	.69
Adult Autism Spectrum Quotient (ASQ)	20.51 ± 0.70	18.76 ± 0.80	1.64	.10
Interpersonal Reactivity Index (IRI)	39.76 ± 0.99	40.29 ± 1.03	−0.38	.71
Childhood Trauma Questionnaire (CTQ)	56.20 ± 0.80	56.00 ± 0.91	0.16	.87
Individualism and Collectivism Scale (ICS)	5.31 ± 0.11	5.36 ± 0.12	−0.31	.76
Prosocial Tendency Measure (PTM)-altruism	15.93 ± 0.43	16.76 ± 0.40	−1.41	.16
After treatment				
PANAS-Positive	25.68 ± 1.48	24.46 ± 1.19	0.64	.52
PANAS-Negative	12.85 ± 0.57	13.60 ± 0.86	−0.73	.47

rating scores as dependent variables revealed no significant main effect of treatment group or type of player or interactions before the experiment (likeability: player $F_{2,160}$=0.22, P=.81; treatment $F_{1,80}$=0.15, P=.70; interaction $F_{2,160}$=0.72, P=.49; trustworthiness: player $F_{2,160}$=0.25, P=.78; treatment $F_{1,80}$=0.15, P=.71; interaction $F_{2,160}$=0.35, P=.71; valence: player $F_{2,160}$=1.03, P=.36; treatment $F_{1,80}$=0.57, P=.45; interaction $F_{2,160}$=0.27, P=.76; Figure 3a). However, after the Observe session during which subjects watched the victim player being excluded, there were significant main effects of player but no treatment main effects or interactions (all Ps>.27) due to ratings of the victim players being higher than those for excluder players for all 3 dependent variables (likeability: player $F_{1,80}$=37.25, P<.001, η^2_p=.32; excluder=44.87±1.80, victim=59.26±1.76, P<.001, Cohen's d=0.90; trustworthiness: player $F_{1,80}$=16.10, P<.001, η^2_p=.17; excluder=49.86±1.91, victim=59.85±1.67, P<.001, d=0.62; valence: player $F_{1,80}$=4.31, P=.04, η^2_p=.05; excluder=53.31±1.76, victim=58.33±1.72, P=.04, d=0.32; Figure 3b), confirming successful experimental manipulation. Moreover, the decreased ratings for the excluders remained stable after subjects played with them during the PLAY run, except for valence (likeability: $F_{2,160}$=17.92, P<.001, η^2_p=.18, excluder=54.25±1.39, victim=57.74±1.70, new=61.43±1.47, excluder vs victim P=.01, d=0.25, excluder vs new P<.001, d=0.56, victim vs new P=.02, d=0.26, trustworthiness $F_{2,160}$=7.83, P<.001, η^2_p=.09, excluder=56.95±1.32, victim=57.80±1.66, new=62.00±1.52, excluder vs new P=.001, d=0.39, victim vs new P=.01, d=0.29; valence $F_{2,160}$=1.38, P=.26, η^2_p=.02). There were no main treatment or interaction effects (Ps all >.26). Furthermore, the effect of the manipulation remained stable after 1 week with continued main effects of player (likeability $F_{2,160}$=6.06, P=.003, η^2_p=.07; excluder=53.28±1.51, victim=59.38±1.94, new=57.70±1.88, excluder vs victim P=.002, d=0.39, excluder vs new P=.03, d=0.29; trustworthiness: $F_{2,160}$=6.97, P=.001, η^2_p=.08, excluder=54.41±1.42, victim=60.65±1.91, new=60.24, excluder vs victim P=.004, d=0.41, excluder vs new P=.004, d=0.38; valence $F_{2,160}$=4.36, P=.01, η^2_p=.05, excluder=58.34±1.51, victim=63.23±1.73, P=.004, d=0.33; Figure 3c–d).

Manipulation Check and Empathic Responses

At the end of the experiment, all subjects reported that they realized 1 player was excluded during the Observe session, further confirming successful manipulation. To examine the effects of OXT on subjects' empathy scores for the victim player, an independent 2 sample t tests was performed but revealed no significant differences between the treatment groups (PLC=63.62, OXT=58.97, t=0.98, P=.33, Cohen's d=0.224).

Behavior During the Play Phase of the Paradigm

For the Play condition, the percentage of ball tosses to each of the other 3 players served as the dependent variable and was subjected to a 2 (treatment: PLC/OXT)×3 (players: excluder/victim/new) mixed ANOVA. Results revealed a main effect of player ($F_{2,160}$=7.05, P=.001, η^2_p=.081) and a marginal significant interaction effect between treatment and player ($F_{2,160}$=2.74, P=.068, η^2_p=.033). Post hoc Bonferroni-corrected paired comparisons showed that subjects in both groups threw more balls to the victim than to the excluder players (victim=36.7%, excluder=30.28%, P=.002, Cohen's d=0.690). Further exploratory analysis of the interaction effect demonstrated that the OXT group threw significantly more balls to the excluder player relative to the PLC group (to excluder player: PLC=27.97%, OXT=32.60%, t=−2.46, P=.016, Cohen's d=0.543; Figure 4). In terms of the actual money subjects in the 2 groups earned during the final 2 rounds, there was no significant difference (PLC=3.45±0.03 RMB, OXT=3.49±0.03 RMB, t=−1.02, P=.31). All subjects actually received the same additional amount (5 RMB) at the end of the experiment.

Neural Activation Changes During the Cyberball Task

The task-related network engaged during the observation of social exclusion and effects of OXT on the underlying neural activity (contrast, exclusion>inclusion) were firstly investigated during the Observe session. Analysis of neural changes during the Observe session in the combined PLC and OXT groups at the whole brain level revealed significantly increased activity in the PCC, left midcingulate cortex, precuneus, left inferior parietal lobule, and right pSTS when subjects observed the victim being excluded (see supplementary Table 1; supplementary Figure 1). In line with the lack of OXT effects on the post Observe

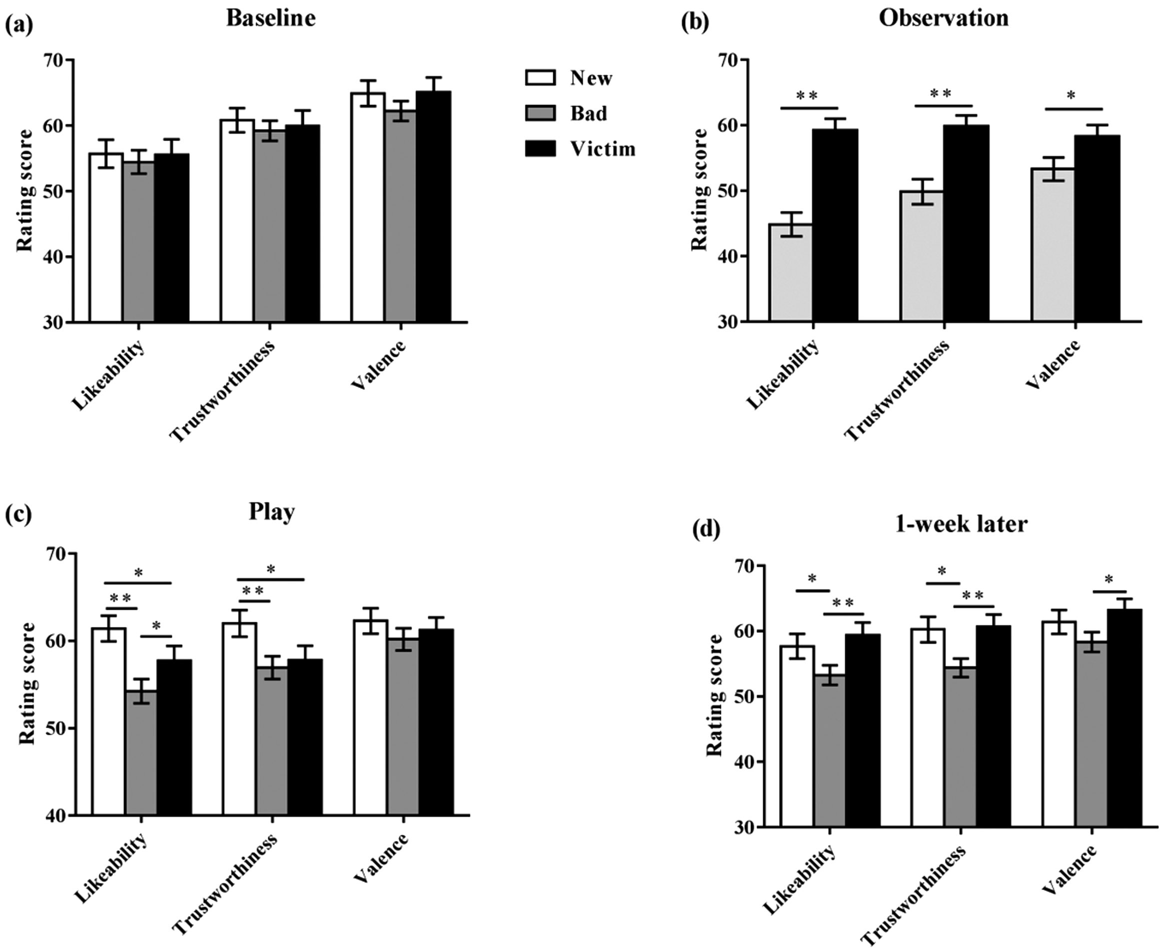

Figure 3. Rating scores of likeability, trustworthiness, and valence in combined oxytocin and placebo-treated groups for (a) before treatment, (b) after treatment during the Observe session, (c) after Play session, (d) 1-week after treatment and observing and playing the Cyberball game. *$P < .05$, **$P < .005$.

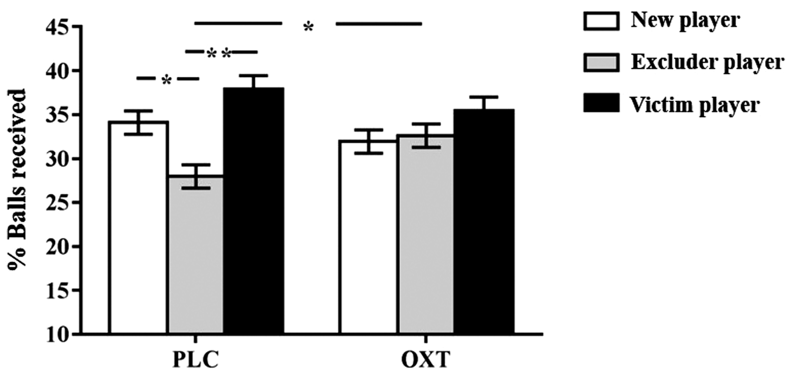

Figure 4. Percentage (mean ± SEM) of balls that participants threw to the excluder, new, and victim players, respectively. *$P < .05$, **$P < .005$.

behavioral ratings, no significant neural differences were observed between the treatment groups. Thus, any group differences during the subsequent Play session were unlikely to be driven by effects of OXT during the preceding encoding phase of the social interaction.

For the Play session, a 2 (treatment: PLC/OXT) × 3 (player: excluder/victim/new) mixed ANOVA using the flexible factorial model in SPM was performed on the whole brain level, but no significant results were found (FWE-corrected $P < .05$). Based on the behavioral results indicating that OXT administration specifically increased the proportion of throws made to the excluder player, an independent *t* test was performed to examine neural activity differences between the treatment groups during this condition. Results at the whole brain level indicated regional-specific significantly stronger left medial orbitofrontal cortex (mOFC) activity ($k = 106$, $t = 4.40$, x/y/z: −6/24/−6, $P = .047$; Figure 5) when playing with excluder players in the OXT group compared with the PLC group (FWE-corrected $P < .05$). In line with the behavioral findings, exploratory *t* tests revealed no significant treatment effects on neural activity when playing with the victim or the new player (both Ps > .348).

Associations Between Trait Altruism Behavior Ratings and Neural Activity

A potential modulatory influence of pretreatment variations in trait altruism (PTM scores) on behavioral and neural responses was investigated using a correlation analysis. No significant associations between the proportion of balls thrown to the 3 different players and PTM scores were found in either the PLC (excluder: r = –0.172, P = .283; victim: r = 0.091, P = .57; new: r = 0.075, P = .64) or OXT (excluder: r = –0.131, P = .413; victim: r = 0.227, P = .154; new: r = –0.114, P = .478) group or differences between the groups (all Ps > .41). Correlations between left mOFC activity and PTM scores during play with the excluder were also examined in the PLC and OXT groups. Results revealed that PTM scores were negatively associated with mOFC activity following OXT but not PLC and that the difference between the groups was also significant (PLC: r = 0.294, P = .094; OXT: r = –0.329, P = .047; Fisher's z = 2.59, P = .040, Cohen's q = 0.28, Bonferroni corrected; Figure 6). This shows that OXT particularly increased left mOFC activity in individuals with lower trait altruism. HI was not associated with either behavior or mOFC activity.

Follow-up Assessment After One Week

Accuracy on memory for the faces of the different players was assessed in both groups during a surprise recognition memory test 1 week after the initial Cyberball games; however, both groups achieved a very high accuracy (all OXT-treated subjects scored 100% accuracy as did 38/41 of the PLC-treated ones) and so no meaningful statistical comparison could be conducted. A 2 (treatment: PLC/OXT) × 3 (player: excluder/victim/new) mixed ANOVA using the willingness to replay rating scores as a dependent variable revealed a main effect of player ($F_{2,160}$ = 10.46, P < .001, η^2_p = .116), with subjects reporting a stronger preference to play with the victim and new players again compared with the excluder players (excluder = 3.36 ± 0.27 vs victim = 4.89 ± 0.32, P = .002, Cohen's d = 0.562; excluder vs new = 4.93 ± 0.29, P < .001, d = 0.611). A treatment × player interaction ($F_{2,160}$ = 3.55, P = .031, η^2_p = .042) showed additionally that whereas subjects in the PLC group were significantly less willing to play again with excluders compared with the victim or new players (excluder vs victim, excluder vs new, both post hoc Ps < .005), this was not the case in the OXT group (both Ps > .097).

Discussion

The current study aimed firstly to establish whether OXT enhanced empathic behavior and neural responses towards observing someone being socially excluded, and secondly promoted altruistic or self-serving behaviors and associated neural responses when these 2 behaviors are in competition. Overall, following observation of a modified Cyberball game, both groups showed strong empathic responses towards the victim players and greater likeability and trustworthiness ratings for them compared with excluder players, but OXT did not potentiate this. Observation of social exclusion was accompanied by increased activity in the mentalizing network, including the PCC, pSTS, IPL, and precuneus; however, activity patterns were also not influenced by OXT. During the subsequent play phase of the paradigm, subjects in both groups threw more balls to the victim

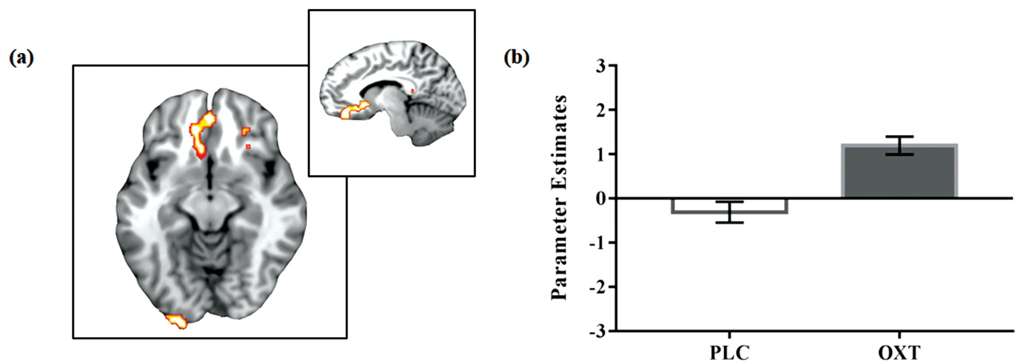

Figure 5. (a) Neural response to excluder player under oxytocin (OXT) > placebo (PLC). P < .05 (family wise error [FWE] corrected, cluster level). (b) Corresponding beta parameters of the left medial orbitofrontal cortex (mOFC) in the PLC and OXT groups.

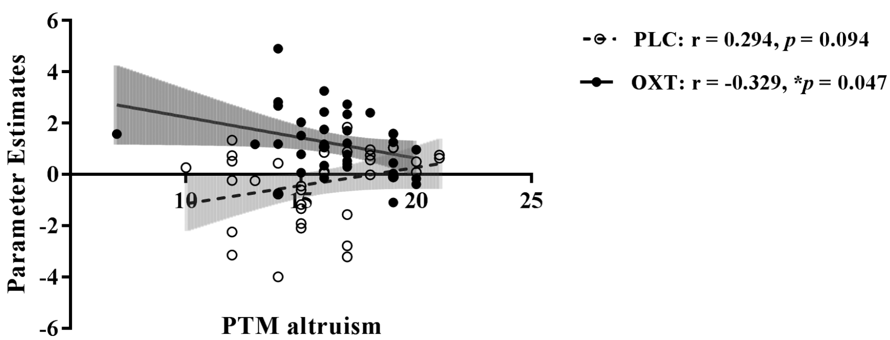

Figure 6. Correlations between pretreatment trait altruism score (PTM) and neural activity when interacting with the excluder player in the placebo (PLC) and oxytocin (OXT) treatment groups. Best-fit line with 95% confidence bands, *P < .05.

player, but this was not enhanced by OXT, suggesting that it did not promote greater altruistic behavior. However, the OXT group threw significantly more balls to the excluder players, suggesting that OXT promoted self-serving decisions since playing with the excluder should potentially lead to a higher monetary pay-off. In line with our hypothesis, increased self-serving behavior following OXT was associated with stronger activation in the mOFC reward system when subjects were playing with the excluder player. Furthermore, OXT established a negative relationship between mOFC activity and trait altruism, an association that was absent following PLC. One week after the Cyberball game while the PLC group expressed a greater preference to play again with the victim and novel players compared with the excluder, in the OXT group there was no such difference, indicating that they maintained their greater interest in playing with individuals who might potentially help them gain larger rewards. Thus, overall, our results demonstrate that when altruistic and self-serving motivations are in competition, OXT rather than promoting altruism actually enhances selfish decision-making.

Our hypothesis that OXT would enhance empathic responses towards the victims of social exclusion was not supported. Previous research showed that OXT enhanced emotional but not cognitive empathy, associated with suppressed amygdala responses (Hurlemann et al., 2010; Geng et al., 2018a). Oxytocin also increased empathic embarrassment in male and female subjects, and this was associated with decreased amygdala and insula cortex responses but with no effect on mentalizing networks (Geng et al., 2018b). Empathic embarrassment can be considered as an example of social pain, and another study has also reported that OXT decreased insula responses to viewing people in pain (Bos et al., 2015). In the current study in both the PLC and OXT groups, there was evidence at the whole brain level for increased activation in core mentalizing regions (for convergent findings, see also Masten et al., 2011) but no responses in the pain network (notably the insula).

In general, empathic ratings by subjects for the victim were not that high and altered activation was only observed in the mentalizing network which we have shown in the context of empathic embarrassment is not influenced by OXT (Geng et al., 2018b). The empathy experienced in the current context may therefore have been more cognitive than emotional. Indeed, since participants could not directly observe the other players and static neutral faces were used, social pain had to be inferred by mentalizing how the victim may emotionally experience exclusion. Since the mentalizing system is a core component of the cognitive empathy (Shamay-Tsoory et al., 2009), this may explain why OXT failed to have any impact on empathic ratings or associated likeability and trustworthiness ratings for the victim due to its greater influence on emotional rather than cognitive empathy.

Our original hypothesis that where altruistic and self-serving motivations were in competition OXT would enhance altruistic responses was also not supported. Overall, while participants in both groups threw more balls to the victim player, indicative of an altruistic response and validating the experimental manipulation, OXT had no effect on this. Similarly, both groups rated the likeability and trustworthiness of excluder players lower than that of victims after observing the game and also 1 week later after playing it, but again this was not influenced by OXT. This finding agrees with previous studies showing that subjects exhibit greater prosocial behavior towards individuals observed to be socially excluded (Masten et al., 2011; Van Der Meulen et al., 2016). On the other hand, subjects in the OXT group threw a significantly greater proportion of balls to the excluder player, indicative of an enhanced self-serving motivation since the latter would have been perceived as being more likely to reciprocate, leading to greater financial gain. A previous study has reported that OXT can enhance strategic reasoning in decision-making (Aydogan et al., 2018), and it is possible that our current results could also reflect an OXT effect on strategic decision-making. However, in the current paradigm the obvious strategy for subjects to gain more money had already been clearly demonstrated to them by the excluder players during the observation session. Furthermore, after the observation session all subjects revealed awareness of this strategy since they identified the differences in the relative gains obtained by excluders as opposed to the victim. Thus, during the Play session it would seem more likely that OXT was only influencing whether subjects decided to use this prior-demonstrated strategy to gain their additional personal monetary reward.

While a number of previous studies have demonstrated that OXT can facilitate altruistic behaviors in terms of cooperation, generosity, trait judgements and valuing other's possessions, these have mainly involved contexts where personal costs to individuals were absent or low (Andari et al., 2010; Declerck et al., 2010; Zhao et al., 2016, 2017). The finding that under circumstances where there is perceived to be a potential cost of altruism in terms of reduced personal gain argues for the primary function of OXT as enhancing the motivation for resource acquisition. Where individuals do exhibit costly altruistic behavior, this is paralleled by increased empathic concern and altered activation in the ventral tegmental area, caudate, and subgenual anterior cingulate, which are important for promoting social attachment and caregiving (FeldmanHall et al., 2015). Although OXT has been shown to modulate neural processing in these regions in social and nonsocial contexts (e.g., Mickey et al., 2016; Zhao et al., 2019), it did not affect activity in this circuitry during the present paradigm, further indicating its lack of effect on promoting altruism.

Previous studies have reported that OXT can promote lying to benefit in-group members, although not purely for self-gain (Shalvi and De Dreu, 2014), and reduce honesty for personal gain in a competitive environment (Aydogan et al., 2017b). However, OXT can also promote pure self-serving lying to increase personal gain when there is no risk of discovery (Sindermann et al., 2018) and increase acceptance of self-benefit, but not other types of moral dilemmas (Scheele et al., 2014). Interestingly, OXT effects on self-serving lying for financial gain are modulated by OXT receptor genotype (Sindermann et al., 2018). Taken together and in line with our current results, accumulating evidence therefore suggests that OXT can promote personal self-interest in some contexts.

On the neural level, increased self-serving behavior following OXT was associated with increased mOFC activation when subjects interacted with excluder players. The mOFC is involved in monitoring associations between previous stimuli with reward and tracking response-outcome probabilities during changing reward contingencies (Elliott et al., 2000; Kringelbach and Rolls, 2004). Moreover, the mOFC codes the value of different behavioral options including that of expected monetary gains (Breiter et al., 2001) and its activity increases with monetary reward magnitude (O'Doherty et al., 2001). Thus, increased mOFC responses in the OXT group may reflect an enhanced value of the expected greater monetary reward when cooperating with the excluder player. Our findings are in line with previous studies demonstrating that OXT enhances activity in brain reward regions in social contexts, such as when viewing a romantic partner's face (Scheele et al., 2013; nucleus accumbens and ventral tegmentum), receiving affective touch (Scheele et al., 2014; orbitofrontal cortex); and receiving social feedback to promote learning (Hu et al., 2015; putamen). One study has also reported that OXT increases activity in the putamen during monetary reward and loss anticipation (Nawijn et al., 2016), and oxytocin receptors are known to be strongly expressed in the human brain reward system (Quintana et al., 2019).

Additionally, OXT produced a negative association between PTM trait altruism and mOFC activation that was absent following PLC. This suggests that at the neural level OXT particularly increased the value of the potential monetary gain in subjects with low baseline altruistic tendencies. Possibly individuals with high trait altruism are less likely to experience a greater anticipation of gaining a greater monetary reward by playing with the excluder under OXT, as a result of greater feelings of guilt evoked by having to exclude other players, and notably the victim.

While both behavioral and neural effects of OXT observed in the current paradigm indicate a shift towards a self-serving rather than altruistic motivation it is notable that the pattern of altered bias is quite subtle. Under OXT, subjects do not actually play more with excluders than with either victim or novel players and effectively exhibit an egalitarian playing pattern that is unlikely to generate feelings of exclusion in any of the other players. This contrasts with the PLC group who show a clear pattern of excluding the excluders compared with both victim and novel players. Thus, OXT may only promote self-benefit behavior if it does not damage others and cause feelings of guilt. Indeed, this is supported by findings that OXT increases lying for self-gain when individuals know that there is no chance their lies will be discovered or will reduce the financial gain of others (Sinderman et al., 2018). Alternatively, it might be argued that subjects in the PLC group are exhibiting altruistic punishment towards the excluders and OXT is reducing the desire to inflict such punishment. However, altruistic punishment is strongly associated with altered amygdala function (Scheele et al., 2012), and there was no evidence for differential amygdala responses in the PLC and OXT groups. While OXT can promote altruistic punishment of defectors, and feelings of anger and disappointment towards them in the Prisoner's dilemma game, it also increases cooperation with them thereby increasing self-gain (Aydogan et al., 2017a). Thus, in the current context OXT may primarily bias individuals towards an optimal self-gain strategy, although without simultaneously doing so by overtly damaging others emotionally. Clearly, to further establish this it would be necessary to investigate the effects of OXT under circumstances where increasing self-gain would also significantly damage others emotionally.

There are several limitations to the present study. Firstly, the victim observed being excluded in the game was a stranger to the participant and if they had been a partner, relative, or other in-group member then OXT may have had the opposite effect by enhancing empathic and altruistic behaviors rather than self-serving ones. Secondly, only male participants were included and a number of studies have reported opposite neural and behavioral effects of OXT in males and females (Scheele et al., 2014; Gao et al., 2016; Luo et al., 2017). Thus, in a similar situation OXT may have facilitated altruistic rather than self-serving behavior in women. Thirdly, the Cyberball game is an online dynamic virtual game intended to simulate real social interactions and subjects may not be completely convinced that they are interacting with others. Importantly though, only 3 subjects questioned afterwards if the other players involved were in fact real, whereas the majority involved in the study did not do so, suggesting that they did believe they were real. Nevertheless, it remains possible that if interactions with other players were direct face to face results might have been different. Lastly, the Cyberball paradigm can incorporate additional factors, such as deception and anxiety about being ostracized by others. As such, it may not exclusively examine altruistic and selfish behaviors, although we showed no differential effects of treatment on subjects' mood during the course of the experiment. Future studies may consider employing additional paradigms to elicit altruistic and selfish behaviors.

In summary, our current findings demonstrate that when self-serving and altruistic behaviors are in competition OXT promotes increased self-benefit behavior associated with increased activation in the mOFC, indicative of greater reward anticipation. Furthermore, the effects of OXT on mOFC are strongest in individuals with lower trait altruism. Thus, OXT tends to bias individuals towards acquisition of resources for self-benefit rather than altruistic behavior, although this may not extend to the point where it generates strong negative feelings in others or feelings of guilt and risk of punishment for social norm violations.

Supplementary Materials

Supplementary data are available at International Journal of Neuropsychopharmacology (IJNPPY) online.

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Statement of Interest

None.

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