Intranasal Oxytocin Reduces Attentional Bias to Food Stimuli

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Abstract

Attentional biases to food-related stimuli have been demonstrated in response to hunger as well as during restrained eating. Such biases are often associated with obesity, but healthy-weight individuals who do not self-report hunger have also demonstrated attentional biases to stimuli signalling food using laboratory-based cognitive tasks. Levels of the anorectic neuropeptide oxytocin are elevated by food intake and, when administered intranasally, oxytocin inhibits food intake in the laboratory. To investigate whether oxytocin can affect appetite via an action on attentional processes, 40 adults (29 women; mean age 24.0 years old) self-administered 24 IU of oxytocin or placebo intranasally. Forty minutes after administration, participants ate a small snack to maintain alertness and ameliorate deprivation-induced hunger before starting a computerized dot-probe attentional bias task that presented 180 trials of paired visual stimuli comprising neutral, food, social and/or romantic images (500 ms presentation time). Reaction times to probe stimuli that appeared after the offset of the visual images indicated a significant attentional bias to food pictures after placebo; this effect was significantly attenuated by oxytocin, $p < .001$. The effect of oxytocin on attentional bias to the food pictures was not altered by the type of stimulus paired with the food image, and was independent of BMI, age, sex, self-rated eating behaviour, and self-reported parental bonding; however, the effect was modulated by self-reported food cravings and trait stress. The findings support and extend previous work which has suggested that oxytocin can counteract attentional biases to food-related stimuli in a sample with anorexia by demonstrating the same effect for the first time in a cohort who do not have an eating disorder.

1. INTRODUCTION

Attentional biases towards food that arise from hunger have been demonstrated using an array of attentional-test paradigms, such as the emotional attention-blink test (Piech, Pastorino, & Zald, 2010), the visual dot-probe task (Tapper, Pothos, & Lawrence, 2010) and the word dot-probe design (Mogg, Bradley, Hyare, & Lee, 1998). These hunger-driven attentional biases to food stimuli, and increased neural sensitivity to food reward, have been identified in normal-weight as well as overweight and obese people (Brignell, Griffiths, Bradley, & Mogg, 2009; Stice, Spoor, Ng, & Zald, 2009; Volkow, Wang, & Baler, 2011). For example, using eye-tracking measures and a visual dot-probe task, people with obesity showed a bias towards food pictures that persisted in the satiated state (Castellanos et al., 2009), a finding replicated by Werthmann et al. (2011), who also found a correlation between the extent of bias and increased food cravings using eye-tracking. Attentional biases to food-related cues may be attributed to enhanced food craving, both in people with obesity and in healthy-weight participants, as demonstrated by functional magnetic resonance imaging (fMRI) studies of normal-weight and obese-weight individuals viewing food images (Rothemund et al., 2007; Stoeckel et al., 2008). A person's cravings for food might be expected to reflect an increased salience for, or preoccupation with, food. This is supported by experimentally enhanced vigilance towards food in a dot-probe task being correlated with food salience (Jones & Rogers, 2003; Timmerman & Gregg, 2003), and by increased craving being associated with stronger attentional biases to food identified using eye-tracking (Werthmann, Roefs, Nederkoorn, & Jansen, 2013).

Increased preoccupation with food is also a consequence of restrained eating (Herman & Polivy, 1975), and a number of studies have linked restrained eating to attentional biases for food-related stimuli, although the direction of the effects is not consistent. Dietary restraint can influence eating behaviours with positive and negative outcomes, depending on how the construct is interpreted (Schaumberg, Anderson, Anderson, Reilly, & Gorrell, 2016). Thus, some studies have found that restrained eaters demonstrate an increased avoidance of food stimuli (e.g. Boon, Vogelzang, & Jansen, 2000), whilst others have reported elevated attention towards food stimuli (e.g. Hollitt, Kemps,

Tiggemann, Smeets, & Mills, 2010) or no effect of dietary restraint (Donofry et al., 2019). Several parameters, such as procedural differences, cultural norms (see Meule, 2020), participant characteristics (e.g. Mills, Weinheimer, Polivy, & Herman, 2018), and the instrument used to measure restrained eating (see Polivy & Herman, 2017), are likely to influence the relationship.

Central and peripheral oxytocin release is triggered by eating (Blevins & Ho, 2013) and multiple factors influence its anorectic actions (Sabatier, Leng, & Menzies, 2014). In fasted participants rating high-calorie food pictures, hypothalamic activation was detected via fMRI, an effect that was attenuated by oxytocin. However, after fasting, oxytocin has not been shown to reduce food intake in healthy-weight participants (Ott et al., 2013; Thienel et al., 2016; van der Klaauw et al., 2017), although in fed participants, oxytocin reduces snack intake 15 minutes after lunch (Burmester, Higgs, & Terry, 2018; Burmester, Gibson, Butler, Bailey, & Terry, 2019). Additionally, oxytocin-driven attentional shifts away from food-related stimuli in women with anorexia who previously showed biases towards food have been demonstrated in the laboratory (Kim, Oh et al., 2014). The same attentional bias to food images was not demonstrated in women with bulimia nervosa or binge eating disorder (BED); moreover, oxytocin increased vigilance to food (Leslie, Leppanen, Paloyelis, & Treasure, 2020). This increased vigilance, however, was driven by the five participants with BED and disappeared when these participants were removed from the analysis.

In humans and animals, the phylogenetically highly conserved neuropeptide oxytocin is involved in promoting social behaviours. Neural, genetic, and experimental evidence point towards oxytocin enhancing empathy, social cognition and memory, bonding and attachment, and prosocial behaviour (Li et al., 2015; MacDonald & MacDonald, 2010; Notzon et al., 2016), leading to the social salience hypothesis of oxytocin, whereby oxytocin modulates attention to social cues (Shamay-Tsoory & Abu-Akel, 2016). Although oxytocin's effects can vary according to context (Dumais & Veenema, 2016; Olff et al., 2013), its promotion of social bias is particularly robust and has even been demonstrated in the rhesus monkey, where reduced attention to negative facial expressions in the dot-probe paradigm was seen after nasally applied oxytocin (Parr, Modi, Siebert, & Young, 2013).

These dual roles for oxytocin of promoting bonding while reducing appetite for food are supported by neural evidence that the ventromedial nucleus of the hypothalamus — a site known to play an important role in energy balance and behaviour related to reproduction — expresses high levels of oxytocin receptors that reciprocally regulate these two functions (Leng & Ludwig, 2008; Leng et al., 2008; McCarthy, Kleopoulos, Mobbs, & Pfaff, 1994; Tribollet, Barberis, Jard, Dubois-Dauphin, & Dreifuss, 1988). Eating is one of a small number of primary reinforcers that stimulate mesolimbic reward circuits without conditioning, and accumbal and striatal dopamine is attenuated by oxytocin (Blevins & Ho, 2013) to reduce motivation for hedonic consumption (McGregor & Bowen, 2012). Although ventromedial hypothalamic neurons appear to contribute to the motivational transfer from food-related incentives to reproductive ones (Leng et al., 2008; McCarthy et al., 1994), this mechanism cannot wholly explain motivational or attentional shifts mediated by oxytocin. That is, the motivational shift from food to sexual targets fails to explain how the administration of intranasal oxytocin creates an attentional bias towards social stimuli that are not sexual (Domes et al., 2013; MacDonald & MacDonald, 2010; Shamay-Tsoory & Abu-Akel, 2016). The shift away from food-focussed attention also has clinical importance for individuals with eating disorders whose attentional bias towards food is well established (Aspen, Darcy, & Lock, 2013).

Emerging evidence has demonstrated an attentional bias towards food in healthy-weight individuals that is independent of hunger. Electrophysiological measures assessing postprandial performance on a word-search paradigm revealed that participants' attention was strongly affected by food stimuli and correlated with BMI (Kumar, Higgs, Rutters, & Humphreys, 2016). Kim and colleagues (2014) demonstrated an attentional bias to food not only in an anorexic experimental group but also amongst healthy controls. In the healthy group, however, the bias was not reduced by oxytocin. Findings that oxytocin-induced reductions in attentional bias in women with anorexia were preceded by decreases in salivary cortisol levels suggest that food-related anxiety may have been lowered by the anxiolytic effects of oxytocin in people with anorexia (Leppanen et al., 2017), whereas this effect may not occur in healthy eaters for whom food is not a threat (Churchland & Winkielman, 2012).

The potential of oxytocin to alter attentional food biases in normal eaters has not been yet explored directly. Given the distinct pathways in the medial prefrontal cortex for feeding and bonding that oxytocin regulates, and the transfer from food-related incentives to reproductive ones via oxytocin receptors in the ventromedial nucleus of the hypothalamus (Leng et al., 2008; McCarthy et al., 1994), attentional bias procedures that incorporate stimuli representing food, social, and sexual bonding will allow comparisons of oxytocin's effects across the three different stimulus types. The current study is the first time that three types of stimuli relating to different motivations that are modulated by oxytocin have been examined alongside each other.

A dot-probe task design was adopted, based on two studies that showed effects of oxytocin on attention: Leppanen et al. (2017) showed that oxytocin reduced attentional bias to food in people with anorexia, and di Simplicio, Massey-Chase, Cowen, and Harmer (2009) demonstrated that oxytocin reduced reaction times to fearful facial expressions. Contrasting the effects of oxytocin on food-related stimuli with its effects on other kinds of stimuli that are presumed to be relevant to oxytocin's actions, here social and romantic images, has not yet been investigated. Further, demonstrating whether oxytocin-induced alterations in the salience of food-related stimuli are identifiable in a non-clinical population, might be beneficial to those who need to lose weight. The experimental aims were concealed, and we measured a number of variables that have been shown to influence endogenous oxytocin effects and that have also been associated with food-related biases. Levels of restraint on the DEBQ, high food cravings, and high trait stress were expected to covary with vigilance to food and, in line with previous research (Kumar et al., 2016), an overall bias towards food-related stimuli was expected that would be attenuated by intranasal oxytocin. It was also expected that oxytocin would shift attention from food to romantic and/or social stimuli.

2. METHOD AND MATERIALS

The study received a favourable ethical opinion from the Research Ethics Committee at Kingston

University in accordance with the principles of the Declaration of Helsinki, 2013.

2.1 Study Design

The experiment was a double-blind, repeated-measures crossover design. The main outcome variable was the effect of oxytocin or placebo on response times to food vs neutral pictures. All hypotheses were pre-specified before data collection; the analytic plan was pre-specified, and no data-driven analyses were carried out.

2.2 Participants

Forty-two well-rested adult university students aged between 19 years and 38 years ($M = 24.02$ yrs; $SD = 4.78$ yrs) with body mass indexes (BMI) ranging from underweight at 15.43 kg/m^2 to obese at 35 kg/m^2 ($M = 23.73$ kg/m^2; $SD = 4.39$ kg/m^2) were recruited in exchange for course credits. One participant was underweight and four participants were obese. All participants self-reported as healthy. Two participants were excluded as they did not complete the online surveys, leaving forty participants, 11 men and 29 women. Five participants (one male) were left-handed. Individuals on a vegan diet, with diabetes or food allergies were excluded due to the food provided. Pregnant and breastfeeding women (by self-report) were also excluded from participation due to their altered oxytocin function and sensitivity (e.g. Crowley, Parker, Armstrong, Spinolo, & Grosvenor, 1992; Fenelon, Poulain, & Theodosis, 1993). Altered endogenous oxytocin function is associated with high emotional arousal or stress (e.g. bereavement, financial windfall) so participants reporting such events were also excluded (Engelmann, Ebner, Landgraf, Holsboer, & Wotjak, 1999; Kovacs, 1986). To participate, individuals had to confirm on the day to the researcher that they had not consumed alcohol or non-steroidal anti-inflammatories during the previous 12 hours at least.

2.3 Materials

Intranasal sprays containing 24 IU of oxytocin or vehicle (placebo) were self-administered by participants in accordance with timing and dose-response work by Spengler et al (2017). Detailed information about the nasal sprays can be found in previous studies by this group (see Burmester,

Higgs, and Terry, 2018). All participants consumed a readily catabolisable chocolate bar (Kitkat®, 40g, 233 kcal) and either a carton of apple or orange juice (200ml, 91 kcal or 84 kcal respectively). This food was designed to boost blood-sugar levels during the attention task to minimise fatigue and reduce deprivation-induced hunger that might have increased attention to food pictures. Height was measured using a wall ruler, and Koogeek biometric impedance scales were used to weigh participants. Images were displayed using a 20-inch monitor, table-mounted at head height approximately 60 cm from the participant with a fixed keyboard for responses. For task presentation and recording of the responses, Superlab presentation software (Version 5.0, Cedrus Corporation, CA, USA) was used.

2.3.1 Questionnaires

The Dutch Eating Behaviour Questionnaire (DEBQ; Van Strien, Frijters, Bergers, & Defares, 1986) is a well-validated measure of restrained, emotional, and external eating. A higher score reflects higher levels of the eating problems. To assess trait levels of food craving, the 39-item Food Cravings Questionnaire trait subscale (FCQ-T) was used, which is the most frequently used instrument for the assessment of food cravings and was developed to assess cravings that relate to palatable food intake in addition to physiological hunger (Cepeda-Benito, Gleaves, Williams, & Erath, 2000). Scores on the FCQ-T have been found to be positively associated with BMI, eating pathology, low dieting success, and increases in state-food craving during cognitive tasks involving appealing food stimuli. The State Trait Anxiety Inventory (STAI: Spielberger, Gorsuch, & Lushene, 1970) measures trait and state anxiety and has been widely used in oxytocin research (Gordon et al., 2008; Heinrichs et al., 2003; Tops, Van Peer, Korf, Wijers, & Tucker, 2007). The 20-item Revised UCLA Loneliness Scale version 3 (Russell, 1996), was used, which measures subjective feelings of loneliness as well as feelings of social isolation. The scale is widely used in psychology and contains positive and negative statements about social relations. To assess the degree to which participants were 'in love', Rubin's widely validated 'Romantic Love Scale' (1970) was completed during both visits to account for possible inter-sessional changes but also to maintain an identical procedure across visits.

2.3.2 Picture Stimuli

Forty pictures of palatable salty and sweet foods together with forty neutral common household objects were selected from Birmingham University's Food Research Database; food items and household objects were matched carefully for colour, complexity, and shape by the database developers. Images were then randomly allocated into two groups of 20 pairs to be used in each session. Although the emotionality of images was not tested beforehand, so may have varied, Birmingham University's Food Research Database is a well-validated tool used in previous similar research (Birmingham University's food research database: Allen et al., 2016). Food images were all ready-to-eat and processed foods (e.g. slices of pizza or cake). Social and romantic pictures from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999) were validated by 215 respondents for typicality within their category, and the top 40 pictures of each category were randomly allocated into two equal sets (set A and set B). All pictures were three inches high and four inches wide with their original scales used.

2.4 Procedure

Participants attended twice, about a week apart. At the first session, participants provided informed consent by reading through the participant information sheet and signing a consent form. At the start of both experimental sessions, participants self-administered 24 IU of oxytocin or placebo, depending on session, supervised by a researcher. Participants provided their age and were then blind-weighed by the researcher. Height was then measured, and the participant's age, gender, and handedness were recorded. Participants then watched a neutral video (*Life of Plants*, BBC, David Attenborough) for about half an hour. At 40 minutes post-inhalation, participants consumed the snack and drink before undertaking the dot probe task with the picture set A or set B used in counterbalanced fashion. To avoid any potential drug effects on questionnaire responses, participants completed questionnaires at the end of the experiment, after taking part in both oxytocin and placebo conditions. using a link to an online Qualtrics survey later on their last testing day.

2.4.1. Dot Probe Task

Participants were seated in front of a monitor and informed that they would be presented with a series of pairs of images (trials) presented side-by-side on the screen, and that one image would disappear to be replaced by a black dot (solid circle, Arial, size 50, black on a white background). At the beginning of each trial a central fixation cross would be presented for 500 ms, immediately followed by a picture pair for 500 ms. To avoid reaction times that reflected responses to the previous set of pictures, the importance of looking at the fixation cross in between trials was emphasised. After picture offset, the dot probe appeared at the location of either the right or the left picture and remained on screen until the participant pressed one of the response keys: the "F" (left) or "J" (right) keys on the keyboard, marked with blue and green tape respectively. Participants were instructed that they should indicate the dot position as quickly as possible without compromising accuracy. After a valid response there was a 500 ms interval, then the fixation cross of the next trial was presented. Practise trials were undertaken by each participant until they were satisfied that they understood the task; typically participants practised for just one or two trials. A total of 180 trials per session were administered, comprising 20 food vs neutral, 20 social vs romantic, 20 romantic vs food, 20 social vs food, and 10 neutral vs neutral. A different set of pictures was used for each session (Set A and Set B), which were presented in a counterbalanced design. Table 1 shows the pairing scheme and position of the probe behind the picture used for both sets. The picture locations (left or right), dot probe locations (left or right) and presentation order were randomised for each participant.

Table 1

Dot Probe Stimulus Presentation Scheme: Stimulus type pairings and their Organisation Across Left/Right Visual Fields.

Left Visual Field	Right Visual Field
10 food	• 10 neutral
10 neutral	• 10 food
10 romantic	• 10 food
10 social	• 10 food
10 neutral	• 10 neutral
10 romantic	• 10 social
10 social	• 10 romantic
10 food	• 10 social
10 food	• 10 romantic
• 10 food	10 neutral
• 10 neutral	10 food
• 10 romantic	10 food
• 10 social	10 food
• 10 neutral	10 neutral
• 10 romantic	10 social
• 10 social	10 romantic
• 10 food	10 social
• 10 food	10 romantic

The dot represents the location of the probe stimulus for that pairing.

3. RESULTS

3.1 Data preparation

Data were prepared and analysed using IBM SPSS version 25. All trials with error responses or response latencies below 200 ms were removed from the results, as values below 200 ms might indicate that a response was not based on perception of the stimulus (Ehrman et al., 2002). Previous research has commonly eliminated latencies either over 1000 ms or 1500 ms, or on the basis of their standard deviation from the mean. In this data set, there were no outliers between 1000 ms and 1300

ms, but thirty-three cases were greater than 1300 ms, some six standard deviations above the mean reaction time. The boundary for exclusion was therefore 1300 ms, a set point also used in previous research as a suitable compromise between 1000 ms and 1500 ms (Kujawa et al., 2011). Overall, under 1% of responses were discarded.

3.1 Analysis of Attentional Bias

The means and standard deviations for congruent responses to probes associated with neutral and food picture types, in both the placebo and oxytocin condition are shown in Figure 1. A 2 (drugs: oxytocin or placebo) x 2 (picture: food or neutral) repeated-measures ANOVA was conducted that revealed a main effect of drug [$F(1,39) = 76.89$, $p < .001$, partial $\eta^2 = .66$] whereby administration of oxytocin significantly increased response times to the dot probe in comparison with placebo administration. There was also a significant interaction between drug and picture type [$F(1,39) = 20.14$, $p < .001$, partial $\eta^2 = .34$]. When the sex of the participant was added to the model as a between-subjects factor, there were no interactions with the drug condition [$F(1,38) = 0.21$, $p = .65$], picture type [$F(1,38) = 0.52$, $p = .47$] or drug and picture type [$F(1,38) = 1.34$, $p = .25$].

A paired-samples t test confirmed that response times to the congruent dot probe behind food pictures after oxytocin ($M = 567.58$ ms, $SD = 30.21$ ms, see Figure 1) were significantly longer compared with after placebo ($M = 487.75$ ms, $SD = 42.35$ ms): $t(39) = 8.23$, $p < .001$, $d = 1.3$, indicating that oxytocin reduced vigilance to food pictures. A second paired-samples t test confirmed that response times to the congruent dot probe behind neutral pictures after oxytocin ($M = 552.11$ ms, $SD = 39.67$ ms) compared with placebo ($M = 531.49$ ms, $SD = 24.09$ ms) were also significantly longer: $t(39) = 2.70$, $p = .01$, $d = 0.43$, indicating that oxytocin also reduced vigilance to neutral pictures. This suggests that oxytocin has a generalised slowing effect on reaction times that was more pronounced for food stimuli.
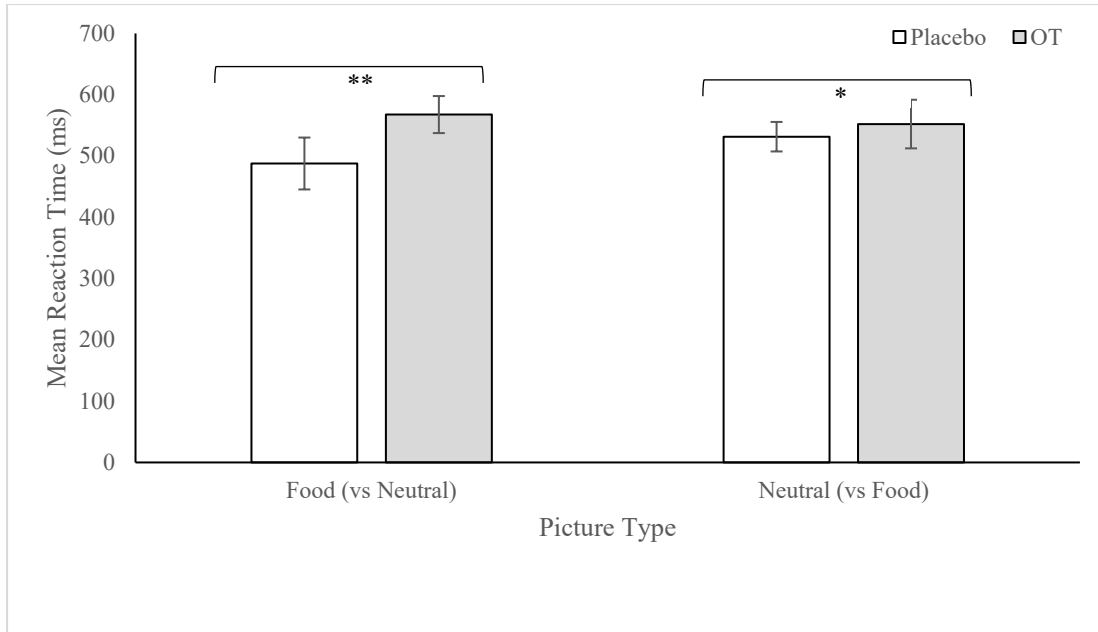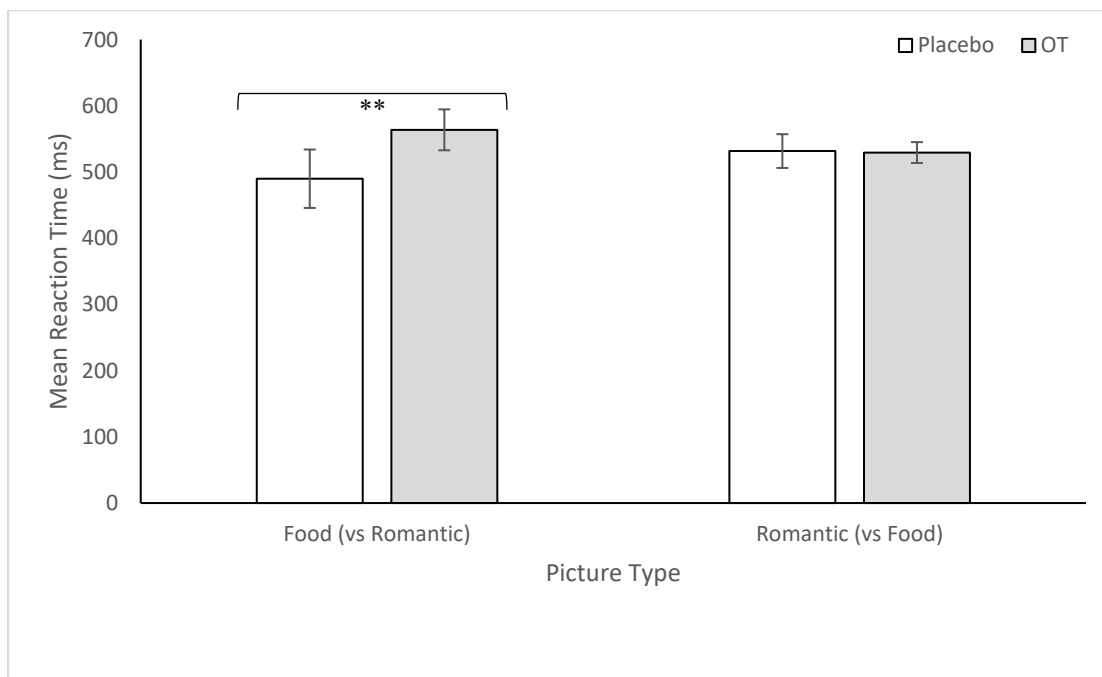
Figure 1

Mean (*SD*) Reaction Times (ms) to Food Congruent vs Neutral Congruent Picture Probes in Placebo and Oxytocin Conditions of Dot Probe Task

3.3 Food versus Social Pictures and Food versus Romantic Pictures

The means and standard deviations for congruent responses to probes associated with food, romantic or social picture types are presented in Figures 2 and 3 for both drug conditions. To compare food and romantic images, a repeated-measures 2 (drug: oxytocin vs placebo) x 2 (picture: food vs romantic) ANOVA was conducted. The main effect of drug [$F(1,39) = 53.46, p < .001$, partial $\eta^2 = .58$] was significant meaning that administration of oxytocin lengthened reaction times irrespective of the type of picture viewed. There was no main effect of picture type [$F(1, 39) = 0.59, p = .44$]. Figure 2 illustrates the significant interaction between drug and picture type, which revealed that oxytocin only reduced attention to food stimuli [$F(1,39) = 49.75, p < .001$, partial $\eta^2 = .56$]. When participant romantic scores were added as a covariate to the model, there were no interactions with the drug condition [$F(1,38) = 0.65, p = .42$], picture type [$F(1,38) = 0.71, p = .79$] or drug and picture type [$F(1,38) = 1.00, p = .33$].

A paired-samples *t* test confirmed that response times to the congruent dot probe behind food pictures (vs romantic) after oxytocin ($M = 563.71$, $SD = 30.92$) compared to after placebo ($M = 489.89$, $SD = 44.13$) were significantly longer: $t(39) = 7.92$, $p < .001$, $d = 1.25$, indicating that oxytocin reduced vigilance to food pictures. A second paired-samples *t* test confirmed that response times to the congruent dot probe behind romantic pictures after oxytocin ($M = 529.41$, $SD = 15.76$) compared to after placebo ($M = 531.67$, $SD = 25.50$) were not significantly longer: $t(39) = 0.52$, $p = .61$, indicating that oxytocin did not reduce vigilance to romantic pictures. This suggests that oxytocin had no effect on response times to the dot probe behind romantic pictures but reduced vigilance to food pictures.

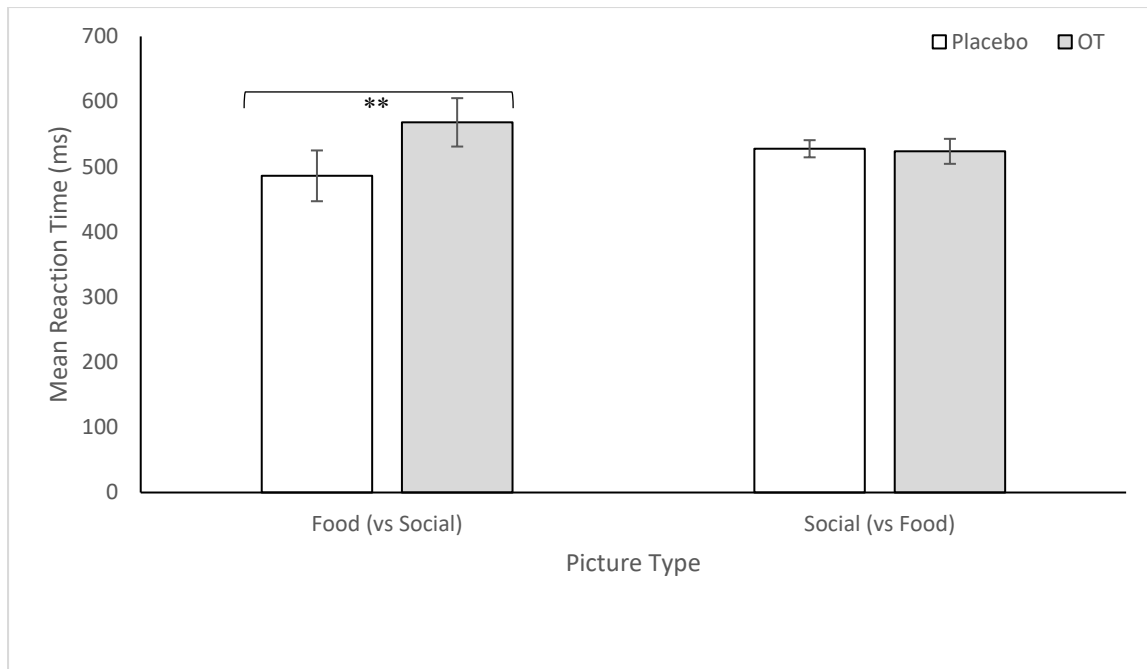*Note.* Error bars are standard deviations; ** $p < .001$

Figure 2

Mean (*SD*) Reaction Times (ms) to Food Congruent and Romantic Congruent Picture Probes in Oxytocin and Placebo Conditions of the Dot Probe Task

A repeated-measures 2 (drug: oxytocin vs placebo) x 2 (picture: food vs social) ANOVA was

conducted to compare food and social stimuli. Administration of oxytocin increased mean response times overall [$F(1,39) = 67.12$ $p < .001$, partial $\eta^2 = .63$], but there was no main effect of picture type on response times [$F(1, 39) = 0.14$, $p = .71$]. Figure 3 shows that there was a significant interaction between drug and picture type [$F(1, 39) = 68.41$, $p < .001$, partial $\eta^2 = .64$] such that oxytocin reduced attention paid to food stimuli only. When participant romantic scores were added as a covariate to the model, there were no interactions with the drug condition [$F(1,38) = 0.72$, $p = .40$], picture type [$F(1,38) = 0.15$, $p = .70$] or drug and picture type [$F(1,38) = 1.17$, $p = .29$].

Further paired-samples t tests confirmed that response times to the congruent dot probe behind food pictures (vs social) after oxytocin ($M = 568.11$ ms, $SD = 37.13$ ms) compared to after placebo ($M = 486.02$ ms, $SD = 38.97$ ms) were significantly longer: $t(39) = 8.85$, $p < .001$, $d = 1.4$, indicating that oxytocin reduced attention to food pictures. A second paired-samples t test confirmed that response times to the congruent dot probe behind social pictures after oxytocin ($M = 523.63$ ms, $SD = 19.18$ ms) compared to after placebo ($M = 527.60$ ms, $SD = 13.16$ ms) were not significantly longer: $t(39) = 1.08$, $p = .29$, indicating that oxytocin did not reduce attention to social pictures. This suggests that oxytocin had no effect on response times to the dot probe behind social pictures but reduced vigilance to food pictures.
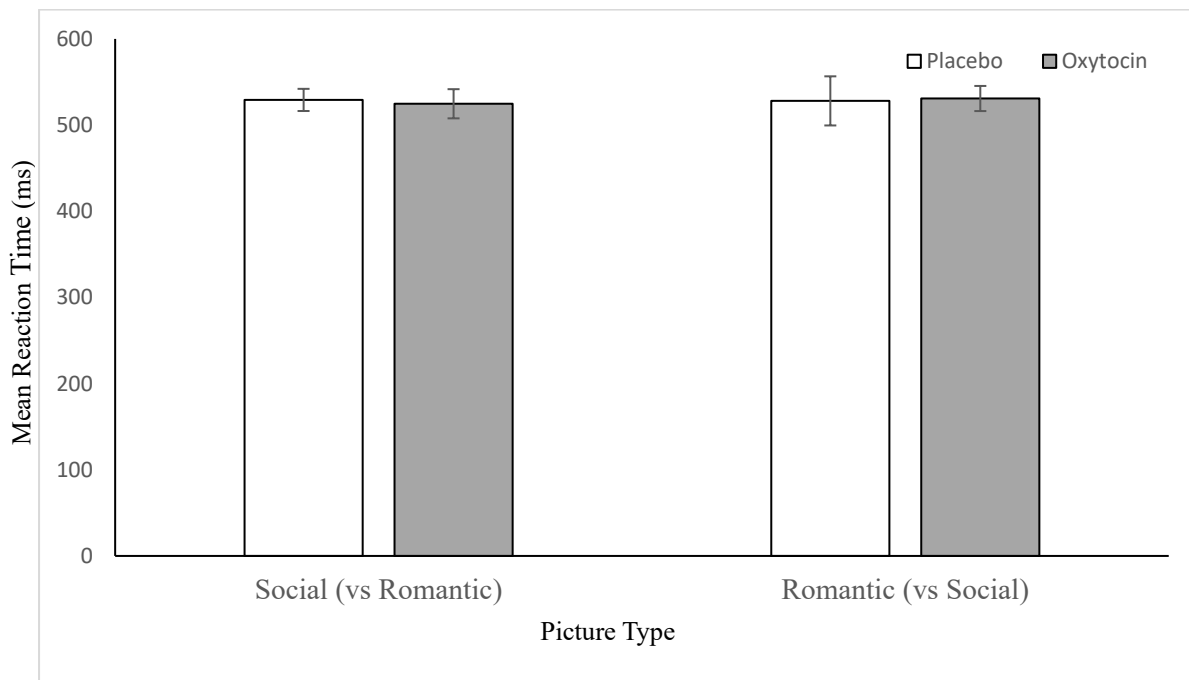
Note. Error bars are standard deviations; ** *p* < .001

Figure 3

Mean (*SD*) Reaction Times (ms) to Food Congruent and Social Congruent Picture Probes in Oxytocin and Placebo Conditions of the Dot Probe Task

3.4 Social and Romantic Pictures

To assess whether oxytocin impacted attention to social and romantic picture probes when paired together, placebo and oxytocin conditions were compared using *t* tests. . Paired *t* tests for responses to the romantic pictures (vs social) after placebo (*M* = 526.30, *SD* = 27.69) and after oxytocin (*M* = 530.85, *SD* = 14.94) revealed no significant difference between the oxytocin or placebo conditions, $t(39) = 0.89$, $p = .38$. There was also no significant difference between the social (vs romantic) images in the placebo (*M* = 528.77, *SD* = 12.88) and oxytocin (*M* = 523.89, *SD* = 16.75) conditions, $t(39) = 1.55$, $p = .13$.
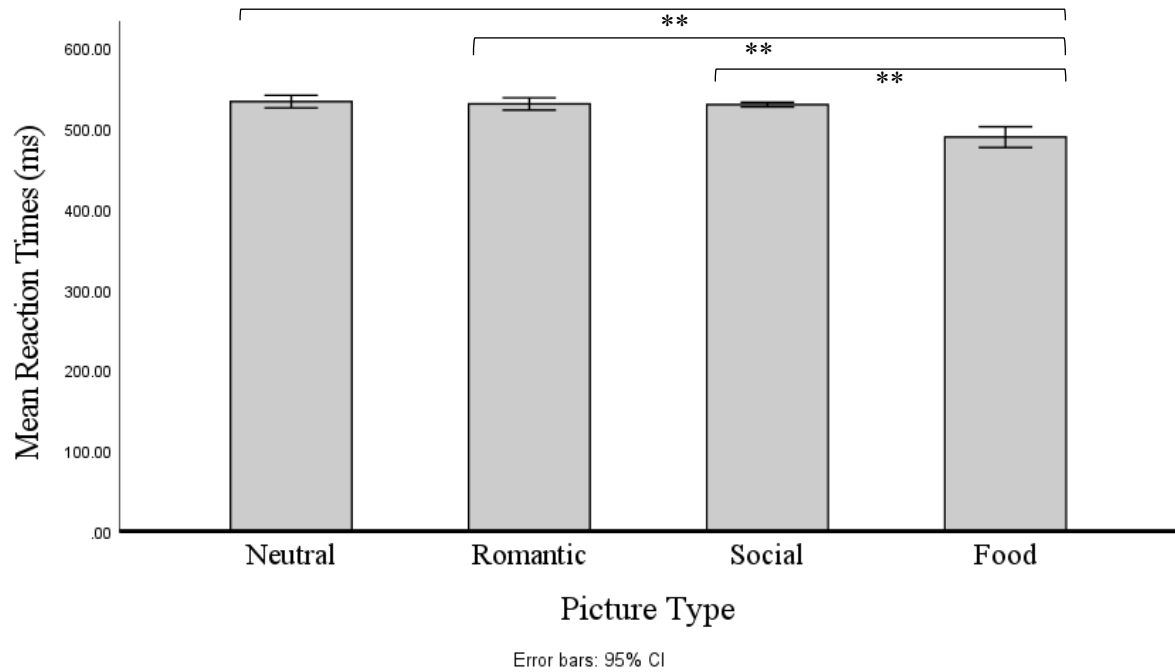
Figure 4

Mean (*SD*) Reaction Times (ms) to Social Congruent and Romantic Congruent Picture Probes in Oxytocin and Placebo Conditions of the Dot Probe Task

3.5 Overall Responses in Oxytocin and Placebo Conditions

To explore the differences in responses after placebo for all types of picture, a repeated-measures ANOVA was used. Reaction times for neutral (*M* = 531.89, *SD* = 24.37), romantic (*M* = 528.98, *SD* = 23.86), social (*M* = 528.18, *SD* = 8.08), and food were found to statistically differ (*M* = 487.95, *SD* = 40.12): $F(3,117) = 23.08$, $p < .001$, partial $\eta^2 = .372$, see Figure 5. Pairwise comparisons showed that responses to the probe behind food pictures were significantly faster than to the probes behind neutral, romantic, and social, all $p < .001$.
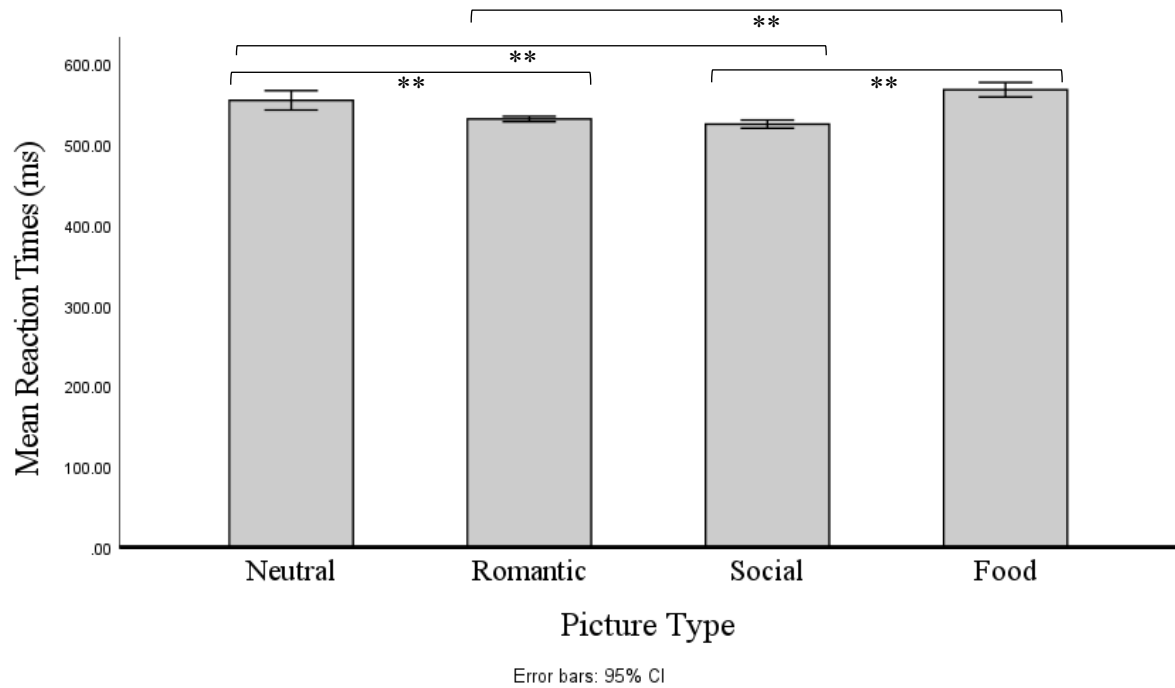
** *p* < .001

Figure 5

Mean (*SD*) Reaction Times (ms) in the Placebo Condition of the Dot Probe Task

To probe the differences in responses after oxytocin administration for all types of picture, a repeated-measures ANOVA was also used. Reaction times for neutral (*M* = 525.26, *SD* = 37.72), romantic (*M* = 530.13, *SD* = 10.41), social (*M* = 523.76, *SD* = 15.96), and food (*M* = 566.35, *SD* = 28.31), were found to statistically differ: $F(3,117) = 24.51$, partial $\eta^2 = $ *p* < .001, .386, see Figure 6. Pairwise comparisons revealed significant differences between neutral and romantic (*p* = .004), neutral and social (*p* < .001), romantic and food (*p* < .001), social and food (*p* < .001).

Figure 5. Mean (*SD*) Reaction Times (ms) Placebo Conditions of the Dot Probe Task

* *p* < .05; ** *p* < .001

Figure 6

Mean (*SD*) Reaction Times (ms) in the Oxytocin Condition of the Dot Probe Task

3.5 Questionnaire Data and Food Bias

The means and standard deviations (SD) for questionnaire scores are presented in Table 2. To assess whether participant characteristics influenced the attenuating effect of oxytocin on attentional bias towards food, questionnaire data were analysed as covariates in a series of repeated-measures ANCOVAs with food bias scores in the two drug conditions as the repeated-measures factor.

Table 2. Means (*SD*) for participants' questionnaire scores (n = 40)

	M	*SD*
STAI-trait	46.23	5.01
BMI	23.73	4.39
Loneliness	37.68	9.57
PBI Care-Neglect	49.88	15.75

PBI Overprotection	29.63	15.05
Romantic Love	77.53	17.22
FCQ – total	147.60	28.29
DEBQ - Restrained	3.56	1.30
DEBQ - External	1.88	0.82
DEBQ - Emotional	1.95	0.75

In addition to re-running the RMANOVA examining oxytocin's effects of food bias by excluding the five participants with obesity or underweight from the main analysis (no change, p < .001), a RMANCOVA using the full range of BMI scores showed that BMI did not interact with oxytocin's reduction of food bias $F(1, 38) = 2.04$, $p = .16$, indicating that oxytocin's effects in this experiment were independent of BMI. The mean STAI-trait score was significantly higher than normative averages [normative: M (SD) = 40.40 (10.10)] for trait anxiety in a one-sampled t test: $t(39) = 14.44$, $p < .001$. Trait anxiety showed a significant interaction with oxytocin's effects on food bias: $F(1,38) = 8.85$, $p = .005$, suggesting that trait anxiety increased the effect of oxytocin on bias scores. In the DEBQ, one-sample t tests showed that the mean scores for restraint [$t(39) = 3.54$, $p = .001$], external [$t(39) = 10.10$, $p < .001$], and emotional eating [$t(39) = 8.77$, $p < .001$] were all different from normative scores with restrained eating in the normative samples being lower than this cohort, but the normative scores for external and emotional eating were higher. No interaction, however, was found between oxytocin's reduction of food bias and any of the subscales of the DEBQ: restraint subscale [$F(1,38) = 2.77$, $p = .10$], external subscale [$F(1,38) = 0.38$, $p = .54$], emotional eating: $F(1,38) = 1.54$, $p = .22$. The mean romantic score for romantic love in this cohort was 77.53, which a one-sampled t test showed was below mean normative scores of 89.46 [$t(39) = 4.38$, $p < .001$].   However, romantic scores did not interact with oxytocin's reduction of food bias, : $F(1, 38) = 0.12$, $p = .73$. No reliable normative data were found for FCQ scores. There was a significant interaction between overall food cravings and oxytocin's reduction of food bias: $F(1,38) = 5.36$, $p = .026$, indicating that food cravings decreased the effect of oxytocin on bias scores. Scores on the loneliness scale were not significantly different from normative data $t(39) = 1.07$, $p = .29$, and did not interact with food bias

scores: $F(1, 38) = 0.01$, $p = .93$.

4. DISCUSSION

In a sample of 40 adults, intranasal oxytocin reduced an attentional bias to food stimuli in a dot probe experiment using neutral and food pictures after ingestion of a snack to boost blood sugar concentrations. Despite oxytocin's generalised lengthening of reaction times to both food and neutral picture probes, oxytocin's effect on food stimuli was significantly greater. The oxytocin-led shift away from food and neutral stimuli was independent of BMI, loneliness, and eating behaviour as measured by the DEBQ, but trait stress and food cravings covaried with food bias scores. Response times to food-picture probes in relation to romantic- or social-stimuli probes were greater after oxytocin than after placebo, meaning participants' attention was less focused on the food stimuli after oxytocin when presented alongside affiliative stimuli. No lengthening of reaction times or differential effects were seen after oxytocin with romantic or social picture probes.

This finding draws together the work using oxytocin to modify attentional bias and research uncovering an attentional bias towards food in the general population. It is also in line with previous research demonstrating oxytocin's effectiveness at changing attentional bias using food and face pictures presented for 500 ms or above (Brüne et al., 2013; Kim, Kim et al., 2014). However, in the previous experiments by the Brüne and Kim groups, the cohorts were anorexic, whereas in this study an attentional bias to food was found in a non-anorexic sample that was not selected according to any particular weight characteristic.

Loeber, Grosshans, Herpetz, Kiefer and Herpetz (2013) proposed two psychological processes underpinning the motivation for food consumption. The first involves the perception of palatable food that initiates cognitive and motivational approach processes, such as attention allocation to food cues that enhances salience attribution. The second process is the self-control required to resist food consumption. It appears that oxytocin may reduce perceptual, motivational, and cognitive processes

to alter attentional bias to food, rather than inhibitory mechanisms, since oxytocin has altered attentional biases in those with anorexia but was not successful in potentiating food intake (Kim et al., 2014). However, assessing self-control processes in those with anorexia is problematic and oxytocin's capacity to increase top-down self-control has not been yet been fully explored in healthy participants. It should also be noted, though, that the speed of processing is indicative of, but not a proxy for, attention. Oxytocin's attenuation of the motivation to eat is consistent with preclinical studies and brain imaging research showing that the anorectic effects of oxytocin on ingestive behaviour downregulate activity in reward circuitry, including the ventral tegmental area, putamen, caudate nucleus, NAc and amygdala (Baracz et al., 2012; Sabatier et al., 2014; Striepens et al., 2013). Thus, since oxytocin has also been shown to regulate the cognitive control of inhibitory processes mediated by prefrontal regions (Striepens et al., 2016), further research into oxytocin's modulation of self-control processes using paradigms such as go-no go tasks is warranted.

The range of participant BMI scores in this study not only reflects that of the general population, and therefore enhances the generalisability of its results, but it also enabled us to examine whether BMI interacts with the effects of oxytocin on vigilance towards food. The lack of correspondence in this experiment between BMI and an attentional food bias does not agree with previous research suggesting that being overweight or obese is associated with a greater attentional bias towards food (Brignell et al., 2009) or that oxytocin's effects are greater in obese than lean men (Thienel et al., 2016). It is likely that participants in the study were unaware of the experimental aims or the relevance of their body mass to the study. In the Thienel et al. and Brignell et al. studies, obese participants specifically were recruited via targeted advertisements and, as part of the selection procedure, completed eating behaviour questionnaires. Attentional processing by participants who self-select as obese may be different from that of naïve participants. However, the relationship between food bias and BMI may be moderated by other factors. In a sample of overweight participants recruited to a study on slimming, the external eating component of the DEBQ and the personality trait of impulsivity were associated with a greater attentional bias towards food pictures (Bongers et al., 2015).

Motivational states, such as hunger, can alter the magnitude of conditioned responses; moreover, the state of hunger increases attentional bias to food in the general population. A limitation of this study was that hunger and fullness ratings were not obtained from participants. However, to minimise fatigue and prevent deprivation-induced hunger, participants were provided with a snack before completing the dot probe task. It is also possible that consuming palatable food beforehand primed participants to be vigilant towards food cues and the results reflect oxytocin's weakening of the priming effect. Small amounts of food can stimulate the appetite and increase attention to food (Zheng, Lenard, Shin, & Berthoud, 2009) and Konorski termed the ensuing increased locomotor activity and attention to olfactory stimuli related to food a "hunger reflex" (Konorski, 1973; Pavlov, 1897). Cornell, Rodin, and Weingarten (1989) first demonstrated this priming effect, or cue reactivity, in humans: Exposure to pizza or ice cream potentiated subsequent eating of that food in food-sated participants. A recent meta-analysis found that consuming palatable food prospectively significantly alters subsequent eating behaviour (Boswell & Kober, 2016). However, it is not clear that attention to picture probes is a reliable proxy for eating behaviour and thus is altered by prior consumption of palatable food. In this study, an effect of oxytocin on reducing attentional bias to food images occurred despite any potential augmentation of interest in food pictures due to the consumption of a snack prior to the task. Future studies should explore whether a snack consumed before an attentional bias task, alters participant responses to food cues, either by way of a priming effect or via an effect of elevated glucose on attention.

Methodological differences between the Kim et al. (2014) study and the present experiment may have contributed to the lack of attentional bias modification by oxytocin in normal eaters in the Kim group that was demonstrated in this experiment. Increased attention in the dot-probe paradigm within the anorexic cohort may be, at least partly, due to increased threat processing, as has been demonstrated in individuals with anxiety disorders towards, for example, spiders (Öhman & Soares, 1994). However, trait anxiety was higher than normative averages in this cohort and covaried with food bias scores, so oxytocin may, therefore, be effective at attenuating attentional bias differently in people with anorexia

than in healthy eaters. In people with anorexia, oxytocin may modulate the increased threat sensitivity present when exposed to food-related cues, whereas in normal eaters, oxytocin may attenuate the reward processes. The food-related images used by the Kim group included items that were related to food (e.g. cooking utensils) and food that was not high valence (e.g. celery). Although both anorexic groups and healthy controls were found to have attentional bias to food-related stimuli, the three types of food-related stimuli were collapsed to produce a single bias result. Low or medium valence stimuli used by Kim et al. (2014) may trigger increased attention in anorexic groups but not healthy controls, meaning that the stimuli were not of equal valence across groups. The high-valence food and neutral pictures in this dot-probe study were from the validated University of Birmingham database, and the romantic and social pictures were rated for typicality by a large number of people (189) compared to other studies that use just four 'judges' (e.g. Mogg et al., 2000). The high valence of all non-neutral stimuli used in this experiment may partially account for the significant findings.

Although attentional biases to social and romantic stimuli were not explicitly examined in this dot probe since no direct comparisons were made with neutral stimuli, response times to romantic and social pictures were as quick as the food response times in the placebo condition, and similar to the attentional bias scores observed when food pictures were viewed alongside neutral pictures. The similarly quick response times to the probes behind romantic, social, and food pictures in the placebo condition suggest that attention across these stimuli was equally distributed in the placebo condition. Given the body of literature showing that oxytocin influences attention toward social stimuli in males (Di Simplicio et al., 2009; Domes et al., 2013), females (Kim et al., 2014; Kim, Eom, Yang, Kang, & Treasure, 2015), autistic individuals (Kanat et al., 2017; Xu et al., 2015), and rhesus monkeys (Parr et al., 2013), the finding that social response times did not change after oxytocin is surprising. One reason for oxytocin's lack of effect on social stimuli in this study could be that previous research used negative and positive pictures of faces as social stimuli, whereas this experiment used pictures of social scenes. If oxytocin's mechanism of action is to reduce the amygdala response to negative or threatening stimuli, facial expressions—particularly eyes—may be more salient stimuli.

Previous attentional research on oxytocin's effect on romantic stimuli could not be found. However, Scheele et al. (2013) demonstrated that oxytocin's enhancing effects on men viewing female faces was specific to their romantic partners only. The generic romantic stimuli used in this experiment may not, therefore, convey sufficient valence. Further research could extend this study by contrasting social and romantic images with neutral ones to examine whether attentional bias towards them exists, and whether it persists under oxytocin.

In summary, despite a relatively small sample size, a significant attentional bias towards food-related stimuli in a non-clinical adult population was eliminated with 24 IU of intranasal oxytocin, pointing towards a mechanism that might underpin oxytocin's effects on appetite. This specific cognitive effect of oxytocin on food images did not generalize to other kinds of appetitive stimuli that are widely considered to be sensitive to the effects of oxytocin. Future work could examine whether this attentional change by oxytocin also diminishes appetite. These results are preliminary evidence of the potential of oxytocin as an agent for modification of attentional bias towards food, which may have important implications for people with obesity or eating disorders.

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