Intranasal Oxytocin Alters Attention to Emotional Facial Expressions, Particularly for Males and Those with Depressive Symptoms

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Abstract

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Ariel Boyle

Intranasal oxytocin (OT) can enhance emotion recognition, perhaps by promoting increased attention to social cues. Some studies indicate that individuals with difficulties processing social information, including those with psychopathology, show more pronounced effects in response to OT. As such, there is interest in the potential therapeutic use of OT in populations with deficits in social cognition. The present study examined the effects of intranasal OT on the processing of facial features and selective attention to emotional facial expressions, as well as whether individual differences in depressive symptom severity predict sensitivity to intranasal OT. In a double-blind placebo-controlled within-subject design, eye tracking was used to measure attention to facial features in an emotional expression appraisal task, and attention to emotional expressions in a free-viewing task with a quadrant of multiple faces. OT facilitated the processing of positive cues, enhancing the maintenance of attention to the mouth region of happy faces and to happy faces within a quadrant, although the latter effect fell short of conventional statistical significance. Further, persons with depressive symptoms, and particularly males, were sensitive to OT's effects. For males only, OT, relative to placebo, increased attentional focus to the mouth region of all faces. Individuals with depressive symptoms showed less attentional focus on angry (males only) and sad facial expressions, and more attention to happy faces (particularly for males). Results indicate increased sensitivity to OT in males and persons at risk for depression, with OT administration promoting a positive bias in selective attention to social stimuli

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Contribution of Authors

Mark Ellenbogen and Aaron Johnson designed the study. Research assistants collected the data. Ariel Boyle conducted the statistical analyses and wrote the first draft of the manuscript. Mark Ellenbogen revised the manuscript, as did Aaron Johnson. All authors contributed to and approved of the final manuscript.

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Intranasal Oxytocin Alters Attention to Emotional Facial Expressions, Particularly for Males and Those with Depressive Symptoms

Oxytocin (OT) is a neuropeptide produced primarily in the paraventricular and supraoptic nucleus of the hypothalamus that is known to influence a wide range of physiological and cognitive processes, as well as social behaviors, through interactions with the central nervous system and peripheral organs (Bethlehem et al., 2013; Veening & Olivier, 2013). Given evidence of prosocial behaviors and improvement in social cognition following intranasal OT administration, there is interest in the potential therapeutic use of OT in clinical populations, particularly those characterized by deficits in social behavior and social information processing (McClure & Nowicki, 2001; Peled-Avron et al., 2020). One aspect of social cognition influenced by OT is emotion recognition. Intranasal OT has been shown to increase the accuracy of identification of basic emotional expressions (Di Simplicio & Harmer, 2016; Ellenbogen, 2017; Leppanen et al., 2017; Prehn et al., 2013; Schulze et al., 2011). These effects have been found for happy faces in emotion recognition tasks where stimuli are presented for short durations (e.g. 500ms; Marsh et al., 2010) or in masked recognition tasks where stimuli are presented with limited conscious awareness (Graustella & MacLeod, 2012; Marsh et al., 2010; Schulze et al., 2011; Shahrestani et al., 2013), and for negative emotions, such as fear, under conditions of longer stimulus presentation (Fischer-Shofty et al., 2010; Kirkpatrick et al., 2014; Shahrestani et al., 2013).

The identification of an emotion is accomplished largely by extracting information from the face. Evidence suggests that individuals are predisposed to process faces in a holistic manner (Tanaka & Farah, 1993), and that configural processing, the analysis of the configuration of facial features, optimizes face identification (Macrae & Lewis, 2002). Featural processing, the processing of individual facial features, however, has been shown to be advantageous for making categorical judgements of faces, such as for sex, race, and emotional expression (Macrae & Martin, 2007; Martin et al., 2012). Feature-based cues seem to have differential importance in the identification of different emotional expressions. The availability of the mouth region of the face as a cue of emotion leads to greater accuracy in identification of happy and disgusted faces than the availability of the eye region, whereas for expressions of anger, sadness, and fear, this pattern is reversed (Calder et al., 2000). Feature-based processing may be favored under challenging conditions, including brief stimulus presentation, whereas in the absence of such challenge configural processing prevails (Macrae & Martin, 2007; Martin et al., 2012). Using eye-tracking methodology, intranasal OT has been shown to increase attention to the eye region of the face in humans (Auyeung et al., 2015; Gamer et al., 2010) and non-human primates (Dal Monte et al., 2014; Kotani et al., 2017), although not all studies have found this effect (Domes et al., 2010; Hubble et al., 2017b; Lischke, Berger, et al., 2012). Enhanced attention to the eye region of faces has been observed across neutral (Gamer et al., 2010; Guastella et al., 2008; Wang et al., 2020) and emotional facial expressions (i.e. happiness, fear, sadness; Gamer et al., 2010; Hubble et al., 2017a; Tollenaar et al., 2013), but not for angry faces (Domes, Steiner, et al., 2013; Wang et al., 2020). Similar to these studies, there is evidence that OT facilitates the

processing of both positive and negative expressions (Leknes et al., 2013). For instance, activity in the ventral tegmental area, an area involved in the coding of salience of stimuli, increased following intranasal OT in response to both expressions of anger and happiness (Groppe et al., 2013). Taken together, these studies show consistent effects of OT on attention to the eyes across most emotional and neutral stimuli. This is consistent with the social salience hypothesis which posits that OT increases the salience of social cues in the environment and can have both positive and negative effects on cognition and behaviour (Shamay-Tsoory & Abu-Akel, 2016).

Intranasal OT might also have different effects on attention to emotional facial expressions across different stages of stimulus processing (Ellenbogen, 2017). Some evidence indicates that OT influences the early stages of attentional processing (Schulze et al., 2011; Tollenaar et al., 2013). Other studies of early processing find that OT promotes more flexible processing, facilitating disengagement of attention from briefly presented negative emotional expressions (Ellenbogen et al., 2012), and increased attention to briefly presented positive facial expressions (Domes et al., 2013). Consistent with the notion of flexibility, OT was found to dampen the processing of angry faces for individuals who showed vigilance to these faces under placebo, while promoting attention to angry faces for individuals who showed avoidance of attention to these faces under placebo (Kim et al., 2014).

There is increasing evidence that the effects of OT on social cognition are moderated by individual traits. The effects of intranasal OT on empathic accuracy were more pronounced among individuals with deficits in social cognition than those with no such deficit (Bartz et al., 2010; Bartz et al., 2011), particularly for male participants (Bartz et al., 2019). In a study of emotion recognition with subtle (hidden) facial expressions of emotion, participants lowest in emotional sensitivity showed the greatest improvements in the processing of emotional faces following intranasal OT relative to placebo (Leknes et al., 2013). Because many forms of psychopathology are associated with deficits in social cognition, OT appears to have more robust effects in persons at risk for, or having, a mental disorder than healthy controls (Alvares et al., 2012; Bate et al., 2014; Bradley et al., 2019; Xu et al., 2015). Individuals with depressive symptoms show difficulties in certain domains of social cognition, including attentional biases to mood-congruent stimuli at the level of elaborative processing (Ellenbogen & Schwartzman, 2009), as well as emotion recognition (Lee et al., 2005). In persons with major depressive disorder, OT has been shown to improve emotion recognition accuracy (MacDonald et al., 2013) and promote more flexible stimulus processing - reducing attention to negative facial expressions and increased attention to positive expressions (Domes et al., 2016; Ellenbogen et al., 2012). Depressed persons may also be highly sensitive to intranasal OT. OT reduced the ability to inhibit processing of sad faces relative to placebo in persons with high depression scores, whereas among those with few depressive symptoms, there was no effect of OT on inhibition (Ellenbogen et al., 2013).

Despite evidence that persons with depressive symptoms may be sensitive to intranasal OT, as well as interest in the potential therapeutic use of OT in these populations (Clarici et al., 2015; De Cagna et al., 2019; MacDonald et al., 2013; Netherton & Schatte, 2011), there is

relatively little research on the associations between depressive symptoms and effects of OT on various aspects of face processing. Relative to placebo, OT attenuated an attentional bias to angry faces among persons with depressive symptoms (Ellenbogen et al., 2012). One study examining effects of OT on eye gaze to social stimuli in depressed patients found no drug effects, although the stimuli used in this study were videos of faces with expressions morphing from neutral to emotional (Rutter et al., 2019), unlike the static images used in most other studies (Wang et al., 2020). Furthermore, tasks assessing effects of OT on attention to social cues are often constrained by differing task demands associated with the different tasks used (e.g. dot-probe, inhibition, visual search, etc.) and do not assess how OT may affect selective attention to emotional stimuli among individuals with depressive symptoms under more naturalistic conditions in the absence of task demands.

The present study aimed to investigate the effects of intranasal OT on selective attention to emotional facial expressions and the allocation of attention to facial features of emotional expressions. Furthermore, we examined whether depressive symptoms are associated with heightened sensitivity to OT relative to placebo, as measured by changes in attention within and between emotional facial expressions. In a double-blind placebo-controlled within-subjects design, participants completed two face-viewing tasks. The first task (Single Face task) involved viewing faces of different emotions, one at a time, while eye tracking was used to measure eye movements and gaze durations on two regions of the face – the eyes and the mouth. The second task (Quadrant Face task) involved passive viewing of a quadrant of faces while eye tracking was used to measure eye movements and gaze durations to the different emotional expressions in each quadrant (happy, angry, sad, neutral).

Given previous findings that OT enhances attention to the eye region of the face (Auyeung et al., 2015; Gamer et al., 2010), we hypothesized that in the Single Face task, where attention to facial features was measured, OT would increase the number of fixations and time spent gazing on the eye region of faces. Although we expected to observe these effects across both positive and negative facial expressions (Hubble et al., 2017a; Leknes et al., 2013), we hypothesized that expressions of positive emotion would elicit the most robust drug effects (Domes et al., 2013; Guastella, Mitchell, & Mathews, 2008; Marsh et al., 2010; Xu et al., 2015). Consistent with this hypothesis, we also predicted that in the Quadrant Face task, OT would facilitate selective attention to the happy faces within the quadrant. We expected that OT's effects on both tasks would be particularly strong among individuals high in depressive symptoms (Ellenbogen et al., 2013). We also examined whether participants' sex might influence OT's effect on selective attention to faces. We had no a priori hypotheses concerning sex differences in the effects of OT during either task. Studies have found higher sensitivity to OT in both male (Bartz et al., 2019; Herzmann et al., 2013) and female participants (Ma et al., 2018), as well as no differences between sexes (Ellenbogen et al., 2012; McClure et al., 2020; Rutter et al., 2019).

Methods

Participants

Healthy adults aged 18 to 35 years were recruited through online classified advertisements (e.g., Craigslist). Exclusion criteria included: smoking more than 5 cigarettes a week, use of marijuana in the past two months, current drug use (excluding alcohol, caffeine, or nicotine), history of illicit drug use or use of prescription medication. Individuals with abnormal/uncorrected vision, current axis-1 DSM-IV mental disorder, current serious or chronic medical condition, history of antidepressant use, or past participation in OT research. Female participants who were pregnant or lactating were excluded from the study. Female participants who had endorsed engaging in unsafe sex in the past two months were required to take a pregnancy test prior to participation in the study.

The final sample consisted of 61 adults (32 females, M_{age}=24.44, SD=4.27, age range= 18-35 years). 62.3% of participants self-endorsed as Caucasian. Males and female participants did not differ in age, M_{diff}=1.39, $t(50)$=1.26, p=.214, nor in depressive symptoms, Range=0-32; Males: M=7.14, SD=5.17; Females: M=7.75, SD=6.67; Difference: M=-.61, $t(59)$=-.40, p=.69.

Materials and measures

Beck Depression Inventory – II (Beck et al., 1996)

The BDI-II is a 21-item self-report measure of the presence and severity of depressive symptoms. The measure has good internal consistency, with Cronbach's α ranging from .83 to .96, and good test-retest reliability, with *r* values ranging from .73 to .96 (Wang & Gorenstein, 2013). Furthermore, the BDI-II shows good convergent and discriminant validity, correlating more strongly with BDI-I scores and other measures of depression, *r* ranging from .66 to .94, than with measures of other constructs, including substance use and chronic pain, *r* being less than .4 (Wang & Gorenstein, 2013).

Eye Tracking

Eye movements were captured using the EyeLink 1000 Host PC application system for binocular eye tracking. Participants' head movements were restricted using a chin rest, allowing a camera mounted to a desktop monitor positioned 70cm in front of the participant to record their eye movements during the completion of the study's computer tasks. The mean calibration error was less than .5 degrees, with no single point surpassing one degree. Eye tracking was used to measure the following gaze behaviors as indices of attentional focus: time to first fixation [i.e. time elapsed from the beginning of a trial before first fixating on an area of interest (AOI) and number of AOIs visited before the first fixation on a particular AOI], duration of first fixation on an AOI, and percentage of total fixations and dwell time made on an AOI throughout a trial. A fixation was defined as a period of sustained gaze on an AOI and its surrounding .5 degree region, lasting at least 50 milliseconds. Dwell time was defined as the total amount of time on a trial of a task spent fixating on an AOI.

Single Face Task

This task was based on the one used by Guastella, Mitchell and Dadds (2008). Participants were presented with 42 (trials) images of a face displaying one of seven expressions (happy, fearful, sad, angry, disgusted, surprised, or neutral) for five seconds (image size: 562 x 762 pixels) on the center of the computer screen. Images were selected from the NimStim Face

Stimulus Set (Tottenham et al., 2006) and presented in random order, with trials balanced across sex and ethnicity of the models. Participants were instructed to look at the monitor for the duration of the task. In order to ensure sustained attention to the faces, participants were required to rate each face on the dimensions of unpleasant-pleasant or unfriendly-friendly using a 7-point scale following stimulus offset. Eye tracking was used to measure participants' gaze behaviors in relation to two AOIs, the area around the eyes and the area around mouth of the face. Both AOIs were the same size.

Quadrant Face Task

This task was based on the one used by Eizenman et al. (2003). The task consisted of 20 trials presented for ten seconds each, with two seconds elapsing between trials, where participants freely viewed four emotional facial expressions (happy, sad, angry, or neutral) arranged in a quadrant (size of quadrant: 1024 x 768 pixels). The position of each facial expression in the quadrant was randomized, and trials were balanced across sex and ethnicity of the models. Participants were instructed to look at the computer monitor for the duration of each trial. Images were selected from the NimStim Face Stimulus Set (Tottenham et al., 2006). Eye tracking was used to measure participants' gaze behaviors in relation to four AOIs, each being one of the faces in the quadrant.

Procedure

Following informed consent, participants completed an online questionnaire in order to determine their eligibility to participate in the study. Eligible participants then completed two laboratory sessions held one week apart. Female participants taking oral contraceptive were scheduled to participate in the study on days when the active pill is taken. Females not taking oral contraceptive (25 participants) were scheduled for both test sessions within 0–11 or 17–25 days of the first day of menstruation in order to avoid large discrepancies in circulating hormones over the estrous cycle.

During the first laboratory session, participants provided written informed consent and completed a medical history questionnaire as well as the BDI-II. The study consisted of a double-blind within-subject design: each participant participated in one laboratory session under the influence of intranasal OT and one under the influence of placebo in randomized order. In accordance to established guidelines (Guastella et al., 2013), participants self-administered intranasal OT (*Syntocinon*, Novartis) or a placebo nasal spray matching the inactive ingredients of the active drug administration. Participants administered three sprays of OT or placebo into each nostril, totaling a 24IU dose. Participants rested and relaxed for 30-minutes, reading neutral reading material or listening to music, prior to beginning the experimental tasks. Participants then completed the two eye-tracking tasks, as well as two autobiographical memory tasks and a modified anti-saccade task assessing inhibition (not presented here) in random order. The eye-tracking tasks were administered sequentially – the Single Face task was always completed following the Quadrant Face task. Following the completion of the second laboratory session, participants were debriefed and compensated $70 CAD for their participation. The study's

procedures were approved by the Human Research Ethics Committee at Concordia University (Montréal, Canada).

Statistical Analyses

We conducted 2 (Drug condition: Oxytocin, Placebo) x 2 (Sex: Male, Female) x 4 (Emotional expression: Happy, Negative, Neutral, Surprise) mixed design ANOVAs, with drug condition and emotional expression as within-subject variables, on eight dependent variables in the Single Face task: time elapsed before first fixation, logarithmic transformations of duration of first fixation, and percentage of fixations and dwell time to the eye and mouth regions of faces. For the Quadrant Face Task, we conducted 2 (Drug condition) x 2 (Sex) mixed design ANOVAs on the following dependent variables: percentage of fixations and dwell time to each of the facial expressions in the quadrant, duration of first fixation on each expression in the quadrant, as well as time elapsed and number of faces visited before the first fixation on each face in the quadrant (Sad, Angry, Neutral, Happy). Greenhouse-Geisser corrections were applied in cases of violations of sphericity. Pairwise t-tests were conducted following significant main or interaction effects, and Bonferroni corrections for multiple comparisons were applied. Statistical assumptions were tested, with results showing acceptable levels of homogeneity of variance and normality. For the Single Face task, analyses were conducted both with and without combining results from sad, angry, fearful, and disgusted expressions into a broader category of negative emotional expressions. The results did not differ between the two analyses. Therefore, the results of the negative emotional expression category are reported here.

In order to examine whether depressive symptoms moderate the effects of OT on indices of attentional focus on both tasks, we conducted hierarchical multiple regressions predicting differences between conditions (oxytocin minus placebo) on the dependent variables listed above. Because dwell time and number of fixations are highly related, however, we only used the percentage of total fixations in the regression analyses. Further, given that the time elapsed and the number of faces visited before the first fixation on a face in the Quadrant task are highly related, we only used the number of faces visited in the regression analyses. Independent variables were entered in the following two steps: (1) sex and depression (BDI-II) scores, and (2) depression X sex interaction term. In order to interpret depression X sex interactions, we conducted additional analyses using the Johnson-Neyman technique performed by the PROCESS macro for SPSS. This technique identifies the value(s) of the depressive symptom scores demarcating the region(s) in which there was a significant conditional effect of sex on changes in our indices of attentional focus.

Results

Effects of drug condition on indices of attention allocation during the viewing of emotional facial expressions

For both eye tracking tasks, there were no main effects of drug, or sex X drug interactions, affecting overall gaze behaviors, including average time spent dwelling on any AOI and number of total fixations made during a trial (data not shown). The duration of first fixation

on each AOI was assessed for both tasks, but no drug or drug X Sex effects were found, therefore this outcome is not reported below (see Supplemental Tables 1-2).

Single Face Task

Time to First Fixation. No main effect of drug condition or participant sex on the time to first fixation on the eye or mouth regions of faces were found (see Table 1). The main effect of emotion on the latency of first fixations on the eye region of the face was significant (F(2, 120)=3.27, p=.041, η^2_p =.05), however pairwise comparisons using Bonferroni corrections revealed no statistically significant differences between the latency of first fixation on the eye region of any two emotional expressions. There was a main effect of emotion on the latency to first fixate on the mouth region of the face (F(3, 95)=5.75, p=.002, η^2_p =.14), such that the shortest latencies before the first fixation on the mouth were for negative expressions. There were no interaction effects between variables influencing the time taken before a first fixation on the eye or mouth regions of faces.

Total Fixation and Dwell Time. Contrary to our hypotheses, there was no main effect of drug condition, sex, or interactions between variables affecting the percentage of fixations or dwell time to the eye region of faces of any expression (see Table 3). There was a main effect of emotional expression on the percentage of fixations (F(2, 116)=74.04, p=.00, η^2_p =.56) and dwell time (F(2, 124)=76.03, p=.00, η^2_p =.56) to the eye region of faces. The highest percentages of fixations and dwell time to the eyes were elicited by happy and neutral faces, followed by negative expressions (see Table 3). In sum, attention to the eyes of any facial expression was not affected by exposure to OT compared to placebo.

Although no main effects of drug condition or sex were found, there was a main effect of emotion on the percentage of fixations (F(2, 137)=15.38, p=.00, η^2_p =.21) and dwell time on the mouth (F(2, 132)=15.72, p=.00, η^2_p =.21). Negative facial expressions elicited more attention to the mouth than did happy, neutral, or surprised faces. Interestingly, there was a significant interaction between drug condition and sex, such that OT elicited higher percentages of fixations (F(1, 59)=5.04, p=0.029, η^2_p =.08) and dwell time (F(1, 59)=4.33, p=.042, η^2_p =.07) to the mouth region of faces relative to placebo in males but not females. There was also an interaction between drug condition and emotion, such that OT elicited higher percentages of fixations (F(2, 144)=3.21, p=.034, η^2_p =.05), but not dwell time, to the mouth region of the face relative to placebo in response to happy (M_{diff}=1.76, p=.020, 95%CI [.28, 3.23]) and surprised faces (M_{diff}=1.54, p=.050, 95%CI [.00, 3.07]), but not neutral or negative expressions. The results suggest that OT enhances overall attentional focus to the mouth region of happy and surprised faces relative to placebo, and that males are more sensitive than females to OT's effects on attention to the mouth region of faces. These findings, in combination with the null findings for the latency and duration of the first fixation on the mouth, suggest that OT is influencing maintenance of attention at the later stage of stimulus processing.

Quadrant Face Task

Time to First Fixation. There were no main effects, nor any interaction effects between drug condition and participant sex affecting time elapsed and number of faces visited before the first fixation on any facial expression (see Table 2).

Total fixation and dwell time. An effect of drug condition on percentages of fixations ($F(1,59)=3.29$, $p=.075$, $\eta^2_p=.05$) and dwell time ($F(1,59)=3.88$, $p=.054$, $\eta^2_p=.06$) to happy faces was found, although these fell short of conventional levels of statistical significance (see Table 4). Larger percentages of fixations on happy faces were observed following OT than placebo (Fixations: $M_{diff}=2.01$, p=.075, 95%CI [-.21, 4.24]; Dwell time: $M_{diff}=2.57$, p=.054, 95%CI [-0.04, 5.17]). There was no main effect of sex nor any interactions between sex and drug condition affecting percentages of fixations or dwell time on any face in the quadrant.

Depressive symptoms as a moderator of the effects of OT on indices of attentional focus

Single Face Task

Time to First Fixation. Hierarchical multiple regressions revealed that BDI-II scores predicted time to first fixate on the mouth region of negative and neutral faces (see Table 5). Participants higher in depressive symptoms were slower to first fixate on the mouth of neutral facial expressions following OT relative to placebo. In contrast, participants higher in depressive symptoms were also quicker to first fixate on the mouth of negative facial expressions following OT relative to placebo. Neither depressive symptoms nor the sex X depression interaction predicted differences between drug conditions in the latency of first fixation on the eyes for all facial expressions. In contrast, the sex X depression interaction predicted differences between drug conditions in latency of first fixation on the mouth region of negative and surprised facial expressions.

Among individuals in the top 31.1% of BDI-II scores, males and females showed different responses to OT relative to placebo, such that OT elicited shorter latencies to first fixations on negative expressions relative to placebo for male participants, but longer latencies following OT relative to placebo for females [BDI=9.74, $t=2.02$, $p=.05$, 95%CI [.00, 533.53]]. The same pattern was observed for the latency before first fixation on surprised faces among individuals in the top 15.4% of BDI-II scores [BDI=12.43, $t=2.01$, $p=.05$, 95%CI [.00,1550.40]]. While OT administration, relative to placebo, hastened the speed to first fixation on negative and surprised facial expressions among male participants reporting depressive symptoms, it had the opposite effect among depressed female participants (see Figure 1).

Percentage of total fixations. BDI-II scores predicted percentage of fixations to the mouth region of surprised faces (see Table 5). Participants with depressive symptoms engaged in larger percentages of fixations to the mouth region of surprised faces following OT relative to placebo. Neither depressive symptoms nor the sex X depression interaction predicted differences between drug conditions in percentage of fixations to the eye region of any of the facial expressions. In contrast, the sex X depression interaction predicted differences between drug conditions in percentages of fixations to the mouth region of surprised faces. Among individuals in the top 36.1% of depressive symptoms, males were more sensitive to OT than females, showing larger increases in percentage of fixations [BDI=8.06, $t=-2.00$, $p=.050$, 95%CI [-5.97,

.00]] to the mouth region of surprised faces following OT relative to placebo (see Figure 2). None of the overall regression models assessing other facial expressions of emotion were significant. In sum, participants reporting depressive symptoms, particularly males, were more sensitive to OT's effects on attentional focus on surprised facial expressions, at both first fixation and across the trial, compared to those with low depression scores.

Quadrant Face Task

Time to First Fixation. Depressive symptoms were positively associated with a higher number of quadrants visited before the first fixation on the sad face following OT relative to placebo (see Table 6). The sex X depression interaction was associated with differences between drug conditions in the number of faces visited before first fixation on angry faces. Among those in the top 13.1% of depressive symptoms, male participants showed an increase in number of faces visited before the angry faces following OT relative to placebo, whereas for females there was a decrease [BDI=13.81, *p*=.05, 95%CI [-.72, .00]]. In sum, depressive symptoms were associated with delays in attentional focus to sad faces following OT administration relative to placebo, and this was also the case for angry faces, but only for males reporting high depressive symptoms.

Percentage of total fixations. As participants reported higher depressive symptoms, participants fixated less frequently on sad faces (see Table 6). There was an interaction between sex and depressive symptoms affecting the differences in total percentage of fixations between drug conditions on sad, happy, and angry faces, albeit the effect on fixations to sad faces fell short of conventional levels of statistical significance. Neither depressive symptoms nor the sex X depression interaction was associated with differences between drug conditions in percentage of fixations to neutral faces.

Among those in the top 6.6% of depressive symptoms [BDI=16.13, *t*=-2.00, *p*=.050, 95%CI [-15.90, .00]], males were more sensitive than females to OT's increase of percentage of fixations to happy faces relative to placebo. Among individuals in the top 24.6% depressive symptoms, males showed different responses following OT compared to placebo than females, with OT decreasing the percentage of fixations on angry faces for males relative to placebo, but increasing these for females [BDI=10.16, t=2.00, p=.050, 95%CI=.00, 4.27] (see Figure 3). The results suggest that males and females high in depressive symptoms show different responses to OT relative to placebo. Relative to depressed female participants, OT increased overall attentional focus to happy faces and decreased attentional focus to angry faces in depressed male participants.

Discussion

The aim of the present study was to examine the effects of intranasal OT on selective attention to emotional facial expressions and facial features, as well as determine whether depressive symptoms are associated with heightened sensitivity to OT relative placebo. There were three key findings in the present study. First, the administration of OT, relative to placebo, increased attentional focus (as indicated by the percentage of fixations and time spent dwelling throughout a trial) on the mouth region of faces expressing happiness or surprise when viewing a

single face. Second, male participants and those reporting high depressive symptoms were more sensitive to intranasal OT than female participants and those with low depressive scores. OT, relative to placebo, increased attentional focus to the mouth region when viewing a single face for males, but not females. Participants with high depressive symptoms increased attentional focus to the mouth region of faces expressing surprise, as well as delayed initiation of fixation and lower overall attentional focus on sad expressions within an array of faces. Of interest, male participants with high depressive symptoms were particularly sensitive to exogenous OT. Among those high in depressive symptoms, male participants showed larger increases in attentional focus to the mouth region of a face expressing surprise and to happy faces in an array than females following OT, relative to placebo. Third, male and female participants also exhibited opposing effects of OT. While males with depressive symptoms showed delayed onset of fixations and decreased overall attentional focus on expressions of anger among an array of faces following OT, females showed a hastened onset of fixations and increased overall attentional focus towards angry faces. Taken together, the administration of OT augmented attention to the mouth region of faces expressing positive affect and uncovered evidence of increased sensitivity as well as opposing effects to exogenous OT in males and persons with depressive symptoms compared to females.

Contrary to our hypothesis, we found no evidence that intranasal OT increased attention to the eye region of faces. Rather, intranasal OT elicited higher percentages of fixations to the mouth region of happy and surprised faces relative to placebo. While a number of studies have found that intranasal OT enhances attention to the eye region of the face (Auyeung et al., 2015; Gamer et al., 2010; Guastella, Mitchell, & Dadds, 2008; Hubble et al., 2017a; Tollenaar et al., 2013), other studies have failed to replicate the effect (Domes et al., 2010; Hubble et al., 2017b; Le et al., 2020; Lischke, Berger, et al., 2012). Methodological differences may account in part for the differences in findings, such as the use of static pictures (Hubble et al., 2017b) rather than video clips (Hubble et al., 2017a) or differences in the duration of stimulus presentation. The single face viewing task used in the present study presented static images for five seconds, whereas several past studies have used shorter stimulus durations. For instance, Wang et al. (2020) used a masked emotion recognition task where target facial expressions were presented for 1500ms and participants were asked to identify the emotion as quickly as possible, and found that OT increased gaze to the eye region of angry, fearful and neutral faces. Given evidence that OT enhances emotion recognition at early stages of processing (Schulze et al., 2011), but that at longer stimulus durations effects of OT are generally not observed, or observed only for emotions that are harder to detect (e.g. fear), it has been suggested that there may be a ceiling effect in which effects of OT are observed at shorter stimulus durations (Hubble et al., 2017b; Le et al., 2020; Shahrestani et al., 2013). Thus, one possible consequence of the long stimulus exposure duration in the present study is that attention to the eyes might have reached a ceiling effect following the placebo administration. Eyes are often fixated on more than any other feature of the face during emotion identification (Eisenbarth & Alpers, 2011; Spezio et al., 2007; Wells et al., 2016). Indeed, in our study percentages of fixations and dwell time to the eye region

of the face exceeded 60%. Consistent with this hypothesis, studies that have observed effects of OT on gaze to the eyes report percentages of fixations or durations of gaze on the eye region of around 40% or lower (Auyeung et al., 2015; Gamer et al., 2010; Hubble et al., 2017a), whereas a number of studies that have not found effects of OT on gaze to the eyes report percentages of fixations or gaze duration above 40% (Domes et al., 2010; Lischke, Berger, et al., 2012).

Another methodological difference between tasks is that participants in the present study were instructed to evaluate the valence (that is pleasant/unpleasant, friendly/unfriendly) of each facial expression. In contrast, previous studies assessing the effects of intranasal OT on eye gaze have used tasks in which task demands consisted of gaze cueing, identification of emotion, or free viewing. Similarly to the present study, the task used by Domes et al. (2010) required participants to evaluate facial expressions on degree of arousal as opposed to the specific emotion conveyed by the expression, and they did not observe effects of OT on eye gaze. Perhaps OT's effects on attentional focus within facial expressions may be less apparent during tasks that require more general and fine-grained evaluations of emotional stimuli.

The finding that OT increased the number of fixations to the mouth region of the face was specific to happy and surprised faces is consistent with evidence of OT's prosocial effects. Evidence suggests that OT particularly improves the processing of positive affect at various levels of processing (Domes et al., 2013; Graustella & MacLeod, 2012; Xu et al., 2015). While expressions of surprise fall mid-way on the continuum of positive and negative affect, they can be interpreted as conveying positive affect, and may explain the similar effects of OT for surprised and happy faces (Calvo & Nummenmaa, 2016). In addition, the ambiguity of valence for expressions of surprise may have made these expressions particularly difficult to evaluate in terms of friendliness and pleasantness, the two ratings that participants had to make following each face presentation. Perhaps this difficulty may explain in part the effects of OT on attention to surprised faces, given that OT's effects are generally more robust during the performance of tasks that are higher in difficulty (Cardoso, Ellenbogen, et al., 2014; Hubble et al., 2017b). Further, enhanced attention to the mouth region of faces may be particularly beneficial for happiness and surprise, as the mouth region plays a larger role in the identification of these expressions than for other emotions (Bassili, 1979; Beaudry et al., 2014; Wegrzyn et al., 2017). Perhaps OT's effects on attention to prosocial stimuli, the complexity in identifying surprised faces, and the importance of the mouth in identifying happy and surprised faces contributed to the present finding that intranasal OT increases attentional focus to the mouth region of happy and surprised faces.

One of the key findings of the study was that male participants exhibited greater attentional focus on the mouth region of single faces following OT administration than female participants, and that depressed male participants exhibited a larger OT-induced increase in attentional focus to happy faces when viewing an array of faces than depressed females. There is increasing evidence of sex differences in the effects of OT on behavior (Ma et al., 2018; Xu et al., 2020; Zhu et al., 2019), cognition (Plasencia et al., 2019; Shi et al., 2020), and neuroendocrine function (Chen et al., 2016; Chen et al., 2020; Feng et al., 2015; Lieberz et al.,

2020). The present findings are consistent with a number of studies showing more pronounced effects of OT in males, than in females (Herzmann et al., 2013; Zhu et al., 2019). For instance, OT has been shown to increase empathic accuracy for males low in social proficiency, but not for males high in social proficiency, or females regardless of social proficiency (Bartz et al., 2019). It has been suggested that the sex differences in response to OT may be related to differences in amygdala activation in males and females following intranasal OT. A number of studies show that for males, OT dampens amygdala activity to negative social cues (Chen et al., 2016; Gamer et al., 2010; Kirsch et al., 2005) and increases amygdala activity (Gamer et al., 2010) and functional connectivity between the amygdala and other regions of the social salience network in response to positive social cues (Rilling et al., 2018). Among females, the findings for studies of exogenous OT are mixed, with evidence that there is no such dampening of amygdala activity in response to negative social cues (Chen et al., 2016), evidence of enhanced activation of the amygdala in response to threatening social cues (Domes et al., 2010; Lischke, Gamer, et al., 2012), and an absence of improved functional connectivity between the amygdala and other regions of the social salience network following positive social interactions that was observed in men (Rilling et al., 2018). Moreover, OT reduced functional connectivity between the amygdala and other regions of the social salience neural network in response to negative social interactions in females, but hardly in men (Rilling et al., 2018). The amygdala plays a role in the processing of salient stimuli and their reward value, and is involved in allocating resources to processing these stimuli (Adolphs, 2010). It is hypothesized that OT may increase the reward value or salience of positive social interactions and decrease the stress response to negative interactions for males, while decreasing the reward value or salience of positive social interactions among females (Chen et al., 2020). These sex differences in neural responses to salient stimuli following OT administration may explain why male participants showed a more robust increase in attention to positive facial expressions and decreased attentional focus to negative facial expressions than females following an OT challenge.

Partially consistent with our prediction, changes in attentional focus following OT administration were most pronounced among participants reporting symptoms of depression. Unexpectedly, these effects were largely found among male participants. Individuals high in depressive symptoms showed enhanced response to OT relative to placebo, including decreased attentional focus on sad faces, as measured by the latency to initiate the first fixation and proportion of overall fixations on sad faces. Among those high in depressive symptoms, males showed larger increases in maintenance of attention to happy faces within the quadrant than females following OT, relative to placebo. In addition, depressed male participants showed a decrease in attentional focus to angry faces following OT administration, while depressed females showed the opposite. There is some evidence that clinical populations show more robust effects of intranasal OT administration than non-clinical samples (Cardoso, Kingdon, et al., 2014), and that this heightened sensitivity extends to populations at risk of psychopathology, including those with attachment insecurity (Wang et al., 2020), trait anxiety (Alvares et al., 2012), and depressive symptoms (Ellenbogen et al., 2013). The present findings are consistent

with a previous study of selective attention using a reaction time attentional cueing task, which found that OT attenuated an attentional bias to masked angry faces for participants reporting depressive symptoms (Ellenbogen et al., 2012). Further, the present findings are consistent with evidence that individuals with difficulties in social cognition show improvements in social information procession following OT, and particularly for males (Bartz et al., 2019). The presence of depressive symptoms is associated with attentional bias to sad emotional stimuli (Ellenbogen & Schwartzman, 2009), as well as an absence of normative bias towards positive emotional stimuli (Armstrong & Olatunji, 2012; Bodenschatz et al., 2018; Duque & Vázquez, 2015; Koster et al., 2011). Our findings suggest that intranasal OT dampened the negative attentional bias and promoted a positive bias for individuals with symptoms of depression. These results must be interpreted with caution, however, given that results observed among participants with higher depression scores are based on a small group of individuals within the sample, and that within this group, there are more female participants with higher depression scores than male participants.

While OT decreased the negative attentional bias among individuals high in depressive symptoms in the free viewing quadrant task, it must be noted that a hastening of the initiation of fixations to the mouth region of negative facial expressions was observed for males, but not females, high in depressive symptoms in the single face viewing task. Given that the single face viewing task required evaluation of the valence of facial expressions, increased attention focus to facial features may have been advantageous in that task, particularly for negative facial expressions, of which there were multiple kinds to distinguish (i.e., sadness, anger, fear, disgust).

A key strength of the present study was the use of eye-tracking to measure selective attention and attentional focus. Eye-tracking eliminates some of the confounds present in other experimental paradigms, such as dot-probe tasks, where using reaction time as an index of attention allocation introduces confounding factors, such as response execution (Armstrong & Olatunji, 2012). Further, eye tracking can measure attention under more natural conditions, with fewer task demands (Liang et al., 2017). There are also study limitations that should be noted. While our single face viewing task involved appraisal of the valence of facial expressions, we did not measure emotion identification outright, and therefore cannot conclude whether OT's effects on attention allocation to the mouth region of the face are advantageous for emotion identification. Further, the study sample consisted of healthy adults with a range of severity of depressive symptoms, but none had major depressive disorder. Additional research would be needed to determine the extent to which these results generalize to a clinical population. Another limitation of the study is that the pathways and precise timing by which intranasal OT influences social cognition are not fully known. There are questions surrounding the effectiveness of the intranasal methodology in directly reaching the brain (Leng & Ludwig, 2016). However, there is increasing evidence that the intranasal route allows for the transport of OT and similar molecules to the brain (Martins et al., 2020; Quintana et al., 2018). Further research is needed, however, in order to elucidate the precise pathway, dosage, and timing to maximise OT's effects in the brain. Nevertheless, our results expand on the growing body of literature pointing to individual

differences in sensitivity to OT by suggesting that individual characteristics including sex and symptoms of psychopathology may be key in determining for whom intranasal OT may facilitate social information processing, and to what extent.

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Table 1

Descriptive Statistics for Latencies of First Fixations (in ms) in the Single Face Task

	Oxytocin		Placebo	
	M	SD	M	SD
MOUTH				
Happy				
Male	1628.35	779.81	1672.07	689.96
Female	1614.79	503.52	2038.91	809.87
Total	1620.70	629.44	1879.00	772.57
Negative				
Male	1351.31	532.43	1372.90	515.57
Female	1554.14	475.62	1471.35	503.16
Total	1465.73	504.73	1428.43	504.26
Neutral				
Male	1521.04	720.87	1839.15	955.07
Female	1847.87	764.65	1749.18	737.01
Total	1705.41	754.24	1788.40	828.43
Surprise				
Male	1627.02	699.99	1552.80	662.54
Female	1589.02	686.86	1663.75	683.46
Total	1605.58	683.66	1615.39	667.89
EYES				
Happy				
Male	16.03	22.77	31.74	44.20
Female	53.91	204.32	49.75	150.07
Total	35.90	148.91	41.19	112.38
Negative				
Male	15.69	21.55	49.48	100.75
Female	34.18	78.06	63.11	183.93
Total	25.39	58.75	56.63	149.21
Neutral				
Male	21.33	42.64	82.89	201.10
Female	39.23	127.62	64.03	195.86
Total	30.72	96.67	72.99	196.93
Surprise				
Male	19.29	37.05	116.97	220.37
Female	56.91	133.76	118.07	401.85
Total	39.03	101.21	117.55	325.72

Note. $N_{eyes} = 61$. $N_{mouth} = 39$.

Table 2

Descriptive Statistics for Latencies of First Fixations (in ms) in the Quadrant Face Task

	Time to first fixation (ms)				AOIs visited before first fixation (#)			
	Oxytocin		Placebo		Oxytocin		Placebo	
	M	SD	M	SD	M	SD	M	SD
SAD								
Male	1179.19	404.37	1122.16	320.38	1.82	0.21	1.78	0.21
Female	1200.57	466.38	1259.17	401.35	1.75	0.23	1.78	0.23
Total	1190.41	434.52	1194.04	368.63	1.78	0.22	1.78	0.22
ANGRY								
Male	1301.01	457.15	1386.86	577.45	1.91	0.30	1.89	0.36
Female	1495.29	562.07	1486.83	503.38	1.91	0.35	1.87	0.32
Total	1402.93	519.93	1439.30	537.64	1.91	0.32	1.88	0.34
NEUTRAL								
Male	1197.47	427.77	1238.82	455.11	1.83	0.29	1.80	0.23
Female	1278.41	458.49	1286.94	394.02	1.69	0.25	1.76	0.16
Total	1239.93	442.34	1264.06	421.26	1.75	0.28	1.78	0.20
HAPPY								
Male	1236.61	462.54	1217.10	471.76	1.83	0.31	1.86	0.27
Female	1365.04	395.62	1418.92	528.90	1.88	0.24	1.87	0.20
Total	1303.98	429.99	1322.97	508.64	1.85	0.27	1.86	0.24

Note. N=61

Table 3

Descriptive Statistics for Percentages of Fixation and Dwell Time in the Single Face Task

		Fixations				Dwell Time			
		Oxytocin		Placebo		Oxytocin		Placebo	
		M	SD	M	SD	M	SD	M	SD
MOUTH									
Happy									
	Male	10.03	9.14	7.12	6.31	10.73	10.85	7.89	6.99
	Female	8.37	6.20	7.76	6.52	8.48	6.34	8.36	8.14
	Total	9.16*	7.71	7.46	6.38	9.55	8.77	8.14	7.55
Negative									
	Male	11.41	5.82	10.61	6.12	12.46	6.77	11.71	6.91
	Female	10.11	6.18	11.05	6.88	10.97	6.99	12.05	7.99
	Total	10.73	6.00	10.84	6.48	11.68	6.87	11.89	7.43
Neutral									
	Male	8.70	6.31	7.17	5.40	8.93	6.69	7.60	6.05
	Female	6.84	5.12	7.74	5.66	7.46	5.90	8.11	6.13
	Total	7.72	5.75	7.47	5.50	8.16	6.28	7.87	6.05
Surprise									
	Male	10.83	7.75	8.06	5.45	11.99	8.49	8.92	6.06
	Female	8.02	4.08	7.71	5.25	8.85	4.30	8.45	6.06
	Total	9.35*	6.21	7.88	5.30	10.34	6.76	8.67	6.01
EYES									
Happy									
	Male	66.48	14.90	68.57	12.68	66.58	16.53	69.22	13.15
	Female	71.21	13.32	73.44	15.10	71.24	14.64	73.24	16.38
	Total	68.96	14.18	71.12	14.10	69.02	15.62	71.33	14.95
Negative									
	Male	66.20	10.98	64.75	12.46	66.15	11.90	64.27	13.29
	Female	68.49	12.55	68.38	13.76	68.30	13.26	68.23	14.64
	Total	67.40	11.79	66.65	13.18	67.28	12.58	66.35	14.04
Neutral									
	Male	70.80	12.63	70.12	13.81	71.08	13.06	69.57	15.82
	Female	75.15	10.97	72.79	13.49	74.57	12.06	73.00	14.37
	Total	73.08	11.89	71.52	13.59	72.91	12.56	71.37	15.05
Surprise									
	Male	57.17	10.63	54.59	16.09	55.39	11.47	53.54	16.26
	Female	57.61	14.92	58.68	15.07	55.91	15.57	57.32	15.94
	Total	57.40	12.95	56.73	15.57	55.66	13.66	55.52	16.07

Note. N = 61. * Drug x emotion interaction $p<.05$.

Table 4

Descriptive Statistics for Percentages of Fixations and Dwell Time in Quadrant Face Task

	Fixations				Dwell Time			
	Oxytocin		Placebo		Oxytocin		Placebo	
	M	SD	M	SD	M	SD	M	SD
SAD								
Male	21.82	4.08	23.23	3.61	20.73	4.91	21.89	5.12
Female	22.49	4.95	22.69	4.58	22.41	5.47	22.75	4.85
Total	22.17	4.53	22.95	4.12	21.61	5.24	22.34	4.96
ANGRY								
Male	21.69	3.86	22.52	3.96	21.09	5.15	22.67	5.17
Female	21.49	4.90	21.27	4.78	21.39	5.47	21.39	5.35
Total	21.58	4.40	21.87	4.42	21.25	5.28	22.00	5.26
NEUTRAL								
Male	24.64	5.17	24.30	4.13	24.15	6.73	23.85	4.84
Female	24.14	5.13	26.06	5.47	23.63	6.03	25.84	6.21
Total	24.37	5.11	25.22	4.92	23.88	6.32	24.90	5.64
HAPPY								
Male	29.86	10.26	27.93	8.73	32.40	13.73	29.96	11.46
Female	30.39	12.13	28.29	10.17	31.51	13.91	28.82	11.17
Total	30.14	11.19	28.12	9.43	31.93	13.71	29.36	11.23

Note. N = 61.

Table 5

Regression Analyses Summary for the Single Face Task

	Model/Predictors	B	Beta	t	p	95%CI	R^2	F	df	p	Adjusted R^2	R^2 change	F change	df	Sig. F Change
Time to first fixation															
Mouth															
Happy															
	Overall Model						0.09	1.50	3,44	0.230	0.03	0.00	0.17	1,44	0.683
	Depressive symptoms	-36.64	-0.22	-1.06	0.293	[-106.04, 32.77]									
	Sex*Depression interaction	-19.72	-0.12	-0.41	0.683	[-116.33, 76.89]									
Negative															
	Overall Model						0.16	2.55	3,41	0.069	0.10	0.13	6.43	1,41	0.015
	Depressive symptoms	-35.20	-0.45	-2.16	0.037	[-68.17, -2.22]									
	Sex*Depression interaction	57.15	0.73	2.54	0.015	[11.62, 102.68]									
Neutral															
	Overall Model						0.15	2.87	3,48	0.046	0.10	0.05	2.95	1,48	0.092
	Depressive symptoms	84.01	0.42	2.31	0.025	[10.75,157.28]									
	Sex*Depression interaction	-91.86	-0.44	-1.72	0.092	[199.33, 15.62]									
Surprise															
	Overall Model						0.11	1.87	3,48	0.147	0.05	0.10	5.10	1,48	0.029
	Depressive symptoms	-52.18	-0.26	-1.36	0.181	[-129.50,25.15]									
	Sex*Depression interaction	123.13	0.63	2.26	0.029	[13.48, 232.77]									
Total % fixations															
Mouth															
Happy															
	Overall Model						0.05	1.05	3,57	0.379	0.00	0.01	0.53	1,57	0.468

	Depressive symptoms	0.18	0.19	0.87	0.388	[-0.24, 0.61]									
	Sex*Depression interaction	-0.19	-2.10	-0.73	0.468	[-0.72, 0.34]									
Negative															
	Overall Model						0.06	1.30	3,57	0.285	0.02	0.02	1.02	1,57	0.320
	Depressive symptoms	0.13	0.19	0.86	0.394	[-0.17, 0.42]									
	Sex*Depression interaction	-0.18	-0.28	-1.01	0.317	[-0.55, 0.18]									
Neutral															
	Overall Model						0.08	1.72	3,57	0.170	0.04	0.01	0.66	1,57	0.419
	Depressive symptoms	-0.17	-0.22	-1.01	0.316	[-0.51, 0.17]									
	Sex*Depression interaction	0.17	0.22	0.81	0.419	[-0.25, 0.60]									
Surprise															
	Overall Model						0.14	3.18	3,57	0.030	0.10	0.08	5.18	1,57	0.027
	Depressive symptoms	0.54	0.53	2.57	0.013	[0.12, 0.96]									
	Sex*Depression interaction	-0.60	-0.61	-2.28	0.027	[-1.12, -0.07]									

Table 6

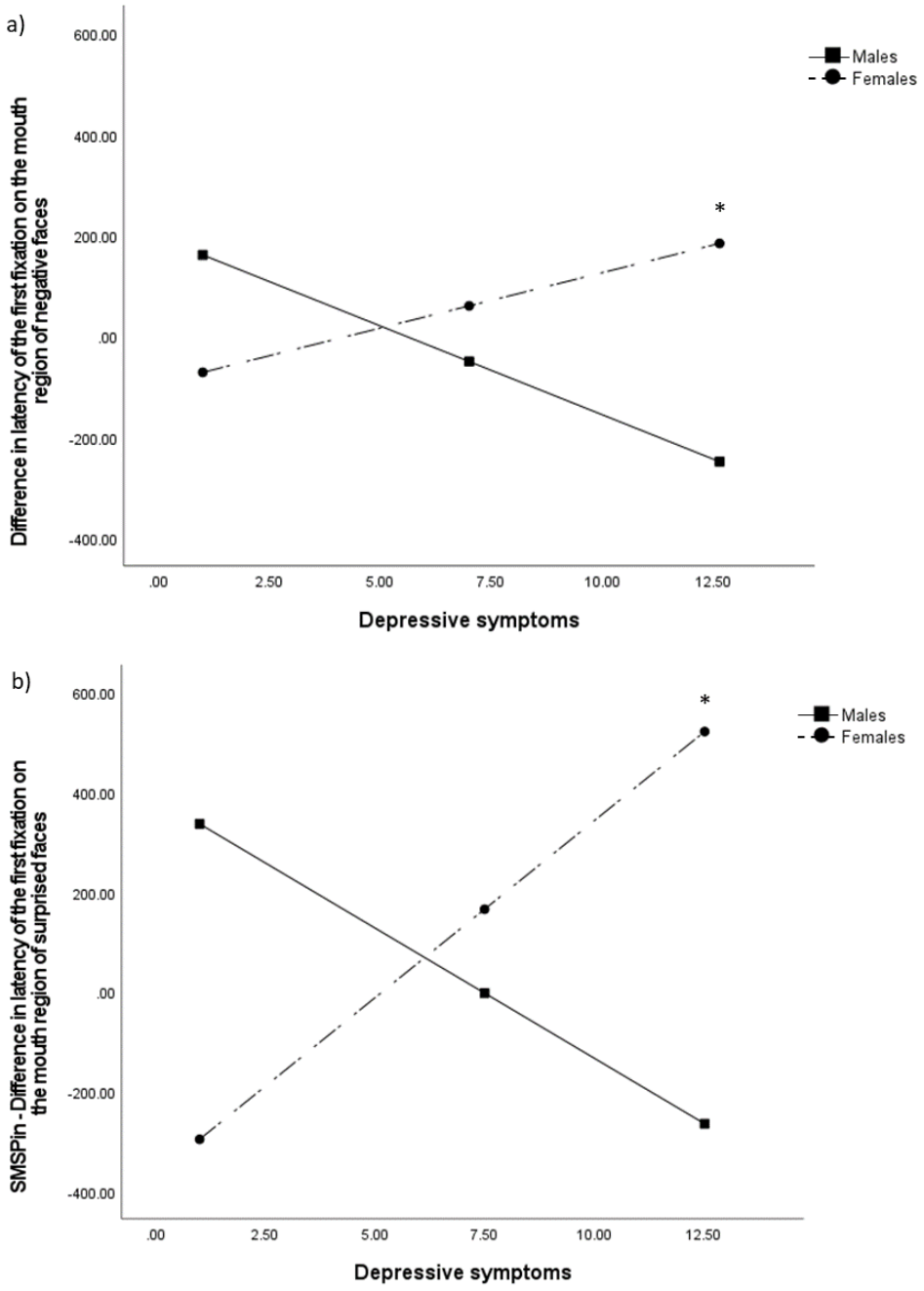
Regression Analyses Summary for the Quadrant Face Task

	Predictor	B	Beta	t	p	95%CI	R^2	F	df	p	Adjusted R^2	R^2 change	F change	df	Sig. F Change
Time to first fixation															
Sad															
	Overall Model						0.09	1.75	3,57	0.166	0.04	0.05	2.97	1,57	0.090
	Depressive symptoms	0.02	0.45	2.10	0.040	[.001, .04]									
	Sex*Depression interaction	-0.02	-0.48	-1.72	0.090	[-0.05, 0.00]									
Angry															
	Overall Model						0.14	3.00	3,57	0.038	0.09	0.13	8.34	1,57	0.005
	Depressive symptoms	0.03	0.39	1.86	0.068	[-0.00, 0.07]									
	Sex*Depression interaction	-0.06	-0.77	-2.89	0.005	[-0.10, -0.02]									
Neutral															
	Overall Model						0.05	1.07	3,57	0.368	0.00	0.01	0.27	1,57	0.604
	Depressive symptoms	0.02	0.26	1.19	0.238	[-0.01, 0.04]									
	Sex*Depression interaction	-0.01	-0.15	-0.52	0.604	[-0.04, 0.02]									
Happy															
	Overall Model						0.01	0.24	3,57	0.872	-0.04	0.01	0.37	1,57	0.544
	Depressive symptoms	0.00	0.07	0.33	0.746	[-0.02, 0.03]									
	Sex*Depression interaction	-0.01	-0.18	-0.61	0.544	[-0.04, 0.02]									
Total % of fixations															
Sad															
	Overall Model						0.09	1.96	3,57	0.130	0.05	0.05	2.99	1,57	0.089
	Depressive symptoms	-0.36	-0.47	-2.18	0.033	[-0.69, -0.03]									
	Sex*Depression interaction	0.35	0.47	1.73	0.089	[-0.06, 0.76]									

Angry															
	Overall Model						0.13	2.94	3,57	0.041	0.09	0.09	5.92	1,57	0.018
	Depressive symptoms	-0.16	-0.25	-1.19	0.240	[-0.43, 0.11]									
	Sex*Depression interaction	0.41	0.65	2.43	0.018	[0.07, 0.75]									
Neutral															
	Overall Model						0.06	1.14	3,57	0.341	0.01	0.01	0.79	1,57	0.378
	Depressive symptoms	-0.09	-0.09	-0.41	0.683	[-0.51, 0.33]									
	Sex*Depression interaction	0.23	0.25	0.89	0.378	[-0.29, 0.75]									
Happy															
	Overall Model						0.10	2.01	3,57	0.123	0.05	0.10	5.97	1,57	0.020
	Depressive symptoms	0.56	0.39	1.83	0.072	[-0.05, 1.17]									
	Sex*Depression interaction	-0.93	-0.67	-2.44	0.018	[-1.69, -0.17]									

Figure 1

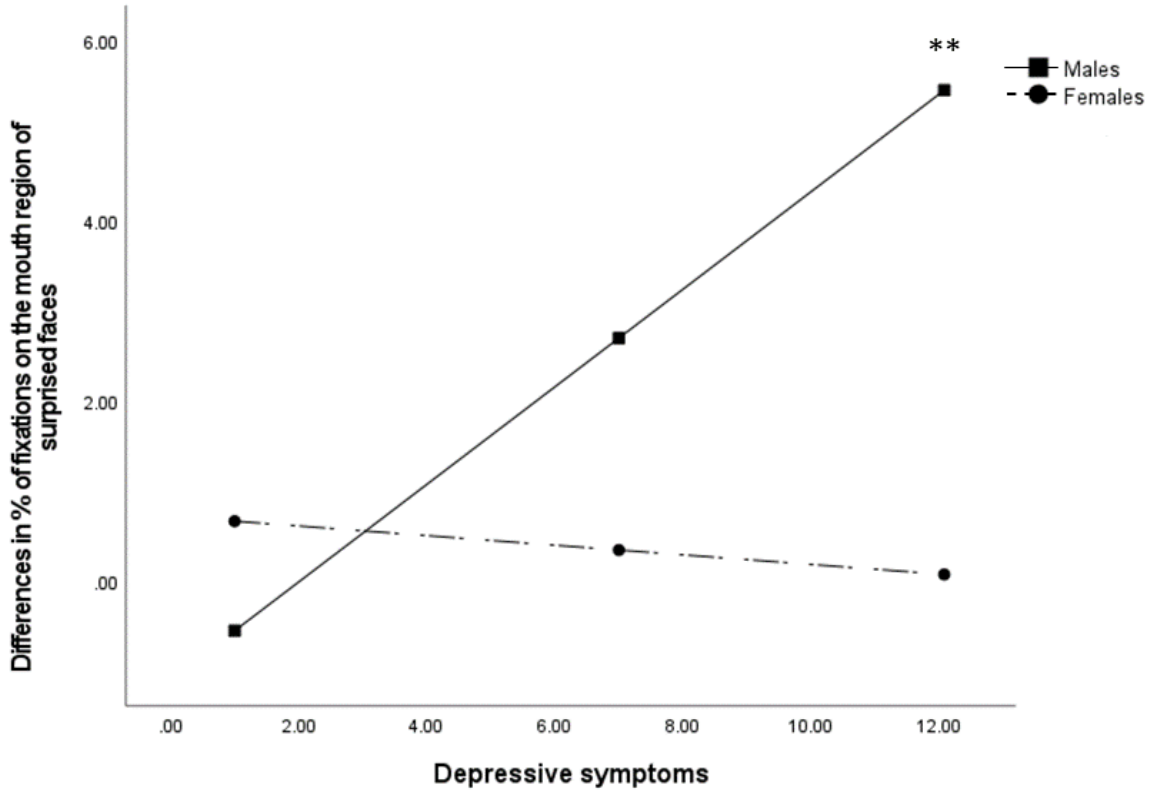
Depression x Sex Interaction Effects on Latencies of First Fixations on the Mouth Region of a) Negative and b) Surprised Facial Expressions Following Oxytocin Relative to Placebo in the Single Face Task.



Note. Difference scores are computed as latencies (in ms) in the oxytocin condition minus those in the placebo condition (OT – PL). *$p < 0.05$

Figure 2

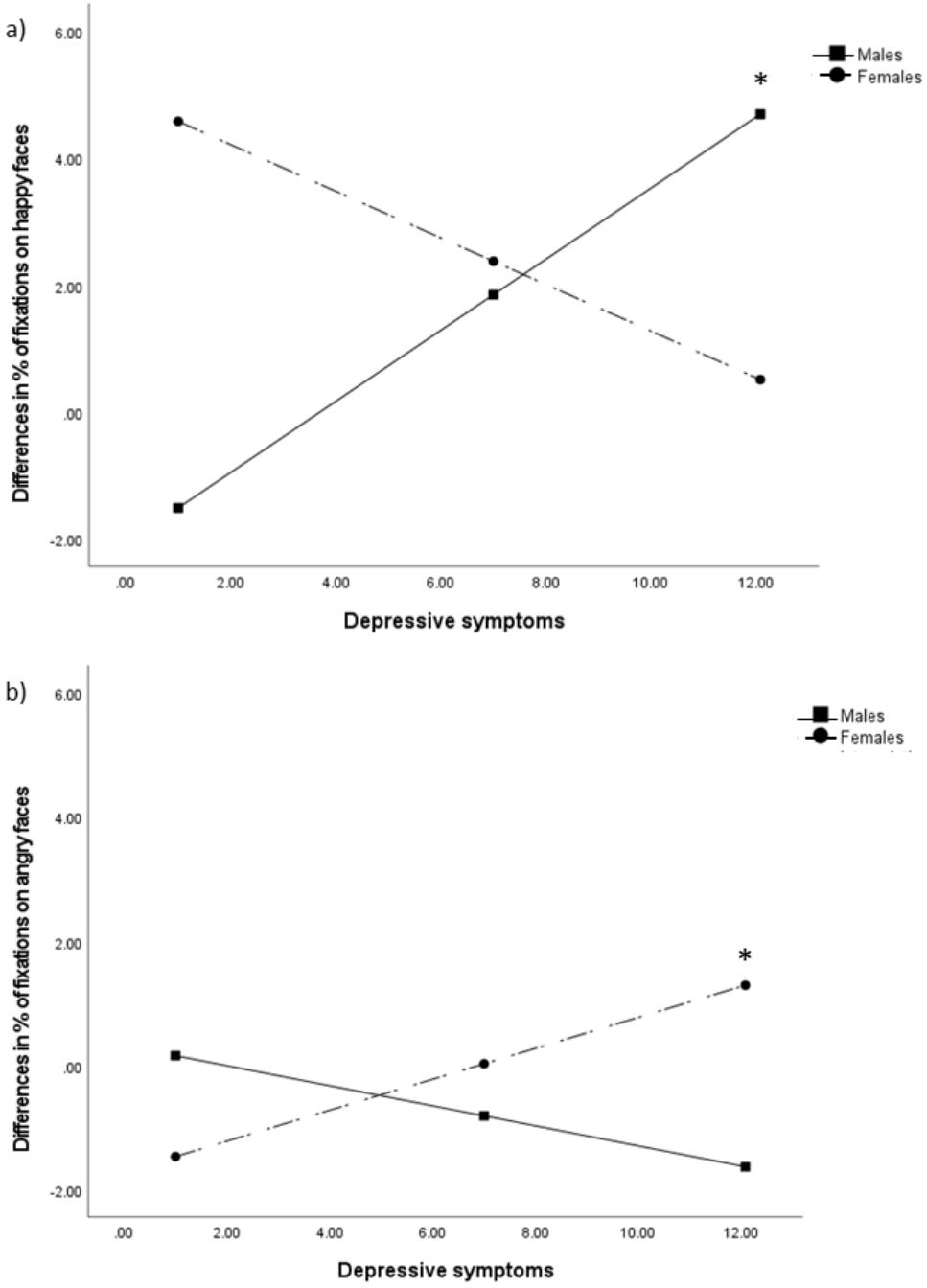
Depression x Sex Interaction Effects on Percentages of Fixations on the Mouth Region of Surprised Faces Following Oxytocin Relative to Placebo in the Single Face Task.



Note. Difference scores are computed as percentages in the oxytocin condition minus those in the placebo condition (OT - PL). ***p* < *0.01*.

Figure 3

Depression x Sex Interaction Effects on Percentages of Fixations on a) Happy and b) Angry Faces Following Oxytocin Relative to Placebo in the Quadrant Face Task.



Note. Difference scores are computed as percentages in the oxytocin condition minus those in the placebo condition (OT-PL). Difference scores are presented here in standardized units. *$p < 0.05$