Published in final edited form as:

Schizophr Res. 2015 March ; 162(0): 52–56. doi:10.1016/j.schres.2015.01.022.

Endogenous Oxytocin Levels Are Associated with the Perception of Emotion in Dynamic Body Expressions in Schizophrenia

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Abstract

Lower endogenous oxytocin levels have been associated with impaired social cognition in schizophrenia, particularly facial affect identification. Little is known about the relationship between oxytocin and other forms of emotion perception. In the current study, 41 individuals with schizophrenia (SZ) and 22 demographically matched healthy controls (CN) completed a forced-choice affective body expression classification task. Stimuli included dynamic videos of male and female actors portraying 4 discrete emotions: happiness, sadness, anger, and neutral. Plasma oxytocin levels were determined via radioimmunoassay. Results indicated that SZ had significantly higher plasma oxytocin concentrations than CN. SZ were also less accurate at identifying expressions of happiness and sadness; however, there were no group differences for anger or neutral stimuli. A group x sex interaction was also present, such that female CN were more accurate than male CN, whereas male SZ were more accurate than female SZ. Higher endogenous oxytocin levels were associated with better total recognition in both SZ and CN; this association was specific to females in SZ. Findings indicate that sex plays an important role in identifying emotional expressions in body gestures in SZ, and that individual differences in endogenous oxytocin predict emotion perception accuracy.

Keywords

Oxytocin; Emotion; Schizophrenia; Psychosis; Emotion Perception

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Contributors: Gregory Strauss, William Keller, Robert Buchanan, James Koenig, and James Gold designed the study. Statistical analyses and writing of the first draft of the manuscript were performed by Gregory Strauss. James Koenig and his lab conducted oxytocin radioimmunoassays. All authors contributed to and approved the final manuscript.

Conflict of Interest: Authors have no conflicts of interest relevant to the current study.

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1.0. Introduction

There is consistent evidence for emotion perception abnormalities in individuals with schizophrenia (SZ) (Kohler et al., 2010). These impairments have been observed across a number of stimulus types (e.g., facial, vocal, audio-visual) and task formats (e.g., identification, differentiation, intensity judgment), and are more pronounced for negative (e.g., fear, anger, sadness) than positive (e.g., happiness, surprise) emotions (Edwards et al., 2002; Kohler et al., 2010). Several variables moderate the magnitude of emotion perception deficits in SZ, including severity of negative and positive symptoms, age, illness duration, antipsychotic medications, phase of illness, and inpatient vs. outpatient status (Kohler et al., 2010; Edwards et al., 2002). Recently, lower endogenous oxytocin levels have also been associated with poorer facial affect perception, particularly among females with SZ (Rubin et al., 2011). Intranasal administration of oxytocin has also been shown to improve several aspects of social cognition in SZ, including facial affect perception (Averbeck et al., 2012; Davis et al., 2013; Davis et al., 2014; Fischer-Shofty et al., 2013; Gibson et al., 2014; Goldman et al., 2011; Pedersen et al., 2011; Woolley et al., 2014). In SZ, aberrant oxytocin functioning may therefore be an important biological correlate of emotion perception abnormalities.

However, facial affect identification is only one form of emotion perception. To determine whether associations between oxytocin and emotion perception are specific to facial affect processing, it will be important to administer tasks using emotional stimuli other than faces. Recently, the field of affective science has developed and validated a series of stimulus sets portraying expressions of emotion in body gestures. Healthy individuals can rapidly and accurately identify discrete emotional states from faceless stimuli depicting body expressions of emotion; such stimuli may be ideal for examining whether the association between oxytocin and emotion perception is unique to faces or a generalizable effect. To our knowledge, only one published study has examined emotion perception in body gestures in participants with SZ. Van den Stock et al. (2011) presented participants with static target photographs displaying a faceless male or female actor portraying either sadness, anger, or fear that had to be matched to one of two simultaneously presented static probe images, one of which displayed the same emotion as the target and the other a foil from another affective category. Results indicated that participants with SZ were less accurate and slower than controls at identifying expressions of anger, sadness, and fear. However, Van den Stock et al (2011) failed to include stimuli representing discrete positive emotions. Therefore, it is unclear whether the valence-related patterns of performance that are observed during facial affect tasks (i.e., impaired perception of negative and intact perception of positive) also occur during the identification of emotion in body gestures. Additionally, it is also unknown whether the perception of emotion in body gestures is associated with endogenous oxytocin levels.

The current study addressed these gaps in the literature by administering a forced-choice affective body expression classification task to a sample of outpatients diagnosed with SZ and demographically matched healthy controls. The following primary hypotheses were made: 1) consistent with Van den Stock et al. (2011) who reported that participants with SZ

performed more poorly than controls across all stimulus conditions, a significant main effect of Group was expected; 2) similar to studies examining emotion perception for facial stimuli (see Kohler et al., 2010), participants with SZ were expected to display poorer performance than healthy controls for negatively valenced, but not positively valenced body gestures; 3) emotion perception impairments were expected to be associated with lower endogenous oxytocin levels in participants with SZ and healthy controls. Several secondary hypotheses were also made in relation to sex differences. It is well documented that females have higher oxytocin levels than males (Carter, 2007). Significant associations between endogenous oxytocin and facial affect perception have also been reported in females with SZ, but not males (Rubin et al., 2011). Given these sex-related effects, we hypothesized that females with SZ would evidence significant associations between oxytocin and the identification of emotion in body gestures, and that these associations would be nonsignificant in males.

2.0. Method

2.1. Participants

Participants included 40 individuals meeting DSM-IV-TR criteria for schizophrenia (SZ) and 22 healthy controls (CN). Individuals with SZ were recruited through the Outpatient Research Program at the Maryland Psychiatric Research Center, and evaluated during a period of clinical stability as evidenced by no changes in medication type or dosage for a period greater than or equal to four weeks. Consensus diagnosis was established via a best-estimate diagnostic approach based on the Structured Clinical Interview for DSM-IV (SCID: First et al., 2001), psychiatric history, and multiple interviews. All SZ participants were prescribed one or more antipsychotics at the time of testing, either alone (clozapine, n=12; haloperidol, n=5; ziprasidone, n=3; aripiprazole, n=1; fluphenazine, n=2; olanzapine, n=2; risperidone, n=4; chlorpromazine, n=1; quetiapine, n=1; thioridazine, n=1) or in combination with another antipsychotic (clozapine and risperidone, n=4; clozapine and haloperidol, n=1; clozapine and quetiapine, n=2; haloperidol and aripiprazole n=1).

CN were recruited through random-digit dialing, word of mouth among recruited participants, and newspaper advertisements. CN had no current Axis I or II diagnoses as established via the SCID (First et al., 2001) and SID-P (Pföhl et al., 1997), no family history of psychosis, and were not taking psychotropic medications. All participants denied a history of neurological injury or disease, medical disorders that could interfere with test results (e.g., cancer, infectious disease, sleep apnea), and did not meet criteria for substance abuse or dependence disorders within the last six months. Lack of recent substance use was confirmed using urine toxicology testing. Female participants completed a pregnancy screen, as this can affect oxytocin levels; no participants were pregnant. All participants provided informed consent for a protocol approved by the University of Maryland Institutional Review Board.

Participants with SZ and CN did not significantly differ in age, parental education, sex, or ethnicity; however, SZ had lower personal education than CN (see Table 1).

2.2. Procedures

Individuals with SZ completed a standard clinical interview that was performed by a clinical psychologist (GPS) trained to MPRC reliability standards (reliability >0.80). After this interview, participants were rated on the Brief Negative Symptom Scale (range 0-78) (BNSS: Kirkpatrick et al., 2011; Strauss et al., 2012ab), Brief Psychiatric Rating Scale (total range 0-126) (BPRS: Overall & Gorham, 1962), and Level of Function Scale (range 0-24) (LOF: Hawk et al., 1975).

Plasma oxytocin levels were determined via radioimmunoassay in extracted samples using a magnetic bead kit from Phoenix Pharmaceuticals, Inc. Samples were assayed in duplicate; the average of these samples was taken as the final oxytocin value. Assay sensitivity was 5 pg/ml with minimal cross reactivity with vasopressin. The coefficient of variation averaged 5-8% across the assay.

2.3. Emotion Perception Measure

A forced-choice affective body expression classification task was administered. Participants were presented with a series of video clips depicting actors wearing full-body grey-scale suits through which no facial expressions could be observed. Stimuli were taken from the Atkinson (2004) full-light body gesture stimulus set, which has been validated for normative accuracy and intensity levels. A total of four practice stimuli were first presented, with one stimulus from each of the four target categories of happiness, sadness, anger, and neutral. Afterwards, 80 stimuli were presented in random order across two blocks, for a total of 40 experimental trials per block. There were 10 unique stimuli (5 male and 5 female actors) from the four target categories, each of which occurred once in each block. Each clip lasted for 3 seconds and repeated on a loop until a manual response was provided. Responses were made via a Cedrus serial response box containing four buttons. Written labels for each of the affective categories were presented on the computer screen at all times just beneath the video display. Labels were in the same position for all trials and all participants, and appeared directly above their corresponding response box keys. A sample trial sequence is presented in Figure 1.

2.4. Data Analysis

A mixed-models ANOVA was conducted to evaluate the primary hypotheses of a main effect of Group and a significant Emotion $\times$ Group interaction. Bivariate correlations were calculated for each group to evaluate associations between plasma oxytocin levels and performance on the emotion perception task. Secondary, exploratory analyses were conducted to evaluate the effect of sex on emotion perception between groups using a Group $\times$ Sex $\times$ Emotion mixed-model ANOVA. Correlations between oxytocin and emotion perception were also evaluated separately for men and women within SZ and CN groups.

3.0. Results

3.1. Group Differences in Plasma Oxytocin Levels

One-way ANOVA revealed that individuals with schizophrenia had significantly higher endogenous oxytocin levels than healthy controls, $F(1, 60) = 2.84, p < 0.02$.

3.2. Emotion Perception of Body Gestures

Emotion perception performance for SZ and CN is presented in Figure 2, panel A. A 2 Group (SZ, CN) $\times$ 4 Emotion (Happiness, Sadness, Anger, Neutral) mixed-models ANOVA revealed a significant effect of Group, $F(1, 61) = 15.6, p < 0.001$, and a significant within-subjects effect of emotion, $F(3, 183) = 13.6, p < 0.001$; however, the Group $\times$ Emotion interaction was nonsignificant, $F(3, 183) = 0.36, p = 0.78$. Follow-up one-way ANOVAs indicated that SZ were less accurate at identifying happiness, $F(1, 60) = 9.92, p < 0.01$, and sadness $F(1, 60) = 19.15, p < 0.001$, and were less accurate overall, $F(1, 60) = 21.41, p < 0.001$, than CN. However, groups did not differ in accuracy for neutral, $F(1, 60) = 1.64, p = 0.21$, or anger, $F(1, 60) = 3.60, p = 0.063$.

Correlations between oxytocin and emotion perception are presented in Table 2 for each group. Higher endogenous oxytocin levels were associated with better total accuracy in both CN and SZ. Additionally, higher plasma oxytocin concentrations were associated with better accuracy for neutral stimuli in CN, and better accuracy for sadness in SZ.

In SZ, poorer identification of sadness was associated with greater severity of BNSS negative symptoms ($r = -0.32, p < 0.05$) and poorer functional outcome ($r = 0.37, p < 0.02$). All other correlations between emotion perception and measures of positive symptoms, negative symptoms, disorganized symptoms, and functional outcome were nonsignificant. Oxytocin and task performance were not significantly associated with chlorpromazine equivalent dosage. Correlations between oxytocin and measures of symptom severity and functional outcome are reported in Strauss et al (in press).

3.3. Sex-Related Effects

ANOVAs indicated that there were no significant Group $\times$ Sex interactions for age [$F(1, 67) = 0.13, p = 0.73$], personal education [$F(1, 67) = 1.53, p = 0.22$], or parental education [$F(1, 67) = 1.91, p = 0.17$], indicating similar sex-related demographics in CN and SZ. Males and females with SZ also did not differ on BPRS psychosis [$F(1, 39) = 1.56, p = 0.22$], BPRS disorganization [$F(1, 39) = 0.81, p = 0.37$], BPRS total [$F(1, 39) = 0.23, p = 0.63$], BNSS total [$F(1, 39) = 0.25, p = 0.62$], or LOF total scores [$F(1, 39) = 0.17, p = 0.68$].

A 2 (Group) $\times$ 2 (Sex) $\times$ 4 (Emotion) Mixed-Models ANOVA revealed a significant Group $\times$ Sex interaction, $F(1, 58) = 5.22, p < 0.03$, and a significant between-subjects effect of Group, $F(1, 58) = 22.69, p < 0.001$ (see Figure 2, panel B). All other main effects and interactions were nonsignificant. One-way ANOVAs indicated that male CN had better total emotion recognition than male SZ, $F(1, 43) = 7.52, p < 0.01$, and that female CN had better total emotion recognition than female SZ, $F(1, 18) = 19.12, p < 0.001$. One-way ANOVAs also indicated no sex differences in overall accuracy for CN, $F(1, 20) = 1.63, p = 0.22$; however, this may be due to limited power. As can be seen in Figure 2B, female CN show a trend toward better accuracy than male CN. In contrast, male SZ had significantly higher total accuracy than female SZ, $F(1, 38) = 4.45, p < 0.05$.

Sex-specific correlations are presented in Table 3. Within the SZ group, sex-specific associations were evident, such that higher endogenous oxytocin was associated with better accuracy for anger stimuli and total accuracy in females. Sex-specific associations between

oxytocin and accuracy were also evident in CN, where males with higher oxytocin had higher happiness, neutral, and total score accuracy, as well as poorer sadness accuracy; there were no significant associations between oxytocin and emotion recognition in CN females. The lack of significant correlations in female CN is likely a function of limited number of female subjects in the CN group and subsequently reduced power. Indeed, the magnitude of correlations observed in female CN is comparable to male CN.

4.0. Discussion

The current study presented some of the first evidence that emotion perception deficits in SZ extend beyond facial and vocal channels and also occur when people with SZ are required to identify emotion in body gestures. Specifically, individuals with SZ displayed poorer performance than CN for body gestures depicting happiness and sadness, but not anger or neutral. These findings extend the results of Van Den Stock et al. (2011), which found that SZ were more impaired than CN at identifying static images of sadness, anger, and fear. At first glance, the current results appear to suggest that the perception of emotion in body gestures yields a finding that is not observed in tasks using facial stimuli- a deficit in identifying expressions of happiness. However, this result may simply reflect that people with SZ were most impaired for the most difficult stimulus type in the body expression task, and are generally least impaired for the easiest stimulus type in prior studies using facial affect tasks. Future studies that equate emotional categories on difficulty and compare identification rates across facial, vocal, and body expression stimuli are needed to adequately examine differential deficits. Interestingly, we did not replicate the deficit in identifying anger in body expressions that was observed in Van den Stock et al (2011). Discrepant findings may reflect differences in stimuli (static vs. dynamic) and task requirements (matching vs. identification) used across these studies. Future studies should utilize multiple body gesture stimuli and tasks (e.g., matching, labeling) within the same study. Furthermore, given that fear recognition has been demonstrated to be particularly impaired in SZ with facial stimuli, future studies should also include fearful body stimuli to evaluate generalization of fear-related deficits.

Findings also extend prior research by suggesting that associations between emotion perception and oxytocin are not specific to facial affect processing. Specifically, we found that in both SZ and CN groups, lower endogenous oxytocin levels were associated with poorer global emotion perception in body gestures. Furthermore, similar to studies finding sex-specific associations between plasma OT and facial affect identification in SZ, the current study found that associations were significant in females with SZ but not males. These findings should be interpreted in light of the significant sex by group interaction (females < males in SZ; males < females in CN), as well as higher overall oxytocin levels in the SZ group. Studies conducted on rodents suggest that oxytocin may indeed have differential effects on females than males, perhaps due to interactions between oxytocin and gonadal hormones (Razzoli et al., 2003). Sex differences in the effects of intranasal administration of oxytocin on emotion perception have also been noted in humans, such that oxytocin increases neural activation in the amygdala in females and decreases it in males (Domes, 2007, 2010). Individuals with SZ also display sex differences in neural activation during emotion perception, with different patterns of cortical and subcortical activations

observed in men and women (Mendrek et al., 2007). Future studies are needed to determine whether sex-related differences in neural response during emotion perception are associated with individual differences in endogenous oxytocin levels in people with SZ.

Overall, these findings add to a growing literature suggesting that oxytocin may play a vital role in emotion perception in SZ. However, certain limitations should be considered when interpreting these results. First, sample sizes were relatively small per group and not ideal for exploring sex differences. Sex-related analyses were underpowered to detect significant effects, especially correlations. Second, several factors may have contributed to discrepant findings between the current and past studies regarding whether endogenous oxytocin levels are abnormal in people with SZ. All participants with SZ were treated with antipsychotics. Drugs that block dopamine receptors may increase plasma oxytocin levels (Kiss et al., 2010), potentially producing group differences in endogenous oxytocin levels that are more driven by medication use than disease. This explanation seems unlikely, however, given that chlorpromazine equivalent dosage was not correlated with plasma oxytocin levels. Individuals with SZ are also more likely to smoke than CN, and smoking may affect plasma oxytocin concentrations. The current study did not record smoking status and it is unclear how smoking may have impacted group differences in oxytocin levels. Fourth, it is difficult to draw firm conclusions regarding the role of oxytocin on brain function given that plasma oxytocin levels gathered here reflect peripheral, rather than central nervous system concentrations. Finally, the extent to which results reflect a problem with oxytocin receptor function is unclear given that receptor function was not measured; it is possible that higher oxytocin levels in SZ represent a compensatory response to a lower sensitivity of the oxytocin receptor to circulating levels of the hormone.

Acknowledgments

The authors would like to thank the participants who completed the study, as well as staff at the Maryland Psychiatric Research Center who contributed to data collection. We are especially thankful to Dana Brady for processing oxytocin levels and members of Dr. Strauss' team who conducted subject recruitment and testing: Lauren Catalano, Adam Culbreth, Bern Lee, Jamie Adams, Travis White, Tehreem Galani, and Carol Vidal.

Role of Funding Source. Research supported in part by US National Institutes of Mental Health Grant P50-MH082999 (WT Carpenter) and a Department of Veterans Affairs Mental Illness Research Education Clinical Centers VISN 5 pilot grant (GP Strauss)

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Figure 1. Sample Trial Sequence for the Emotion Perception Task

Note. This sample trial sequence presents examples of anger and sadness; fixation was presented for 1 second and participants had unlimited time to make a forced-choice response to the stimulus clip that repeated on a loop until response.

Figure 2. Identification of Emotion in Body Gestures in SZ and CN

Note. A = Emotion perception in all schizophrenia vs all control participants; B = Sex differences in emotion perception in controls and schizophrenia; SZ = schizophrenia, CN = control. Bars reflect standard error.

Table 1
Participant Demographic and Clinical Characteristics

	SZ (n = 40)	CN (n = 22)	Test-statistic, p-value
Age	43.73 (11.85)	43.14 (9.44)	F = 0.05, p = 0.81
Participant Education	12.95 (2.08)	15.05 (1.86)	F = 15.47, p < 0.001
Parental Education	13.46 (2.45)	14.18 (2.42)	F = 1.03, p = 0.32
% Male	70.7%	68.2%	$\chi^2 = 0.04$, p = 0.83
Ethnicity			$\chi^2 = 1.12$, p = 0.77
% Caucasian	90.2%	95.5%	
% African-American	4.9%	4.5%	
% Native-American	2.4%	0%	
% Bi-racial	2.4%	0%	
Plasma Oxytocin (pg/ml)	24.46 (7.54)	19.66 (5.86)	F = 6.69, p < 0.02
Symptoms			
BNSS Total	26.08 (16.97)	--	--
BPRS Total	38.97 (9.09)	--	--
BPRS Positive	2.41 (1.13)	--	--
BPRS Negative	2.25 (1.12)	--	--
BPRS Disorganized	1.51 (0.45)	--	--
Functional Outcome			
LOF Total	18.32 (7.01)	--	--
LOF Social	4.55 (2.57)	--	--
LOF Work	1.79 (2.60)	--	--

Note. Data reflect means, standard deviations in parentheses, or percentages within each group. SZ = schizophrenia; CN = control; BNSS = Brief Negative Symptom Scale; BPRS = Brief Psychiatric Rating Scale, LOF = Level of Function scale

Table 2
Spearman Correlations between Plasma Oxytocin and Affective Body Gesture Identification Accuracy

Group	Affective Body Gesture			
	Angry	Happy	Sad	Neutral
SZ (n=40)	0.25	0.11	0.38*	0.16
CN (n=22)	0.04	0.31	-0.28	0.50*
				0.31* 0.54*

Note. SZ = schizophrenia; CN = control;
* p < 0.05

Table 3
Spearman Correlations between Plasma Oxytocin and Affective Body Gesture Identification in Men and Women

Group	Affective Body Gesture				
	Angry	Happy	Sad	Neutral	Total
SZ Male (n=28)	0.13	0.00	0.37	0.07	0.12
SZ Female (n=12)	0.60*	0.47	0.38	0.24	0.77**
CN Male (n=15)	-0.04	0.52*	-0.55*	0.54*	0.55*
CN Female (n=7)	0.26	-0.57	0.47	0.47	0.25

Note. SZ = schizophrenia; CN = control;

* p < 0.05;

** p < 0.01