



Sex-specific associations between plasma oxytocin levels and schizotypal personality features in healthy individuals



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ABSTRACT

Objectives: Oxytocin (OT) has been shown to play a crucial role in the biology of social interaction. Sex differences associated with this neuropeptide system have been reported. OT may serve as an indicator of interpersonal stress, especially in women. The aim of this study was to investigate the sex-specific associations between plasma OT levels and schizotypal personality features, especially in interpersonal dimension, in healthy individuals.

Methods: Ninety six healthy participants, including 41 males and 55 females, were recruited. Fasting blood samples were analyzed by enzyme immunoassay of OT. The Schizotypal Personality Questionnaire (SPQ) was administered. Mann–Whitney *U* test was used to test the difference between male and female. Spearman's ρ correlation analysis (two-tailed) was carried out to examine the association between OT level and SPQ score.

Results: The results showed that OT level was significantly positively correlated with total score and interpersonal dysfunction dimensional scores of the SPQ only in females.

Conclusions: Although the causal relationship remains unclear, our findings provide further evidence to support the sexual dimorphic role of OT in interpersonal biology. Moreover, the effect of sex difference also is taken into consideration.

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1. Introduction

A growing body of evidence from animal and human studies has implicated the role of the neuropeptide oxytocin (OT) in social cognitive functions and social bond formation (Carter, 2013; Carter and Porges, 2013). Research in animals showed OT could activate mesocorticolimbic and nigrostriatal dopamine pathways to establish social bonds and even pair bonding (Abi-Dargham, 2012; Love, 2013; Romero-Fernandez et al., 2013). Human functional imaging studies have also revealed the role of OT in social bond formation (Douglas, 2010; Riem et al., 2012). In addition, sex differences associated with this neuropeptide system have been reported (Fischer-Shofty et al., 2013). Estrogen affects the expression of OT receptors and the responsiveness to OT. Females usually present

with higher levels of OT and more OT receptor expression (Zingg and Laporte, 2003; Carter, 2007). The elevation of OT levels while facing interpersonal distress or psychological stress is also more obvious in females (Turner et al., 1999; Taylor et al., 2006). Sex difference in the neural and behavioral response to oxytocin administration during human social interaction associations has also been reported (Rilling et al., 2014).

Individuals with certain personality characteristics could face long-term social and interpersonal difficulties. For instance, those with schizotypal personality disorder were characterized by acute discomfort with, and reduced capacity for, close relationships, as well as by cognitive or perceptual distortions and eccentricities of behavior (Oldham et al., 2009). Individuals with the schizotypal personality traits who do not fit the diagnosis criteria, have received great attention for their relatively high risk of developing schizophrenia (Fenton and McGlashan, 1989; Raine, 2006). Additionally, it has been shown that two main features of schizophrenia, higher striatal D₂ availability and poorer executive function were noted in healthy individuals with higher schizotypal personality traits (Chang et al., 2011; Chen et al., 2012).

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Interestingly, the effects of the OT on social behavior and social cognitive functions in schizophrenia have been the topic of increasing investigation (Macdonald and Feifel, 2012; Davis et al., 2013; De Berardis et al., 2013). In patients with schizophrenia, endogenous plasma OT concentrations are lower than normal subjects and correlate negatively with psychotic and negative symptoms (Keri et al., 2009; Rubin et al., 2010). Daily extraneous intranasal OT treatment enhances social cognition in schizophrenia (Feifel et al., 2010; Pedersen et al., 2011). Although the underlying mechanisms on schizophrenia remaining unknown, OT's beneficial effects have been speculated to be related its act through regulating mesolimbic dopamine pathways and modulating the activation of amygdala (Domes et al., 2007; Rosenfeld et al., 2011). Rubin et al. (2010, 2011) also revealed sex-specific associations between peripheral OT, social cognition and symptom severity in patients with schizophrenia.

While both the role of OT in the pathophysiology and treatment of schizophrenia have been studied, the relationship between peripheral OT and schizotypal personality characteristics in healthy individuals has not been explored. The current study aims to explore if there are sex-specific associations between peripheral OT levels and schizotypal dimensional features in healthy individuals. Our hypothesis is that sex-specific significant relationships would exist between peripheral OT levels and interpersonal dimension of Schizotypal Personality Questionnaire (SPQ) in healthy individuals as that been demonstrated in patients with schizophrenia.

2. Methods

2.1. Ethics statement

The research protocol was approved by the Ethical Committee for Human Research at the National Cheng Kung University, and written informed consent was obtained from each subject before any procedures were performed.

2.2. Subjects

The participants were enrolled from the community through advertisement. They were recruited as healthy controls in our previous studies (Yang et al., 2007; Yeh et al., 2009, 2012; Hsieh et al., 2010). The individuals were excluded if they were found to have a mental illness/psychiatric disorder after a diagnostic interview, the Chinese version of the Mini International Neuropsychiatry Interview (MINI) (Sheehan et al., 1998). Participants with a history of physical disease, alcohol abuse, or other substance abuse were also omitted from our study. In total, 96 healthy participants, including 41 males and 55 females (8 were menopause), with a mean age of 33.52 years (SD = 12.11) were recruited. The age and OT levels did not differ between male and female, but body mass index (BMI) and smoking rate were significantly higher in male group (Table 1). The mean SPQ score recorded in the current study was similar to those previously reported (Rossi and Daneluzzo, 2002; Vollema et al., 2002).

2.3. Schizotypal personality questionnaire (SPQ)

The SPQ is a 74 true-or-false item self-report screening instrument based on the DSM-III-R criteria for schizotypal personality disorder (American Psychiatric Association, 1987; Raine, 1991). Its total score is 82. It contains cognitive–perceptual (CP), interpersonal (IP), and disorganized dysfunction (Dis) dimensions to identify schizotypal dimensional features in the general population (Raine, 1991; Raine et al., 1994; Chen et al., 1997). The Cronbach's alpha value (for internal consistency) and the intra-class correlation

Table 1
Demographic data, oxytocin levels, and SPQ scores.

	Mean ± SD		Test for the sex difference	
	Male (n = 41)	Female (n = 55)	Mann–Whitney U/ χ^2	p
Age	33.50 ± 11.55	33.54 ± 12.62	−0.12	0.91
Oxytocin level (pg/mL)	26.14 ± 6.13	25.37 ± 5.69	−0.83	0.41
BMI	25.13 ± 3.87	21.20 ± 2.52	5.21	<0.001
Smoker			21.99	<0.001
Yes (N, (%))	14 (34.1)	0 (0.0)		
No (N, (%))	27 (65.9)	55 (100.0)		
SPQ				
Total score	17.98 ± 10.60	15.62 ± 10.36	−1.26	0.21
Cognitive–perceptual subscale	6.93 ± 3.82	5.73 ± 4.65	−2.03	0.04
Interpersonal subscale	7.58 ± 5.38	6.84 ± 5.27	−0.79	0.43
Disorganized subscale	3.34 ± 3.15	3.05 ± 2.91	−0.42	0.67

SPQ: schizotypal personality questionnaire; BMI: body mass index. $p < 0.05$ was significant.

coefficient reliability value (for a one week test–retest) of the Chinese version SPQ were 0.95 and 0.86, based on a Taiwanese community schizotypy study (Chen et al., 1997).

2.4. Measurement of oxytocin

Fasting blood samples were collected between 0800 and 1000 h in heparinized plain tube then centrifuged (2400 rpm for 10–15 min at 4 °C). Plasma was then aspirated and stored at −80 °C until assayed by using the enzyme immunoassay (Elisa Kit for oxytocin, USCN Life Science, Houston). The detectable range for this assay is 12.35–1000 pg/mL. Intra-assay coefficient of variation was 10% and inter-assay CV was 12%. The minimum detectable dose of OT is typically less than 4.87 pg/mL.

2.5. Statistical analysis

Because the SPQ score was not of a normal distribution (p of Kolmogorov–Smirnov test < 0.004), Spearman's ρ correlation

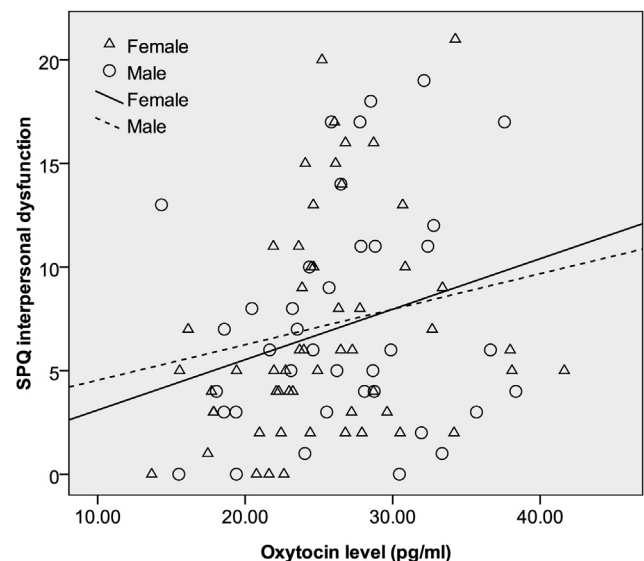


Fig. 1. Positive association between oxytocin level and the interpersonal dysfunction score of SPQ. SPQ: schizotypal personality questionnaire.

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