RESEARCH REPORT

Intranasal Oxytocin Increases Positive Communication and Reduces Cortisol Levels During Couple Conflict

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Background: In nonhuman mammals, the neuropeptide oxytocin has repeatedly been shown to increase social approach behavior and pair bonding. In particular, central nervous oxytocin reduces behavioral and neuroendocrine responses to social stress and is suggested to mediate the rewarding aspects of attachment in highly social species. However, to date there have been no studies investigating the effects of central oxytocin mechanisms on behavior and physiology in human couple interaction.

Methods: In a double-blind placebo-controlled design, 47 heterosexual couples (total $n = 94$) received oxytocin or placebo intranasally before a standard instructed couple conflict discussion in the laboratory. The conflict session was videotaped and coded for verbal and nonverbal interaction behavior (e.g., eye contact, nonverbal positive behavior, and self-disclosure). Salivary cortisol was repeatedly measured during the experiment.

Results: Oxytocin significantly increased positive communication behavior in relation to negative behavior during the couple conflict discussion ($F = 4.18$, $p = .047$) and significantly reduced salivary cortisol levels after the conflict compared with placebo ($F = 7.14$, $p = .011$).

Conclusions: These results are in line with animal studies indicating that central oxytocin facilitates approach and pair bonding behavior. Our findings imply an involvement of oxytocin in couple interaction and close relationships in humans.

Close social relationships play a key role for wellbeing and longevity in humans (1–3). It has been suggested that this beneficial effect of social relationships and particularly of positive couple interaction is mediated through a reduced reactivity of physiological stress systems, namely the hypothalamic-pituitary-adrenal (HPA) axis and the autonomous nervous system (ANS) (4–6). Conversely, marital discord and specifically hostile behavior during couple conflict in unhappy relationships have been shown to substantially impair psychological and physiological well-being (7–9). To date, it is unclear which neurophysiological mechanisms mediate both the beneficial effects of happy close social relationships on psychobiological stress systems as well as the negative effects of repeated and intense couple conflict.

A large body of evidence links the central activity of the neuropeptide oxytocin with affiliative behavior as well as with stress reduction in nonhuman mammals (10,11). In line with this research, initial studies suggest similar social and stress-reducing effects of oxytocin in humans. Notably, recent neuropharmacological research has shown that neuropeptides gain access to the human brain after intranasal administration (12), providing a useful method for studying the central nervous effects of oxytocin in humans (13). Intranasal oxytocin was found to reduce

endocrine and psychological responses to social stress (14), to modulate social memory (15,16), and to increase trust and eye-gazing (17,18) and the ability to infer the mental state of another person ("mind-reading") (19). In line with this, the hormone was shown to attenuate amygdala responses to emotional faces (20,21) and during prosocial behavior (22).

The effects of intranasal oxytocin in human couple interaction have not been investigated so far. Given that oxytocin seems to promote pair bonding behavior in nonhuman mammals and social approach behavior in humans, we hypothesized that oxytocin might affect communication and stress responsiveness in human couples.

In this study, we investigated the effects of a single dose of intranasal oxytocin in comparison with placebo on interaction behavior and HPA axis activity during a laboratory couple conflict discussion.

Methods and Materials

Forty-seven heterosexual couples ($n = 94$ subjects), aged 20–50 years, who were married or had been cohabiting for at least 1 year participated in the study. Exclusion criteria for participation were smoking, chronic mental or physical illness, medication intake and, for women, the intake of hormonal contraceptives, current pregnancy, and breastfeeding. All women were investigated during the luteal phase of their menstrual cycle. Subjects were informed that we were interested in hormonal influences on couple communication and that they would receive either oxytocin or placebo before a conflict conversation in the laboratory. All couples gave written informed consent and were offered 100 Swiss Francs for participation. The study was approved by the ethics committee of the University of Zurich and the Canton of Zurich.

To assess equivalence among oxytocin and placebo groups, the General Health Questionnaire (GHQ) (23), the Relationship Questionnaire (PFB) (24), and the Short Chronic Stress Scale (SSCS) (25) were analyzed in all subjects before participation in the study. Experiments took place in the laboratories of the Department of Psychology at the University of Zurich between 5:00 PM and 7:30 PM to control for diurnal variation in salivary

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Received June 13, 2008; revised October 8, 2008; accepted October 8, 2008.

cortisol. Salivary free cortisol was repeatedly assessed with Salivette collection devices (Sarstedt, Sevelen, Switzerland) at baseline (−50 min relative to the onset of the conflict discussion), immediately before conflict (−1 min), and after conflict (+15, +25, +35, +50 min). Saliva samples were stored at −20°C until required for analysis with a commercially available chemiluminescence immunoassay (CLIA; IBL Hamburg, Germany) with inter- and intra-assay coefficients of variation below 10%.

After the baseline saliva assessment and a pregnancy test in women, subjects rated the intensity of 23 pre-determined areas of couple conflict (24) with regard to their own relationship. Couples chose two topics (e.g., finances, educational issues, leisure time) of continuing disagreement for the later discussion (26–28). After this procedure, in a double-blind design based on the randomization table prepared by the study pharmacy, couples self-administered either 40 IU (5 puffs in each nostril) of oxytocin (Syntocinon Spray, Novartis, Basel, Switzerland) or placebo intranasally under the supervision of the study coordinator.

Forty-five minutes after drug administration, couples were asked to discuss the conflict issue that they had chosen previously during the following 10 min (29). Couples were alone in the room and were videotaped during this conflict discussion. After the conflict discussion, all subjects were asked to evaluate the discussion with a standard evaluation questionnaire (30) on self-perceived aspects of the conflict (e.g., validity of the task, stressfulness of the task).

During the following 60 min, saliva samples were taken repeatedly and couples watched a documentary (31) to prevent them from talking or ruminating about the conflict any further. Finally, participants received the financial incentive and left the laboratory at 7:30 PM.

Conflict behavior was coded with an adapted version of the Specific Affect Coding System (SPAFF) (26,32) and the Coding System for Marital and Family Interaction (KPI) (33) with a computer-aided system of analysis (Computer Aided Observation System [CAOS]) (34). Two trained raters who were blind with regard to the subjects' group assignment coded nonverbal (e.g., eye contact, nonverbal positive behavior, nonverbal negative behavior) and verbal behavior (e.g., curiosity/care, emotional self-disclosure, agreement, contempt, belligerence, defensiveness). Inter-rater reliability (Cohen's kappa) was .66 for nonverbal categories and .80–1.0 for verbal categories. The total score was calculated as the relative duration of positive behavior (e.g., eye contact, emotional self-disclosure, nonverbal positive behavior) as a ratio of the relative duration of negative behavior (e.g., contempt, defensiveness, belligerence, nonverbal negative behavior). Before calculating the sum score, all behavior categories were z-transformed.

Baseline differences between groups were analyzed with t tests. Univariate analyses of variance with the group factor oxytocin versus placebo and the covariates chronic stress level (25) and scores of pre-determined areas of couple conflict (24) were calculated in order to analyze cortisol and behavior. For nonparametric self-rating data, Mann-Whitney U tests were calculated. Cortisol values were log-transformed by $lnCort = \ln(x + 1)$ to yield unskewed response variables. Salivary cortisol levels were interpreted on the basis of the area under the curve with respect to the increase (AUC_i), which allows a sensitive measure of physiological changes over time (35). Data were analyzed with SPSS 14 (SPSS, Chicago, Illinois).

Results

The two groups did not significantly differ in any demographic or baseline characteristics (age, body mass index, years of education, duration of relationship, relationship quality, chronic stress, and general health symptoms), in baseline cortisol levels (−50 min relative to the onset of the conflict), or cortisol levels immediately before conflict (−1 min) (Supplement 1).

Oxytocin significantly increased the duration of positive behavior in relation to negative behavior during the couple conflict [$F(1,43) = 4.18$, $p = .047$, partial $\eta^2 = .09$; Figure 1A], with no differences between women and men. Oxytocin did not affect the total duration of positive or negative behavior during the conflict discussion.

Participants rated their behavior as "very much like at home" (median = 5.0, range: 2–6) and the topics as "very representative
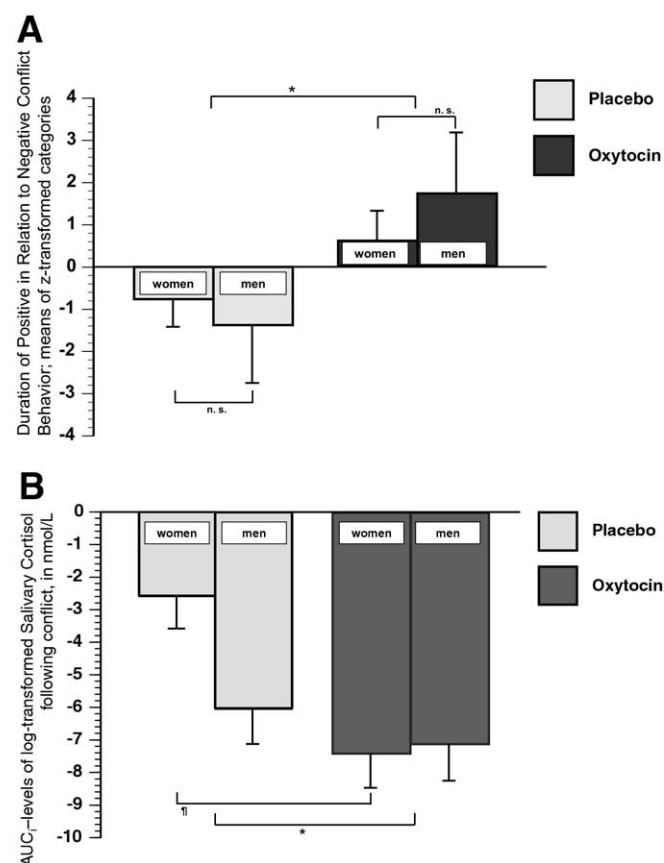
Figure 1. (A) Duration of positive conflict behavior in relation to duration of negative conflict behavior during couple conflict in the laboratory, categorized on the basis of the Specific Affect Coding System. The levels represent the means of z-transformed duration in positive behavior (eye contact, interest, emotional self-disclosure, validation, caring, nonverbal positive behavior) in relation to the z-transformed duration of negative behavior (criticism, contempt, defense, domineering, belligerence, stonewalling, nonverbal negative behavior, interruption) in women (n = 23) and men (n = 23) with intranasal oxytocin or women (n = 24) and men (n = 24) with placebo during the 10-min conflict discussion. **(B)** Areas under the individual response curves with respect to increase (AUC_i) of log-transformed salivary cortisol after couple conflict in the laboratory. The AUC_i includes the four measures of saliva hormone levels after the 10-min conflict in women (n = 23) and men (n = 23) with oxytocin or women (n = 24) and men (n = 24) with placebo (intranasal administration). Error bars are SEM. To convert cortisol from nmol/L to mg/dL, divide by 27.59. *5% level of significance; ¶10% level of significance.

of everyday life conflicts" (median: 5.0, range: 4–6). The stressfulness of the conflict was evaluated as "relatively low" (median: 2.0, range: 1–5). There were no gender or group differences between the oxytocin and placebo group in the self-evaluation of the conflict discussion. As expected, salivary cortisol did not increase during conflict, with no significant time effect and no significant group or gender differences in salivary cortisol courses (Supplement 2). However, oxytocin induced significantly decreasing cortisol concentrations after the conflict compared with placebo [salivary cortisol (AUC_i): $F(1,43) = 7.14$, $p = .011$, partial $\eta^2 = .14$, Figure 1B], again with no main effect of gender. The interaction of group and gender was marginally significant [$F(1,43) = 3.19$, $p = .081$, partial $\eta^2 = .07$], with lower cortisol levels in women with oxytocin compared with women with placebo than in men with oxytocin compared with men with placebo (Figure 1B).

Regression analyses controlling for the influence of gender and substance did not show a significant association of behavior and cortisol [$\beta(2_{regression}, 91_{residual}) = -.110$, $p = .291$, ns].

Discussion

The findings of this initial study on the effects of intranasal oxytocin on human couple interaction suggest that oxytocin increased the duration of positive behavior in relation to negative behavior during a conflict discussion and reduced salivary cortisol levels after this conflict in both women and men.

A large body of studies in nonhuman mammals suggests an involvement of central oxytocinergic mechanisms in the regulation of attachment behavior and affiliation (for reviews see 10,36). Our data on behavior during couple conflict concur with data from these animal studies. Most notably, in our study oxytocin did not increase positive behavior in total but did increase positive behavior in relation to negative behavior. According to Gottman (26), this ratio of positive to negative interactions is a potent predictor of positive long-term relationship outcomes. Notably, the effect of oxytocin on behavior reported here is significant but indicates a small effect size. On the basis of a one-time substance administration after years of relationship interaction, this is not surprising. It would be most relevant, however, to investigate long-term substance effects on couple interaction in future studies.

The cortisol results presented here also add to research that relates central oxytocin to stress and anxiety reduction in animals (37–40) and in humans (14,20,21). In accordance with this literature, our data suggest an important mediating role of oxytocin in the stress-buffering effects of positive social interaction, supposedly due to an increased availability of positive relationship memories (15,16), increased trust (17), and decreased levels of anxiety (20,21) and stress (14) during social interaction.

The lack of a salivary cortisol increase reported here might be interpreted in terms of a lack of stressfulness of the task. Indeed, only a small number of studies have reported actual increases in corticosteroids after a laboratory conflict (41,42), which deserves further attention. Cortisol increases in the laboratory were reported to be highest when the situation is perceived as unpredictable and socio-evaluative (43), and when the predominant emotion is anxiety rather than anger (44). These characteristics might not typically be present in couple conflicts.

It is important to note that we did not find gender differences in behavior after oxytocin administration and only a relatively small gender × substance interaction in cortisol measures.

Interestingly, this interaction effect does not parallel the results in behavior, which suggest stronger substance effects in men than in women. These results might contradict results from animal studies, which suggest a stronger effect of oxytocin in females than in males (45,46). To date, most of the studies investigating the effects of oxytocin in humans have restricted their samples to male volunteers, showing anxiolytic, stress-buffering, and prosocial effects of intranasal oxytocin in men (for review see 13,47). Future studies should include both genders to determine whether the sexual dimorphism in the behavioral effects of oxytocin known from several vertebrate classes (48) also holds for human behavior.

To summarize, our results suggest that oxytocin might be an important central nervous mechanism involved in the stress-protective and health-promoting role of positive couple interaction (49,50). These findings might prove helpful for the development of deeper insights into the neurobiology of close relationships in humans. They might therefore stimulate future research on psychobiological treatment options in couple therapy as well as in psychiatric disorders with particular impairment in social relationships, such as autism and personality disorders.

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