Hormones and Behavior 56 (2009) 108–111

Contents lists available at ScienceDirect

Hormones and Behavior

journal homepage: www.elsevier.com/locate/yhbeh

Social closeness increases salivary progesterone in humans

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ARTICLE INFO

Article history:
Received 23 October 2008
Revised 12 February 2009
Accepted 19 March 2009
Available online 9 April 2009

Keywords:
Progesterone
Altruism
Affiliation
Social closeness

ABSTRACT

We examined whether interpersonal closeness increases salivary progesterone. One hundred and sixty female college students (80 dyads) were randomly assigned to participate in either a closeness task with a partner versus a neutral task with a partner. Those exposed to the closeness induction had higher levels of progesterone relative to those exposed to the neutral task. Across conditions, progesterone increase one week later predicted the willingness to sacrifice for the partner. These results are discussed in terms of the links between social contact, stress, and health.

The neuroendocrine basis of social bonds has important implications for our understanding of affiliative behavior in humans, including links between social contact, stress, and health (Brown and Brown, 2006). Much of the neuroendocrine work has examined centrally released hormones and transmitters like oxytocin (OT), vasopressin (AVP), and beta-endorphin (B-ENDO), which are associated with bond-relevant behaviors such as social memory and the formation of partner preferences (Carter, 1998; Ferguson et al., 2001).

Hormones such as oxytocin are selectively released under circumstances that promote social closeness—for example, birth and sexual behavior (Carter, 1998). New human evidence suggests that perception of another's trust leads to higher levels of circulating OT in the observer, but not to differences in cortisol or other hormones such as testosterone (Zak et al., 2005).

In the context of "cues" for social closeness, OT is causally related to behaviors that may be considered altruistic (i.e., incurring cost to benefit another). OT administration induces, and OT antagonists block, parental investment behavior and maternal responsiveness in rats, mice, voles, and sheep (Carter, 1998). Among humans, peripheral OT increases associated with trust predict increased monetary donations to a partner (Zak et al., 2005). And, nasal administration of OT increases monetary donations to a partner if the two are financially interdependent (Kosfeld et al., 2005).

Despite these findings, the neuroendocrine basis of social bonding in humans is difficult to study because centrally released OT, AVP, and b-ENDO can only be assessed through invasive methods (spinal tap) or tracer-based brain imaging methods (PET). Although these hormones can be measured peripherally, blood levels of OT and AVP have a different source than brain levels and it is unclear to what extent they're correlated with central levels of the same hormone (Carter et al., 2007).

Recent findings suggest that progesterone, a hormone which can be assessed in saliva, is one that indexes an individual's motivation to bond with others. For example, higher levels of progesterone in humans are associated with greater affiliation motivation—deriving satisfaction from positive relationships with others (Atkinson, 1958). Women who take oral contraceptives (which contain progestins) have higher levels of affiliation motivation relative to women not taking oral contraceptives or men (Schultheiss et al., 2003). As progesterone levels rise in the course of women's menstrual cycle, higher progesterone levels are predictive of greater affiliation motivation

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[1] Dr. Wirth was supported by an NIH Training Grant, T32 MH 18931.

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doi:10.1016/j.yhbeh.2009.03.022

(Schultheiss et al., 2003). And, the results of experimental studies have shown links between progesterone and increased affiliation motivation (Wirth and Schultheiss, 2006), and between movie-induced arousal of affiliation motivation and progesterone increases in both women and men (Schultheiss et al., 2004).

This suggestive evidence for a role of progesterone in human bonding parallels evidence for such a role in other animals. Progesterone is involved in parental and sexual behavior in mammals (Young and Insel, 2002). The hormone allopregnanolone (ALLO), which is synthesized from progesterone in the brain and endocrine glands, increases sexual behavior as well as non-sexual affiliative behavior in rodents (Frye et al., 2006). Blocking ALLO in rodents decreases time spent with conspecifics (Frye et al., 2006). Social isolation causes a decrease in brain and plasma ALLO (Serra et al., 2007), and ALLO reduces separation distress in rat pups (Zimmerberg et al., 1994).

Based on stimulating effects of oxytocin on progesterone release (Miyamoto and Schams, 1991), Schultheiss et al. (2004) speculated that changes in progesterone levels may reflect changes in levels of centrally released oxytocin. Progesterone and OT display other interrelationships; for example, progesterone causes increases in OT receptors in the brain (hypothalamus) (Bale et al., 1995); thus, progesterone increase during affiliation may serve to increase the brain's sensitivity to OT. However, these hypotheses are difficult to evaluate given the difficulties of assessing hormone levels and receptor densities in the human CNS. Alternatively, it may be possible to examine whether progesterone increases are triggered by bond-relevant circumstances, as is the case for some CNS hormones. To our knowledge, however, interpersonal causes and consequences of progesterone increases in humans have not been studied. Thus, the present study was designed primarily to examine whether progesterone is increased by circumstances that promote social closeness.

A subsidiary goal of the proposed study was to explore whether progesterone increases are related to altruistic motivation, as would be expected with the hormone oxytocin (reviewed above). Although no studies we are aware of have examined this possibility, a recent evolutionary theory of altruism suggests that the hormonal basis of social bonds is effectively a motivational system designed to trigger the suppression of self-interest when necessary to promote and prioritize the well-being of another person (Brown and Brown, 2006). If this is true, and if progesterone is part of the neuroendocrine basis of social bonds, then we might expect progesterone to also be associated with a willingness to sacrifice for another person.

We randomly assigned female dyads to a closeness induction (Session 1) and then measured their progesterone levels and their willingness to risk their life for their partner (sacrifice). Dyads then played a cooperative computerized card game and then came back one week later to play a second round of the computer game (Session 2). During Session 2 we once again measured progesterone levels and the willingness to risk one's life for the partner. We hypothesized that the closeness induction would lead to a greater increase in progesterone levels (relative to the control condition) during Session 1, and that progesterone increase would be related to the willingness to sacrifice for the partner.

Method

Participants

One hundred and sixty female college students from the University of Michigan were recruited to participate in a study on social coordination to be conducted across two sessions, one week apart. They were offered $20 in base payment, and were told that individual earnings from an online cooperative card game they would play typically ranged between $40 and $60. Detailed analysis of play data, including the effects of emotions on play strategy, will be reported elsewhere.

Measures

Hormone measures

Salivary measures provide a reliable, non-invasive way to assess unbound steroid hormones in humans (Riad-Fahmy et al., 1983). We collected and processed saliva samples following procedures described in Schultheiss et al. (2004). Salivary progesterone levels were determined by solid-phase 125-I radioimmunoassay (Coat-A-Count, Diagnostic Products CorpSiemens). We also used the same procedure to measure salivary cortisol, a stress hormone (to distinguish effects on progesterone increase from general effects on the stress response). We measured hormones using 400 μl saliva samples in combination with water-diluted standards (analytic range: CORT, 0.5–50 ng/ml; PROG, 5–400 pg/ml) and overnight incubation at room temperature. Average lower limits of detection (Mean B0 − 3*SD) were 6.3 pg/ml for progesterone assays and 0.1 ng/ml for cortisol assays. Pooled saliva from several male and female volunteers were included in each assay, as well as low and high lyphocheks (LCs; 27 and 101 pg/ml for progesterone assays; 1.5 and 3.5 ng/ml for cortisol assays). Average recovery values for LCs were 90.21 and 90.76% for low and high LCs in progesterone assays, and 119.47 and 119.12% for low and high cortisol LCs. Average intra-assay CVs were 21.03% and 9.98% for progesterone and cortisol assays, respectively. Participants were not excluded as a function of timing of the menstrual cycle, so they were asked to report menstrual cycle information as well as whether they were using hormonal contraceptives (7 women) or other hormonally active medications (3 women). Although the findings reported in this paper are based on the entire sample, the findings do not change if women taking these hormonally active medications are excluded from the analyses.

Manipulation check

Participants indicated *perceived closeness* with their interaction partner by choosing one of 7 response options on the single-item Inclusion of Other in Self (IOS) Scale (Aron et al., 1992). The IOS depicts a series of increasingly overlapping circles and participants are asked to choose the set of circles that best describes their relationship to their partner. This measure has been shown in previous work to be sensitive to the closeness task used in this study, and its reliability and validity are well-established.

Willingness to risk one's life

Participants reported their willingness to suppress self-interest for their partner by responding to the single item "I would risk my life for [my partner in this study]" on a 5-point Likert-type scale, ranging from 1, "strongly disagree" to 5, "strongly agree." This item was chosen from the 7-item Investment Scale, developed by Brown (2000), to operationalize an individual's willingness to suppress self-interest in order to provide costly resources to another person. The original scale was developed for use within existing relationships and evidenced good psychometric properties, including high reliability (Cronbach's alpha = .94), and good convergent and discriminant validity. The entire scale was not used in the present study because the original items were designed to assess behaviors that typically occur in the context of long-term relationships (e.g., I would drop out of school or quit work if this person got sick and needed my help). The risking life item, however, was used because it could reasonably be endorsed by virtual strangers who would be unlikely to have future encounters outside of the study.

Dyadic interaction tasks

Female dyads were randomly assigned to a closeness induction or to a control task, and then played a cooperative computerized card

game with a partner immediately after the task (Session 1), and one week later (Session 2). The control task was also a social task that involved a partner, but was not designed to produce feelings of closeness. Because we were interested in testing the hormonal effects of social closeness, a "social" as opposed to a "solo" control task was chosen to reduce the chance that any progesterone changes would be due to either the mere presence of others, or the concept of having a partner.

Social closeness task

Participants were told that the purpose of this task was to "get to know each other a bit." Early in the first session, each pair was given a packet of 16 questions drawn from the Closeness Generating Procedure developed by Aron et al. (1997). Example questions include: *"Given the choice of anyone in the world, whom would you want as a dinner guest?" "What is the greatest accomplishment of your life?"* Partners took turns answering each question first.

Control task

Participants in the control group were told that their task was to proofread an article together with the goal of correcting as many errors as possible. By random assignment, one member of the dyad received the "edited version" of a high-level botany manuscript, whereas the other member received the "unedited version," containing inserted errors. The participant with the edited version was instructed to read aloud while the participant with the unedited version listened and made corrections in red ink in the margins. After 10 min, participants switched roles.

Procedure

To control for diurnal variation in hormone levels, all sessions were held between 12:00 and 19:00. Four (previously unacquainted) participants were randomly assigned into two dyads and each dyad was ushered to a separate laboratory room. Two dyads were tested in each session to accommodate a switch in partners before the game for half the participants. For privacy, when participants provided saliva samples and completed written measures, they sat with their backs facing each other at individual workstations across the room. When they completed tasks jointly, they each moved to a small table in the center of the room and sat across from each other. After providing informed consent, they provided a saliva sample and completed an IOS (T1). Then, by random assignment, dyads either completed the closeness task or the control task, each for approximately 20 min. Following the joint task, they provided another saliva sample and completed an IOS and the measure of sacrifice (T2). Participants then played a cooperative card game in which each of two players was assigned to a different role with distinct rules for playing the card game. These different roles had to be coordinated to maximize a monetary outcome, either through speed or by solving a problem with the fewest number of attempts (Cohen and Bacdayan, 1994). Once players "discovered" efficient ways of cooperating, they could improve their score with successive trials if they recognized complex patterns that could be solved in similar ways. By random assignment, partners played the game either with their same partner from the closeness or neutral task, or with a new partner. Seven days later, participants returned to the laboratory to play the cooperative card game again, with the same partner with whom they played the game the prior week. Although performance on the card game was not the focus of the present study (and analyses will be reported elsewhere), the cooperative nature of the card game was expected to lead to variations in progesterone during Session 2. Thus, before and after this second session of card game play, participants provided a saliva sample and completed the same written measures as in T1 and T2, respectively (T3 and T4).

Results

Table 1 presents the means and standard deviations for self-report and hormonal measures for participants with reliable hormonal data for all time points ($N = 141$). As shown in Table 1, the closeness activity caused increases in closeness (IOS) and progesterone. A robust linear regression conducted using STATA 9.0 (Stata Corp. College Station, Texas), with subjects clustered by dyad, tested the effects of the closeness task on post-task progesterone, controlling for progesterone at baseline. This model ($N = 141$, multiple $R^2 = .63$) revealed that closeness task subjects had higher post-task progesterone ($\mu = 47.62$ pg/ml) than did those in the control condition ($\mu = 37.68$ pg/ml; $B = 9.99$, $p < .05$). All analyses were also conducted omitting outliers on progesterone variability; results remained substantively identical. As shown in Table 1, progesterone tended to decline between baseline and the post-task assessment for control condition subjects, consistent with previous studies (Wirth and Schultheiss, 2006), whereas it tended to remain constant or increased among closeness task subjects. No such result was found for change in cortisol over the same period, ($B = -0.07$, $p = .63$).

We next examined whether progesterone increase during Session 1 (T1 to T2) or Session 2 (T3 to T4) would predict altruistic motivation. During Session 1, across conditions, change in progesterone did not significantly predict altruistic motivation, and neither did change in cortisol ($ps > .30$). However, during Session 2, ($n = 130$) increased progesterone (from T3 to T4) predicted greater altruistic motivation ($Beta = .32$, $p < .001$). No such effect was found for increased cortisol over the same period ($Beta = -.13$, $p = .14$). The association of increased progesterone (from T3 to T4) with altruistic motivation remained significant when controlling for altruistic motivation during Session 1, and when progesterone in Session 2 was examined as a residualized variable (T4 values holding constant baseline T3 values). Findings did not significantly differ across conditions.

Table 1
Means (SDs) of all measures as a function of time and experimental condition.

	Closeness induction ($N = 68$)		Neutral task ($N = 73$)	
	Before game	After game	Before game	After game
Self-report measures				
Closeness (IOS)[a,b]	1.60 (.79)	3.16 (1.05)	1.73 (.99)	2.82 (1.27)
Willingness to risk One's life	Not measured	2.22 (1.21)	Not measured	2.01 (1.05)
Hormone measures				
Progesterone[a,c]	46.00 (42.99)pg/ml	47.62 (58.57)pg/ml	45.47 (43.47)pg/ml	37.68 (33.24) pg/ml
Cortisol[c]	2.19 (1.66) ng/ml	1.60 (1.16) ng/ml	2.09 (1.84) ng/ml	1.50 (1.36) ng/ml

[a] Indicates a significant effect ($p < .05$) of type of social interaction induction (closeness task versus neutral task) on pre-post values.
[b] Indicates that there is no significant dyadic-level variation in this measure, so effects over time were analyzed using repeated measures ANOVA.
[c] Indicates significant dyadic-level variation so effects over time were analyzed using robust estimation of variance (STATA's *robust* option).

Discussion

Our results demonstrate that a closeness induction caused increased progesterone, but not cortisol, levels. Although we found no evidence of a relationship between progesterone and willingness to sacrifice shortly after the closeness induction, an increase in progesterone one week later was predictive of the willingness to sacrifice during that time. This effect was found across conditions, when presumably all individuals had developed some level of closeness with their game partner. A similar effect was not found for cortisol.

To our knowledge, these results are the first to demonstrate hormonal changes associated with an experimental manipulation of closeness. These results are also the first to link progesterone to self-reported willingness to risk one's own life for another person. Of course our results are also limited. The link between progesterone and sacrificial behavior is correlational, so we cannot be sure that progesterone is causally related to the motivation to suppress of self-interest. And, although the finding of a link between closeness and progesterone increase was based on an experimental manipulation, there were differences between our closeness task and our control task that may have confounded our results. For example, the closeness task involves personal questions that may have caused individuals to feel more aroused than those in the control condition. Consequently the finding that the closeness condition led to an increase in progesterone may be due to the fact that progesterone is also an indicator of activation of the stress response (Paul and Purdy, 1992), as opposed to the possibility that progesterone is part of the neuroendocrine basis of social bonds. However if this were the case, we might have expected the closeness condition to also cause an increase in cortisol, which did not happen. Nevertheless, future research should employ the use of different types of controls that may equate the arousal level and valence of the two conditions, or that utilize a solo control condition to isolate the effects of social closeness on progesterone. At the very least, the findings from the present study highlight the need to study the possible role of progesterone as a potential mechanism for social bonding.

Our results are consistent with findings for the hormone oxytocin (OT), in that cues for closeness and interdependence have been shown to trigger OT release (Zak et al., 2005), and exogenous administration of OT stimulates altruistic behavior in the context of interdependence (reviewed in Brown and Brown, 2006). The similarity between oxytocin findings and the results of this study may be due to links between oxytocin and progesterone (Miyamoto and Schams, 1991; Bale et al., 1995) however a test of this possibility awaits the development of new technology and future research. At the very least, our findings suggest that progesterone is part of the neuroendocrine basis of social bonds, and are broadly consistent with a new evolutionary theory of altruism which argues that the hormonal basis of social bonds (including oxytocin) enables individuals to suppress self-interest when necessary in order to promote the well-being of another person (Brown and Brown, 2006).

Our results may also illuminate the mechanism by which helping behavior promotes health (Brown et al., 2003). Of interest, many hormones/peptides involved in affiliation and helping behavior cause reductions in stress and anxiety. For example, OT increases during stress, and it reduces stress effects (e.g., corticosteroid levels and blood pressure, Uvnas-Moberg, 1998; Light et al., 2005). Progesterone also plays a role in stress (Paul and Purdy, 1992), including reducing anxiety in humans and other animals via its metabolite, the hormone allopregnanolone (ALLO) (Soderpalm et al., 2004). ALLO acts on receptors for gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the mammalian brain. In fact, ALLO has similar efficacy and potency to benzodiazepines at GABA receptors (Majewska et al., 1986). Decreased stress could be both a prerequisite for and a consequence of affiliation, social bonding, and altruistic behavior, which is consistent with a role for progesterone and ALLO in these behaviors. Due to links with decreased stress responding, progesterone may also represent one of several mechanisms explaining the well-documented positive health effects of social contact (House et al., 1988).

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