Research Report

aps ASSOCIATION FOR PSYCHOLOGICAL SCIENCE

Psychological Science
21(1) 3–7

DOI: 10.1177/0956797609356507
http://pss.sagepub.com
SAGE

Are Plasma Oxytocin in Women and Plasma Vasopressin in Men Biomarkers of Distressed Pair-Bond Relationships?

Shelley E. Taylor, Shimon Saphire-Bernstein, and Teresa E. Seeman
University of California, Los Angeles

Abstract

Young adults in couple (pair-bond) relationships reported on the positive and negative aspects of their relationships and had blood drawn and assayed for oxytocin and vasopressin. Elevated plasma oxytocin was associated with distress in the pair-bond relationship for women, but not for men. Vasopressin, which is closely related to oxytocin in molecular structure and significantly related to male pair-bond behavior in animal studies, was elevated in men experiencing distress in the pair-bond relationship, but not in women. Controlling for estradiol and testosterone did not alter these findings. We conclude that plasma oxytocin in women and plasma vasopressin in men may be biomarkers of distressed pair-bond relationships.

Keywords

gender, oxytocin, relationships, relationship distress, vasopressin

Received 3/5/09; Revision accepted 6/11/09

Identifying the psychological and biological bases of human affiliation is critical for understanding how relationships protect or threaten health and well-being. The purpose of this investigation was to evaluate whether plasma vasopressin (AVP) may be a biomarker of distress in the pair-bond relationship in men, and to replicate and extend previous findings that plasma oxytocin (OT) may be a biomarker of distress in the pair-bond relationship in women.

OT is perhaps best known for its links to social bonds, including maternal bonding (Feldman, Weller, Zagoory-Sharon, & Levine, 2007), affectionate behaviors between partners (Light, Grewen, & Amico, 2005), and displays of romantic love (Gonzaga, Turner, Keltner, Campos, & Altemus, 2006). However, research has also found that elevated plasma OT is associated with relationship distress, especially in the pair-bond relationship, among older (Taylor et al., 2006) and younger (R.A. Turner, Altemus, Enos, Cooper, & McGuinness, 1999) women, as well as in animals (Grippo et al., 2007). In the present study, we further pursued this link between elevated OT and relationship distress.

Little is known about the relation of AVP to social behavior, especially in humans. Animal studies indicate that AVP, a neuropeptide that is highly similar to OT in molecular structure, is related to partner preference formation and mate guarding in male prairie voles (Winslow, Hastings, Carter, Harbaugh, & Insel, 1993). However, there is no evidence directly linking AVP to pair-bond behavior in humans. We predicted that, as a male counterpart to OT, AVP may be elevated in men experiencing distress in the pair-bond relationship.

Method

Participants

Eighty-five young adults in self-characterized committed relationships (62% female and 38% male; mean age = 21.60 years, range = 18–34) participated in a study that related social psychological variables to plasma OT and AVP. The average age of the men and women did not differ. Most of the participants had completed some college, but 15 had a high school diploma only, and 6 had completed at least some graduate work. Eight participants (6 women, 2 men) were married (1 was separated). One participant had children. People taking any medication affecting endocrine function, including birth control pills, were excluded from the study.

Measures

Participants completed individual difference measures on-line prior to the laboratory session, including optimism (Scheier, Carver, & Bridges, 1994), mastery (Pearlin & Schooler, 1978), extraversion (Eysenck & Eysenck, 1975), perceived stress (Cohen, Kamarck, & Mermelstein, 1983), the Brief Symptom Inventory (Derogatis, 1975), the Mood and Anxiety Symptom

Corresponding Author:
Shelley E. Taylor, Department of Psychology, University of California, Los Angeles, 1285 Franz Hall, Los Angeles, CA 90095-1563
E-mail: taylors@psych.ucla.edu

Questionnaire (MASQ; Watson et al., 1995), and the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961).

Participants also completed a measure originally developed for the Mid-Life in the United States (MIDUS) study, a composite measure of socially supportive and unsupportive relationship behaviors that enjoys wide use in the relationship literature (see Schuster, Kessler, & Aseltine, 1990). Psychometric properties were originally reported by R.J. Turner, Frankel, and Levin (1983). Respondents rated their partner (on 7-point scales) on the following items: "How often they make too many demands on you," "how often they make you feel tense," "how often they argue with you," "how often they criticize you," "how often they let you down when you are counting on them," "how often they get on your nerves," "how much they really care about you" (reverse-coded), "how much they understand the way you feel about things" (reverse-coded), "how much they appreciate you" (reverse-coded), "how much you can rely on them for help if you have a serious problem" (reverse-coded), "how much you can open up to them if you need to talk about your worries" (reverse-coded), and "how much can you relax and be yourself around them" (reverse-coded). Responses were averaged to create an index of partner relations (relationship-distress scale; $\alpha = .84$). The high internal reliability of the measure in this study is similar to that reported in other studies.

Within a week of completing these measures, participants had blood drawn at the University of California, Los Angeles, Clinical Research Center to have their basal levels of OT, AVP, estradiol, and testosterone assessed. All blood draws took place in the midafternoon and were conducted by a nurse. Blood samples were drawn into serum tubes containing aprotonin (500 kallikrein-inhibiting units, or KIU, per ml of blood). The samples were centrifuged at 1,600 × g for 15 min at 4 °C. The plasma was transferred to a plastic tube and stored at –80 °C. Frozen samples were batched and shipped overnight on dry ice to a Clinical Laboratory Improvement Amendments–certified analytical laboratory (Salimetrics, LLC, State College, PA).

Assay procedures

On the day of assay, samples were completely thawed at room temperature, centrifuged at 1,500 × g (at 3,000 rpm) for 10 min and pipetted into appropriate test wells. OT was assayed using a commercially available immunoassay (enzyme-linked immunosorbent assay, or ELISA, kit; Assay Designs, Inc., Ann Arbor, Michigan, Catalogue No. 900-153).[1] The sample was diluted X5 and 100 µl was used in the assay, which had a lower limit of sensitivity of 11.7 pg/ml and an upper limit of 1,000 pg/ml. The intra-assay coefficient of variation (CV) was 12.7%. The interassay CVs, estimated across 15 separate runs for high control (550 pg/ml) and low control (71 pg/ml), were 15.0%, and 26.3%, respectively.

AVP was assayed using a commercially available immunoassay (Assay Designs, Inc., Catalogue No. 900-017). The sample was diluted X2 and 100 µl was used in the assay. The assay had a lower limit of sensitivity of 3.39 pg/ml and an upper limit of 1,000 pg/ml. The intra-assay CV was 7.4%. The interassay CVs, estimated across 10 separate runs for high control (507 pg/ml) and low control (36 pg/ml), were 21.8%, and 25.5%, respectively.

Testosterone was assayed using a commercially available immunoassay without modification to the manufacturer's recommended protocol (Salimetrics, Catalogue No. 1-2402). The test used 25 µl of serum, and had a lower limit of sensitivity of 1.0 pg/ml and an upper limit of 600 pg/ml. The intra-assay CV was 7.3%. The interassay CVs, estimated across six separate runs for high control (200 pg/ml) and low control (20 pg/ml), were 11.3% and 18.4%, respectively.

Estradiol was assayed using a commercially available immunoassay without modification to the manufacturer's recommended protocol (Salimetrics, Catalogue No. 1-3702). The test used 100 µl of serum, and had a lower limit of sensitivity of 0.5 pg/ml and an upper limit of 32 pg/ml. The intra-assay CV was 8.4%. The interassay CVs, estimated across six separate runs for high control (25 pg/ml) and low control (6 pg/ml), were 9.1% and 16.0%, respectively.

All plasma samples were tested in duplicate; values that varied by more than 5% were tested again.

Results

One woman with an OT value exceeding mean OT by 3 standard deviations was excluded from the OT analyses, and three women were excluded from the AVP analyses because their baseline levels exceeded 3 standard deviations from average. Men and women did not differ significantly in baseline OT (women: 248.75 pg/ml, $SD = 180.01$; men: 273.45 pg/ml, $SD = 234.36$), $t(83) = -0.546$, $p = .586$, or in baseline AVP (women: 71.73 pg/ml, $SD = 47.50$; men: 67.09 pg/ml, $SD = 33.38$), $t(81) = 0.482$, $p = .631$. The correlation between OT and AVP was not significant, $r = .056$, $p > .60$.

Means for the relationship-distress scale were 2.75 for women ($SD = 0.78$) and 2.69 for men ($SD = 0.76$). Men and women did not differ significantly on this measure, $t(83) = 0.36$, $p = .72$.

As Table 1 shows, plasma OT (but not AVP) was significantly correlated with relationship distress in women (Fig. 1), and plasma AVP (but not OT) was significantly correlated with

Table 1. Correlations Between Basal Vasopressin and Oxytocin and Relationship Distress in Men and Women

Participant gender	Vasopressin	Oxytocin
Men	.54** (.52**)	−.03 (−.02)
Women	.16 (.18)	.34* (.34*)

Note: Correlations in parentheses are partial correlations controlling for estradiol (in women) and testosterone (in men).
*$p < .02$. **$p < .01$.

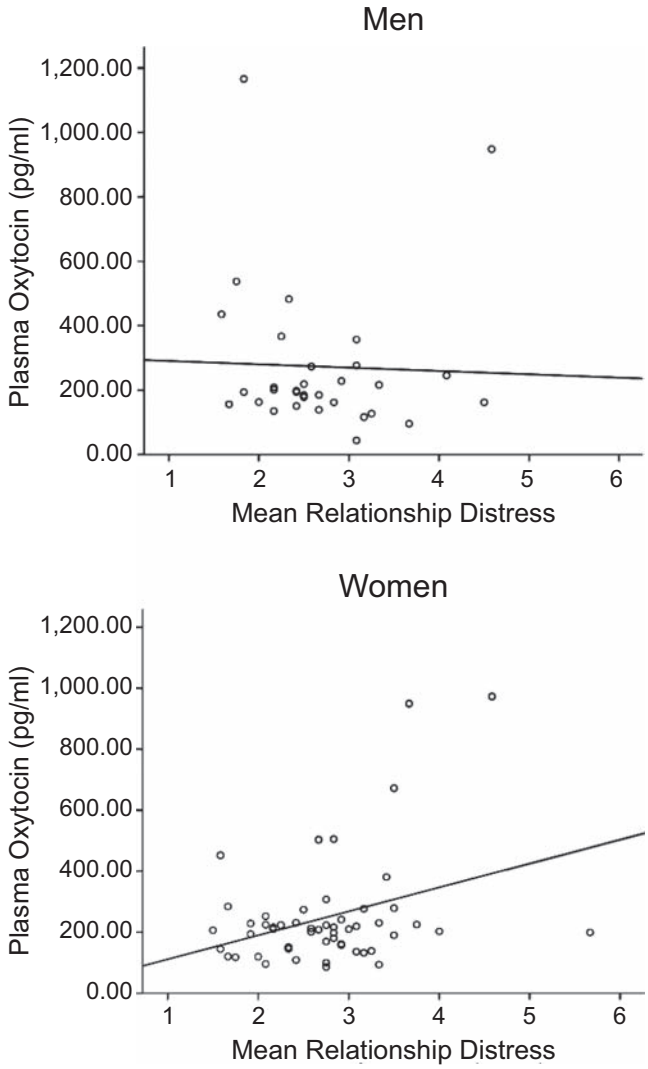

Fig. 1. Scatter plots (with regression lines) of the relation between plasma oxytocin and relationship distress among women (bottom panel) and men (top panel).

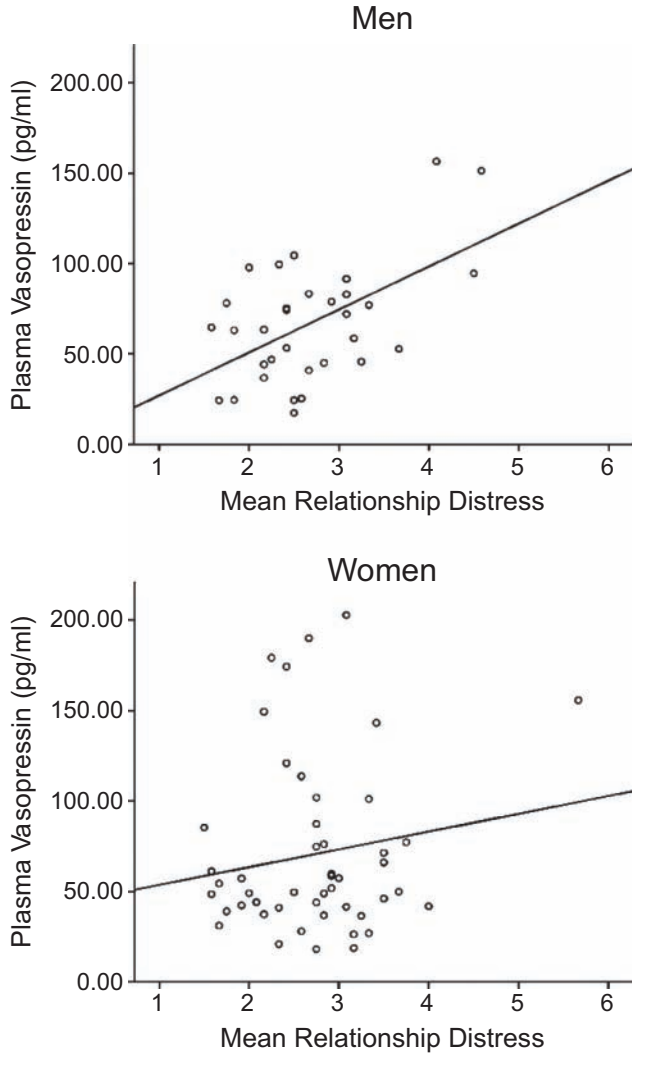

Fig. 2. Scatter plots (with regression lines) of the relation between plasma vasopressin and relationship distress among women (bottom panel) and men (top panel).

relationship distress in men (Fig. 2). Inclusion of the AVP outliers negligibly changed the correlation reported for women in Table 1, $r = .18$, $p = .21$. The relation of OT to relationship distress was significantly stronger in women than in men, Fisher's $z = 1.663$, $p = .048$ (one-tailed), and the relation of AVP to relationship distress was significantly stronger in men than in women, Fisher's $z = 1.898$, $p = .029$ (one-tailed). One-tailed tests were used because we predicted the direction of the effects.

The correlations were recalculated for positive and negative relationship characteristics separately, and analyses revealed strong, significant positive correlations between AVP (for men) and OT (for women) and unsupportive relationship characteristics, and strong significant negative correlations between AVP (among men) and OT (among women) and supportive relationship characteristics. The correlations changed negligibly when controlling for age. The correlations were also recalculated controlling for testosterone (which influences AVP release in men) and estradiol (which influences OT levels in women) levels, and the patterns were the same (see Table 1).

We also examined the relationships between AVP and OT and the individual difference measures noted earlier. The only significant correlation was between OT and depression, as assessed by the BDI, $r = .40$, $p < .01$, in women only. The correlations between OT and relationship distress were recalculated controlling for depression, and the results did not change.

Discussion

The present findings replicate two earlier studies suggesting a relationship between plasma OT and relationship distress in women (Taylor et al., 2006; R.A. Turner et al., 1999). The results extend this previous research by showing that the

relation does not hold for men and that it is not accounted for by potentially related individual differences.

Because AVP appears to be the male counterpart of OT in women, and is similar in molecular structure to OT but regulated by testosterone, a viable hypothesis is that AVP serves similar relationship functions in men as OT serves in women (Taylor et al., 2000). Consistent with this reasoning, the results indicated that AVP, but not OT, is significantly related to distress in the pair-bond relationship in men, but not in women. This is the first study to report this relationship. Recent research has suggested that genetic variation in the AVP receptor 1a gene (AVPR1A) is related to pair-bonding behavior in men (Walum et al., 2008), and this finding is consistent with a role for AVP in pair-bond behavior in humans as well.

Why would plasma OT and AVP be biomarkers of relationship distress in women and men, respectively? The primary social relationship in monogamous species is the pair bond. Humans are (serially) monogamous, and so the pair bond may be significant not only for its obvious reproductive functions, but also for meeting vital needs of nourishment and safety more generally. Accordingly, a biological signal that this relationship is threatened may be adaptive.

The exact pathways by which plasma OT and AVP are elevated in response to distressing relationships remain unknown, however, as the kind of invasive research that would answer this question is not possible in humans. A tentative hypothesis is that because OT and AVP are largely prosocial hormones, levels may rise in response to distress as a signal to affiliate with others because the pair-bond relationship is threatened. This is conjectural, however, in the absence of animal research identifying the specific pathways.

The question arises as to the direction of causality in these correlational data. Although human data do not speak directly to this issue, a recent study (Grippo et al., 2007) compared isolated and nonisolated female prairie voles and found that in the isolated voles, plasma OT levels rose significantly. This finding is consistent with the interpretation that relationship distress leads to a rise in OT in women (and potentially, AVP in men).

A considerable research literature on both animals and humans has related exogenous administration of OT to reduced psychological and biological stress responses (see Carter, Lederhendler, & Kirkpatrick, 1999, for a review). The present results might seem to contradict those findings. In fact, both the current findings relating elevated plasma OT to greater relationship distress and previous findings relating OT to reduced psychological distress are quite robust, and it is likely that the two sets of findings reflect different psychological and biological processes. For example, OT is known to rise both with the need for social contact and in response to social contact. When social relationships are not comforting, it is possible that OT passes into the bloodstream without involving the downstream opioid and dopamine pathways that are believed to account at least partially for the calming, relaxing effects sometimes attributed to OT alone. This idea is speculative, however, and it is difficult to resolve this question with research on humans. Possibly, future animal research will resolve this apparent but reliable paradox. It should also be noted that elevations in plasma OT and AVP do not necessarily always or only signal relationship distress (e.g., Feldman et al., 2007; Gordon et al., 2008). There are many reasons why a hormone may get into the bloodstream, and so the same end point does not ensure uniformity of the underlying processes (i.e., equifinality). In any case, one reliable lesson from studying the biobehavioral interface is that the expectation of tight, linear relationships between hormones and specific psychological states is unlikely to be met.

Limitations of the study include the fact that length of relationship was not measured. However, length of relationship is not a good indicator of relationship qualities: Intensity, obsessiveness, engagement, and sexual interest are reported in both short-term and long-term relationships (Acevedo & Aron, 2009). We also note that the findings relating OT to relationship quality in this report are virtually identical to those reported in a study from our laboratory of older women, whose relationships were, in many cases, several decades long (Taylor et al., 2006). Thus, length of relationship is unlikely to be a significant factor in the dynamics reported here.

A second limitation concerns the variability in the assays. The intra-assay and interassay CVs were fairly high. Unfortunately, at present, good alternative assays are not commercially available. We note, however, that variability in the assays works against the likelihood of finding significant effects.

Conclusions

The present study supports the conclusion that plasma OT (but not AVP) in women and plasma AVP (but not OT) in men may be biomarkers of relationship distress. The findings are largely distinctive to relationship distress and are not accounted for by individual differences in potentially related personality traits. As such, the results contribute to a growing understanding of the psychological and biological bases of affiliation.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interests with respect to their authorship and/or the publication of this article.

Funding

This research was supported by a grant from the National Science Foundation (SES-0525713).

Note

1. Salimetrics, in consultation with Assay Design, determined that it was appropriate to eliminate the extraction step.

References

Acevedo, B.P., & Aron, A. (2009). Does a long-term relationship kill romantic love? *Review of General Psychology*, *13*, 59–65.

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, *4*, 561–571.

Carter, C.S., Lederhendler, I.I., & Kirkpatrick, B. (1999). *The integrative neurobiology of affiliation*. Cambridge, MA: MIT Press.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*, 385–396.

Derogatis, L.R. (1975). *Brief Symptom Inventory*. Baltimore: Clinical Psychometric Research.

Eysenck, S.B.G., & Eysenck, H.J. (1975). *Manual of the Eysenck Personality Questionnaire*. London: Hodder & Stoughton.

Feldman, R., Weller, A., Zagoory-Sharon, O., & Levine, A. (2007). Evidence for a neuroendocrinological foundation of human affiliation: Plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. *Psychological Science*, *18*, 965–970.

Gonzaga, G.C., Turner, R.A., Keltner, D., Campos, B., & Altemus, M. (2006). Romantic love and sexual desire in close relationships. *Emotion*, *6*, 163–179.

Gordon, I., Zagoory-Sharon, O., Schneiderman, I., Leckman, J.F., Weller, A., & Feldman, R. (2008). Oxytocin and cortisol in romantically unattached young adults: Associations with bonding and psychological distress. *Psychophysiology*, *45*, 349–352.

Grippo, A.J., Gerena, D., Huang, J., Kumar, N., Shah, M., Ughreja, R., & Carter, C.S. (2007). Social isolation induces behavioral and neuroendocrine disturbances relevant to depression in female and male prairie voles. *Psychoneuroendocrinology*, *32*, 966–980.

Light, K.C., Grewen, K.M., & Amico, J.A. (2005). More frequent partner hugs and higher oxytocin levels are linked to lower blood pressure and heart rate in premenopausal women. *Biological Psychology*, *69*, 5–21.

Pearlin, L.I., & Schooler, C. (1978). The structure of coping. *Journal of Health and Social Behavior*, *19*, 2–21.

Scheier, M.F., Carver, C.S., & Bridges, M.W. (1994). Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): A reevaluation of the Life Orientation Test. *Journal of Personality and Social Psychology*, *67*, 1063–1078.

Schuster, T.L., Kessler, R.C., & Aseltine, R.H. (1990). Supportive interactions, negative interactions, and depressed mood. *American Journal of Community Psychology*, *18*, 423–438.

Taylor, S.E., Gonzaga, G., Klein, L.C., Hu, P., Greendale, G.A., & Seeman, T.E. (2006). Relation of oxytocin to psychological stress responses and hypothalamic-pituitary-adrenocortical axis activity in older women. *Psychosomatic Medicine*, *68*, 238–245.

Taylor, S.E., Klein, L.C., Lewis, B.P., Gruenewald, T.L., Gurung, R.A.R., & Updegraff, J.A. (2000). Biobehavioral responses to stress in females: Tend-and-befriend, not fight-or-flight. *Psychological Review*, *107*, 411–429.

Turner, R.A., Altemus, M., Enos, T., Cooper, B., & McGuinness, T. (1999). Preliminary research on plasma oxytocin in normal cycling women: Investigating emotion and interpersonal distress. *Psychiatry*, *62*, 97–113.

Turner, R.J., Frankel, G., & Levin, D.M. (1983). Social support: Conceptualization, measurement, and implications for mental health. In J.R. Greenley & R.G. Simmons (Eds.), *Research in community and mental health* (pp. 67–111). Greenwich, CT: JAI Press.

Walum, H., Westberg, L., Henningsson, S., Neiderhiser, J.M., Reiss, D., Igl, W., et al. (2008). Genetic variation in the vasopressin receptor 1a gene (AVPR1A) associates with pair-bonding behavior in humans. *Proceedings of the National Academy of Sciences, USA*, *105*, 14153–14156.

Watson, D., Clark, L.A., Weber, K., Assenheimer, J.S., Strauss, M.E., & McCormick, R.A. (1995). Testing a tripartite model: II. Exploring the symptom structure of anxiety and depression in student, adult, and patient samples. *Journal of Abnormal Psychology*, *104*, 15–25.

Winslow, J.T., Hastings, N., Carter, C.S., Harbaugh, C.R., & Insel, T.R. (1993). A role for central vasopressin in pair bonding in monogamous prairie voles. *Nature*, *365*, 545–548.