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Plasma Vasopressin and Interpersonal Functioning

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Abstract

The neuropeptide vasopressin has traditionally been associated with vasoconstriction and water reabsorption by the kidneys. However, data from experimental animal studies also implicate vasopressin in social bonding processes. Preliminary work suggests that vasopressin also plays a role in social behaviors in humans. The goal of this cross-sectional study was to evaluate associations among plasma vasopressin and self-reported interpersonal functioning in a sample of married couples. During a 24-hour admission to a hospital-based research unit, 37 couples completed measures of interpersonal functioning and provided blood samples for neuropeptide analyses. Results showed that vasopressin was associated with markers of interpersonal functioning, but not with general psychological distress. Specifically, greater plasma vasopressin levels were related to a larger social network, fewer negative marital interactions, less attachment avoidance, more attachment security, and marginally greater spousal social support. These results indicate that vasopressin is likely implicated in different relationship maintenance processes in humans.

Keywords

vasopressin; social functioning; couples; social support; marital quality

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Arginine vasopressin (AVP) is a neuropeptide that has traditionally been associated with the regulation of vasoconstriction and water reabsorption by the kidneys (Vincent and Su, 2008). However, mounting evidence from animal studies also implicates AVP in social behaviors (Caldwell et al., 2008). To date, only a handful of studies have examined the role of AVP in social bonding processes in humans.

Manipulation of central AVP levels via intra-nasal peptide administration facilitated perceptions of friendliness in females, but diminished perception of friendliness and recognition of negative facial expressions in males (Thompson et al., 2006; Uzefovsky et al., 2011). Furthermore, intra-nasal AVP administration increased the likelihood of reciprocated cooperation (i.e., they gave money back to their partner when the partner had initially entrusted them with some money), but it did not impact initial trust behavior in a Prisoner's Dilemma game (Rilling, et al., 2011). Pharmacological AVP manipulation thus impacts cognitive and behavioral responses during interaction with strangers.

Different markers of vasopressinergic activity have been related to social bonding and marital quality. Gene polymorphisms of the AVP V1a receptor have been associated with autism, a disorder characterized by social behaviors deficits and verbal and non-verbal communication difficulties (Kim, et al., 2002; Wassink, et al., 2004; Yirmiya et al., 2006). Among healthy individuals, AVP V1a receptor polymorphisms have also been related to a greater likelihood of being married, decreased frequency of marital conflict, and perception of better marital quality in males and in their female partners (Walum, et al., 2008). Moreover, higher plasma AVP levels have been related to greater self-reported marital distress in men, but not in women (Taylor et al., 2010). In contrast, higher levels of plasma AVP were associated with lower frequencies of negative communication behaviors during a marital interaction task among both males and females (Gouin, et al., 2010).

Results of experimental animal studies parallel human data. Pharmacological manipulation of AVP improved social memory and recognition (Engelmann and Landgraf, 1994), facilitated social bonding (Cho et al., 1999; Winslow et al., 1993), promoted paternal care (Parker and Lee, 2001), and increased inter-male and maternal aggression (Bester-Meredith et al., 1999; Wersinger et al. 2007). Collectively, these data implicate AVP in a range of processes involved in interpersonal relationships initiation and maintenance.

Given the paucity of data linking AVP with interpersonal processes in humans, the purpose of this cross-sectional study was to examine the associations of plasma AVP with a range of indicators of interpersonal functioning. We predicted that in a sample of non-depressed, married individuals, plasma AVP would be more strongly associated with indices of interpersonal functioning than with markers of psychological distress.

Methods

Participants

As part of a larger study on marital stress and wound healing, 37 heterosexual, married couples (74 participants) were recruited through newspaper and radio ads, notices posted on campus and in the community, and referrals from other participants (Kiecolt-Glaser, et al., 2005). Exclusion criteria included 1) health problems or related medications that had an obvious immunological or endocrinological component or consequence for wound healing (e.g., cancer, recent surgeries, strokes, diabetes mellitus, peripheral vascular disease, conditions such as asthma or arthritis that required regular use of anti-inflammatory medications), 2) blood pressure medication, smoking, or using excessive alcohol or caffeine, and 3) pregnancy, current involvement in breastfeeding, or anti-diuretic medication use. All women were scheduled during the follicular phase of their menstrual cycle. The Institutional

Biomedical Research Review Committee approved the project; all subjects gave written informed consent prior to participation.

Protocol

Individuals participated in a 24-hour visit at a hospital-based research unit. Upon admission at 7:00 AM, a heparin well was inserted in each participant's arm to facilitate blood sample collection throughout the day. Couples subsequently underwent a blistering procedure for the wound healing study and participated in two marital interaction tasks, as described elsewhere (Kiecolt-Glaser, et al., 2005). The psychological distress and marital quality questionnaires were completed during the adaptation period in the morning. The social network, social support, and attachment style questionnaires were administered after the experimental tasks in the afternoon. Throughout the admission, couples were encouraged to drink water regularly to facilitate blood draws and prevent AVP fluctuations due to changes in plasma osmolarity. Blood samples for AVP were taken at 7:45 AM (baseline) and 12:00 PM (after the second interaction task).

Self-report measures

Psychological distress—The Beck Depression Inventory (BDI) assessed cognitive and vegetative depressive symptoms in the past two weeks (Beck et al., 1988). The Beck Anxiety Inventory (BAI) assessed anxious symptoms in the past two weeks (Beck et al., 1988). Higher scores on these measures indicated greater psychological distress.

Interpersonal functioning—The Social Network Inventory (SNI) provided an index of social integration by evaluating regular participation in different types of social roles (Cohen et al., 1997). The types of relationships and social roles evaluated included spouse, parents, parents-in-law, children, other close family member, close neighbors, friends, coworkers, fellow volunteers, member of religious and non-religious groups. Individuals with larger social network had higher scores on this measure.

The Social Support Questionnaire (SSQ) quantified the perceived availability of social support (Sarason et al., 1983). Participants were asked to list who they could turn to or rely on when they were faced with a given sets of circumstances. Examples of items include: “who can console you when you are very upset?”, and “who can you really count to help out in a crisis situation?” Two indexes were derived from the scales: 1) number of times the spouse was mentioned as a source of support and 2) the total number of people (excluding the spouse) listed as available to provide support when needed. Because 73% of the sample listed their spouse as a support provider for all the situations listed, a dichotomous variable distinguishing whether the participants listed their spouse as being supportive in all vs. some of the situations described was created. Higher scores indicated greater perceived social support.

The Marital Adjustment Test (MAT) assessed marital adjustment and satisfaction (Locke and Wallace, 1959). Participants were asked to rate their current level of happiness in their marriage, and the degree agreement with their spouse on several topics such as finance, in-laws, or sexual relations. Higher scores were associated with greater relationship satisfaction.

The Test of Negative Social Exchanges (TENSE) is an 18-item questionnaire assessing the frequency of occurrence of negative social interactions in the past month (Ruehlman and Karoly, 1991). Participants completed two versions of the questionnaire: one referring to marital interactions and one referring to non-marital interactions. The total score was

computed by summing the average of each subscale. Higher scores were indicative of more frequent negative social interactions.

Adult attachment style was measured using both categorical and continuous measures of attachment. With the Hazan and Shaver's categorical attachment style measures, participants indicated their degree of agreement to one-sentence descriptions of secure, anxious, and avoidance attachment style using a 6-point Likert scale (Hazan and Shaver, 1987). Higher scores represented greater endorsement of the specific attachment style. The Experiences in Close Relationships-Revised (ECRr) is a 36-item scale assessing attachment style at a dimensional level (Brennan et al., 1998). It comprised two subscales evaluating attachment anxiety and avoidance. Higher scores were associated with greater attachment anxiety and avoidance, respectively.

Plasma Vasopressin Assay—Plasma was kept chilled and immediately frozen at -80° prior to thawing for assays. The plasma was diluted in assay buffer (1:4) to give results reliably within the linear portion of the standard curve. Plasma AVP was assayed in duplicate by enzyme immunoassay (Assay Designs, Ann Arbor, MI), per kit instructions. This EIAs are highly sensitive (minimal detection levels = 4 pg/ml vasopressin) with very little antibody cross-reactivity for other neuropeptides. For the vasopressin EIA kits, the cross-reactivity between oxytocin and vasopressin was $<0.04\%$. All samples were run in duplicates. The inter- and intra-assay coefficients of variation were less than 8% for the assay. The raw vasopressin values obtained ($m = 75.75$ pg/ml, $SD = 62.19$) were similar to those reported in the Taylor et al., (2010) study using the same assay (women mean = 71.73 pg/ml, $SD = 47.50$; men mean = 67.09 pg/ml, $SD = 33.38$). Due to technical difficulties, peptide analyses were not performed for one participant.

Statistical analysis—To account for the dependency between the husband and the wife data, hierarchical linear models treating each individual as nested within a couple were fitted with interpersonal functioning variables as dependent variables and AVP as independent variable (Kenny & Kashy, 1991). Intercepts were estimated as random effects, but all the slopes of the level-1 predictors were constrained to be equal because estimating a random effect for these variables may lead to non-convergence problems with dyadic data (Newsom and Nishishiba, 2002). Restricted maximum likelihood was used as the estimation method given the study sample size. A grand mean centering of the independent variables was performed to facilitate the data interpretation.

As reported elsewhere, levels of AVP in the two blood samples were highly correlated ($r = .87$, $p < .001$) and the marital interaction task did not lead to significant changes in AVP, $F(1,73) = 0.01$, $p = .93$ (Gouin, et al., 2010). The two peptide measurements were therefore averaged to provide a better estimate of the basal AVP values. Spearman's rho correlations were used for the bivariate analyses because of the non-normal distributions of some of the study variables. For the multivariate analyses, a log₁₀ logarithmic transformation normalized the positively skewed distributions of AVP and the Experiences in Close Relationship-Revised's continuous attachment variables. Given the skewed response distributions with the Hazan & Shaver's categorical attachment measure, 3-level categorical variables were created for the attachment avoidance and anxiety variables and a dichotomous variable was computed for the attachment security variable. Gender was effect coded (-1 : men and 1 : women) to facilitate interpretation. The covariates included in the models were age and sex. The α significance level was set at .05. Statistical analyses were performed using SAS version 9.2.

Results

Most participants ($n = 68$) were Caucasian (91.3%), 3 were African-American, 2 Hispanic and 1 Asian. About half (56.5%) of the sample had a college education. Participants' ages ranged from 22 to 73 years with a mean of 38.47 ($SD = 11.99$). Couples had been married from 2 to 39 years, with a mean of 11 years ($SD = 9.63$). Most participants (78%) had only been married once. Couples had two children on average ($SD=1.63$) with a range of 0 to 5. Table 1 provides the descriptive statistics of the participants' psychological and social characteristics.

Age was not associated with AVP, β (SE) = $-.0004$ (.003), $p = .91$. There was no significant gender difference in AVP levels, β (SE) = $-.06$ (.07), $p = .42$. Length of marriage was not significantly correlated with the peptide, β (SE) = $.11$ (.10), $p = .27$. Household income was not related to AVP, β (SE) = $.008$ (.02), $p = .58$. The within-couple intra-class AVP correlations between the husband and the wife was $\rho = .08$. Table 2 includes the Spearman's rho correlations among the study variables.

Table 3 presents the associations between measures of psychological and interpersonal functioning and plasma AVP. The psychological distress indices of depression and anxiety were not significantly related to AVP. Among the interpersonal functioning variable, greater plasma AVP was associated with a larger social network (Figure 1), less negative marital interactions (Figure 2), lower attachment-related avoidance (Figure 3), greater attachment-related security (Figure 4), and marginally with greater spousal social support. Notably, for the self-reported negative social interaction (TENSE) and social support (SSQ) measures, the spousal versions, but not the general interpersonal relationships versions of the measures, were related to AVP levels. No significant gender differences were observed in the relationships between interpersonal functioning and AVP, all p 's $> .19$.

Discussion

This study evaluated the relationships among plasma AVP and interpersonal functioning. Among these married couples, peripheral AVP was associated with a range of indicators of positive interpersonal functioning such as a larger social network, fewer negative marital interactions, less attachment avoidance, more attachment security, and, marginally, more spousal social support. Given that AVP was associated with different facets of interpersonal functioning, these data support the hypothesis that AVP may be involved in a range of interpersonal relationships initiation and maintenance processes in humans.

Consistent with research in animals implicating AVP in the formation of social bonds in both males and females (Cho, et al., 1999; Winslow, et al., 1993), circulating AVP levels were significantly related to facets of interpersonal functioning, but not to psychological distress. Furthermore, on two measures distinguishing general interpersonal functioning from marital functioning, AVP was only associated with aspects of marital quality. Interestingly, in non-human primates, AVP administration increased social contact with a partner, but not with a stranger (Jarcho et al., 2011). In humans, intra-nasal AVP manipulation increased reciprocated cooperation, but not initial trust behavior in a Prisoner's Dilemma game (Rilling, et al., 2011). These data suggest that AVP may be specifically implicated in relationship maintenance processes.

In the current study, plasma AVP was associated with indices of positive interpersonal functioning. In contrast, among individuals with personality disorders, greater cerebro-spinal fluid AVP levels were associated with a history of aggression (Coccaro et al., 1998). Furthermore, among partnered undergraduate students, higher plasma AVP levels were related to greater marital distress in men, but not in women (Taylor et al., 2010). Moreover,

AVP administration decreased perception of friendliness to neutral faces in men (Thompson et al., 2006). While these data support the role of AVP in social behaviors in humans, the directionality of the association between AVP levels and interpersonal functioning varies across studies. Interestingly, similar results have been found for the closely-related nonapeptide oxytocin (Grewen et al., 2005; Taylor, et al., 2006). These findings raise the possibility that individual and contextual differences might influence the association between the peptide and social behaviors (Bartz et al., 2011).

A large body of literature implicates AVP in the activity of the hypothalamic-pituitary-adrenal axis (Aguilera and Rabadan-Diehl, 2000). Furthermore, plasma AVP levels were elevated in a subgroup of patients with major depression in some (van Londen, et al. 1996; Goekoop, et al., 2006) but not all studies (Parker, et al., 2011). In the current study, plasma AVP was not associated with markers of psychological distress. This is likely due to the fact that participants in the current sample reported very low levels of psychological distress (mean BDI score = 2.33; BDI clinical cut-off score = 14; Beck, et al. 1988). It is possible that a different pattern of associations might emerge in samples taken in a more stressful context or among clinically depressed individuals.

A limitation of the study is the fact that AVP was measured from plasma. Although the AVP that is detected in plasma is likely made in the brain, it is unclear to what extent peripheral AVP is related to levels of the peptide in specific brain regions (Landgraf and Neumann, 2004). Furthermore, because of the cross-sectional design of the study, the current data do not speak to the causality or direction of the relationships among peptide levels and social functioning. Thus, high levels of AVP as well as the patterns of behavior measured here might both be secondary to other central processes. Moreover, a large number of statistical tests were conducted given the study's sample size, inflating the possibility of type I errors. However, it is important to note that AVP was significantly related to several measures of interpersonal functioning, but not to measures of psychological distress.

The present results extend our understanding of the role of AVP in social behaviors in humans. Among married couples, higher levels of AVP were associated with a range of indicators of positive interpersonal functioning. Future work should focus on identifying the specific relationship maintenance processes modulated by the vasopressinergic system.

Acknowledgments

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Highlights

- Healthy, married couples provided blood samples and completed questionnaires.
- Greater plasma vasopressin levels were related to better interpersonal functioning.
- Vasopressin related to social integration, attachment style, and marital quality.

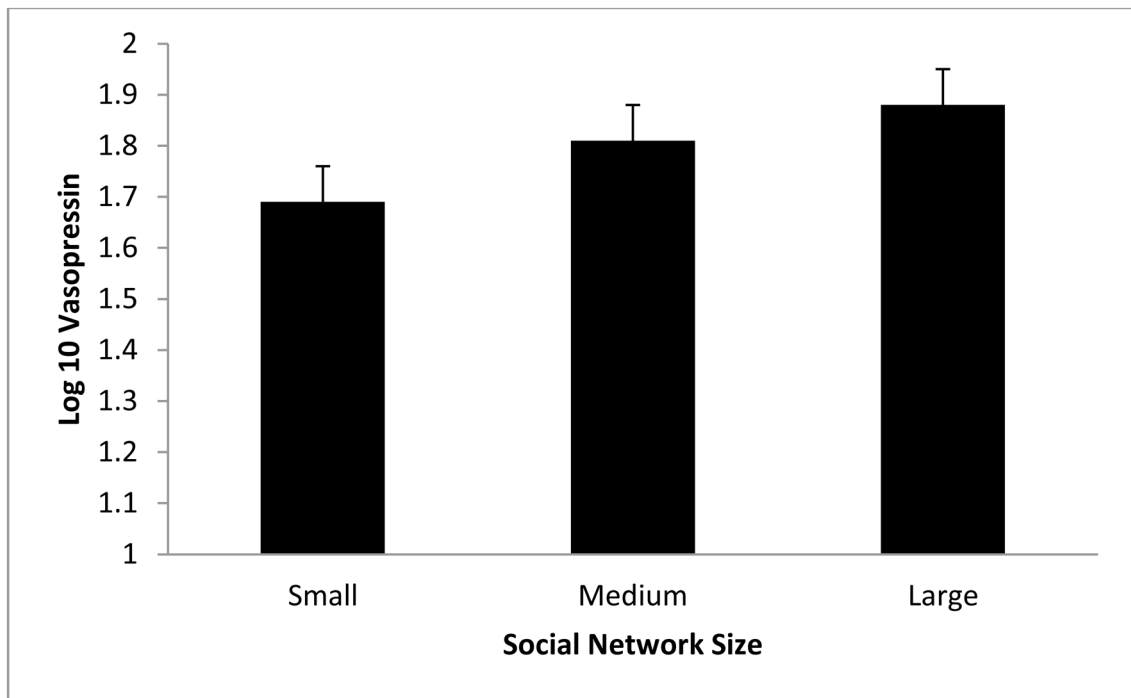


Figure 1. Relationship between plasma vasopressin and social integration. Results revealed that vasopressin was significantly associated with the number of regular social roles, $p = .05$. For illustration purposes, the social integration variable (SNI) was divided into tertiles. Error bars represent standard errors of the mean.

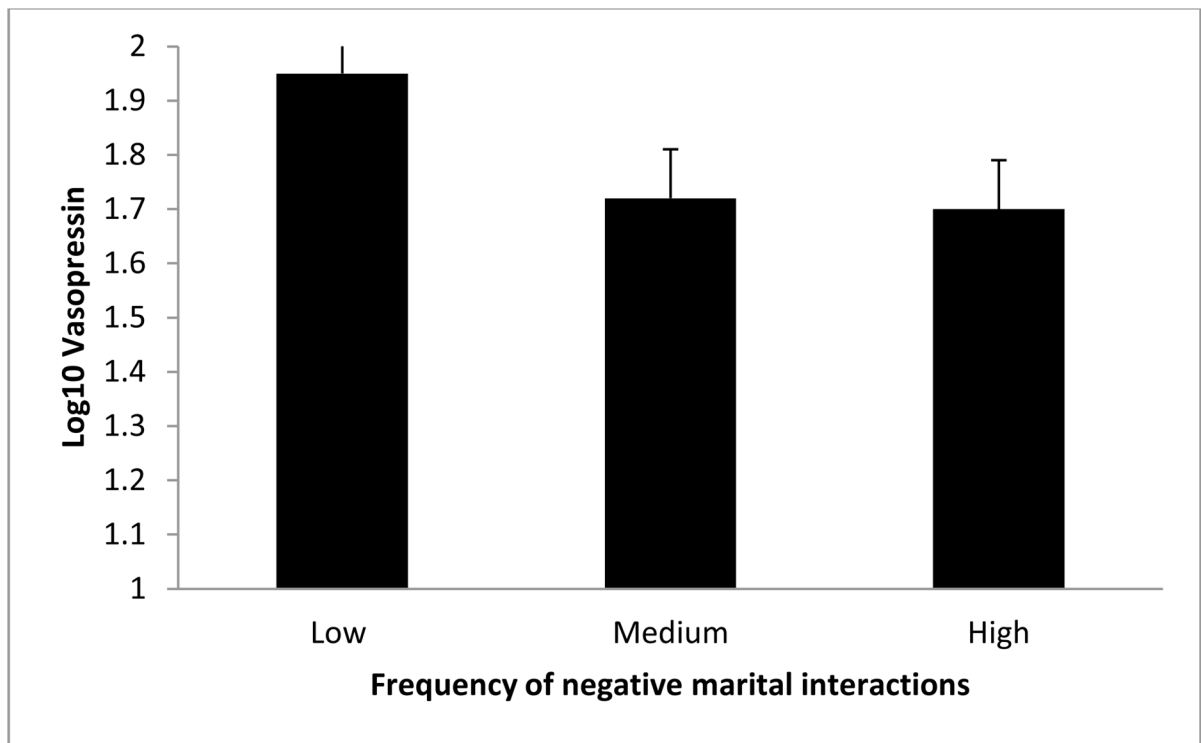


Figure 2. Relationship between plasma vasopressin and the frequency of negative marital interactions. Results revealed that vasopressin was significantly associated with the frequency of negative marital interactions, $p = .03$. For illustration purposes, the negative marital interaction variable (TENSE) was divided into tertiles. Error bars represent standard errors of the mean.

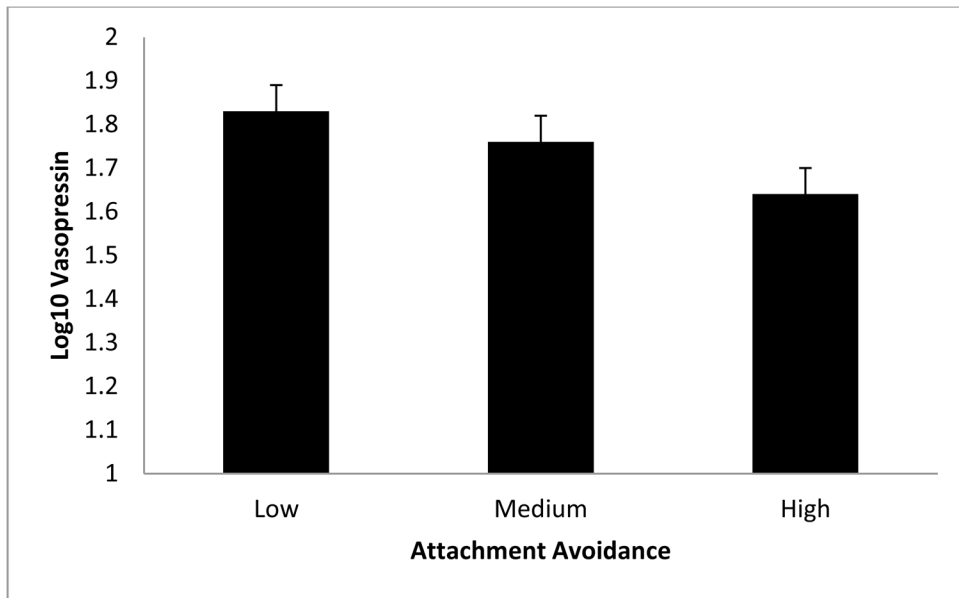


Figure 3. Relationship between plasma vasopressin and Hazan and Shaver's attachment avoidance. Results revealed that vasopressin was significantly associated with attachment avoidance, $p = .03$. Error bars represent standard errors of the mean.

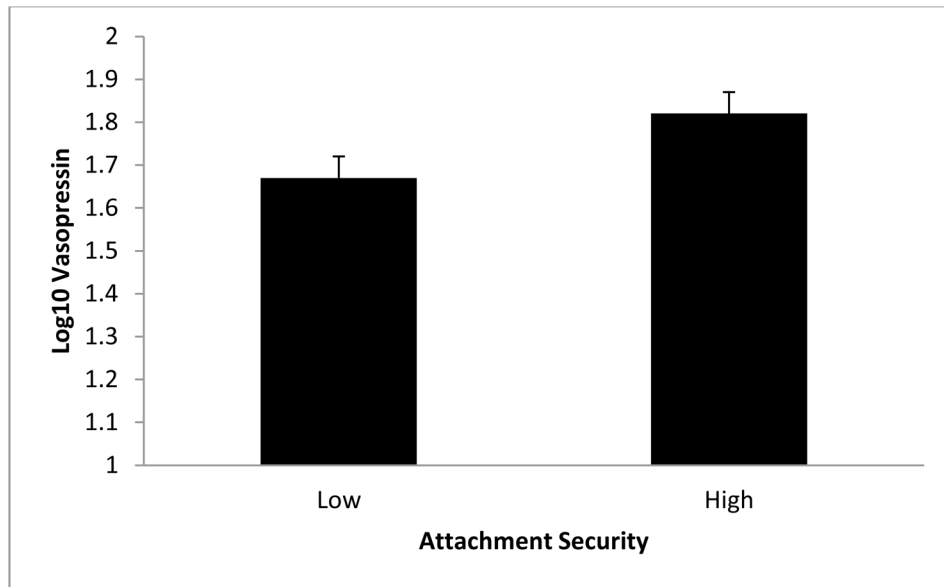


Figure 4. Relationship between plasma vasopressin and Hazan and Shaver's attachment security. Results revealed that vasopressin was significantly associated with attachment security, $p = .04$. Error bars represent standard errors of the mean.

Table 1

Study participants' psychological and social characteristics.

	M (SD)	Range
Depression (BDI)	2.33 (2.38)	0–12
Anxiety (BAI)	5.11 (4.33)	0–21
Social Network Size (SNI)	7.29 (1.77)	3–12
Spousal social support (SSQ)	5.4 (1.34)	0–6
Non-spousal social support (SSQ)	17.42 (11.42)	0–48
Marital Satisfaction (MAT)	113 (25.50)	39–155
Negative Marital Interactions (TENSE)	1.95 (2.32)	0–11.65
Negative Non-Marital Interactions (TENSE)	1.56 (1.67)	0–7.20
Hazan & Shaver Attachment anxiety	2.03 (1.41)	1–6
Hazan & Shaver Attachment avoidance	2.37 (1.62)	1–6
Hazan & Shaver Attachment security	4.23 (1.55)	1–6
ECR-R Attachment Avoidance	2.23 (.95)	1–5.94
ECR-R Attachment Anxiety	2.39 (.92)	1–5.39

Table 2

Spearman's rho correlations among the study variables.

	AVP	BDI	BAI	SNI	SSQ-S	SSQ-NS	MAT	TENSE-S	TENSE-NS	ATT-Av	ATT-Ax	ATT-S	ECR-Av	ECR-Ax
AVP	1	-.09	0.3	.24*	.29*	.01	.13	-.30	-.18	-.24*	-.5	.19	.02	.08
BDI		1	.26*	-.07	-.14	-.01	-.32*	.23*	.33*	.37*	.25*	-.24*	.39*	.36*
BAI			1	.05	-.19	-.11	-.20	.13	.13	.14	.09	-.12	.02	.30*
SNI				1	.04	.21	-.02	-.01	.02	-.22	-.12	.40*	-.13	-.13
SSQ-S					1	.24*	.41*	-.33*	-.17	-.15	-.11	.26*	-.34	-.04
SSQ-NS						1	-.14	-.07	.20	-.20	-.12	.32*	.04	.03
MAT							1	-.41*	-.35*	-.19	-.22	.22	-.40*	-.27*
TENSE-S								1	.62*	.25*	.17	-.23*	-.20	.15
TENSE-NS									1	.37*	.21	-.22	.26*	.12
ATT-Av										1	.30	-.61	.31	.07
ATT-Ax											1	-.41*	.27*	.33*
ATT-S												1	-.29*	-.12
ECR-Av													1	.32*
ECR-Ax														1

AVP: Vasopressin; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; SNI: Social Network Index; SSQ-S: Social Support Questionnaire- Spousal version; SSQ-NS: Social Support Questionnaire-Non-Spousal version; MAT: Marital Adjustment Test; TENSE-S: Test of Negative Social Exchange-Spousal version; TENSE-NS: Test of Negative Social Exchange-Non-Spousal Version; ATT-Av: Hazan & Shaver Attachment avoidance; ATT-Ax: Hazan & Shaver Attachment anxiety; ATT-S: Hazan & Shaver Attachment security; ECR-Av: Experiences in Close Relationships-Avoidance Scale; Experiences in Close Relationships-Anxiety Scale.

* indicates $p < .05$

Table 3

Social functioning and plasma AVP levels.

	β (SE)	p-value
Depression (BDI)	-.14 (.12)	.24
Anxiety (BAI)	.05 (.14)	.71
Social Network Size (SNI)	1.37 (.69)	.05**
Spousal social support (SSQ)	.33 (.17)	.06*
Non-spousal social support (SSQ)	-.88 (4.29)	.83
Marital Satisfaction (MAT)	7.92 (9.84)	.42
Negative Marital Interactions (TENSE)	-.25 (.11)	.03**
Negative Non-Marital Interactions (TENSE)	-.14 (10)	.18
Hazan & Shaver Attachment avoidance	-.73 (.32)	.03**
Hazan & Shaver Attachment anxiety	-.25 (.33)	.45
Hazan & Shaver Attachment security	1.71 (.83)	.04**
ECR-R Attachment Avoidance	.02 (.07)	.78
ECR-R Attachment Anxiety	.01 (.06)	.88

* $p < .10$;** $p < .05$