Genetic variation in the vasopressin receptor 1a gene (*AVPR1A*) associates with pair-bonding behavior in humans

Hasse Walum*[†‡], Lars Westberg[†§], Susanne Henningsson[§], Jenae M. Neiderhiser[¶], David Reiss[‖], Wilmar Igl*, Jody M. Ganiban**, Erica L. Spotts[††], Nancy L. Pedersen*, Elias Eriksson[§], and Paul Lichtenstein*

*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Box 281, S-171 77 Stockholm, Sweden; [§]Department of Pharmacology, Institute of Neuroscience and Physiology, University of Gothenburg, Box 431, S 405 30 Gothenburg, Sweden; [¶]Department of Psychology, Pennsylvania State University, University Park, PA 16802; [‖]Yale Child Study Center, Yale University, New Haven, CT 06520; **Department of Psychology, The George Washington University, Building GG 2125 G St NW, Washington, DC 20052; and [††]Behavioral and Social Research Program, National Institute on Aging, Bethesda, MD 20892-9205

Edited by Solomon H. Snyder, Johns Hopkins University School of Medicine, Baltimore, MD, and approved July 14, 2008 (received for review March 28, 2008)

Pair-bonding has been suggested to be a critical factor in the evolutionary development of the social brain. The brain neuropeptide arginine vasopressin (AVP) exerts an important influence on pair-bonding behavior in voles. There is a strong association between a polymorphic repeat sequence in the 5′ flanking region of the gene (*avpr1a*) encoding one of the AVP receptor subtypes (V1aR), and proneness for monogamous behavior in males of this species. It is not yet known whether similar mechanisms are important also for human pair-bonding. Here, we report an association between one of the human *AVPR1A* repeat polymorphisms (RS3) and traits reflecting pair-bonding behavior in men, including partner bonding, perceived marital problems, and marital status, and show that the RS3 genotype of the males also affects marital quality as perceived by their spouses. These results suggest an association between a single gene and pair-bonding behavior in humans, and indicate that the well characterized influence of AVP on pair-bonding in voles may be of relevance also for humans.

monogamy | neuropeptide | polymorphism | social behavior

Primate social organization is often characterized by bonded relationships, and recent analyses suggest that it may have been the particular demands for pair-bonding behavior that triggered the evolutionary development of the primate social brain (1). The brain neuropeptide arginine vasopressin (AVP), acting through the receptor subtype V1aR, plays a key role in the regulation of pair-bonding behavior in male rodents, as revealed by a series of elegant studies on closely related vole species, i.e., montane voles (*Microtus montanus*), meadow voles (*Microtus pennsylvanicus*), and prairie voles (*Microtus ochrogaster*) (2). In prairie voles, which in contrast to montane and meadow voles are socially monogamous and highly social, pair-bond formation and related behaviors are facilitated by AVP and prevented by a V1aR antagonist (3). Supporting the theory that the striking difference in pair-bonding between monogamous and nonmonogamous voles is related to the influence of AVP on this behavior, the neuroanatomical distribution of V1aR differs considerably between these vole species (4) and is associated with sexual and social fidelity among prairie voles (5). Moreover, partner preference is enhanced in the nonmonogamous meadow vole when the V1aR density is increased in relevant brain areas by using viral vector gene transfer (6). Although there are no major differences in the coding sequence of the gene encoding V1aR (*avpr1a*) between prairie, montane or meadow voles, the former species displays a 428-base pair sequence in the 5′ flanking region that is not found in the latter two species. When the *avpr1a* of the prairie vole, including the sequence in the 5′ region, is transgenically inserted into the nonmonogamous species mouse (7), more pronounced social behavior, similar to that displayed by prairie voles, is generated. Furthermore, variation in the 5′ flanking region of prairie vole *avpr1a* affects brain expression of the gene and alters intraspecific variation in partner preference (8).

Human *AVPR1A* is situated on chromosome 12q14–15 (9). Whereas there is no sequence in the human *AVPR1A* 5′ flanking region homologous to the one found in prairie voles, humans do have three repetitive sequences in this region that are polymorphic: A $(GT)_{25}$ dinucleotide repeat, a complex $(CT)_4$-TT-$(CT)_8$-$(GT)_{24}$ repeat (RS3), and a $(GATA)_{14}$ tetranucleotide repeat (RS1) (10). Although as yet not consistently replicated, previous studies have revealed associations between *AVPR1A* repeat polymorphisms and autism (11–13), age at first sexual intercourse (14), and altruism (15), suggesting that these repetitive sequences may have an impact on human social behavior.

The aim of this study was to investigate whether variability in the 5′ flanking region of *AVPR1A* affects pair-bonding behavior in humans as it does in prairie voles. To this end, the three repeat polymorphisms of the *AVPR1A* were genotyped in adult men and women from the Twin and Offspring Study in Sweden (TOSS), comprised of 552 same-sex twin-pairs and their spouses/partners (16). All subjects were assessed with respect to various indices of the quality of the marital relationship, including a new scale–the Partner Bonding Scale (PBS)–which is comprised of items that correspond to the behavioral patterns observed when measuring features of pair-bonds among nonhuman primates.

Results

The allele and genotype distributions of the three repeat polymorphisms (RS1, RS3, and GT_{25}) were similar to what has been reported in previous studies (10, 11, 17) and did not deviate from Hardy–Weinberg equilibrium. After correction for multiple tests, there was a significant global P value for an association between the RS3-repeat polymorphism and the outcome of the PBS for men ($P < 0.01$ after a Bonferroni correction of the six tests), but not for women (Table 1). No associations were found for the other *AVPR1A* polymorphisms. When comparing the mean scores of the PBS for each RS3 allele (Table 2), this value was found to be significantly lower for men carrying allele 334 than for those not carrying this allele ($F_{1,130} = 16.35, P < 0.0001$,

Author contributions: H.W., L.W., S.H., J.M.N., D.R., J.M.G., E.L.S., N.L.P., E.E., and P.L. designed research; W.I. contributed new reagents/analytic tools; H.W. analyzed data; and H.W. and L.W. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

Freely available online through the PNAS open access option.

[†]H.W. and L.W. contributed equally to this work.

[‡]To whom correspondence should be addressed. E-mail: hasse.walum@ki.se.

This article contains supporting information online at www.pnas.org/cgi/content/full/0803081105/DCSupplemental.

NEUROSCIENCE

Table 1. Association between the different microsatellite polymorphisms in the *AVPR1A* 5′ flanking region and the Partner Bonding Scale

Men				Women			
Repeat	*df*	*F*	*P*	Repeat	*df*	*F*	*P*
GT_{25}	21, 148	0.39	0.99	GT_{25}	18, 138	1.05	0.41
RS1	16, 187	1.03	0.43	RS1	15, 197	0.99	0.46
RS3	19, 157	2.48	0.001	RS3	21, 166	1.19	0.27

Only genotypes for which $n > 10$ were included in the analyses.

$d = 0.27$; $P < 0.001$ after correction for the 11 tests). In addition, a dose-dependent effect of the number of 334 alleles on the PBS score (Table 3) was found, with carriers of two alleles showing the lowest scores. The size of these effects were $d = 0.27$ between men not carrying any 334 allele and 334 heterozygotes, and $d = 0.38$ between men not carrying any 334 allele and 334 homozygotes. After Bonferroni correction, no RS3 allele other than the 334 allele displayed a significant association with scores on the PBS.

The association between the RS3 polymorphism and the scores of the PBS prompted us to examine to what extent an influence of this polymorphism on marital quality could be detected when using other measures than the PBS. To this end, we first assessed whether carriers of allele 334 reported more marital problems than men without it, by using an item collected from a life event questionnaire based on the Social Readjustment Rating Scale (18), asking whether the male subjects had experienced marital crisis or threat of divorce during the last year. In line with our assumption, carriers of the RS3 allele 334 responded affirmatively more often to this question (Table 3). Fifteen percent of the men carrying no 334 allele reported marital crisis, whereas 34% of the men carrying two copies of this allele reported marital crisis, suggesting that being homozygous for the 334 allele doubles the risk of marital crisis compared with having no 334 allele.

The validity analysis, reported in the *Materials and Methods* section, showed that unmarried individuals scored significantly lower than married subjects on the PBS. Thus, we hypothesized that men carrying the RS3 allele 334 more often were involved in a relationship without being married. The allele 334 was indeed associated with marital status (Table 3); the frequency of nonmarried men being higher among 334 homozygotes (32%) than among men with no 334 alleles (17%).

Table 2. Association between different RS3 alleles and the Partner Bonding Scale in men

Allele	Freq	Percent	Mean	*df*	*F*	*P*
320	21	2.3	48.8 (6.21)	1, 12	1.52	0.24
330	92	9.9	47.6 (7.18)	1, 37	0.21	0.65
332	128	13.8	47.5 (6.45)	1, 50	0.06	0.81
334	371	40.0	46.2 (6.23)	1, 130	16.35	<0.0001
336	359	38.7	47.6 (6.35)	1, 133	1.51	0.22
338	170	18.3	48.3 (6.21)	1, 77	4.73	0.03
340	263	28.4	47.5 (6.56)	1, 106	0.40	0.53
342	30	3.2	47.0 (4.49)	1, 12	0.05	0.82
344	23	2.5	45.6 (6.43)	1, 8	1.64	0.24
346	126	13.6	46.7 (6.87)	1, 60	1.30	0.26
348	37	4.0	47.9 (8.47)	1, 16	0.36	0.55

Analyses were performed by comparing individuals carrying one or two of an allele with individuals not carrying this allele. Freq, Frequency, denoting number of individuals carrying one or two of the given allele. Mean, Mean value for the Partner Bonding Scale (standard deviation within brackets). Only alleles for which $n > 10$ were included in the analyses. Six alleles were thereby excluded.

Next we investigated whether the genotype of the men influenced marital quality as perceived by their spouses. For this purpose, we used the Dyadic Consensus, Dyadic Satisfaction, Dyadic Cohesion, and Affectional Expression subscales from the Dyadic Adjustment Scale (DAS) (19), measures frequently used to evaluate the quality of marital relationships. As hypothesized, the marital quality, as perceived by the wives, was significantly associated with the RS3 genotype of their husbands. Women married to men with one or two 334 alleles scored significantly lower on the Affection Expression, Dyadic Consensus, and Dyadic Cohesion subscales than did women married to men without the 334 allele (Table 4), and effect sizes ranged from $d = 0.14$–0.20. However, the difference between carriers of one or two 334 alleles that was observed when analyzing the outcome of the PBS for the men was not found for the rating conducted by their spouses. When the women's ratings were adjusted for the husbands' scores on the PBS, a considerable change of regression estimates (β) was obtained; suggesting that the behaviors assessed by the PBS mediate the association of the 334 allele with the wives' reported quality of the marital relationship.

Discussion

The results from the current study suggest an association between a *AVPR1A* polymorphism and human pair-bonding behavior possibly analogous to that reported for voles (8). One of the most common RS3 alleles, the allele 334, was associated with perceived partner bonding in men as assessed by using the PBS. This association could be detected also by assessing marital problems and marital status in men, and the perception of the quality of the marital relationship expressed by their spouses. That an association between the studied gene and items reflecting pair-bonding was found only in men is consistent with the fact that the influence of vasopressin on social behavior is more prominent in male than in female voles (20).

Although the functional importance of the RS3 polymorphism of the *AVPR1A* remains to be clarified, an association between the length of the RS3 repeat and the amount of hippocampal mRNA in human postmortem tissue has been reported (15). Moreover, a recent study in healthy subjects suggests that the 334 allele is associated with increased activation of amygdala, a brain region known to be of importance for pair-bonding behavior (17). The conclusion of our study (that the 334 allele of the RS3 polymorphism influences brain function) is well in line with previous observations.

The possible influence of AVP on social interactions has led researchers to suggest an involvement of this transmitter in conditions characterized by social deficits, for example, autism and autism-related conditions. This theory has gained support from studies assessing the possible association between *AVPR1A* and risk for autism (11–13) and other traits related to interpersonal relationships (15). Although it is difficult to compare the results of these studies to those of our study, it is of interest to note that one of these studies suggests the 334 allele to be over-transmitted to subjects with autism (11). The observation that a gene variant, which according to our data, is negatively associated with the ability to interact within a relationship, may enhance the risk for a condition characterized by impaired social impairments of social relatedness and communication is obviously noteworthy.

The effect size (d) for the influence of the studied allele on PBS scores when comparing men who carry one or two 334 alleles with those who do not carry any was 0.27. This is comparable with what has been reported in large metaanalyses of the association between a DRD4 polymorphism and the personality trait novelty seeking ($d = 0.32$) (19) and that between a serotonin transporter polymorphism and neuroticism ($d = 0.23$) (20), despite the fact that the outcome of the PBS, unlike

Table 3. Effect of 0, 1 or 2 334 alleles on male reports on the Partner Bonding Scale, marital crisis, and marital status

Measure	Number of 334 alleles 0	1	2	*df*	*F*	*P*
Mean score for the Partner Bonding Scale in the three groups						
Partner Bonding Scale	48.0 (6.50)	46.3 (6.16)	45.5 (6.71)	2, 143	8.40	0.0004
Frequency and column-wise percentage of subjects reporting marital crisis/threat of divorce in the three groups						
Have you experienced marital crisis or threat of divorce during the last year?						
No	469 (85%)	277 (84%)	27 (66%)	2, 143	5.00	0.008
Yes	81 (15%)	51 (16%)	14 (34%)			
Frequency and column-wise percentage of subjects being married or cohabiting in the three groups						
Marital status						
Married	457 (83%)	275 (84%)	28 (68%)	2, 143	4.36	0.01
Cohabiting	96 (17%)	52 (16%)	13 (32%)			

Values for the Partner Bonding Scale are means with standard deviation in brackets.

novelty seeking and neuroticism to some extent is influenced not only by the informant but also by his/her partner.

It is notable that an association was found between the RS3 repeat of the *AVPR1A* and indices of pair-bonding behavior in a cohort in which all subjects had been married or cohabiting for at least five years. Tentatively, such an association would be even stronger in a population also comprising subjects not involved in any long-term romantic relationships. It would also be of importance to assess the possible influence of this polymorphism on measures of pair-bonding that are more objective than self-report, such as proneness for cohabiting versus living alone, marriage, and divorce. However, of some interest in this context is our observation that men that were homozygous for the 334 allele were more likely to be unmarried than other men, despite the fact that the cohabiting individuals in our sample had been in a relationship persisting for at least five years and that in the vast majority of all of these couples, both individuals were biological parents to a adolescent child, ranging in age from 11- to 22-years-old. This finding is in line with the observation that unmarried men displayed lower scores on the PBS (see *Materials and Methods*) and may tentatively reflect a lower degree of commitment in those being unmarried.

The relatively small effect size of the *AVPR1A* polymorphism on traits tentatively reflecting pair-bonding in males observed in this study clearly does not mean that this polymorphism may serve as a predictor of human pair-bonding behavior on the individual level. However, by demonstrating a modest but significant influence of this gene on the studied behavior on the group level, we have provided support for the assumption that previous studies on the influence of the gene coding for V1aR on pair-bonding in voles are probably of relevance also for humans.

Materials and Methods

Subjects. The study consisted of 552 twin pairs and their spouses from the second cohort of the Twin and Offspring Study in Sweden (TOSS), a two-cohort study of twin parents, one adolescent child, and the spouse/partner, for which detailed measures of parent-child relationships, marital relationships, personality, attachment style, and the mental health of all study participants were collected (16). Participants were mostly middle class and born between 1944 and 1971. Consistent with the population of Sweden, the vast majority were Caucasian. A more detailed description of the sample is available in a previous article by Neiderhiser and coworkers (16). The same-sex twins included in the study were required to have a relationship of at least five years with their partner; whereas 82% were married, 18% were cohabiting but unmarried. For simplicity, both married and unmarried cohabiting individuals are referred to as ''husband,'' ''wife,'' or ''spouse.'' The twins and their spouses were first sent a questionnaire that was followed by a home visit, during which additional questionnaires were administered. DNA was extracted from mouthwash samples that were collected by using a DNA self-collection kit. Zygosity was determined primarily by genotyping. There were 238 monozygotic (MZ) pairs

NEUROSCIENCE

Table 4. Association between 334 alleles in men and their wives' reports of marital qualities

Quality		No 334 (mean)	One or two 334 (mean)	β	*df*	*F*	*P*
Affectional expression	Unadjusted	18.0 (2.99)	17.4 (2.92)	−0.64	1, 113	10.08	0.002
	Adjusted	—	—	−0.39	1, 111	4.30	0.04
Dyadic consensus	Unadjusted	65.4 (8.11)	63.9 (8.57)	−1.46	1, 117	6.92	0.01
	Adjusted	—	—	−0.82	1, 115	2.46	0.12
Dyadic cohesion	Unadjusted	19.5 (4.34)	18.9 (4.10)	−0.60	1, 116	4.27	0.04
	Adjusted	—	—	−0.20	1, 114	0.53	0.47
Dyadic satisfaction	Unadjusted	43.3 (3.14)	43.2 (2.92)	−0.12	1, 111	0.49	0.49

Mean, Mean value on the outcome for the different DAS Scales for wives with standard deviation within brackets. Adjusted, Analysis with the Partner Bonding Scale included as a covariate. The category of subjects not carrying any 334 allele was used as reference group when constructing the regression estimates (β). Analyses of adjusted values were only performed for the scales that were significantly associated with the 334 allele in the unadjusted analysis.

and 314 dizygotic (DZ) pairs. In total, 2,186 adult individuals were included in the study, of which 1,899 provided usable DNA samples.

Partner Bonding Scale. The pair bond is a critical element in the study of the evolution of primate social organization (21). Pair bonds among nonhuman primates are generally assessed by measures of partner specific affiliative interaction, proximity, and reciprocity between two individuals (22–24). Furthermore, the strength and stability of the bond is related to its persistence through time (25). In accordance with the behavioral domains observed when studying pair-bonding among nonhuman primates, items were collected from the DAS (19), a frequently used assessment of the quality of marital relationships and similar dyads, the Support Seeking and Giving (SSG) (26) assessment measuring subjects' engagement with other people, and the Marital Instability Scale (MIS) (27). Partner specific affiliative interaction was measured by the occurrence of partner exclusive actions (for example, ''How often do you kiss your mate?''). Proximity measures, which in nonhuman primates are measured as the amount of spatial closeness between two individuals, were assessed by two types of items: The proband's experiences of closeness to other people (for example, ''I don't like when other people come too close to me'') and items concerning the proband's motivation to spend time together with their spouse (for example, ''How often are you and your partner involved in common interests outside the family?''). Because one requirement for inclusion in the TOSS dataset was that the adult individuals were part of a dyadic relationship that had persisted for at least five years, no information about the final length of the pair-bonds were available. Instead the proband's reports of their attitudes toward the stability of the relationship (for example, ''Have you discussed a divorce or separation with a close friend?'') were used as individual indicators of future persistence of the relationship. No relevant measures of reciprocity could be found in the TOSS dataset. Thus, of a total of 49 items, 18 questions (7 DAS, 10 SSG, and 1 MIS) were considered relevant measures of human pair-bonding. A factor analysis was performed, and items with loadings <0.4 on the first principal component were excluded [see supporting information (SI) Table S1] resulting in the final PBS, which were created as the sum of 13 items (7 DAS, 5 SSG, and 1 MIS), with scores ranging from 5 to 66. The reliability, as measured with Cronbach's alpha, was 0.79. Validity estimates of the PBS and the original subscales of the validated questionnaires showed plausible patterns of moderate to high correlation coefficients (r = .40–.75). These results were confirmed by our findings on known-groups validity, which showed significant differences between married and nonmarried subjects ($F_{1,105} = 28.28$, $P < 0.0001$), with nonmarried subjects scoring lower on the PBS. We also observed that subjects that had experienced during the last year marital crisis/threat of divorce scored significantly lower on the PBS than those who had not ($F_{1,162} = 186.22$, $P < 0.0001$).

By using the fact that the studied population comprised twin pairs, we finally made an assessment of the heritability of this parameter in the studied cohort. The intraclass correlation for the scale was 0.27 for monozygotic (MZ) and 0.03 for dizygotic (DZ) males. The corresponding figures were 0.47 and 0.33 for females. Heritability according to Falconer's formula ($h^2 = 2(r_{MZ} - r_{DZ})$) (28) was 0.27 for men and 0.28 for women, similar to what has been observed for marital satisfaction (29) and divorce (30).

Microsatellite Genotyping. The GT_{25} repeat polymorphism was amplified with primers 5′-TGTCAGACAAAACGCTGTTC-3′ (forward) and 5′-TGTGGCTTTA-AAAGTTATCCAG-3′ (reverse), the RS3 repeat polymorphism was amplified with primers 5′-TCCTGTAGAGATGTAAGTGC-3′ (forward) and 5′-gtttcttTCT-GGAAGAGACTTAGATGG-3′ (reverse) (11, 12, 17), and the RS1 repeat polymorphism was amplified with primers 5′-AGGGACTGGTTCTACAATCTGC-3′ (forward) and 5′-ACCTCTCAAGTTATGTTGGTGG-3′ (reverse) (11, 12). The fluorescently labeled DNA fragments were analyzed by size with automated capillary electrophoresis by using an ABI PRISM 3730 Genetic Analyzer (Applied Biosystems).

Statistical Analysis. Statistical associations between the continuous and categorical predictors on the one hand and continuous and binary criteria on the other were estimated by using Generalized Linear Mixed Effects Models (GLMM). As earlier studies have shown that the effects of vasopressin on pair-bonding behavior differ between sexes (20), all analyses were performed for men and women separately.

To take the correlated data structure into account and to avoid estimation problems, different variance-covariance matrices were modeled for monozygotic twins, spouses to monozygotic twins, dizygotic twins, and spouses to dizygotic twins. Each of these four groups had a cluster size of $n = 2$. The correlations between individuals in these groups were calculated by using R-side random effects with an unstructured variance-covariance matrix. The model for continuous outcomes assumed normal distribution of residuals with an identity link function between the predictor term and the criterion. Dichotomous outcomes were assumed to be binary distributed with a logit link function. The parameters were estimated based on the residual log pseudo-likelihood (RSPL), which is equivalent to restricted maximum likelihood (31). All statistical analysis was performed by using the *Statistical Analysis System* (SAS), Version 9.1.3 (32), and generalized linear mixed effects models were implemented by using the PROC GLIMMIX procedure.

ACKNOWLEDGMENTS. This project was supported by National Institute of Mental Health Grant R01MH54610, Bank of Sweden Tercentenary Foundation Grant J2004–0036:1, and a postdoctoral fellowship sponsored by the Brain Foundation, Sweden (to L.W.).

1. Dunbar RI, Shultz S (2007) Evolution in the social brain. *Science* 317:1344–1347.
2. Young LJ, Wang Z (2004) The neurobiology of pair bonding. *Nat Neurosci* 7:1048–1054.
3. Cho MM, DeVries AC, Williams JR, Carter CS (1999) The effects of oxytocin and vasopressin on partner preferences in male and female prairie voles (Microtus ochrogaster). *Behav Neurosci* 113:1071–1079.
4. Insel TR, Wang ZX, Ferris CF (1994) Patterns of brain vasopressin receptor distribution associated with social organization in microtine rodents. *J Neurosci* 14:5381–5392.
5. Ophir AG, Wolff JO, Phelps SM (2008) Variation in neural V1aR predicts sexual fidelity and space use among male prairie voles in semi-natural settings. *Proc Natl Acad Sci USA* 105:1249–1254.
6. Lim MM, *et al.* (2004) Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene. *Nature* 429:754–757.
7. Young LJ, *et al.* (1999) Increased affiliative response to vasopressin in mice expressing the V1a receptor from a monogamous vole. *Nature* 400:766–768.
8. Hammock EA, Young LJ (2002) Variation in the vasopressin V1a receptor promoter and expression: Implications for inter- and intraspecific variation in social behaviour. *Eur J Neurosci* 16:399–402.
9. Thibonnier M, *et al.* (1996) Structure, sequence, expression, and chromosomal localization of the human V1a vasopressin receptor gene. *Genomics* 31:327–334.
10. Thibonnier M, *et al.* (2000) Study of V(1)-vascular vasopressin receptor gene microsatellite polymorphisms in human essential hypertension. *J Mol Cell Cardiol* 32:557–564.
11. Kim SJ, *et al.* (2002) Transmission disequilibrium testing of arginine vasopressin receptor 1A (AVPR1A) polymorphisms in autism. *Mol Psychiatry* 7:503–507.
12. Wassink TH, *et al.* (2004) Examination of AVPR1a as an autism susceptibility gene. *Mol Psychiatry* 9:968–972.
13. Yirmiya N, *et al.* (2006) Association between the arginine vasopressin 1a receptor (AVPR1a) gene and autism in a family-based study: Mediation by socialization skills. *Mol Psychiatry* 11:488–494.
14. Prichard ZM, Mackinnon AJ, Jorm AF, Easteal S (2007) AVPR1A and OXTR polymorphisms are associated with sexual and reproductive behavioral phenotypes in humans. Mutation in brief no. *981 Online Hum Mutat* 28:1150.
15. Knafo A, *et al.* (2007) Individual differences in allocation of funds in the dictator game associated with length of the arginine vasopressin 1a receptor RS3 promoter region and correlation between RS3 length and hippocampal mRNA. *Genes Brain Behav* 7:266–275.
16. Neiderhiser JM, *et al.* (2007) Father-adolescent relationships and the role of genotype-environment correlation. *J Fam Psychol* 21:560–571.
17. Meyer-Lindenberg A, *et al.* (2008) Genetic variants in AVPR1A linked to autism predict amygdala activation and personality traits in healthy humans. *Mol Psychiatry*, epub ahead of print.
18. Holmes TH, Rahe RH (1967) The Social Readjustment Rating Scale. *J Psychosomatic Res* 11:213–218.
19. Spanier GB (1976) Measuring Dyadic Adjustment: New scales for Assessing the Quality of Marriage and Similar Dyads. *J Marr Fam* 38:15–28.
20. Winslow JT, *et al.* (1993) A role for central vasopressin in pair bonding in monogamous prairie voles. *Nature* 365:545–548.
21. Fuentes A (2002) Patterns and Trends in Primate Pair Bonds. *Internat J Primatol* 23:1573–8604.
22. Krebs JR, Davies NB (1997) *Behavioral Ecology* (Blackwell, London).
23. Fuentes A (2000) Hylobatid communities: Changing views on pair bonding and social organization in hominoids. *Am J Phys Anthropol* 43:33–60.
24. Hinde RA (1983) *Primate Social Relationships*: *An Integrated Approach* (Blackwell, Oxford).
25. Rasmussen DR (1981) Pair-bond strength and stability and reproductive success. *Psycholog Rev* 88:274–290.
26. Simpson JA (1990) Influence of attachment styles on romantic relationships. *J Person Soc Psychol* 59:971–980.
27. Booth A, Johnson D, Edwards JN (1983) Measuring Marital Instability. *J Marr Fam* 45:387–394.
28. Falconer DS, Mackay TF (1996) *Introduction to Quantitative Genetics*. (Longman, Harlow).
29. Spotts EL, *et al.* (2004) Genetic and environmental influences on marital relationships. *J Fam Psychol* 18:107–119.
30. Jockin V, McGue M, Lykken DT (1996) Personality and divorce: A genetic analysis. *J Pers Soc Psychol* 71:288–299.
31. SAS Institute, Inc. (2006) The GLIMMIX Procedure (Sas Institute, Cary, NC). Available from http://support.sas.com/rnd/app/da/glimmix.html. Accessed January 7, 2008.
32. SAS Institute Inc. (2007) SAS/STAT Software (Version 9.1.3) (SAS Institute, Cary, NC).