## Genetic Influence on Reproductive Behavior in Female Rhesus Macaques

## Commentary on Cherkas et al. (2004). Genetic Influences on Female Infidelity and Number of Sexual Partners in Humans: A Linkage and Association Study on the Role of the Vasopressin Receptor Gene (AVPR1A). *Twin Research, 7*, 649–658.

Andrea Trefilov,<sup>1</sup> Peter J. P. Croucher,<sup>2</sup> Michael Krawczak,<sup>2</sup> and Jörg Schmidtke<sup>1</sup>

<sup>1</sup> Abteilung für Humangenetik, Medizinische Hochschule Hannover, Hannover, Germany
<sup>2</sup> Institut für Medizinische Informatik und Statistik, Christian-Albrechts-Universität, Kiel, Germany

In a recent paper published in this journal, Cherkas et al. (2004) provided evidence that the number of sexual partners and the level of infidelity of human females are partly determined by genetic factors. The authors argued that female promiscuity and the genetic variants underlying it exist because unfaithful behavior would have been evolutionarily advantageous (Cherkas et al., 2004). A genome-wide linkage scan led to the identification of three suggestive, but nonsignificant, linkage regions for genes controling infidelity and sexual partner number on chromosomes 3, 7 and 20. However, none of these regions contain an obvious candidate gene for the behavioral traits in question. The authors therefore suggested further linkage and association studies to be carried out on hormone and hormone-receptor genes. Although the study of Cherkas et al. (2004) was the first to demonstrate a genetic basis for infidelity and sexual partner number in humans, substantial evidence for the heritability of these traits in animals, particularly birds and rodents, has already been reported (Blomqvist et al., 2002). Interestingly, no comparative data exist for nonhuman primates. Such studies would be of particular relevance in this context, given the evolutionary proximity of nonhuman primates to humans.

The study by Cherkas et al. (2004) has prompted us to reevaluate genotype data for the 5HTTLPR polymorphism in the serotonin transporter gene promoter (chromosomal location in man: 17q11.1–q12), which has previously been analyzed by our own group in relation to the social, and in particular the reproductive, behavior of monkeys (Krawczak et al., 2005; Trefilov et al., 2000). Our studies were based on large-scale molecular genetic paternity assessment exercises in the free-ranging colony of rhesus macaques (*Macaca mulatta*) maintained by the Caribbean Primate Research Center, Cayo Santiago, Puerto Rico (Nürnberg et al., 1998). The 5HTTLPR polymorphism has two alleles, L (long) and S (short). The latter is known to be associated with various stress-related psychological and psychiatric traits in humans and other primates (for references, see Krawczak et al., 2005; Trefilov et al., 2000). In rhesus macaques, we found that 5HTTLPR modulates the reproductive life history of males. Rhesus macaques live in social groups of strict female descent from which the majority of native males disperse following puberty. The age at dispersal is associated with the 5HTTLPR genotype (Trefilov et al., 2000), and the age at reproduction is also influenced by the 5HTTLPR genotype in males, but not in females (Krawczak et al., 2005).

Reproduction in rhesus macaques is based entirely on female choice and females prefer mating partners novel to their social group (Berard, 1999). In order to verify whether female reproductive choice was also related to 5HTTLPR genotype in the Cayo Santiago colony, we revisited the genotype data of all females with infants of known paternity (n = 210). The average number of offspring per female was 2.8 (597/210), with a maximum of 9. Of the 139 females who had at least two offspring, some 115 (83%) had conceived all their infants from different males (Table 1). Interestingly, the proportion who had at least two offspring from the same male differed significantly between females of different 5HTTLR genotype (LL: 20%; LS: 10%; SS: 38%; Fisher's exact p = .033). In a pairwise comparison, only the difference between LS and SS females attained statistical significance (p = .020). Thus, LS females appear to be significantly more promiscuous than SS females, although it is unclear whether this difference is due to a dominant effect of the L allele or reflects heterosis.

Of the 25 male-female dyads that produced more than one offspring, and for which the migratory status of the sire was known, five involved a male still

Address for correspondence: Jörg Schmidtke, MD, Institute of Human Genetics, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany. E-mail: schmidtke.joerg@mh-hannover.de

Table 1	
Female Promiscuity and 5HTTLR Genotype	
Diversity of sirehood	Genotype

'	71			
	LL	LS	SS	
$n_o = n_s$	53	54	8	
$n_o > n_s$	13	6	5	
Total	66	60	13	

Note:  $n_o = n_s$ : number of offspring of given female equal to number of different sires, that is, all offspring have been conceived from a different male.

 $n_o > n_s$ : number of offspring of given female larger than number of different sires, that is, at least two offspring have been conceived from the same male.

residing in his birth group. A similar proportion was observed among dyads with only one offspring (93 out of 526). Therefore, familiarity to partners does not appear likely to have been a major factor in determining the number of sexual partners of females. It is worth noting, however, that in none of the five dyads involving a recurrent, native male partner was the female of LS genotype.

Our data provide the first evidence for nonhuman primates of a genetic influence on the number of sexual partners chosen by females. Although the serotonin transporter gene is not located in any of the reported regions of suggestive linkage with human female fidelity (Cherkas et al., 2004), our findings suggest that the serotonin system, in particular the SHTTPLR polymorphism, should be an important future target for research into the genetic basis of female sexual behavior.

## Acknowledgments

Supported by grant P40 RR03640 from the National Center for Research Resources awarded to the Caribbean Primate Research Center, Puerto Rico.

## References

- Berard, J. (1999). A four-year study of the association between male dominance rank, residency status and reproductive activity in rhesus macaques (*Macaca mulatta*). *Primates*, 40, 159–175.
- Blomqvist, D., Andersson, M., Kupper, C., Cuthill, I. C., Kis, J., Lanctot, R. B., Sandercock, B. K., Szekely, T., Wallander, J., & Kempenaers, B. (2002). Genetic similarity between mates and extra-pair parentage in three species of shorebirds. *Nature*, 419, 613–615.
- Cherkas, L. F., Oelsner, E. C., Mak, Y. T., Valdes, A., & Spector, T. D. (2004). Genetic influences on female infidelity and number of sexual partners in humans: A linkage and association study of the role of the vasopressin receptor gene (AVPR1A). *Twin Research*, 7, 649–658.
- Krawczak, M., Trefilov, A., Berard, J., Bercovitch, F., Kessler, M., Sauermann, U., Croucher, P., Nürnberg, P., Widdig, A., & Schmidtke, J. (2005). Male reproductive timing in rhesus macaques is influenced by the SHTTLPR promoter polymorphism of the serotonin transporter gene. *Biology of Reproduction*, 72, 1109–1113.
- Nürnberg, P., Sauermann, U., Kayser, M., Lanfer, C., Manz, E., Widdig, A., Berard, J., Bercovitch, F. B., Kessler, M., Schmidtke, J., & Krawczak M. (1998).
  Paternity assessment in rhesus macaques (*Macaca mulatta*): Multilocus DNA fingerprinting and PCR marker typing. American Journal of Primatology, 44, 1–18.
- Trefilov, A., Berard, J., Krawczak, M., & Schmidtke, J. (2000). Natal dispersal in rhesus macaques is related to serotonin transporter gene promoter variation. *Behavior Genetics*, 30, 295–301.