doi:10.1093/scan/nsn015 SCAN (2008) 3, 89–90

In this Issue

Genetic contributions to sensitive parenting

A professor from whom I took a course in graduate school asserted that journals could serve one of two functions: an archival function for articles that nailed down the details of an often paradigm-specific effect or a heuristic function, in which all the details of the findings were not yet nailed down, but the work could serve as an inspiration to others. He was squarely on the side of the heuristic function.

A similar point may be made about journal articles. Some address all the details of a modest question, whereas others are sufficiently exciting, despite leaving questions unanswered, as to have an energizing effect on the field. Such is the case with the Bakermans-Kranenburg and van IJzendoorn article, 'Oxytocin Receptor (*OXTR*) and Serotonin Transporter (*5-HTT*) Genes Associated with Observed Parenting'. The article reports findings from an ongoing study of problem behavior in toddlers. Children with externalizing behavior problems worked on puzzles that were beyond their capabilities, and the ways in which their mothers offered help were assessed. The results indicated that mothers with the less efficient genotypes of the 5-HTTLPR (s/s) and the oxytocin receptor gene (OXTR, AA/AG) showed less sensitive parenting.

These findings are among the earliest to tie genetic predispositions to differences in normal social behavior. Much previous work has focused on identifying genetic risks for clinical disorders, such as autism or depression. Although this clinical approach is undeniably important for clarifying risk factors for well-defined disorders, the approach restricts the range of the phenotype, thereby limiting the applicability of the results to normal social behavior. The Bakermans-Kranenburg and van IJzendoorn approach instead treats the target behavior, namely maternal sensitivity, as a continuously distributed outcome, and thus provides a statistically sensitive approach that directly addresses variation in a common and important social behavior, namely mothering.

The particular genes explored by this group merit note. The serotonin transporter gene has long been a favorite target of investigators looking for genetic bases of psychological functioning, most particularly, psychological distress. With fair reliability, the s/s genotype of the 5-HTTLPR has been tied to risk for major depressive disorder and to depressive symptomatology in normal populations, especially in conjunction with a harsh early family environment or a stressful current environment (Caspi *et al.*, 2003; Taylor *et al.*, 2006). The Bakermans-Kranenburg and van IJzendoorn article is one of the first studies to tie the serotonin transporter gene to normal social behavior. These findings raise intriguing questions, such as how generalizable these effects might be. Do the effects extend beyond maternal sensitivity to other relationships? What other social behaviors might be influenced? Might the s/s genotype of the 5-HTTLPR be connected to social behavior in offspring not only via genetic inheritance of the s-variant, but also by exposure to the behavior of a relatively insensitive parent (Francis *et al.*, 1999)?

The findings regarding the OXTR gene are exciting as well. In the past, as is the case for the 5-HTTLPR, investigators have focused primarily on the potential role of these genes as risk factors for clinically based disorders, and the oxytocin system has, for example, been implicated in autism (Jacob *et al.*, 2007). Research increasingly documents the important role that oxytocin plays in animal social behavior and, most recently, in human social behavior as well. Studies administering exogenous doses of oxytocin in humans have related oxytocin to interpersonal trust and empathy, among other social behaviors. However, a disadvantage of the experimental paradigm is that exogenous administration may not mimic the effects of oxytocin changes that occur naturally in the context of the social environment. As such, a paradigm such as the current one avoids those problems.

The pathways linking these genes potentially to each other and to the outcome of maternal sensitivity represent an exciting direction for future work. The discussion implies that serotonin transport affects oxytocin release, which may exert effects on maternal sensitivity both by enhancing social behavior directly and indirectly via the hedonic effects of relaxation and social contact. Future work can address this and related pathways.

The focus on maternal sensitivity and a young sample are particularly significant features of this study. Numerous investigations have shown that the nurturance or harshness of the early family environment has an enduring effect on offspring mental and physical health across the lifespan (Repetti *et al.*, 2007). Although genetic expression is influenced by aspects of the current environment as well, the effects of the early family environment may be especially enduring because the developing structure and functioning of the brain appears to be strongly influenced by social interactions during this period. The elegant studies

conducted by Michael Meaney and his group (Liu *et al.*, 1997; Meaney, 2001; Weaver *et al.*, 2004), as well as related studies in monkeys by Steven Suomi and colleagues (Suomi, 1991), point to the pivotal role that maternal sensitivity plays in a broad range of offspring social behaviors, ranging from exploratory behavior in novel situations, status within a dominance hierarchy, impulsive behaviors and fearfulness, as well as epigenetic effects on the offspring's own parenting behavior (Francis *et al.*, 1999). The Bakermans-Kranenburg and van IJzendoorn paper does not address the behavioral effects on offspring, of course, but their future work is potentially poised to do so.

Another significant contribution of the paper is its demonstration that researchers interested in the dynamics of social behavior, in this case in the developmental context, can add potency to their findings by adding information at the genetic level. The question 'nature or nurture?' has largely faded from scientific consciousness, as investigators increasingly recognize the powerful influences of genes and gene–environment interactions on human behavior. This paper, thus, represents not only an exciting advance in its own right, but also a model for how researchers interested in addressing the interplay of nature and nurture might proceed.

In the context of G × E interactions, the authors raise the intriguing question as to whether associations between the serotonin and oxytocin genes and social behavior may be especially pronounced in mothers in deprived settings and/or experiencing high levels of stress. In other words, do the less efficient genotypes of the 5-HTTLPR and OXTR confer risk for compromised social behavior primarily in high stress environments? The current report builds on the authors' previous work examining genetic bases of parenting behaviors, in which they found that genes tied to less efficient dopaminergic system functioning, coupled with daily hassles, had negative effects on maternal sensitivity but that the more efficient genetic variants actually protected against adverse effects of daily hassles (Bakermans-Kranenburg and van IJzendoorn, 2007). Similar findings may be uncovered for the 5-HTTLPR-OXTR pathway, as the phenotypic expression of the 5-HTTLPR is known to be sensitive to the beneficence of the social environment (Caspi *et al.*, 2003; Taylor *et al.*, 2006). Accordingly, one might expect to see gene–environment interactions in which these genes are implicated in insensitive social behavior primarily in high-stress environments, effects that may actually reverse in nurturant environments. The authors did not find this G × E interaction in this study, but as they note, the relative educational homogeneity of the sample may make it hard to see such an interaction in a small sample.

There are, of course, important issues that remain to be addressed. The authors note the relatively modest contribution of genetic factors in their investigation. Complex phenotypes, such as sensitive parenting, typically show small relations to specific genes, and so the small amount of variance accounted for is not surprising. Replication with a larger sample is needed. There are limitations of the sample and procedures as well. To what extent will the findings extend beyond this sample, namely the mothers of 2-year-old children with externalizing problems? Do these genes relate to parenting of children without identifiable problems? Do the effects extend to fathers as well as mothers? Are the effects confined to frustrating situations? Might we expect to see these genes related to insensitivity in other kinds of social behaviors, such as relations with partners or friends? (Note that marital distress is not related to these genes in this study). Are these genes implicated in social behavior generally?

These are some of the provocative questions that this article raises. And so, in the best tradition of heuristically based pieces, without nailing down every loose end, this research team has succeeded in stirring interest, guiding future thinking and providing a model for testing these and other exciting questions regarding genetic bases of social behavior.

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REFERENCES

Bakermans-Kranenburg, M.J., van IJzendoorn, M.H. (2007). Research review: genetic vulnerability or differential susceptibility in child development: the case of attachment. *Journal of Child Psychology and Psychiatry*, *48*, 1160–73.

Bakermans-Kranenburg, M.J., van IJzendoorn, M.H. (in press). Oxytocin receptor (*OXTR*) and serotonin transporter (*5-HTT*) genes associated with observed parenting. *Social Cognitive and Affective Neuroscience*.

Caspi, A., Sugden, K., Moffitt, T.E., et al. (2003). Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science*, *301*, 386–9.

Francis, D., Diorio, J., Liu, D., Meaney, M.J. (1999). Nongenomic transmission across generations of maternal behavior and stress responses in the rat. *Science*, *286*, 1155–8.

Jacob, S., Brune, C.W., Carter, C.S., Leventhal, B.L., Lord, C., Cook, E.H. (2007). Association of the oxytocin receptor gene (OXTR) in Caucasian children and adolescents with autism. *Neuroscience Letters*, *417*, 6–9.

Liu, D., Diorio, J., Tannenbaum, B., et al. (1997). Maternal care, hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal responses to stress. *Science*, *277*, 1659–1662.

Meaney, M.J. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annual Review of Neuroscience*, *24*, 1161–92.

Repetti, R.L., Taylor, S.E., Saxbe, D. (2007). The influence of early socialization experiences on the development of biological systems. In: Grusec, J. and Hastings, P., editors. *Handbook of Socialization*. New York, NY: Guilford, pp.124–52.

Suomi, S.J. (1991). Up-tight and laid-back monkeys: individual differences in the response to social challenges. In: Brauth, S., Hall, W. and Dooling, R., editors. *Plasticity of Development*. Cambridge, MA: MIT Press, pp. 27–56.

Taylor, S.E., Way, B.M., Welch, W.T., Hilmert, C.J., Lehman, B.J., Eisenberger, N.I. (2006). Early family environment, current adversity, the serotonin transporter polymorphism, and depressive symptomatology. *Biological Psychiatry*, *60*, 671–6.

Weaver, I.C.G., Cervoni, N., Champagne, F.A., et al. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience*, *7*, 847–54.