HOW GENE-ENVIRONMENT INTERACTIONS CAN INFLUENCE EMOTIONAL DEVELOPMENT IN RHESUS MONKEYS

Stephen J. Suomi, Ph.D.

Laboratory of Comparative Ethology
National Institute of Child Health & Human Development
National Institutes of Health

INTRODUCTION

The question of whether the characteristics that make us unique as individuals are largely determined by our heritage or shaped by our personal experiences has been debated since at least the time of Aristotle. Selective breeding was practiced by those who grew plants or raised animals long before anything was known about specific genes, and assertions by educators and philosophers alike that “the child is the father of the man” predated by centuries any formulation of explicit theories of reinforcement by twentieth century behaviorists. In recent years we have heard claims by some behavioral geneticists that going shopping or getting a divorce is highly heritable, as well as arguments not about whether personality is determined by experience but whether the experience that really counts is with one’s parents or with one’s peers (e.g. Harris, 1998). Clearly, the nature-nurture debate is not exactly new.

What has been relatively new among those who study development is an emerging realization that the basic questions underlying the nature-nurture debate over the years may have been largely misguided. Instead of arguing whether behavioral and biological characteristics that appear during development are genetic in origin or the product of specific experiences, these individuals acknowledge that both genetic and environmental factors can play crucial roles in shaping individual developmental trajectories. Indeed, major efforts have been initiated by behavioral geneticists, among others, to determine the relative contributions of specific genetic and environmental factors to a variety of physical, physiological, cognitive, emotional, and behavioral features exhibited by different humans and animals. Other investigators have been more interested in determining to what extent developmental phenomena are the result of interactions between genetic and environmental factors (Collins et al., 2000; Rutter, 2001).

This chapter summarizes some recent research examining the development of emotional regulation in rhesus monkeys, with a major focus on identifying certain genetic and environmental factors -- and their multiple interactions -- that consistently predispose some monkeys to be unusually fearful in novel or mildly challenging circumstances and others to be excessively and inappropriately aggressive. In both cases, difficulties in the regulation of these
two emotions not only are evident early in life but also appear to be linked to a variety of behavioral and physiological problems that emerge later in development and typically persist thereafter.

By way of background, it is now generally accepted that humans do not have a monopoly on emotionality. Indeed, over a century ago Darwin (1872) argued that some mammals are clearly capable of expressing emotions, and an impressive body of recent research has demonstrated that many mammals possess the same basic neural circuitry and exhibit the same general patterns of neurochemical change that have been implicated in human emotional expression (e.g., Panksepp, 1998). Monkeys and apes, in particular, display characteristic patterns of emotional expression that seem strikingly similar to, if not homologous with, those routinely exhibited by infants and young children in virtually every human culture studied to date. To be sure, some complex emotions such as shame are most likely exclusively human, but those apparently require cognitive capabilities well beyond those of human infants and nonhuman primates of any age (cf. Lewis, 1992). Most other emotions are clearly expressed soon after birth by human and nonhuman primate infants alike, and they appear to serve as highly visible and salient social signals to those around them (cf. Suomi, 1997b). Among the most obvious are expressions of fear and those of anger and rage associated with aggression.

Ethologists have long argued that these basic patterns of emotional expression each serve important adaptive functions, having been largely conserved over mammalian evolutionary history. Consider the case of fear: In a world filled with predators and competitors who have the potential to maim or even kill, an individual fully without fear is unlikely to survive very long. On the other hand, excessive or inappropriate fear can essentially paralyze any individual, in effect limiting those very interactions with the environment needed to obtain the physical and social sustenance necessary for survival. Thus, while every human and nonhuman primate is born with the capacity to be fearful, each must learn which particular stimuli merit fearful responses, as well as how to inhibit the expression of fear in non-threatening situations that present little risk to life or limb (Suomi & Harlow, 1976).

Similarly, the capability to engage in aggressive attack and defense in the service of protecting
self, family, and friends from predators and competitors is seemingly crucial for the survival of the individual and the maintenance of any social group across successive generations. However, excessive and/or inappropriate aggression by any individual has the potential of destroying the very social fabric that binds the group together. The expression of aggression must therefore be regulated, i.e., individual group members must come to know which social stimuli merit an aggressive response and which do not, and for those that do, to what degree, and for how long, if the group is to maintain its social cohesion over time. Indeed, learning how and when to avoid an aggressive encounter and when and how to end it once begun may be at least as important as learning how and when to start or respond to an aggressive act (Suomi, 2000a).

The development of proficiency in the regulation of fear and aggression appears to be especially important for those advanced primate species whose members live in large social groups that are well defined in terms of both kinship relationships and social dominance hierarchies. Among the most complex are those of rhesus monkeys (Macaca mulatta), a highly successful species of macaque monkey that lives throughout most of the Indian subcontinent and beyond. In their natural habitats rhesus monkeys typically reside in large, distinctive social groups (termed “troops”) composed of several female-headed families, each spanning three or more generations of kin, plus numerous immigrant adult males. This form of social group organization derives from the fact that all rhesus monkey females spend their entire life in the troop in which they were born, whereas virtually all males emigrate from their natal troop around the time of puberty and eventually join other troops. Rhesus monkey troops are also characterized by multiple social dominance relationships, including distinctive hierarchies both between and within families, as well as a hierarchy among the immigrant adult males (Lindburg, 1971).

The complex familial and dominance relationships seen in rhesus monkey troops seemingly require that any well-functioning troop member not only be able to regulate its expressions of fear and aggression but also to become familiar with the specific kinship and dominance status of other monkeys toward whom those emotions might be expressed. An impressive body of both laboratory and field data strongly suggest that the acquisition of such knowledge represents an emergent property of the species-normative pattern of socialization that rhesus monkey infants experience as they are growing up (Sameroff & Suomi, 1996).
NORMATIVE DEVELOPMENT OF EMOTIONAL REGULATION IN RHESUS MONKEYS

Rhesus monkey infants are born with the capacity to express multiple emotions, including both fear and anger. These infants begin life highly dependent upon their biological mother for essentially all of their initial biological and psychological needs, and they spend virtually all of their first month in almost continuous physical contact with their mother. During this time a strong and enduring social bond between mother and infant naturally emerges (Harlow, 1958). This bond, largely homologous with Bowlby’s (1969) characterization of human mother-infant attachment, is unique in terms of its exclusivity, constituent behavioral features, and long-term duration – it is like no other relationship a monkey will experience again in its lifetime, except (in reciprocal form) for females when they grow up to become mothers themselves (Suomi, 1999).

Once an infant has developed an attachment relationship with its mother it can use her as a “secure base” from which to begin exploring its immediate social and nonsocial environment. Most infant monkeys soon learn that if they become frightened or otherwise threatened, they can always run back to their mother for immediate safety and comfort via mutual ventral contact. Numerous studies have documented that initiation of ventral contact with the mother promotes rapid decreases in hypothalamic-pituitary-adrenal (HPA) activity, as indexed by a drop in plasma cortisol concentrations (e.g., Gunnar et al., 1981; Mendola et al., 1978), and in sympathetic nervous system arousal, as indexed by reductions in heart rate (e.g., Reite et al., 1987), along with other physiological changes commonly associated with soothing. Secure attachment relationships thus help infants learn to manage the fears they will inevitably experience in the course of exploring their ever-expanding world. On the other hand, if a rhesus monkey infant develops an insecure attachment relationship with its mother, both its ability to regulate fear and its willingness to explore may be compromised, consistent with Bowlby’s observations regarding human attachment relationships (Bowlby, 1988; Suomi, 1999).

During their second and third months of life rhesus infants begin interacting with monkeys other than their mother, and they soon develop distinctive social relationships with specific individuals.
outside of their immediate family, especially with peers -- other infants of like age and comparable physical, cognitive, and social capabilities. Following weaning (usually in the fourth and fifth months) play with peers emerges as a predominant social activity for young monkeys and essentially remains so until puberty (Rupprecht et al., 1974). During this developmental period play interactions become more and more behaviorally and socially complex, increasingly involving interaction patterns that appear to simulate most aspects of adult social behavior. By the time they reach puberty, most rhesus monkey juveniles have had ample opportunities to develop, practice, and perfect behavioral routines that will be crucial for normal adult functioning, especially with respect to dominance interactions and aggressive exchanges.

Aggression typically emerges in a young monkey's behavioral repertoire prior to 6 months of age, and it initially appears in the context of rough-and-tumble play (Symonds, 1979). Shrieking, hair-pulling, wrestling, and other forms of physical contact are basic components of rough-and-tumble play directed toward peers, occurring with increasing frequency among males in the second half of their first year of life and, in fact, becoming their predominate form of play behavior throughout the juvenile years. Although some form of virtually all of the basic physical components of adult aggressive exchanges can be seen in these rough-and-tumble play bouts, the intensity of such interactions is usually quite controlled and seldom escalates to the point of actual physical injury -- if it does, the play bout is almost always terminated immediately, either via adult intervention or by one or more of the participants backing away themselves. The importance of these play bouts with peers for the socialization of aggression becomes apparent when one considers that rhesus monkey infants reared in laboratory environments that deny them regular access to peers during their initial months inevitably exhibit excessive and socially inappropriate aggression later in life (cf. Suomi & Harlow, 1975).

The onset of puberty is associated with major life transitions for both males and females, involving not only major hormonal alterations, pronounced growth spurts, and other obvious physical changes, but also major social changes for both sexes. Males experience the most dramatic social dislocations; when they leave home they sever all social contact not only with their mother and other kids but also with all others in their natal social group. Virtually all of these adolescent males soon join all-male ‘gangs,’ and after several months to a year most of them
then attempt to join a different troop, usually composed entirely of individuals largely unfamiliar to the immigrant males (Berard, 1989). The process of natal troop emigration is exceedingly dangerous for adolescent males -- the mortality rate from the time they leave their natal troop until they become successfully integrated into another troop can approach 50%, depending on local circumstances (e.g., Dittus, 1979). Recent field studies have identified and characterized striking variability in both the timing of emigration and the basic strategies followed by these males in their attempts to join other established social groups.

Adolescent females, by contrast, never leave their natal troop. Puberty for them is instead associated with increases in social activities directed toward maternal kin, especially when they begin to have offspring of their own. Indeed, the birth of a new infant (especially to a new mother) often has the effect of bringing extended family members closer both physically and socially and, in the process, providing a buffer for the new mother and her infant from external threats and stressors. These females' ties to both family and troop are facilitated throughout adulthood by appropriate regulation of fear and aggression; conversely, these ties can be compromised whenever such emotional regulation goes awry (Suomi, 1998).

**INDIVIDUAL DIFFERENCES IN THE REGULATION OF FEAR**

While the basic developmental sequence outlined above are typical for most rhesus monkeys growing up both in the wild and in captive social groups, there are nevertheless substantial differences among individuals in the precise timing and relative ease with which they make major developmental transitions, as well as how they manage the day-to-day challenges and stresses that are an inevitable part of complex social group life. In particular, recent research has identified a subgroup of individuals, comprising approximately 15-20% of both wild and captive populations, who seem excessively fearful. These monkeys consistently respond to novel and/or mildly challenging situations with extreme behavioral disruption and pronounced physiological arousal, including significant and often prolonged activation of the HPA axis, sympathetic nervous system arousal, and increased noradrenergic turnover (Suomi, 1986).

These excessively fearful or "untight" monkeys can usually be identified during their first few weeks of life. Most begin leaving their mothers later chronologically and exploring their
physical and social environment less than other infants in their birth cohort. Highly fearful youngsters also tend to be shy and withdrawn in their initial encounters with peers -- laboratory studies have shown that they exhibit significantly higher and more stable heart rates and greater secretion of cortisol in such interactions than do their less reactive age-mates. However, when these monkeys are in familiar and stable social settings they become virtually indistinguishable, both behaviorally and physiologically, from others in their peer group. In contrast, when fearful monkeys encounter extreme and/or prolonged stress, their behavioral and physiological differences from others in their social group usually become exaggerated (Suomi, 1991a).

For example, young rhesus monkeys growing up in the wild typically experience functional maternal separations during the 2-month-long annual breeding season when their mothers repeatedly leave the troop for brief periods to consort with selected males (Berman, Rasmussen, & Suomi, 1994). The sudden loss of access to its mother is a major social stressor for any young monkey and, not surprisingly, virtually all youngsters initially react to their mother's departure with short-term behavioral agitation and physiological arousal, much as Bowlby (1960, 1973) has described for human infants experiencing involuntary maternal separation. However, whereas most youngsters soon begin to adapt to the separation and readily seek out the company of others in their social group until their mother returns, highly fearful individuals typically lapse into a behavioral depression characterized by increasing lethargy, lack of apparent interest in social stimuli, eating and sleeping difficulties, and a characteristic hunched-over, fetal-like posture (Suomi, 1991b). Laboratory studies simulating those naturally occurring maternal separations have shown that relative to their like-reared peers, highly fearful monkeys not only are more likely to exhibit depressive-like behavioral reactions to short-term social separation but also to show greater and more prolonged HPA activation, more dramatic sympathetic arousal, more rapid central noradrenergic turnover, and greater immunosuppression (Suomi, 1991a). These differential patterns of biobehavioral response to separation tend to remain remarkably stable throughout prepubertal development and may be maintained through adolescence and even into adulthood (Suomi, 1995). There is compelling evidence of significant heritability for at least some components of these differential patterns of separation response (e.g., Higley et al., 1993).
In naturalistic settings fearful rhesus juveniles have greater adrenocortical activity, higher parasite loads, and lower antibody titers following asthmus vaccination than do others in their birth cohort (Ludenslager et al., 1993; 1999). When they reach adolescence, fearful males tend to emigrate from their natal troop at significantly older ages than the rest of their male cohort and, when they do finally leave, they typically employ much more conservative strategies for entering a new troop than do their less-reactive peers. Such strategies actually appear to enhance the prospects of surviving the emigration process for these fearful males (Rasmussen, Fellows, & Suomi, 1990). Thus, even though excessive fearfulness apparently puts an individual male at increased risk for adverse biobehavioral reactions to stress throughout development, there are some circumstances where this characteristic may actually be adaptive (Suomi, 2000b).

A parallel situation exists for females: Highly fearful young mothers in the wild tend to reject and punish their infants at higher rates around the time of weaning than do other mothers in their troop (Rasmussen, Timme, & Suomi, 1997), and in the absence of social support they appear to be at increased risk for infant neglect and/or abuse (Suomi & Ripp, 1983). Yet, under stable social circumstances these fearful females may not only turn out to be highly competent mothers but also often achieve relatively high positions of social dominance (Rasmussen, Timme, & Suomi, 1997; Suomi, 1999). In sum, excessive fearfulness in infancy appears to be associated with increased risk for developing anxious- and depressive-like symptoms, and potential problems in parenting in response to stressful circumstances later in life, but such long-term outcomes are far from inevitable.

Recent research has demonstrated that individual differences in biobehavioral measures of fearfulness obtained during infancy are also predictive of differential responses to other situations experienced later in life. One of the most striking of these involves differences in the propensity to consume alcohol in a “happy hour” situation. Over the past decade J. D. Higley and his colleagues have developed an experimental paradigm in which group-living rhesus monkeys are given the opportunity to consume an aspartame-flavored 7% ethanol beverage, a non-alcoholic aspartame-flavored beverage, and/or plain tap water for daily 1-hour periods within their familiar social group (e.g., Higley et al., 1991). Falke et al. (2000) found that monkey infants who exhibited high levels of plasma cortisol following brief separations at 6 months of
age subsequently consumed significantly more alcohol in this “happy hour” situation when they were 5 years of age than did monkeys whose 6-month cortisol responses were more moderate, independent of gender or rearing background. These monkeys appeared to be self-medicating in that particular situation.

INDIVIDUAL DIFFERENCES IN THE REGULATION OF AGGRESSION
A second subgroup of rhesus monkey exhibit problems in regulating their aggressive behavior. These monkeys, comprising approximately 5-10% of the population, seem unusually impulsive, insensitive, and overtly aggressive in their interactions with other troop members. Impulsive young monkeys, especially males, often are unable to moderate their behavioral responses to rough-and-tumble play initiations from peers, frequently escalating initially benign play bouts into full-blown, tissue-damaging aggressive exchanges (Hagley, Suomi, & Linnola, 1996). Not surprisingly, most of these males tend to be avoided by peers during play bouts and as a result they become increasingly isolated socially. In addition, they appear unwilling (or unable) to follow the “rules” inherent in rhesus monkey social dominance hierarchies. For example, they may directly challenge a dominant adult male, a foolhardy act that can result in serious injury, especially when the juvenile refuses to back away or exhibit submissive behavior once defeat becomes obvious. Impulsive juvenile males also show a propensity for making dangerous leaps from treetop to treetop in outdoor settings (Mehlman et al., 1994).

Overly impulsive monkeys, male and female alike, consistently exhibit chronic deficits in central serotonin metabolism, as reflected by unusually low cerebrospinal fluid (CSF) concentrations of the primary central serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA). Laboratory studies have shown that these deficits in serotonin metabolism emerge early in life and tend to persist throughout development, as was the case for HPA responsiveness among highly fearful monkeys. Monkeys who exhibit such deficits are also likely to show poor state control and visual orienting capabilities during early infancy (Champoux, Suomi, & Schneider, 1994), poor performance on delay-of-gratification tasks during childhood (Bennett et al., 1999), and excessive cerebral glucose metabolism under mild isoflurane anesthesia as adults (Doudet et al., 1999). In addition, both laboratory and field studies have reported that individual differences in 5-HIAA concentrations are highly heritable among monkeys of similar age and comparable
Recent field studies have found that the timing of natal troop emigration typically experienced by impulsive males is seemingly the reverse of that shown by fearful males, with a long-term prognosis that is not particularly promising. Ostracized by their peers and frequently attacked by adults of both sexes, most of these excessively aggressive young males are physically driven out of their natal troop prior to the onset of puberty and long before most of their male cohort begins the normal emigration process (Mehlman et al., 1995). These males tend to be grossly incompetent socially and, lacking the requisite social skills necessary for successful entrance into another troop or even to join an all-male gang, most of them become solitary and typically perish within a year (Higley et al., 1996b).

Young females who have chronically low CSF levels of 5-HIAA also tend to be impulsive, aggressive, and generally rather incompetent socially. However, unlike the males, they are not expelled from their natal troop but instead remain with their families throughout their lifetime, although studies of captive rhesus monkey groups suggest that these females usually remain at the bottom of their respective dominance hierarchies (Higley et al., 1996a). While most of these females eventually become mothers, recent research indicates that their maternal behavior often leaves much to be desired (Suomi, 2000a). In sum, rhesus monkeys who exhibit poor regulation of impulsive and aggressive behavior and low central serotonin turnover early in life tend to follow developmental trajectories that often result in premature death for males and chronically low social dominance and poor parenting for females.

As was the case for excessively fearful monkeys, overly impulsive and aggressive individuals tend to consume excessive amounts of alcohol when placed in the afore-mentioned “happy hour” experimental paradigm. Interestingly, their pattern of alcohol consumption during the 1-hour sessions appears to be more like “binge-drinking” than the “self-medication” pattern typically exhibited by excessively fearful individuals (Higley, Suomi, & Linnola, 1996). Recent studies have demonstrated a significant relationship between degree of alcohol intoxication and serotonin transporter availability in these monkeys (Heinz et al, 1998), as well as among alcohol intake, innate tolerance, and serotonin transporter availability (Higley et al., in press).
EFFECTS OF EARLY PEER REARING ON THE REGULATION OF FEAR AND AGGRESSION

Although the findings from both the field and laboratory studies cited above have consistently shown that differences among rhesus monkeys in their expressions of fearfulness and impulsive aggression tend to be quite stable from infancy to adulthood and are at least in part inheritable, this does not mean that they are necessarily fixed at birth or are immune to subsequent environmental influence. To the contrary, an increasing body of evidence from laboratory studies has demonstrated that patterns of emotional expression can be modified substantially by certain early social experiences, especially with respect to early attachment relationships.

Perhaps the most compelling evidence comes from studies of rhesus monkey infants raised with peers instead of their biological mothers. In these studies infants typically have been permanently separated from their biological mothers at birth, hand-reared in a neonatal nursery for their first month of life, housed with same-aged, like-reared peers for the rest of their first 6 months, and then moved into larger social groups containing both peer-reared and mother-reared age-mates. During their initial months, these infants readily establish strong social bonds with each other, much as mother-reared infants develop attachments to their own mothers (Harlow, 1969). However, because peers are not nearly as effective as typical monkey mothers in reducing fear in the face of novelty or in providing a "secure base" for exploration, the attachment relationships that these peer-reared infants develop are almost always "anxious" in nature (Suomi, 1995). As a result, while peer-reared monkeys show completely normal physical and motor development, most appear to be excessively fearful --- their early exploratory behavior tends to be somewhat limited, they seem reluctant to approach novel objects, and they tend to be shy in initial encounters with unfamiliar peers (Suomi, 1997a).

Even when peer-reared youngsters interact with their rearing partners in familiar settings, their emerging social play repertoires are usually retarded in both frequency and complexity. One explanation for their relatively poor play performance is that their peer partners have to serve both as attachment figures and playmates, a dual role that either mothers or mother-reared peers have to fulfill. Another obstacle faced by peer-reared monkeys is that all of their early play
bouts involve partners who are basically as socially incompetent as themselves. Perhaps as a result of these factors, peer-reared youngsters typically drop to the bottom of their respective dominance hierarchies when they are subsequently housed with mother-reared monkeys their own age (Higley, Suomi, & Linnola, 1996).

Several prospective longitudinal studies have found that peer-reared monkeys consistently exhibit more extreme behavioral, adrenocortical, and noradrenergic reactions to social separation than do their mother-reared cohorts, even after they have been living in the same social groups for extended periods (e.g., Higley & Suomi, 1989; Higley, Suomi, & Linnola, 1992). Such differences in reactions to separation persist from infancy to adolescence, if not beyond. Interestingly, the general nature of the separation reactions exhibited by peer-reared monkeys seems to mirror that shown by “naturally occurring” highly fearful mother-reared subjects. In this regard, peer-rearing early in life appears to have the effect of making rhesus monkeys generally more fearful than they might have been if reared by their biological mothers (Suomi, 1997a).

Early peer-rearing has another long-term developmental consequence for rhesus monkey -- they tend to become excessively aggressive, especially if they are males. Like the previously described impulsive monkeys growing up in the wild, peer-reared males initially exhibit overly aggressive tendencies in the context of juvenile play; as they approach puberty, the frequency and severity of their aggressive episodes typically exceed those of their same-age mother-reared counterparts. Peer-reared females tend to groom (and be groomed by) others in their social group less frequently and for shorter durations than mother-reared females, and, as noted above, they usually stay at the bottom of their respective dominance hierarchies. The differences between peer-reared and mother-reared age-mates in rates of aggression and grooming and in dominance rankings remain relatively robust throughout the prepubertal and adolescent years (Higley, Suomi, & Linnola, 1996). Peer-reared monkeys also consistently have lower CSF concentrations of 5-HIAA than their mother-reared counterparts. These group differences in 5-HIAA concentrations appear well before 6 months of age, and they remain stable at least throughout adolescence and into early adulthood (Higley & Suomi, 1996). Thus, peer-reared monkeys exhibit the same general tendencies that characterize excessively impulsive wild-living (and mother-reared) rhesus monkeys, not only behaviorally but also in terms of decreased
serotonergic functioning.

Given these findings, it should perhaps come as no surprise that peer-reared adolescent monkeys as a group consume larger amounts of alcohol under comparable ad libitum conditions than their mother-reared agemates (Higley, Hasert, Suomi, & Linnoila, 1991). They also rapidly develop a greater tolerance for alcohol and, as previously noted, this tendency appears to be associated with differences in serotonin turnover rates (Higley et al., in press) and with differential serotonin transporter availability (Heinz et al., 1998). In sum, early rearing with peers seems to make rhesus monkey infants both more fearful and more impulsive, and their resulting developmental trajectories not only resemble those of naturally occurring subgroups of rhesus monkeys growing up in the wild.

**GENE-ENVIRONMENT INTERACTIONS**

Studies examining the effects of peer-rearing and other variations in early rearing history (e.g., Harlow & Harlow, 1969), along with the previously cited heritability findings, clearly provide compelling evidence that both genetic and early experiential factors can affect a monkey’s capacity to regulate expression of fear and aggression. Do these factors operate independently, or do they interact in some fashion in shaping individual developmental trajectories? Ongoing research capitalizing on the discovery of a polymorphism in one specific gene – the serotonin transporter gene – suggests that gene-environment interactions not only occur but also can be expressed in multiple forms.

The serotonin transporter gene (5-HTT), a candidate gene for impaired serotonergic function (Lesch et al., 1996), has length variation in its promoter region that results in allelic variation in 5-HTT expression. A heterozygous “short” allele (S) confers low transcriptional efficiency to the 5-HTT promoter relative to the homozygous “long” allele (L.L), raising the possibility that low 5-HTT expression may result in decreased serotonergic function (Heils et al., 1998), although evidence in support of this hypothesis in humans has been decidedly mixed to date (e.g., Furlong et al., 1998). The 5-HTT polymorphism was first characterized in humans, but it also appears in a largely homologous form in rhesus monkeys but interestingly not in many other species of primates and other mammals (Lesch et al., 1997).
We recently utilized polyclonal recombinant (PCR) techniques to characterize the genotypic status of monkeys in the studies comparing peer-reared monkeys with mother-reared controls described above with respect to their 5-HTT polymorphic status. Because extensive observational data and biological samples had been previously collected from these monkeys throughout development, it became possible to examine a wide range of behavioral and physiological measures for potential 5-HTT polymorphism main effects and interactions with early rearing history. Analyses completed to date suggest that such interactions are widespread and diverse.

For example, Bennett et al. (2002) reported that CSF 5-HIAA concentrations did not differ as a function of 5-HTT status for mother-reared subjects, whereas among peer-reared monkeys individuals with the LS allele had significantly lower CSF 5-HIAA concentrations than those with the LL allele. One interpretation of this interaction is that mother-rearing appeared to "buffer" any potentially deleterious effects of the LS allele on serotonin metabolism. A different form of gene-environment interaction was suggested by the analysis of alcohol consumption data: whereas peer-reared monkeys with the LS allele consumed more alcohol than peer-reared monkeys with the LL allele, the reverse was true for mother-reared subjects, with individuals possessing the LS allele actually consuming less alcohol than their LL counterparts (Bennett et al., 1998). In other words, the LS allele appeared to represent a risk factor for excessive alcohol consumption among peer-reared monkeys but a protective factor for mother-reared subjects. In another set of analyses, Champoux et al. (in press) examined the relationship between early rearing history and serotonin transporter gene polymorphic status on measures of neonatal neurobehavioral development during the first month of life and found further evidence of maternal "buffering." Specifically, infants possessing the LS allele who were reared in the laboratory neonatal nursery showed significant deficits in measures of attention, activity, and motor maturity relative to nursery-reared infants possessing the LL allele, whereas both LS and LL infants who were being reared by competent mothers exhibited normal values for each of these measures.

In sum, the consequences of having the LS allele have been found to differ dramatically for peer-reared and mother-reared monkeys: whereas peer-reared individuals with the LS allele exhibit
deficits in measures of neurobehavioral development during their initial weeks of life and reduced serotonin metabolism and excessive alcohol consumption as adolescents, mother-reared subjects with the very same allele are characterized by normal early neurobehavioral development and serotonin metabolism, as well as reduced risk for excessive alcohol consumption later in life. Indeed, it could be argued on the basis of these findings that having the “short” allele of the 5-HTT gene may well lead to psychopathology among monkeys with poor early rearing histories but might actually be adaptive for monkeys who develop secure early attachment relationship with their mothers.

IMPLICATIONS FOR UNDERSTANDING THE DEVELOPMENT OF EMOTIONAL REGULATION IN HUMANS

Earlier in this chapter it was argued that emotional regulation represents a process that is not limited to humans. To what extent can studies of its development and possible biological correlates in rhesus monkeys enhance our understanding of how genetic and environmental factors might influence the development of emotional regulation in children, particularly those who display debilitating fearfulness or excessive aggression as they are growing up? To be sure, rhesus monkeys are clearly not furry little humans with tails but rather members of another (albeit closely related) species, and one should be especially cautious when making comparisons between humans and other primate species with respect to the expression of fearful and aggressive behavior, given that there exist obvious age, gender, and cultural differences in what is considered excessive or abnormal for humans. Nevertheless, there appear to be some general principles emerging from research with rhesus monkeys that might be relevant for the human case.

First, the results of these studies have clearly demonstrated that both nature and nurture are at play in the development of most, if not all, biobehavioral features of excessive fearfulness and impulsive aggressiveness. On the one hand, evidence of significant heritability has been reported for certain neonatal reflex and activity patterns, HPA reactivity, CSF 5-HIAA concentrations, and behavioral expressions of both fear and aggression. On the other hand, many of these studies have also demonstrated significant effects of differential early rearing experiences on the developmental trajectories of virtually all of these very same behavioral and
physiological systems, their significant heritabilities notwithstanding. Thus, the manner in which a rhesus monkey has been reared can markedly affect its pattern of neonatal reflex development, its daily distribution of activity states, its propensity to activate its HPA axis and to exhibit fear in the face of novelty, as well as its likelihood of escalating play bouts into aggressive episodes, and its chronic CSF concentrations of 5-HIAA, respectively, no matter how many genes might be involved in each instance. Clearly, both nature and nurture can contribute to the development of both excessive fearfulness and impulsive aggressiveness in this species -- and most likely in other primate species as well.

Perhaps the more interesting principle concerns the manner and degree to which heritable factors can interact with environmental influences to shape individual developmental trajectories with respect to these two emotions. The recent findings that a specific polymorphism in the serotonin transporter gene is associated with different behavioral and biological outcomes for rhesus monkeys as a function of their early social rearing histories suggest that more complex gene-environment interactions may actually be responsible for the phenomena in question. Whether comparable instances of gene-environment interactions can be demonstrated for other biobehavioral characteristics is currently the focus of ongoing research efforts; preliminary findings to date have been exceedingly encouraging in that respect. Nevertheless, even highly definitive demonstrations of additional gene-environment interactions would scarcely begin to address issues regarding the actual cascades of protein synthesis presumably initiated by expression of the genes in question, the extent and manner in which such expression might be enhanced, blocked, or otherwise modified by specific environmental factors, and the biological pathways and mechanisms through which such expression might be translated into specific physiological and behavioral characteristics exhibited by individual monkeys. While nature and nurture can obviously interact, exactly how, when, and why has yet to be fully determined -- be it for rhesus monkeys or for our fellow humans.

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