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Psychobiology of Intergenerational Effects of Trauma

Evidence from Animal Studies

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INTRODUCTION: RATIONALE FOR ANIMAL STUDIES

Systematic scientific study of the effects of trauma on humans has always faced formidable methodological challenges and both ethical and practical obstacles. The most scientifically rigorous study designs—prospective longitudinal experiments, preferably double-blind in nature—are virtually nonexistent, appropriately precluded by the ethical standards of every civilized society. Instead, some reliance on retrospective data inevitably occurs, at least for part of the period under study (e.g., the time prior to the beginning of the trauma). Practical considerations also hinder prospective studies of the long-term consequences of trauma, especially those that involve life-span or multigenerational perspectives. It simply takes too long for humans to grow up (and old) for such prospective longitudinal studies to be feasible in most cases. As a result, retrospective reports provide the basis for much of our current knowledge base regarding long-term consequences of trauma.

This is not to say that retrospective data are without legitimacy or value in scientific inquiry. To the contrary, such data have clearly informed major areas of knowledge in traumatology and many other fields. Sophisticated epidemiological designs and analyses are currently at least on a par with most prospective approaches; there is nothing inherently nonscientific about such retrospective methodology. However, retrospective data of any and all forms are not sufficient in and of themselves to provide unambiguous scientific proof of causality, and that represents an absolute limitation.

In many areas of inquiry in traumatology, retrospective data are often rich in detail, objective in nature, and certifiably accurate (e.g., medical or archival records). Such retrospective data can be of great utility in understanding specific trauma-related phenomena. In

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contrast, for investigations focusing on the psychobiological correlates and consequences of trauma, reliance on retrospective approaches poses real problems. The biggest problem is that relevant retrospective psychobiological data rarely exist. The very kinds of measures typically used to document the psychobiological effects of stress and/or trauma (e.g., stress hormone levels, central neurotransmitter metabolite concentrations, or various measures of immunological functioning) are unlikely to be found in typical medical records, let alone in any sort of community or state archives.

Quantitative indices of these psychobiological measures are even less likely to be found in the memories of the vast majority of individuals who have experienced traumatic events or episodes. The human memory system is arguably one of the wonders of nature, and the capacity to recall specifics of circumstances, impressions, and emotions associated with trauma has provided the raw data for an expanding area of legitimate, indeed exciting, scientific inquiry and clinical application. However, experiences must be encoded as well as accessed for memory to be operative, and humans rarely, if ever, routinely monitor most of their psychobiological functioning in an objectively quantifiable fashion, let alone encode such information into memory. Of course, virtually all of us are aware of at least some of our visceral psychobiological experiences, especially during and following periods of stress (e.g., the experience of a "pounding" heart or the flushing of the face), and such memories are often intense and exceedingly long-lasting. However, it is difficult, if not impossible, to quantify such psychobiological memories in a scientifically useful fashion, especially when the memories go back many years and/or across generations.

Given the problems inherent in carrying out prospective longitudinal studies of long-term psychobiological consequences of trauma and the relative absence of relevant and scientifically useful retrospective data in humans, it should not be surprising that much of what we currently know in this area comes from research with animals. Prospective longitudinal experiments are the rule rather than the exception in animal studies of the psychobiology of stress. Current legal guidelines and ethical standards permit experimental designs with animals that involved preplanned exposure to stressful circumstances of systematically varied type, intensity, and duration, as well as the opportunity for rigorous and long-term follow-up. In these designs, variables deemed extraneous can be explicitly controlled for, in marked contrast to the "experiments of nature" that characterize much of human trauma research. Animal researchers are usually able to collect a much wider range of psychobiological measures in a more rigorous and direct fashion over more extended periods (including periods prior to exposure to trauma) than is typically feasible in human studies. Finally, and perhaps most relevant for this volume, the vast majority of animal species grow up much more rapidly and have considerably shorter life spans and generational turnovers than do humans. Thus, prospective experiments investigating long-term and intergenerational psychobiological consequences of stress in animals are clearly feasible and often practical, whereas comparable human research remains largely hypothetical.

Of course, findings from animal studies can be useful in furthering our understanding of the effects of trauma on humans only to the extent that there is generalizability between the human and animal phenomena under study (Harlow, Suomi, & Gluck, 1972). Such generalizations are not always possible. For example, given that humans have unique linguistic abilities in both the communicative and the mental imagery realms, it seems exceedingly unlikely that any animal model could be developed that would faithfully represent much of either realm. On the other hand, there are many aspects of psychobiological functioning in humans that are shared essentially in toto with many other animal species, homologous even down to the molecular level of gene functioning (Suomi & Immelmann, 1983). It is in these specific areas that

animal models of psychobiological response to trauma are most likely to provide useful insights regarding possible cross-generational effects of trauma in humans.

BASIC PATTERNS OF PSYCHOBIOLOGICAL RESPONSE TO STRESS IN ANIMALS

Research on the effect of early experiences and, in particular, the influences of exposure to "trauma" early in ontogeny has been ongoing for at least four decades. Clearly, we have accumulated a greater understanding of the consequences of these experiences and some of the mechanisms underlying the variety of persistent changes that have been observed. For many reasons, the laboratory rodent has been the animal most extensively investigated. The laboratory rodent has a relatively short life span; thus, the long-term effects of neonatal trauma can easily be studied. The laboratory rodent breeds well in captivity; therefore, experimental subjects are readily available. Finally, it is possible to examine the neural correlates of the now well-documented changes in both behavior and physiological function that are altered by exposure to trauma neonatally. Examining changes in brain mechanisms that follow early experiences is difficult in primates and almost impossible in humans. What has become progressively clearer is that the effects of early experience with traumatic events depend upon a number of critical variables. Among these are (1) the age of onset of the experience, (2) the type of traumatic event, and (3) the intensity and duration of the experience. There are undoubtedly other variables that can modify outcomes. For example, there is increasing evidence that the genetic background of the organism can modify the outcome of exposure to early trauma.

Given the fact that this problem has been studied for many years, we do not attempt a comprehensive review of all the outcome measures that have been investigated. Rather, we focus on aspects of behavior associated with emotionality and on one of the major physiological systems associated with the response to stress, namely, the hypothalamic–pituitary–adrenal (HPA) axis. One of the major endocrine responses following exposure to stress is the increased secretion of specific hormones from the adrenal (glucocorticoids). In the rodent, the primary glucocorticoid is corticosterone (CORT), whereas in the primate and human, cortisol is synthesized and secreted by the adrenal. Release of the adrenal hormones is a result of a "neuroendocrine cascade" that involves specific release of a hormone, corticotropin-releasing hormone (CRH), from the brain, which, in turn, regulates the output of adrenocorticotropic hormone (ACTH) from the pituitary that is required to activate the adrenal to increase the secretion of glucocorticoids. Although much of the research on the effects of early experience on the endocrine response to stress has measured either CORT or cortisol as the dependent variable, it is always assumed that an increase in the levels of adrenal hormones reflects the response of the brain to stress.

In the original studies (Levine, Chevalier, & Korchin, 1956), infant rats were subjected to a brief daily exposure to a painful stimulus and were compared to another group of rats that were removed daily from their mothers for the same period of time but not subjected to the painful experience. An additional group received no experience and remained with the mother without any disturbance. As adults, these animals were tested in a learning paradigm that involved learning to avoid a noxious stimulus (conditioned avoidance learning). Surprisingly, the rats that either experienced the painful event or were removed from the mothers neonatally showed the appropriate adaptive response and learned to avoid the noxious stimuli very rapidly. In contrast, those animals who presumably had the best of all possible worlds failed

to learn to avoid and showed excessive emotional reactivity when exposed to aversive stimuli as adults. Subsequent research (Levine, 1960), using a variety of behavioral probes designed to examine emotionality, demonstrated that these early experiences, traditionally called early handling (EH), resulted in an adult that was significantly less emotionally aroused. It is somewhat unfortunate that these procedures have been termed *early handling,* since this implies some form of positive physical contact, which is not at all descriptive of the actual experimental treatments and implies that these procedures involved stroking and gentling. The critical manipulation in these studies actually turned out to be the removal of the infant from the mother for brief periods of time. The additional exposure to painful stimuli did not seem to override the importance of the brief disruption of mother–infant interactions.

An extensive series of studies conducted for more than three decades (cf. Meany *et al.* [1993] for the most recent review) have examined the response of the HPA axis in EH rats. The results revealed changes in the endocrine responses to stress that were consistent with the reduction in emotional behavior. Thus, CORT secretion in response to a number of different stressors was reduced in EH animals when compared to their nontreated counterparts. Furthermore, following the initial increase in CORT, the EH rats showed a more rapid return to basal levels, indicating a more efficient negative feedback. Of particular importance is that these changes in the HPA axis of EH animals have been found to be a function of permanent structural and functional alterations of the brain mechanisms that are part of the regulation of the HPA axis (Meany *et al.,* 1993). The crucial message is that there is a great deal of plasticity in developing nervous systems, which can be affected by early experiences and appear to permanently alter later neuroendocrine activity. To what extent other brain structures are also affected remains to be determined.

We have discussed the EH model at length since it has received a great deal of attention. This, however, is only one of several experimental manipulations that have been observed to have long-term effects. Other neonatal experiences result in outcomes that are paradoxical to those seen with EH. Recently, two different methods of maternal separation in rats have been shown to result in an hyperactive HPA axis, as well as increased emotionality. Whereas the EH paradigm involved removing the rat pup from the mother for periods of time between 5 and 15 minutes per day, the critical period for these treatments is between 3 and 14 days of age. If the length of separation is increased to 3 hours daily during this period, the adult rat now exhibits a significantly greater CORT response than the pups that were separated for 15 minutes daily (Meaney *et al.,* 1993). Further prolonged daily separated animals show a greater increase in corticotropin releasing factor (CRF mRNA) when compared to nonhandled (NH) and handled subjects (Plotsky & Meaney, 1993). These results are very recent; thus, behavioral changes have not been explored extensively. However, the evidence does suggest that there are changes in the central nervous system (CNS) that are consistent with the hyperactivity of the HPA axis in these animals.

Recently, a different type of maternal separation has been shown to also produce persistent changes in HPA function. In these studies, pups are separated from the mother for 24 hours at different ages. If pups are separated early in development (days 3–4) and then reunited with the mother, they exhibit a pattern of HPA hyperactivity when tested as juveniles. In contrast, if the separation occurs between days 11–12, these animals hyposecrete ACTH and CORT (Van Oers & Levine, 1998, unpublished observations). There is also evidence that deprivation between days 3–4 results in long-term functional and structural changes in the brains of the early deprived rats (Levine, 1994). Thus far, there have been no behavioral studies conducted using this model of maternal deprivation. Thus, it appears that all forms of early experiences that we presume to be traumatic result in permanent alterations in the CNS regulation

of the neuroendocrine responses to stress in these rodents. There is no evidence that these changes are reversible.

There is also evidence for intergenerational effects of EH. In an extensive series of studies, Denenberg and colleagues (Denenberg, 1970; Deneberg & Whimby, 1963) examined the influence of the mothers' postnatal experience on their offspring. The primary measures used were body weight and open field behavior (a presumed measure of emotionality). Although there was clear evidence of intergenerational effects, they were complex and depended not only on the maternal postnatal experience but also interacted with the rearing conditions (cf. Denenberg, 1970).

Most of the research on intergenerational effects has studied behavior as the outcome variable. Levine (1967) reported that weanling rats of EH mothers showed a reduced CORT response to novelty when compared to weanlings of nonhandled mothers. Handling the pups of previously handled mothers did not affect the CORT response, whereas EH of offspring of NH mothers once reduced the CORT response to the same level that was seen in the pups of EH mothers.

PRIMATE STUDIES OF PSYCHOBIOLOGICAL RESPONSIVENESS TO STRESS

The knowledge base regarding the psychobiological consequences of stress in primates is considerably less extensive than it is in rodents, both in terms of breadth and depth. However, those findings that have emerged from stress research with primates have been remarkably congruent with what is known for rodents, at least where straightforward comparisons have been feasible. In this respect, there have been relatively few surprises to date.

On the other hand, the rich behavioral and emotional repertoires and cognitive capabilities of monkeys and apes provide opportunities for modeling aspects of human stress response patterns that are simply not feasible with rodents. Significantly, it is possible with primates to investigate patterns of covariance between specific behavioral and emotional responses and concomitant psychobiological reactions during and following stressful periods. Many of these behavioral and emotional response patterns seem remarkably congruent with those seen in humans. The correspondence between human and nonhuman primates is perhaps even greater for most physiological systems, which is not surprising in light of the extensive genetic overlap among monkeys, apes, and humans (e.g., humans share approximately 94% of their genes with rhesus monkeys and over 98% with chimpanzees; cf. Lovejoy, 1981). These behavioral and emotional patterns provide a face validity for primate models that simply cannot be matched by those with rodents.

A case in point can be seen in studies of psychobiological response to social separation in primates. Short-term separation from family and/or friends is essentially as obsequious a phenomenon for most wild-living monkeys and apes as it has been for humans throughout recorded history. Such separations can be stressful or routine (or both), depending on the circumstances and the individuals involved. For example, virtually every rhesus monkey infant born into a wild troop experiences repeated short-term separations from its mother when she consorts with different adult males during the troop's annual breeding season (Berman, Rasmussen, & Suomi, 1994). The universal reactions of these infants to such involuntary maternal separation is one of significant behavioral disruption and physiological arousal, much as Bowlby has described for human infants experiencing involuntary maternal separation (Bowlby, 1960, 1973). Although most of these rhesus monkeys youngsters soon get over their

initial period of protest and subsequently seek out the company of other troop members during their mothers' absence, about 20% instead become lethargic and withdraw from all social contact (Suomi, 1991), reminiscent of Bowlby's description of separation-induced "despair" in some human infants and children.

Experimental studies of social separation in captive nonhuman primates have been carried out under a variety of laboratory conditions for over 30 years. These studies of mother–infant separation have consistently found that, as in the wild, captive-living infant monkeys and apes initially respond to separation with behavioral agitation, characterized by dramatic increases in locomotor activity and "coo" vocalizations, and a cessation of exploratory and play behaviors. Maternal separation also typically activates the HPA axis, as indexed by sharp increases in levels of plasma cortisol and ACTH, and increased turnover of the noreadrenergic system, as indexed by decreased cerebral spinal fluid levels of norepinephrine (NE) and increased levels of the NE metabolite 3-methoxy-4-hydroxyphenylglycol (MHPG), as well as elevated heart rate, indicating sympathetic arousal.

Although most infant monkeys in these laboratory studies begin to return to preseparation levels of behavioral and physiological functioning within a few hours, some individuals continue to display profound behavioral and physiological reactions for several days, if not longer, as is the case for some individuals in the wild. Virtually all of these young separated monkeys essentially show spontaneous recovery when reunited with their mothers, although physical contact with mother remains elevated, and social play reduced, relative to preseparation levels, for days or even weeks following reunion (e.g., Seay, Hansen, & Harlow, 1962).

Many investigators have noted the parallels between these reactions to separation and Bowlby's characterization of prototypical separation reactions in human infants and young children. Parametric studies have demonstrated that numerous factors can influence various features of reaction to maternal separation in nonhuman primates, including species, age at separation, nature of the attachment relationship with mother prior to separation, duration of separation, nature of the separation (and reunion) environment, and availability of substitute caretakers during the time away from the mother (e.g., Mineka & Suomi, 1978). What is clear, however, is that forced separation from the mother is almost always a traumatic experience for primate infants, at least initially, and it almost always results in profound behavioral and emotional disruption, along with dramatic activation of several physiological systems. It is also clear that there are marked individual differences within primate species in the relative severity and duration of separation-induced distress.

An increasing body of data has documented long-term consequences for at least some individuals who have experienced traumatic maternal separation early in life. These individuals tend to react to subsequent stressful situations with exaggerated behavioral and physiological reactions (e.g., greater and more prolonged elevation of cortisol levels) relative to individuals who did not experience the early trauma or those who did but whose reactions at the time were mild. Other forms of early trauma or stress (e.g., exposure to extreme fear-provoking stimuli) appear to have generally parallel psychobiological consequences (cf. Suomi, 1995).

In some cases, the long-term effects of early stress or trauma are expressed in domains seemingly far removed from the initial experience. For example, squirrel monkey males who experienced brief maternal separations in their first few months of life undergo puberty many months earlier on average than nonseparated cagemates (Levine, Weiner, & Coe, 1993). Rhesus monkey adolescents who experienced maternal deprivation during their first 6 months of life tend to consume significantly more alcohol in a "happy hour"–like situation than monkeys reared by their mothers during that initial 6 months (Higley, Hasert, Suomi, & Linnoila, 1991). Rhesus monkey females who were neglected or abused by their own mothers during infancy

have a much higher incidence of neglecting and/or abusing their own firstborn offspring than primiparous females who received normal caregiving from their own mothers during infancy (Ruppenthal, Arling, Harlow, Sackett, & Suomi, 1976; Seay, Alexander, & Harlow, 1964). Adolescent male rhesus monkeys who likewise experienced inadequate parenting as infants are much more likely to exhibit explosive bouts of impulsive aggression and have lower rates of central serotonin turnover than their normally reared agemates (Higley, Linnoila, & Suomi, 1994). These diverse examples clearly demonstrate that early experience with trauma can have significant long-term (and sometimes lifelong) consequences for both behavioral and psychobiological functioning.

What about the possibility of cross-generational transmission of some effects of early trauma in primates? Are there ways in which trauma experienced in one generation of primates can be "transmitted"—in the form of behavioral and/or psychobiological dysfunction—to the next generation? With humans, the answer seems to be relatively clear, as evidenced by numerous chapters in this volume. Humans, of course, can use oral and written language to recall and retell past experiences, including pleasant as well as terrifying ones, to members of subsequent generations. Nonhuman primates have neither oral nor written language (as we know it). Are there other ways by which traumatic experiences of one generation of monkeys or apes could have specific and significant behavioral and psychobiological consequences for subsequent generations? The data to date suggest at least three modes for such cross-generational transmission in primates. The first mode is via observational learning; the second encompasses maternal treatment of offspring, and the third involves prenatal mechanisms. Each is considered in turn.

Cross-Generational Transmission via Observational Learning

One potential way for the effects of trauma experienced by members of one generation to be passed on to the next generation is via observational learning. Among humans, observational learning provides a highly efficient means of transmitting certain types of information between individuals or groups. Observational learning and related forms of knowledge acquisition (e.g., social facilitation, imitation, and direct modeling) do not require language to be effective as "teaching devices" (although appropriate use of language usually facilitates the process) and hence can be used with individuals who are not fluent in the language of the "teacher" or "model," such as preverbal infants and toddlers or members of a different culture.

The degree to which animals are capable of learning via observation has been the subject of considerable research and even more debate over the years. At issue have been arguments regarding the operational definition of observational learning, sufficient and necessary conditions for its demonstration, the nature and scope of information that can be effectively transmitted, and differences between and within species in its efficacy. Although a discussion of these issues is well beyond the scope of this chapter, it is worth noting that (1) simian primates (i.e., monkeys, apes, and humans) are usually considered to have the most advanced observational learning capabilities among all animals (e.g., Seyfarth & Cheney, 1990), and (2) some types of information are much more readily and effectively transmitted via observational means than are others. For example, capuchin monkeys (*Cebus apella*), a species of primates with unusual tool-using capabilities, are quite capable of using observational learning techniques to discover the location of preferred food types but are surprisingly unable to learn how to use a particular tool to access such food by watching the performance of a skilled model; instead, they must learn individually on a trial-and-error basis (Visalberghi & Fragaszy, 1990).

In contrast, chimpanzee juveniles apparently acquire considerable tool-using proficiency simply by watching their mothers in action.

The potential for observational learning to provide a mechanism for cross-generational transmission of the effects of trauma is nicely illustrated through some elegant experiments by Susan Mineka and her colleagues regarding the acquisition of snake "phobias" by rhesus monkeys born and raised in captivity (Mineka, Davidson, Cooke, & Keir, 1984). The original impetus for these studies came from the long-standing observation by researchers working with captive primates that whereas virtually every wild-caught subject brought into laboratory settings spontaneously exhibited an intense fear of snakes, few if any laboratory-born subjects ever displayed any evidence of fearful or avoidant behavior, or any indications of emotional arousal, when exposed to live or artificial snakes. Such observations obviously challenged previous assumptions that primates have an "innate" fear of snake-like stimuli and additionally raised the question as to how wild-born monkeys and apes actually acquired their "universal" snake phobia.

Mineka hypothesized that observational learning might provide the vehicle by which fear of snakes could be acquired by primates growing up in habitats that contained snakes—that youngsters might learn such fears by observing the reactions of their mothers and others in their social group to the presence of snakes and other potential predators. In an exquisitely controlled series of studies, she was able to demonstrate clearly and convincingly that juvenile monkeys previously indifferent to live snakes quickly acquired an intense fear of snake stimuli when they observed another monkey (especially their mother) exhibit a fearful reaction to their presence. The juveniles' acquired fearful responses included visceral as well as behavioral components. Most importantly, the emergence of such psychobiological reactions in the presence of a fearful model was immediate (always within a single exposure) and essentially permanent (virtually impossible to extinguish) (Mineka *et al.,* 1984).

It is easy to see how such a mechanism for acquiring fear of potentially lethal stimuli would be adaptive in the wild. This very specific form of observational learning is quickly and permanently acquired. Furthermore, it occurs without requiring the juvenile to have any actual physical contact with snakes (e.g., a bite or constriction) in order to develop an intense aversion to them or to similar stimuli. Indeed, one can envision how generation after generation of rhesus monkeys could readily sustain such an intense aversion without any individual actually getting killed or injured by snakes throughout this process.

This example serves as an illustration of how the consequences of traumatic experience for certain individuals might be passed on to progeny via observational learning mechanisms. To the extent that such individuals continued to exhibit emotionally intense reactions in the face of stimuli associated with the original trauma, the likelihood that their offspring would acquire a parallel behavioral and psychobiological response set to the same or similar stimuli would clearly be enhanced if such observational learning mechanisms were indeed operative. Unfortunately, to date, there have been precious few studies directly examining whether observational learning of specific fears associated with previous trauma actually occurs among wild-living primates, although the data that do exist appear promising. For example, Seyfarth, Cheney, and Marler (1980) demonstrated that young vervet monkeys rapidly learn to respond to different alarm calls by older group members with predator-specific escape behaviors (e.g., seeking cover in response to a "raptor" call vs. climbing a tree in response to a "snake" call). Such learning undoubtedly occurs via observation of the specific escape behaviors (and associated emotional arousal) shown by adults, especially kin, and apparently does not require observation of actual predation to be effective.

Thus, there exist at least some data from both laboratory and field studies suggesting that monkeys can indeed pass specific fears on to the next generation. To be sure, a great deal remains to be learned about this phenomenon, including sufficient and necessary conditions for its occurence, the magnitude and duration of physiological concomitants, and its specificity and generalizability to other stimuli and situations. Nevertheless, the evidence to date clearly establishes that observational learning can provide one pathway for intergenerational transmission of the consequences of trauma, a pathway that does not require either spoken or written language to be effective.

If monkeys are indeed capable of developing aversive psychobiological response patterns to stimuli toward which they observe their parents responding with fear and avoidance, it would seem likely that humans have at least as powerful observational learning capabilities. Such capabilities need not require language for effective cross-generational transmission; indeed, they might occur in spite of language. Perhaps the most striking aspect of the observational learning of specific fears in monkeys is its permanence: Mineka and her colleagues expressed some surprise as to how difficult it was to extinguish such emotional response patterns once acquired. Other investigators (e.g., LeDoux and his colleagues) have demonstrated a limbic system–based emotional memory system that operates essentially independent of any cortical input (such as linguistic information; cf. LeDoux, 1986). It may well be that emotional responses acquired via observational learning in humans are similarly highly resistant to extinction. If such responses are not dependent on language for either their acquisition or their long-term maintenance, then it may also be the case that language-based interventions or therapies might be relatively ineffective in extinguishing such acquired fears.

Cross-Generational Transmission via Effects on Maternal Behavior

A second way in which the consequences of traumatic stress can be transmitted to the next generation is through effects on maternal behavior. This can occur in primates when trauma and its sequelae compromise an individual's capabilities as a parent. Inadequate parenting, in turn, can affect an offspring's well-being and adaptive capabilities, both in the short and long term. Such effects include physiological functioning as well as behavioral competence.

Unlike the case for observational learning of trauma consequences, the database in primates documenting long-term effects of inadequate parenting on progeny is quite impressive. Over 30 years ago, Harlow and his colleagues demonstrated convincingly that rhesus monkey "motherless mothers," that is, females who were raised in isolation, with surrogates or with peers—but not with their own mothers—were at exceedingly high risk for showing major deficits in their care of firstborn offspring, including high rates of neglect and abuse (Seay *et al.,* 1964). Subsequent research in Harlow's laboratory demonstrated that (1) the nature and duration of the early deprivation was predictive of subsequent deficits in maternal behavior; (2) there were several ways in which the risk for "motherless mothers" exhibiting inadequate maternal behavior could be significantly reduced; these "interventions" were most effective when they were introduced during these females' juvenile and adolescent years; and (3) even in the absence of such intervention (and especially in its presence), the risk for inadequate maternal behavior by motherless mothers toward their second-born and subsequent offspring was greatly reduced (Ruppenthal *et al.,* 1976). These findings suggested that even the most severe early deprivations need not inevitably result in aberrant maternal behavior; instead, effective preventive interventions could be developed in most cases.

Other primate researchers have examined the effects on maternal behavior of less severe and long-lasting environmental stressors than total maternal deprivation initiated at birth. For example, Rosenblum and his colleagues demonstrated that changes in food accessibility and availability for mothers had clear-cut "carryover" effects to their treatment of offspring, over and above any effects on their interactions with others in their social group (Andrews & Rosenblum, 1994). Other researchers have found predictable relationships between changes in a mother's position in her group's dominance hierarchy and disruption of her behavior with her offspring. These effects, seen in both laboratory and field studies, are most pronounced when mothers exhibit dramatic drops in status, but they also can occur in the face of general instability of dominance relationships (e.g., that result from changes in overall group composition).

What is the nature and extent of cross-generational psychobiological consequences of stress or trauma experienced by a mother? One general consequence that seems to transcend the specific types of trauma experienced by the mother involves the compromising of a secure attachment relationship with her infant. Offspring of stressed-out monkey mothers are much less likely to develop and maintain secure attachment relationships than those whose mothers live in stable, benign social settings. In turn, infants with insecure attachments are less likely to use their mothers as a secure base to explore their physical and social environment throughout their first year of life (Suomi, 1995). One long-term consequence emerges in play patterns with peers. Monkey juveniles with insecure maternal attachments typically play less often and are less sophisticated in their interactions with securely attached peers. When they reach adolescence, monkeys who grew up with insecure early attachments are at risk to develop impulsive, socially incompetent, and often inappropriately aggressive patterns of response to seemingly neutral social stimuli. They usually end up at or near the bottom of their peer group's dominance hierarchy (Higley & Suomi, 1996).

Perhaps the most dramatic long-term consequence for offspring of mothers exposed to stress is their own subsequent psychobiological responses to novel and/or stressful stimuli or circumstances. In a word, offspring of stressed-out mothers tend to overreact both behaviorally and physiologically to their own encounters with stress. For example, infants and juvenile monkeys with anxious attachments react to brief separation not only with more extreme and more prolonged behavioral disruption, but also with higher and longer lasting elevations of plasma cortisol, greater central NE turnover, and a greater degree of immune system suppression than their securely attached agemates (Suomi, 1995). Other risks associated with disrupted early maternal experiences may be more subtle, sometimes masked for years. For example, Rosenblum and his colleagues found that monkeys whose mothers experienced variable food availability when they were infants were in turn much more behaviorally and physiologically reactive (e.g., greater HPA activation and monoamine turnover) when exposed to a pharmacological challenge as adolescents (Rosenblum *et al.,* 1994).

One of the most intriguing long-term consequences of disruption of an infant's early attachment relationship with its caregiver is the effect on its own capabilities as a parent when it becomes an adult. An increasing body of data collected in both laboratory and field environments has documented remarkable specificity of cross-generational consequences of deficits in parenting behavior: Female monkey infants who experienced certain abnormalities in the care they received from their own mothers (or substitute caregivers) tend to exhibit virtually identical or highly similar abnormalities toward their own offspring when they become parents themselves. Such cross-generational specificity is especially clear-cut in terms of patterns of ventral–ventral contact (cradling) between monkey mothers and infants.

Numerous studies have shown that ventral–ventral contact is crucial for developing and sustaining normal attachment relationships in Old World monkeys and apes. Typically, infants

in these species spend virtually all of their initial days and weeks of life in ventral–ventral contact with their mother, and they gradually reduce the frequency and duration of such contact in the ensuing weeks and months. Indeed, some investigators have viewed ventral–ventral contact as a rough index of, or proxy for, maternal "warmth." At any rate, several studies have reported a highly predictive relationship between the precise amount and developmental pattern of ventral–ventral contact a female receives from her mother as an infant and the amount and patterning of contact she directs toward offspring when she becomes a mother herself. For example, females who experienced greater than normal amounts of ventral–ventral contact as infants tend to contact their own infants excessively, whereas females who were relatively contact-deprived as infants tend to be contact-shy with their own offspring (Fairbanks, 1989). These predictive relationships are especially strong when the early contact experience is most aberrant, as in the case of peer- or surrogate-reared females (Champoux, Byrne, Delizio, & Suomi, 1992).

Recent theoretical and empirical work on long-term consequences of differential early attachment relationships in humans has also focused on possible cross-generational continuities in attachment style, including specific parenting behaviors. The results to date have generally been highly congruent with the primate data described earlier. For example, mothers who experienced secure attachments as infants and young children tend to develop secure attachments with their own infants, whereas those who experienced avoidant, ambivalent, or disorganized attachment with their mothers tend to promote avoidant, ambivalent, and disorganized-like attachments, respectively, as mothers themselves. Current attachment theorizing attributes these infancy-to-parenthood continuities in attachment type to internalized "working models" initially based on early memories and periodically transformed by more recent experiences (e.g., those accrued during adolescence). Such "working models" are generally thought to involve complex cognitive imagery and mental representational capabilities not usually ascribed to monkeys or even to apes. However, the primate data clearly suggest that such "advanced" human cognitive capabilities need not be prerequisites for cross-generational transmission of specific patterns of parental behavior. Indeed, they raise the distinct possibility that more "primitive" emotional memory processes might also be involved in the parallel human phenomenon (cf. Suomi, 1995).

Cross-Generational Transmission via Prenatal Mechanisms

A third way in which the psychobiological consequences of trauma might be transmitted across generations of primates involves prenatal mechanisms. According to this view, normal developmental processes transpiring during gestation might be comprised as a result of stress experienced by the mother-to-be during her pregnancy. Such effects could occur either by relatively direct means, for example, via transmission of maternal cortisol across the placental barrier resulting in fetal exposure to high and/or chronic glucocorticoid elevation, or through more indirect mechanisms, for example, changes in fetal nutrition resulting from stress-induced changes in maternal eating behavior, or fetal reactions to stress-induced physical and/or physiological changes in the intrauterine environment.

Recent research by Schneider and her colleagues strongly suggests that such prenatal mechanisms are more than merely hypothetical in nature (Schneider, 1992). These researchers subjected pregnant rhesus monkeys to brief (10 minutes) periods of exposure to a mild stressor 5 days per week for 8 weeks during pregnancy (normal gestation for rhesus monkeys is 21–22 weeks). The daily stressor involved removing each pregnant female from her home cage, placing her in a smaller cage in a darkened room, and randomly administering three 10-second noise

bursts from a 1300 Hz horn at 115 db over a 10-minute period, then returning the pregnant female to her home cage. This procedure routinely produced short-term behavioral agitation and brief cortisol elevation in the pregnant females but no obvious effects on their home-cage behavior or food consumption. The offspring of these females were then compared with offspring of females who had not been exposed to the noise stressor, but whose living arrangements and diets were otherwise identical during pregnancy. Both prenatally stressed and control infants were nursery-reared from birth and socialized with peers in order to eliminate potential variance resulting from differential postnatal treatment by their mothers, and their subsequent behavioral, cognitive, and physiological development was systematically monitored as they grew up in comparable physical and social environments.

Schneider and her colleagues found significant differences between prenatally stressed and control infants on numerous measures, both behavioral and physiological, throughout development. In general, the prenatal exposure to stress had the effect of making these monkeys more reactive to mildly stressful events and situations throughout development. For example, when these monkeys were placed in a novel playroom filled with toys and unfamiliar peers, they were less likely to explore the playroom, manipulate the toys, or initiate interactions with peers than were the offspring of control mothers who had not experienced the stress during pregnancy. Prenatally stressed monkeys also exhibited greater and more prolonged elevation of plasma cortisol and ACTH during their playroom sessions than did their agemates who were not prenatally stressed. Similar behavioral and physiological differences emerged when these monkeys were briefly separated from their respective social groups as juveniles and adolescents. Thus, 10-minute daily exposure to unpredictable noise over an 8-week period during pregnancy was sufficient to produce long-term behavioral and physiological effects in the offspring under subsequent conditions of environmental novelty and challenge (Clarke & Schneider, in press).

Schneider and her colleagues also studied another group of rhesus monkey infants whose mothers had experienced a physiological stressor on a daily basis over the same part of pregnancy as described earlier. In this case, the stressor involved exogenous adminstration of ACTH, which had the effect of briefly raising these females' plasma cortisol levels even though they remained in their home cases during this procedure. The postnatal effects on their offspring were remarkably similar to those resulting from prenatal exposure to the unpredictable noise. These youngsters likewise exhibited increased stress reactivity, as indexed by behavioral disruption and elevated plasma cortisol and ACTH, when faced with novel or challenging situations throughout development (Schneider, 1992).

These findings suggest that different types of prenatal stress that result in maternal glucocorticoid elevation have common consequences, most notably the tendency to "overreact" both behaviorally and physiologically to postnatal environmental challenges. In this respect, prenatally stressed monkeys clearly resemble individuals who experienced trauma in their early postnatal life, either directly or indirectly, as a result of their mothers' previous experience with trauma. The common feature is increased reactivity to subsequent environmental stressors. Such increased reactivity clearly does not require human linguistic or other advanced cognitive capabilities to become a prominent part of an individual's psychobiological response repertoire.

INTERACTIONS AND IMPLICATIONS

The research described in the preceding sections provides clear-cut evidence, obtained from prospective longitudinal experiments, demonstrating that nonhuman primates are indeed capable of transmitting long-term psychobiological effects of trauma across generations via

at least three different mechanisms. In each case, the long-term effects include physiological as well as behavioral features or propensities, and in two of the three cases, the mechanisms of transmission have been documented in natural social groups of primates living in the wild as well as those studied in laboratory settings. None of the three mechanisms—observational, maternal, and prenatal—require language capabilities on the part of either the initiating or receiving generation for the transmission to take place.

These three mechanisms differ considerably with respect to the potential specificity and timing of the cross-generational transmission. Observational learning, in theory, is quite specific with respect to the type of stimulus that generates the cross-generational psychobiological effects; on the other hand, it can transpire at any time and to anyone in an individual's social sphere. Psychobiological effects of trauma transmitted via maternal behavior patterns involve a much wider range of stimuli and situations that potentially can affect how a mother acts, but such effects are typically limited to offspring and, then, largely to their period of maternal dependence. Effects of trauma that are transmitted via prenatal mechanisms can theoretically come from anything that raises a pregnant female's cortisol levels, but those effects are obviously limited to the period of pregnancy and affect only the fetus. Despite these differences, it can be argued that each mechanism can produce remarkably similar consequences for those in the next generation—increased behavioral and physiological reactivity in the face of environmental novelty and/or challenge.

Although these three pathways for cross-generational transmission can be distinguished from one another on a number of dimensions, they clearly need not be mutually exclusive. Rather, it is easy to envision how they might interact within a given individual and/or have cumulative effects for that individual. Consider, for example, what might transpire if a rhesus monkey female in the middle of her second pregnancy lived through a series of violent thunderstorms that uprooted many trees and bushes, killing some members of her social group, including relatives, in the process. One immediate consequence would be acute and dramatic elevation of the female's cortisol levels during the storms, producing effects on the fetus that would be reflected postnatally in increased psychobiological reactivity to subsequent stressful situations.

In addition, the habitat destruction and social disruption created by the series of storms might well have long-term consequences for the young mother after her infant was born. Specifically, her food supply might be more variable and less predictable, the habitat destruction might make her and the rest of her social group more vulnerable to predation, and her position in the group's dominance hierarchy might plummet as a result of loss of social support her now-deceased relatives might have provided. Each of these factors could compromise the care of her new infant, increasing its psychobiological reactivity in the face of subsequent stressors over and above any bias resulting from its prenatal stress experiences. In contrast, the consequences of the same factors for the female's firstborn offspring would likely be considerably less than those for its younger sibling, because it had not received comparable prenatal stress and, being older, would not have been as dependent on the mother during the time her maternal capabilities were being influenced by long-term sequelae of the storms.

Finally, the infant who experienced the storm prenatally might additionally be especially sensitive to the effects of subsequent violent storms, particularly if it witnessed storm-related fear responses by its mother to flashes of lightning or claps of thunder. To be sure, its older sibling (and others in the social group) might also witness the mother's reactions and indeed might have some of their own. However, it seems likely that the infant's psychobiological reaction would be even more extreme because (1) the mother would have greater salience as a model, and (2) the infant's threshold for responding would be lower and the magnitude and

duration of response greater as a long-term consequence of the previous prenatal and maternal experiences. Such exaggerated responses to tropical storms might well be expected to continue throughout the infant's lifetime—and possibly be transmitted to any offspring she herself might have in the future.

This admittedly hypothetical example illustrates one way in which different modes of cross-generational transmission of psychobiological effects of trauma can interact and/or have cumulative long-term consequences for certain individuals. While carefully controlled prospective laboratory experiments can clearly identify, differentiate, and even isolate specific modes, nature is usually much messier in its "natural experiments." This is doubtlessly as true for humans as it is for rhesus monkeys and other primates.

What implications do these studies of the cross-generational psychobiological consequences of trauma in nonhuman primates have for consideration of the human case? To be sure, monkeys are not furry little humans with tails but rather members of other species, albeit with considerable genetic overlap and some commonality in evolutionary history. Furthermore, as previously mentioned, monkeys and apes lack the linguistic capabilities that make our history, our cultures, and our experiences—both good and bad—uniquely human. Nevertheless, it seems hard to believe that the same mechanisms that permit cross-generational transmission of psychobiological effects of trauma in nonhuman primate species would not be operative in humans as well. Such mechanisms require no special cultural traditions, special instructions, or advanced cognitive or linguistic capabilities to transpire—and they have undoubtedly transpired generation after generation for millions of years in our closest primate relatives. On the other hand, our unique human capabilities do enable us to study these phenomena, to try to comprehend how and why they occur, and to consider how they might contribute to cross-generational effects of trauma on ourselves and our progeny. We will fail to engage such capabilities at our own peril.

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