Primary maternal preoccupation revisited: circuits, genes, and the crucial role of early life experience

James F. Leckman, Linda C. Mayes, and Donald J. Cohen
Child Study Center, Yale University School of Medicine, New Haven, Connecticut, USA

Abstract
Parental caregiving includes a set of highly conserved set of behaviors and mental states that may reflect both an individual's genetic endowment and the early experience of being cared for as a child. This review first examines the mental and behavioral elements of early parental caregiving in humans. Second, we consider what is known of the neurobiological substrates of maternal behaviors in mammalian species including some limited human data. Third, we briefly review the evidence that specific genes encode proteins that are crucial for the development of the neural substrates that underlie specific features of maternal behavior. Fourth, we review the literature on the "programming" role of epigenetic factors in shaping subsequent maternal behavior. We conclude that there are critical developmental windows during which the genetically determined microcircuitry of key limbic-hypothalamic-midbrain structures are susceptible to early environmental influences and that these influences powerfully shape an individual's responsivity to psychosocial stressors and their resiliency or vulnerability to various forms of human psychopathology later in life.

Introduction
In 1956 Donald Winnicott, a pediatrician and psychoanalyst, drew attention to "primary maternal preoccupations." He described this state as "almost an illness" that a mother must experience and recover from in order to create and sustain an environment that can meet the physical and psychological needs of her infant. Winnicott speculated that this special state began towards the end of the pregnancy and continued through the first months of the infant's life. Although this concept has been incorporated into subsequent clinical formulations of disordered mother-infant interactions, it has received relatively little scientific attention especially in consideration of the normative developmental trajectory of parenting.4-10

This review focuses initially on recent efforts to characterize further in normative groups of adults - early parental preoccupations - and the care taking behaviors they engender. Next, we consider recent advances in our understanding of the genetic, epigenetic, and neurobiological substrates of maternal behavior in model mammalian species and their potential relevance for understanding risk and resiliency. For example, some of the studies reviewed suggest that aspects of maternal behavior are non-genomically transmitted from one generation to the next and that the nature of the maternal care received in infancy may "program" aspects of infant's response to stress later in life and have enduring consequences in their approach to the world.11,12 If similar mechanisms are at work in human populations, they may provide a basis for successful early intervention programs13,14 and may deepen our understanding why some individuals are more vulnerable, or conversely more resilient, to certain forms of psychopathology.15,16

Point-of-view and initial caveats
Before reviewing any specific findings, it may be useful to articulate our evolutionary point-of-view concerning developmental psychopathology. The human brain is a remarkable product of evolution. While the basic machinery of the vertebrate brain has been in place for more than 450 million years, the exploration of variations leads to the appearance of our species less than 100,000 years ago. In the struggle for life, certain traits have come to predominate. Elements in our mental and behavioral repertoire related to successful reproduction were certainly the focus of the greatest selective pressures. The selection of a mate, bearing of viable offspring, and the formation of parental commitments that will sustain an infant through a lengthy period of dependency are just a few of the crucial complex, interdependent processes needed for individual survival and hence, species viability. Although most of our biological and behavioral potentialities are likely called upon at one point or another in the service of these goals, there must be highly conserved brain-based systems that are specifically activated at developmentally appropriate moments to achieve and sustain these processes. We hypothesize that a thorough understanding of these "normal" processes will also lead to deeper insights into our vulnerability to develop a range of psychopathological outcomes.17

Despite the intuitive appeal of evolutionary explanations, it is also worth noting a few caveats. First, these explanations typically are population-based and fail to account for why a particular individual is affected. Any adequate account of disease pathogenesis requires that environmental events that impinge on CNS development be considered. Second, species and strain differences can be pronounced so that generalizations across species can be misleading. Finally, the empirical testing of specific evolutionary theories may prove to be difficult, if not impossible.

Early Parental Love
For the most part, empirical studies of the early parent-child relationship have been child centered. Most reports have focused on the...
development of attachment behaviors in the child and on the mo-
ment-to-moment observable, behavioral functioning of the parent-
infant dyad. These points of focus have revealed the highly special-
ized nature of parental verbal and non-verbal behaviors with very 
young infants, and the importance of early synchrony and reciprocity 
in parent-child interactions, and the critical impact of early experi-
ences on the child’s subsequent attachment behaviors toward the 
parent—and later in other intimate relationships.18-22 They have un-
derscored the potential negative impact of early parental deprivation 
and neglect on the development of socialization capacities and the 
importance of parental marital adjustment, self-esteem, and social 
supports for successful adaptation to parenting a newborn and in-
fant.23-26 However, relatively neglected in these lines of research have 
been the thoughts of the parents regarding their roles as parents and 
the place of the infant in their inner lives, and the relationship of these 
thoughts to their behaviors with the infant.

As noted above, Winnicott described an altered mental state that 
he termed “primary maternal preoccupation” that characterizes the 
first weeks of a mother’s relationship with the infant.1 Suggesting that 
such a state of preoccupation or a state of “heightened sensitivity” 
develops toward the end of pregnancy and lasts for the first few post-
natal weeks, he likened it to a withdrawn or dissociated state that in 
the absence of pregnancy and a newborn would resemble a mental 
illness of acute onset. In this period, mothers are deeply focused on 
the infant to the apparent conscious exclusion of all else, and this 
preoccupation heightens their ability to anticipate the infant’s needs, 
learn his/her unique signals, and over time to develop a sense of the 
infant as an individual. Winnicott emphasizes the crucial importance 
of such a stage for the infant’s self-development and the development-
mental consequences for infants when mothers are unable to tolerate such 
a level of intense preoccupation.

Similar to the notion of primary maternal preoccupation, others 
have suggested that for both mothers and fathers, there is an initial 
critical period of “engrossment” with the infant in which all other 
concerns and realities assume a lesser role in day to day life.27 In a 
prospective longitudinal study of 82 parents, we have documented 
the course of early preoccupations and found that they peak around 
the time of delivery.3 Although fathers and mothers displayed a similar 
time course, the degree of preoccupation was significantly less for 
the fathers in our study. For example, at two weeks after delivery 
mothers of normal infants, on average, reported spending nearly 14 
hours per day focused exclusively on the infant, while fathers re-
ported spending approximately half that amount of time.9

The mental content of these preoccupations includes thoughts of 
reciprocity and unity with the infant, as well as thoughts about the 
perfection of the infant. For example, we found that 73% of the moth-
ers and 66% of the fathers reported having the thought that their baby 
was “perfect” at three-months of age.9 These idealizing thoughts may 
be especially important in the establishment of resiliency and the 
perception of self efficacy.

These parental preoccupations also include anxious intrusive 
thoughts about the infant. In a longitudinal study of 120 couples 
during their first pregnancy and in the six months after birth, women 
reported increasing levels of worry toward the end of their pregnancy 
and 25 to 30% described being preoccupied with worries about car-
ing for the infant postpartum.28 Immediately before and after birth this 
figure may be substantially higher. In our study, we found that 95% 
of the mothers and 80% of the fathers had such recurrent thoughts about 
the possibility of something bad happening to their baby at eight 
months of gestation. In the weeks following delivery this percentage 
declined only slightly to 80% and 73% for mothers and fathers, re-
spectively, and at three months these figures were unchanged.9 After 
delivery and on returning home, most frequently cited were concerns 
about feeding the baby, about the baby’s crying, one’s adequacy as a 
new parent, and thoughts about the infant’s well-being.8 Conditions 
such as these are more commonly reported among parents of very sick 
preterm infants, infants with serious congenital disorders or malfor-
mations or infants with serious birth complications.29 Less commonly, 
intrusive thoughts of injuring the child beset the new mother (or 
father) that can in turn lead to postpartum obsessive-compulsive dis-
order or depression or both.29

Nursing and feeding are the parental behaviors that are perhaps 
most associated with a new infant. Women describe breast feeding as 
a uniquely close, very physical, at times sensual experience and one 
that brings a particular unity between the mother and her infant.9 In 
some instances, mothers appear not to experience breast feeding as an 
interpersonal event but rather as a moment when they and the infant 
are joined as one. Grooming and dressing behaviors carry a special 
valence inasmuch as they permit the closeness between parent and 
infant and are times for close inspection of the details of the infant’s 
body and appearance.

Even before the child is born parents preoccupy themselves with 
creating a safe, clean, and secure environment for the infant. Major 
cleaning and renovation projects are commonplace as the human 
form of nest building unfolds. After birth, unimpeded access and safety 
are among the parents’ uppermost concerns. Safety issues include the 
cleanliness of the infant and the infant’s immediate environment, tak-
ing extra care not to drop the infant, as well as protection from poten-
tial external threats. After birth this same sense of heightened respon-
sibility lead parents to check on the baby frequently, even at times 
when they know the baby is fine.9

Viewed from an evolutionary perspective, it seems nearly self-
evident that the behavioral repertoires associated with early parenting 
skills would be subject to intense selective pressure.30-32 For one’s 
genes to self-replicate, sexual intimacy must occur and the progeny of 
such unions must survive. Pregnancy and the early years of an infant’s 
life are fraught with mortal dangers. Indeed, it has only been during 
the past century that infant mortality rates have fallen from over 100/ 
1,000 live births in 1900 to about 10/1,000 in 1984.33 Little wonder 
then that a specific state of heightened sensitivity on the part of new 
parents would be evolutionarily conserved.

It is also worth noting that becoming a new parent often comes at 
high physiological and mental cost. For nursing mothers there is the 
need to increase their caloric intake as well as to remain well hydrated. 
There is also a revaluing of what is important in life. Care giving is just 
one of several competing motivational systems for parents. Parents 
must also consider the needs of the other children in the family, their 
occupational duties, the needs of the marital relationship and the 
demands of the larger social group so that the advent of a new infant 
involves an adjustment in the parent’s hedonic homeostasis as they 
establish lasting reciprocal social bonds and make room in their inner 
lives for a new family member.37

Finally, too much or too little primary parental preoccupation may 
be problematic. Too much can lead to obsessive-compulsive-like 
states34 and to little may set the stage for abuse or neglect in vulner-
able, high-risk families.

Neural Circuitry of Maternal Behavior

Although the central nervous system events that accompany parental 
care in humans are largely unknown, it is likely that there is a substan-
tial degree of conservation across mammalian species.35 Classical le-
son studies done in rodent model systems (rats, mice, and voles) have
Gene knockout technology has provided new insights into the molecular basis of maternal behavior that are congruent with the existing neurobiological literature. At least nine genes have been identified that are necessary for the expression of one or more aspects of maternal behavior. These genes encode for three transcription factors: three enzymes, including dopamine beta hydroxylase and neuronal nitric oxide synthase; two receptors, including the prolactin and the estrogen receptor; and one neuropeptide, oxytocin. By way of illustration, we briefly review two of these genes, Paternally expressed gene-3 (Peg3) and Dopamine beta hydroxylase (Dbh).

Paternally expressed gene-3. Peg3 is an imprinted gene. Imprinted genes display differential expression according to their parental origin. Normally, only the paternally derived Peg3 allele is expressed. Peg3 contains two zinc finger motifs and likely acts as a transcription factor. Li and co-workers disrupted Peg3 by inserting a bgeo selection cassette into its 5' coding exon. Pups born to Peg3/−/− mutant mothers failed to survive. While only 8% of litters born to mutant mothers grew to weaning age, 83% of litters born to wild-type females survived. The offspring of mutant females and wild-type males (+/+ X +/-) also failed to thrive, suggesting that the genotype of the mother, not the father, was relevant for their survival. Since these pups inherited the active paternal Peg3 allele and the silent maternal allele, they should develop as normal adults. The fact that so few pups survived suggested that there was a defect in maternal behavior. Mutant primiparous mothers were subjected to a behavioral assay of nurturing behaviors. These animals were deficient in nest building, pup retrieval, and nursing.

Normally in rodent brain, high levels of Peg3 expression are present in a number of hypothalamic nuclei (MPOA and PVN) as well as the MA, BNST, hippocampus, and olfactory bulb. Further, histological examination revealed that the Peg3/−/− mothers had fewer oxytocin-positive neurons in the PVN.

Dopamine beta hydroxylase. Noradrenergic neurons in the brain project from brainstem nuclei and innervate virtually all areas of the brain and spinal cord. The enzyme Dbh synthesizes the adrenergic receptor ligands norepinephrine (NE) and epinephrine. Thomas and colleagues disrupted the Dbh gene in mice. Mice homozygous for the Dbh mutation (Dbh/−/−) died in utero, of apparent cardiovascular failure. Dbh/−/− mice could be rescued at birth by provision of adrenergic agonists or a synthetic precursor of NE, L-threo-3, 4-dihydroxyphenylserine (DOPS), in the maternal drinking water from embryonic day 9.5 until birth. The majority of these rescued animals became viable adults. When subjected to behavioral tests, the same circuitry being involved. For example, Fleming and co-workers have found that first-time mothers with high levels of circulating cortisol were better able to identify their own infant’s odors. In these same primiparous mothers, the level of affectionate contact with the infant (affectionate burping, stroking, poking and hugging) by the mother was associated with higher levels of salivary cortisol. Both of these findings support the hypothesis that our stress response systems are adaptively activated during the period of heightened maternal sensitivity surrounding the birth of a new infant.

Finally, we also regard this circuit as being crucially involved in the formation of any reciprocal social/emotional bonds such that genetically mediated alterations in this circuit may lead to the social deficits seen in autism and other pervasive developmental disorders.
Dbh -/- mice displayed some difficulty learning an active avoidance paradigm and a simple motor task.

In a subsequent study, Thomas and Palmiter demonstrated impaired maternal behavior across virtually all domains evaluated. Pups were observed scattered within the bedding around the nest. Often pups were not cleaned, and their placentas remained attached. Milk was not detected in the stomachs of most pups born to Dbh -/- females, which suggests that the pups were not nursing despite the presence of normal mammary gland tissue. Cross-fostering experiments revealed that almost all litters in which Dbh -/- dams were paired with experienced wild type pups were raised to weaning. This observation demonstrates that the Dbh -/- dams can nurse and that lactation is not impaired.

The impairment in maternal behavior in the Dbh -/- animals could reflect a developmental deficit caused by NE deficiency or it could represent a physiological deficit. To distinguish between these possibilities DOPS was used to restore transiently NE to the mutant females. When mutant females were injected with DOPS on the morning after birth, maternal behavior was not restored, and all pups subsequently died. However, when mutant females were injected with DOPS on the evening prior to birth, over half of the litters survived. Even more pups survived when DOPS was injected both in the evening before and on the morning after birth.

These findings suggest that NE may play a key role in initiating a realignment of the dam’s sense of what is salient and important in the environment. Interestingly, in 85% of the mutant females, the rescue of maternal behavior by DOPS extended to the mother’s subsequent pregnancies even in the absence of DOPS injections. However, DOPS injections did not significantly enhance pup retrieval by mutant virgin females.

In sum, gene-targeting studies have demonstrated that at least nine certain genes including Peg3 and Dbh are necessary for the development of maternal behavior. We conclude that the basic microcircuitry responsible for mediating maternal behavior (Figure 1) is at least, in part, genetically determined. Indeed, the limbic-hypothalamic-midbrain circuit implicated by the gene knockout studies is the same circuit identified by the classical lesion studies. Strikingly, some of the genetically mediated deficits in maternal behavior can be restored through early environmental manipulations.

Non-genomic Influences on Maternal Behavior

Thus far, several experimental interventions have been shown to have effects on aspects of maternal behavior including licking and grooming, high arched backed nursing, and aggression towards an intruder. More recently, other rodent maternal behaviors have also been systematically evaluated. In general, these findings suggest that maternal behavior in the days following birth serves to “program” the subsequent maternal behavior of the adult offspring as well as establishing the pups’ level of hypothalamic-pituitary-adrenal responsiveness to stress. This complex programming also appears to influence aspects of learning and memory. Further, many of the brain regions are implicated in these experimental interventions are the same as those identified in the knockout gene and earlier lesioning studies. Although we review in detail a series of recent rodent studies, investigations in social primates also highlight the importance of early mothering in determining how the daughters will mother. It is also clear that the effects of early maternal deprivation in primates may be difficult to reverse, as many maternally deprived monkeys, as adults, are able to function normally under usual conditions but are unable to cope with psychosocial stressors.

**Handling and brief separations (15 minutes per day) from pups**

Repeated handling of pups in conjunction with brief maternal separations induces more licking and grooming by the rat dams. The handling procedure used in the Liu study involved removing the mother and then rat pups from their cage, placing the pups together in a small container, and returning the animals 15 min later to their cage and their mothers. The manipulation was performed daily for the first 21 days of life. This manipulation resulted in more than a doubling of the time the dam spent licking and grooming her pups. The licking and grooming behavior is also highly correlated with high arched back nursing postures.

As adults, the offspring of mothers that exhibited more licking and grooming of pups during the first 10 days of life showed reduced plasma adrenocorticotropic hormone (ACTH) and corticosterone responses to acute restraint stress, as well as increased hippocampal glucocorticoid receptor mRNA expression, and decreased levels of hypothalamic corticotropin-releasing factor (CRF) mRNA. Subsequent studies by the same group of investigators, have shown that the offspring of these high licking and grooming mothers also show reduced acoustic startle responses, and enhanced spatial learning and memory.

**Handling and prolonged separations (3 hours per day) from pups**

In contrast, repeated handling of pups in conjunction with prolonged maternal separations induces deranged maternal behavior including a reduction in licking and grooming by the rat dams and reduced maternal aggression. Similarly, the adult offspring show increased neuroendocrine responses to acute restraint stress and airpuff startle including elevated levels of PVN CRF mRNA and elevated plasma levels of ACTH and corticosterone. These animals also show an increased acoustic startle response, and enhanced anxiety or fearfulness to novel environments.

**Handling and early adoption within first 3-6 hours**

Early adoption has been found to be associated with increased maternal licking behavior. In the same study, early adoption within the first 3-to-6 hrs after birth was found to prevent the prolonged stress-induced secretion of corticosterone evident in early separated offspring that were returned to the nest with their biological mother. Similarly, as adults the early-adopted pups demonstrated lower novelty-induced locomotion and improved recognition performance in a Y-maze compared to the early separated offspring. However, later adoption at either 5 or 10 days resulted in a prolonged stress-induced corticosterone secretion, increased the locomotor response to novelty, and disrupted cognitive performance in the adult offspring.

**Cross-fostering studies**

It has been observed that rodent mothers display naturally occurring variations in maternal licking/grooming and arched-back nursing. Since the licking/grooming behavior occurs most frequently before or during arched-back nursing, the frequencies of these two behaviors are closely correlated among mothers. In a subsequent cross-fostering study, investigators determined that the amount of licking and grooming that a female pup receives in infancy is associated with how much licking and grooming she provides to her offspring as a new mother. They also reported that the low licking and grooming dams could be transformed into high licking and grooming dams by handling. More impressively they also found that this change was passed on to the next generation – that is that the female offspring of the low licking and grooming dams became high licking and grooming mothers if
they were either cross-fostered by high licking and grooming dams or if they were handled. The converse was also true, namely that the female offspring of the high licking and grooming dams became low licking and grooming mothers if they were crossed-fostered by low licking and grooming dams.

These naturally occurring variations in licking, grooming, and arched back nursing have also been associated with the development of individual differences in behavioral responses to novelty in adult offspring. Adult offspring of the low licking, grooming, and arched back nursing mothers’ show increased startle responses, decreased open-field exploration, and longer latencies to eat food provided in a novel environment.14

Furthermore, Francis and coworkers demonstrated that the influence of maternal care on the development of stress reactivity was mediated by changes in gene expression in regions of the brain that regulate stress responses. For example, adult offspring of high licking, grooming, and arched back nursing dams showed increased hippocampal glucocorticoid receptor mRNA expression as well as increased expression of NMDA receptor subunit and brain-derived neurotrophic factor mRNA, and increased cholinergic innervation of the hippocampus.15 In the amygdala there are increased central benzodiazepine receptor levels in the central and basolateral nuclei. In the PVN there is decreased CRF mRNA in the PVN. These adult pups also show a number of changes in receptor density in the locus ceruleus including: increased alpha2 adrenoreceptors, reduced GABA A receptors, and decreased CRF receptors.16

In another recent study, oxytocin receptor binding levels were examined in brain sections from high and low licking, grooming, and arched back nursing animals sacrificed either as non-lactating virgins or during lactation.17 Examination of the MPOA and the intermediate and ventral regions of the lateral septum disclosed that oxytocin receptor levels were significantly higher in lactating females compared with non-lactating females. Lactation-induced increases in oxytocin receptor binding were greater in high compared with low licking, grooming, and arched back nursing females in the BNST and ventral region of the septum. Francis and colleagues suggest, therefore, that variations in maternal behavior in the rat may be reflected in, and influenced by differences in oxytocin receptor levels in the brain.

In sum, despite genetic constraints, the nature of early caregiving experiences can have enduring consequences on individual differences in subsequent maternal behavior, anxiety regulation and patterns of stress response. Data from animal studies indicate that the interval surrounding the birth of the rat pup or the rhesus infant is a critical period in the life of the animal that likely has enduring neurobiological and behavioral consequences.

In the final section of this review we consider whether there is any evidence in human studies of similar effects?

**Early Life Experience, Risk and Resiliency**

Increasing clinical and epidemiological data supports the view that exposure to early adverse environments underlie vulnerability to altered physiological responses to stress and the later expression of mood and anxiety disorders.18-20 Among the most important early environmental influences is the interaction between the primary caregiver and the infant. Building on the early work of Bowlby and colleagues,21 efforts to characterize this reciprocal interaction between caregiver and infant and to assess its impact have provided a powerful theoretical and empirical framework in the fields of social and emotional development.22 Over the past 30 years, clear evidence has emerged that significant disturbances in the early parent-child relationship (reflected in such things as child abuse and neglect or insecure attachments) contribute to an increased risk for developing both internalizing and externalizing disorders.23 While early adversity and insecure attachment may not be a proximal cause of later psychopathology, it appears to confer risk. Conversely, longitudinal studies of high-risk infants suggest that the formation of a special relationship with a caring adult in the perinatal period confers a degree of resiliency and protection against the development of psychopathology later in life.24

Similar to the findings observed in rodents by Liu, Francis and colleagues,25 a growing body of evidence also indicates that human caregivers’ levels of responsivity to their children can be traced in part to the caregivers’ own childrearing histories and attachment-related experiences.26 Caregivers’ attachment-related experiences are hypothesized to be encoded in “internal working models” of self and others that establish styles of emotional communication that either buffer the individual in times of stress or that contribute to maladaptive patterns of affect regulation and behavior.27 In the next section, we review the results of early intervention programs with high-risk families. The focus is primarily on interventions begun in the pre- or peri-natal period and that included random assignment to either the experimental intervention group or to a comparison group.

**Early interventions to reduce insecure attachments**

Based on the empirical work suggesting the critical importance of early parent-infant relationships, at least six home visitation studies with random assignment have been reported that have aimed to reduce rate of relationship disturbances between high-risk mothers and their infants.28-30 Five of the six studies focused on low SES populations, and one focused on mothers who adopted children of different nationalities. Five out of the six interventions reported reductions in the rates of insecure attachment and the sixth31 reported fewer negative attachment behaviors. Four of these home visitation programs employed health care professionals as visitors, while the fifth employed a combination of nurses, para-professionals, and non-professionals. Three studies began in the prenatal period.28,32,34 The duration of the programs varied with two programs lasting only 3-4 months, another lasting on average 8.5 months, and the remainder lasting between 12-24 months. Unfortunately, none of these studies has examined long-term effects on child emotional and behavioral adjustment.

In sum, while it appears that the quality of infant-mother attachment is malleable, the long-term impact of such adjustments on risk and resiliency to later psychopathology remains in doubt. The results of the one adoption study are also difficult to interpret, as there was no assessment, antecedent or otherwise, of the biological parents.

**Early interventions to improve child behavioral adjust-ment**

Thus far there have been at least three selective intervention studies with random assignment and prenatal initiation and at least one-year duration focused on child behavioral adjustment. The first set of studies was based on an intervention model that included home visits, parent meetings and medical care.35,36 It showed early effects at 2 and 3 years of age that attenuated by 5 years of age. A second intervention that also included home visits by nurses, parent meetings, and medical care showed less of an effect early on at 4 years of age that became significant at 5 and 6 years of age.36-38 Finally, a third set of studies that included home visits by nurses that began prenatal and continued for 30-months has shown a remarkable number of positive outcomes as late as 15 years of age.38,39 For example, this
Conclusions
Behavioral, neurobiological, and genetic and neurobiological studies in model mammalian systems have the potential to inform clinical practice, particularly early intervention programs for high-risk expectant parents. “Good enough” genes combined with “good enough” parental care are needed to ensure positive outcomes in childhood and beyond. Among these positive outcomes is a resilience to subsequent adversities in life and the capacity to be a good enough parent for the next generation. Consequently, it is possible that effective early intervention programs may have consequences for generations. Measures of “primary parental preoccupations” may be useful in future early intervention programs as an index of change within a key domain of functioning.

Close collaborations between clinicians and the designers of model intervention programs have been long standing. These collaborations are now beginning to include neuroimagers, developmental neurobiologists, and geneticists. Our capacity to study genes and the brain has never been stronger. Future studies should permit the examination of how successful early intervention programs influence brain development, problem solving abilities, stress response, as well as vulnerability to later psychopathology.

Acknowledgements
Aspects of this work were presented as the 20th Annual Daniel Prager Lecture, The George Washington University, May 2000, Washington, DC. The Korczak Foundation (JFL, DJC); the Harris Programs in Perinatal Mental Health (LCM, JFL, DJC); and grants from the National Institutes of Health MH49351, HD03008, MH30929, DA06025, DA00222 (LMC), and RR06022.

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Something remarkable is happening in the hitherto hermetically sealed worlds of neurobiology and psychoanalysis. Here is an article linking an aspect of the mind as described by Winnicott, with the brain as it is beginning to open out to molecular genetics. What are the implications for the clinician? Does this post-Descartian revolution matter? Or is it just a question of “pretty pictures” that are no more than epiphenomena when it comes to the workings of the inner world? In a general sense there is no doubt that the thrust behind neuropsychanalysis is important. To discover that there are biological aspects to ideas such as primary maternal preoccupation that link human psychology with that of other mammals is reassuring for psychoanalysts who have been so long under attack from a hostile and philosophically philistine scientific community. At the same time to be shown unequivocally that genetic and hormonal factors underpin many of the behaviours we are interested in is a useful counterweight to the mentalistic excesses of psychoanalysis. We need to be more cautious in our tendency to ascribe unconscious volition to infants and their carers whose behaviours may in reality driven more by biology than intentionality.

More specifically, the studies cited in this review suggest as psychoanalysts have long suspected that environmental events, especially those that are traumatic, can inscribe themselves in the brain in such a way as to have become “biological”, with often devastating long term implications for healthy psychological functioning. The notion of gene expression and of regulator genes, going back to the pioneering work of Jacob and Monod in the 1960s, suggests mechanisms by which such phenomena can occur. Nurture can determine nature and vice versa.

From the perspective of personality disorder research it was interesting to learn that factors that interfere with primary maternal preoccupation analogues in rodents can have long term effects on the infant’s subsequent reproductive competence. Using an (admittedly retrospective) life course methodology we have found that patients suffering from BPD have a much higher incidence of what we call ‘inauspicious beginnings’ than controls. Thus maternal bereavement in pregnancy, being an unwanted or “wrong” sex child, or loss of father before birth, all seem to cluster in those whose subsequent adult relationship capacities will be compromised. The evidence that rodent mothers who licked and groomed their offspring more had less stressed infants suggest possible preventive interventions for at risk infants and mothers. Resilience researchers will be looking for further studies identifying factors that can mitigate the long-term effects of such early trauma, and their possible genetic and biological underpinning.

The finding that the main impact of such early intervention studies was to lengthen the gap between first and subsequent child is particularly intriguing. Evolutionary theorists have argued that in conditions of deprivation and stress, having large numbers of closely spaced infants may be an appropriate reproductive strategy, whereas in more favourable environments smaller numbers of more widely spaced children confers selective advantage. In our contemporary societies however a 60 month interval would be highly unusual. Here perhaps we are seeing the interaction not just of genes and minds but also of sociology. Studies of chimp in the wild suggest that they often have a gap of as long as four years between first and second child, so in biological terms a 60 month gap is not unusual. Here however child care is communal, as it is in most traditional human societies. Given low infant mortality, the pressure to produce a playmate for a single two or three year old is much less where the child is reared in close proximity to cousins than in the nuclear families of the western world. Thus a comprehensive child care programme would need not just offer parenting skills to parents, but also to provide affordable and psychologically sensitive nursery arrangements that would support the mother delaying her next child until sufficient investment had been made to buffer stress, genetically and psychologically.

In sum, this article enhanced my ‘hedonic homeostasis’; further reviews and original work in this field are eagerly awaited. How about tackling the genetics and biochemistry of the paranoid-schizoid position, or an exposition of the neurochemistry of oedipus as a next project?

Correspondence:
Email: j.a.holmes@btinternet.com