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Infant bonding and attachment to the caregiver: Insights from basic and clinical science

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Abstract

The bonding and early life attachment between the infant and caregiver is a dynamic, bidirectional process involving caregiver nurturing of the infant, as well as complementary infant behavior that elicits parental care. Attachment appears to have a dual function. The first function is to ensure the infant remains close to the caregiver in order to receive necessary care for survival. Interestingly, animal research has shown that both nurturing and painful stimuli associated with the caregiver support attachment. Secondly, the quality of attachment and its associated sensory stimuli organize the brain to define the infant's cognitive and emotional development. Specifically, the patterning and quality of care regulate the infant's brain function and behavioral expression that determines long-term emotional regulation. These issues, presented within an historical view of infant attachment, highlight the importance of integrating human and animal research in understanding infant care.

Keywords

attachment; premature infants; odor; sensitive period

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Introduction

A common feature of many species is the formation of a mutual attachment between infant and caregiver that ensures the pair maintains contact. This attachment formation must engage both a maternal behavioral system for provision of care and a behavioral system in the infant that elicits parental care, thus beginning the complex dance of reciprocal attachment. The quality of care received from the mother also programs the infant's emotional and cognitive development by helping to sculpt the developing brain. Since infants must identify their caregivers, a unique pathway for rapid attachment learning appears to support the attachment formation, where robust and rapid attachment learning occurs that is akin to the “imprinting” described for avian species. This occurs in both the mother and the infant, although this review focuses solely on the infant. The characteristics of the infant's attachment to the mother undergo considerable changes as the infant matures into an independent organism.

Traditionally, the term attachment has been confined to the more complex cognitive, highly specific attachment exhibited by the time children reach their first birthday[1,2]. This original idea of attachment relates to its theoretical formation and the complex, cognitive representation of the attachment figure seen in older infants and children. However, newborns show specific, highly specialized behavior that can be characterized as attachment or bonding that is influenced by learning and experience. This behavior begins *in utero* and adapts to accommodate the changing world as the infant is born and matures. According to this more recent view, high-risk infants, such as premature infants, are vulnerable to forming lower quality attachments to their caregivers as a result of disrupted critical experience with the mother during pre- and post-natal development. A better understanding of the complex nature of early life caregiver-infant relationships may help us improve environments and outcomes for at risk infants.

Attachment to the mother begins in utero

At birth, the full term infant is attracted to the mother's voice and smell, including the scent of amniotic fluid[3,4]. This attraction to the mother's sensory stimuli is the first sign of the infant's attachment and bonding to the mother. This attachment begins during the last trimester of pregnancy, when auditory and olfactory systems become functional, allowing the fetus to learn about the mother's voice and odors. In the womb, the fetus is suspended in amniotic fluid, causing the olfactory mucosa and its receptors to be bathed in waves of this fluid during infant swallowing and thumb sucking. While the uterine acoustic environment is dominated by the rhythmic sound of the mother's blood flow, the mother's voice is carried through her bones and amniotic fluid to the fetal ears[5]. We know that fetal experience with these stimuli is important in shaping the newborn infant's response because experimental manipulation of the amniotic fluid's smell and of sound exposure have profound effects on the newborn's response to these stimuli[6–8]. Based on the animal literature, these stimuli appear to acquire significance through two mechanisms – through fetal learning and through shaping the development of the fetal brain's sensory systems[5,9,10].

At birth, these familiar auditory and olfactory stimuli hold particular salience for the infant, as the infant suddenly transitions into a world filled with new sensory experiences, including new sights, sounds, textures, and temperatures. Indeed, maternal voice and odors may ease the infant's transition into extra-uterine life. Amazingly, a newborn placed on the mother's ventrum will crawl to the mother's breast, as it is a potent source of maternal odor but also a similarly potent source of amniotic odor[11]. Even on the first day of life, infants orient to their mother's odor and are soothed, when crying, by their mother's odor[4,12,13]. These behaviors seem to be expressed even in response to the odors of other mothers, but infants

show significantly more mouthing to their own mother's odor[12]. In summary, these data suggest that the maternal odor organizes the infant's behavior for nursing[14]. Infants also orient to their mother's voice and will either decrease or increase their sucking rate in order to hear that voice in an operant conditioning paradigm[3,15]. Importantly, these infant responses to maternal cues also elicit care giving from the mother. The mutual infant-caregiver attachment is strengthened during this finely tuned dance of social behaviors as the infant and mother continue to learn about one another.

Over the first few days of life, these basic attachment behaviors to the mother change as the infant learns about additional maternal features, such as her face, odors and voice[3,16–18]. The newborn infant prefers the odor of amniotic fluid over breast/maternal odors, although this preference reverses after a week of experience with nursing[19]. Interestingly, bottle fed infants show a decreased preference to maternal odors over the first week of life, perhaps due to their reduced exposure to maternal odors compared to breast fed infants[7,20]. Even bottle fed infants, however, prefer maternal odors to the odor of formula[19,21]. It should be noted that the caregiver is also learning about the baby. Indeed, the infant's face, vocalizations, touch, and odor are all rapidly learned by its caregivers[22–26].

While it is impossible to conclusively determine if infants learn their mother's odors, robust learning has been demonstrated in newborn infants using both sounds[5] and odors[9]. In this review, however, we will only describe odor learning. Infants must learn to respond appropriately to their environment by responding to important stimuli while ignoring irrelevant stimuli. While biological predisposition occurs to some maternal odors because of the `odor signature'[27], learning about other aspects of the world and the caregiver is also important[7,9,28,29]. Odor learning and its importance was demonstrated by infant odor preference learning for perfume worn by the mother, which dissipated when the mothers stopped wearing the perfume[16]. This odor learning was also demonstrated in a more controlled classical conditioning experiment[9]. Specifically, infants were presented with a novel odor for 30-seconds with concurrent tactile stimulation similar to a massage or caressing. Standard learning control groups were also included, such as infants that received the odor alone or the odor-massage in a non-contingent manner. One day later, the infants, now just 24–96 hours old, were given presentations of test odor-only presentations, as a test of learning preference to the odor. Only the infants who had received the odor with concomitant massage showed increased levels of activity and head turns towards the odor, indicating that complex classical conditioning to an odor could occur in newborns. In a more naturalistic experiment, an odor placed in infant bassinets for a day produced a preference for that odor, presumably due to the handling, feeding and nurturing paired with that odor[30]. Thus, research indicates that infants' exposure to natural or artificial odors can enhance or attenuate infants' reactive behavior based on their postnatal experiences with that odor.

Importance of attachment

The critical importance of the mother-infant attachment was noted by Sigmund Freud[31] who suggested that neuroses in adults were caused by aberrant experiences. Our current understanding of the complexity of the infant's first social relationship, however, underwent a paradigm shift in the 1950's. As documented below, it was the synthesis of research on nonhuman animals and clinical observations of hospitalized and orphaned children who were separated from their mothers highlighted the critical importance of early life attachment and its importance for infant mental health.

During the 1950s clinical observations of orphaned and hospitalized children by Rene Spitz[32] and James Robertson[33] showed detrimental effects of separating the child from the caregiver. Specifically, children expressed extreme emotional distress at separation, which

became progressively more depressive-like and subsequently compromised their recovery. This observation of the detrimental effects of caregiver-infant separation initiated a change in hospital visitation policies that enabled parents to visit their children throughout their hospital stay. It should be noted that, within a certain time range and within certain contexts, separating an infant from the mother does not irrevocably damage the infant. Indeed, as eloquently described in the work of Sir Michael Rutter[2], maternal deprivation must be viewed not only as a break in a relationship but also as a break in the *function* of the relationship between the infant-mother. It should also be noted that infants frequently have access to other caregivers, such as the father, who can also provide the infant with both the bonding relationship and the sensory stimulation required for normal development.

Concurrent animal work highlighted the role of experience in attachment formation, gradually replacing the notion of attachment as an entirely innate process to a more complex understanding that included a biological predisposition for attachment requiring experience for expression and healthy development. This work showed that the notion of newborns innately knowing their caregiver was too simplistic. Imprinting research in chicks by researchers such as Konrad Lorenz, Niko Tinbergen and John Hinde first illustrated the importance of experience in attachment formation[34]. At birth, chicks are biologically predetermined to form an attachment, although they have a limited period of time – a "critical" or "sensitive" period in early life when the infant can learn or "imprint" on their caregiver. The attachment system is straightforward, where the chicks attach to the first moving object they see, which under normal circumstances is their mother. The chicks express learned attachment to their caregiver through their following or proximity seeking of the mother. This discovery was an important breakthrough because it illustrated that there must be a neural circuit for attachment, however it also indicated that experience plays a critical role in attachment and bonding More recently, the neural basis of imprinting, which accounts for both the biological predisposition to attach and the mechanisms underlying the learning aspect of imprinting, has been identified in chicks. These underlying mechanisms involve simplistic brain circuitry, including the dorsocaudal neostriatal complex[35,36]. While imprinting provides some insight into human attachment, it cannot model all aspects of human attachment and its associated flexibility, resiliency, and children's ability to make bonds with multiple caregivers across longer periods in early childhood.

Additional nonhuman primate research by Harry Harlow[37,38] and his colleagues' further expanded our understanding of attachment. This work highlighted the organizing function of attachment by showing that disruption of the mother-infant bond disturbs infant emotional and cognitive development. Findings from Harlow's work on infant monkeys appeared to mirror the strong emotional and physical stunting of orphaned and hospitalized infants separated from their mothers. This work emphasized the importance of maternal nurturing of the infant that went beyond food and perfunctory care.

Rodent research in the 1950's also contributed to our understanding of early life experience and development. Specifically, rodents were provided with different types of sensory stimuli (handling, mild shock), or the infant rodents were separated from their mother. Any of these interventions were capable of dramatically modifying later life emotionality, such as fear, and novelty seeking[39,40]. Stressful stimuli occurring prenatally can also program the earliest maternal behaviors towards the offspring as well as later life behaviors in the offspring. In one study, when stress hormone was administered to pregnant dams during early gestation, the dams displayed altered nursing behaviors, and the newborn pups of treated dams showed decreased juvenile social play and a blunted acoustic startle reflex in adolescence and adulthood, effects that were predicted by frequency of milk ejections in the dams[41]. Together, this research indicates that sensory stimuli and experience alters infant behavior directly but also indirectly by altering maternal care.

Thus, findings in various disciplines from humans and other animals began to present a similar story – early life experience was important for programming emotionality. Through a synthesis of these clinical observations and basic research, a new view of the mother-infant relationship emerged. It was postulated that infants have a biological attachment system that involves learning to identify the caregiver. It also indicated that attachment went beyond the immediate infant-caregiver relationship and highlighted a function of attachment to suggest that the quality of maternal care determines the long-term emotional well-being of the infant. This new view of the mother-infant dyad was facilitated by discussions and meetings of a diverse set of animal researchers and clinicians and resulted in the paradigm shift, as described above, in our understanding of attachment formation.

The psychiatrist John Bowlby[42] had a significant role in integrating this updated view of the mother-infant relationship into our understanding of human attachment, eventually leading to the formulation of his important Attachment Theory. His interest in human attachment was established as a result of his clinical observations of disturbed children who were deprived of their mothers in childhood. However, his understanding of attachment was also based on the animal models noted above and discussions with animal researchers. Specifically, Bowlby's attachment theory suggests that due to the critical importance of attachment for survial, evolution has led children to become biologically pre-programmed to form attachments to their caregiver. Bowlby describes that the attached child exhibits proximity-seeking behavior to the caregiver because the caregiver provides protection and a sense of safety to the child. Once the attachment is formed, the child uses the caregiver as a secure base to explore the world and develop other relationships. It is important to note that Bowlby believed that the child's attachment was built over the first year of life as the child forms a representational mental model of the self and others based on its earliest relationship to its mother. Mary Ainsworth[43], a student and collaborator of John Bowlby, elaborated on his attachment theory and developed the widely used Strange Situation Test to characterize attachment quality. This test was developed in order to define the child's attachment quality. It places the child in a series of seven increasingly challenging situations (e.g. mother ignoring the child, the mother leaving the child and a stranger entering the room) to trigger attachment behaviors and uncover possibly disrupted attachment styles of the child. Bowlby's Attachment Theory and the Strange Situation Test greatly increased our understanding of different qualities of attachment and gave rise to a prolific second generation of attachment researchers.

Animal research and early life experience

Due to ethical concerns, the type of research questions we can address in humans is generally limited to correlations, while questions of causation can generally be assessed only through the study of disease. Thus, scientists must rely on animal research to access causation and define underlying mechanisms of behaviors, such as attachment, in a more precise and controlled manner. However, the direct translation of animal research to humans requires both caution and an understanding of unique species-specific ecological niches, with a particular awareness of the increasingly complex cognitive processes involved in human attachment relative to other animals.

Nonhuman primates exhibit some aspects of the complex cognitive processes of human attachment and provide an excellent experimental model. Indeed, nonhuman primate research by Harlow and his associates generated clues about the importance of sensory stimulation provided by the mother in producing healthy cognitive and emotional development[37]. For example, a young infant monkey separated from its mother fared better if given access to a tire swing during the separation. However, social interactions with peers,

which provide a richer source of sensory stimulation (peer rearing) resulted in even better outcomes, albeit still compromised[44].

Paradigm shifting rodent research in the laboratory of Myron Hofer, a psychiatrist interested in a child's bereavement following the death of the caregiver, produced insights into how these sensory stimuli could overcome or repair effects of maternal deprivation[45]. Hofer described the unique role of sensory stimuli from the mother as controlling the behavior, brain, and physiology of rat pups and suggested that these altered sensory experiences were important for development. The mother was viewed as a “hidden regulator” of pup behavior and physiology through her sensory stimulation of the pups. By systematically removing and replacing the sensory stimuli normally provided by the mother, he determined that the patterning and intensity of these sensory stimuli were critical for controlling the pup's homeostasis. For example, tactile stimulation from the mother licking or touching the pup increased excretion of growth hormone, while her warmth increased levels of the neurotransmitter norepinephrine (NE), critical for pups' attachment learning. Other stimuli, such maternal odor increased behavioral activity in the pups and indicated that different sensory stimuli each regulate different behavioral and physiological systems. Removal of these regulating sensory stimuli, as occurs during separation from the mother, produced dysregulation of the pups' brain functioning and behavior. Hofer further suggested that the short-term effects of maternal separation produce an animal geared to attracting the caregiver, although prolonged separation (i.e. long-term removal of the “hidden regulators”) results in a de-synchronization of different physiological systems depending on the specifics of the separation paradigm (i.e. whether other pups are present, whether body temperature is maintained, or whether pups can still smell the maternal odors, for example). Long-term disruptive effects on adult emotionality are the results of physiological dysregulation, which ultimately produces an animal that does not show adaptive behaviors (i.e. inappropriate fear, cognitive impairment, or anxiety). The age and timing of the animal during the experiment produce different long-term outcomes. Importantly, these effects of maternal behavior on pups include epigenetic changes that are transmitted across generations to continue to control emotionality in the next generation[46,47].

Animal research and the neurobiology of attachment

Animal research has facilitated our understanding of human attachment by shedding light on the brain's circuitry used to support attachment. It is important to note that the neural circuit for attachment in children has not been identified and cannot be identified based on the limits of existing technology. Therefore, we must continue to rely on the assumption that a neural circuit in the child's brain supports attachment as we explore circuitry and neurochemistry in other species. This research has been pivotal in our ability to understand and treat children with attachment disorders and the psychiatric problems that co-occur with these disorders as a result of absent, neglectful, or abusive caregivers. However, much additional animal and human research is still needed.

Currently, animal research is helping us characterize infant attachment circuitry in other species, including chicks, rodents, and nonhuman primates. While it is clear that the circuitry is quite different in avian and mammalian species, a common feature across species is that it is pre-wired to evoke rapid learning and identification of the caregiver, followed by a unique sequence of infant behaviors designed to elicit caregiving from the mother. In the rodent, the high level of NE in the brain produced during the birth process is physiologically paired with the mother's diet-dependent *natural* odors to stimulate the learning required for pups to identify and approach their mother and to initiate nursing[48]. This process has been mimicked in the lab by substituting maternal odor with artificial odors, such as a peppermint, and injecting the pup with NE to produce an artificial maternal odor that works

just as well as natural maternal odor in controlling pup social interactions with the mother[49,50,]. This learned odor has properties powerful enough to produce proximity-seeking behavior in the infant, control pups' social interactions with the mother, and enable nipple attachment for nourishment. It should be noted that the human infant has a surge of NE at birth[51,52] and it has been speculated that a similar mechanism is utilized by human infants learning about their mother[53].

However, as Bowlby observed, children also attach to abusive or neglectful caregivers. The proposed ecological explanation for this seemingly paradoxical attachment is that an infant will attach to its caregiver, regardless of the care quality, because the infant's survival is dependent on that care[14]. The wide phylogenetic representation of attachment to an abusive caregiver includes chicks, rodents, dogs and nonhuman primates[54–58].

For example, if an electric shock is administered to a chick during imprinting it still supports learning to follow the surrogate caregiver, although the same stimulus results in avoidance just hours after the critical period for imprinting closes[55,59]. Similarly, shocking an infant dog or rat results in a strong attachment to their caregiver[57,58,60,61]. Finally, nonhuman primate and human infants exhibit strong proximity-seeking behavior toward an abusive mother[62,63].

What, then, is the neurobiological mechanism that allows for aversive or painful stimuli paired with an odor to result in an odor preference? Research on abusive attachment from our lab suggests that the lack of plasticity in the infant amygdala may play a leading role[58], since the amygdala has been shown to be critical for learning fear in adults[64,65]. Interestingly, the amygdala is not activated during attachment learning in the infant rat pup with an abusive caregiver, nor in our more controlled classical fear conditioning experiments where pups learn attachment odors[57,66,67]. This suggests that the amygdala is neither activated during social interactions with the mother in infancy nor during encounters with aversive stimuli. These findings have only been demonstrated in infant rats. They are strikingly different from findings in older animals where the amygdala is readily evoked by aversive stimuli as well as during fear classical conditioning[68–72]. This has been shown in both rodents and humans. Additionally, as has been suggested by research in nonhuman primates, the amygdala may not be associated with early life infant attachment but is involved in social behavior in adulthood[73,74]. Furthermore, work by Nim Tottenham and colleagues suggests that the child's amygdala is not as readily engaged as the adult amygdala[75]. Together, these data suggest unique attributes of early infancy that support infant attachment: the infant brain is not an immature version of the adult brain but appears to support learning approach responses, while inhibiting learned avoidance responses. This occurs presumably to ensure infants approaching their caregiver regardless of the quality of care received. However, at least in the rodent, it should be noted that while odor pain conditioning does enhance attachment odor in infancy, it is associated with later life mental health problems including depressive-like behaviors and limbic system (amygdala, hippocampus) dysregulation[57,58,61].

Pediatrics and attachment

Pediatric primary care provides a unique opportunity to detect infants at risk for attachment disorders[76]. Based on findings in basic research, specific observational tools have been developed for the use in primary care[77]. In a cross-sectional study of mothers and infants at an urban hospital clinic, we are currently assessing the prevalence of at risk infants, utilizing screening tools recommended by the American Academy of Pediatrics. Preliminary data analyses of 133 mother-infant dyads show that 34% of infants exhibit concerning behavior six months postpartum in this high risk, low socio-economic status population with a high

prevalence of maternal psychiatric disorders (e.g. 26% with maternal depression)[78]. Finally, these findings underline the importance of translating results from basic research in human and animal studies into clinical practice and policy guidelines. Deciding how to make use of findings from basic research in pediatric practice, however, can be a challenging task. The newborns' preference for their mother's smell, for example, has been successfully used to facilitate breastfeeding in both pre-and full-term babies[79,80]. Likely, there is no harm to mother or newborn in this practice, and the advantages of breastfeeding for both mother and newborn are well known[81]. Utilizing the soothing effect of maternal odors in order to ease the newborn's pain during invasive procedures, on the other hand, might not be an entirely judicious clinical decision. This practice might reduce the newborn's immediate stress response during the procedure, and might thus also reduce the clinician's stress response, as the newborn might cry less, as has been described in an excellent study by Goubet and colleagues[82]. Since odor conditioning has been demonstrated in newborn, this practice, however, could result in conditioning of the newborns who would learn to associate pain with their mother's odor. This is of particular importance for premature infants who undergo a multitude of painful procedures during their first months of life. In addition, premature infants often spend long periods separated from their mother; this might interfere with their ability to form a representation of their mother that integrates her odor with her warmth, voice, touch etc. Associating maternal odor with pain might thus be confusing to the newborn and interfere with development bonding to the mother and secure attachment patterns. In summary, it might be prudent not to make universal recommendations to expose newborns to their mother's scent[83], as depending on the situation, this exposure might also have detrimental impact on their long-term development.

Concluding remarks

Infant attachment and bonding to the caregiver is widespread across animal species where the survival of the young is dependent upon a caregiver. The main function of attachment is to maintain contact between the infant and the caregiver to ensure infant survival. While infant-caregiver dyads are biologically predisposed to attach, learning about the caregiver is an additional determinant of the success and quality of attachment formation. The biological predisposition for attachment in infants appears to be mediated by a unique learning circuit that produces rapid, robust learning about the caregiver in both nurturing and abusive situations. Although attachment to an abusive caregiver seems contradictory, it may occur because the infant is programmed to ensure its own survival, which can only be achieved via continued contact to the caregiver, despite the poor quality of care provided. Attachment also contributes to infant developmental outcomes such as emotionality, cognition, and overall mental health, as it is associated with specific caregiving patterns and levels of caregiving intensity. These specific patterns and intensity levels of stimulation to the infant's sensory systems can directly influence brain development.

Understanding this dual role of attachment in ensuring care and sculpting infant neural and behavioral development provides a unique perspective when determining the level of care required for premature infants. It remains difficult, however, to separate the effects of disrupted early-life attachment from the critical health issues associated with care of the preterm infant. Bi-directional translational research is key to advancing our understanding of attachment during the early infant period. While human studies inform questions asked by animal researchers, animal research helps define mechanisms of basic functions and uncover unexpected results. Such interplay between human and animal research helps us optimize infant attachment formation, resulting in enhanced long-term outcomes for the both full term and preterm infants.

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Synopsis

Infant attachment to the caregiver is critical for survival and the initial programming of life-long emotionality and cognitive capabilities. We review attachment/bonding in the newborn and capitalize on animal research to provide clues to potential mechanisms that mediate the profound enduring effects of this early life experience.