Neurobiology of Infant Attachment

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Abstract

A strong attachment to the caregiver is critical for survival in altricial species, including humans. While some behavioral aspects of attachment have been characterized, its neurobiology has only recently received attention. Using a mammalian imprinting model, we are assessing the neural circuitry that enables infant rats to attach quickly to a caregiver, thus enhancing survival in the nest. Specifically, the hyper-functioning noradrenergic locus coeruleus (LC) enables pups to learn rapid, robust preference for the caregiver. Conversely, a hypo-functional amygdala appears to prevent the infant from learning aversions to the caregiver. Adult LC and amygdala functional emergence correlates with sensitive period termination. This study suggests the neonatal brain is not an immature version of the adult brain but is uniquely designed to optimize attachment to the caregiver. Although human attachment may not rely on identical circuitry, the work reviewed here suggests a new conceptual framework in which to explore human attachments, particularly attachments to abusive caregivers.

Keywords

mother-infant interactions; olfactory bulb; norepinephrine; attachment; imprinting; locus coeruleus; amygdala; learning; classical conditioning; abuse; corticosterone; sensitive period; stress

INTRODUCTION

The powerful influences of infant experiences on adult life are well established with strong support from both clinical and basic research, beginning with Freud. More recently, the psychiatrist John Bowlby proposed that infant relationships define future relationships and stressed the importance of understanding early attachment to the mother (Bowlby, 1965). He characterized human infant attachment in a specific, defined framework that permitted testing in an experimentally refined protocol easily applied to humans. Beyond that, his characterization of attachment is relevant throughout the animal kingdom. First, Bowlby noted that infants rapidly form an attachment to the caregiver. The classic example is imprinting in chicks, although human infants can also rapidly learn about the mother during the hours following birth (DeCasper & Fifer, 1980). Second, Bowlby noted infants undergo considerable abuse while remaining attached to the caretaker. In the avian model of imprinting, chicks will continue to follow their mother during the imprinting period even while being shocked (Hess, 1962; Salzen, 1970). Naive post-critical period chicks (only hours older) are quickly able to learn an aversion to a surrogate mother when given similar shock presentations. A similar experiment in young dogs showed that puppies will learn a strong attachment to a handler providing shock or rough treatment (Fisher, 1955; cited in Rajecki, Lamb, & Obmascher, 1978). This phenomenon extends to primates. The Harlows (1965) showed that nonhuman...
primate infants of abusive mothers still exhibited strong attachment, and recent work on a colony of abusive nonhuman primates shows similar results (Maestripieri, Tomaszczyki, & Carroll, 1999; Sanchez, Ladd, & Plotsky, 2001). Moreover, human children, even those abused by their caregiver, generally exhibit a strong attachment to that caregiver (review—Helfer, Kempe, & Krugman, 1997). We have hypothesized that this attachment system may have evolved to ensure that altricial animals easily form a repertoire of proximity-seeking behaviors to the primary caregiver, regardless of the quality of the care they receive (Hofer & Sullivan, 2001).

In general, altricial species rely, at least to some extent, on learning about the mother to form attachment. This is exemplified in the avian imprinting model with its temporally defined sensitive period when the learning process is rapid and robust, although sensitive periods can be found in many species during developmental stages critical for survival. For example, postpartum animals quickly learn about their offspring; animals learn to identify their mate and, as described here, infants learn about their caregiver (Brennen & Keverne, 1997; Insel & Young, 2001; Marlier, Schaal, & Soussignan, 1998; Moffat, Suh, & Fleming, 1993; Okere & Kaba, 2000).

**Mammalian Imprinting Model**

To assess the neurobiology of infant attachment, we have developed an infant rat model that conforms to the characteristics of attachment initially described by Bowlby. First, Bowlby stated that the infant rapidly forms an attachment to the caregiver. As illustrated in Figure 1 (top), neonatal rats very rapidly and easily learn an odor preference, although learning becomes more adult-like after postnatal day (PN) 10 (lower Fig. 1). We modeled this rapid odor learning outside the nest using a classical conditioning paradigm in which a novel odor was paired with a positive stimulus such as stroking (left Fig. 1; Pedersen, Williams, & Blass, 1982; Sullivan, Brake, Hofer, & Williams, 1986a; Sullivan, Hofer, & Brake, 1986b). This learning occurs naturally in the nest to the maternal odor, although the preference can also be acquired to a novel odor applied to the mother (Galef & Kaner, 1980; Roth & Sullivan, 2005; Sullivan, Wilson, Wong, Correa, & Leon, 1990; Terry & Johanson, 1996). Rapid odor learning may be a critical component of the altricial rat’s survival because a newborn rat has limited sensory input (olfactory, somatosensory) and depends on learning its mother’s odor for approach to the mother and nipple attachment (Polan & Hofer, 1999; Shair, Masmela, Brunelli, & Hofer, 1997). This period of unique odor learning ends at PN 10 and is called the sensitive period (Sullivan, Landers, Yeaman, & Wilson, 2000a; see lower Fig. 1 where learning is more adult-like). The second attachment characteristic defined by Bowlby is that infants will undergo considerable abuse while remaining attached to the caretaker. As is illustrated in Figure 1 (right, top), neonatal (PN6) rat pups learn to approach an odor even after pairing that odor with a painful stimulus (0.5 mA shock), although older (PN12; lower right) pups easily learn to avoid an odor paired with shock on the previous day (Sullivan et al., 2000a). Specifically, using a classical conditioning paradigm, pups exposed to an odor while receiving either a shock (0.5 mA) or tail pinch subsequently express a preference for that odor (Camp & Rudy, 1988; Moriceau & Sullivan, 2004b; Sullivan et al., 1986a,b, 2000a). This shock-induced learning and preference acquisition is not due to pups’ inability to feel pain, since shock threshold varies little during this period of development (Barr, 1995; Emerich, Scalzo, Enters, Spear, & Spear, 1985; Stehouwer & Campbell, 1978; Sullivan et al., 2000a).

While shock-induced preference acquisition may appear paradoxical, it may have developed to prevent pups from learning an aversion to the mother when being handled roughly in the nest. Indeed, rough treatment of pups by the mother is common in the nest. Mothers frequently step on pups when entering and leaving the nest or retrieve pups by a leg rather than at the nape of the neck. During these painful interactions, pups emit vocalizations associated with pain.
The benefits of a system preventing pups from learning an aversion to the mother are obvious since pups need to exhibit approach behaviors to procure the mother’s milk, warmth, and protection. Thus, in the altricial rat pup, the neonatal learning system seems specifically designed for attachment and is expressed behaviorally as an enhanced ability to acquire learned odor preferences and a decreased ability to acquire learned odor aversions (reviews—Hofer & Sullivan, 2001; Sullivan, 2001, 2003).

It should be noted that neonatal rats are able to learn aversive conditionings if an odor is paired with malaise (> 1.0 mA-strong shock or LiCl), since pups easily learn about interoceptive but not exteroceptive cues (Campbell, 1984; Haroutunian & Campbell, 1979; Miller, Molina, & Spear, 1990; Rudy & Cheatle, 1977, 1978; Spear, 1978; Spear & Rudy, 1991). However, while odor illness associations are easily learned by pups away from the mother, this learning is diminished if LiCl conditioning is done while pups are suckling (Martin & Alberts, 1979; Melcer, Alberts, & Gubernick, 1985).

During the sensitive period (PN1–9, age when pups show enhanced preference learning and attenuated aversion learning), neonatal rats are confined to the nest. It is appropriate to learn only preferences, not aversions, in a situation where only the mother and other pups are encountered. However, as the sensitive period terminates around PN10, walking develops and the probability of leaving the nest greatly increases (Bolles & Woods, 1965). At this stage of development, pups require a more complex learning system more suited to the extra-nest environment. As illustrated in Figure 1 (lower, PN12), the more mobile pup is more adult-like, with a discriminating learning system to deal with the increasingly complex environment. Specifically, aversions are more easily learned and odor preferences are less easily learned, enabling pups to deal more appropriately with stimuli outside the nest. As is reviewed below, the pup’s learning circuitry appears to show remarkable correspondence to its changing behavioral needs as its mobility increases.

### Long-Term Importance of Odors Learned in Infancy

In rats, early attachment-related odors appear to retain value into adulthood, although the role of the odor in modifying behavior changes from that used during infancy (attachment to the mother) to that used in adulthood (reproduction). Work done independently in the labs of Celia Moore (Moore, Jordan, & Wong, 1996) and Elliot Blass (Fillion & Blass, 1986) demonstrated that adult male rats exhibited enhanced sexual performance when exposed to the odors experienced in infancy. These results are consistent with observations in other species on the influence of early experience on adult mate preference, such as avian imprinting (Slagsvold, Hansen, Johannessen, & Lifjeld, 2002; Ten Gate & Vos, 1999).

### Neural Circuitry Underlying Neonatal Attachment Learning

It is curious that neonatal rats can be classically conditioned, since brain areas known to be important in adult learning may not yet be functional (e.g., amygdala, hippocampus, frontal cortex; Fanselow & Rudy, 1998; Nair & Gonzalez-Lima, 1999; Rudy & Morledge, 1994; Sananes & Campbell, 1989; Stanton, 2000; Sullivan et al., 2000a; Verwer, Van Vulpen, & Van Uum, 1996). Thus, the infant rat must use a different learning circuit from adults, presumably one designed through evolution to provide rat pups with the neural circuitry required to survive and optimize attachment to a caregiver (Hofer & Sullivan, 2001). Three brain structures have been shown to have a role in the neonatal rat’s sensitive period for heightened odor learning: the olfactory bulb, the noradrenergic locus coeruleus (LC), and the amygdala. The adult circuit for odor learning appears more complex and includes the olfactory bulb, piriform cortex, hippocampus, amygdala, and orbitofrontal cortex (Hess, Gall, Granger, & Lynch, 1997; Ramus & Eichenbaum, 2000; Roullet, Datiche, Lienard, & Cattarelli, 2004; Schettino & Otto, 2001;
Schoenbaum, Chiba, & Gallagher, 1999; Sevelinges, Gervais, Messaoudi, Granjon, & Mouly, 2004; Tronel & Sara, 2002).

**Olfactory Bulb**

In sharp contrast to learning in adult rats, neonatal odor learning produces changes in the olfactory bulb. The bulb is a simple structure with functional cell groupings called glomeruli that are intermediary between the input from the receptors on the olfactory nerve and the output via mitral cell dendrites. The glomerulus response in neonatal rats to an odor is modified after learning, with a corresponding change in the output signal of the olfactory bulb via the mitral cells. Importantly, this learning-induced olfactory bulb change occurs both naturally in the nest and in controlled learning experiments (McLean, Harley, Darby-King, & Yuan, 1999; Moriceau & Sullivan, 2004b; Sullivan & Leon, 1986; Sullivan et al., 1990; Wilson, Sullivan, & Leon, 1987; Yuan, Harley, & McLean, 2003; Yuan, Harley, McLean, & Knopfel, 2003; Yuan, Mutoh, Debardieux, & Knopfel, 2004; Zhang, Okutani, Inoue, & Kaba, 2003). As with the behavioral changes in attachment, the olfactory bulb neural changes described here are retained into adulthood and their acquisition is dependent upon experiences during infancy (Pager, 1974; Woo & Leon, 1988).

Recordings of mitral cells during learning indicate that the excitatory response of mitral cells to the CS odor continues throughout learning in the paired group (odor-reward), but habituation occurs in the control groups (Wilson & Sullivan, 1992). Molecular events within mitral cells during learning may provide insight into how the olfactory bulb response to the learned odor is permanently changed (McLean et al., 1999; Yuan et al., 2003; Zhang et al., 2003). Within minutes of acquisition, cAMP levels, induced by neurotransmitters binding, increase CREB phosphorylation (pCREB) and lead to changes in protein synthesis that allow a long-term CS-UCS association trace to form in mitral cells (Fig. 2). Research by the McLean and Harley group shows that manipulation of CREB directly alters learning induced molecular events; mutant CREB mice (too little CREB) fail to learn. This learning-induced cascade of molecular events has been identified in a wide variety of species across development, suggesting that the molecular biology underlying memory storage is highly conserved across both development and species (Carew, 1996; Carew & Sutton, 2001; Kandel, 2001; Rankin, 2002). However, while learning-induced intracellular events appear unchanged with development, as outlined here, the neural circuitry involved in olfactory memory shows marked changes with development.

**Locus Coeruleus (LC)**

The LC is a pontine nucleus and the sole source of norepinephrine (NE) for the olfactory bulb (McLean & Shipley, 1991; Shipley, Halloran, & De la Torre, 1985). In sharp contrast to the role of NE in neonatal learning, the LC is not necessary for adult learning, although NE enhances or attenuates memories during consolidation in adults (Roozendaal, Nguyen, Power, & McGaugh, 1999). In the neonate, the NE from the LC is both necessary and sufficient for neonatal learning. Related experiments found that an odor preference can be rapidly acquired by activation of olfactory bulb NEβ-receptors with isoproterenol paired with odor stimulation (Langdon, Harley, & McLean, 1997; Sullivan, Zyzak, Skierkowski, & Wilson, 1992) or by direct stimulation of the LC, the source of olfactory bulb NE (Sullivan, Wilson, Lemon, & Gerhardt, 1994; Sullivan, Stackenwalt, Nasr, Lemon, & Wilson, 2000b). Moreover, destroying the LC or preventing olfactory bulb NE receptor binding prevents neonatal odor learning (Sullivan et al., 1992, 2000b). While many other neurotransmitters have a role in neonatal rat learning, NE appears particularly important in learning-induced neural plasticity in development (dopamine-Weldon, Travis, & Kennedy, 1991; Zhang, Okutani, Yagi, Inoue, & Kaba, 2000; serotonin-McLean, Darby-King, Sullivan, & King, 1993; McLean et al., 1999;
Yuan et al., 2003; GABA-Okutani, Zhang, Yagi, & Kaba, 2002; Okutani, Zhang, Otsuka, Yagi, & Kaba, 2003; and opiates-Barr & Rossi, 1992; Kehoe & Blass, 1986; Roth & Sullivan, 2001, 2003). For example, within the olfactory bulb, NE is required for the maintenance of the prolonged mitral cell response necessary for acquisition of an odor preference and olfactory bulb learning-induced changes (Wilson & Sullivan, 1991). A similar role for NE appears to reemerge in adult olfactory learning critical for survival, such as mating and infant care (Brennen & Keverne, 1997; Fleming, O’Day, & Kraemer, 1999; Moffat et al., 1993; Okere & Kaba, 2000).

The LC’s changing role in learning appears to be caused by developmental changes in the LC. Neonates show prolonged excitation of the LC and it releases enormous amounts of NE compared to the level released after the sensitive period (Rangel & Leon, 1995). This decrease in NE release is controlled by functional changes in the maturing LC: (1) inhibitory α2 noradrenergic autoreceptors become functional and quickly terminate the LC’s excitatory responses to stimuli; (2) LC excitatory α1 autoreceptor function becomes limited and no longer temporally extends the LC’s response to sensory stimuli; and (3) decreases in electronic coupling of LC neurons limits the coordination of LC neuron firing (Marshall, Christi, Finlayson, & Williams, 1991; Nakamura & Sakaguchi, 1990; Nakamura, Kimura, & Sakaguchi, 1987; Winzer-Serhan & Leslie, 1999). Given these observations, we hypothesize that the hyperactivation of the LC before PN10 is responsible for enhanced odor preference learning, and that maturation of the LC signals the termination of the sensitive period for learning in rat pups.

Support for the role of the maturing LC terminating the sensitive period comes from a recent experiment from our lab (Moriceau & Sullivan, 2004a). As illustrated in Figure 3, the sensitive period for olfactory learning was reinstated after the sensitive period had terminated by recreating the autoreceptor characteristics of the neonatal LC. Specifically, a relative odor preference was acquired by PN 14 pups (post-sensitive period) when an odor was paired with LC pharmacological manipulations that reinstated the LC’s sensitive period low autoinhibition and high autoexcitation. This was done through activation of the LC by acetylcholine concurrently with the blockade of LC inhibitory autoreceptors (α2 antagonist, idazoxan) and activation of the LC excitatory autoreceptors (α1 agonist, phenylephrine) during an odor presentation. These data strongly suggest that the sensitive period, at least in part, is terminated through functional autoreceptor changes within the LC. Furthermore, these data also suggested that the olfactory bulb remains plastic in post-sensitive period pups since simply changing the LC autoreceptors (i.e., changing endogenous NE levels) was sufficient to induce an odor preference. We addressed this issue further by directly increasing olfactory bulb NE in post-sensitive period pups and again found odor preference conditioning. Specifically, an odor associated with bilateral olfactory bulb infusions of an NE β-receptor agonist produced a conditioned approach to that odor even after the end of the normal sensitive period. It should be noted that the olfactory bulb is still developing during the neonatal period (Guthrie & Gall, 2003; Malun & Brunjes, 1996).

### Amygdala

In the adult rat, the amygdala is important for the acquisition of the odor-shock induced odor aversion called conditioned fear (Cahill, McGaugh, & Weinberger, 2001; Fanselow & Gale, 2003; Fanselow & LeDoux, 1999; Fendt & Fanselow, 1999; Maren, 2003; McGaugh, Cahill, & Roozendaal, 1999; Pape & Stork, 2003; Pare, Quirk, & LeDoux, 2004). Evidence suggests that the lack of a functional amygdala during neonatal odor-shock conditioning may underlie pups’ difficulty in learning fear. First, behaviors associated with amygdala function emerge around PN10: inhibitory conditioning, passive avoidance and olfactory-conditioned aversions (Blozovski & Cudennec, 1980; Collier, Mast, Meyer, & Jacobs, 1979; Myslivecek, 1997;
Sullivan et al., 2000b). Second, amygdala lesions during the neonatal sensitive period (PN1–9) do not prevent the acquisition of an odor preference, although slightly longer training is required (Sullivan & Wilson, 1993). A similar lesion in the adult greatly retards fear conditioning, and the unique recovery traits of a neonatal amygdala cannot account for the dramatic differences in neonatal and adult amygdala lesions (Higley, Hermer-Vazquez, Levitsky, & Strupp, 2001; Maren, 1999). Third, the amygdala does not appear to participate in acquisition of odor-shock induced odor preference during the sensitive period (Fig. 4; Sullivan, 2001; Sullivan et al., 2000b). However, following the termination of the sensitive period, when odor-shock conditioning produces an odor aversion, the amygdala is involved in learning. Fourth, similarly to conditioned fear, unconditioned fear of natural odors does not emerge until PN10 when the amygdala begins to participate in the odor response (Takahashi, 1994; Wiedenmayer & Barr, 2001).

Immaturity of the amygdala may account for its lack of participation in neonatal sensitive period learning. Amygdala neurogenesis continues until PN14, although major nuclei subdivision occurs around PN7 (Bayer, 1980; Berdel & Morys, 2000; Berdel, Morys, & Macieiewska, 1997; Morys, Berdel, Jagalska-Majewska, & Luczynska, 1999). Synaptic development begins to appear around PN5 with a dramatic increase between PN10–20, reaching adult levels by PN30 (Mizukawa, Tseng, & Otsuka, 1989). Behavioral data on the development of amygdala-dependent behaviors suggest that sequential maturation of specific amygdala microcircuits may be important (Hunt & Campbell, 1999; Richardson, Paxinos, & Lee, 2002; Sananes, Gaddy, & Campbell, 1988). Specifically, freezing first emerges in the olfactory, auditory, and visual systems at PN10, 16, and 18 respectively. Learning ability for specific fear-related behaviors within a sensory system also emerges sequentially. In odor-fear conditioning, pups learn freezing, heart rate and startle at PN10, 15, and 21 respectively, whereas in visual fear conditioning, pups exhibit learned freezing, heart rate and startle at PN18, 23, and 30 respectively. Ontogenetic connectivity of the amygdala with motor-related neural areas may also play a role in the ontogenetic emergence of these learned behaviors.

The attenuation of odor aversion conditioning during the sensitive period may also be due to immature major neural connections between the amygdala and other brain areas important in conditioning. For example, amygdala-hippocampus connections are still undeveloped, and the primary cortical input to the hippocampus from the entorhinal cortex is still developing (Crain, Cotman, Taylor, & Lynch, 1973; Fanselow & Rudy, 1998; Nair & Gonzalez-Lima, 1999; Rudy & Morledge, 1994; Stanton, 2000). Furthermore, neonatal learning may not involve the cortex, and the frontal cortex is still undeveloped during this early neonatal period (Landers & Sullivan, 1999a,b; Verwer et al., 1996).

Sensitive Period Learning and the Hypothalamic-Pituitary-Adrenal Axis (HPA)

During stress, the adrenal gland can release corticosterone (CORT), but the early HPA system is limited in function, resulting in attenuated CORT release in response to shock during the neonatal sensitive period (Levine, 1962a). For example, while the adult rat responds to shock with a robust CORT response, the neonatal rat does not (Levine, 1962a, 2001; Van Oers, De Kloet, Whelan, & Levine, 1998). The attenuated neonatal CORT response appears to limit pups’ ability to express unlearned fear (predator odor), learned odor aversions (also called conditioned fear), passive avoidance and inhibitory conditioning. These behaviors normally emerge at PN10–11 (the end of the sensitive period) but can be delayed or advanced ontogenetically simply by removing the source of CORT or by prematurely elevating CORT levels (Bialik, Pappas, & Roberts, 1984; Blouzovski & Cudennec, 1980; Collier et al., 1979; review—Myslivecek, 1997; Takahashi, 1994; Takahashi & Rubin, 1993; Takahashi, Turner, & Kalin, 1991). Previous work has shown potent CORT effects on the neonatal LC, amygdala,
hippocampus, frontal cortex and HPA axis that last until adulthood using the maternal
deprivation paradigm (Dent, Smith, & Levine, 2001; Eghbal-Ahmadi, Avishai-Eliner, Hatalski, & Baram, 1999; Francis, Caldji, Champagne, Plotsky, & Meaney, 1999; Swiergiel, Takahashi, & Kalin, 1993). While CORT has strong effects on adult memory formation, its role in adult learning appears to be modulatory (McGaugh & Roozendaal, 2002). These data suggest that stress during early infancy may be capable of modifying the neural systems underlying attachment and hence the adult functioning of these brain areas.

Recent data from our laboratory support the hypothesis that CORT levels are critical in determining characteristics of early odor learning. We used our paradoxical odor-shock (0.5 mA) conditioning paradigm that produces an odor preference during the sensitive period (Moriceau & Sullivan, 2004b). Specifically, we assessed the effects of manipulating CORT levels on learning during the sensitive period (PN8 pups had their normally low CORT levels increased) or post-sensitive period (PN12 pups had their CORT levels decreased by adrenal gland removal at PN8). As is illustrated in Figure 5, injections of CORT (3 mg/kg, ip) 30 min prior to PN8 conditioning prevented the learning of a shock-induced odor preference and prevented the acquisition of the olfactory bulb learning-induced neural (enhanced 2-DG uptake) changes. Moreover, PN12 CORT-depleted (by adrenalectomy) pups demonstrated shock-induced odor preference learning and acquisition of the olfactory bulb neural changes. CORT replacement in ADX PN12 pups enabled pups to learn a shock-induced odor aversion and prevented the olfactory bulb learning-induced changes. These data suggest that low levels of CORT are critical to ensure neonatal rat pups’ attachment to their mother and that neonatal rat pups have unique learning abilities to ensure the olfactory-based attachment to the mother.

Furthermore, we were able to alter the developmental expression of unlearned fear (predator odor) through manipulations of the CORT system similar to those described previously (Moriceau, Roth, Okotoghaide, & Sullivan, 2004). As is illustrated in Figure 6, PN8 pups injected with CORT (3 mg/kg, ip) 30 min prior to presentation of adult male odor showed behavioral expression of fear through freezing and demonstrated activation of the basolateral complex of the amygdala (measured by Fos-positive cells). Also, PN12 CORT-depleting PN12 pups retard the normal expression of fear and the basolateral complex of the amygdalal does not appear to participate. These data suggest that low CORT levels block pups expression of fear (freezing) and attenuate amygdala activation.

Consequences for Adult Behavior

Early life experiences, including early attachment experiences, have an enormous impact on adult life in rodents, nonhuman primates, and humans (Denenberg, 1963; Harlow & Harlow, 1965; Levine, 1962b; Rosenzweig, Bennett, Diamond, Wu, Slagle, & Saffran, 1969; Schore, 2001). The documented overlap in brain areas associated with our attachment model, general early experiences, and later psychiatric problems strongly suggests that the neonatal effects are mediated through the LC, amygdala, cerebellum and HPA axis, as well as presumably nonfunctional neonatal rat brain areas such as the hippocampus and frontal cortex (Dent et al., 2001; Francis et al., 1999; Gutman & Nemeroff, 2002; Heim & Nemeroff, 2001; Kaufman, Plotsky, Nemeroff, & Charney, 2002; Levine, 2001; Perry, Pollard, Blakely, Baker, & Vigilante, 1995; Teicher et al, 1997). Together, these data suggest a potential mechanism for the enduring effects of early attachment on adult psychiatric wellness.

In summary, the present review outlines unique characteristics of neonatal learning that facilitate the infant rat’s attachment to the mother. Specifically, pups exhibit enhanced preference learning and attenuated aversion learning. Considering the necessity of infant maternal odor preference learning for survival (nipple attachment, huddling, orientation), it is
beneficial for pups to quickly learn a preference for the maternal odor and block aversion learning that would interfere with pups’ attachment to the mother.

This review also suggests that pups’ unique neural circuitry underlying infant learning may have evolved to ensure infants rapid attachment to the mother. This circuitry is not simply due to the absence or immaturity of brain structures but rather to the brain having unique characteristics: the olfactory bulbs encode learning, the noradrenergic LC is both necessary and sufficient for the preference learning, and lack of amygdala participation underlies pups’ attenuated aversion learning. This NE dependent learning is similar to the neural basis of other survival dependent behaviors in reproduction across species.

References


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FIGURE 1.
Mean number of CS odor choices (±SEM) in an olfactory Y-maze test. Pups were trained during the sensitive period (PN6) with pleasant odor-stroke conditioning (upper left) or aversive odor-shock (0.5 mA) conditioning (upper right), although pairings of either reward produced a subsequent odor preference at his early age. Older pups (lower), after the sensitive period (PN12), show more discriminating conditioning characteristic of adult animals; odor-stroke conditioning (lower left) was ineffective at producing an odor preference and odor-shock conditioning (lower right) produced a subsequent odor aversion.
FIGURE 2.
Schematic representation of olfactory bulb input from the noradrenergic locus coeruleus, which is important in inducing early olfactory learning. If the odor is paired with a reward, activation of NE (β-receptors increases cAMP levels, which combined with the high levels of Ca++, activates a cascade resulting in pCREB-mediated changes in gene transcription. These changes could result in odor-specific changes in mitral cell odor coding that would reflect the learned significance of the odor to the animal (Sullivan et al., 2000b; Yuan et al., 2003).
FIGURE 3.
Mean number of choices toward the CS odor (±SEM) during the Y-Maze test. To revert the older LC to the neonatal LC, during acquisition we infused the LC with acetylcholine (ACh) concurrently with $\alpha_1$ agonist (potentiates autoexcitation; phenylephrine) and $\alpha_2$ antagonist (prevents autoinhibition; idazoxan) during an odor presentation. This caused pups to subsequently express a learned odor preference compared with each of the control groups.
FIGURE 4.
Amygdala activity, as measured by 14C auto-radiography, of sensitive period pups (PN8) does not appear to participate in odor-shock conditioning and may underlie pups’ difficulty in learning odor aversions. Older pups, past the sensitive period, have an amygdala that participates in learning and easily form odor aversions (Sullivan et al., 2000a).
FIGURE 5.
Mean number of CS odor choices (±SEM) in an olfactory Y-maze test (left) and mean level of odor-induced olfactory bulb focal $^{14}$C 2-deoxyglucose uptake (±SEM; right). Pups were trained during the sensitive period (PN8; top) or after the sensitive period (PN12; lower) with odor-shock conditioning.
FIGURE 6.
Mean number of immobility/freezing responses (±SEM; left) and mean number of Fos-positive cells in the basolateral complex of the amygdala (±SEM; right). Pups were trained during the sensitive period (PN8; top) or after the sensitive period (PN12; lower).