SECTION 5

Emotion and temperament

Emotional processes are of basic importance to survival and to individual functioning in human and non-human animal species. They provide primary appraisals of the world that have been highly conserved in evolution. In the course of human development, these emotional processes come to interact with language and higher cognitive processes, providing layers of emotional complexity and subtlety seen only in humans. Emotional brain systems serve the functions of evaluating, avoiding and coping with threat and loss, yet they are also critically important in the development of conscience, prosocial behavior, cohesive social relationships and other adaptive behaviors. Emotions can also become dysregulated, leading to distressing and disabling emotional disorders. Individuals vary in their propensity to experience and express emotions, and these differences can be observed early in development in humans and other animals. Individual differences in emotionality are part of the area of study that we call temperament, and they provide a place to begin in the study of adaptive and maladaptive trajectories of human development.

Neuroscientific studies have begun to elucidate the brain structures, pathways and chemical processes involved in normal emotions and emotional disorders. In elegant studies of laboratory animals (LeDoux, 1996, 2000; Davis, Walker & Lee, 1998; Davis & Shi, 1999) researchers have begun to characterize the brain structures and pathways related to components of emotion, especially those involved in aspects of fear and stress. These include evaluations identifying potentially threatening sensory stimuli as emotionally significant, as well as autonomic and behavioral expressions of emotion.

Concurrently, in human developmental studies, remarkable links have been found between the emotions and the development of important social outcomes. For example, temperamental individual differences in fearfulness have been linked to the early development of conscience, with more fearful children showing stronger conscience development (Kochanska, 1991, 1995, 1997). Interactions between temperament and child rearing have also been found, indicating that children can reach the outcome of moral development via different routes, depending on their temperament and early experience (Kochanska, 1997). More fearful children benefit from parents’ gentle reasoning approaches, whereas less fearful children benefit from positive attachment relations in the development of conscience.

Several brain mapping studies have investigated regions of the brain that are functionally related to the evaluation of facial emotions. In one study, Blair, Morris, Frith, Perrett and Dolan (1999) found that when subjects viewed pictures of sad facial affect, cerebral blood flow in the left amygdala was directly related to the intensity of the expression. Previously, investigators had reported that persons with antisocial personality features have impairments in fear conditioning, fear-potentiated startle and the electrodermal response to distress cues (Blair, Jones, Clark & Smith, 1997). On the basis of these and other findings, Blair proposed that persons with antisocial personality features have early impairments in amygdala activity and responsiveness to distress cues, leading to an impaired violence inhibition mechanism. He suggests that moral socialization (i.e. the inhibition of violence and other forms of antisocial behavior) is less likely to be achieved through punishment (classically conditioned fear) than through the promotion of empathy (the response to distress cues in others). Parental gentle reasoning approaches as studied by Kochanska (1995) and others are particularly likely to make use of these empathic processes.

Recently, neuroscientific studies of laboratory animals and humans have begun to consider important developmental issues. In animal studies, early individual differences in vulnerability to fear and stress have also been identified (Adamec, 1991), with evidence that the stress experience itself can sensitize individuals to subsequent stress proneness who did not previously demonstrate strong fear and stress reactions (Adamec, 1997; Adamec, Kent, Anisman, Shallow & Merali, 1998). Thus, current work continues to demonstrate the necessity of considering environmental influences and their interaction with individual dispositions in the development of behavior patterns.

There is also emerging evidence of the influence of the environment on gene expression. Several of these studies have involved examination of the 5-HTT gene, where the short version is associated with impaired regulation of the neurotransmitter serotonin (Bennett et al., under
review; Champoux et al., in preparation). By identifying rhesus monkeys carrying the short versus long 5-HTT gene and varying their early rearing history, researchers have begun to show that deficits associated with the short version develop as a function of the rearing environment. When monkeys reared only with other baby monkeys are compared to those reared with their mothers, sometimes interactive and sometimes additive effects are noted.

For example, during the first month of life, for monkeys raised without mothers, short allele animals perform more poorly on tests of behavioral organization than long allele animals. When reared with mothers, however, their performance does not differ from that of long allele animals (Champoux et al., 1999). When dominance is examined in older monkeys, those animals with the short allele tend to be higher on the dominance hierarchy, as do animals reared with their mothers: here the gene and environment seem to add together to predict dominance. Alcohol drinking in adolescent monkeys falls somewhere in between. Monkeys with the short allele drink more than those with the long allele, but mother-rearing may temper the effect, although the statistical interaction only approached traditional levels of significance (e.g. p < 0.07). Thus, the predictive power of knowing whether the animal carried a short or long allele of the serotonin transporter gene appears to depend on the behavioral outcome and the rearing history. This compels studies of how genes come to be expressed over the course of development in interaction with the environments the individual experiences.

Emotion regulation has been found to be critical in human and animal developmental research. Self-regulatory abilities – whether they involve the regulation of physiology, emotion or behavior – have important connections to environmental input as well as to underlying physiological functioning. The study of self-regulation involves multiple levels of analysis, including the social level, as indicated in the rhesus monkey research. In animal research, alterations in opioid levels have also been found to influence animals’ social contact-seeking, soothability and social confidence (Martel, Nevison, Simpson & Keverne, 1995; Panksepp, Nelson & Bekkedal, 1997), and lowering of norepinephrine levels has been linked to increased risk for despair to social separations (Kraemer & McKinney, 1979; Kraemer, Ebert, Schmidt & McKinney, 1989, 1991). Finally, researchers of human children have produced evidence that both the child’s relationship with his or her primary caregiver and the caregiver’s observable behaviors contribute to the child’s patterns of emotion regulation (Tronick, 1989; Cassidy, 1994).

Scientific work on the emotions is proceeding on three broad fronts, each arising from a distinct intellectual tradition. The first tradition is the developmental study of emotion and temperament in infants and children, following the tradition of psychological research. This approach identifies ways in which the child differs from the adult, traces development of basic dispositions over time, and identifies both change and continuity in children’s characteristics. Historically, this area has lagged behind cognitive developmental research, but current interest in the topic is increasing.

The second approach follows cognitive science and neuropsychological traditions, focusing to date largely on adult human issues, and using modern brain imaging procedures (e.g. position emission tomography (PET), functional magnetic resonance imaging (fMRI), computational electroencephalography (EEG)) that highlight neural pathways for emotional processing. The research is recent and its contributions similarly have lagged behind a cognitive analysis. To date, few of the affective imaging studies have been conducted within a developmental framework.

The third intellectual tradition, emerging from behavioral neuroscience and psychobiology, has a longer history. It has largely focused on animal brain research, using a large number of direct manipulations. These include lesions, electrical stimulation (affecting cell bodies and fibers of passage), chemical brain stimulation (selectively affecting cell bodies), neural tract tracing, and psychopharmacological challenges. These studies have revealed specific circuits in generating emotional states and behaviors. Animal research appears to be particularly effective in relating specific brain structures, neuronal pathways and chemical processes to the dissociable components of emotion, including evaluation, and autonomic and behavioral expression. At the same time, it is important to recognize the limitations of animal studies. These include neuroanatomical differences among species, problems in making inferences about an animal’s psychological (especially conscious) state on the basis of its observed behaviors, problems in extrapolating from studies of fear to the full range of human emotions, the need to study distinctly human behaviors (e.g. psycholinguistic aspects of emotion), as well as the need to understand distinctly human emotional disorders.

In this section, we argue that efforts must be made to capitalize on complementary contributions of these different traditions and methods to the cognitive neuroscientific and developmental study of emotion, temperament and related disorders. In our view, a new research tradition is required where these three approaches – the developmental, adult and the animal –
can work together to yield a fully integrated developmental affective neuroscience. In addressing issues of synthesis, we are very much in need of better conceptual and research tools for the affective neuroscience of development. How can results of detailed animal research be translated to human functioning? How can research methods used with adults be properly applied to developing children? Opportunities for interdisciplinary training in developmental psychology and developmental neuroscience are also needed in this effort. Only a few programs are currently training neuroscience researchers to work with children on developmental questions and vice versa, and most of these do not include training in developmental psychology. A concerted training effort is needed to produce a cadre of developmentally sensitive neuroscience researchers. These and additional future directions will be elaborated at the conclusion of this report.

Progress in some aspects of the emotions has also been much more rapid than others. Research on the negative emotions, particularly fear and stress, is the most advanced. On the other hand, an understanding of the neuroscience and development of the positive emotions—affiliation, attachment and positive affectivity—and other aspects of negative affect, such as anger and sadness, have lagged behind. Because research on fear and stress is more advanced than research on the other emotions, we now briefly review theory, method and research in this area. In presenting this discussion of fear and stress, we note the importance of interactions across emotional systems and fundamental issues of emotion regulation, including social and attentional self-regulation, that are basic to advancing our understanding of temperamental and emotional development.

**Fear and stress research**

Fear research is well established in behavioral neuroscience and in many respects is closely aligned with ongoing stress research, in part because the systems share many neurochemical controls, such as CRF (corticotropin-releasing factor; Dunn & Berridge, 1990). The details of fear conditioning and stress responsivity that have been worked out at this level may have important implications for human research and therapeutic practice (Panksepp, 1990, 2000; LeDoux, 1996), and we elaborate methods and results of this research in this part of the report.

**Theories**

The neural circuits underlying fear and defensive behavior as studied in animal models involve multiple systems (LeDoux, 2000; see Figure 5.1). In conditioned fear, nuclei of the amygdala appear to play critical roles in evaluating the significance of threatening stimuli and orchestrating its behavioral, autonomic and neuroendocrine expressions. Information from sensory channels flows through the thalamus to the lateral nucleus of the amygdala. The lateral nucleus also receives projections from the hippocampus, subiculum and entorhinal cortex, as well as from many association cortical areas. From the lateral nucleus, information flow is through the basal and accessory basal nuclei of the amygdala, supporting conditioned aversion responses, and thence to the central nucleus.

The central nucleus of the amygdala (CEA) projects broadly to areas in the hypothalamus and brainstem that support defensive behaviors, including the central gray. Pathways through the central gray are thought to be important in the inhibition of response and pain suppression. Pathways through the lateral hypothalamus and parabrachial regions regulate sympathetic and parasympathetic activity, which together manage the balance of the autonomic nervous system. Pathways through the bed nucleus of the stria terminalis (BNST) terminate on the paraventricular nuclei of the hypothalamus (PVN) to regulate the production of glucocorticoids in response to threat. Combined, these influences on autonomic and hypothalamic–pituitary–adrenocortical systems link the central processing of threat with the orchestration and activation of hormonal stress systems (pituitary–adrenal and sympathetic–mediullary). Nonetheless, because stress hormones in the periphery regulate energy trafficking essential for supporting high affective arousal, the activity of these hormones is not specific to the fear system. However, research on the hypothalamic–pituitary–adrenocortical system has long been associated with research on fear and threat.

In addition to the pathways involved in orchestrating fear/stress, understanding individual differences in vulnerability to fear has also been a focus of research in neuroscience. Recently, much attention has been focused on corticotrophin-releasing hormone (CRH). This neuroactive peptide is released not only by the paraventricular region of the hypothalamus but also in many other brain regions. Indeed, the CEA is a major site for CRH activity where infusions of CRH are anxiogenic, and dysregulation of CRH systems has been proposed to play a role in a variety of stress-related psychiatric disorders, including anxiety, depression and eating disorders (Nemeroff, 1996; Rosen & Schulkin, 1998). From a developmental perspective, CRH hyperproduction is believed to play a central role in the suppression of physical growth through effects on growth hormone production observed in syndromes.
Figure 5.1 Neural pathways of conditioned fear (LeDoux, 2000).

such as psychosocial dwarfism (Johnson, Kamilaris, Chrousos & Gold, 1992; Uhde, 1994; Friess, Wiedemann, Steiger & Holsboer, 1995; Ghizzoni, Vottero, Street & Bernasconi, 1996). Two CRH receptor subtypes have been identified, with the first, CRH1, being expressed primarily in areas involved in fear and anxiety (Steckler & Holsboer, 1999). Specific agonists and antagonists for CRH1 differentially affect both conditioned and unconditioned fear behavior, while manipulation of CRH2a receptors tends to affect consummatory behaviors (e.g. sexual behaviors, feeding). However, CRH1 does not appear to only mediate fear/stress responding. These receptors are broadly distributed in the frontal cortex where they appear to also influence executive functioning, attention, and the conscious experience of emotion.

Early experiences related to the quality of care received by the infant appear to have long-lasting effects on the CRH system, perhaps helping to explain the combination of anxiety and diminished self-regulatory competence expressed by individuals reared in less than optimal early care environments (Heim, Owen, Plotsky & Nemeroff, 1997b). Notably, however, most of the research on CRH and on the hypothalamic–pituitary–adrenocortical system has been conducted in rodents. Research in primates suggests that elements of the CRH story may differ among species. For example, CRH1 predominates in the frontal cortex in the rat, but in rhesus monkeys it appears that CRH2 may be the major receptor in the frontal cortex (Sanchez, Young, Plotsky & Insel, 1999). Efforts to translate research on animals to studies of human development are sorely hampered by the lack of basic normative, descriptive studies of neurobiology, particularly developmental neurobiology beyond the prenatal period.

While attention has focused on the CRH system, the physiology of stress encompasses multiple systems. However, two systems are most intimately involved: the sympathetic–adrenal system and the hypothalamic–pituitary–adrenocortical system (Axelrod & Reisine, 1984). These systems support behavioral, as well as physiological, responses to threat (De Kloet, 1991). In the brain, stress and emotion systems overlap and interact. Stress systems are not, however, emotion systems, and the relations between their activity and emotional behavior differ depending on the organism’s developmental level, the nature of the threat or challenge, and the context. With regard to the CRH system, there is increasing evidence that extra-hypothalamic CRH and CRH in the PVN are differentially
regulated, with extra-hypothalamic CRH being much more closely associated with fear and anxiety (Coplan et al., 1996). Elevations in cortisol related to PVN CRH activity thus may or may not correlate with CRH activity in limbic and cortical regions regulating fear behavior. It follows that peripheral measures of stress physiology should not be employed as adjunct measures of emotion. These measures instead tell us about the physiological costs of adaptation to emotionally charged situations.

Temperament and early experience

In human developmental and temperament research, differences in the threshold for activation of fear circuits in the amygdala have been posited to underlie extreme variations in fear or inhibition to the unknown (Kagan, 1994), and fear has been a major topic of study in children’s temperament (Rothbart & Bates, 1998). Evidence that the activity of CRH (possibly operating through the CRH1 receptor) in the CEA and BNST plays a critical role in these fear circuits, together with evidence that elevated glucocorticoids may increase CRH activity in these areas, has led a number of researchers to posit that experiences shaping reactivity and regulation of the hypothalamic–pituitary–adrenocortical system may affect individual differences in the propensity to experience fear (Schulkin, McEwen & Gold, 1994; Heim, Owen, Plotsky & Nemeroff, 1997a, 1997b). Research in rodents and non-human primates suggests that early experiences may play a critical role, particularly those associated with variations in the amount and quality of early caregiving (Higley, Suomi & Linnola, 1992; Caldji et al., 1998; see review by Gunnar, 1998). There is also increasing evidence that these early experiences may be more critical for individuals who are genetically predisposed to heightened fearfulness (Fernandez-Teruel, Escorihuela, Castellano, Gonzalez & Tobena, 1997).

Most of the studies supporting this aspect of the early experience hypothesis have been conducted with rats. Beginning with studies of handling, this work has progressed to the point where the ‘maternal transducers’ are fairly well understood (Caldji et al., 1998). In rats, disturbances to the nest can affect how much the mother licks and grooms her offspring and the degree to which she adopts the arched back nursing posture. Manipulations that enhance these behaviors appear to shape a less reactive fear–stress system as the animal matures, while those that reduce these behaviors result in a more reactive fear–stress system. Natural variations among mothers, maintained over generations of offspring, have similar effects. In adulthood, compared to animals from high licking and grooming mothers, animals from low licking and grooming mothers exhibit a reduced number of glucocorticoid receptors in the hippocampus (presumably important in containing elevations in glucocorticoids to stressors) and increased CRH mRNA activity in the central nucleus, bed nucleus and brain stem areas regulating norepinephrine and peripheral sympathetic nervous system activity. The effects are also seen more for CRH1 than CRH2 receptors (Plotsky, personal communication, June 2000).

Similar effects of disturbances in primate maternal behavior have been observed among monkeys reared only with peers and monkeys whose mothers were subjected to unpredictable foraging demands during their first year of life, although the neurobiological information for primates is not as detailed (Coplan et al., 1996). Studies in humans are generally lacking, although there is one report on children reared under highly deprived conditions in orphanages in Romania which showed that, 6.5 years after adoption, cortisol levels across the day are elevated for these children compared to family-reared children or children from Romania adopted close to birth (Gunnar, 2000). Perhaps in a similar vein, studies of children, chronically abused (for years) during early childhood, who, in addition, have post-traumatic stress disorder of several years’ duration, also have elevated cortisol and epinephrine urinary excretion compared to low risk, psychologically healthy controls (De Bellis et al., 1999a). These children also exhibited significant differences in brain anatomy, having smaller cerebral volumes and larger ventricles, with these differences correlated with duration and age of onset of abuse (De Bellis et al., 1999b).

There is thus strong expectation that stress systems are fairly plastic early in life, and that early experience shapes stress reactivity and regulation (Meaney et al., 1996). The data contributing to this belief are largely from animals, and we are in great need of studies that can test whether these findings also apply to human development. If the animal work proves to have a bearing on the human case, however, this will support our concerns with providing adequately supportive care to infants and young children. Indeed, the animal data suggest that in depriving environments infants develop highly reactive stress systems that potentially pose risks for their later physical and psychological health.

Because the analogies to humans are provocative, it is tempting to view these animal models as reflective of the human condition. However, we simply do not know whether these rat models have implications for human children. The psychobiology of infant rats is very different from that of human infants. Rats are born less mature than humans. In particular, their brains are less
developed at birth. Despite having more mature brains at birth, human children also undergo a prolonged and extensive period of postnatal brain development (Black, Jones, Nelson & Greenough, 1998). The areas of the brain that develop the most postnatally are rich in receptors for cortisol (Steckler & Holsboer, 1999). It seems possible that the psychosocial regulation of cortisol postnatally in children will play a role in how their brains develop. Structures of most interest would be the hippocampus (involved in learning and memory), because of the well-documented effects of elevated cortisol on cell death; the amygdala and its connections to other brain regions (because of its documented role in fear and stress responding); the anterior cingulate (a brain structure in the frontal cortex involved in effortful attention and inhibitory control) which is also rich in cortisol receptors and shows a protracted period of postnatal development; and the frontal cortex.

Research on fear and anxiety is ripe for translation into studies of infants and young children. Many of the techniques used in the adult and animal work, such as fear-potentiated startle, can be effectively used with infants and young children (Schmidt & Fox, 1998). While we are limited in our ability to administer psychopharmacological challenges to children as we can with laboratory animals and informed and consenting adults, there may be opportunities to study the effects of clinically indicated medications in pediatric patients – at least to the extent that confounding variables, such as the patient’s illness, can be addressed. Rodent studies of early experience using high and low stress-reactive strains have shown that high stress-reactive strains are more sensitive to qualities of maternal care, with improved care resulting in the shaping of a less reactive/fearful neurobiology. Human research on extremely inhibited and uninhibited children indicates that high inhibition is less stable over early childhood than low inhibition (Fox, Henderson, Rubin, Calkins & Schmidt, 2001). This may indicate a similar sensitivity to qualities of the early care environment for the highly inhibited children. As this example indicates, and there are many others that could be used, the neuroscience literature on fear and early experience is ripe for intersection with our equally rich body of basic behavioral data on fearful temperament and its development.

**Adult imaging studies**

Brain imaging studies of the adult human brain have also begun to elucidate the structures, connections and chemical process involved in normal emotions (Benkelfat, Nordahl & Semple, 1990; Pardo, Park & Raichle, 1993; George et al., 1995; Mayberg, Liotti, Jerabek, Martin & Fox, 1995; Kosslyn et al., 1996; Lane, Reiman, Ahern, Schwartz & Davidson, 1997a; Lane, Reiman & Bradley, 1997b; Reiman et al., 1997; Schneider et al., 1997; Koepp et al., 1998; LaBar, Gatenby, Gore, LeDoux & Phelps, 1998; Lane et al., 1998; Lang et al., 1998; Whalen et al., 1998a, 1998b; Dougherty et al., 1999; Dolan & Morris, 2000; LeDoux, 2000; Reiman, Lane, Ahern, Davidson & Schwartz, 2000), the recognition of facial emotions (Sergent, Ohta, MacDonald & Zuck, 1994; Morris et al., 1996, 1998; Phillips et al., 1997) and emotional disorders (Reiman et al., 1986, 1989, 2000; Baxter, Phelps & Mazzotta, 1987; Buchsbaum et al., 1987; Mountz et al., 1989; Nordahl et al., 1989, 1990; Swedo, Schapiro & Grady, 1989; Benkelfat, Nordahl & Semple, 1990; Baxter, Schwartz & Bergman, 1992; Davidson, 1992; Drevets et al., 1992; Swedo, Pietrini & Leonard, 1992; Wik et al., 1993; Dager, Marro, Richards & Metzger, 1994; McGuire et al., 1994; Rauch et al., 1994, 1995, 1996; Bremner et al., 1995, 1997; Dager, Strauss, Marro, Richards & Metzger, 1995; Ketter et al., 1996; Shin et al., 1999).

In several PET and fMRI brain mapping studies, researchers have sought to characterize the neuroanatomical correlates of normal human emotion, to determine how the implicated brain regions are related to emotional type (e.g. happy, sad, disgust, fear, guilt, and anticipatory anxiety), emotional dimensions (e.g. valence and autonomic arousal) and the nature of the emotional stimulus (e.g. different kinds of unconditioned and conditioned simple sensory, complex sensory, interoceptive sensory and cognitive stimuli). For example, researchers have investigated the neuroanatomical correlates of film- and recall-generated primary emotions (Lane et al., 1997a; Reiman et al., 1997). Film- and recall-generated emotion were each associated with significantly increased cerebral blood flow, a marker of local neuronal activity, in the vicinity of medial prefrontal cortex and thalamus, suggesting that these regions participate in aspects of emotion that do not depend on the nature of the emotional stimulus. Film-generated emotion was associated with significantly greater increases in cerebral blood flow bilaterally in the occipito temporo parietal cortex (visual association areas) and a region that includes the anterior temporal cortex, amygdala and hippocampal formation (limbic and paralimbic areas in the anterior temporal lobe). Recall-generated sadness was associated with significantly greater increases in cerebral blood flow in the vicinity of anterior insular cortex (another paralimbic area, which has been functionally related to the production of several internally generated negative
emotions, including anticipatory anxiety and biochemically induced panic attacks, as well as the perception of temperature, pain and offensive tastes.

The researchers postulate that limbic and paralimbic areas in the anterior temporal lobe are preferentially involved in an evaluation procedure that invests exteroceptive sensory stimuli with emotional significance (among other things, serving as an external alarm center). In addition, the anterior insular region is preferentially involved in investing cognitive and interoceptive sensory stimuli with emotional significance (among other things, serving as an internal alarm center). Studies of laboratory animals and patients with lesions in medial prefrontal cortex implicate this region in the extinction of conditioned fear (Morgan, Romanski & LeDoux, 1993) and restraint from socially inappropriate emotions (Damasio, 1994). Thus, this region could be involved in the inhibition of excessive expressions of emotion or the monitoring of the individual’s emotional state in order to make personally relevant decisions.

Non-invasive brain mapping techniques could be effectively used to investigate the development of neural systems and cognitive operations involved in evaluating stimuli as emotionally significant, those involved in the inhibition of excessive emotions, and those related to the developmental neurobiology of affective, anxiety and phobic disorders. Since studies of sham rage in laboratory animals suggest that the cerebral cortex is critically involved in the inhibition of excessive emotions (Bard & Rioch, 1937), indicating that one or more cerebral structures participates in the individual’s inhibition of emotions, the developmental neurobiology of emotional inhibition and self-regulation may also be an especially ripe target for investigation in infants and children.

In brain mapping studies, researchers have investigated how different regions of the brain and related mental operations participate in dissociable components of emotion, including the evaluation procedures that label information as emotionally meaningful, the autonomic, facial and other behavioral expressions of emotion, and the conscious experience of emotion. For example, researchers used a selective attention paradigm and the International Affective Picture System (Lang, Bradley & Cuthbert, 1995) to investigate regions of the brain that are functionally related to the conscious experience of emotion (Lane et al., 1998). In comparison with selective attention to the spatial features of pictures (indoors, outdoors or indeterminate), selective attention to emotional experience (pleasant, unpleasant or neutral) was associated with increased cerebral blood flow in a brain region that includes the rostral anterior cingulate and medial prefrontal cortex.

Kihlstrom postulates that the difference that makes for consciousness is the connection between cognitive and perceptual processes and an integrated representation of the self that resides in working memory. If, like dorsolateral cortex, the medial prefrontal/rostral anterior cingulate region is involved in working memory, it could contribute to the conscious experience of emotionally significant information received from limbic and paralimbic connections. Non-invasive brain mapping techniques could be used to investigate the developmental neurobiology of emotional experience, considering how these and other emotional processes are involved in the developmental pathophysiology of alexithymia (a condition associated with emotional arousal in the absence of emotional experience). They might also consider how emotional learning in childhood might improve the capacity for intimacy, love, and the ability to adapt to adversity and stress (Lane, Nadel & Kaszniaik, 2000). Empathy has been documented to enhance prosocial behavior in children (Lennon, Eisenberg & Carroll, 1986) and to be important in the inhibition of violence (Blair et al., 1997, 1999).

Studies of children with and without a familial risk for antisocial personality disorder could confirm and further characterize the roles of amygdala dysfunction and hyporesponsiveness to distress cues in the developmental neurobiology of this disorder, further characterize the role of responsiveness to distress cues in moral socialization, and determine how empathy training (i.e. heightening children’s attention to the effect of their misbehavior on others) might bolster the violence inhibition mechanism and decrease the risk of antisocial behavior. It is important to note, however, that in developmental studies negative affect to the distress of others does not always lead to prosocial behavior. Empathic distress, when too intense, may be experienced as aversive, leading to a self-related focus and lower levels of prosocial behavior (Eisenberg & Fabes, 1990). These data suggest that interventions to promote an attentional focus on the needs of other rather than the self may be another important aspect of moral education.

Imaging studies of the adult human brain have provided new information about some of the brain regions functionally related to aspects of normal anticipatory anxiety and fear and those that are functionally related to the pathophysiology and treatment of anxiety and phobic disorders. To investigate the neuroanatomical correlates, PET was used to study patients before, during and after the anticipation of an electric shock (Reiman et al., 2000). After controlling for the potentially confounding effects of blood flow in the temporalsis muscles and the internal carotid arteries,
increases in cerebral blood flow were observed in the vicinity of anterior insular cortex, anterior temporal and temporoparietal cortex, a region that includes anterior cingulate and medial prefrontal cortex, caudate and thalamus, the cerebellar vermis and the midbrain. Since the anterior insular cortex has been implicated in brain imaging studies of anticipatory anxiety, lactate-induced panic, cholecystokinin-induced anxiety, the perception of temperature and pain, and taste, this paralimbic area could participate in the evaluation procedure that labels internal stimuli as potentially threatening.

As previously suggested, the anterior cingulate/medial prefrontal region could participate in the conscious experience of, attentional response to, or behavioral response to the anxiety-provoking situation. The researchers postulate that the cerebellar vermis, which has been implicated in several imaging studies of anxiety and experimentally induced anxiety syndromes, could participate in the behavioral response to the anxiety-provoking situation or cognitive features of anxiety that remain to be elucidated; and they postulate that the thalamus and caudate are involved in a basal ganglia–thalamic–frontal circuit that participates in the integrated expressions of anxiety. This study, as well as a study implicating anterior insular cortex in the response to aversive visual imagery (Kosslyn et al., 1996), illustrates how imaging studies can provide information about additional layers of emotional complexity (in this case, the emotional response to cognitive stimuli) that are difficult to study in laboratory animals and are especially relevant to the emotional lives of human beings.

To help bridge the gap between studies of fear in laboratory animals and humans, researchers used echoplanar fMRI to investigate the role of the amygdala in the acquisition and extinction of conditioned fear to a visual cue (LaBar et al., 1998). The amygdala/peri-amygdaloid complex was observed during both conditioned fear extinction and acquisition: the amygdala response during fear acquisition was correlated with autonomic measures, and the amygdala response during fear extinction was temporally graded. This study provides an excellent example of the opportunity to use imaging to help bridge the gap between studies in human and non-human species and it provides a foundation to begin relating studies of conditioned fear in laboratory animals to different forms of fear, anxiety and other emotions in adults and children.

Several studies have used imaging techniques to investigate regions of the brain that are involved in the predisposition to, elicitation of and treatment of anxiety syndromes. For instance, patients have been studied before and after the provocation of panic attacks, post-traumatic stress syndrome, specific and social phobic anxiety, and obsessive–compulsive anxiety syndromes. Non-invasive brain mapping studies in the developing child could further characterize how these and other brain regions are functionally related to the genetic and non-genetic predisposition to, natural history of, and possible prevention of these common, distressing and disabling psychiatric disorders.

**Methodological issues**

Many of the methodologies used in emotion studies were discussed in Section 2, including behavioral genetics (page 257), human imaging (pages 259–264), EEG asymmetry (pages 264–265), autonomic measures (pages 265–266) and fear-modulated startle (page 266). Additional methodologies are described below.

**Animal studies**

Studies of the neurobiology of emotions in laboratory animals have capitalized on (a) brain stimulation techniques (including electrical methods affecting both cell bodies and fibers of passage and chemical methods affecting cell bodies), (b) lesions (again including general electrolytic and more specific chemical methods) and (c) peripheral and central psychopharmacological and hormonal challenges that excite or inhibit neurochemically selective systems. In addition, there are a large number of routine biological correlates of emotion including (a) peripheral and central hormones and neurochemistries; and (b) brain recording of neural system activities, including EEGs, single and multiple unit recordings, and imaging techniques that provide information about brain activity (e.g. cFos visualization), which provides an overall estimate of neuronal fields activated; also (c) anterograde and retrograde neural tract tracing techniques can provide information about the connections between brain regions implicated in studies of emotion; and (d) a variety of neurochemical and molecular methods can be used to investigate how local neurotransmitter, neuropeptide, neuropeptide, membrane channels and intracellular events contribute to the neurobiology of emotion and other behaviors (e.g. immunocytochemical methods, in vivo and in vitro autoradiographic methods, and the measurement of gene expression through in situ hybridization).

In specific behavioral procedures, a variety of fear assays are used in animal studies. Techniques for the study of fear can be broken up into those that use classical aversive conditioning and those that do not, and the specific measures used may reflect learning or unconditional behaviors (for summaries see Panksepp, 1998a, 2000). The most common techniques are those
that use punishment and learned measures (including a
great number of avoidance and escape tasks). The next
most common are procedures that use punishment, but
observe the unconditional behaviors of animals (e.g.
freezing and flight in response to shock), or direct
stimulation of brain fear circuits (defensive burying of
shock prods, and startle responses to loud sounds). In
one of the most elegant and productive examples,
LeDoux (1996) and his colleagues characterized the
effects of selective brain lesions that follow the flow of
sensory information on a rat’s behavioral and auto-
nomic response (freezing and an increase in mean
arterial pressure, respectively) to classically conditioned
fear to simple sensory stimuli (e.g. a pure sound or a
flashing light). Davis and his colleagues, characterizing
the effects of selective brain lesions on the conditioned
fear-potentiated startle response, have used a similar
approach (Davis et al., 1998). Progress has also been
made in the study of spontaneous fear behaviors that do
not use strong punishments but rather employ animals’
tendencies to exhibit anxiety (e.g. freezing and dimin-
ished social and other appetitive behaviors) in the
presence of species-specific anxiety stimuli such as open
areas, bright lights, and the presence of predatory odors
(e.g. cat smell in rats), as well as their responsiveness to
novel stimuli.

Animal studies of conditioned fear, fear-potentiated
startle, and response to novel or noxious stimuli have
provided important information about the brain re-
gions, pathways and chemical processes that participate
in aspects of fear and anxiety. To capitalize on this
information in the study of human emotion, similar
elicitors and measurements of emotion need to be used
(when ethically and logistically possible) in the study of
human adults and children, with the findings from these
studies compared to other, more ecologically valid forms
of fear, anxiety and other emotions. Most assays of fear
in developmental research involve unconditioned beha-
viors in response to novelty or high intensity stimula-
tion. To date, there has been little study of learned fear
responses and their relation to unconditional fear
reactions in human development, and this is an area in
which more work is needed.

Human developmental studies

Developmental assays of the emotions include modifica-
tions of emotional facial expression coding methods.
These coding methods were designed to measure discrete
emotional states in adults (the Facial Action Coding
System; Izard, 1983) and Affex (Izard, Dougherty &
Hembro, 1983) use formulas derived from prototypical
adult facial expressions to categorize basic emotions in
young children. The Max measure also codes for
emotion blends.

Although the Max measures of joy and interest
appear to be differentiable early in life, several studies
suggest problems in differentiating the negative affects
in infancy (see review by Oster, Hegley & Nagel, 1992;
Matias & Cohn, 1993). The facial affect coding method
is also highly time and labor intensive, and there is
difficulty maintaining consistency across multi-site and
longitudinal studies (Cohn, Zlochower, Lien, Hua &
Kanade, 2000). However, recently attempts have begun
to develop a computerized automated face analysis that
might greatly facilitate coding of facial affect (Cohn et
al., 2000). Even when reliably measured, however,
facial coding systems do not take into account other
behavioral indicants of emotion such as positive and
negative vocalization and the child’s movement toward
or away from the stimulus. Other coding systems for
emotion measurement have attempted to take these
multiple channels into account (e.g. Lewis & Michael-
son, 1982; Rothbart, Derryberry & Hershey, 2000).

Developmental assessment of emotion in infancy has
also used measures of infant temperament, including
caregiver-report questionnaires (see reviews by Rothbart
& Mauro, 1990; Rothbart, Chew & Gartstein, in press),
teacher-report questionnaires, caregiver-report inter-
views and questionnaires, and direct observations of
temperament in the home or laboratory (see review by
Laboratory Temperament Assessment battery (LAB-
TAB; Goldsmith & Rothbart, 1991) uses multiple
episodes to elicit five different dimensions of tempera-
ment (fearfulness, activity level, anger proneness, inter-
est/persistence, and joy/pleasure). Laboratory measures
of the emotions in temperament studies are related to
parent-report measures, both concurrently and over
time (Bridges, Palmer, Morales, Hurtado & Tsai, 1993;
Rothbart & Bates, 1998; Goldsmith, Lemery, Buss &
Campos, 1999; Rothbart et al., 2000), although in one
recent study they were related to aspects of father report
only (Kochanska, Tjebbes & Forman, 1998).

Modification of measures applied to children of
different ages are required due to developmental
changes in emotion expression and effective elicitors of
emotion. Just as translations and mapping from animal
to human studies and from adult research to studies of
children are basic to developmental affective neuro-
sience, so appropriate translation of measures from one
human developmental period to another is a desider-
atum. For example, in the study of temperamental
behavioral inhibition, 21-month-olds’ responses have been coded for withdrawal, crying, clinging to the mother, facial indications of distress, and extended latency to approach a novel person or object (Garcia-Coll, Kagan & Reznick, 1984). Later in life, indices of behavioral inhibition have included slow approach to play with peers and response to the interviewer (Kagan, Reznick, Clarke, Snidman & Garcia-Coll, 1984).

Although some progress has been made in the development of emotion and temperament assays, research methods for the study of human emotion are in urgent need of further development. Without good behavioral measures of the emotions, neuroscience studies of the development of affect will be greatly hampered. For example, strong behavioral tools will be necessary to investigate links between gene and environment effects in molecular genetics work or in other basic neuroscience research. The tools are also necessary to characterize behavioral development of the emotions in a systematic way.

In developmental studies, fear is usually assessed through observations of infants or young children exposed to relatively unconditioned fear stimuli, such as intense and unpredictable mechanical toys, masks or a stranger approach (Goldsmith & Rothbart, 1991; Rothbart et al., 2000). Considerable stability of fear reactions is found between laboratory measures in infancy and mother reports of fear in middle childhood (Rothbart et al., 2000). Kagan (1998) and others have nevertheless questioned the use of parental reports, citing biases in parent perceptions. Laboratory observations, although free from potential problems of parental bias, are themselves also vulnerable to bias, in that the period of observation is short, the range of behaviors may be constricted, and there can be strong carryover effects from one measurement episode to another (Rothbart & Bates, 1998). Matheny and colleagues (Matheny, Riese & Wilson, 1985) argued in favor of multimethod assessments that include both laboratory and maternal assessments, and more research is currently being conducted that adopts such an approach (Calkins & Johnson, 1998; Kochanska et al., 1998; Goldsmith et al., 1999).

Cortisol measures

In addition to the human imaging, genetic and psychophysiological methods described in Section 2, adrenocortical activity has also been measured in plasma and salivary cortisol in studies of fear and stress. Cortisol is the hormonal end product of the hypothalamic–pituitary–adrenocortical system in humans, whose production varies fairly rhythmically during the course of the 24 h day/night cycle. Cortisol levels also change in response to both physiological and psychological elicitors, helping the organism mount a response to physical and emotional challenges (De Kloet, 1991). In using cortisol as a measure of stress or emotional reactivity, then, the aim is to compare changes in cortisol levels from basal to stressor conditions, with consideration to the activity of the diurnal system (Stansbury & Gunnar, 1994).

Measuring cortisol is a simple procedure (Kirschbaum & Hellhammer, 1989). Assays have now been adjusted to measure cortisol in small samples of free-flowing saliva (Riad-Fahmy, Read, Walker & Griffiths, 1982). Several reliable assays are available designed to operate on as little as 50 μl (literally a few drops) of saliva. Salivary flow rate has little measurable effect on the assay and, unlike measures of catecholamines, normal activity and movement do not affect cortisol concentrations (Kirschbaum & Hellhammer, 1994). Finally, cortisol is highly stable. As long as evaporation does not occur and mold does not grow, saliva can be left at room temperature for several weeks or more without affecting cortisol concentrations (Kirschbaum & Hellhammer, 1994). This means that subjects can collect samples at home, store them in their refrigerator and mail them to the laboratory for assay.

While salivary cortisol is relatively easy to measure, several types of error can enter into its assessment. The most common is to fail to control for the circadian rhythm in hormone production. Subjects need to be tested at the same time of day. Because of the severe restrictions this places on the researcher, those who are merely adding cortisol as an adjunct measure of emotion sometimes ignore this stricture. Across subjects, the difference between morning and afternoon, for example, does not correlate with baseline or response levels of cortisol. However, within subjects, higher baselines and smaller increases to stressors are typically observed earlier in the day. Stimulants used to produce saliva flow can also interfere with some assays because these typically lower the pH of saliva. Milk and milk-based products contain cortisol, and when these are present in the mouth they can affect assessment. There have been many studies of caffeine, nicotine and other substances that may affect circulating cortisol levels (see Kirschbaum & Hellhammer, 1989, 1994). Control for these substances is necessary in order to accurately measure cortisol production.

While cortisol can be measured in saliva, assessing other levels of the lateral hypothalamic–pituitary–adrenocortical axis requires more invasive procedures that limit their use in studies with children. Both adrenocorticotropin (ACTH) and cortisol can be
measured in plasma. CRH can be measured in cerebrospinal fluid, but this is feasible in humans only under very limited conditions. Numerous studies have shown that assessment of different levels of the system yield different information. Thus a pattern of low ACTH and normal cortisol levels is often observed in chronically stressed populations (De Bellis et al., 1994b). High ACTH influence on the adrenal results in enlargement of the adrenal’s capacity to produce cortisol. Maintenance of basal levels now requires less ACTH. Whenever feasible, it is preferable to assess both the adrenal and pituitary level of the system, and to use pharmacological probes to assess different levels of the axis.

CRH enhances fear-potentiated startle in animals. We do not know what effect stressors that elevate glucocorticoids and activate the CRH system have on EEG laterality or potentiated startle in children. While children cannot be given glucocorticoids solely for research purposes, the widespread use of steroids for their anti-inflammatory effects means that large numbers of children are taking steroids for medicinal reasons. Manipulations surrounding their use are feasible. Of even greater importance is the widespread use of glucocorticoids and glucocorticoid receptor antagonists in neonatology. Premature infants receive steroids to foster lung maturity (e.g. Garland et al., 1999) and drugs that occupy glucocorticoid receptors (e.g. spironolactone that acts on MR receptors; e.g. Young, Lopez, Murphy-Weinberg, Watson & Akil, 1998) to help dry out the lungs. All of these treatments should produce elevated levels of glucocorticoids during a period of time in human brain development that is most equivalent to the period during which early experience manipulations have been shown to affect later fear–stress system responsivity in the rodent (Vazquez, 1998). We know almost nothing, however, about how these treatments affect the development of the fear–stress system in humans. Randomized trials are feasible, because controversy exists over the most efficacious use of glucocorticoid-manipulating drugs in neonatology.

One of the more intriguing avenues for analysis that has not yet been mined is to link studies of caregiving and its role in modulating activity of the hypothalamic–pituitary–adrenocortical axis with electrophysiological studies (EEG asymmetry and emotion-modulated startle). There is now fairly strong evidence from several laboratories that secure attachment relationships block or prevent elevations in cortisol that would typically be observed when toddlers act frightened or distressed (Nachmias, Gunnar, Mangelsdorf, Parritz & Buss, 1996; Spangler & Grossmann, 1997; Spangler & Schiee, 1998). Similarly, the amount of focused attention and stimulation provided by the childcare provider for children 3–5 years of age influences whether cortisol levels increase over the childcare day or not, with these effects greater for children who are described as more negative in emotionality and poorer in effortful control (Dettling, Parker, Lane, Sebanc & Gunnar, 2000).

Both sets of findings allow one to hold ‘temperament’ constant and analyze the impact of elevated glucocorticoids. Because, once elevated, cortisol’s effects on the central nervous system are fairly prolonged, one could imagine manipulating glucocorticoid levels naturalistically and then testing children in the electrophysiological environment. These kinds of studies would contribute to our understanding of whether neurobiological models of early experience that emphasize the role of caregiving and later vulnerability to anxiety and depressive disorders can be translated from animal studies to the human case. Presumably, a secure attachment relationship or sensitive/responsive care, if it prevents or reduces elevations in stress hormones, may also reduce the stress sensitization of neural circuits involved in fear and defensive motivation.

The study of stress

There are some unique new ways to manipulate and monitor the consequences of rather modest stress experiences of animals, which may make such lines of research ethically more manageable: for instance, it is now recognized that a single instance of social defeat can result in remarkably long-lasting bodily and behavioral effects in rats (Ruis et al., 1999). Also, early stress can have long-lasting consequences on many aspects of brain and behavior of animals (Meaney et al., 1991; Ladd, Owens & Nemeroff, 1996; Heim et al., 1997a, 1997b). Detailing of such issues is an essential prerequisite for understanding intersystemic interactions.

In animal research, some of the most important future goals should be to determine the extent to which the vigor of stress-related systems can be modified by early experiences. The malleability of these emotional systems needs to be studied in detail at both neurochemical and neuroanatomical level. The most compelling long-term findings that could be translated to developmental studies come from animal kindling studies, where the sensitivity of affective systems to incoming stimuli can be increased by electrically stimulating specific emotional circuits. Recent data indicate that such effects can also be reversed by specific neurochemical maneuvers such as pre-stress administration of CCK antagonists (Adamec, Shallow & Budgell, 1997). The extent to which
such effects can occur in youth and extend into adulthood (Schmidt & Schulkin, 1999), the extent to which they are relevant to other aspects of emotion or emotional disorders, and how such tendencies can be reversed need to be studied neurobiologically (e.g. Fernandez, Bravo, Sanhueza & Inzunza, 1998; Caldji, Francis, Sharma, Plotsky & Meaney, 2000). At present, translations between basic animal research on emotional systems and human practice are tenuous at best. However, to help highlight how connections between basic neuroscientific knowledge of these systems and child emotional development can be achieved, the following perspectives may be useful.

It is now known that the long-term stress responsiveness of an organism is strongly related to maternal bonding/separation issues (Schmidt & Schulkin, 1999), but the details are rather surprising. For instance, rats exhibit a very modest glucocorticoid response to many, but not all, stressors beginning around postnatal day 4 and extending to postnatal day 14. Twenty-four hours of maternal separation, a dramatic threat to the pup's viability, result in different fear–stress system organization depending on whether the separation occurs at the beginning or near the end of this period. When stressed during the early neonatal period (3–4 days of life), animals exhibit an exaggerated stress response when they grow older. On the other hand, older neonates (11–12 days of age), who already show a vigorous stress response, exhibit comparatively less stress at an older age (van Oers, De Kloet & Levine, 1998). Thus, the long-term developmental consequences of neonatal stress can be diametrically different depending on exactly when the stress occurred (Heim et al., 1997b). Long-term changes in stress responsivity may have effects on how human emotions and cognitions interact later in life (i.e. early trauma that is not remembered may have subconscious long-lasting effects on adult personality), but no clear evidence is at present available on such issues.

We also need to be cautious in translating the specifics of this research to humans. The 3- to 5-day-old rat pup's brain is probably comparably in development to the infant during the last trimester of gestation (a time now included in the perinatal period because of our capacity to keep premature infants alive). In contrast, the 11- to 12-day-old rat pup may be more comparable to the human toddler or preschooler. However, whereas the rat pup on postnatal days 11–12 is beginning to emerge from the time when it is difficult to elevate glucocorticoids to many stressors, the human child at around 11–12 months is entering a period during which it is difficult to elevate them as long as the child has access to sensitive and responsive caregivers.

Thus, much translational activity is needed to understand the implications of the elegant rodent work for human development.

**Relations of fear to other systems**

Interactions among fear and other emotional systems are bound to be extensive simply from anatomical considerations (Bandler & Keay, 1996; Panksepp, 1998b; McDonald, Shammah-Lagnado, Shi & Davis, 1999), but a great deal of fundamental work characterizing each of the basic emotional systems needs to be conducted before these interactions can be discussed in any detail. For example, it is reasonable to expect that producing stressful negative affect, whether it be specific forms of anger or fear, or more generalized forms of negative arousal, would be expected to modify all other positively motivated appetitive behavior.

Fear and anger are also expected to influence one another. On the one hand, fear is viewed as being important in the socialization of anger expression, while on the other hand fear can foster hostile behavior that serves a protective function. Both fear and anger are associated with threats to well-being and are capable of activating peripheral systems that increase metabolism and support fight/flight responses. Distinguishing between fear and anger using peripheral physiological measures is often not easy, and simple dichotomies (NE associated with anger, E with fear) have not proven useful. Similarly, factor analyses of questionnaire temperament/personality instruments with scales for anger and fear result in both negative affects loading on the same factor in childhood, although the two constructs appear to be more differentiated in infancy (Rothbart & Bates, 1998). Whether this reflects an overlapping neurobiology or merely a functional relationship is not known.

One way to differentiate these affects is to use different eliciting situations in the laboratory, e.g. novel and intense stimuli for fear, and goal blockage for anger. These responses in infancy differentially predict parent-reported fear and anger in middle childhood (Rothbart et al., 2000). Facial expression coding has also been devised to distinguish fear and anger in infants and young children, as noted above. However, both fear and anger can elicit crying. Situations that are expected to produce fear, such as maternal separation, can elicit intense crying. Facial coding schemes applied to such data have identified anger as the emotional response. Whether this is the case, or whether intense crying produces facial configurations that no longer distinguish the emotional elicitor of distress is not known.
Both fear and anger affects are expected to play a motivational role in orchestrating responses to threat. Threat of harm is seen as the basis for fear, while threats to goal attainment constitute a basic elicitor for anger. Perception of threat and the degree of threat perceived should be affected by expectancies about outcomes, which in turn depend on one’s resources for managing threat. Both development, as it affects knowledge and behavioral competencies, and experience, as it affects expectancy, threat appraisal and the individual’s coping responses, should influence the nature of the stimuli, thresholds for activation, and intensity of negative affect experienced.

Caregivers constitute the infant and young child’s primary resource for managing threat. Emotional expressions serve a communicative function, often serving to mobilize and orchestrate responses of caregivers. Early in development it is assumed that emotional behavior is more or less reactive, while later in development children are believed to use emotional expressions more instrumentally to gain the resources they need to manage threat. This may mean that children come to associate the expression of fearful affect in the presence of a responsive caregiver with removal of the threat or actions that protect and calm the child. Similarly, in responsive caregiving environments, children may come to associate the expression of anger with the removal of the offending stimulus and/or responses from caregivers that support the child’s attempts to overcome obstacles and achieve goals. Either way, emotional expression may become dissociated from activation of the physiological responses necessary to manage threats that overwhelm coping resources. Dissociation between negative emotional expressions and peripheral measures such as cortisol and adrenaline production are often found, particularly in the context of secure emotional relationships. This suggests that the analysis of the neurobiological substrates of fear and anger needs to be undertaken with an eye to the child’s history of care, the nature of the child’s adaptations, and consideration of the contextual cues that might influence children’s expectations of adult aid.

Attentional orienting is related to the expression and experience of negative emotionality. In some instances, the ability to control attention allows infants to moderate distress. For example, Johnson, Posner and Rothbart (1991) found that 4-month-old infants’ ability to disengage visual attention in the laboratory was related to maternal reports of the child being less susceptible to negative affect and distress to limitations, and being more soothable. Harman, Rothbart and Posner (1997) found that infants’ orienting had a soothing effect, but only for as long as the distracting stimulus was presented. Rothbart, Ziaie and O’Boyle (1992) also found that infants often look away from locations they find distressful. Individual differences were also found, with disengagement of attention related to lower distress and higher smiling and laughter in laboratory measures. Moderate relations have been reported between differences in reactivity and the tendency to sustain attention (Rothbart, 1981; Ruff, 1988). Ruff and Rothbart (1996) suggest that infants who are prone to distress might be less attentive than infants who are not. Therefore, children who show negative emotionality as a temperamental trait may have the most difficulty controlling their attention as a regulatory strategy.

More effort directed toward addressing issues related to fear and stress is likely to greatly enhance our understanding of other emotional systems and the nature of their interactions with fear and stress. These systems include anger, positive affect and affiliation. Finally, a study of attentional systems and their interaction with emotions will be critical to our understanding of emotional development. We now consider some of the challenges in seeking new knowledge in each of these areas.

Other emotional and temperament systems

Anger

In comparison with fear and stress, the level of neuroscientific knowledge for anger systems is modest, and there has been comparatively little investment in working out the fine details of aggression systems. This research is particularly timely, however, given societal concern about the tragedy of violence in young children. In human research, much observational work has been done on the development of anger and aggression in children (Coie & Dodge, 1998; Mascolo & Griffin, 1998). In animals, Panksepp (1998a) describes rage or anger as involving neurocircuits that run from medial areas of the amygdala through the stria terminalis to the medial hypothalamus to the periaqueductal gray. As such, this circuitry overlaps with pathways mediating peripheral glucocorticoid and epinephrine production. This is not surprising because rage, particularly if it motivates attack, would require activation of the peripheral stress hormones involved in the fight side of the fight/flight system that support heightened energy use, preparation for wounding, and shunting of blood to muscles.

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Reviews of research on early-onset behavior problems suggest critical links to emerging self-regulatory capacities and the ability to exert self-control in a variety of social and non-social contexts (Campbell, 1995). Behavior problems may be rooted in problematic behavioral and emotional control and negative temperament (Caspi, Henry, McGee & Moffitt, 1995). Research focusing on precursors of behavior problems has emphasized negative affect in infancy and childhood (Calkins & Dedmon, 2000). Early research studies focused on undifferentiated negative affectivity (Bates, Maslin & Frankel, 1985). However, there is evidence that at least two stable behavioral patterns of negative affectivity are observable in infancy. One such pattern may be characterized by anger, low tolerance for frustration and high heart rate variability (Stifter & Fox, 1990; Braungart-Rieker & Stifter, 1996); a second pattern is marked by withdrawal, fear, low heart rate variability and right frontal EEG asymmetry (Kagan, Reznick & Snidman, 1987; Fox, 1989; Calkins & Fox, 1992; Calkins, Fox & Marshall, 1996).

These two types of negative behavior may differ in origin and may lead to very different behavioral outcomes later in development (Fox & Calkins, 1993). One outcome for fearful infants is in the direction of shyness and internalizing problems (Kagan, Reznick & Snidman, 1988; Calkins & Fox, 1995). In contrast, recent data on anger reactions in older children demonstrate relations to later externalizing-type behavior problems (acting-out, aggression, impulsivity) and difficulty in peer interactions (Eisenberg, Murphy, Maszk, Smith & Karbon, 1995). Increased understanding of anger and its relation to self-regulation may allow development of programs and preventive parent training that will lead to better regulation of anger and aggression. As previously suggested, it would be helpful to consider the differential roles of punishment (i.e. classical conditioning) and empathy training (i.e. enhancement of Blair’s (1997, 1999) violence inhibition mechanism by promoting attention to distress cues in others) in the primary prevention, secondary prevention and treatment of antisocial personality features.

Positive affect

The study of positive emotional systems will also be an important growth area in the new field. This work in humans has very recent origins. In psychology, for example, the field of ‘positive psychology’ is currently establishing itself as a domain of study (Seligman & Csikszentmihalyi, 2000). In these authors’ words, ‘research on positive emotions and behaviors allows us to recognize that: ... psychology is not just the study of pathology, weakness and damage; it is also the study of strength and virtue. Treatment is not just fixing what is broken; it is nurturing what is best. Psychology is not just a branch of medicine concerned with illness or health; it is much larger. It is about work, education, insight, love, growth, & play’ (p. 7).

In animal research, however, a good deal of work has been done on positive, appetitive brain systems. At present, one can divide research in the area into three general categories.

(1) Positive affects emerging from appetitive behaviors: there is growing consensus for a distinct positive appetitive motivational system in the mammalian brain. Some have called it a behavioral activation system (Gray, 1982), a wanting system (Berridge & Robinson, 1998), a behavioral facilitation system (Depue & Collins, 1999), and others the expectancy/seeking system (Panksepp, 1998a). All agree that dopamine is a key component of this system (Ikemoto & Panksepp, 1999). The positive affect correlates that can be detected in human frontal EEG asymmetry studies (e.g. left frontal arousal in positive emotions) described in Section 2 may reflect this same dimension.

(2) Positive affects emerging from receipt of reward and ensuing consummatory responses such as eating and sexual activities (Berridge & Robinson, 1998; Pfaff, 1999).

(3) Positive affects emerging from basic playful interactions (Panksepp, Siviy & Normansell, 1984; Vanderschuren, Niesink & Van Ree, 1997; Pellis & Pellis, 1998).

In complex and at present poorly understood ways, issues of drug abuse appear to be closely related to some of these systems (Berridge & Robinson, 1998; Wise, 1998; Ikemoto & Panksepp, 1999).

A large number of procedures are available to study the neural substrates of appetitive motivation, ranging from the standard approach of intracranial self-stimulation at electrode sites along the trajectory of the ascending mesolimbic dopamine systems, to various measures of arousal of this system, most prominently single neuron activity profiles (Schultz, 1998), in vivo voltametry and dialysis procedures (for summary see Ikemoto & Panksepp, 1999), as well as direct intracranial administration of specific neurochemical agents (McBride, Murphy & Ikemoto, 1999). Currently, PET and, to a lesser extent, single photon emission computed tomography (SPECT) can provide information about the characteristics of several neurotransmitters (e.g. the dopamine D2 and transporter receptors, the serotonin 5-HT1a and 5-HT2 receptors, cholinergic muscarinic...
receptors, benzodiazepine receptors and opiate mu receptors). The dopamine transporter receptor is relevant to the study of reward and drug addiction. PET can also provide indirect estimates of synaptic neurotransmitter concentrations, including dopamine, acetylcholine, serotonin and endorphins. Combining the latter technique with a cognitive-activation paradigm, Koepf et al. (1998) demonstrated increased synaptic concentrations of dopamine in the striatum as adult human subjects performed a rewarding video, thus providing a link between neurochemical studies of reward in humans and laboratory animals.

While PET, SPECT and other imaging techniques associated with radiation exposure have limited applicability to the study of infants and children, other techniques (e.g. model tasks, see Section 2) may be able to bridge the gap between neurochemical studies in adults and other kinds of studies in children. Complementing these neurochemical studies, there are a host of behavioral measures including the analysis of motor activity and sniffing patterns in rodents (Rossi & Panksepp, 1992) and various novelty seeking and place preference measures (Schechter & Calcagnotto, 1993).

In human developmental studies, one of the three broad factors emerging from factor analytic work has been labeled surgency (Rothbart, Ahadi, Hershey & Fisher, in press). With primary loadings from scales assessing positive affect and anticipation, activity level, and impulsivity, surgency is related to both externalizing behavior problems and prosocial helping. In the laboratory, infants’ latency to approach objects and their smiling and laughter are positively related, and these laboratory measures predict later surgency as measured by parent report (Rothbart et al., 2000).

Affiliation
Attachment/affiliation research is a growth field in behavioral neuroscience, and has the potential to yield major breakthroughs in our understanding of affiliative emotional processes, especially the neurophysiological and neurochemical nature of the secure base and separation distress, both of which are essential for a detailed understanding of social bonding (Panksepp, 1981; Panksepp, Siviy & Normansell, 1985; Kalin, Shelton & Barsdale, 1988; Kalin, Shelton & Lynn, 1995; Keverne, Nevinson & Martel, 1999). The analysis of separation distress mechanisms started with the opioid theory of social attachment (Panksepp, Herman, Villberg, Bishop & DeEskaínazi, 1980; Panksepp, 1981), which, across the years, has garnered substantial support (e.g. Kalin et al., 1988, 1995; Keverne et al., 1999). More recently it has been expanded substantially to include many other neurochemical systems (Panksepp, Normansell, Herman, Bishop & Crepeau, 1988), most prominently those based on the neuropeptide oxytocin. Maternal behavior systems of the brain have been studied in rodent models (Numan, 1994; Fleming, O’Day & Kraemer, 1999). At the same time, developmental research drawing upon attachment theory has stressed the role of maternal sensitivity and subsequent child strategies as playing a formative role in the development of emotional regulation (Cassidy, 1994; Sroufe, 1996; Gunnar, 1998). Brain imaging studies, which could be applied to the study of non-human primates and adult humans, may provide additional information about the neuroanatomical and neurochemical correlates of attachment.

Effortful control
By the time they are 5 or 6, children have come a long way in developing the ability to regulate their expression of the emotions. Some of this developing regulatory capacity probably reflects the development of frontal lobe functioning as discussed in ‘Control processes’ in Section 3. Behavioral research on emotion regulation, however, suggests that experience also plays a role, and we are beginning to understand the factors of early experience and adult caregiving associated with better emotion regulation. The intersection of these two points suggests critical studies, including (1) correlational studies linking tasks assessing functions such as effortful control to children’s emerging emotion-regulatory competence, and (2) research examining whether experiences that enhance emotion regulation also enhance the frontal functions that we presume help mediate the regulation of emotions.

Recent approaches to the study of individual differences in temperament during infancy and early childhood have conceptualized these differences in terms of variability in both emotional reactivity and attentional self-regulation (Rothbart & Derryberry, 1981; Gunnar, Porter, Wolf, Rigatuso & Larson, 1995; Stifter & Braungart, 1995; Calkins & Johnson, 1998). In infancy, the child’s success at regulation depends heavily on the parent’s sensitivity and responsivity to emotional expression and the child’s need for intervention. During infancy and early childhood, children gradually acquire the necessary emotion-regulation skills and strategies that enable them to cope with a variety of developmental challenges (Kopp, 1982, 1989; Tronick, 1989; Cicchetti, Ganiban & Barnett, 1991). The ability to use self-regulating behaviors becomes critical as the child is gaining independence, control and an identity separate from the caregiver. This development appears to be supported by the maturation of executive attentional
mechanisms, particularly the anterior attention system (Posner & Rothbart, 1998) involved in children’s effortful control of action and emotion.

Temperament, defined as individual differences in emotional and attentional reactivity and self-regulation, includes individual differences in attentional effortful control (Rothbart & Bates, 1998; Kochanska, Murray & Harlan, 2000). Model tasks for the assessment of effortful control have been adapted from adult neuroimaging studies to assess children’s performance in conflict situations (Carlson & Moses, 2000; Kochanska et al., 2000; Berger, Jones, Rothbart & Posner, 2000; Gerardi-Caulton, 2000), requiring children to inhibit a dominant response in order to perform a subdominant response. Children’s performance on these tasks has been linked to emotional and behavioral regulation and to performance on theory of mind tasks, as well as to children’s development of conscience. Although it is believed that effortful control begins to emerge at the end of the first year of life, its active development continues through the preschool years and into adoles-
cence (Casey, Giedd & Thomas, in press), and additional developmental research on attention and attention–emotion interactions will provide a major contribution to developmental affective neuroscience. Functional brain imaging studies find increased activity in medial prefrontal cortex, which could possibly reflect the inhibition of excessive emotion (Lane et al., 1997b; Reiman et al., 1997). Studies of Phineas Gage and others with medial frontal lobe damage report that they appear to have difficulty monitoring their emotional responses in order to make personally relevant decisions (Damasio, Grabowski, Frank, Galaburda & Damasio, 1994).

Functional brain imaging studies frequently find increased activity in lateral prefrontal cortex during the performance of difficult force-choice tasks, perhaps related to the active inhibition of the inappropriate choice in order to make the correct response. Several functional brain mapping studies suggest that anterior cingulate cortex can be subdivided into a more anterior affective region, which is involved in the processing of emotional information and the production of normal

![Diagram](image_url)

**Figure 5.2** Areas of activation and deactivation in the anterior cingulate during the processing of cognitive and emotional tasks (after Bush, Luu & Posner, 2000).

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and pathological emotions, and a more posterior cognitive region, which is involved in cognitively demanding tasks, divided attention tasks, working memory and motor response selection (Bush, Luu & Posner, 2000) (Figure 5.2).

In a structural MRI study of older children, the size of the right anterior cingulate cortex was correlated with their ability to inhibit a prepotent response (Casey et al., 1997a), and in a fMRI study, activity in the anterior cingulate cortex in children and adults was correlated with the number of false alarms (Casey et al., 1997b). As noted above, anterior cingulate cortex can be subdivided into more anterior affective and more posterior cognitive regions (Bush et al., 2000). Together, imaging, lesion and cognitive studies promise to clarify how the divisions of the anterior cingulate cortex work in concert with other brain regions to regulate behavior, and how they evolve during the course of human development. Studies are needed to further clarify the role of these frontal lobe regions and other brain structures, chemical processes and cognitive operations in the inhibition of excessive emotion, the relationships among emotion, emotion-monitoring and decision-making, rational decision-making, and their development.

As noted above, behavior problems may be rooted in problematic behavioral and emotional control and negative temperament (Caspi et al., 1995). Calkins and Dedmon (2000) report that aggressive 2-year-olds display patterns of both behavioral and physiological regulation in laboratory situations that differ from their non-aggressive counterparts. Recent data on anger reactions in older children also demonstrate relations between anger management strategies and later externalizing-type behavior problems (acting-out, aggression, impulsivity) and difficulty in peer interactions (Eisenberg et al., 1995). These studies suggest that the temperamental dimension of anger may be related to subsequent externalizing behavior problems through the failure to develop self-regulation behaviors that might modify early negativity. Similarly, research on fear and inhibition suggests that poor regulation of that affect may be linked to shyness, internalizing disorders and anxiety (Fox, Schmidt, Calkins, Rubin & Coplan, 1996; Kagan & Snidman, 1999; Schwartz, Snidman & Kagan, 1999). Increasing understanding of self-regulation through attention and effortful control is thus of great societal importance.

Summary

This section reviews how the emerging field of developmental affective neuroscience promises to shed new light on the neural systems, cognitive operations, and the genetic and environmental factors involved in the regulation of emotion and temperament. It will also contribute to an understanding of the pathogenesis, treatment and possible prevention of emotional disorders, as well as normal behaviors such as attention, decision-making and empathy, in which aspects of emotion and temperament may play an important part.

Much progress has been made in understanding the fear system as expressed in animals and human beings. Temperamental differences in such dimensions as fear, smiling and laughter, and effortful control have proven to be measurable, and to shed light on the development of underlying mechanisms.

To fulfill the promise of this area we recommend an investment of resources in (a) the area of human emotional development research, with a strong emphasis on instrument development, (b) the areas of affective brain imaging and cognitive models, (c) the area of animal research, and (d) perhaps most critically, the effort to bridge existing gaps between each of these areas. Promising areas of inquiry include, but are not limited to, the study of positive affect, fear, the inhibition of excessive or inappropriate anger, sadness, affiliation, the interaction between emotion and attention, and factors that may be involved in the vulnerability to and possible prevention of emotional-related disorders.

We support an investment in (i) the training of developmental scientists who understand the components, capabilities, limitations and complementary roles of methods used in these areas and who can translate this understanding into productive research; (ii) developmental scientists who will create, test and apply techniques to permit the translation of findings across each of these areas (e.g. the development of common elicitors and markers of emotions in laboratory animals, human adults and human children); (iii) developmental researchers involved in the interrelated areas of emotion, attention, decision-making and self-regulation; (iv) scientists in the areas of imaging, cognitive modeling and animal research whose primary focus is not development but who demonstrate the commitment to help translate their research to the field of affective developmental neuroscience and help train affective developmental neuroscientists; and (v) developmental scientists who will translate new findings from these areas and others (e.g. genetics) into the creation and testing of programs that modify maladaptive emotionally relevant behaviors (e.g. antisocial activities and addictive behaviors), promote adaptive emotionally relevant behaviors (e.g. empathy and mature interpersonal relationships) and reduce the risk of emotion-related disorders.


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