PRIMATE NEUROETHOLOGY

Circuits of emotion in the primate brain

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ABSTRACT (~250 Words)

Circuits of emotion comprise a multitude of subcortical and cortical structures of the primate brain, and can be conceptualized as a series of nested circuits. The core circuit of emotion contains structures that are mainly subcortical and phylogenetically older. These structures initiate autonomic and motor responses associated with the expression of emotion. Changes in attention and vigilance are also intrinsic components of these responses. Structures overlaying the core circuit (i.e. intermediate structures) are fully or partially corticalized, and phylogenetically newer. They combine information about external stimuli with internal signals, producing a single representation that contributes to the evaluation of and response to emotional events. Several additional structures are incorporated into an extended emotional circuit that provides further information to intermediate structures about the emotional content of stimuli, expected outcomes, and contextual contingencies that determine behavioral options under changing circumstances.

The amygdala - a structure central to emotional processing – is comprised of nuclei associated with core or intermediate circuits. The centromedial (subcortical) nuclei are among the core structures; they are closely linked to autonomic and somatic effectors. The basolateral (cortical) nuclei are part of the intermediate structures that evaluate the emotional significance of incoming stimuli, modulate attention and memory in affiliate cortical structures, and signal the appropriate behavioral options to core structures. Examples of the dissociation between core and intermediate nuclei of the amygdala are described.

The picture that emerges when evaluating these nested loops is that, regardless of phylogenetic age, structures are recruited to aid in the evaluation of - and behavior towards - stimuli that are meaningful for that species. The outcomes of evaluation are borne out in immediate behaviors and in long term changes such as memory formation and trait changes in levels of stress or anxiety. Together, the nested circuits that enact short and long-term changes in the individual underlie the complex social repertoire of primates.
I. Introduction

Emotions are coordinated brain-body states that allow animals to cope with the challenges of their physical and social environment. Emotional states are characterized by a specific configuration of inputs (triggering events), outputs (autonomic and somatic responses), and the neural processes that mediate their transformation. Many emotional states, especially acute states such as fear or anger, are coupled with enhanced perceptual processing, decision making, action selection, and increased energetic expenditure.

The brain-body state triggered by a threatening facial expression, a common event in the daily life of a macaque, exemplifies the phenomena ascribed to emotion. When a mid-ranking male monkey is confronted with a threat, the covert autonomic and overt behavioral responses that are triggered by observing this display are the results of a complex process of evaluating the emotional and social significance of that display given the present internal state of the viewing monkey. This evaluation takes into account the identity of the displaying monkey; he is recognized as a dominant male, with a well-groomed, muscular body, red-pigmented face, and large, symmetrical canines. The display is directed to the closest ally of the viewer. Based on this evaluation, the viewer decides whether to flee the scene of an imminent confrontation, or to rush to defend his ally. For either action, the autonomic system sets the organism in a “higher gear”. The animal is more vigilant, the sensory threshold for threat-related stimuli is lowered, reaction time is shortened, and widespread sympathetic effects lock the internal organs in a functional mode biased toward energy expenditure.

A completely different brain-body state is triggered by an affiliative approach, signaling the intention to groom. Such an approach, especially if there is a history of affiliative interaction between the players, leads to relaxed postures, accompanied by vagal tone, increased levels of oxytocin, and often by gestures of reciprocation.

The behavioral outcomes of brain-body activation are not unique to a particular emotion; the initiating factors of emotions and the internal states they generate are much more diverse than the relatively limited behavioral repertoire available for their expression. The autonomic and behavioral expressions of emotions are therefore, low-dimensional and highly reproducible across situations and individuals. In contrast, the stimuli that evoke emotional expressions are often high-dimensional, and their emotional content dependent also on context and the emotional states preceding the stimulus. In light of the contrast between the extremely rich array of stimuli that can generate emotions and the restricted set of expressive affordances, the central process of evaluating the emotional significance of all stimuli and events encountered by the organism is essentially a process of dimensionality reduction.

This dimensionality reduction takes place in nested circuits, in which phylogenetically older regions form a core circuit (Fig. 1). The core circuit is localized primarily in the brainstem and midbrain and produces low-dimensional output (e.g., heart rate and blood pressure can increase or decrease, other effects, such as piloerection, sweating, pupil dilation, contraction of various muscles, etc., also have few degrees of freedom). Additional circuits are superimposed on this core. They encompass subcortical and cortical areas that carry out complex computations on high-dimensional inputs, but ultimately funnel their outputs through the core structures. In this framework, the core structures elaborate low-dimensional affordances based on a limited set of stimuli (e.g.,
defensive behaviors towards predators) while the outer circuits elaborate high-dimensional internal states to deliver the optimal behavioral choices (e.g., learning that one can attack the member of a rival group only when the attack cannot be witnessed by those who could retaliate).

Conservation of the phylogenetically old, core structures does not imply that they perform the same, ‘old’ functions across extant species; rather, the emotional brain of primates can be thought of as a palimpsest in evolutionary terms. Even the function of homologous structures across species may have been co-opted for new or species-specific purposes. Thus, even as we refer to core structures that are conserved across vertebrates, mammals, or primates, their functions may vary according to species-specific, ecological and ethological demands.

The first section of this chapter will identify the main structures that comprise the emotional circuits of the primate brain. The second section describes what is known about the neural basis of emotional processes, from the association of stimuli to positive or negative outcomes, to the interplay between the perception and expression of social signals. Reflecting the biases in the literature, our descriptions will emphasize the macaque genus, and the function of the amygdala, the most highly connected component of the emotional brain (Young et al., 1994).

II. The organization of emotional circuits

A. Core structures

Core structures are those whose activity generates a relatively restricted array of emotional responses (autonomic or somatic) via short pathways that link inputs to outputs. These include: sensory, motor, and autonomic centers of the brain stem, the periaqueductal gray (PAG), the deep layers of the superior colliculus, the hypothalamus, and the centromedial (subcortical) nuclei of the amygdala (Fig 1).

Sensory, motor and autonomic centers of the brainstem

All the afferent signals from the sensory organs of the head and body (with the exception of olfaction) and all the viscerosensory signals from the internal organs converge in the brainstem. Several complex behaviors such as foraging, feeding, flight and fight, response to pain, and reproduction can be initiated and maintained from the level of the brainstem alone (Blessing, 1997). Heart rate, respiration, digestion, elimination, even immune function is coordinated directly from the brainstem. The brainstem also contains a reticular system that plays an important role in vigilance and behavioral activation in response to both emotional and neutral stimuli. Based on the collateral signals it receives from all the ascending sensory pathways, the reticular system generates a tonic output projected toward the cortex (Blessing, 1997).

Several neurotransmitters that are produced in the brainstem determine emotional traits and mediate emotional states, either by direct-synaptic or modulatory activity. The levels of norepinephrine (NE), produced in the locus coeruleus of the brainstem are increased during vigilance, anxiety, acute fear, and other forms of emotional stress. When levels of serotonin (5-HT), secreted by the raphe nuclei are low, animals are more aggressive and/or depressed. Dopamine (DA), a neurotransmitter associated with reward
and pleasure, is produced by the ventral tegmental area and substantia nigra. The gigantocellular nuclei of the reticular formation produce acetylcholine (Ach) that maintains the excitability and coherence of activity across multiple cortical areas. A bundle of axons carry these and other neurotransmitters from the brainstem to the cortex; these axons form the medial forebrain bundle that terminates in the prefrontal cortex but gives out massive collaterals to the hypothalamus (Fig. 1B). The hypothalamus, therefore, registers the level of vigilance through NE, the presence of rewards through DA, and other signals related directly to the activity of the brainstem monoaminergic neurons.

Of particular importance for emotions are two nuclei of the brainstem: the nucleus of the solitary tract (NTS) and the parabrachial nuclei (Fig. 1D). The NTS is the main visceral sensory nucleus that contains an elaborate viscerosensory map of the body. This map and the “feeling of the body” contained wherein, is broadcast to higher cortical areas (e.g. the insula and anterior cingulate cortex) where internal sensations are associated with external stimuli. Ascending fibers from many cranial nerves report to the NTS the state of all internal organs of the head and body; these signals are either transformed in the NTS into descending commands targeting sympathetic and parasympathetic effectors that coordinate autonomic reflexes, or are transmitted via the thalamus to higher cortical centers. The parabrachial nuclei regulate respiration but they also receive visceral sensory information and information about pain and temperature. The majority of emotional states are associated with changes in respiration that are controlled, in part, by the parabrachial nuclei. Stimulation of this area causes a rapid inhale followed by apnea – a gasp (von Euler and Trippenbach, 1976), a typical respiratory behavior for surprise, pain, fear, etc.

The brainstem, therefore, is both a relay for higher-level centers of emotion and a first stage processing center that elaborates species-specific somatic and autonomic behaviors in situations of importance.

Periaqueductal gray (PAG)

The PAG has important sensory and motor functions in emotion. It is a major integration and descendent modulatory center of the pain pathways, but also a key center that engages the autonomic nervous system (Bandler et al., 2000) in conjunction with the brainstem centers mentioned above. A few important ethological functions distinguish the PAG from the brainstem centers, namely, its role in vocalizations and aggression.

Species-specific vocalizations are coordinated via the PAG, as demonstrated by electrical stimulation (Jürgens, 1994). This is achieved by indirect control of the laryngeal and respiratory muscles via the reticular formation of the brainstem, (Davis et al., 1996). Motor commands for vocalization are initiated in the PAG under descending input from the orbital and medial prefrontal cortex. These two prefrontal systems are also linked to PAG activity during maternal perception of their offspring (Bartels and Zeki, 2004). Prefrontal projections contact discrete regions of the PAG that, in turn, connect to different regions of the hypothalamus, forming parallel loops that link higher cognitive aspects of emotion and social behavior, with expressive and homeostatic/regulatory components of the core circuit (Bandler et al., 2000).

Aggression related to rage and defensive behaviors is coordinated jointly by the PAG and the lateral hypothalamus. The PAG is not involved, however, in attack
associated with predation. Complex local neural and pharmacological mechanisms regulate the level of aggression within the PAG. The neural networks that coordinate different forms of aggression are reciprocally inhibitory and the output of each network is potentiated or dampened by different neurotransmitters: glutamate generally enhances, while opioid peptides typically dampen aggression (Gregg and Siegel, 2001).

A fascinating but unsolved problem in primate neuroethology is the neural site and mechanism of establishing the connections between social status and aggression. Given the fluctuating status of males in a macaque society, the links between rank and aggression is expected to be highly flexible. Serotonin levels and the efficiency of serotonin transporters have been invoked as the major determinants of trait aggression, but state aggression appears to be regulated by prefrontal-PAG/hypothalamic-brainstem mechanisms relying on a different set of neurotransmitters and steroid hormones.

**Superior Colliculus (SC)**

A central role of the SC is to guide and modulate visual orientation. The SC contains sensory, motor, and multimodal maps that control the initiation and execution of saccades (for an early review, see Sparks and Hartwich-Young, 1989). In addition to its sensorimotor function, the deep layers of the SC are a critical node in the core circuit of in emotion and social behavior.

Electrical stimulation of the rodent SC elicits orienting responses and species-specific defensive behaviors, and in some cases approach behaviors (Dean et al., 1989). Stimulation also causes changes in respiration, blood pressure and heart rate (Keay et al., 1988), reduces pain threshold (Redgrave et al., 1996), and causes desynchronization of the cortical electroencephalogram (EEG), which is the cortical signature of heightened attention and vigilance. These autonomic responses might be produced via the bidirectional connections of the SC with the PAG, and with the motor and sensory nuclei of the brainstem. The SC may trigger the re-allocation of visual attention in response to emotionally salient stimuli via connections with the amygdala and the mesencephalic reticular formation, involved in the elaboration of eye movements. Indeed, lesions or local infusion of neurotransmitter antagonists in the SC block fear-potentiated startle (Waddell et al., 2003; Zhao and Davis, 2004).

Compared to rodents, where the neural circuitry and pharmacology of colliculus-dependent defensive and anti-nociceptive effects have been worked out in detail, little is known about how these pathways function in primates. Recent work indicates that bicuculline-mediated disinhibition of the SC in monkeys increases defensive emotional reactivity (Cole et al., 2006), and decreases species-specific social behaviors (Ludise Malkova, personal communication). This outcome is only partially overlapping with the outcome of the same manipulations in the amygdala, indicating that the role in social behavior of these two structures is not entirely redundant.

Finally, the SC has been implicated in detecting emotionally salient visual stimuli without the contribution of cortical visual pathways. A strong argument in favor of this proposal comes from ‘blindsight’ patients and animals with uni or bilateral visual cortical damage. Subjects report being unaware of stimuli, yet are able to navigate visual obstacles, produce defensive movements in response to looming stimuli, and detect or even discriminate visual stimuli, including threatening images of facial expressions (Stoerig and Cowey, 1997; de Gelder et al., 1999; Morris et al., 2001; Liddell et al.,
One of several proposed pathways for these preserved abilities includes the SC, the pulvinar, and the amygdala, which show functional connectivity in neuroimaging experiments and the predicted processing deficits when lesioned (Morris et al., 1999; Morris et al., 2001; Vuilleumier, 2003; Ward et al., 2005). A colliculo-pulvinar pathway might be important for vision early in development (Wallace et al., 1997), enabling rapid orienting and vigilance toward sudden, potentially dangerous stimuli, but may be less efficient for calculated responses to complex visual arrays. Although blindsight patients are notable for their lack of awareness of their intact visual abilities, these parallel visual pathways may normally function under conditions of visual awareness (Pessoa et al., 2005).

**Hypothalamus**

The hypothalamus is a collection of nuclei concerned primarily with homeostasis through autonomic and endocrine mechanisms, but it also coordinates basic, drive related behaviors, e.g., feeding, reproduction, aggression. Many of these functions, especially those that involve species-specific “instinctive” behaviors coordinated by central pattern generators are redundant and overlapping with similar functions controlled by the brainstem. A unique contribution of the hypothalamus in emotion is related to hormone production: the arcuate nucleus controls neuroendocrine function, the supraoptic and paraventricular nuclei release oxytocin and vasopressin (hormones of affiliation and social bonding) and corticotropin releasing hormone that initiates a cascade of events to supply cortisol in situations of emotional stress.

The hypothalamus receives input from the brainstem and spinal cord via the medial forebrain bundle (Fig. 1B). These inputs carry signals about the state of all internal organs. Intrinsic sensory neurons in the hypothalamus are specialized to sense the composition of the internal milieu and correct reflexively any deviation from normal.

Like the brainstem, the hypothalamus contains networks of neurons that often form patterns generators and control behavioral, endocrine, and regulatory functions. These networks are under the influence of higher centers. For example, inputs from the amygdala signal the emotional value of a stimulus or event, and can trigger, when appropriate, the classical stress response via the hypothalamic-pituitary-adrenal (HPA) axis. Descending inputs from the amygdala, anterior cingulate cortex (ACC), and prefrontal cortex modulate the role of the hypothalamus in territoriality, aggression, the desirability of food, mates, etc. Reward-related signals from the ventral tegmental area, and nucleus accumbens, but also from the orbitofrontal cortex (OFC) and anterior cingulate, mediate reward-based learning and action selection. Inputs from the reticular formation, the basal forebrain (nucleus basalis), and the bed nucleus of the stria terminalis contribute to the control of attention and vigilance. The majority of these connections are reciprocal, closing loops that combine the internal state of the organism with the external stimuli and initiate (or block), basic, drive-related behaviors (Appenzeller and Oribe, 1997).

**The subcortical nuclei of the amygdala**

The amygdala contains a heterogeneous collection of nuclei with dissociable functions. Together these nuclei carry out the evaluation of stimuli, the initiation of autonomic and somatic responses most appropriate for each stimulus, and the modulation
of the ‘gain’ of perceptual, motor, and memory processes associated with emotional stimuli.

The subcortical nuclei are connected primarily with subcortical structures and are involved in attention and autonomic functions. The central and medial nuclei, but also the anterior amygdaloid area and the bed nucleus of the stria terminalis (BNST) are part of the subcortical group (Amaral et al., 1992). These nuclei receive and send projections from and to the hypothalamus and the brainstem and via these connections control autonomic function. For example, the amygdala modulates heart rate and cardio-respiratory reflexes via connections to the dorsal motor nucleus of the vagus and the nucleus of the solitary tract. Facial expressions are controlled by direct projections to the lower motor neurons in the facial nucleus (Fanardjian and Manvelyan, 1987). Likewise, salivation, lacrimation, respiration, pupil dilation, pain perception, etc., are modulated by direct connections with the respective centers of the brainstem. Finally, the amygdala can modify the output of all major neurotransmitter systems originating in the brainstem: direct projections from the central nucleus to the VTA influences dopamine release (Gallagher, 2000); projections to the locus coeruleus set the level of vigilance and cortical “preparedness” via widespread projections that release norepinephrine over the entire cortex (Amaral and Sinnamon, 1977); direct projections from the central nucleus to the nucleus basalis of Meynert, influence acetylcholine levels in the brain (Davis and Whalen, 2001). Finally the central nucleus emits projections to the hypothalamic areas where pro-hormones and releasing factors are synthesized.

B. Intermediate structures

Compared to the core, these structures elaborate the representations of stimuli and stimulus combinations that are evaluated in these circuits, and label them with emotional valence. The outputs of the intermediate structures are higher-dimensional than the outputs of the core structures; they control somatic and autonomic effectors via the core structures. The high-dimensional representations generated by these structures are shared with multiple neocortical areas involved in attention, perception, memory, and decision making. Note that intermediate structures do not overlap with the classical concept of the “limbic system” (Maclean, 1949). The intermediate structures include the basolateral (cortical) nuclear group of the amygdala, the mediodorsal nucleus of the thalamus, the insula, the anterior cingulate cortex (ACC), and the orbitofrontal cortex (OFC).

Amygdala, basolateral complex

The cortical nuclei of the amygdala, also called the basolateral complex, contain neurons of cortical type and receive and send connections primarily from and to the neocortex. One role of these nuclei is to evaluate the emotional significance of stimuli. These nuclei receive highly processed sensory information from all sensory modalities (Amaral et al., 1992; Stefanacci and Amaral, 2002). Olfactory signals arrive from the piriform cortex, gustatory information from the insula, somatosensory, auditory, and visual information from association cortices in the parietal and temporal lobe. Coarsely processed sensory information also arrives here directly from the thalamus (Romanski and LeDoux, 1992). Viscerosensory signals in the amygdala come from the insula or
from the nucleus of the solitary tract. Based on these inputs, which converge with inputs from the medial and orbital prefrontal cortex, the cortical nuclei of the amygdala determine the positive, negative, or neutral significance of all stimuli. The outcome of this evaluation is sent back to the cortex via widespread feedback projections (Fig 1A). Output projections reciprocate the inputs but also project to multiple stages of sensory processing, including primary sensory areas, e.g., area 17, or V1. These nuclei also project to the subcortical nuclei of the amygdala, which, in turn, project to autonomic and somatic effectors. Signals from the amygdala modulate attention, perception, and memory and are carried by excitatory connections that terminate in the layer II of the neocortex. There, they compete for synaptic sites with adjacent or more distant cortical areas (Freese and Amaral, 2006).

Mediodorsal nucleus of the thalamus

The mediodorsal thalamus (MD) is an obligatory station in the higher-level interconnections of emotion circuits (Jones, 2007). This nucleus connects the prefrontal intermediate structures – the ACC and OFC – to other emotion-related areas. Its positioning as a ‘nexus’ for the other intermediate structures may account for its known role in object–reward association memory (Gaffan and Parker, 2000).

The insula

The insula is a good example of the diversity and redundancy of functions carried out by the core and intermediate structures of the circuits of emotion. The insula is both the primary cortical center of taste and smell, and a major source of autonomic regulation, redundant with the autonomic functions of the brainstem. In addition, the insula integrates interoceptive signals, pain, and somatosensory stimuli such as various kinds of touch, and re-maps the surface of the body in terms of the quality of stimuli (Augustine, 1996). Social stimuli are also processed in the insula; e.g., facial expressions of disgust, and the “trustworthiness” of faces - stimuli that also activate the amygdala (Phillips et al., 1997; Winston et al., 2002; Engell et al., 2007). Based on these rich inputs, the insula generates a representation of the internal state of the body in which somatic and visceral components are fused and ultimately give rise to empathy, general disposition, and mood stability (Singer et al., 2004).

The anterior cingulate cortex (ACC)

Whereas the insula has mainly sensory and autonomic functions, the anterior cingulate cortex (ACC) hosts both executive and cognitive functions based on extero- and interoceptive signals arriving from the insula, brainstem, basal nucleus of the amygdala, hypothalamus. In addition, certain areas of the ACC (24, 25 and ventral 32) receive strong inputs from the mediodorsal nucleus of the thalamus. All subregions of the ACC receive inputs from the anterior thalamic nuclei (Vogt et al., 1987) that receive, in turn, input from the mammilary bodies of the hypothalamus – a memory-related structure. The diversity of inputs is mirrored by a diversity of functions within the ACC (for review, see Bush et al., 2000; Joseph, 2000).

Among these functions are the control of visceral, skeletal, and endocrine outflow in response to emotional stimuli. The outflow of the ACC targets the amygdala, periaqueductal gray, and several cranial nerve nuclei in the brainstem (V, VII, IX, and
Via the output to the brainstem nuclei, emotional states set up in ACC translate into changes of heart rate, blood pressure, and into vocalizations associated with expressing internal states (e.g., crying, moaning). Note that species-specific vocalizations are also controlled by the periaqueductal gray of the brainstem.

Like the PAG and the insula, the anterior cingulate cortex also functions as a pain center. Compared to the insula where bodily sensations such as pain are mapped according to their subjective quality, the pain representation in the anterior cingulate is more abstract. The same areas of the cingulate cortex are activated by social pain (the feeling of being ignored or rejected) and by physical pain. Finally, mother-infant interactions are also under the influence of a division of the anterior cingulate.

Cognitive functions mediated by the ACC include reward anticipation and social decision making. The control signals for these functions originate from dorsal areas of the anterior cingulate that contain a motor region. The motor region influences motor areas of the brainstem and spinal cord, thereby contributing to the selection of the most appropriate action pattern.

**Orbitofrontal cortex**

Based on patterns of connectivity, the orbitofrontal cortex resembles the amygdala, a structure to which it is also reciprocally connected. High-level sensory inputs from all modalities converge there, and the outputs target the core structures of the emotion circuits including the hypothalamus (from which it also receives inputs) and brainstem autonomic areas.

The orbitofrontal cortex may exert control over the output of the amygdala by way of projections to the intercalated nuclei of the amygdala (for review, see Barbas, 2007). The intercalated nuclei separate the basolateral (cortical) groups of nuclei from the centromedial (subcortical groups) through their GABAergic interneurons. These interneurons may inhibit the transfer of signals from the basolateral complex to the centromedial nuclei, thus blocking the initiation of autonomic responses (Pare and Smith, 1993; Rempel-Clower, 2007). The recently described functions of intercalated nuclei (Likhtik et al., 2008) might explain why a snake in the outdoors is more fear-producing than when experienced in a terrarium. In theory, the orbitofrontal activity could prevent the basolateral signal of danger from activating the central nuclei, ‘heading it off at the pass’, thereby eliminating unnecessary behavioral and autonomic responses.

Collectively, the intermediate structures show partially-overlapping, yet complementary functions. For example, the connectivity of the ACC and OFC suggest that both process reward signals in conjunction with internal and external stimuli and both can influence autonomic and somatic responses that contribute to normal social and emotional behavior. There are important differences, however, between these two areas in terms of their contribution to the evaluation of stimuli and the elaboration of responses. Whereas the ACC integrates reward-related signals with species-specific motor behaviors, the OFC learns to associate and dissociate internal and external stimuli and rewards. Together, they form a unit critical for bringing into register the internal and external state of the world with behavioral choices, the building blocks of emotion and social decision making.
C. Affiliate structures

Affiliate regions are primarily neocortical and are more strongly connected to the intermediate structures than to the core structures. They are capable of processing complex, high-dimensional signals, linking multiple aspects of emotion, such as memory, decision making and action planning to ongoing stimuli and events. Compared to the core and intermediate structures, their role in generating autonomic and reflexive emotional outputs is less direct, often demonstrating their involvement only for a specific set of stimuli and contexts. Though this list will surely lengthen as our understanding of emotion circuits increases, for now, we consider the hippocampus, the lateral temporal lobe, ventrolateral prefrontal cortex, the lateral intraparietal area, and the medial pulvinar.

Hippocampus

Historically, both Papez (1937) and MacLean included the hippocampus in the emotional centers of the ‘limbic system’ (Maclean, 1949). Refined lesion techniques revealed later that the hippocampus does not play a major role in emotion; however, as a central learning and memory structure, it is at the interface between emotion and memory. Episodic memories that are hippocampal-dependent, can have an emotional component that is encoded and stored together with the neutral components; conversely, emotional states are known to influence memory formation, whether by enhancing vigilance and attention at the time of encoding (Easterbrook, 1959; Adolphs et al., 2005), or through the effects of arousal on memory consolidation (McGaugh, 2000; McGaugh, 2004). The strong connections of the hippocampus (or its gateway structures) with the amygdala, orbitofrontal cortex, and medial prefrontal cortex, constitute the anatomical framework on which emotional memories are built (Packard and Teather, 1998; McGaugh, 2004; LaBar and Cabeza, 2006).

An additional role of the hippocampus in emotion and memory derives from its high concentration of glucocorticoid receptors. This makes the hippocampus vulnerable to the neurotoxic glucocorticoids that are released in stressful or highly emotional situations by the hypothalamic-pituitary-adrenal (HPA) axis (Woolley et al., 1990; Watanabe et al., 1992; Sapolsky, 1996). Chronic stress, marked by elevated levels of cortisol, is associated with hippocampal atrophy, reduced neurogenesis, and behavioral changes ranging from memory loss to depression. In humans, personality traits such as self-esteem and an internal locus of control are positively correlated with hippocampal volume (Pruessner et al., 2005). Given its coupling with stress responses, and the association between high stress levels, anxiety, and heightened responses to acute stressors, the hippocampus should be brought back into the fold of emotional circuits, at least when considering the long-term, trait influences on emotion processing.

Lateral temporal lobe

The continuous stretch of cortex from the upper bank of the superior temporal sulcus (STS), through the lower bank, and onto the inferotemporal (IT) gyrus, processes complex visual images, including faces (Gross et al., 1972; Bruce et al., 1981; Perrett et al., 1982; Yamane et al., 1988; Tanaka, 1992). This area of the temporal cortex receives inputs from ‘upstream’ visual areas such as MT, TEO, and V4, and projects to the
orbitofrontal cortex, lateral prefrontal cortex, medial temporal lobe neocortex and amygdala (Seltzer and Pandya, 1978; Baizer et al., 1991; Felleman and Van Essen, 1991). Neurons in these areas show responses to different dimensions of social stimuli, such as face identity, facial expression, head or gaze direction, and body movements (for review, see Rolls, 2007). In addition, the upper bank STS shows multisensory responses that can combine visual and auditory information, such as communication signals (Barraclough et al., 2005; Ghazanfar et al., 2008).

Some evidence that these areas are important for processing socio-emotional cues comes from lesions made in infancy to area TE that lead to temporary deficits in socio-emotional behavior in infants (Malkova et al., 1997b; Bachevalier et al., 2001). The STS is required for normal gaze discrimination, which is important for interpreting the target of an expression (Heywood and Cowey, 1992), and an intact STS and inferior temporal gyrus (ITG) are required for discrimination of configural changes in faces (Horel, 1993), that are important for identification. Taken together, these areas may form a key 'prerequisite' filter for extracting emotion and/or intention from visual social cues such as faces, though the lateral temporal lobe is not the only region poised to play this role.

**Ventrolateral prefrontal cortex (vIPFC)**

The ventrolateral prefrontal cortex, specifically, the inferior prefrontal convexity processes social-emotional information from every sensory modality. This area receives projections from high-level visual areas including the inferotemporal cortex (Ungerleider et al., 1989) and contains neurons that show selective responses to faces (Wilson et al., 1993; O. Scalaidhe et al., 1997) that are similar to the responses of face-selective neurons of the lateral temporal areas. Adjacent to the visual region is an area that shows selective responses to species-specific vocalizations (Cohen et al., 2004; Romanski et al., 2005; Cohen et al., 2006). Selectivity profiles do not fall strictly into featural (tonal/noisy) or functional (food/nonfood, aggressive/apppeasing) borders, though biases in a neuron’s response towards one or the other category can be sufficient to extract this information (Thomas et al., 2001). The inferior prefrontal convexity was recently shown to engage in multisensory processing of audio-visual communication signals (Sugihara et al., 2006), providing one clue to the processing that may occur in this region. Moreover, with its sensitivity for complex, species-specific stimuli, vIPFC activity may ultimately prove to be an important link between the perception of social stimuli and the extraction of their emotional significance. We refer the reader to the chapters in this volume on communication signals and visual processing for further details.

**Lateral intraparietal area (LIP)**

The allocation of spatial attention (Bisley and Goldberg, 2003) and goal-directed selection of actions (Snyder et al., 1997), are two functions ascribed to LIP. More recently, it has also been associated with perceptual decision making (Freedman and Assad, 2006), including enhanced responses when selecting preferred social cues such as images of dominant males, conspecific faces, or female hindquarters (Klein et al., 2008). LIP neurons do not respond selectively in anticipation of social cues when the cues are presented in a predictable, obligatory fashion, but when the monkey makes a choice that triggers the presentation of a given image, the responses predict the value of that image. Here, value was assessed by the amount of juice monkeys would forego to view an
image, using a previously-established paradigm (Deaner et al., 2005). Thus, the LIP might mediate processes by which social cues are embedded in the decision-making networks in the brain, as would be important for action selection during social interactions.

**Medial Pulvinar**

The medial nucleus of the pulvinar is connected to the superior temporal sulcus and gyrus, the amygdala, the insula, orbitofrontal cortex, the frontal pole, and the medial prefrontal cortex including the anterior cingulate cortex (Romanski et al., 1997). This list of structures corresponds to the intermediate layer of the emotional circuit proposed here. The medial pulvinar, like its neighboring structure, the mediodorsal nucleus of the thalamus, may contribute to the integration of signals from nodes of the emotion circuit.

The unique roles played by the affiliate regions, and their recruitment of widely-conserved core regions may be specializations to selective pressures that reward social savvy. The affiliate structures aren’t directly tied to the production of a specific emotion; rather, they enable extraction of appropriate responses to complex constellations of cues and scenarios that are relevant for responding appropriately to the current social situation. In this way, the boundaries segregating structures associated with emotion and with cognition become blurred (Pessoa, 2008), as will become clear when considering the contribution of the aforementioned structures to specific emotional processes.

**III. Processing emotion: circuits in action**

A basic rule of survival is to approach food sources and potential mates (appetitive stimuli), and avoid danger such as predators (aversive stimuli). Biologically prepared appetitive or aversive stimuli elicit emotional/motivational states, and are processed primarily by the core of the emotional brain. The structures of the core circuits are highly conserved across species, but component neurons are often tuned to stimuli with species-specific significance (e.g. odors of predators, pheromones, etc). The appetitive-aversive dichotomy, although not mapped onto different circuitry, has proven to have great heuristic value for deciphering the neural circuitry of emotion in animals.

Our most complete understanding to date of the most basic and most shared emotion across all species - fear- comes from aversive conditioning in rats. Fear has been studied using an aversive stimulus such as foot shock, often in association a cue such as a tone (LeDoux, 2000; Davis and Whalen, 2001; Fanselow and Gale, 2003).

Approach behaviors, which do not correspond to a state as clearly defined as fear, have been studied using food reinforcement (Everitt et al., 2003; Holland and Gallagher, 2004). In rats, the amygdala alone can support fear conditioning, whereas appetitive conditioning and reward devaluation paradigms require the joint contribution of the amygdala and frontal cortex.

Pavlovian conditioning in primates suggest a conservation of neural structures (Baxter and Murray, 2002), and possibly mechanisms (Salzman et al., 2007) that support this basic form of emotional learning. The main difference might be that emotional processing from the core structures radiates in primates to larger array of partially or fully corticalized structures that re-process emotion and link it to memory, planning, and
decision making. The essential difference derives from the major role of social stimuli to elicit emotions in primates. We will consider first the evidence for aversive and appetitive conditioning in primates, before describing how social stimulus evaluation is intrinsically related to emotional circuits.

A. Aversive emotional states

Unconditioned fear

Some stimuli are known to produce fearful or startle responses in monkeys (Davis et al., 2008). The central nucleus of the monkey amygdala is necessary for the expression of unconditioned, but also of conditioned startle. Monkeys with lesions of the central nucleus also lack the normal apprehension to the sight of a snake (real or fake), as determined by the latency to retrieve food in its presence (Kalin et al., 2004; Davis et al., 2008). In addition, monkeys without a central nucleus fail to demonstrate normal freezing (Kalin et al., 2004) that typically accompanies the appearance of a human intruder. Finally, lesions of the central nucleus reduced cortisol levels, indicating that an intact amygdala is necessary for generation of normal stress responses. In rats, too, the central nucleus is associated with production deficits in fearful situations. But in rats, the lateral/basolateral complex is necessary for learning about predictors of fearful or aversive stimuli (LeDoux, 2000).

Conditioned fear responses

A subset of neurons in the monkey amygdala respond selectively to stimuli that predict an aversive, unconditioned stimulus (US), such as a puff of air directed at the face or eyes (Paton et al., 2006). Neuronal responses to the air puff and the stimuli that predict it (conditioned stimuli, CS) ramp up during learning, and fall off during extinction, suggesting they may reflect the updated value of the association to the aversive unconditioned stimulus. Although patients with amygdala damage are able to learn CS-US associations, they are unable to express fear, or the anxious anticipation of the noxious stimulus (Bechara et al., 1995). Moreover, conditioned stimulus learning and extinction are associated with changes in BOLD responses in the ventromedial prefrontal cortex and amygdala of humans (Büchel et al., 1998; LaBar et al., 1998; Phelps et al., 2004). The following reviews consider the fear conditioning literature in more detail (LeDoux, 2000; Phelps, 2006).

The predominance of fear-conditioning as a model for emotional learning has led to the implicit assumption that the structures necessary for processing fearful stimuli are specialized for fear. To determine whether structures such as the amygdaloid nuclei function as ‘fear modules’, involving only negative affect, it is important to demonstrate that they do not act more generally in emotional learning, involving either positive or negative affect.

B. Appetitive emotional states

Conditioned appetitive responses

Classical conditioning can also be used to study positive emotional states, by pairing an initially neutral stimulus, such as a visual stimulus, with reward. For example,
A study in marmosets showed that the amygdala is not necessary for appetitive conditioning per se (Braesicke et al., 2005). In this study, the overt behaviors indicating anticipation of reward (looking and scratching at a food barrier) persisted in amygdala-lesioned animals, despite a reduction in the physiological signs of arousal during that anticipatory phase. It was as though the habit of orienting towards a conditioned stimulus remained, even when the underlying incentive was no longer present. This suggests that some aspects of positive affect require an intact amygdala.

Consistent with this observation, neural responses in the macaque amygdala follow the timecourse of learning the association between an image and juice reward, just as a previously-mentioned population of amygdala neurons ‘tracks’ learning of image-punishment associations (Paton et al., 2006). For a more detailed examination, we refer the reader to reviews of the role of the amygdala in reward and positive emotion (Baxter and Murray, 2002; Everitt et al., 2003; Murray, 2007).

Lesion studies implicate both the amygdala and orbitofrontal cortex in the flexible selection of cues that predict specific rewards, though each plays a distinct role in the process. Overall preferences for desirable foods are unchanged after lesions or disruption of the amygdala (Malkova et al., 1997a; Wellman et al., 2005; Machado and Bachevalier, 2007b; Murray and Izquierdo, 2007), or of the orbitofrontal cortex (Machado and Bachevalier, 2007b) indicating that these structures are not necessary to encode the primary reinforcement value of foods. Indeed, behavioral responses are appropriately diverted away from food that has been devalued through satiation (Machado and Bachevalier, 2007a). Moreover, neither structure is necessary to discriminate which objects are associated with food reward in a concurrent discrimination task. Yet when a preferred food is devalued, lesions to either the amygdala and/or the contralateral orbitofrontal cortex lead to continued selection of objects associated with the satiated (devalued) reward, when a normal response would be to switch, selecting the food reward that had not been devalued. Curiously, upon seeing the underlying food reward, only monkeys with orbitofrontal lesions actually took the reward. These monkeys selected the non-devalued food when given a choice between the two, indicating that satiation indeed changed the value representation of the food. These monkeys only fail when given a choice between the cues predicting the foods, falling back on their learned behaviors to previous conditioned associations. Having selected the single, devalued food, they take it despite satiety for it, unlike monkeys with amygdala lesions. Thus, both the orbitofrontal cortex and the amygdala share a role in updating behaviors towards previously learned associations based on current preferences or motivational state, and the integrity of both structures is required for updating the value of a reinforcer (Baxter et al., 2000). These results are also consistent with a study of instrumental extinction (Izquierdo and Murray, 2005).

In contrast to the nuanced distinctions in the roles played by the amygdala and orbitofrontal lesions in encoding the value of reinforcers, the anterior insula may be more directly involved in representing the reward value of foods. As secondary olfactory and primary gustatory cortex, cells in the insula show reduced firing rates to preferred odors or foods following satiation (Rolls, 2000). When orbitofrontal lesions include part of agranular insular cortex, monkeys continue to select foods after being fed to satiety (Machado and Bachevalier, 2007b; Machado and Bachevalier, 2007a). Thus, the insula
may be central source of behavioral responses to some rewarding (appetitive) stimuli, such as food.

The use of similar appetitive and aversive conditioning paradigms in primates and in rodents reveals a large overlap in the structures involved. This implies a conservation of the potential mechanisms of emotional learning (Everitt et al., 2003; Holland and Gallagher, 2004; Phelps, 2006; Murray, 2007).

Although the emotional behavior of rodents cannot be reduced to food and predators, and social stimuli are likely processed by the circuit that evaluates reinforcers, little is known about the “social brain” in rodents (Panksepp, 1998). In primates, however, it is clear that the majority of emotional states are centered on social interactions; for many primate species, individuals live within elaborate social dominance hierarchies. Here, appropriate responses to members of the group can reduce the threat of attack or increase access to food, reproductive partners, or to allies that indirectly reduce threats and increase access to rewards. Indeed, the majority of emotional states in such primate species occur during social interactions. These socio-emotional interactions depend on the identity and dominance status of the participants, as well as on the recent history of aggression/affiliation, and perhaps most critically on the social signals (facial expressions) displayed by interacting conspecifics.

C. The social envelope: the relationship between expressions and emotions.

Expressions can be regarded both as the externalization of the emotional state of the displayer, and as intentional signals aimed at another individual. At the receiving end, expressions can induce emotional states in the observer. Importantly, expressions map most closely onto the state of the sender; how it is interpreted by an observer will depend on additional factors. For example, an aggressive expression indicates the perturbed state of the sender, but if the sender is a meek juvenile monkey, or if the expression is directed at another individual, it would have little effect on an adult monkey observer. Thus, we will begin by describing the expressions generated by an individual based on that individual’s emotional state, before considering how expressions can evoke emotional responses in observers. We will focus on macaque expressions, allowing us to describe neural structures associated with the generation and perception of expressions, expanding to incorporate what is known in humans or other members of the primate order, where possible. The three poles suggested in the macaque expression literature (Mason, 1985; Deputte, 2000; Partan, 2002) are avoidance, which maps directly onto other fearful or avoidance behaviors, affiliation, which corresponds to appetitive behaviors, and the additional pole of aggression, a ‘strictly social’ addition that arises as a consequence of dominance status.

Generating expressions

Avoidance (fear grimace, scream)

In macaques, a cluster of expressions indicate the presence of an aversive stimulus, including the fear grimace and scream. The fear grimace is characterized by horizontally retracted lips, revealing upper and lower teeth, and retracted ears. It can also be accompanied by a high-pitched, shrill vocalization, or ‘scream’ (Partan, 2002).
Affiliation (lip smack, coo, groom present)
Expressions indicating a desirable or appetitive stimulus include the lip smack, coo and grunt. The lip smack is produced by puckering the lips and smacking them together, with the chin held up and ears retracted. The coo is a single tonal vocalization made while making an ‘oo’ shape with the lips. The groom present, common to many primate species, is a body-gesture made by exposing a vulnerable part of the body by extension, such as by raising the arm or turning the head away to expose the neck, or, by turning one’s back, all in close proximity to an individual invited to groom. The act of grooming that may follow has been used as a measurement of the degree of affiliation (Seyfarth and Cheney, 1984). Affiliative behaviors trigger neural reward states: grooming is accompanied by beta-endorphin release in CSF; blocking the mu-opioid receptor increases groom invitations and grooming durations, and opiate delivery decreases grooming invitations (Keverne et al., 1989).

Aggression (open-mouth stare, pant-threat)
The most typical expression of aggressive or threatening gestures in the macaque is the open-mouth threat (or stare), characterized by directed gaze and an opening of the mouth so that lips form an ‘o’ shape, with the upper teeth covered by the lips. Ears are forward or are flapped, and head is lowered, the eyes are fixated on the receiver of the threat, and the facial display is often accompanied by a body lunge toward the target. The pant-threat is a staccato noisy (broadband) vocalization, often occurring as a triplet. Consistent with the presumed emotional correlates of this vocalization, the pant-threat appears to be mediated by stress levels. A reduction of stress hormone output leads to fewer pant-threat vocalizations under stressful conditions (Bercovitch et al., 1995).

Neural basis for the generation of expressions
Facial expressions reflect the internal state of approach, avoidance, or aggression of the displaying animals. Whereas the involvement of some neural structures appears to be restricted to the generation of a subset of expressions (e.g. aggressive displays), other structures, such as the amygdala, are involved in generating a wide array of expressions, possibly selecting which class of responses is appropriate for a given situation.

Avoidance: Monkeys that were given neonatal amygdala lesions show more fear responses (more grimaces and screams) towards a novel peer monkey than do intact monkeys (Bauman et al., 2004b), but show fewer fear response than intact monkeys do when separated from their mother, e.g., fewer screams (Bauman et al., 2004a). Likewise, in a study of young monkeys who had just received amygdala lesions, there was diminished fear expression towards a stimulus that should have been threatening: the introduction of a novel adult male (Kalin et al., 2001). The ability of these monkeys to respond, but at inappropriate times or with abnormal frequency, suggests that the amygdala may be one structure important for appropriate evaluation or expression of fearful situations, but not for the generation of the response per se.

Affiliation: When faced with a novel adult male (a threatening stimulus), young amygdala-lesioned monkeys delivered fewer affiliative vocalizations (coos) than did
monkeys with an intact amygdala (Kalin et al., 2001). They also barked less and showed less submissive behavior. In contrast, when paired with a peer monkey, monkeys with neonatal amygdala lesions produced more affiliative expressions than intact monkeys (Bauman et al., 2004b). This is consistent with the suggestion that the amygdala is not required for the generation of expressions – regardless of emotional state – rather, it seems to play a role in determining the appropriate gestures in a particular context. We will return to this point in our discussion of the perception of expressions and their link to emotional state.

**Aggression:** In marmosets, stimulation of the ventromedial hypothalamus produces aggressive vocalizations, and lesions to the anterior hypothalamus or the pre-optic area lead to a reduction in aggressive vocalizations towards an intruder (Lloyd and Dixson, 1988). In macaques, stimulation of the anterior hypothalamus, pre-optic area, and the BNST lead to an increase in aggressive vocalizations (Robinson, 1967) and aggressive behaviors towards subordinate monkeys (Alexander and Perachio, 1973). Thus, proper expression of aggressive behaviors involves, at a minimum, the hypothalamus, BNST and as previously mentioned the periaqueductal gray and possibly the anterior cingulate cortex.

**Perceiving and evaluating expressions**

Although expressions indicate the emotional state and/or the intentions of an individual, the dominance hierarchy of macaque societies imposes additional factors on the interpretation of an expression, such as the rank, sex, and identity of the sender, and of the receiver, as well as the ranks of the close affiliates of both. Recent social exchanges and their outcomes may also weigh into the interpretation of a given expression. What is the evidence that monkeys are sensitive to expressions, and to associated social factors? In this section, we explore the neural substrates for perceiving and properly interpreting expressions.

**When a threat is threatening.**

In general, when observing a social encounter, an aggressive response is one that escalates an encounter, ultimately predicting an attack, whereas an affiliative response is one that invites or predicts those interactions that decrease the probability of attack. An avoidance response is one that disarms or prevents an encounter, leading to a break in the interaction. It follows that aggressive gestures directed at an observer are generally arousing and threatening to the observer; directed affiliative gestures may be arousing, but not threatening, and directed avoidance gestures should not be arousing or threatening.

Images of expressions elicit in the macaque brain stimulus-specific responses in several areas of the temporal cortex, as well as in the hippocampus, amygdala, and prefrontal cortices, as shown by imaging studies (Hoffman et al., 2007; Hadj-Bouziane et al., 2008; Tsao et al., 2008). Neurons in the inferotemporal cortex or STS (Hasselmo et al., 1989) and amygdala (Gothard et al., 2007; Kuraoka and Nakamura, 2007) respond selectively to facial expressions. In the amygdala, the same fraction of neurons respond to threatening, appeasing, or neutral stimuli, but the firing rates are higher for threatening
faces. The heightened response to threats is a matter of degree; all types of expressions can elicit selective amygdala responses (Gothard et al., 2007). Of note, many amygdala neurons responded most strongly to a specific combination of identity and expression, not to expressions in an identity-invariant manner. This would provide a neural means of perceiving expressions embedded in the appropriate social context, something monkeys with lesions to the amygdala or orbitofrontal cortex are unable to do. Proper interpretation of an expression is a prerequisite for generating context-appropriate expressions. Recall that the generation of appropriate expressions was impaired in monkeys with amygdala lesions (Kalin et al., 2001; Bauman et al., 2004a, b). It’s possible that the process of evaluating expressions simply does not occur independently of the context in which the expression is displayed. Here, ‘context’ can be ascertained from physical attributes and attitudes of the sender that co-occur with the expression, such as gaze and body direction, age, gender, and dominance rank deduced from recognizing the sender’s identity and physical markers of fitness. Context could also reflect the presence, proximity, and gestures of other individuals, or of a sender’s history of behaviors associated with an expression, as well as the recent activity of the colony. We will explore the evidence for neural sensitivity to these contextual factors, and the effects they may have on the evaluation of emotion-laden stimuli.

Head and gaze direction
Expressions directed away from the observer, towards an unseen target are ambiguous. Without knowing the target of the expression, the appropriate response is unclear and requires additional information gathering, such as orienting in the direction of display. Indeed, averted expressions in monkeys are more arousing than are expressions directed at the observer (Hoffman et al., 2007). Because an important factor in the perception of expressions is an assessment of the target of an expression, the direction of head and gaze of a displaying monkey are important to the proper interpretation of an expression.

Neurons sensitive to body, head, and eye gaze direction are found in the superior temporal sulcus of the temporal lobe (Perrett et al., 1985), and lesions to this region produce gaze-discrimination deficits (Heywood and Cowey, 1992). In addition, the central nucleus of the amygdala, which is known to influence autonomic output, shows greater BOLD activation for averted- than for directed-gaze faces, consistent with physiological measures of arousal in response to the same stimuli (Hoffman et al., 2007). The STS sends strong projections to the basolateral amygdaloid nuclei, which, in turn, project to the central nucleus, thereby providing a putative circuit for perceiving and redirecting attention based on the intended target of a seen expression. These results are consistent with a more general roll for the central nucleus in the detection of saliency, and the re-allocation of attention (Whalen, 2007).

Dominance rank
The asymmetrical allocation of valued resources such as space, food, and agonistic interactions within groups of macaques is evidence of a dominance hierarchy, with the commonly-studied rhesus macaque demonstrating one of the most linear, despotic hierarchies of all macaque species (Flack and de Waal, 2004; Thierry, 2004). Sensitivity to social dominance is a pervasive facet of macaque behaviors, from its effects on the latency to approach foods, to female orgasm rate, which increases with the
dominance rank of the males in a pair (Troisi and Carosi, 1998). Even in an isolated, experimental setting, responses to pictures of familiar conspecifics, demonstrates sensitivity to dominance rank. Low-ranking macaques will follow the gaze of a monkey looking away, regardless of the rank of the stimulus monkey. High-ranking monkeys, however, will only follow gaze of other high-ranking monkeys (Shepherd et al., 2006). Thus, the aforementioned neural sensitivity to head and gaze-direction could also be influenced by the status of both the observing and stimulus monkeys. Consideration of rank will be important in future studies of macaque circuits of emotion.

Kin and affiliation

Macaque mothers differentiate between threats directed at them or towards their infants; the presence of a dominant female is threatening to both, a subordinate female is a threat to their infants, and young daughters are non-threatening to both groups (Maestripieri, 1995). Understanding the neural substrates for macaques’ sensitivity to social status is difficult, however; most of our knowledge of social behaviors comes from field studies void of neural manipulations. Those studies measuring social behaviors in monkeys following lesions have focused on the role of the amygdala. Qualitative descriptions of the effects of amygdala lesions or lesions extending into other medial temporal lobe regions, included withdrawal, submission, and drop in rank when placed in large-group settings (Rosvold et al., 1954; Dicks et al., 1969). Somewhat different results were obtained through the quantitative behavioral assessment of amygdala-lesioned monkeys placed in randomized dyads (Emery et al., 2001). Under these conditions, introduction to another, unlesioned, monkey produced more affiliative approach behaviors than those seen for introductions between pairs of unlesioned monkeys. Monkeys with neonatal amygdala lesions also show enhanced contact, in this case with their mothers. These two observations support the idea that the amygdala is involved in the inhibition of certain types of behaviors, primarily affiliative behaviors, (Sally Mendoza, personal communication). In addition, despite the ability to generate the full repertoire of expressions and vocalizations, during perturbations in the social environment, monkeys with neonatal amygdala lesions generate inappropriate responses, either vocalizing more or less than controls, depending on the situation, or failing to return to their mothers after forced separation (Kalin et al., 2001; Bauman et al., 2004a, b). In contrast, hippocampal-lesioned monkeys showed none of these behaviors. It is not clear what components of the amygdala are responsible for these aberrations, but the results are consistent with the suspected role of the basolateral amygdala in evaluating the proper constellation of cues to update behavioral responses. Clearly, more information is needed to understand what, if any, additional structures are implicated in identifying and altering responses to expressions based on kin relationships and social bonds.

Traits and states

In addition to functional architecture that allows the evaluation of stimuli, the emotional circuits of the brain are influenced by genetic make-up and by early life experience that establish the ‘baseline’ or tonic output even in the absence of a changing input. The temperament, affective style, or personality traits, of the animal depend on this output. Anxiety-related personality traits in monkeys, for example, have been linked to the polymorphism of the regulatory region of the gene for transporter-facilitated uptake
of serotonin (5-hydroxytryptamine or 5-HT) (Suomi, 2006). Secure attachment, or lack thereof, to the mother, combined with the presence of short or long allele of the serotonin transporter gene or of the monoamine oxidase A gene promoter is predictive of risk taking behaviors, resiliency to adverse social situations, and the ability of monkeys to control aggression, (Newman et al., 2005; Suomi, 2006). Individual differences in tonic autonomic output or ‘trait’ behaviors will influence the degree and possibly character of emotional states evoked by changing inputs. Likewise, keeping track of which individuals are highly reactive will assist the interpretation of the likely consequences of a given expression.

D. Multi-dimensionality and pluripotency within emotion circuits

The literature on appetitive conditioning suggests there are no ‘dedicated’ fear circuits, rather emotional stimuli with negative and positive valence are evaluated by the same or highly overlapping circuits. Likewise, the structures implicated in the evaluation of social stimuli overlap, at least partially, with those the process conditioned approach/avoidance behaviors, demonstrating a co-opting of approach/avoidance processing into the social domain. In addition, all stimuli with uncertain or ambiguous emotional significance engage the amygdala and related structures (Whalen, 2007). This raises the question: to what extent do structures within circuits of emotion evaluate ‘emotional’ stimuli exclusively?

A comparison of the neural responses elicited by unfamiliar objects, food items, fear-producing objects, and a variety of facial expressions indicated that all classes of stimuli elicit stimulus-selective response in the monkey amygdala (Gothard et al., 2007). Whether these images engage the amygdala because they are unfamiliar with ambiguous value or their “neutrality” is encoded as part of a more general process of stimulus evaluation remains to be clarified. The quasi-equanimous allocation of the processing resources of the amygdala to negative and positive stimuli is best illustrated by the response to social stimuli, such as facial expressions. Although fearful faces are the least discernable expression for patients with amygdala damage (Adolphs et al., 1994; Sprengelmeyer et al., 1998; but see Rapcsak, 2003) and hemodynamic changed in the human amygdala appear larger in response to fearful and angry faces than to neutral or happy faces (for review, see Zald, 2003), neurons in the monkey amygdala show only a small increase in firing rate for threatening faces compared to neutral or appeasing faces (Gothard et al., 2007).

Neurons in the monkey amygdala that are selective for facial expressions, respond by either increasing or decreasing their firing rate. Positive facial expressions (appeasing faces) are more often encoded by significant decreases of firing rates than threatening faces that cause most often significant increases in firing rate. The number of neurons allocated to process positive, negative, and even neutral stimuli is roughly equivalent, and the global activation is significantly above baseline for all facial expressions. There was indeed a short-lived excess of population firing rate for threatening faces, but the size of the difference between the threatening and appeasing faces was smaller than the size of responses to any type of facial expressions compared to baseline. Nevertheless, the observed difference between aggressive and appeasing facial expressions is sufficient to account for neuroimaging results obtained by subtraction analyses using the same facial
expressions (Hoffman et al., 2007). Our observation that the monkey amygdala processes aversive and appetitive stimuli equally is in line with earlier neurophysiological and behavioral studies of the monkey amygdala (Fuster and Uyeda, 1971; Sanghera et al., 1979; Nakamura et al., 1992; Ono and Nishijo, 1992; Wilson and Rolls, 1993; Paton et al., 2006).

It appears, therefore, that the monkey amygdala performs the operations of aversive conditioning and appetitive conditioning elucidated in rats but, in addition, carries out important social processing that is not biased in favor of stimuli with a particular emotional valence. If a structure traditionally placed at the heart of emotional processing demonstrates processing of stimuli irrespective of emotional valence, other structures in circuits of emotion may do the same.

CONCLUSIONS:

1. A variety of neural structures contribute to the processing of emotions. For didactic purposes, the neural circuits of emotion can be divided into core structures that are the proximal sources of autonomic and motor responses associated with the expression of emotion. These emotional expressions are closely tied to - and in certain cases include - vigilance, orienting and the reallocation of attention to emotionally salient stimuli. Intermediate structures are those that generate more complex representations that place in emotional register the external and internal milieu, and flexibly link perceptual and motor components of an emotional response. Several additional structures serve an extended emotional circuit, providing further information about the emotional content of stimuli, expected outcomes, and contextual contingencies that determine which emotional response should be delivered and under what circumstances. All regions, taken together, afford adaptive responses to changes in the social environment.

2. The amygdala is a key structure for the evaluation of emotional stimuli. Based on interaction with affiliate structures, the amygdala controls the emission of signals toward the core structures that orchestrate the expressions of emotions. Much of our current understanding is based on the treatment of the amygdala as a unitary structure due, in part, to methodological limitations. Nevertheless, the subcortical and cortical nuclei, when scrutinized, fall into distinct roles in emotional circuits on both anatomical and functional grounds.

3. Emotional responses can be broken down into the immediate evaluation and response to changes in the environment and to long-term modifications that can shape future responses, or even regulatory states of the animal (e.g. stress hormone levels). Whereas core and intermediate areas may afford rapid responses, the high-dimensional information available to intermediate and affiliate areas may be useful for constructing multiple contingencies for subtly varying sets of inputs. They may also support memory for these contingencies, and set into motion longer-term changes thereby shaping both traits and states related to emotions.
Figure 1. Structures contributing to circuits of emotion in the macaque. Core structures are shown in red, intermediate structures in orange and affiliate structures in yellow. A. Coronal section through several key structures. Arrows indicate connections between structures, depicted on the left hemisphere. Structure names are listed on the right hemisphere. Connections are shown only for structures visible in this image plane. The basolateral amygdala had bidirectional connections with the STS, anterior cingulate, and the insula, and projects to the central nucleus of the amygdala. The central nucleus, in turn, sends projections to the hypothalamus. B. Sagittal section depicting several key structures and the medial forebrain bundle (MFB). The MFB (black line) contains fibers originating in several neuromodulatory centers in the brainstem and midbrain, and projecting to the hypothalamus and the prefrontal cortex. Neuromodulator-specific fiber tracts continue on to ennervate other regions of neocortex (see text). C. Horizontal (axial) section at the level depicted by the blue line in A. Conventions as in A. The brainstem (indicated by the periaqueductal gray arrows) projects to several structures including the hippocampus, amygdala and superior temporal sulcus, among other structures. D. Schematic diagram of brainstem connections subserving circuits of emotion. Conventions as in A. This diagram loosely depicts the ventral surface of the brain, including several core brainstem nuclei. Sensory nuclei include those from cranial nerves V, VII, IX, X. Motor nuclei include those from cranial nerves III, IV, V, VI, VII, IX, X, XI, XII. The periaqueductal gray (not labeled) is the vertical gray bar connected to the superior colliculus and the reticular formation. Abbreviations: ACC – anterior cingulate cortex, BLA – basolateral amygdala, BS – brainstem, CeA – central nucleus of the amygdala, HIP – hippocampus, HY – hypothalamus, INS – insula, M – motor cranial nerve nuclei, NTS – nucleus of the solitary tract, OFC – orbitofrontal cortex, PAG – periaqueductal gray, PB – parabrachial nucleus, RF – reticular formation, S – sensory cranial nerve nuclei, SC – superior colliculus, STS – superior temporal sulcus.


