Anatomy and Physiology of Human Emotion:
Vertical Integration of Brainstem, Limbic, and Cortical Systems

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The neural organization of human emotion spans multiple levels of the brain, from the elementary adaptive reflexes of the lower brainstem, to the complex visceral and somatic integration of the hypothalamus and thalamus, to the control of memory and cognition in limbic-cortical networks. At each level, there are implications not only for the experience and expression of emotion, but for the effective motivation of behavior.

At the level of the pontine brainstem, for example, there are neural representations of elementary patterns of laughing and crying. These emotional displays become disinhibited when lesions disrupt the fiber tracts mediating limbic and cortical modulation of the brainstem responses (Rinn, 1984). Anencephalic infants, born with only a brainstem, show well organized facial displays of pleasure and distress (Buck, 1988). At the pontine level, we also find critical motivational mechanisms in the nuclei of the ascending monoamine projection systems that regulate arousal and alertness according to both internal states and environmental events (Bloom, 1988). The challenge for a neuropsychology of emotion is to explain how the elementary levels of the neuraxis are coordinated with higher cortical systems to control behavior adaptively.

In this chapter, we review the basic outlines of the anatomy and physiology of human emotion, describing the multiple levels of emotional control that have resulted from the progressive elaborations of the mesencephalic, diencephalic, and telencephalic levels of visceral, reflexive, and behavioral organization in vertebrate evolution. We emphasize the need to understand vertical integration, how these levels coalesce effectively. Two principles may help with this problem of understanding vertical integration. The first principle is Jacksonian hierarchic integration through inhibitory control, through which fixed-action lower circuits are subordinated to the representational flexibility of higher networks. The second, and related, principle is encephalization, through which higher, general-purpose brain networks take on the functions formerly served by lower, fixed-action circuits. By sketching the outlines of all of the major emotion control circuits of the mammalian brain, and then considering these in light of the complex
psychological qualities of human emotion, we attempt to formulate more clearly, even if we can not answer satisfactorily, the fascinating question of vertical integration of human brain systems.

**Overview of Evolutionary Neuroanatomy**

The hierarchic architecture of the human brain can be understood through a developmental-evolutionary analysis. Seen from the perspective of engineering or computer science, the human brain presents a convoluted and confusing circuit architecture. This architecture makes sense only when it is recognized to be the end point of the progressive differentiation of the brain in vertebrate evolution. Given the requirement for continuous functioning of each generation, the foundation circuitry remained in place, and new structures were differentiated to modify, rather than replace, the primordial adaptive mechanisms. The major episodes of functional transformation were associated with new structures of nerve network anatomy elaborated at the anterior end of the neural tube. These are now marked by the major divisions of the neuraxis seen in embryogenesis (rhombencephalon, mesencephalon, diencephalon, telencephalon).

Accounts of human emotion typically emphasize the telencephalic structures (basal ganglia, limbic circuits, and cortex). But it is well-known in clinical neurology that both diencephalic (thalamus, hypothalamus) and mesencephalic (pontine reticular nuclei) structures are critical not only to vegetative controls and primitive drives, but to the fine regulation of attention and cognition. Many lines of evidence suggest these subcortical circuits are essential to the cortical representation of emotional experience and behavior as well. In this chapter, we briefly outline the major control circuits at each level of the neuraxis, and we provide examples of how mesencephalic and diencephalic influences may be integral to human emotion.

The brainstem circuits have been strongly conserved in vertebrate evolution, with the core nuclei and connections of the amphibian motor system easily traced in the human brainstem (Sarnat & Netsky, 1974). In contrast, the architecture of the telencephalon has become highly unique in each avian and mammalian species. A key insight to mammalian cortical architecture has been achieved in recent years by the study of the connectivity of the primate cortex (Pandya, Seltzer, & Barbas,
1988b). This research has suggested that the mammalian neocortex evolved from the limbic structures at two points of origin, with the archicortical base of the cingulate gyrus, parietal lobe, and dorsal frontal lobe (the spatial or “where” pathway) emergent from the hippocampus, and the paleocortical base of the inferior temporal and orbital frontal lobe (the object or “what” pathway) emergent from primitive olfactory cortex. A theoretical challenge, so far unmet, is to determine whether there are unique emotional and motivational properties of these limbic divisions that are integral to their mnemonic and cognitive functions. In this chapter, we outline the anatomical organization of the dorsal and ventral corticolimbic networks, and we raise the question of the differing motivational and emotional functions of these divisions of the cortex.

The human brain shows a massive frontal cortex and functionally differentiated cerebral hemispheres. As other chapters of this volume will illustrate, these cortical features have been primary targets for theorizing on the uniqueness of human cognition and emotion. In the present chapter, we will emphasize that the study of neuroanatomy and neurophysiology not only points out the evolved hierarchy of the human brain; it leads directly to the question of how the flexible operations of the human cortex have come to coexist with the homeostatic drives, arousal mechanisms, and adaptive reflexes of the limbic structures, striatum, and brainstem.

We address this question with two classical principles of brain function. These emerged from the developmental-evolutionary analysis of the last century that is again popular in biology (Pennisi, & Roush, 1997). The first is Hughlings Jackson’s principle of hierarchic integration through inhibitory control (Jackson, 1879). Along with his contemporaries, Jackson was impressed by the evolutionary order in the anatomy of the brain, which is traced by the progressive differentiation in embryogenesis. Observing that brainstem reflexes disappear as the infant matures, but then reappear following cortical lesions, Jackson proposed that the higher (e.g., telencephalic) brain structures evolved to extend, inhibit, and modulate, rather than replace, the earlier (e.g., mesencephalic) functional systems. Only in rare instances (e.g., the pyramidal motor tract) does a higher brain structure actually replace or bypass lower structures. From this perspective, we may better understand the various forms of disinhibitory psychopathology seen in
humans with brain lesions. We may also understand how complex patterns of human emotional experience and behavior are the composite of hierarchic, vertical integration, through which cortical representation networks are regulated by limbic and brainstem control mechanisms.

The second principle is encephalization. It is complementary to Jacksonian hierarchic integration in emphasizing the increasing functional dominance of higher systems with increasing complexity in the phylogenetic order. Encephalization is the evolutionary mechanism through which special-purpose controls in the periphery (e.g., lateral inhibition in the avian retina) are taken over by general-purpose controls in the central nervous system (e.g., lateral inhibition in the mammalian thalamus). A principle such as this is essential to explain how human emotional responses can be so elaborated in time, removed from proximal stimuli. From this perspective, the subcortical circuits that were once complete mechanisms for evaluating the sensory context and motivating fixed action patterns now must support the more extended adaptive processes of the telencephalon. These are processes of continually integrating past experience, evaluating the significance of events while delaying gratification, and planning the future. Compared to the reflexive fixed action patterns that comprise the motivational systems of simple vertebrates, the increasing complexity of mammalian emotional systems can be seen as the continued extension of the brain’s representation of information in space and time.

In the simplest vertebrates, exemplified in surviving species by *amphioxus*, the primitive brain responded reflexively to local stimuli, such as tactile contact or pain. With the evolution of sense organs for information from “distant” sources, such as smell or hearing, more complex brain structures such as the olfactory cortex and thalamus evolved the specialized synaptic networks to process distant information. Sarnat and Netsky (1974) point out that, by processing distant information in advance of contact, the vertebrates with special senses could afford the increased delay in processing caused by to the increased number of synapses in the higher (e.g., diencephalic) nerve networks. We suggest that the human brain represents the continuation of this primordial principle, with progressively greater extension of the reflex arc (stimulus-response complex) in space and time.
The network architecture of the telencephalon shows the limbic structures as pivotal for connecting the sensory representational networks of the posterior brain to the action organization networks of the anterior brain. The limbic circuits and thalamus are also pivotal in funneling the widespread cortical inputs to the key regulatory systems of the brainstem, which then project broadly to tune the arousal and motivational state of the entire neuraxis. The evolutionary trend toward organizing perception and behavior according to “distant” information appears to be extended in the human brain, through memory capacities that allow continual integration of past experience to anticipate the events of the future. These memory capacities cannot be understood by a strictly cognitive analysis. The complex corticolimbic interaction of the massive human cortices is regulated adaptively, by motivational and emotional controls of limbic and subcortical systems.

Subcortical Bases of Emotion

Emotions comprise specialized neurophysiological subsystems that control motor, autonomic, and sensory processing. For a coherent theory of emotion, it is necessary to understand how these component subsystems are coordinated by higher level structures to produce adaptive emotional states. A number of advances in integrative capacity appear to have accompanied the evolution of motivational systems within the brainstem and limbic system.

Component Brainstem Subsystems

The component subsystems arise from cell groups and nuclei located primarily within the spinal cord and lower brainstem. Many of these cell groups serve effector functions through their descending influence upon peripheral muscles and organs. Within the caudal medulla, for example, the medial tegmental field controls the axial trunk and head muscles, whereas the more rostral red nucleus controls the distal limb muscles. Other cell groups control specific behaviors such as chewing, vocalization, facial expressions, eye movements, and locomotion. In addition to these somatic functions, medullary cell groups regulate various autonomic reflexes. Some regions
appear to control sympathetic activity (e.g., the rostral ventrolateral medulla), whereas others are concerned with parasympathetic functions (e.g. nucleus ambiguus). (Holstege, Bandler, & Saper, 1996; Loewy, & Spyer, 1990; Van Bockstaele, Pieribone, & Aston-Jones, 1989).

While these effectors control specific behaviors, additional brainstem systems serve a more general function of adjusting the gain of spinal transmission. These include descending projections employing serotonin (raphe pallidus and raphe obscurus), norepinephrine (locus coeruleus), and dopamine (A11 cell group). The monoamines’ relatively diffuse projections throughout the ventral horn of the spinal cord appear to be modulatory; i.e., they do not activate the motorneurons, but enhance responses to inputs converging from other brainstem systems. In addition, they inhibit the transmission of sensory information as it ascends within the dorsal horn, thereby promoting analgesia in stressful situations. These descending modulatory systems appear to adjust the balance between motor and sensory processing within the spinal cord (Holstege, 1991; Holstege, et al., 1996; White, Fung, Jackson, & Imel, 1996).

A third set of brainstem components includes ascending projections to the forebrain. Traditionally associated with the reticular activating system, these systems include (among others) norepinephrine (locus coeruleus), serotonin (dorsal and median raphe), dopamine (ventral tegmental area), and acetylcholine (nucleus basalis) projections. These cell groups appear responsive to emotional stimuli, and their target effects are primarily modulatory (i.e., facilitating or attenuating converging sensory information). Such effects are consistent with recent studies showing how emotional states regulate attention (Niedenthal, & Kitayama, 1993). It has been suggested, for example, that during positive states, noradrenergic projections may promote an expansive, present-centered state of cortical processing. In contrast, negative states may recruit dopaminergic projections to promote a more focused, future-oriented attentional state (Tucker, & Williamson, 1984).

**Integrative Brainstem Mechanisms**
When viewed as a whole, the brainstem consists of discrete subsystems serving somatic, autonomic, and modulatory components. To produce emotional behaviors, however, these components must be coordinated by higher level structures. Although such coordination is facilitated by limbic and cortical projections, its primitive basis can be found within the brainstem itself. Some of these integrative mechanisms are relatively specific. For example, the nucleus paragigantocellularis provides the main source of sympathetic drive within the organs of the autonomic nervous system, while at the same time providing the most potent afferent input to the locus coeruleus. Such projections suggest a mechanism for coordinating the ascending noradrenergic influence upon the forebrain with sympathetic tone throughout the body (Aston-Jones, Chiang, & Alexinsky, 1991; Van Bockstaele, et al., 1989).

More rostral brainstem structures appear to provide more elaborate integrative influences. The midbrain periaqueductal gray (PAG) possesses descending projections to somatic, autonomic, and modulatory cell groups, allowing it to coordinate their activity in patterns related to general motivational states. Recent findings indicate that the PAG is organized into columns of cells, with each column related to a motivational pattern. The lateral column organizes active forms of defensive behavior, and appears particularly responsive to superficial pain. Stimulation of the intermediate region of the lateral column elicits confrontational defensive behavior (i.e., defensive aggression) and blood flow to the face, whereas stimulation of the caudal region of the lateral column elicits flight behavior and increased blood flow to the limbs. Both of these defensive patterns are accompanied by increased heart rate and a non-opioid analgesia. In contrast, the adjacent ventrolateral column orchestrates a more passive strategy in response to deep pain. This pattern involves a cessation of ongoing motor activity, hyporeactivity, hypotension, decreased heart rate, and opioid mediated analgesia. In its primitive form, the passive pattern may serve defensive purposes (e.g., playing dead), or it may it may serve recuperative functions following serious injury (Bandler, & Keay, 1996; Bandler, & Shipley, 1994). Future studies of the PAG promise a better understanding of some of the brain’s most basic emotional functions, both in
terms of their identity (e.g., defensive, recuperative, sexual) and in terms of their patterned organization.

**Integrative limbic Influences**

The more recently-evolved limbic structures that surround the brainstem serve a number of functions central to emotion and cognition. In terms of emotion, these circuits provide higher levels of integrative control over the brainstem. At the diencephalic level, the hypothalamic nuclei receive extensive exteroceptive and interoceptive sensory information, and innervate multiple brainstem structures. Hypothalamic projections to the motor and autonomic pools of the lower brainstem allow for a fine tuning of homeostatic functions based on a detailed, integrative monitoring of ongoing metabolic conditions (Swanson, 1987). By means of additional projections to the pituitary, the hypothalamus (paraventricular nucleus) can coordinate peripheral endocrine activity in light of ongoing somatic, autonomic and modulatory activity (Loewy, et al., 1990). In addition, hypothalamic projections appear capable of regulating brainstem integrative mechanisms. For example, the ventromedial hypothalamus exerts a descending inhibitory influence upon cell groups within the PAG that are responsible for defensive aggression. It has been suggested that such suppression of brainstem aggressive tendencies has been crucial in the evolution of prosocial behaviors involving trust, play, and affection (Panksepp, 1986).

Hypothalamic projections also regulate the fearful forms of defense organized within the brainstem. Gray (1996) has suggested that the hypothalamus and PAG function together, along with the amygdala, as part of a distributed fight-flight system. The PAG mobilizes defensive behavior given proximal sources of threat (e.g., pain, a predator) when there is little time for analysis. If the threat is very close and allows no avenue of escape, then fighting is elicited, but given more distance or more room for escape, then undirected flight is elicited. In contrast, the ventromedial hypothalamus mobilizes defense in situations involving more distal threats and more time for sensory analysis. The hypothalamic organization takes the form of directed escape behavior, and it is coordinated by regulating the PAG and recruiting additional brainstem regions.
involved in orientation (superior colliculus) and locomotion (cuneiform nucleus) functions. It is worth emphasizing that these primitive forms of defensive behavior are based upon threats that are physically present and temporally urgent. Several theorists have suggested that they give rise to emotional states of *panic*, which are distinct from the anticipatory states of *anxiety* orchestrated by higher limbic and cortical circuitry (Graeff, 1991; Gray, & McNaughton, 1996). The evolutionary progression in motivation can be seen as moving from reflexive responses to systems that engage defensive or other adaptive behavior in the face of proximal stimuli to systems that maintain an emotional state to bias the organization of behavior appropriately (e.g., a threatened posture) over extended intervals of time.

*Limbic Anticipatory Functions*

More anticipatory emotional capacities appear to have evolved along with two telencephalic limbic structures, the amygdala and hippocampus. Both of these structures have extensive descending inputs to the hypothalamus, and the amygdala also projects throughout the brainstem. Although the amygdala is a complex structure with multiple nuclei, recent evidence suggest a crucial role in associating exteroceptive information with information concerning rewarding and aversive outcomes. Such learned associations allow the amygdala to organize emotional activity in light of potential rather than actual events. For example, when a rat is exposed to an auditory tone that signals an impending shock, the auditory information is delivered to the amygdala’s lateral nucleus. The amygdala can respond based on relatively crude input delivered from the thalamus or on more highly processed information from the cortex. In either case, an immediate conditioned fear response is initiated by projections from the lateral nucleus to the basal nucleus (which projects to the ventromedial hypothalamus) and the central nucleus (which projects to the brainstem) (Davis, 1992; Petrovich, Risold, & Swanson, 1996; Savander, Go, LeDoux, & Pitkanen, 1995).

Although it is supported by activity within the PAG and the hypothalamus, the amygdaloid fear response differs from the more primitive forms of explosive and directed escape. In Gray’s (1996) terms, the amygdala facilitates anticipatory, active avoidance. Thus, the response integrates a
more flexible set of response options in relation to a potential, impending danger. Because these options depend upon complex, distal sensory information, the amygdala must be crucially involved in coordinating response and attentional functions. In locomotion, for example, the animal must employ attention to seek out sources of threat (to avoid) and safety (to approach). Such flexibility is based upon the amygdala’s control over more ballistic brainstem and hypothalamic functions. In addition, projections to response-programming mechanisms within the basal ganglia and frontal cortex allow a finer tuning of selected response options. Furthermore, the amygdala projects (together with the PAG and hypothalamus) to the brainstem’s ventral tegmental area, allowing it to adjust the focused attentional state related to the ascending dopaminergic projections. Finally, the amygdala projects extensively upon the sensory and association areas within the posterior cortex, allowing a more direct modulation of the sensory information that is converging upon the response systems. Thus, the amygdala’s integrative capacities are quite extensive, coordinating somatic, autonomic, and sensory processing within the brainstem, limbic system, and cortex.

A final telencephalic structure, the hippocampus, provides a mix of subcortical and cortical functions. In addition to its well-known role in spatial processing (Nadel, 1991), recent findings seem to be converging on a general role of the hippocampus in memory (Eichenbaum, Otto, & Cohen, 1994). In contrast to the amygdala, which is involved in associative memory processes involving discrete objects, the hippocampus appears more concerned with memory for contextual and relational information. Various researchers have described this capacity in terms such as working, declarative, and configural memory as opposed to reference, procedural, and associative memory. A simple example involves the conditioning of a fear reaction to background contextual information, apart from the conditioned stimulus itself (LeDoux, 1995). Consistent with these functions, it has been suggested that the hippocampus contributes to defensive behavior by providing contextual information that complements the object-information processed within the amygdala (LeDoux, 1996). This allows another type of anticipatory emotional function, based on contextual properties of the environment rather than discrete threatening objects.
The hippocampus has also been viewed as central to a behavioral inhibition system (Gray, 1996), which provides a fourth level to the hierarchy extending from the PAG to the hypothalamus to the amygdala. Gray (1996) suggests that the hippocampal formation contributes to defensive behavior in situations where active avoidance is in conflict with an equally strong approach tendency. Specifically, the behavioral inhibition system performs a conflict resolution function by determining which of the competing tendencies is most appropriate to the current (often spatial) context and suppressing the inappropriate options (and memories). This capacity relies on hippocampal projections to the fear-related circuits within the amygdala and hypothalamus, to response programming mechanisms of the basal ganglia, and to association and motor areas of the cortex. These outputs orchestrate a complex form of anticipatory anxiety, involving extensive contextual processing, competing response options, and an emphasis on inhibition.

In summary, subcortical emotional functions are carried out through a hierarchy of projections that integrate multiple motor, autonomic, modulatory, and endocrine subsystems. Although we have emphasized the descending influences, emotional states also coordinate many ascending subsystems, such as the massive forebrain projections from the locus coeruleus, ventral tegmental area, hypothalamus, amygdala, and hippocampus. These combined descending and ascending influences suggest that emotional states facilitate a vertical integration of processing systems across the brainstem, limbic system, and cortex. As these systems evolved, the higher level structures enabled flexible and integrative motivational systems based on increasingly distal and anticipatory sensory processing. This progression continued with the evolution of mammalian cortical networks.

Anatomy and Physiology of Cortical Systems

In reptiles and amphibians the cortex is only incipient, with a highly undifferentiated organization. Based upon his comparative anatomical studies, Herrick proposed that cortical morphogenesis is shaped by adaptation of cortical regions to subcortical inputs (Herrick, 1948).
The primitive pallium (hemisphere) can be divided into two fields: the paleocortex (olfactory) and the archicortex (hippocampal). Based upon modern anatomical findings, and a consideration of the subcortical and brainstem connections, we can use Herrick’s reasoning to see how the two fields of the pallium differentiated under the influence of unique subcortical inputs.

Archicortical and Paleocortical Routes of Corticolimbic Evolution

These two fields may be traced in Nauta’s pivotal study of the anatomy of the primate frontal lobe (Nauta, 1964). In studying the efferent connections of the prefrontal cortex, Nauta noticed that it was organized into two routes. One route originates from the medial prefrontal areas and travels via the cingulum bundle and terminates in the medial temporal lobe (subiculum and entorhinal areas). The second route (the uncinate fasciculus) connects the orbitofrontal cortex with the temporal pole, insula, and amygdaloid complex. Nauta remarked that the observed duality in the organization of prefrontal efferents may reflect something fundamental about the organization of the brain.

The anatomical separations of dorsal and ventral cortical systems led Sanides (1970) to propose that the cerebral cortex evolved along two lines of differentiation, one from the primitive paleocortex and the other from the archicortex. The archicortex gave rise to cortices on the mediodorsal surface, and the paleocortex gave rise to cortices on the ventrolateral surface of each hemisphere (Pandya, Seltzer, & Barbas, 1988a; Sanides, 1970). For example, the hippocampus gives rise to the cingulate cortex on the medial surface of the cerebral hemisphere. In the frontal lobe the anterior cingulate gives rise to cortex on the medial (such as the supplementary motor area) and dorsolateral surface. In contrast, the paleocortex gave rise to the orbitofrontal cortex and then ventrolateral frontal region. In monkeys, the principle sulcus is where the two trends converge on the lateral surface; in humans it is the inferior frontal sulcus. Sanides noted that the connectional findings by Nauta (Nauta, 1964) may reflect the differential organization of the cerebral cortex according to these two trends.
More recent evidence has verified the initial work of Sanides and Nauta. Based upon extensive studies detailing the architectonic and architecture of cortical connections in primates, Pandya and his associates (Pandya, et al., 1988a) found that cortices and structures within each trend show a preferential pattern of connectivity. Similar to the pattern of connections reported by Nauta, Barbas and colleagues found that the hippocampus, although projecting to both trends within the prefrontal areas, sends denser projections to the mediodorsal prefrontal cortex (Barbas, & Blatt, 1995), and that the amygdala's projections to the prefrontal limbic cortex were densest at caudal orbitofrontal regions (Barbas, & De Olmos, 1990).

The separation of the archicortical (dorsal) and paleocortical (ventral) trends is not limited to connections between limbic structures with the prefrontal cortex. It appears that the dual trends represent a fundamental way in which the brain is organized; this pattern holds for both motor (Barbas, & Pandya, 1986) and visual areas (Barbas, 1988). For example, the ventrolateral visual cortices (derived from the paleocortex), which are involved in the processing of object information, is preferentially connected with the ventrolateral and basal prefrontal cortex, and the medial and dorsolateral visual cortices, which are involved in visuospatial processing, are preferentially connected with the medial and dorsolateral prefrontal cortex (Barbas, 1988; Barbas, 1995). This pattern of connections with the visual areas no doubt contributes to the spatial functions of the mediodorsal prefrontal cortex (Fuster, 1989; Goldman-Rakic, Funahashi, & Bruce, 1990) and the object functions of the ventral and lateral prefrontal cortex (Wilson, O Scalaidhe, & Goldman-Rakic, 1993).

Additionally, Pandya and his colleagues (Pandya, et al., 1988a; Pandya, & Yeterian, 1990) noted that corticocortical connections reflect the evolutionary progression of the cortex. That is, the pattern of cortical projections follows the sequence of cortical differentiation, such that a given area has dense connections with its precursor and successor and lesser connections with evolutionary distant regions. More recent areas send projections to older areas via the supragranular layers and receive reciprocal projections to layer I. The older areas receive projections in layer IV and send efferents from their infragranular layers. The functional
significance of this architecture is that sensory areas which receive extensively processed information are densely connected with limbic centers involved in the control of motivation and memory. Furthermore, limbic control of information processing occurs most abundantly in the processing layers of sensory areas involved in complex and holistic information.

Cortico-limbic Mechanisms of Memory and Cognition

The clarification of cortical anatomy by Pandya and associates has shown the patterns of connectivity that must constrain efforts to frame computational models of memory in neuroanatomical terms (McClelland, McNaughton, & O'Reilly, 1995; Treves, & Rolls, 1994). The evolutionary analysis helps to explain why the limbic system forms the base for both sensory integration and motor organization: the cortex evolved through differentiating from limbic structures. This analysis also explains why corticolimbic pathways are essential to memory functions: it is the motivationally significant information which gains consolidation in memory (Kornhuber, 1973). The adaptive significance of sensory information—the extent to which it resonates with core concepts of needs and values—is what determines whether that information will be allocated processing capacity in a limited memory store.

Given the anatomical distinction between archicortical and paleocortical divisions of the cortex, it may be that the dorsal and ventral trends operate under different memory mechanisms, perhaps with different motivational biases. Mishkin and colleagues (Bachevalier, & Mishkin, 1986; Mishkin, 1982; Mishkin, & Murray, 1994; Mishkin, & Phillips, 1990) have outlined two memory circuits. One circuit consists of the mediodorsal nucleus of the thalamus, the amygdala, and the ventromedial aspects of the prefrontal lobe. We refer to this circuit as the ventral circuit to emphasize the paleocortical components within this system. The second circuit involves the anterior nucleus of the thalamus, the hippocampus, and the mediodorsal prefrontal lobe (cingulate). We refer to this circuit as the dorsal circuit to emphasize the cingulate cortex and the hippocampus, both belonging to the archicortical trend.
As described above, the hippocampus and the dorsal circuit may be important not only to spatial memory, but to memory for context (Nadel, 1992; Nadel, & Moscovitch, 1997). Based upon findings that the hippocampus is important to the processing and encoding of nonreinforced stimuli, Pribram (Pribram, 1991) suggested that the hippocampus supports the contextual representation in which behaviors occur. Similarly, Nadel (Nadel, 1992) believes that the hippocampal memory system emphasizes the unique aspects of an event to be remembered. Thus, memory supported by the hippocampal system would resemble a key aspect of episodic memory.

As suggested by the studies of lesions to the inferotemporal pathway (Ungerleider, & Mishkin, 1982), the ventral memory circuit is important to memory for objects rather than spatial locations. Nadel has suggested that the ventral circuit’s contribution may be generalized to categorical memory; that is, memory based upon identity of objects (Nadel, 1992). Consistent with a context versus category distinction, Gaffan (Gaffan, 1994) found that lesions to the fornix and perirhinal regions (dorsal circuit) result in recognition memory for complex scenes, whereas lesions to the amygdala (ventral circuit) result in deficits for food preference learning.

Although the theoretical analysis of corticolimbic function has yet to take advantage of the new insights of connectional anatomy, there have been suggestions that the motivational functions of limbic circuitry may be considered in neuropsychological models memory. Several lines of evidence show that corticolimbic pathways must be intact for memory consolidation to occur (Squire, 1986). Because patients with hippocampal and medial temporal damage may be impaired in new learning, but not in access to previously learned material, the assumption has been that the neocortex is adequate for storage and retrieval of memory, once the limbic structures and paralimbic cortices have participated in the consolidation process (Squire, 1986).

Nadel and Moskovitch (Nadel, et al., 1997) have recently reviewed the literature on human amnesia, and have drawn conclusions that may point to the importance of motivational factors in memory access. They point out that the evidence is actually fairly weak for full access to memories laid down before the medial temporal insult, particularly if memory is tested for autobiographical information rather than general semantic knowledge. Therefore, intact limbic structures may be
important to retrieval as well as consolidation of memory. The fact that the limbic contribution is particularly important accessing autobiographical memory is consistent with the view that the limbic system is important to evaluating the emotional and motivational significance of information to be retained in memory (Kornhuber, 1973).

**Descending Projections for Emotional Control**

In addition to showing how subcortical controls are brought to bear on the cognitive functions of the cortex, the evidence on the anatomy of corticolimbic networks provides important insight into the cortical influences on subcortical systems. Nauta’s (1964) initial delineation of the dorsal and ventral pathways of the frontal lobe showed the connections through which the frontal lobe can modulate limbic function, and these pathways have been confirmed by recent anatomical studies (Barbas, et al., 1986). Two carefully-studied examples, the startle response and primate emotional vocalizations, illustrate the role of cortical and limbic networks in regulating brainstem emotional systems.

The startle response shows how emotional states modulate brainstem function in humans as well as rodents and carnivores (Lang, Bradley, & Cuthbert, 1990; Vrana, Spence, & Lang, 1988). The startle response is a simple reflex mediated by a brainstem circuit of five synapses (auditory nerve, ventral cochlear nucleus, nuclei of the lateral lemniscus, nucleus reticularus pontus caudallis, spinal interneuron) plus the neuromuscular junction. This circuit is modulated by higher control from limbic structures, particularly the amygdala (Davis, Hitchcock, & Rosen, 1987). In humans, complex emotional states, engaging widespread cortical networks (such as when subjects view photographic slides of nudes or mutilated bodies), result in inhibition of the startle response for pleasant states and facilitation for aversive states (Lang, et al., 1990; Vrana, et al., 1988). The implication is that the cognitive representations of the cortex are associated with an appropriate adaptive set established across multiple levels of the neural hierarchy. Although startle may not be a significant motivational mechanism in humans, the orderly modulation of this reflex illustrates the
role of emotional states in linking a variety of systems, including postural, motor, sensory, and visceral, up and down the neuraxis.

The differential roles of cortical and limbic influences in regulating emotional systems was particularly clear in Ploog’s investigations of the monkey’s emotional vocalizations (Ploog, 1981). Ploog showed that the monkey’s calls are organized at the most basic level in discrete motor nuclei of the lower brainstem. At the next level, these nuclei are subordinated to the species-specific patterned motor sequences which are organized in the midbrain. For the motor sequences to show modulation by the animal’s current emotional state, the contributions of the limbic structures (amygdala and hippocampus) are required. The limbic cortical (cingulate) control of this hierarchy comes into play for what Ploog calls “voluntary call initiation,” in which the limbic-brainstem hierarchy is recruited in service of more complex goal-oriented behavior. At the final level, the neocortical control becomes important for “voluntary call formation,” in which frontal and motor cortices bypass the midbrain pattern generators to articulate specific vocalizations.

Ploog suggests that an elaboration of this neocortical control of vocalization may underlie human language capacity (Ploog, 1992). At the same time, he points out that the human brain has undergone expansion of structures such as anterior thalamic nuclei that link frontal cortex to the limbic system. Ploog’s analysis is consistent with the observations of disinhibited emotional displays in humans with cortical lesions (Brodal, 1969; Monrad-Krohn, 1947). Human vocalizations can thus be seen to involve not only the direct cortex-to-brainstem pyramidal pathways, but the hierarchy of pathways that integrate limbic with diencephalic and lower brainstem control of emotional vocalization.

Vertical Integration of Motivational and Emotional Systems

The anatomy and physiology of emotional systems is thus complex, comprising an evolved hierarchy of control processes. For a neuropsychological theory to account for the anatomical and
physiological evidence, a critical issue is vertical integration, how the control processes are coordinated across the multiple levels of the neuraxis. Fundamentally, human emotion encompasses the primitive reflexes and homeostatic drives of the vertebrate brain. Vertical integration must explain how these reflexes and drives can act to shape attention and memory, while at the same time becoming subordinated to more complex processes of cognitive representation.

In addition to the cortical modulation of subcortical responses, the extensive memory and cognitive capacities of the human cortex are dependent on adequate regulatory control by limbic and brainstem mechanisms. An important task for a neuropsychological theory of emotion is to explain how subcortical controls have evolved from direct, reflex-like adaptivity to provide generic support functions, such as arousal control, significance evaluation, and action motivation, to support the ongoing, cognitively-mediated sensorimotor integration that characterizes human behavior. We suggest that modern neuroanatomy and neurophysiology continue to support Jackson’s hierarchic, evolutionary model, specifically as applied to understanding human motivation and emotion.

Hierarchic Anatomy of Emotion and Memory

Connectivity implies function. Although this has always been the assumption of the anatomical method, modern connectionist models provide specific examples of how patterns of connectivity constrain the functional architecture of distributed networks (McClelland, McNaughton, & O’Reilley, 1995) (Rumelhart, & McClelland, 1986). Papez’s initial formulation of a limbic system came from observations of connectivity, indicated by the propagation of seizures through the dorsal limbic circuitry (Papez, 1937). The hierarchic organization of emotional behavior was recognized in MacLean’s pioneering studies of the limbic system (MacLean, 1993; Pribram, & MacLean, 1953). Maclean emphasized that the development of the cingulate cortex in mammals occurred with the appearance of fundamentally new forms of behavior, including social attachment and play. We can now recognize that these new capacities are essential to support the increasingly
extended juvenile period that allows the plasticity of the mammalian cortex (Tucker, Luu, & Pribram, 1996).

Several lines of evidence suggest that limbic mechanisms are critical to the integration of motivational controls with the cognitive capacities of human cortical networks. Mesulam proposes that the ascending cholinergic projections of the nucleus basalis provide modulatory control over the limbic-cortical interactions in memory consolidation (Mesulam, 1988). Studies of the cholinergic projections to the sensory input pathways of the amygdala show increasingly strong cholinergic modulation as the pathways approach the limbic system. Mesulam suggests that the cholinergic control may be important for gating cortical information exchange into and out of the 

limbic system.

However, the majority of the cortical areas do not project to the nucleus basalis; rather it is controlled primarily by the limbic structures and paralimbic cortices. Thus, an important aspect of the memory architecture of the mammalian cortex shows a fan-in of control, through which the limbic areas respond to the motivational and emotional content of the limbic-cortical traffic, determine the feedback to be applied to the nucleus basalis, and the nucleus basalis then projects back in a fan-out pattern to regulate widespread regions of limbic-cortical traffic (Mesulam, 1988).

Because the connections between cortical regions and limbic structures are required for memory consolidation (Squire, 1992), we can look to corticolimbic physiology for clues to the mechanisms for motivating memory consolidation. The hippocampus shows a particular affinity for the process of long-term potentiation, a model of Hebbian learning in which afferent input to a neuron results in a permanent potentiated response if it is associated with simultaneous activation of that neuron by another source (Gustafsson, & Wigstrom, 1988; Teyler, 1986). The reactivity of limbic structures is shown by the electrophysiological phenomenon of kindling. Electrical stimulation anywhere in the cortex tends to elicit responses from the amygdala and hippocampus preferentially. This observation of limbic excitability in animal studies parallels the tendency of epileptic seizures to focalize in the medial temporal lobes in humans. In the animal studies, repeated stimulation may “kindle” increasingly amplified responses from the limbic structures, propagating throughout the
The eventual result may be a pathological facilitation of corticolimbic excitability, evidenced by spontaneous seizures (Dichter, & Ayala, 1987).

Long-term potentiation is typically considered as a model of learning, whereas kindling is typically considered as a model of epilepsy. However, the relevance of corticolimbic sensitization to general mechanisms of learning and memory is shown by the finding that kindled seizures can be classically conditioned (Janowsky, Laxer, & Rushmer, 1980). The relevance of motivational control of corticolimbic excitability has been suggested by evidence of limbic sensitization in both normal and pathological forms of emotional responses (Harkness & Tucker, in preparation; Sapolsky, 1992; Tucker, & Luu, in press). Harkness and Tucker propose that a traumatic emotional response induces a pattern of limbic reactivity involving the same electrophysiological and endocrine mechanisms as kindling. Thus, subsequent exposure to a traumatic stimulus may elicit a response that is disproportional to the stimulus, unless the sensitization caused by the traumatic history is appreciated (Harkness & Tucker, in preparation).

**Mechanisms of Limbic Drive**

A different perspective on the contributions of limbic networks to cortical function has been provided by studies of emotional disorders in patients with temporal lobe epilepsy. Flor-Henry (Flor-Henry, 1969) observed that, for those epileptics who develop major psychiatric symptoms, patients with a left temporal focus were more likely to show a schizophreniform disorder, whereas those with a right temporal focus were more likely to show an affective disorder. A consistent set of observations, with a more direct parallel with hemispheric psychological functions, has been gathered in psychometric studies of temporal lobe epileptics by Bear and Fedio (Bear, & Fedio, 1977).

Bear and Fedio used not only self-ratings but observer ratings of the patients, and found what appeared to be an exaggeration of the pathological hemisphere’s psychological processes. Consistent with Flor-Henry’s observations, the right temporal epileptics showed affective instability and emotional expressiveness in their behavior, possibly suggesting an exaggeration of
the right hemisphere’s role in affective prosody and emotional communication. As if reflecting an exaggeration of the left hemisphere’s verbal cognitive capacities, the left temporal epileptics were found to show an “ideative” pattern of traits, with a preoccupation with intellectual, philosophical, and religious concerns.

The Bear and Fedio findings were predictably controversial, but they have been replicated in independent samples (Fedio, 1986; Fedio, & Martin, 1983). Although these findings may seem at first to confirm characterizations of the right hemisphere as emotional and the left hemisphere as non-emotional, closer inspection shows that the psychological operations of the epileptic hemisphere were charged with emotional significance for the left as well as right sides. The left temporal patients were obsessed with the personal importance of their intellectual concerns, often writing long treatises on the topics. To explain the exaggerated personal significance associated with the intellectual as well as affective behavior, Bear and Fedio proposed that the epileptic disorder resulted in a “functional hyperconnection” of limbic areas with the cortex.

These several observations on limbic reactivity may provide a way of understanding, in both psychological and neurophysiological terms, how limbic areas use their privileged connectivity with subcortical control systems to motivate memory consolidation and therefore cognitive processing. These observations may also help to integrate the emphasis on vertical integration in the present chapter with the evidence on hemispheric specialization reviewed in other chapters of this volume (Gainotti; Davidson). The massive human cortices provide extensive, but limited, representational capacity. The selection for a representation to be consolidated within cortical networks is based upon the adaptive resonance it recruits within limbic structures and paralimbic (archi and paleo) cortices. The adaptive resonance may be extended in time, as in ruminations, obsessions, and fantasies. The linked networks from sensory areas to limbic cortex (Pandya, & Yeterian, 1985) are engaged by this resonance, stabilizing memory representations in a distributed fashion across the paralimbic and neocortical levels.

As Pandya and associates have pointed out, the “back-projections” from limbic toward cortical areas are as extensive as the “forward projections” carrying sensory data from primary sensory
cortex to the intermediate association areas to paralimbic cortex. In modern psychological theories of perception, the perceptual process is seen as one in which memory and expectations resonate with, and shape the organization of, sensory input (Shepard, 1984). Shepard emphasizes the active, constructive role of memory by suggesting that perception is “hallucination constrained by the sensory data” (Shepard, 1984). In the context of the cortico-limbic architecture for perception, we would add that the resonance is shaped by inherent motivational constraints incorporated with the representation at the paralimbic level. Because they are the most densely interconnected of cortical networks, the paralimbic cortices provide a global, integrative, and yet undifferentiated, mnemonic context for cognition. Given their connectivity to subcortical controls, and their intrinsic excitability, the paralimbic cortices may provide the motivational drive for evaluating and consolidating significant contents in memory.

The physiology of motivated perception may thus be seen as a kind of arbitration across layered networks, anchored at the superficial layers by sensory analyzers, and energized in the deep layers by a resonance of the information with a global representation of adaptive need states (Derryberry, & Tucker, 1991). Because the paralimbic representations are the composite of the person’s developmental experience, the “limbic drive” structuring perception is formed not just by immediate homeostatic needs, but by more extended processes of self-representation. In this manner, the self may be understood as the implicit context of autobiographical memory. In normal personalities, there is an effective arbitration of perception between limbic drive, with its inherent motivational, self-referential constraints, and the requirements for maintaining veridical and complex representations in the neocortex. Judging from the personality disorders of temporal lobe epileptics, limbic drive occurs not only in the emotionally expressive right hemisphere, but in the verbal and analytic left hemisphere as well. We may speculate that the charged intellectualizations of the left temporal lobe epileptics may have their counterparts in disorders in which limbic kindling may be psychopathological rather than neuropathological, such as in the forced ruminations of the obsessive, or the rigid delusions of the paranoid (Shapiro, 1965). In contrast, excessive limbic drive may take a more affectively labile form within the right hemisphere,
supporting the loose modes of self-regulation of the histrionic, psychopathic, and impulsive personalities (Tucker, 1981).

Motive Persistence

Although the distorted cognition in emotional disorders may be most easily understood in terms of temporal-limbic dysfunction, there are more subtle deficits of motivation that occur with damage to the frontal lobe that result in profound deficits in life adjustment. Patients with mild frontal lesions may appear entirely normal to clinical examination and cursory neuropsychological testing. Despite the popular “working memory” notion of frontal lobe function, the memory deficits of these patients are typically not a significant feature of their clinical presentation (Squire, 1987). Yet within a short time of returning to work and family life, frontal patients often experience complete failures of adjustment. The problem seems to be not just a memory defect, but an inability to motivate ongoing behavior in relation to long-term goals (Lezak, 1983; Luria, 1973).

The frontal lobe’s expansion in human evolution may support a vertical integration of multiple adaptive systems to allow complex behavior to be organized over time. The massive cortical networks provide cognitive representational capacity, yet this capacity is not effective unless it is controlled in relation to the adaptive challenges that humans must organize over increasingly extended intervals of time. Extended challenges, such as keeping a job, or keeping a relationship, are the tasks at which frontal lesioned patients fail. As recognized in classical formulations, the frontal cortex mediates between the motivational and emotional representations in limbic areas and the organization of action in premotor areas (Nauta, 1971; Pribram, 1950). In doing so, the frontal networks are able to integrate functions such as arousal control that require contributions from lower as well as higher levels of the neuraxis (Luria, & Homskaya, 1970; Yakovlev, & Lecours, 1967).

In the extended plasticity of frontal networks through the long human juvenile period, cortical representations appear to form that mirror not only the perceptual operations of the posterior brain, but the regulatory controls of limbic and subcortical structures. The effect seems to be a kind of
encephalization of vertical integration, such that, toward the end of the juvenile period, human frontal cortical networks may be prepared to take on increasing control of the multiple levels of the neural hierarchy required for effective self-regulation.

_Intrinsic Motivation: The Cognitive Means Become the End_

The study of neuroanatomy and neurophysiology thus uncovers many mechanisms of emotion and motivation that humans share with primitive vertebrates. It also points to structures and mechanisms that are unique to the human brain. The increasing emphasis on “distant” events, evident in the progression from mesencephalic to diencephalic controls in primitive vertebrates, can be seen as a simple principle that continues to describe evolution of motivation in the executive functions of the human frontal lobes.

Although a thorough knowledge of the vertebrate control systems is essential for understanding human neuropsychology, the human cortex appears to represent and subsume motivational and emotional processes to an extent unknown among other mammals. Instead of stereotyped, species-specific motivations, humans acquire flexible, and highly idiosyncratic, patterns of motivation as neural plasticity shapes and reshapes the cortical mantle over a 20-year juvenile period.

To allow the extended neural plasticity of massive cortical networks, subcortical control systems appear to have become redirected from reflexive, immediate influences on behavior to take on the increasingly complex support operations for the corticolimbic matrix. Thus the task of arousal control is important not just to facilitate a reflex, but to facilitate memory consolidation across distributed cortical networks. The task of detecting the adaptive significance of a perception is important not just to release an endocrine secretion, but to code a sensory pattern for the limbic resonance that excites corticolimbic consolidation.

In many ways, the neurophysiology of human motivation has become encephalized in a way that inverts the relation between cortical and subcortical systems. Whereas the cortex was initially a device for elementary representation and memory, supporting the integration between the
stimulus and response circuits in the reflexes of the subcortical control systems, in human
evolution the tables are turned. The support of cortical operations has now become the primary
task of the subcortical systems. Although humans continue to struggle with biological needs, there
are now people who are motivated, at least for a few brief moments of their lives, by intellectual
interests. Activities such as curiosity, reasoning, or the search for understanding are a kind of
inversion of the vertebrate control hierarchy. The corticolimbic networks that once served a
subordinate support function for brainstem adaptive mechanisms have now commandeered the
motivational systems to support cognition as an end in itself.
References


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