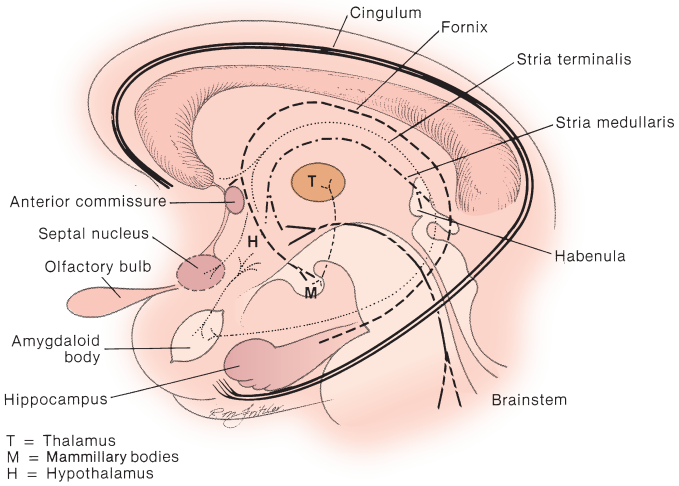

Fig. 4.2 Interlinking Neuron Network Within the Limbic Network. (Adapted from Kandel ER, Schwartz JH, Jessell TM. *Principles of Neural Science*. 4th ed. New York: McGraw-Hill; 2000.)

CLINICAL CASE 4.1

A patient example of limbic interactions can be found in a case description of a middle-aged woman admitted to the intensive care unit (ICU) with multiple pelvic fractures and diagnosed with severe internal bleeding, kidney failure, pneumonia, pulmonary emboli, and severe clotting in the lower extremities. The physician took her husband aside to let him know that she was going to die, to which her husband replied, "I understand. Juggling one system problem is easy, juggling two systems takes a little practice, and three-system involvement may challenge the best medical skill. She is presenting four or five body system failures, and you are sure no one can juggle that many problems." The doctor said yes, and the patient's husband then said, "Please keep juggling and don't worry about me, because if you do, I would then be one more ball to juggle." And it did seem that every time the doctors got a handle on a body system problem, another system would fail. She required services from an endocrinologist, infection control specialists, interventional radiologists, a pulmonologist, a hematologist, a vascular surgeon, an internal medicine specialist, a urologist, and a nephrologist. Each specialist shared his or her limited experience with a complex clinical problem like this and that there was nothing in the literature to help his or her respective understanding. After 2{1/2} months in the ICU, the woman survived. The physician who had foretold her death met again with the patient and her family. He stated, "How are you still alive? I know what we did medically, but that was not enough to keep you alive." And he was right. No model within each respective field could account for her recovery. However, the piece not considered within her medical management was the beliefs and spiritual strength of the patient and her family, a positive limbic network influence on the function of each failing body system.

investigating potential interactions of other systems with nuclei within the limbic network. This is no longer the case, as neuroscience research has helped to identify the critical nature of behaviors modulated or influenced by the limbic network. Based on research at a cellular level,[11–13] a consciousness level,[14–17] a bodily systems level,[18–20] and a quantum level[21–23] it is now clear that many systems are affected by the complex limbic network, and most notably, the motor systems.[24–31] A patient example of the complex and critical interactions between the limbic network, body systems, and its influence upon human behavior can be considered in Clinical Case 4.1.

The Limbic Network "MOVEs" Us

Moore[32] eloquently describes the limbic network as the area of the brain that moves us. The word *MOVE* can be used as a mnemonic for the functions of the limbic network that drive movement. As seen in Fig. 4.3 the *M* (motivation, memory) depicts the drive component of the limbic network; the *O* (olfaction) refers to the sense of smell and of other sensory inputs that drive motor, emotional, or visceral responses; the *V* (visceral) outlines the visceral and autonomic responses that serve as an indicator of the limbic network state; and *E* (emotional), the value or significance of individual feelings, attitudes, and beliefs that possess emotional significance for attention and learning.

Motivation

"The most powerful force in rehabilitation is motivation."[26] Without motivation the individual will not attend to the task and the neurobiology of learning will not occur. Motivation drives our motor system to develop motor programs that will enable us to perform and execute movements with the most efficient patterns available. In addition, motivation drives our ability to integrate the somatosensory map of functional skills[2] (cortical) and attention (limbic) necessary to process both sequential and simultaneous components (parts) of the movement task to be learned (whole).

Moore[32] considers motivation and memory as part of the MOVE system. Esch and Stefano[33] link motivation with reward, illustrating how the limbic network "learns" through repetition and reward. They state that the concept of motivation includes drive and satiation, goal-directed behavior, and incentive. They recognize that these behaviors maintain homeostasis and ensure the survival of the individual and the species. Motivation mediated by limbic (forebrain) and subcortical structures forms an interlocking neural network with the cognitive representation within the frontal regions and thus plays an important role in movement execution.[26,34]

Memory

The brain stores sensory and motor experiences as memory. Current theory supports a "dual memory system," each utilizing different pathways in the nervous system. Terms such as *verbal* and *nonverbal* and *intrinsic* and *extrinsic* have been given to these two memory systems. For this discussion, two specific categories of learning—*procedural* and *declarative*—will be used, although in today's neuroscience environment, the terms *implicit* and *explicit* memory are used as frequently. The limbic network plays a key role in both declarative and procedural aspects of memory and learning.[35–38] Before the limbic network's impact on learning and memory can be delved into, a clear understanding of what is meant by these functions is needed. Declarative (explicit) memory entails the capability to recall and verbally report experiences. This recall requires deliberate conscious effect, whereas the procedural counterpart is the recall of "rules, skills, and procedures (implicit),"[39] which can be recalled unconsciously. Both categories of learning have been correlated to limbic function.[40–42] These systems do not operate autonomously, and many therapeutic activities seem to combine these memory systems to achieve functional behavior.[39] The limbic amygdala and hippocampal structures and their intricate circuitries play a key role in the declarative aspect of memory.[35–38] The hippocampus may be more concerned with sensory and motor signals relating to the external environment, whereas the amygdala is related

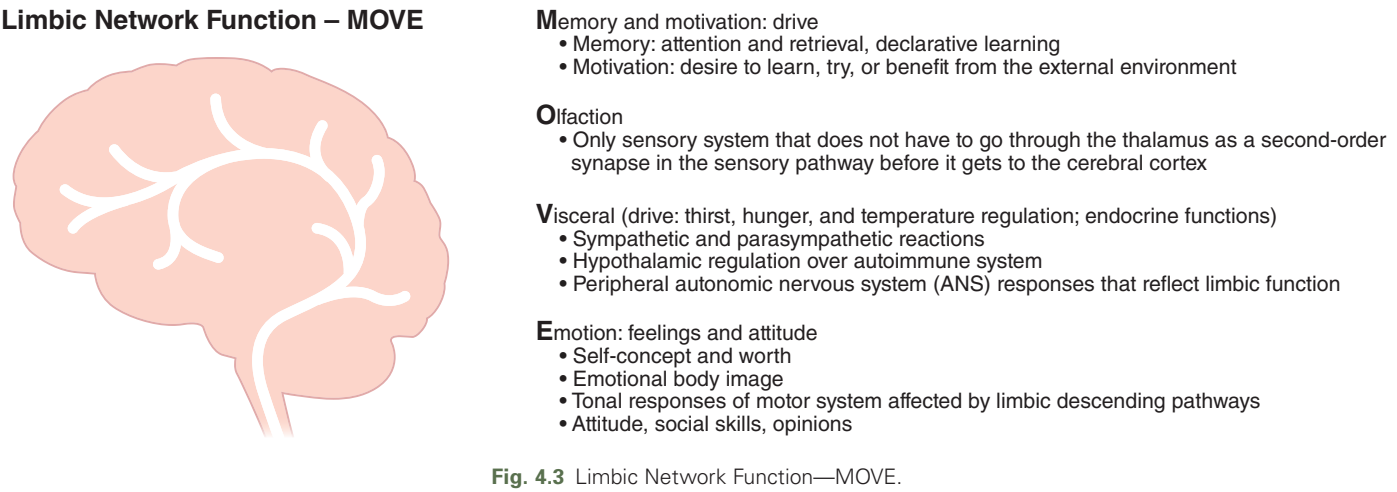

Fig. 4.3 Limbic Network Function—MOVE.

more to those of the internal environment. They both contribute in relation to the significance of external or internal environmental influences.[43,44–49] Procedural learning is vital to the development of sequence-specific learning and motor control. Acquisition and learning (memory) of new motor tasks involves dopaminergic projections from the VTA to the primary motor cortex for motor execution and initiating neuroplastic change, and from the NAc for the reward and reinforcement of that motor learning. The dorsal prefrontal cortex and the ACC are more active in the skill acquisition phase of motor learning than in the execution of pre-learned motor skills, consistent with the need for motivation as a requisite. Consolidation and retention occur as information passes through the limbic network nuclei; it is stored in cortical areas and retention and retrieval occurs without limbic involvement.[10,50–54]

Olfaction

The *O* refers to olfaction, or the incoming sense of smell, which exerts a strong influence on alertness and drive. This is clearly illustrated by the billions of dollars spent annually on perfumes, deodorants, mouthwashes, and soap as well as scents used in stores to increase customers' motivations to purchase. Olfactory input first synapses within the olfactory bulb. Subsequently, afferents travel to and synapse within the cerebral cortex without second-order synapse in the thalamus, as well as with structures within the limbic network. Although collaterals do project to the thalamus, unlike all other sensory afferent information, olfaction does not need to use the thalamus as a relay center to access the cortical structures.[39,55] Olfactory input that enters the limbic network may be used to calm or to arouse the patient, based upon the specific odor selected; for example, the use of aromatherapy to promote muscle relaxation prior to therapeutic massage.[56,57] Thus olfaction indirectly influences motor output via the limbic network's influence on muscle tone through brain stem modulation of the indirect or "emotional" motor pathways. Through brain stem connections to the reticular activating system, olfaction can have a powerful effect upon alertness. The evaluation of this system seems even more critical when a patient's motor control system is locked, with no volitional movement present. Research has shown that retrieval processing and retrieval of memory have a distinctive emotionality when they are linked to odor-evoked memories.[58,59]

Beyond olfaction, input from the other senses may not be reaching the cortical levels, such as in patients with lesions in the internal capsule or thalamus, and the patient may have a sensory-deprived environment. If the sensory input to the patient is deprived, the limbic network may place the patient in a "limbic low" state and the patient may withdraw physically or mentally, lose focus or attention, decrease motivation, and demonstrate a decrease in motor tone and output. Conversely, if the sensory input to the patient is excessive, whether through internal (patient/systems generated) or external (therapist, environment generated) feedback, the limbic network may go into an alert, protective mode, or "limbic high" state. The patient may withdraw physically or mentally, lose focus or attention, decrease motivation, and become frustrated or even angry. The resultant overload on the reticular system may be the reason for the shutdown of the limbic network versus dysfunction of the limbic network itself. Both are part of the same neuroloop circuitry and as such, in either situation, the CNS will not function optimally and learning will diminish. All these behaviors may be expressed within the hypothalamic-autonomic system as motor output, no matter where in the loop the dysfunction occurs. Having a functional understanding of the neuroanatomical sectors and their relationships with each other helps therapists unravel some of the challenging patient presentations after CNS insult.[60,61]

Therapists often try to increase motor activity through sensory input; however, they must cautiously avoid indiscriminately bombarding the sensory systems. The limbic network may demonstrate overload from stimulation at the same time the spinal motor generators reflect inadequate activation. One way that a therapist might assess for potential limbic overload would be to closely monitor the autonomic nervous system (ANS) responses, such as blood pressure, heart rate, internal temperature, and sweating, versus observing or measuring muscle tone.

Visceral or Autonomic

The *V* represents visceral or autonomic drives to movement. At the heart of the limbic network is the hypothalamus, the primary regulator of autonomic and endocrine functions. The hypothalamus controls and balances homeostasis of the internal and peripheral (skin) organ systems through regulation of sympathetic and parasympathetic reactions. Protective drives such as thirst, hunger, temperature regulation, and sexuality are controlled by this system.[39] However, the hypothalamus is also an important modulator of the limbic network, given its direct connections with the limbic midbrain,[39] the amygdala, and hippocampus, as well as close reciprocal interaction with most centers of the cerebral cortex, brain stem, and spinal cord. As such, the fact that autonomic and somatomotor responses controlled by the hypothalamus are closely aligned with the expression of emotions[62–65] and strong emotions and emotionally linked memories can change or support movement has clearly been established.[66]

Of clinical importance is that autonomical responses may reflect the presence of a limbic network imbalance that may go unnoticed by therapists. For example, patients with unstable body temperature regulation may exhibit signs of hypothalamic-pituitary involvement and overactivity.[39] Similarly, severe sweating of the palms or increased oral motor activity may be the first sign that the stress of an activity is becoming overwhelming to a patient. A therapist must continually monitor the patient's response behaviors to ascertain that they reflect true or desired motor output and not limbic influences over the motor system.

Emotional

E relates to emotions: the feelings, attitudes, and beliefs that are unique to that individual. These beliefs include psychosocial attitudes and prejudices, ethnic upbringing, cultural experiences, religious convictions, and concepts of spirituality.[67] When stimuli or tasks are endowed with emotional value or significance, a patient's attention is drawn to those with emotional significance, selecting these for attention and learning. Emotionally charged events will leave a more significant impression and enhance subsequent recall. All these aspects of emotions are strongly linked to the amygdaloid complex of the limbic network, and activity within the frontal lobe.[34,68,69] As a primary emotional center, it regulates not only our self-concept but our attitudes and opinions toward our external environment and the people within it. One aspect of self-concept is the emotional component of body image. A second self-concept deals with the patient's perceived worth or value to society, the world, and their role within it.[70] Both of these attitudes may be changed through enhanced mood or positive experience, enabling emotions to influence what is perceived and learned via the amygdala's reciprocal connections with the cortex.

Preconceived attitudes, social behaviors, and opinions have been learned by filtering the input through the limbic network. If new attitudes and behaviors need to be learned after a neurological insult, the status of the amygdalar pathways seems crucial. Damage to these limbic structures may prevent learning[71]; thus socially maladaptive behavior may persist, making the individual less likely to adapt to the social environment. It is often harder to change learned social behaviors than any other type of learning.[72–75] Because our feelings, attitudes, values, and beliefs drive our behaviors through both attention and motor responses, the emotional aspect of the limbic network has great impact on our learning and motor control. If a patient is not motivated to participate and places little value on a motor output, then low complacency results, and little learning will occur.[76–78] On the other hand, if a therapist places an extremely high value on a motor output as the expression of motor control success without interlocking that with the patient's sense of control, the behavioral response (limbic influence) may lead to inconsistency, lack of compliance/participation, and thus lack of motor learning and carryover.[76] In addition, it can cause the patient significant stress, which can prevent recovery and in some cases, cause disease.[79]

Repeated experience of reinforcement and reward leads to learning, changed expectancy, changed behavior, and maintained performance.[80] Emotional learning through the limbic network is very hard to unlearn once the behavior has been reinforced over and over.[81,82] For that reason, motor behavior that is strongly linked to a negative emotional response might be a very difficult behavior to unlearn. Repetition of motor performance with either the feeling of emotional neutrality or the feeling of success (positive reinforcement) is a critical element in the therapeutic setting. Consistently making the motor task more difficult just when the patient feels a need to succeed may decrease positive reinforcement or reward, lessen the patient's motivation to try or participate, and decrease the probability of true independence once the patient leaves the clinical setting. When pressure is placed on therapists to produce changes quickly, strategic and meaningful repetition and thus long-term learning are often jeopardized. Rapid progression based solely upon therapist/clinic requirements may impede progress and yield a dramatic effect on the quality of the patient's life and the long-term treatment effects once he or she leaves the medical facility. Motor control theory (see Chapter 3) coincides with limbic research regarding reinforcement. Inherent feedback within a variety of environmental contexts allowing for error with correction leads to greater retention.[83] Repetition or the opportunity to practice a task (motor or cognitive) in which the individual desires to succeed will lead to long-term learning.[84] Without practice or motivation, the chance of successful motor learning is minimized. This continues to highlight the importance of both therapeutic environment and therapeutic alliance, which we will discuss in greater detail.

Multiple nuclei and interlinking circuits of the limbic network play crucial roles in behavioral and emotional changes[85–87] and declarative memory.[9,86–102] The loss of any link can affect the outcome activity of the whole circuit. Thus damage to any area of the brain can potentially cause malfunctions in any or all other areas, and the entire circuit may need reorganization to restore function.

THE NEUROSCIENCE OF THE LIMBIC NETWORK

The limbic network comprises a group of nuclei, tracts, and cortical areas that lie beneath the cortex and surround the thalamic structures. All of the areas of the limbic system are interconnected with each other through both simple and complex reverberating neural pathways. There are extensive connections between the limbic system and the hypothalamus and brain stem structures, these together play a substantial role in the regulation of homeostasis and autonomic control. Similarly, there are extensive connections to the structures of the basal ganglia, thus influencing motivation to move, as well as initiation and modulation of motor output.[103] A limited overview of the anatomy and physiology of the limbic network is presented in the following sections, designed to guide our understanding of the limbic network. The complexities of the network and its complex circuitry can be found upon deeper review of primary and secondary evidence.[7,39,104–108]

Neuroanatomy

Basic Structure and Function

Broca[109] first conceptualized the anatomical regions of the limbic lobe as forming a ring around the brain stem. Today, neuroanatomists do not differentiate an anatomical lobe as limbic, but rather refer to a complex network that encompasses cortical, diencephalon, and brain stem structures.[39] This description is less precise and includes (but is not limited to) the orbitofrontal and prefrontal cortex, hippocampus, parahippocampal gyrus, cingulate gyrus, dentate gyrus, amygdaloid body, septal area, hypothalamus, and some nuclei of the thalamus.[39,110–114] Anatomists stress the importance of looking at the interrelated structures, pathways, and functional loops within the complex limbic region.[85,115]

The limbic network can be best visualized as consisting of both cortical and subcortical structures, with the hypothalamus located at the central position (Figs. 4.4 and 4.5). The hypothalamus is surrounded by a circular alignment of the subcortical limbic structures linked with one another and the hypothalamus. These subcortical structures include the amygdalar complex and the hippocampal formation as the major input structures, and the anterior nuclei of the thalamus (limbic thalamus), as well as the NAc, the fornix, and the septal nuclei areas. The septal area projects to emotion-generating

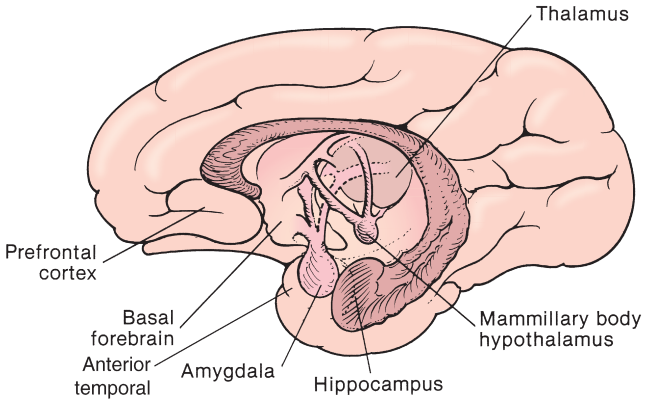

Fig. 4.4 Anatomy of the Limbic Network: Schematic Illustration.

areas and plays an important role in feelings of social connectedness and bonding. The fornix contains major efferent fibers from the hippocampus, as well as carrying some afferent fibers to the hippocampus from structures in the thalamus and basal forebrain.[116] The cingulate fasciculus carries amygdalic and hippocampal projections to and from the prefrontal cortex, linking many basic perceptual strategies, such as body schema, hearing, vision, and smell, to the emotional and learning centers of the limbic network.[117]

The subcortical structures are again similarly surrounded by a ring of cortical structures collectively called the *limbic cortex*, which includes the frontal cortex, the ACC/gyrus, the parahippocampal gyrus, and the uncus. The limbic network circuitry contains parallel and reverberating connections between the subcortical and limbic cortex structures, the anterior nuclei of the thalamus *(limbic thalamus)*, as well as to the limbic forebrain NAc and limbic midbrain structures: VTA and midbrain raphé nuclei of the basal ganglia. There are neuroanatomists who include the olfactory system and the basal forebrain area (cognition and memory) within the network as well (see Fig. 4.5). Olfaction is included as part of a "mesolimbic" system, linking olfaction to the midbrain structures of the NAc and the VTA.

Vitally linked to the limbic network is the excitatory reticular activating system and other brain stem nuclei of the midbrain. Some consider components of the midbrain a very important region for emotional expression.[92] Derryberry and Tucker[92] found that attack behavior aroused by hypothalamic stimulation is blocked when the midbrain is damaged and that midbrain stimulation can be made to elicit "attack behavior" even when the hypothalamus has been surgically disconnected from other brain regions. Recent research has clearly identified the neurochemical precursors to this aggressive behavior.[39,62,118–120] This "septo-hypothalamic-mesencephalic (midbrain)" continuum, connected by the medial forebrain bundle (see Fig. 4.5), is suggested as vital to the integration and expression of emotional behavior.[121] The linking of other brain structures to emotions came initially from the work of Papez,[122] who first identified the hippocampal-fornix circuit. He saw this as a way of combining the "subjective" cortical experiences with the emotional subcortical (hypothalamic) contribution. Earlier, Broca[109] labeled the cingulate gyrus and hippocampus "circle" as "the great limbic lobe." Today, the concept of the limbic network and its interaction with sensory inputs and motor expression has become extremely complex.[123] Mood can change motor output, and motor activity can change mood.[124,125]

Klüver and Bucy[126] linked the anterior half of the temporal lobes and the amygdaloid complex to the limbic network. They showed changes in behavior, with specific loss of the amygdaloid complex and anterior hippocampus input, resulting in (1) restless overresponsiveness, (2) hyperorality, or examining objects by placing them in the mouth, (3) psychic blindness of seeing and not recognizing objects and the possible harm they may entail, (4) sexual hyperactivity, and (5) emotional changes characterized by loss of aggressiveness. These changes have been named the *Klüver-Bucy syndrome*.[127] Myriad connections link the amygdala to the olfactory pathways, the frontal lobe and cingulate gyrus, the thalamus, the hypothalamus, the septum, and

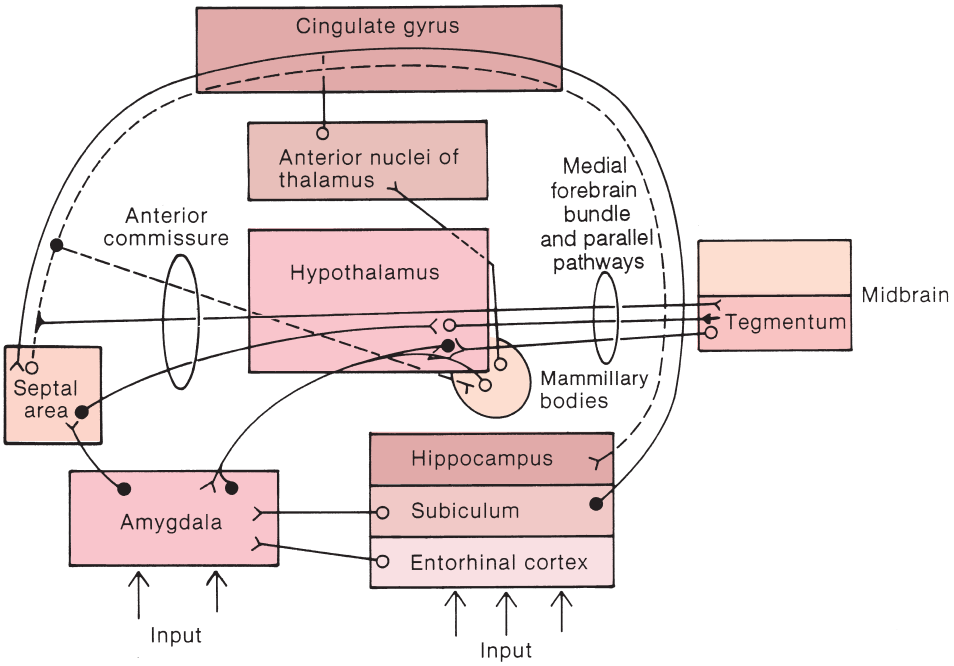

Fig. 4.5 Limbic network circuitry with parallel and reverberating connections and with medial forebrain bundle.

the midbrain structures of the substantia nigra, locus coeruleus, periaqueductal gray matter, and the reticular formation. The amygdala receives feedback from many of these structures it projects to by reciprocal pathways.

At the heart of the limbic network is the hypothalamus. The hypothalamus, in close reciprocal interaction with most centers of the cerebral cortex and the amygdala, hippocampus, pituitary gland, brain stem, and spinal cord, is a primary regulator of autonomic and endocrine functions and controls and balances homeostatic mechanisms. Autonomical and somatomotor responses controlled by the hypothalamus are closely aligned with the expression of emotions.[62–65]

In the temporal lobe, anteromedially is the amygdaloid complex of nuclei, with the hippocampal formation situated posterior to it. Located medial to the amygdala is the basal forebrain nuclei, which receive afferent neurons from the reticular formation, the hypothalamus, and the limbic cortex. From this basal forebrain, efferents project to all areas of the cerebral cortex, the hippocampus, and the amygdaloid body, providing an important connection between the neocortex and the limbic network. These nuclei represent the center of the cholinergic system, which supplies acetylcholine to limbic and cortical structures involved in memory formation.

Interlinking the Components of the System

The limbic network has many reciprocating interlinking circuits among its component structures, which provide for much functional interaction as well as allow for continuing adjustments with continuous feedback (see Fig. 4.2).[39,62] Neuroimaging has helped reduce uncertainty concerning the anatomical pathways, and neurochemistry has widened the possibilities of variations across synaptic connections.[128–130] The largest of the interlinking pathways is the fornix, providing efferent and afferent connections to the hypothalamus and connecting the limbic network structures.[131] The stria terminalis, another of the linking circuitry components, originates in the amygdaloid complex and follows a course close to the fornix to end in the hypothalamus and septal regions. The amygdala is also directly connected to the septal region by a short pathway, the *diagonal band of Broca.* These pathways serve as foundation for emotion memory and bonding. A third pathway, the uncinate fasciculus, connects the amygdala and the orbitofrontal cortex serving as a foundation for decision making.[39,132,133]

The medial forebrain bundle and other parallel circuits (see Fig. 4.5) are vital connections of the limbic network.[134] These pathways course through the lateral hypothalamus to terminate in the cingulate gyrus in its ascending limb and in the reticular formation of the midbrain in its descending part; these pathways have strong interconnections and control over the periaqueductal gray area, and thus influence upon descending modulation of pain signals.[135]

Commissural fibers from the vestibular nuclei run through the lateral medullary reticular formation (parvicellular reticular formation [PCRF]) and connect the vestibular nucleus to the reticular formation. The PCRF and the solitary nucleus receive both vestibular and nonvestibular input from the cortex, cerebellum, and the limbic network and are considered functionally as the "vomiting center." It also receives heavy input from the chemoreceptor region in the floor of the fourth ventricle (area postrema), resulting in vomiting in response to noxious chemicals. The PCRF also projects fibers to the parabrachial nuclei that contain the respiratory centers and to the hypoglossal nucleus to activate and coordinate the protective gag reflex.[136] Visceral autonomic input from multiple sources, including the vestibular nuclei, converges on the parabrachial nucleus. The locus ceruleus and autonomical brain stem nuclei also receive vestibular nuclear input.[137–141] Thus cardiovascular activity and respiration (brain stem–mediated autonomic activity), as well as vomiting, are highly influenced by the status of the vestibular system and the limbic system. This helps us to understand how cold to the neck or forehead, pressure to the wrist, or taste or olfactory input of ginger depresses autonomic reactions and nausea in response to chronic vestibular or interneuronal connection problems. There are three different types of drugs that neuroanatomically suppress or modulate vestibular input and thus have a dramatic effect on dizziness and nausea.[142] Additionally, functional magnetic resonance imaging (fMRI) confirms that there is increased activity within the inferior frontal cortex when nausea is induced by either vestibular stimulation or ingestion of an emetic.[143] This research supports that there is a strong interconnection among vestibular input, limbic nuclei, and autonomic responses.[144]

There are also connections between the parabrachial nucleus and higher brain centers, including the amygdala, which is known to be critical in the development of conditioned avoidance, such as found in agoraphobia, as an example. Thus vestibular input results in a sensory stimulus that may induce a state of general autonomic discomfort as a trigger of avoidance that precedes the onset of a panic attack.[14,136,138,144] Vestibular firing rates are further modulated and regulated by the dorsal raphe nucleus of the midbrain and rostral pons. The dorsal raphe nucleus is the largest producer of serotonin in the brain, which further explains the significant linkage between vestibular dysfunction and anxiety, and sleep deprivation and anxiety.[145]

Additionally, animal research has shown that bilateral vestibular lesions result in changes in the morphology and function of the hippocampus, specifically associated with hippocampal atrophy. The hippocampus contributes to spatial and gravitational orientation, cognition, learning, and memory (spatial and nonspatial), which are symptoms and functional limitations often identified by individuals with vestibular dysfunction.[146–154]

Central pattern generators found in the caudal brain stem and the spinal cord are understood to generate fixed rhythmic motor output patterns such as biting and swallowing. These motor tracts receive direct and indirect afferent information from the periphery and are part of the interneuronal projection system to motor neurons, contributing to the activity within the motor neuron pool.[155–157] Their output is linked to the proximal (axial) and distal motor control system through the ventromedial and lateral descending motor pathways, modulated by a variety of structures, and regulated by the prefrontal area.[135,158–162] Their output is also strongly linked to the limbic network, resulting in an emotional context linked to the motor output.[158,163] The functional motor implication of these tracts is determined by whether the fibers project as part of the medial or lateral descending system. The medial components of this system originate within the medial portion of the hypothalamus, and the lateral portion originates in the limbic network (lateral hypothalamus, amygdala, and bed nucleus of the stria terminalis). The medial system, through the locus coeruleus, periaqueductal gray matter, and raphe spinal pathways, contributes to the general level of activity of both somatosensory and motor neurons. As such, the limbic network can have an effect on both somatosensory input and motor output. A change in activity in this system can alter the level of excitation at the first order synapse, thus altering the processing or sensitivity to that afferent information as it enters the nervous system. Similarly, it can alter the level of motor activity and thus motor output or expression, which may account for the increase in extensor muscle tone and extension seen with anger and the flexion and decrease muscle tone seen with depression. The lateral system seems to be involved in more specific motor output related to emotional behavior and may explain some of the loss of fine motor skill when one is placed in an emotional situation such as competition. The clinical relevance of this information highlights the

need during patient examination to differentiate whether observed postural/muscle tone abnormalities are deficits within the motor system itself, or are a result of limbic system influence on that motor output. The clinician would need to observe and assess the emotional state, as well as how it changes with patient mood or activity, or with modification of the therapeutic environment. If the abnormal state consistently alters with mood shifts of control of emotional variables, then limbic involvement causing motor control disturbances could be identified. Human social behavior requires motor expression, yet that behavior is driven through the limbic circuitry.[164–167]

These links enable the limbic network itself and the non–limbic-associated structures to act as one neural task system. No portion of the brain, whether limbic or nonlimbic, has only one function.[39] Each area acts as an input-output station. At no time is it totally the center of a particular effect, and each site depends on the cooperation and interaction with other regions. The concept of neuroplasticity within the motor system and motor learning is well understood by physical therapists, but less understood is the integration of this emotional system interaction with sensory and motor components of motor performance and learning. Research is identifying that these neurocircuitries are present and interactive, and therefore should be considered.[164]

Neurochemistry

Discussion of the limbic network's intricate regulation of many neurochemical substances is not within the scope of this chapter. Yet therapists need to appreciate how potent this system can be with respect to the influence of neurochemical imbalance or loss on motor control, memory, or motor learning. The amount of research reflecting new understanding of the role of neurochemistry in brain function highlights the importance of frequent review of the literatures.[168–176]

More than 200 neurotransmitters have been identified within the nervous system.[39] The hypothalamus, the physiological center of the limbic network (see Figs. 4.1 and 4.5), is involved in neurochemical production and is essential for the passage of information along specific neurochemical pathways within the network. Squire and colleagues[177] consider it the major motor output pathway of the limbic network, which also communicates with every part of this system.

Neuropeptides

The importance of neuropeptides is being recognized relative to the limbic network's role in the regulation of affective and motivated behaviors.[34,39,135,178–180] Certain nuclei of the hypothalamus produce and release these neuroactive peptides, which have long-acting effectiveness as neuromodulators, controlling the levels of neuronal excitation and effective functioning at the synapses. Through their long-lasting effects, they regulate motivational levels, mood states, and learning. These peptide-producing neurons extend from the hypothalamic nuclei to the ANS and to the nuclei of the limbic network, where they modulate neuroendocrine and autonomic activities. Lesions in the medial hypothalamus affect hormone production and thus alter regulation of many hormonal control systems.[39] For example, head injury may lead to medial hypothalamic lesions general hyperactivity, signs of hostility after minimal provocation, as well as huge weight gain resulting from the increase of insulin in the blood (increasing feeding and converting nutrients into fat) and loss of satiety.

The nuclei of the amygdaloid complex represent the center of the cholinergic system, which supplies *acetylcholine* to limbic and cortical structures involved in memory formation. Depletion of acetylcholine in patients with Alzheimer disease relates to memory loss.[135,181–183,184]

Monoamines

The monoamines play a critical role in many aspects of function and dysfunction within the limbic network. As a quick overview, the noradrenergic system (noradrenaline and adrenaline) plays a significant general role in the body's response to stressors. In the brain, the noradrenergic system is located primarily in the locus coeruleus and plays a significant role in modulating behavioral and cognitive function within the cortex.[185] The adrenal corticosteroids also contribute to modulation of long-term potentiation within the hippocampus.[186] Novelty or reward-seeking and motivational behaviors of the limbic network seem to be dopamine dependent,[187] whereas coordination of circadian body rhythm and sleep (critical for motor performance and learning) is influenced by levels of all of the monoamine neurotransmitters.[188–190]

A functional deficiency in monoamines, especially *serotonin*, is hypothesized to be a primary cause of depression.[191,192] The serotonin systems originate in the rostral and caudal raphe nuclei in the midbrain. Ascending serotonergic tracts start in the midbrain and ascend to the limbic forebrain and hypothalamus; they are concerned with mood and behavior regulation. Damage to the ascending pathways contributes to depression as a mood disorder. In addition, newer evidence has highlighted the important role serotonin plays in motor control.[193]

Descending pathways from the raphe nuclei to the substantia gelatinosa are involved in pain mechanisms. Through a complex sequence of biochemical steps, a reduction in serotonin in the raphe nuclei contributes to the increased sensitization of the presynaptic terminals of the cutaneous sensory neurons. Increased central sensitization of these terminals can lead to a hyperactive withdrawal reflex or hypersensitivity to cutaneous sensory input.[39] This would account for the behavior patterns seen in patients with head trauma, when the therapist sees a flexed posture with a withdrawn or depressed affect associated with an extreme sensitivity to touch or even cutaneous input from clothing, air, etc.

Lesions in the lateral hypothalamus lead to damage of *dopamine*-carrying fibers that begin in the substantia nigra and filter through the hypothalamus to the striatum of the basal ganglia. Lesions, either along this tract or within the lateral hypothalamus, lead to aphagia and hypoarousal, as well as marked passivity with decreased functioning. Decreased sensory awareness contributing to sensory neglect is also present in lateral hypothalamic lesions. Disruptions of the indirect (hypothalamic) and direct (independent of hypothalamus) pathways from the mammillary bodies to the anterior thalamus contribute highly to loss of spatial orientation and memory.[194] Bilateral infarcts within the mammillothalamic tract result in acute Korsakoff syndrome.[195]

Dopamine is critical for motor cortex plasticity and motor skill acquisition and learning.[196] Dopamine released from the VTA in the midbrain projects to the primary motor cortex (M1) and enables motor skill acquisition.[52] Moreover, the dopaminergic VTA neurons projecting to M1 are activated when rewards are obtained during motor skill acquisition, but not during task execution in later associative or autonomous stages of motor learning, or when rewards are not associated with performing a skilled movement. Dopamine released from the VTA to the NAc and the frontal cortex plays an important role in reward processing for motor learning.[51] Furthermore, in animal study, destruction of the VTA dopaminergic neurons prevented improvements in forelimb reaching, but learning recovered on administration of levodopa directly into the M1 of these VTA-lesioned animals. Of note is that lesioning the VTA did not affect performance of an already learned skill, meaning movement execution remained intact.[52]

It is hypothesized that the underlying pathophysiological mechanism of one form of schizophrenia involves an excessive transmission

of *dopamine* within the mesolimbic tract system.[39] The dopaminergic cell bodies are located in the VTA and the substantia nigra. Some of these neurons project to the limbic network, specifically to the NAc, the stria terminalis nuclei, parts of the amygdala, and the frontal entorhinal and ACC, serving to modulate the flow of neural activity through the limbic network.[39] The NAc may serve a critical role, acting as a filtering system with respect to affect and certain types of memory through its influence over the hippocampus, frontal lobe, and hypothalamus.[39]

The specific roles of the *noradrenergic* pathway are numerous and affect almost all parts of the CNS. The center for the noradrenergic pathways is located within the caudal midbrain and upper pons. Its nucleus is referred to as the *locus coeruleus.* This nucleus sends at least five tracts rostrally to the diencephalon and telencephalon.[39] Of specific interest for this discussion are the projections to the hippocampus and amygdala, which have an excitatory effect on the regions where they terminate.[39] Thus the activation of this system will heighten the excitation of the two nuclei within the limbic network that are involved in declarative learning and memory. This excitation or hyperactivation may cause "overload" or impair focus of attention and learning.[197] Decreased activity may prevent learning and memory. Attention to task may depend on continuing noradrenergic stimulation. These tracts, travelling rostrally from the midbrain, play a key role in alertness. The correlation of alertness and attention to performance and learning of motor tasks can be demonstrated.[39]

In conclusion, the neurochemistry of the limbic network is intricately linked to the neurochemistry of the brain and the body organs regulated by the hypothalamus. All systems within the limbic circuitry seem to be interdependent, with the summation of all the neurochemistry being the determinants of the specific processing of information. Similarly, the interdependence of the limbic network with almost all other areas of the brain and the activities of those areas at any time reflect the complexity of this system.

Neurobiology of Learning and Behavior

Strub and Black[198] view behavior as occurring on distinct interrelated levels that represent behavioral hierarchies. Starting at level 1, a state of alertness to the internal and external environment must be maintained for motor or mental activity to occur. The brain stem reticular activating system brings about this state of general arousal by relaying in an ascending pathway to the thalamus, the limbic network, and the cerebral cortex. To proceed from a state of general arousal to one of "selective attention" requires the communication of information to and from the cortex, the thalamus, and the limbic network and its modulation over the brain stem and spinal pattern generators.[39,199]

Level 2 of this hierarchy lies in the domain of the hypothalamus and its closely associated limbic structures. This level deals with subconscious drives and innate instincts. The survival-oriented drives of hunger, thirst, temperature regulation, and survival of the species (reproduction) and the steps necessary for drive reduction are processed here, as well as learning and memory. Most of these activities relate to limbic functioning. If an individual or patient is in a perceived survival mode, little long-term learning regarding either cognition or motor programming will occur. Thus making the patient feel safe is initially a critical role for the therapist. This approach may require placing the therapist's hands on the patient initially to take away any possibility of falling. The therapist would first deal with the emotional aspect of the patient's environment and then shift to the motor learning and control component, in which the patient is empowered to practice and self-correct within the program she or he can control.

On level 3 only cerebral cortical areas are activated. This level deals with abstract conceptualization of verbal or quantitative entities. It is at this level that the somatosensory and frontal motor cortices work together to perceptually and procedurally develop motor programs. The prefrontal areas of the frontal lobe can influence the development of these motor programs, thus again illustrating the limbic influence over the motor system.[200–203]

Level 4 behavior is concerned with the expression of social aspects of behavior, personality, and lifestyle. Again, the limbic network and its relationship to the frontal lobe are vital. The shift to the World Health Organization International Classification of Functioning, Disability and Health (WHO-ICF) model, which reflects patient-centered therapy, has actualized the critical importance of this level of human behavior.[204–208]

The interaction of all four levels leads to the integrative and adaptable behavior seen in the human. Our ability to become alert and protectively react is balanced by our previous learning, whether it is cognitive-perceptive, social, or affective. Adaptability to rapid changes in the physical environment, in lifestyles, and in personal relationships results from the interrelationships or complex neurocircuitry of the human brain. When insult occurs at any one level within these behavioral hierarchies, all levels may be affected.

A fifth level of limbic function may one day be recognized as the link between the hard science of today and unexplained medical mysteries of healing. Meanwhile, how might the function of the limbic system explain certain mysteries, such as why some people heal from terminal illnesses spontaneously, others heal in ways not accepted by traditional medicine,[213,214] and others just die without any known disease or pathological condition?[67,105,215,216] It is proposed that a characteristic of the fifth level of limbic function is the patient's strong, emotional belief[67] that he or she will heal or will not heal. How conscious intent drives hypothalamic autoimmune function is being unraveled scientifically, and clinicians often observe these changes in their patients. Through observation it becomes apparent that patients who believe they will get better, often do, and those who believe they will not, generally do not. Whether belief comes from a religious, spiritual, or hard science paradigm, that belief drives behavior, and that drive has a large limbic component. Intellectual curiosity and human compassion motivates practitioners to explore these mysteries that otherwise might remain unexplained, overlooked, disbelieved, or forgotten.

As Western medicine continues to explore the intricate neurochemistry of the limbic network,[209–212] alternative medicine is establishing effectiveness and efficacy for various interventions, approaches, and philosophies (see Chapter 39). The intersection of evidence and treatment efficacy is this: there is an interlocking dependence among somatosensory mapping of the functional skills[2] (cognitive), attention (limbic) necessary for any type of learning, and the sequential, multiple, and simultaneous programming of functional movement (motor). The limbic amygdala and hippocampal structures and their intricate circuitries play a key role in the declarative aspect of memory and learning.[35–38] The dorsal prefrontal cortex and the ACC were activated more when the subjects learned[53,54] a new sequence than they were when subjects simply paid attention to a pre-learned sequence.[51,52] Once this syntactical, intellectual memory is learned and taken out of short-term memory by passing through limbic nuclei, the information is stored in cortical areas and can be retrieved at a later time without limbic involvement.[50]

Limbic Influence on Memory and Motor Learning

Recovery of function after injury may involve mechanisms that allow reorganizing of the structure and function of cortical, subcortical, and spinal circuits. In very young infants, areas within opposite hemispheres may "take over" function, whereas in more mature brains reorganization of existing parallel and silent pathways within and between hemispheres, as well as synaptogenesis are accepted recovery

mechanisms within the expanding knowledge of neuroplasticity.[217–220] For complex behavior, such as in motor functioning requiring many steps, the limbic network, cortex, hypothalamus, basal ganglia, and brain stem work as an integrated unit. As such, damage to one area may cause the whole system to initially malfunction. In addition, a lesion in one area may cause secondary dysfunction of a different area that was not damaged by the primary lesion. Without appropriate task (activity), internal and external environmental challenge designed to promote neuroplasticity, the initial malfunction can become permanent.[221] The optimal rehabilitation timing for neuroplastic change has not yet been firmly established; however, it is accepted that there are key plastic "time windows."[222] The use of drug therapies to alter cellular activity and plasticity within these key windows after CNS damage has become a huge area of pharmaceutical research.[223–229] This line of research is focused on the effect of the sensorimotor representation of movement within the cortex, which is a net effect of the stimulation of multiple pathways. The activation of specific direct, indirect, or modulating pathways engaged during the process of function-induced neuroplasticity, such as those of the limbic network, is less understood.

"Ultimately, to be sure, memory is a series of molecular events. What we chart is the territory within which those events take place."[32] The brain stores sensory and motor experiences as memory. In processing incoming information, most sensory pathways from receptors to cortical areas send vital information to the components of the limbic network. For example, extensions can be found from the visual pathways into the inferior temporal lobe (limbic network).[39,230,231] Visual information is "processed sequentially" at each synapse along its entire pathway, in response to size, shape, color, and texture of objects. In the inferior temporal cortex, the total image of the item viewed is projected. In this way the sensory inputs are converted to become "perceptual experiences." This also applies to other sensory stimuli, such as tactile, proprioceptive, and vestibular. The process of translating the integrated perceptions into memory occurs bilaterally in the limbic network structures of the amygdala and the hippocampus.[39,43,168,232–241]

Before the limbic network's impact on learning and memory can be investigated, a clear understanding of what is meant by these functions is needed. Current theories support a "dual memory system" consisting of different pathways in the nervous system. Terms such as *verbal* and *nonverbal, habit* versus *recognition, intrinsic* and *extrinsic,* and *procedural* and *declarative* have been given to these two memory systems. These systems do not operate autonomously, and many therapeutic activities seem to combine these memory systems to achieve functional behavior.[39] As such, in reality, the complexity of memory is not a two-category system. Verbal and nonverbal memory both interact with declarative function.[242] Even within spatial memory, additional areas of integration and parallel circuitry have been identified.[243,244]

For this discussion, two specific categories of learning—procedural and declarative—will be used, although in today's neuroscience environment, the terms *implicit* and *explicit memory* are used as frequently. Both categories of learning have been correlated to limbic function.[40–42] Declarative (explicit) memory entails the capability to recall and verbally report experiences. This recall requires deliberate conscious effect, whereas the procedural counterpart is the recall of rules, skills, and procedures (implicit),[39] which can be recalled unconsciously.

Procedural learning is vital to the development of motor control. A child first receives sensory input from the various modalities through the thalamus, terminating at the appropriate sensory cortex. That information is processed, a functional somatosensory map is formulated,[2,245] and the information is programmed and relayed to the motor cortex. From there, it is sent to both the basal ganglia and the cerebellum to establish plans for postural adaptations, refinement of motor programs, and coordination of direction, extent, timing, force, and tone necessary throughout the entire sequence of the motor act. Procedural learning and memory do not *require* limbic network involvement as long as an emotional value is not placed on the task. This memory deals with skills, habits, and stereotyped behaviors. Summarizing, the frontal lobe, basal ganglia, and cerebellum are critical nuclei for changing and modulating existing programs.[39] Storage and subsequent retrieval of memory of these semiautomatic motor plans are thought to occur throughout the motor control system.[39] This motor system is involved in developing procedural plans used in moving us from place to place or holding us in a position when we need to stop.[39] The complexity of this process has had an impact on the study of motor control and variables that might affect that control.[246]

Unlike procedural learning and memory, declarative (explicit) learning and memory require the wiring of the limbic network and are closely associated with limbic function. Declarative thought deals with factual, material, semantic, and categorical aspects of higher cognitive and affective processing.[247] A strong emotional and judgmental component is linked with declarative thought. Thus as soon as a motor behavior has value placed on the act, it becomes declarative as well as procedural, and the limbic network may become a key element in the success or failure of that movement.[248,249] Most functional tasks or activities practiced in a clinical setting have value attached to them. That value can be clearly seen by observing the emotional intent placed on the activity by the patient.[250]

Two reciprocal pathways, or circuits, within the limbic network are intimately involved in the process of declarative learning and memory (1) the amygdaloid, dorsomedial thalamic nucleus, and cortical pathways and (2) the hippocampal, fornix, anterior thalamic nucleus, and cortical pathways. Both pathways contribute in relation to the significance of external or internal environmental to learning of a concept or task.[43–49] The amygdala may be more concerned with sensory and motor signals relating to the internal environment, whereas the hippocampus is concerned more with those of the external environment. The hippocampus is rich in stem cells and may be a primary nuclear mass that directs the bodily systems to heal after injury. This is especially true when the external environment is enriched and nurtures the emotional environment for that healing.[251,252]

For initial declarative learning and memory, function of the hippocampus and the amygdala of the limbic network is required.[39] These two structures play an important role within the "cortico-limbo-thalamo-cortical" circuit, which plays a significant role in memory storage.[39] For memory formation to occur in early motor learning (acquisition), there must be a storing of the "neural representation" of the stimuli in the association and the processing areas of the cortex. This "cortico-limbo-thalamo-cortical" circuit serves as the "imprinting mechanism" by which pathway activation by stimulus is reinforced. Limbic involvement in the declarative memory and learning processes creates a chemical bond that allows cortical storage of "stimulus representation" necessary for subsequent recognition and recall of the information.[39,44,233,235,236] Therefore on subsequent stimulation, a stimulus recognition or recall would be elicited. In the associative phases of recall and transfer of learning, stored representations of any interconnected imprints might be evoked simultaneously.[39]

The amygdaloid circuits seem to deal with strongly emotional and judgmental thoughts, whereas the hippocampal circuits are less emotional and more factual. The amygdala may be more involved in emotional arousal and attention, as well as motor regulation, whereas the hippocampus may deal with less emotionally charged learning. It

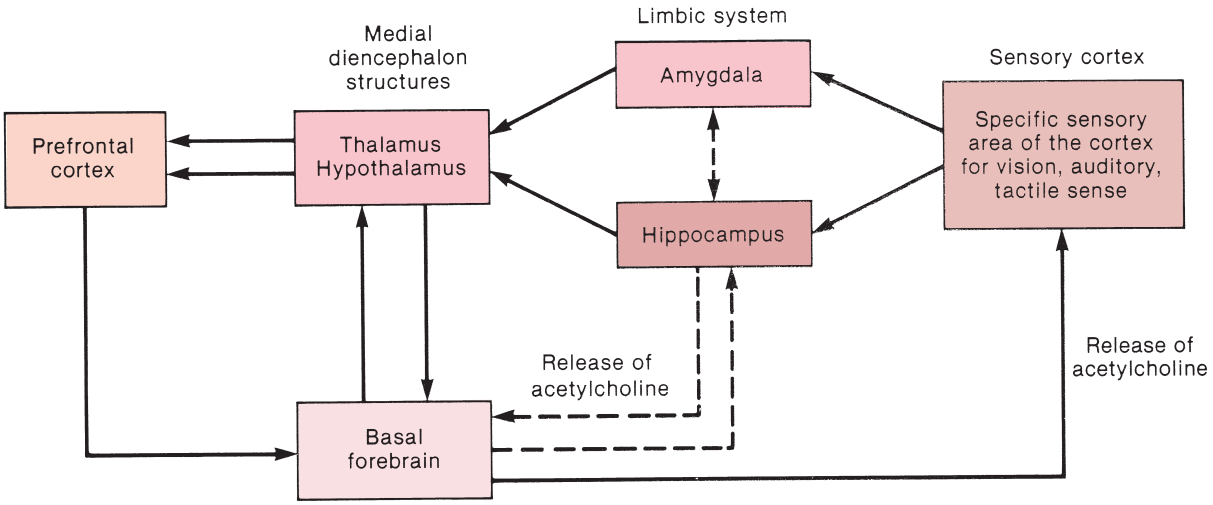

Fig. 4.6 The basal forebrain closes the circuit and causes changes in sensory area neurons, which could lead to correct perception and stored memory. This is neurochemical-dependent.

is postulated that the amygdala is the area of the brain that adds a "positive association," associating a stimulus and reward and placing an emotional value memories or learning. In this way, stimulus and reward are associated by the amygdala, and an emotional value is placed on them.[253,254] These limbic circuits seem crucial in the initial processing of material that leads to learning and memory. Once the thought has been laid down within the cortical structures, retrieval of that specific intermediate and long-term memory does not seem to require the limbic network, although new associations will need to be run through the system.[39,233,235,43]

The hippocampus and amygdala are also linked both structurally and functionally to each other and to specific thalamic nuclei in the medial diencephalon. The medial diencephalon is an important relay station along the pathway that leads from the specific sensory cortical region to the limbic structures in the temporal lobe to the medial diencephalic structures and ends in the ventromedial part of the prefrontal cortex (Fig. 4.6).[39,255,256] A vital processing area for all sensory modalities is located in the region of the anterior temporal lobe. Patients with temporal epileptic seizures and whose temporal lobes have been surgically removed develop global anterograde amnesia—that is, amnesia develops for all senses, and no new memories can be formed. Experimental removal of only the hippocampus does not bring about these changes, although processing is slowed down. When both the hippocampus and the amygdala are removed bilaterally, the amnesia is both retrograde and anterograde. A third component in the memory pathway involves pathways between the amygdala, hippocampus, and the thalamic nuclei in the medial diencephalon. When the medial diencephalic region is damaged by neurological trauma such as strokes, neoplasms, infections, or chronic alcoholism, global amnesias result. Given that the limbic network and the diencephalon cooperate in the memory circuits, the destruction of these pathways causes the same amnesic effect.

As shown in Fig. 4.6, memories may be stored in the sensory cortex area, where the original sensory input was interpreted into "sensory impressions." Today, concepts regarding memory storage suggest that declarative memory is stored in categories similar to a filing system. Those categories or files seem to be stored in several cortical areas bilaterally depending on the context.[257,258] This system allows for easy retrieval from multiple areas. Memory has stages and is continually changing. It was once thought that the hippocampus only dealt with long-term memory, but it is now accepted that it also supports multi-item working memory.[259] To go from short-term to long-term memory, the brain must physically change its chemical structure (a plastic phenomenon). Memory first begins with a representation of information that has been transformed through processing of perceptual systems. The transferring of this new memory into a long-lasting chemical bond requires the neuronal network of the limbic complex. Owing to the multiple tracts or parallel circuits in and out of the limbic network and throughout neocortical systems, patients, even with extensive lesions, can often learn and store new information.[39,260] This may also explain why damage to the limbic network structures does not destroy existing memory nor make it unavailable because it is actually stored in many places throughout the neocortex. The circular memory circuit illustrated in Fig. 4.6 shows only one system. The reader must remember that many parallel circuits function simultaneously. The circular memory circuit shown reverts to the original sensory area after activation of the limbic structures to cause the necessary neuronal changes that would inscribe the event into retrievable stored memory.[261] This information can be recognized and retrieved by activation of storage sites anywhere along the pathway.[39,262] Patients with brain lesions localized in the limbic network components of the amygdala and hippocampus have the ability to acquire and function with "rule-based" games and skills but have lost the capacity to recall how, when, or where they gained this knowledge or to give a description of the games and skills learned. Relating this to clinical performance, patients may develop the skill in a functional activity but not the problem-solving strategies necessary to associate danger or other potentially harmful aspects of a situation that may develop once out of the purely clinical setting.[119,263–266] Similarly, if a patient needs to learn a procedural task such as walking, transfers, eating, and so on, it may be extremely important to direct the attention off the task while the task is being practiced procedurally.

The last station or system to be added to the circuit is the "basal forebrain cholinergic system," which delivers the neurochemical acetylcholine to the cortical centers and to the limbic network, with which it is linked. Visual recognition memory can be augmented or impaired by administration of drugs that enhance or block the action of acetylcholine.[267–269] The loss of this neurotransmitter is linked to memory malfunctioning in Alzheimer disease and plays a key role in dementia problems in Parkinsonism.[270] Currently, many chemicals are being

studied for their influence on brain structures and specially limbic structures.[271,272]

The hippocampus and the amygdala are involved in recognition memory.[273] Hippocampal (indirect) and nonhippocampal (direct and independent) pathways influence the anterior thalamus and thus play an important role in memory, particularly spatial memory and location of objects in space.[194] The the amygdala is necessary for the association of memories derived through the various senses with a specific recognition recall. For example, a whiff of ether might bring to mind a painful surgical experience or the sight of some food may cause a recall of its pleasant smell. Removal of the amygdala brings out the behavior shown in Klüver-Bucy syndrome. For patients with this neurological problem, familiar objects do not bring forth the correct associations of memories experienced by sight, smell, taste, and touch and relate them to objects presented.[274] Association of previously presented stimuli and their responses appear to be lost. Animals without amygdaloid input had different response patterns that ignored previous fears and aversions. Thus the amygdala adds the "emotional weight" to sensory experience. Loss of the amygdala takes away many positive associations and potential rewards, thereby altering the shaping of perceptions that lead to memory storage.

When stimuli are endowed with emotional value or significance, attention is drawn to those possessing emotional significance, selecting these for attention and learning. This would give the amygdala a "gatekeeping" function of selective filtering. The amygdala may enable emotions to influence what is perceived and learned by reciprocal connection with the cortex. Emotionally charged events will leave a more significant impression and subsequent recall. The amygdala alters perception of afferent sensory input and, hence, affects subsequent actions.[36,275,276]

In the human, memory functioning has been associated with the phenomenon of long-term potentiation observed in hippocampal pathways.[39] This potentiation of synaptic transmission, lasting for hours, days, and weeks, occurs after brief trains of high-frequency stimulation of hippocampal excitatory pathways. Whether this long-term potentiation occurs presynaptically, postsynaptically, or both has not yet been established.[39,135,277] The adrenal corticosteroids contribute to modulation of long-term potentiation within the hippocampus.[186] Recent literature has linked a neurotropic factor usually considered for long-term potentiation within the hippocampus as a factor in amygdala-dependent learning, thus reiterating the interaction between these two nuclei and their role in memory and learning.[36]

Learning and memory evoke alterations in behavior that reflect neuroanatomical and neurophysiological changes.[39,210] These alterations include the phenomenon of long-term potentiation as an example of such changes. The hippocampus demonstrates the importance of input of long-term potentiation in associative learning. In this type of learning, two or more stimuli are combined through the "associative" interaction of afferent inputs. As such, tetanizing of more than one pathway needs to occur simultaneously. If only one pathway is tetanized, the effect is decreased synaptic transmission. Thus long-term potentiation serves as one model for understanding the neural mechanism for associative learning. Hormones interact with this neural mechanism, which, if combined with stress, can change the specific circuitry active during the experience.[278] As an example, the amygdala is not only involved in learning related to emotional experiences but is also responsible for changing motor expression or conditioned response generated as part of an autonomic expression, such as with fear.[164,279] Limbic responses to input stimuli need to be differentiated from limbic memory and initiation of a response without the stimuli. Although this is an area of practice not yet fully understood, clinical implications to patient examination and evaluation will be generally discussed later in this chapter.

Limbic Influence on Emotions and Behaviors: The F²ARV and General Adaptation Syndrome Continua

Noback and co-workers[280] state that the limbic network is involved with many of the expressions that make us human, namely, emotions, behaviors, and feeling states. That humanness is highly individual even in patients with normal functioning limbic networks, and even greater variance with involvement of the primary or modulating limbic network structures or pathways.

As a brief clinical example, a patient with severe brain injury with decreased responsiveness (Ranchos Los Amigos Level of Consciousness II–III) may show increased alertness and an increase in base muscle tone or motor function through effective use of sensory stimuli. Alternatively, although the desired response may be improved alertness or a motor response, a patient may become highly oversensitive to a strong odor or noxious tactile stimuli,[281] and the response may become autonomic or behavioral instead, reflected in an increased heart rate or blood pressure, or even as fear or anger.[57] Overstimulation may move the patient into a "protective state of survival," whereas a pleasant/personally desirable smell, touch, or sound (e.g., melody) will more likely lead to "safety." The former can lead to strong emotions or responses such as anger; the latter often leads to bonding, engagement (attention), and motivation to learn.[16]

Both motivation ("feeling the need to act") and concentration ("ability to focus on the task") are interlinked with the limbic network and are both critical to participation in the motor activities. The amygdaloid complex with its multitude of afferent and efferent interlinkages is specially adapted for recognizing the significance of a stimulus, and it assigns the emotional aspect of feeling the need to act. These neuroanatomical loops have tremendous connections with the reticular system. Hence, some authors call it the reticulolimbic network.[39,74] The interaction of the limbic network and the motor generators of the brain stem and ultimate direct and indirect modulation over the spinal system lead to need-directed and therefore goal-directed motor activity. It also filters out insignificant from significant information through selective processing, storing the significant for memory, learning, and recall. These interconnected neuroloop circuitries reinforce the concept that areas have both specialization and generalization and thus work closely together with other areas of the brain.[81,282]

Some of the earliest understanding of the limbic network was limited to that of a primary protective role in "fight or flight." With normally functioning limbic networks, patients can appropriately recognize the significance of a stimulus, effectively filter out insignificant from significant stimuli or information, and appropriately assign a need to act. However, in the impaired patient, inaccurate stimulus interpretation and therefore action/reaction occur. The therapist needs to be aware that a patient may overrespond to stress, frustration, or fear of failure in both cognitive and motor activities. A small or unfiltered stimulus may generate one of two powerful and predictable limbic motor response programs: the fear and frustration, anger, rage, and violence continuum (F²ARV) and the general adaptation syndrome (GAS). The F²ARV and GAS continua are often interrelated in individuals who have direct or indirect limbic network involvement.

Fear and frustration, anger, rage, and violence or withdrawal continuum. One sequence of behaviors used to describe the emotional circuitry of the limbic network through the amygdala is the F²ARV continuum (Fig. 4.7).[74,283,284] This continuum begins with fear or frustration. This fear can lead to avoidance behavior.[285] If the event inducing the fear or frustration continues to heighten, avoidance behaviors can continue to develop.[285] In a simple example, we recall or