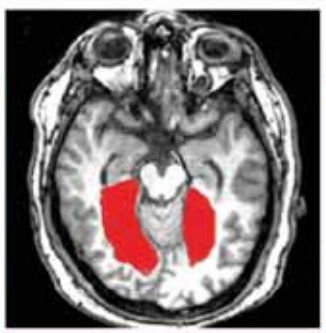
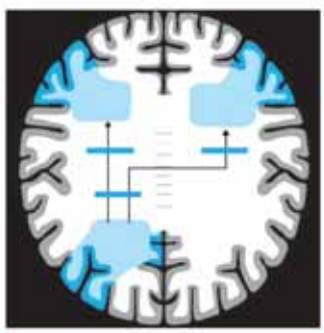
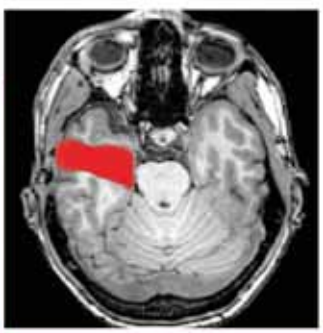
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Higher Neural Functions

A Clinical Approach

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SECOND EDITION

Foreword
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JAYPEE

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10 Emotion and Neurobehavioral Disorders

INTRODUCTION

Emotion, in a subjective sense, refers to our feelings, positive and negative. Objectively, emotion can only be assessed based on an organism's outward behavior as a result of the internal emotions. Emotional responses generally occur based on an organism's current state and future needs.

The emotional systems also impact many other bodily functions. Emotions can increase the heart rate and enhance cardiac function. Respiration can increase. Controlling respiration through techniques, like pranayama, can also modulate the emotional state. Thus, systems are interlinked. Emotional states can also influence the body's immune responses. An entire field of study, psychoneuroimmunology has developed around the discovery that emotional factors can influence immune system activity. There have been cases of "unexplained" cancer cures, apparently because the immune system was able to selectively destroy the tumor cells. Some data suggest that patients' becoming convinced of the hopelessness of their situation may actually accelerate the process of them succumbing to their disease. Patients who have an optimistic outlook may possibly have a better chance.

Emotions are also a major part of our daily activities and experience of life itself. Most human activities are motivated by some form of emotion. Simplistically, it can be said that most activities are based on basic emotions like fear or desire.

Historically, there have been many theories about emotion. Emotion has long been recognized as having at least two distinct elements, which are as follows:

1. The cognitive recognition of the emotion, such as subjective feeling of fear on seeing a wild animal.
2. The physiological response of the body, with increased heart rate and respirations, and possibly sweating.

The original view was that the feeling of fear came first and the autonomic responses followed.

Another school of thought, advanced independently by James and Lange,[1] was that the initial response was actually the body's autonomic response, and the cognitive awareness followed perhaps as a consequence of the autonomic reaction. Another view, called the Cannon–Bard view, held that the cognitive awareness and the autonomic responses occurred simultaneously. Current belief is that all the elements are interlinked.

Emotional Perception

Emotion generally begins in response to stimuli. This can be any exogenous stimuli or, in higher organisms like humans, endogenous stimuli such as memories of an experience. Sensory stimuli can be through the basic sensory modalities of touch, taste, or smell, or through the more complex visual and auditory modalities which undergo significant cortical processing to understand their meaning and significance. An important part of sensory perception in general is this component of emotional perception. This often involves separate direct pathways from the sensory association cortices to the

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amygdala and other emotional centers. The emotional limbic system, as well as cognitive neocortical systems, interact to process the significance of stimuli.

An example of emotional perception dysfunction is a patient admitted with delirium and alcohol withdrawal. He may be combative, fighting off imaginary assailants, and hearing voices that are all very real for him.

Emotional Processing

In lower animals, emotion is an important determinant of outward behavior. The hypothalamus, periaqueductal gray, and several pontine and midbrain nuclei mediate some of the most primitive emotional responses.[2] When an emotionally challenging situation arises, threatening the survival of the individual or the species, a preset behavioral response occurs in lower animals. Such relatively simple behavioral responses are modified in humans. In higher animals, and much more so, in humans, emotional responses are greatly tempered by cognition and executive functions (mediated by phylogenetically newer structures, like the neocortex)[3] to produce intelligent and socially appropriate behavior.

The networks mediating emotion mainly involve the limbic system, including the hypothalamus, thalami, amygdala, hippocampus, midbrain, and pontine structures. The interacting networks mediating the cognitive and emotional interactions in humans mainly involve the cerebral cortex in the prefrontal and cingulate areas. The prefrontal cortex is divided into the orbitofrontal, mesial frontal, and dorsolateral areas. The orbitofrontal and cingulate cortices are, in a sense, the cortical representation of the limbic system.

Emotional responses are modulated by emotional structures and also through networks with cortical structures. This is called "emotional processing" or "emotional cognition". As an example of such emotional cognition, imagine a marketing office where the boss starts Monday morning by announcing, "If anyone has failed to meet their target for last week, I am going to kill them!" For an employee who is so guilty, the normal emotional response to this imminent threat of grievous bodily harm may be tempered by the reassuring knowledge that, "My boss has been saying this every Monday morning for 7 years and has never yet hurt anyone." This emotional intelligence will prevent the usual "fight or flight" response.

The networks involving neocortical structures are involved in deciding the appropriate manner of behavioral responses to emotional stimuli, considering factors such as time, place, and social conventions (e.g., these cortices help the romantic boy understand that it is not the right time to ask the girl to elope if the father is nearby, visibly agitated, and wielding an axe). Lesions of these networks may disconnect frontal cortical monitoring systems from limbic input, resulting in disinhibition of behavior and emotions (potentially producing self-destructive behavior as suggested in the example above).

The limbic cortices (orbitofrontal and cingulate) are involved in the cognitive awareness of emotionally relevant stimuli and insight into the emotional state to help determine the appropriate pattern of emotional expression. They are also involved in emotional rationalization; the insight into one's emotional state (in the example above, the boy might ponder, "Why do I get so nervous when I speak to this particular girl?"). The limbic cortices have a tremendous modulating influence on the limbic system. When one learns to use emotion to one's advantage, this is termed "emotional intelligence". As an example, upon failing an examination, instead of allowing oneself to be plunged into hopelessness, one can use the emotion from the setback to fuel one's determination to do better next time.

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Finally, the outward expression of emotion is through the autonomic and motor systems. The hypothalamus is connected via the mammillothalamic tract with the anterior nucleus of the thalamus. This is connected to the cingulate gyrus. This, in turn, feeds through the hippocampus and then, the fornix back to the hypothalamus. The hypothalamus is involved in autonomic emotional expression. The cingulate gyrus is involved in the cognitive emotional experience. This cognitive awareness is further augmented by cognitive input through networks with other neocortical areas, referred to as emotional coloring. This is depicted in **Figure 1**.

Emotional cognition dysfunction: A well-known example is seen in the movie "Beautiful Mind". Here, a mathematical genius suffers from emotional dysfunction. He does brilliant work, including helping the United States government break Soviet secret codes, but develops progressively debilitating paranoid delusions that he is unable to deal with, rendering him an emotional cripple, helpless, and unable to function.

Emotional Expression

In response to an emotionally-charged stimulus, there is a sense of cognitive awareness as well as an involuntary autonomic response. Emotional expression occurs in different ways, which are given as follows:

- There is an autonomic response mediated through the hypothalamus.
- There may be unconscious, automatic, implicit motor responses mediated through the basal ganglia, and motor cortices.
- There may be a conscious response based on cognitive awareness of the situation and executive functions deciding on the appropriate response.

The outward manifestation of emotion often involves facial expression changes, lacrimation, and changes in respiration. It may be noted that respiratory changes make the major difference between laughing and crying with inspiration in crying and expiration in laughing. There is thought to be a faciorespiratory center in the brainstem that is modulated by multiple areas of the cerebral cortex through inhibition and

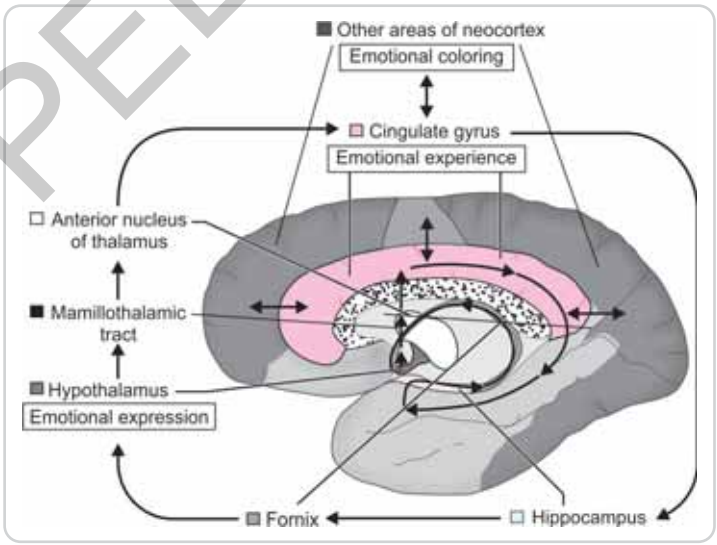


FIG. 1: Brain areas involved in different aspects of emotional cognition.

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excitation. Lesions that result in a loss of inhibition can lead to exaggerated responses to even trivial stimuli, even though affect is the same. Damage to excitatory pathways may result in a bland or flat affect. Damage to both pathways (as seen in multi-infarct states) can result in pathologic laughing or crying, usually spontaneous and unrelated to stimuli.

The outward expression of emotion is performed largely by the motor system. However, other areas of the brain influence this emotional motor expression. Right frontal hemispheric lesions may cause impairment of the voluntary emotional intonation of speech (motor aprosodia) as discussed earlier (in Chapter 3 on "Language"). Lack of voluntary control of emotional expression may adopt another form, namely, accentuated emotional expression, to the point of irrepressible laughing or crying in the absence of feeling any amusement or pain. Pathologic laughing or crying can result from bilateral internal capsular lesions that also involve the basal ganglia, from lesions affecting the substantia nigra, cerebral peduncles, and hypothalamus, and from pronounced involvement of the corticobulbar fibers, such as occurs in severe suprabulbar amyotrophic lateral sclerosis.[4]

It has been postulated that lesions that mainly affect the left hemisphere tend to induce pathologic crying, whereas lesions affecting the right hemisphere is what more commonly produces pathological laughter.[5] Likewise, patients with left hemispheric damage tend to show depression more often than those with right-hemispheric damage.[6] The severity of depression is directly correlated with the proximity of the lesion to the frontal pole. Patients with left brain damage are often anxious, tearful, negative, and abusive, whereas patients with right-hemispheric damage are indifferent and jocular, further suggesting that the dominant hemisphere may be more concerned with positive feelings and the nondominant hemisphere more with negative ones.[7] Many patients with right-hemispheric damage are to some extant unaware of their deficit and such a denial may prevent the negative effect that the handicap might otherwise have on their mood. Right hemisphere lesions often show undue cheerfulness and indifferent emotional reactions (*anosodiaphoria*).

Let us consider an example of emotional expression dysfunction. A patient was admitted with left hemiplegia on account of a right cerebral infarction. The patient burst into tears on seeing his friend. This quickly resolved, however. When his friend reminded him of a recent amusing anecdote, the patient went into peals of loud and uncontrolled laughter. The patient had disinhibited emotional expression, or emotional incontinence.

In summary, emotions and their expression depend on following factors:

- The state of arousal of the individual (alertness) mediated by the reticular activating system, some thalamic structures, and the prefrontal cortex.
- Vegetative functions mediated in part by the periaqueductal gray and other brainstem regions, the hypothalamus, and limbic structures.[2]
- The ability to perceive the emotional component of various stimuli (such as a friendly face or a threatening utterance) mediated by the amygdala and related networks.
- A previous experience retrieval system (memory) mediated by the hippocampus and other portions of the limbic system.
- The assessment of motivational content and thereby assigning an emotional valence to external as well as internal stimuli, leading to emotional and autonomic arousal, mediated by the anterior cingulate region and the insular cortex.
- Cognitive control and modulation of the emotional experience and autonomic

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arousal by the prefrontal cortex and networks.
- The ability to express emotion by the motor system influenced particularly by the right frontal lobe.

Brain Areas Involved in Emotion

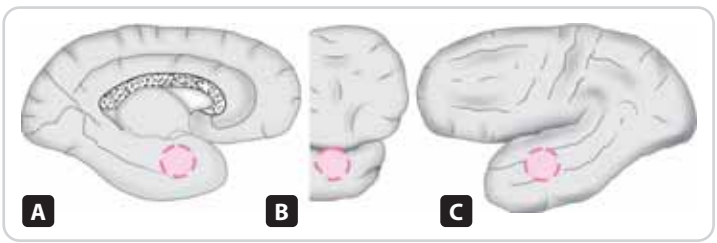
Let us now examine the roles of the various brain areas in greater detail.

Role of the Limbic System and Amygdala

The limbic system and especially the amygdaloid complex is reciprocally connected with multiple cortical sensory systems (polymodal sensory areas) providing information regarding the external world.[8] The amygdala is located subcortically deep to the hippocampus and temporal pole, as shown schematically projected on to the cerebral surface in **Figures 2A** to **C**. The amygdala is important in determining the affective (emotional) significance of stimuli. It appears to play an important role in the amalgamation of detailed information from the sensory cortices on the one hand with the emotional responses such as pleasure, pain, or fear mediated through hypothalamic and visceral and somatomotor centers.[9] Important output from the amygdala are to the hypothalamus and the extrapyramidal motor system (especially the ventral striatum) through the stria terminalis, and to brainstem centers (cardiac and respiratory) through the ventral amygdalofugal pathway.

The amygdala appears to assign a *valence* (emotional and motivational value associated with a stimulus) to stimuli,[10] after evaluating the potential reward or punishment value of these stimuli. Functional neuroimaging has shown the amygdala to be active in emotional situations. One functional magnetic resonance imaging (fMRI) study showed that the right amygdala is selectively sensitive to faces that had been associated with emotional descriptions compared to faces that had been associated with neutral descriptions.[11,12] Amygdala responses are also heightened in response to threatening images, such as guns or knives.[13] These findings suggest that the amygdala is involved in evaluating the emotional significance of stimuli.[14] In lower organisms with amygdala lesions, objects, and events that previously provoked an attack or other strong reaction, no longer to do so. In humans, stimulation of the corticomedial amygdaloid nucleus evokes a display of anger whereas stimulation of the basolateral nucleus does not.

Destruction of the amygdaloid nuclear complex bilaterally tends to abolish aggressive behavior. The primary effect of amygdalectomy on aggression may not be a change in the aggressive threshold, but a change in previously acquired patterns linking particular stimuli with aggressive responses.[15] Such individuals exhibit a flattened affect and diminished subjective responses to emotional stimuli (*placidity* and *taming*) as in the Kluver–Bucy syndrome.[16]



FIGS. 2A TO C: Location of amygdala depicted on: (A) Medial surface; (B) Anterior surface; (C) Lateral surface of the cerebral hemisphere.

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Aggressive behavior becomes inhibited and apathy and placidity ensue.

The amygdaloid nuclei have projections to the dorsomedial nucleus of the thalamus as well as to the cingulate gyrus. Lesions of the dorsomedial nucleus of the thalamus render humans placid and docile. So does bilateral ablation of areas of the cingulate gyrus (area 24). This is an example of how disruption of a network at any point in its path may produce the same dysfunction.

Patients with lesions of the amygdala have difficulty in identifying particular objects as being appropriate or inappropriate for satisfying hypothalamic drives like feeding or reproduction. They may try to ingest inedible objects and direct reproductive drives toward inappropriate objects.[17,18]

Patients with bilateral temporolimbic damage may develop the *Kluver–Bucy syndrome*, characterized by indiscriminate oral and tactile exploration of their environment (*hyperorality* and *hypermetamorphosis*) and changing of sexual preferences.

The emotional disconnection may be modality specific with small lesions in specific locations.[19,20] Bilateral inferior occipitotemporal lesions may sometimes produce *visual hypoemotionality*, an isolated inability to react emotionally to visual stimuli. Patients with such lesions may complain of a total loss of emotional reactions to visual stimuli. For example, a patient may report that he is no longer has interest in erotic visual stimuli that had previously evoked a strong response. However, he may still feel aroused by verbal-auditory or tactile stimuli. This type of modality specific limbic disconnection may extend to fear and aggression.

Sometimes the converse of what is seen in Kluver–Bucy syndrome can be occur. This is usually seen in temporal lobe epilepsy with abnormal neuronal hyperexcitability. Repeated seizure activity can lower the threshold for future seizure activity in a process called kindling. The amygdaloid complex can be particularly susceptible to this process. As a result, patients may have enhanced aggressive and other emotional responses to both drive-related and neutral stimuli.[21,22] They may exhibit a generalized deepening of affective (emotional) associations even in the interictal period (between seizures). This is called *Geschwind syndrome,* and is characterized by exaggerated emotions, sensitivity to moral issues, often with religious and philosophical preoccupation and hypergraphia (a tendency to write at great length).[23,24] As a consequence of strongly-felt emotions, these patients may become overly sensitive to minor issues and experience intense anger. Thankfully, strong moral and philosophical beliefs often preclude violent acts (but it is still a good idea to keep such patients at more than arms' length). When patients do act aggressively, their behavior is typically performed in clear consciousness with intact recollection afterward and often sincere regret. This is distinguished from agitation as a part of complex partial ictal behavior which is typically not recollected afterward.

Role of Prefrontal Cortex

The anterior executive region consists of an area in the anterior cingulate gyrus around the rostrum of the corpus callosum. This area can be functionally simplified into "affect" and "cognition" areas. The affect region includes areas 24, 25, and 33 and has connections with the amygdala, periaqueductal gray matter, and autonomic brain stem nuclei. This area is concerned with assigning an emotional valence to internal and external stimuli, thereby determining the motivational content of the stimuli. The motivational valence to stimuli is assigned by both the anterior cingulate and the insular cortex (discussed later). The insular cortex appears involved with representing the

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physiologic state of the body and has been considered as the limbic sensory cortex. The anterior cingulate, on the other hand, modulates first order autonomic centers, such as the hypothalamus and motor centers, such as the periaqueductal gray region in the brainstem,[25] and has been considered as the *limbic motor cortex*.[26,27]

The other functions sustained by the anterior cingulate region include regulation of autonomic and endocrine function, conditioned emotional learning, the expression of emotionally triggered movements related to painful stimuli, the vocal expression that is linked to emotional expression, and maternal-infant interaction. The separation cry induced by separating the mother from her offspring in a primate is adversely affected by ablation of the anterior cingulate cortex. Moreover, the anterior cingulate cortex is involved in generating the motor act of laughter along with the basal temporal cortex which supplies laughter's emotional content. Patients with small bilateral anterior cingulate (area 24) lesions may be unconcerned in the presence of painful stimuli.[28,29]

Different types of emotional states map to quite specific subregions of the cingulate gyrus.

Excessive cingulate activity can alter the emotional state and expression and influence-related motor and autonomic activity. Elevated anterior cingulate cortical activity can contribute to obsessive-compulsive behavior, tics, and aberrant social behavior. Reduced cingulate activity, such as due to damage from infarcts or tumors, can result in akinetic mutism, depression, diminished self-awareness, motor neglect and impaired motor initiation, reduced response to pain, or aberrant social behavior. Thus, the affect region of the cingulate cortex modulates autonomic activity and internal emotional responses.[30] Overall, the anterior cingulate cortex appears to play an important role in motivation and goal-directed behavior.

Another prefrontal area regulating emotions is the orbitofrontal cortex. Input regarding external stimuli may project from the anterior temporal cortices via the uncinate fasciculus, and inputs about the internal stimuli may project from the hypothalamus via the dorsomedial nucleus of the thalamus, allowing it to play a role in regulating the emotional response to these stimuli.[31,32]

The orbitofrontal circuit has lateral and medial sections. The medial part permits integration of visceral-amygdalar functions with the internal state of the organism and the lateral portion is involved with transformation of limbic and emotional information into contextually appropriate behavioral responses.

In these ways, networks involving the prefrontal cortex may evaluate the internal state of the organism, appreciate the current state of the external world, and help in planning future actions to satisfy current internal drives. This also has to be done in conformity with learned social norms to minimize the chances of adverse or failed outcomes. The prefrontal lobe helps to provide the sound reasoning that if one is hungry, one should go to the store across the street to buy a loaf of bread, as opposed to running in, grabbing it off the shelf, and having to jump into a river to avoid the shopkeeper's friends and aggressive local populace.

Damage to the orbitofrontal cortex results in spontaneous, poorly-thought out, reflexive responses to stimuli in the immediate environment.[33] Patients are impulsive without due consideration of the consequences of their action. Orbitofrontal lesions, thus, lead to irritability and aggressive behavior over trivial provocations with little consideration to social prohibitions.

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The orbitofrontal cortex, especially its lateral part, helps to evaluate external stimuli for their potential for punishment.[12] This has been shown by functional neuroimaging studies in humans.[34] For patients with bilateral orbitofrontal destructive lesions, most social issues are tolerated. However, they may go into a rage when some basic instinctive drives are not satisfied. In contrast, for patients with temporal lobe epilepsy, even apparent trivia may become transcendental issues.

Dysfunction of the orbitofrontal areas in addition produces changes in appetite, in the form of hyperphagia or altered food preferences. The orbitofrontal cortex plays a key role in the evaluation of outcomes (including rewards) and options for action. Dysfunction results in behavioral changes in the form of sexually inappropriate behavior, loss of social decorum, jocularity, argumentativeness, capriciousness, inappropriate preoccupations, and even criminal behavior.

The dysfunction of the orbitofrontal cortex may be only evident from careful history taking or clinical observation of aberrant behavior. The role of the orbitofrontal cortex in social cognition is mentioned below.

The dorsolateral prefrontal cortex is particularly important in mediating the link between emotion and cognitive awareness of the nature of emotional stimuli. It is important in modulating one's emotional expression, tempering it with social prudence and foresight keeping in mind one's needs and goals.

Role of Anterior Temporal Lobe

The temporal pole, especially on the right, has been implicated in evaluating the emotional importance of sensory stimuli. When there is incoming sensory stimuli, the temporal pole plays an important role in evaluating it based on prior knowledge and memory.[35] Therefore, it follows that lesions of the anterior temporal lobes may result in a failure to recognize the emotional and social implications of sensory stimuli leading to behavior that is socially inappropriate and with undesirable consequences.[12] For example, female monkeys with lesions of the temporal poles (sparing the amygdalae), lose their emotional attachment to other monkeys including their own infants.[36] Similarly, emotional detachment from close family members has been seen in patients with bilateral anterior and medial temporal lobe lesions due to herpes encephalitis[37] or the semantic variant of primary progressive aphasia.[38]

The temporal poles are also important in appreciating familiar faces and voices and also the emotional expression on faces. Lesions of the right temporal lobe, as seen in the semantic variant of primary progressive aphasia, may result in the inability to recognize familiar faces and voices. This should be distinguished from cases of prosopagnosia, usually with more posterior lesions, where there is an inability to recognize familiar faces but no problem with recognizing voices.[39]

Patients with the semantic variant of primary progressive aphasia with right-sided involvement often show social withdrawal, irritability, impulsiveness, obsessions and compulsions, and disruption of physiologic drives like appetite and sleep[12,40] Some of these patients may have difficulty exhibiting appropriate facial expressions to social situations, as well as using these cues to understand another person's emotional state.[38] These patients may seem to be cold and arrogant in social interactions.[41]

Patients with bilateral anterior temporal lesions have a bland affect. Patients with epileptogenic foci in the left temporal lobe tend to be paranoid and have antisocial behavior, whereas those with right temporal foci show emotional extremes (elation and sadness) and denial.[42]

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Higher Neural Functions

A Clinical Approach

Salient Features

- This book provides a practical approach to higher neural functions and disorders.
- Initial chapters explore in depth the basic understanding of attention, language, and memory.
- Further chapters deal with cognition, visual and other higher sensory processing, neglect syndromes, apraxia, and neurobehavioral disorders.
- The emphasis is on a clear and logical approach to these fascinating subjects, simplified with numerous case illustrations, figures, and references.
- The simplified but detailed approach to this complex subject should be of value to neurologists, neuroscientists, psychiatrists, general physicians, psychologists, and postgraduate and medical students.

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