

Neural Substrates of Psychotherapeutic Change

II: Beyond Default Mode

George I. Viamontes, MD, PhD; and Bernard D. Beitman, MD

The development of advanced brains that support transcendence of basic appetitive urges to satisfy higher-order demands was motivated by significant evolutionary pressures. The unrestrained pursuit of salient stimuli to serve internal urges is not adaptive in a danger-filled world. In addition, the ability to postpone gratification on the basis of context is essential to the development of social groups. For example, the lowest animals in a social hierarchy must wait to eat until more dominant members of the social group are sated. To make such advanced behaviors possible, special circuits evolved to modulate the internal urges and narrow external focus induced by the reward system. These circuits, whose major components are located in the prefrontal cortex, promote the pursuit of reward in a manner that is consistent with contextual considerations, learned rules, and a vision of the future.

ADAPTIVE CIRCUITS OF THE PREFRONTAL CORTEX

The term prefrontal cortex refers to the region of the brain directly in front of the premotor and motor strips (Figure 1, see page xxx). In humans, the prefrontal cortex represents 30% of the neocortex and facilitates transcendence of the default brain by permitting the consideration of an expanded set of variables before the initiation of actions.¹ It coordinates adaptable, goal-directed behavior that considers internal and exter-

nal circumstances, memory, applicable rules, and projected consequences.

Functional and anatomical considerations have demonstrated three distinct circuits in the prefrontal cortex that modulate complex behavior. The oculomotor circuit, which controls automatic eye movements, is a fourth prefrontal network, but it will not be discussed in this article. All the prefrontal circuits have nodes in the thalamus, cortex, basal ganglia, and globus pallidus/substantia nigra pars reticulata (Figure 2, see page xxx).^{2,3} These circuits are mapped somatotopically and define numerous “channels” through each circuit component.² As described in the section on reward, thalamic circuitry is inhibited tonically by the globus pallidus.² This inhibition can be removed for selected channels through the action of the basal ganglia, which can suppress default pallidal inhibition. Self-excitatory loops that sustain representations of interest in the brain therefore can be selectively activated. Additional “indirect” loops pass through the subthalamic nucleus and external globus pallidus and complement the circuitry described above.²

The three major behavioral circuits in the prefrontal cortex are outlined in the Sidebar (see page xxx).^{2,3} The first circuit, which contains the cingulate gyrus, is involved primarily in the motivation of goal-directed actions. The cingulate gyrus is a heterogeneous area with specific processing modules for emotion, cognition, sensation, and movement.⁴

Important functions of the cingulate are thought to include the motivation of appropriate responses to internal and external stimuli, emotional-cognitive integration, “attention for action,” motor preparation, and conflict monitoring. The cingulate carries out these functions by triggering body states that focus attention on internal and external demands and motivate appropriate action. It generates emotional motivation through its projections to autonomic, visceromotor, and endocrine systems,⁵ and is an important component of reward circuitry (see above).

The cingulate receives cognitive data from the dorsolateral prefrontal cortex⁶ and facilitates emotional-cognitive integration by generating emotional states appropriate to cognitive contents.⁵ Conversely, it conveys emotional information to the dorsolateral prefrontal cortex for cognitive processing. Damage to the cingulate gyrus can result in a state of apathy in which responses to internal and external stimuli are diminished significantly.² At worst, severe cingulate damage results in “akinetic mutism,” a state with little spontaneous movement or speech.²

The cingulate can organize “attention for action” by modulating arousal, motivation, autonomic tone, and attentional focus to drive behavioral responses that address the most salient internal or external stimuli.⁴ Cingulate gyrus–nucleus accumbens circuitry figures prominently in addictive states. The cingulate gyrus



also is thought to generate the autonomic tone necessary to support many types of movement, and it signals behavioral conflicts by increasing arousal and autonomic tone.⁵

The orbitofrontal circuit modulates the pursuit of reward by adding considerations of risk, context, and potential consequences to the behavioral equation. The orbitofrontal cortex is connected reciprocally to the amygdala, and both act in concert to generate emotional states relevant to the pursuit of reward and avoidance of risk. Both the orbitofrontal cortex and the amygdala receive a rich set of inputs from all five sensory cortices, as well as from the insula (Figure 4, see page xxx). These define comprehensive views of both external and internal milieus. The inputs come primarily from downstream regions of the

unimodal cortices; therefore, the information probably is at the whole object rather than the individual feature level.⁶ In addition, sensory inputs are relatively blended and provide multidimensional views of the environment. The amygdala projects to the same sites in the orbitofrontal cortex that receive direct sensory inputs; this arrangement may allow the orbitofrontal cortex to extract the emotional significance of sensory events. Both amygdala and orbitofrontal cortex ignore neutral sensory inputs with no implications of risk or reward and stop responding to any inputs that lose their motivational value.

Barbas and coworkers⁶ have elucidated the layout of orbitofrontal–amygdalar circuitry through experimental work with nonhuman primates. The amygdala can exert both inhibitory and stimulatory

influences on hypothalamic autonomic nuclei. The central nucleus of the amygdala normally inhibits the hypothalamic nuclei, while the basolateral nucleus stimulates it.

The orbitofrontal cortex can suppress autonomic centers through stimulation of the amygdala’s central nucleus.⁶ Activation of this nucleus causes autonomic inhibition. The opposite result, autonomic activation, can be achieved by the orbitofrontal cortex through stimulation of the intercalated masses of the amygdala. This diminishes the default inhibition of hypothalamic nuclei by the amygdala’s central nucleus.

Functionally, the orbitofrontal cortex induces anticipatory body states that promote reward seeking, as well as aversive body states that reduce the likelihood of risky actions.² The orbitofrontal

cortex probably evolved to prevent injury in the pursuit of reward, to facilitate behavioral restraint by animals at lower levels of the social hierarchy, to promote the preferential pursuit of low-risk rather than high-risk rewards that are consistent with internal needs, and to inhibit pursuit of contextually inappropriate rewards, such as seeking food when sated. Humans with orbitofrontal cortex damage usually demonstrate personality changes that include high impulsivity, social inappropriateness, explosive behavior, disregard for rules and consequences, and the inability to use aversive emotions to inhibit risky behavior.²

The dorsolateral prefrontal circuit modulates executive functions. These include organization, problem solving, working memory and memory retrieval, self-direction, the ability to address novelty, and the use of language to guide behavior.² The dorsolateral prefrontal cortex, like the orbitofrontal cortex, receives sensory inputs, although these are primarily from visual, auditory, and somatosensory cortices.⁶ The frontal eye fields (BA8) receive low-level visual in-

SIDEBAR.

The Three Major Behavioral Circuits in the Prefrontal Cortex^{2,3}

1. The anterior cingulate circuit (Figure 2a) with nodes in:
 - The dorsomedial nucleus of the thalamus.
 - Brodmann area 24 of the anterior cingulate gyrus.
 - The ventromedial caudate, ventral putamen, nucleus accumbens, and olfactory tubercle.
 - The rostromedial and ventral globus pallidus.
2. The orbitofrontal circuit (Figure 2b) with nodes in:
 - The ventral anterior and dorsomedial nuclei of the thalamus.
 - Brodmann area 11 and inferomedial Brodmann area 10.
 - The ventromedial caudate.
 - The dorsomedial globus pallidus and substantia nigra pars reticulata.
3. The dorsolateral circuit, with nodes in:
 - The ventral anterior and dorsomedial nuclei of the thalamus.
 - Brodmann area 9 and dorsolateral Brodmann area 10.
 - The dorsolateral caudate.
 - The dorsomedial globus pallidus and substantia nigra pars reticulata.

formation with a degree of detail that rivals what is found in the visual unimodal cortex.⁶ Sensory information is less integrated in the dorsolateral cortex than in the orbitofrontal cortex, possibly facilitating more detailed analysis of specific stimuli.⁶

People with damage to the dorsolateral prefrontal cortex have difficulty organizing behavior to meet internal or external demands and perseverate in their thoughts and speech. Decision making is impaired, and there is a strong tendency to be drawn toward objects and situations with high salience, even if the interaction is contextually inappropriate. These people often engage in utilization behavior, which is the indiscriminate handling of any salient objects encountered. They have significant difficulty with problem solving and are unable to address novelty.²

The dorsolateral prefrontal cortex is the entry point for verbal psychotherapeutic interventions, as it is essential for advanced reasoning and for modulating behavior through the use of words. Mayberg and colleagues⁷ have demonstrated increases in limbic-paralimbic blood

flow in the subgenual cingulate (BA25) and anterior insula in people experiencing sadness. Sad people also demonstrated decreases in blood flow to the right dorsolateral prefrontal cortex and inferior parietal cortex.⁷ These imbalances can be corrected through psychotherapy⁷ (Mayberg, see page xxx).

EMOTIONS AND BODY STATES

According to Rolls,⁸ emotions can be defined as internal states “elicited by rewards and punishers.” Functionally, emotions are powerful motivators that modulate the probability of either engagement or avoidance with respect to objects or situations. Each emotion generates a specific body state through a characteristic pattern of autonomic activation as well as neurotransmitter and hormonal release. These factors promote arousal and move the individual along the engagement–avoidance continuum with respect to the stimuli that generated the emotion. In addition to promoting engagement or withdrawal, emotions amplify the representations that are generating them.

Emotions promote both the storage

CME EDUCATIONAL OBJECTIVES

1. Describe the anatomy and function of the major circuits of the prefrontal cortex.
2. Recognize a variety of neural substrates that have special relevance to the psychotherapeutic process.
3. Identify the basic brain circuitry that controls emotions.

Dr. Viamontes is regional medical director, United Behavioral Health, St. Louis, MO, and assistant clinical professor, Department of Psychiatry, University of Missouri-Columbia, Columbia, MO. Dr. Beitman is professor and chair, Department of Psychiatry, University of Missouri-Columbia.

Address reprint requests to: [ADDRESS & E-MAIL]

The authors disclosed no relevant financial relationships.

and retrieval of relevant memories and provide a sense of experiential continuity, as the autonomic, neurotransmitter, and hormonal changes that accompany them have lasting effects. The lasting effects of emotional arousal also can lead to the nonspecific attachment of emotions to objects and situations that are encountered while the emotional state remains in force. This phenomenon is a source of significant interpersonal and occupational dysfunction and is an area of concern for the psychotherapist. Behaviorally, the drive to engage that can accompany certain emotions is not always a positive factor. People in manic states are an example of this. In addition, engagement can take place for the purpose of aggression. Emotions can amplify a situation to such a level that disengagement becomes difficult, yet the person involved feels compelled to fight physically, verbally, or both. Many patients who seek psychotherapeutic help have problems disengaging from emotional situations.

The following description of the brain's emotional system is based in part on a previous article.⁹ Phillips and colleagues¹⁰ reviewed the brain regions responsible for the generation of emotions and their subsequent regulation. The evaluation of stimuli and the generation of the autonomic, neurotransmitter, and hormonal components of emotions are mediated by a "ventral" processing system with epicenters in the amygdala, the insula, the nucleus accumbens, ventral regions of the anterior cingulate gyrus, and the orbitofrontal cortex (Figure 3, see page xxx).

Barbas and colleagues⁶ mapped the density of projections from primate prefrontal regions to autonomic centers in the hypothalamus. Dense projections originated in the subgenual and rostral cingulate (Brodmann areas 25 and 32, respectively), as well as caudal areas of the orbitofrontal cortex. Moderate projections emanated from cingulate area

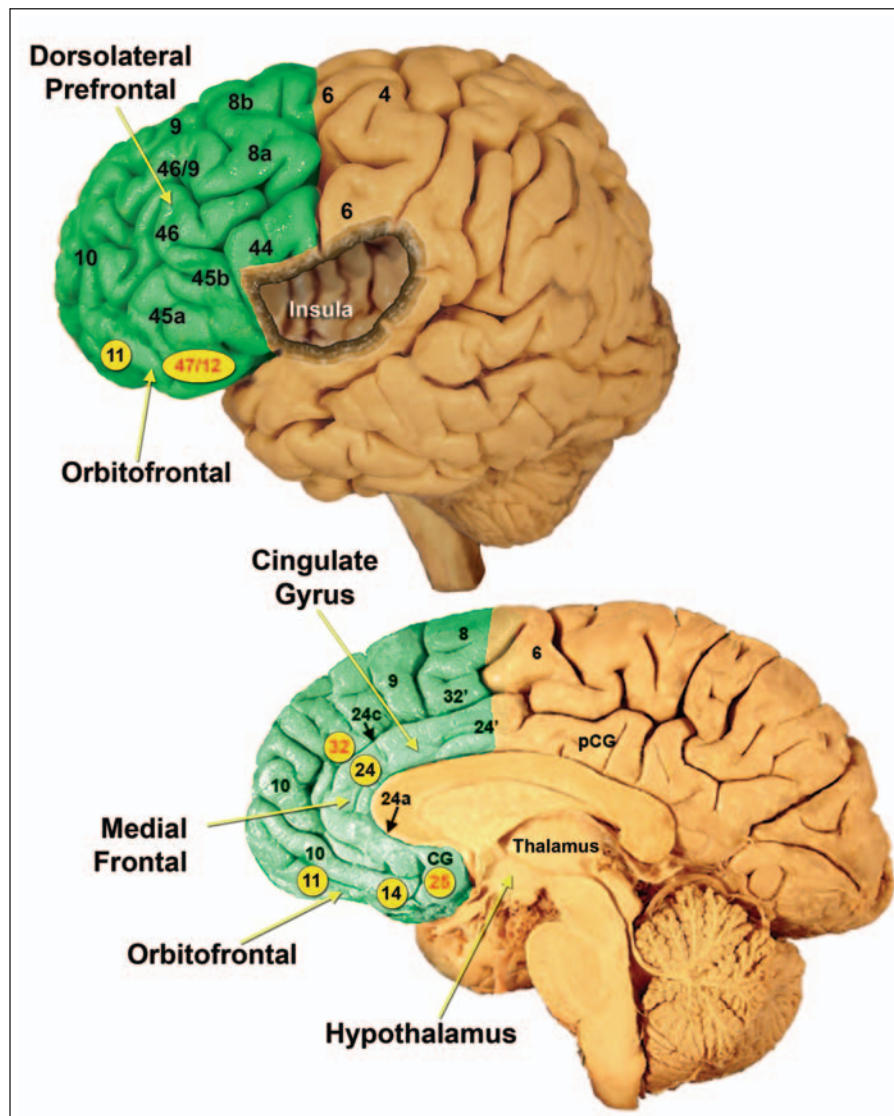


Figure 1. Lateral and medial views of the prefrontal cortex (outlined in green). The prefrontal cortex includes the cortical regions of the brain in front of the premotor and motor strips. Commonly cited regions of the prefrontal cortex include the dorsolateral prefrontal, orbitofrontal, medial frontal, and cingulate cortices. Areas with strong connections to hypothalamic autonomic centers⁶ are in red letters within yellow circles or ovals. Areas with moderate connections to the same areas are in black letters within yellow circles. These regions are able to trigger autonomic body states that can be perceived consciously and are an integral part of emotions. When the evaluation of a situation by these regions does not agree with cognitive assessments, a feeling that something "is not right" is often experienced. (Figure ©2006 G.Viamontes. Used with permission.)

24, as well as orbitofrontal areas 11, 12, 13, and 14 (Figure 1). These special areas in the prefrontal cortex, together with a variety of subcortical nuclei, are the regions that provide the direct autonomic modulation associated with emotions.

The amygdala, as previously described, is an important modulator of responses to objects and situations that signal potential reward or risk. The

amygdala also functions in the recognition of facial expressions, especially angry, threatening, or fearful expressions.⁸ The anterior insula is another important mapping region for emotions. It represents visceral sensations as well as many emotional states that are accessible to consciousness, such as sadness, pain, anticipatory anxiety, guilt, and the recollection of past emotional states.¹⁰

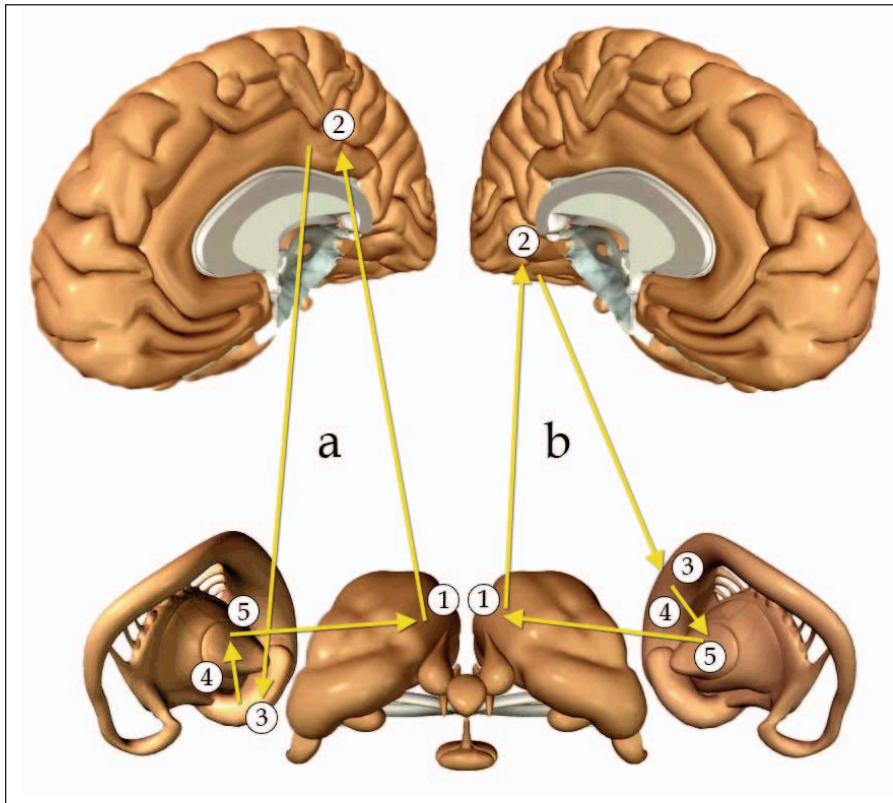


Figure 2. Two of the thalamocortico-striatal-pallidal loops that involve functional nodes in the prefrontal cortex as key components. Figure 2a depicts the loop through the cingulate gyrus and nucleus accumbens. Information is transmitted from the dorsomedial nucleus of the thalamus (1) to the cingulate gyrus (2). Excitatory projections from the cingulate reach the nucleus accumbens (3). The nucleus accumbens sends inhibitory signals to the internal globus pallidus (4). The inhibition from the nucleus accumbens disrupts the tonic inhibition that the internal globus pallidus normally exerts on the thalamus and enhances thalamo-cortical transmission. The circuit can generate a sustained representation that focuses motivation and attention on a particular stimulus. Figure 2b depicts a similar circuit through the orbitofrontal cortex. This circuit courses through the ventral anterior and dorsomedial nuclei of the thalamus (1), the orbitofrontal cortex (2), the dorsolateral caudate (3), the dorsomedial globus pallidus (4), and then back to the thalamus. The dorsolateral prefrontal circuit is not shown. It has nodes in the ventral anterior and dorsomedial nuclei of the thalamus, Brodmann areas 9 and 10, the dorsolateral caudate, the dorsomedial globus pallidus, and then back to the same thalamic nuclei from which the signal originated. Brain images copyright 3B Scientific GmbH 2001. (Excerpted from NEUROteacherTM. Used with permission.)

Both the amygdala and the insula appear to play a role in the identification of the emotional value of stimuli and in the coordination of emotional responses. The ventral striatum, particularly the nucleus accumbens, as described above, is the centerpiece of the brain's reward system. It functions in the identification of objects of potential value and in motivating the organism to pursue the acquisition of these objects. The anterior cingulate appears to function in the generation of the autonomic component of affective states and in the connection of objects and

situations with appropriate motivation. It focuses attention on activities likely to yield high reward and helps to generate mood-related affective states, whether happy or sad.^{4,7}

The dorsal emotional system appears to function in the modulation of emotions in concert with current adaptive demands.¹⁰ The dorsal system includes the hippocampus, the dorsal anterior cingulate, and the dorsolateral regions of the prefrontal cortex¹⁰ (Figure 4, see page xxx). These regions modulate emotional states with respect to context, memory,

and internalized rules. An imaging study examined whether rational reappraisal of negative emotions could result in attenuation of the negative emotional state and found that reframing emotional events in unemotional terms reduced affective intensity.¹¹ The neural correlates of this phenomenon began with activation of the dorsal and ventral regions of the left lateral prefrontal cortex, as well as the dorsomedial prefrontal cortex during the reappraisal procedure. The specific correlates of successful emotional reappraisal involved increased activation of lateral and medial prefrontal cortices combined with decreased activation of the amygdala and medial orbitofrontal cortex.¹¹

Regardless of the therapist's theoretical orientation, the modulation of emotional reactions plays a critical role in the psychotherapeutic process. An understanding of the circuitry that mediates emotions and how these circuits can be influenced through psychotherapy, medication, and physical methods (Mayberg, see page xxx) can be invaluable in the design of novel psychotherapeutic approaches and in the formulation of strategies for combining psychotropic medications and somatic treatments with psychotherapy.

EGO, SUPEREGO, AND ID

Sigmund Freud defined ego, super-ego, and id to segregate three functional modalities whose interplay, in his estimation, were the central drivers of human behavior. Even if one does not agree with Freud's theoretical constructs, it is not difficult to understand the neurobiology that motivated his basic conceptualizations. The three prefrontal circuits described above can be aligned roughly with the phenomena that Freud described.

The dorsolateral prefrontal circuit has many of the attributes of the ego (Figure 4). It facilitates executive functions such as integration of perceptual information,

problem solving, and decision making.^{2,3} Imaging studies have also shown that the dorsolateral prefrontal cortex, possibly in conjunction with the cingulate gyrus, plays a key role in the suppression of unwanted memories.¹³

The manifestations of the id (Figure 5, see page xxx) are very much a function of cingulate gyrus–nucleus accumbens circuitry. This circuit amplifies signals that suggest the attainability of reward and generates body states that motivate pursuit of potential pleasures. In the presence of remembered cues, this circuit can generate overwhelming motivational pressure to engage in reward-producing behavior, as is the case in chemical dependence.

The functions of the superego (Figure 6, see page xxx) are implemented by orbitofrontal–amygdalar circuitry. This functional network evolved to temper the pursuit of pleasure with considerations of context and risk. Orbitofrontal–amygdalar circuits are directly wired to autonomic centers and can produce body states conducive to disengagement and withdrawal. The actions of this circuit set limits on risk-taking and can convey the visceral feelings of potential punishment or embarrassment.

Much of the apparent conflict among the prefrontal circuits in the determination of behavior is a result of parallel processing. Cognitive and emotional centers process information simultaneously, rather than sequentially. In addition, emotional processing often is completed before cognitive evaluation. This can lead to the production of a body state that motivates approach or withdrawal, followed by a cognitive assessment that dictates the opposite. Harmonious integration of cognition and emotions often is not possible even in common social and occupational situations, and the imbalance is even greater when psychopathological processes have altered the relative contributions of emotional and cognitive circuits. High-function-

ing individuals can sense processing discrepancies and use them to advantage in defining behavior. The feeling that “something is not quite right” can be very valuable, for example, during problem-solving or creative pursuits. Conversely, emotional–cognitive dissonance can lead to severely impaired occupational and social behavior and is an important area of concern for the psychotherapist.

NEURAL SUBSTRATES OF PSYCHOTHERAPEUTIC CHANGE

The human brain promotes adaptability by evaluating many variables as it coordinates behavior. The substrate that the brain uses for evaluation is not the external world, or even its direct physical properties. Instead, the brain internalizes peripheral sensory data and edits it according to expectations, using internal content to fill “gaps” and resolve discrepancies. The “meaning” of this composite map is defined by existing feature detectors and their connections, by cognitive and emotional processing, and by prevailing internal states.

Representation is the first level of information processing at which malfunctions can cause psychopathology. Brains that have developed under conditions of neglect or abuse may not possess adequate numbers or types of feature detectors, because exposure to sociocultural information may have been inadequate, and chronic stress is associated with brain simplification, including loss

of cells and neuronal dearborization.¹⁴ Such modifications can save energy and decrease response time, at the cost of diminished powers of discrimination. In this context, the psychotherapist should be aware that basic experiential concepts such as empathy, happiness, and love might not be represented adequately in a patient’s brain. Without such representation, the words that name these concepts have no meaning, and the body states that normally accompany these experiences will not be elicited.

Memory symptoms are common

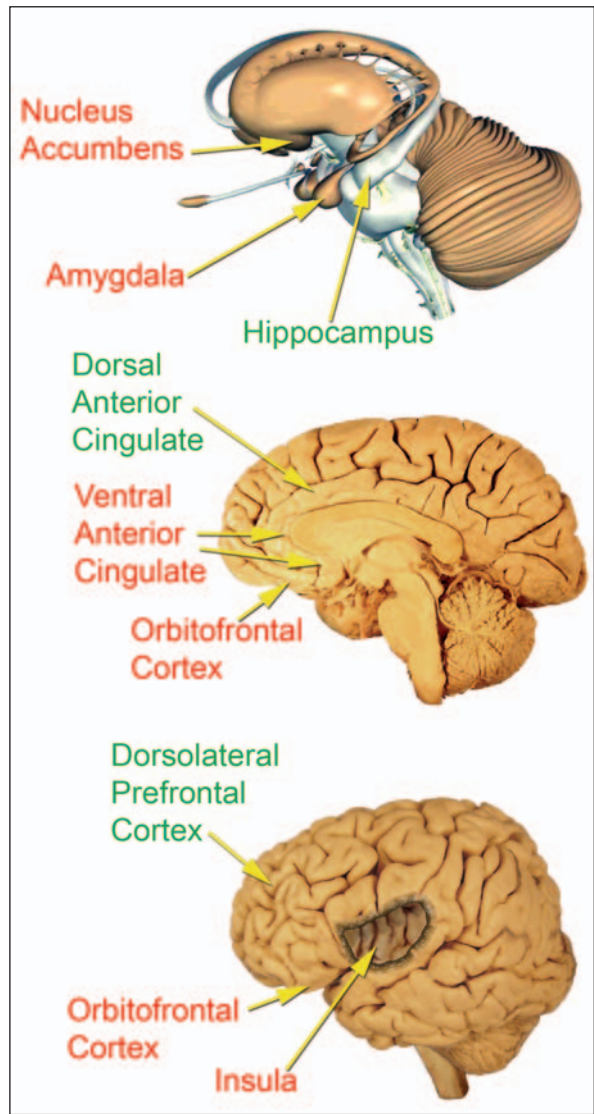


Figure 3. Depiction of the ventral and dorsal systems that generate and regulate emotions.¹⁰ Components of the ventral system are labeled in red, while elements of the dorsal system are in green. (Bottom two images ©2006 G. Viamontes. Used with permission.)

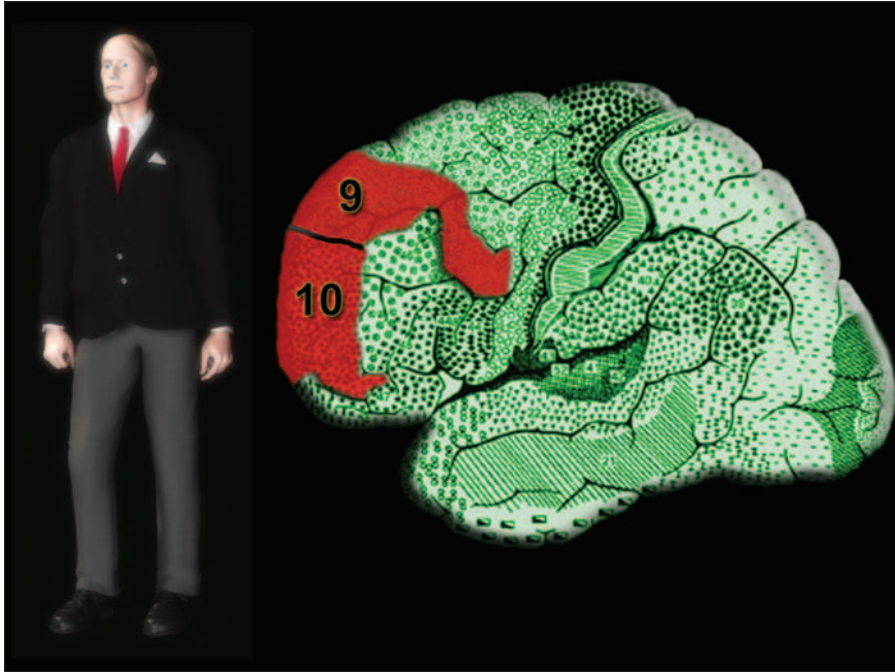


Figure 4. Metaphorical depiction of the ego, as well as the origin of the dorsolateral prefrontal circuit (Brodmann areas 9 and 10) that facilitates classical ego operations such as executive function, problem-solving, organization, working memory, and the use of language to control behavior.

among people in psychotherapy. The classification of memories into phyletic, sociocultural, and idiotypic can assist in defining possible psychopathologi-

cal deficits. People with faulty phyletic memory have serious problems that may be difficult to treat, as they have deficiencies in basic representational or

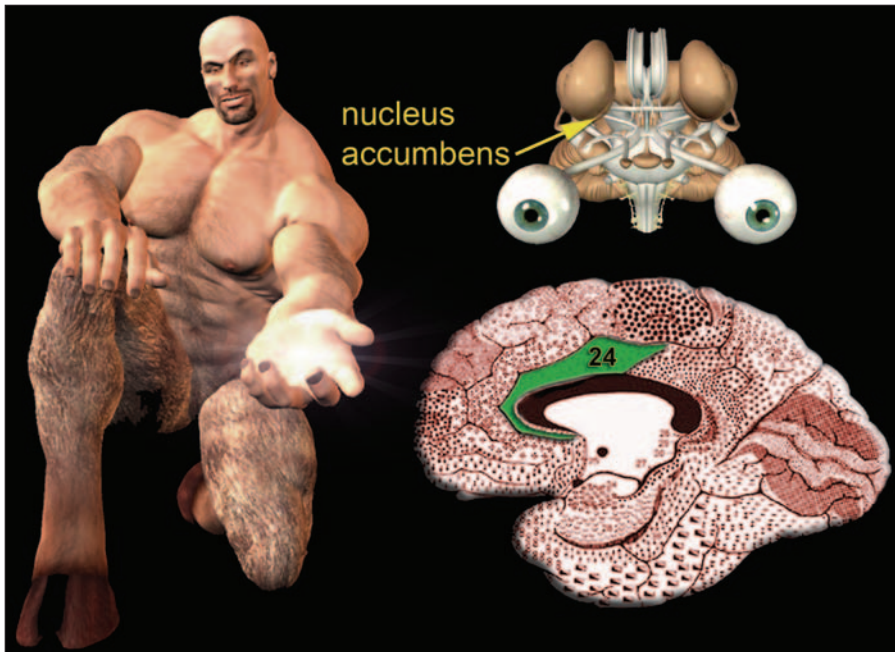


Figure 5. Metaphorical visualization of the id, as well as the cingulate gyrus and nucleus accumbens, which are critical nodes in the circuit that controls classical id functions. This circuit serves in part as the brain's main reward system. Cingulate function motivates behavioral responses to the most salient internal or external stimuli that are being perceived at any given moment.

processing capabilities. Those with dysfunctional sociocultural memories may never have assimilated the basic knowledge and behavioral rules that are necessary for success in occupational and social settings. Dysfunctional idiotypic memories can cause significant behavioral problems because they often generate explosive emotional amplification. In addition, such memories often contain associational patterns that precipitate interpersonal difficulties. We have hypothesized that excessive compression of memories, or the filtering out of many of the details that normally differentiate experiences, can lead to “black or white” thinking, which engenders numerous perceptual and social problems.

The prefrontal circuits described above, which support adaptive behavior by making it possible to consider many variables before responding to a stimulus, are important targets for the psychotherapist. First, dorsolateral prefrontal circuitry must be enlisted to use words as tools for shaping behavior. This circuit is responsible for executive functions, including organization, problem solving, abstract thinking, creativity, strategic planning, and future orientation. Many common psychotherapeutic problems are rooted in suboptimal function within this circuit.

The generation of motivational and emotional states appropriate to context is an important function of the cingulate gyrus.⁵ The amygdala and orbitofrontal cortex, by virtue of their connections to hypothalamic autonomic centers and other subcortical targets, also are able to generate emotional body states. One of the most common conditions for which people seek psychotherapy is emotional dysregulation. Imaging studies have shown that orbitofrontal and amygdalar circuits can be modulated through conscious cognitive processes, such as psychotherapeutic interactions¹¹ (Mayberg, see page xxx).

The orbitofrontal circuit, in concert

with the amygdala, is responsible for tempering the unbridled pursuit of reward or saliency. Deficits in this circuit can present as impulsivity, social inappropriateness, lack of empathy, lack of respect for social conventions, and little response to the threat of personal risk, embarrassment, or punishment. In cases of suspected orbitofrontal dysfunction, the psychotherapist must first determine whether there is any functionality present and then decide whether to try to bolster representations of adverse consequences in connection with inappropriate behaviors. If this circuit appears to be completely nonfunctional, the prognosis for a psychotherapeutic “cure” would be considered poor, as is the case in the treatment of antisocial personality disorder.

SUMMARY

The neural circuitry that supports the generation of adaptive responses to environmental and internal stimuli includes representational, evaluative, emotional, and cognitive components, many of which are located in the prefrontal cortex. Dysfunction in any of these neural circuits will lead to characteristic psychopathological manifestations. An understanding of the neural circuitry that shapes behavior can be invaluable to the psychotherapist for defining the underlying causes of a particular patient’s symptoms and for working with the patient to restore adaptive functioning. To facilitate change, the words of psychotherapy must first point accurately, and in terms that the patient can understand, to the representational, memory, or processing deficits that are maladaptive. As the psychotherapeutic process unfolds, the psychotherapist can help the patient generate new representational capabilities, create new synaptic connections, enhance the complexity of memories, and recruit prefrontal circuitry for optimizing behavior. With the expanded capabilities that accompany psycho-

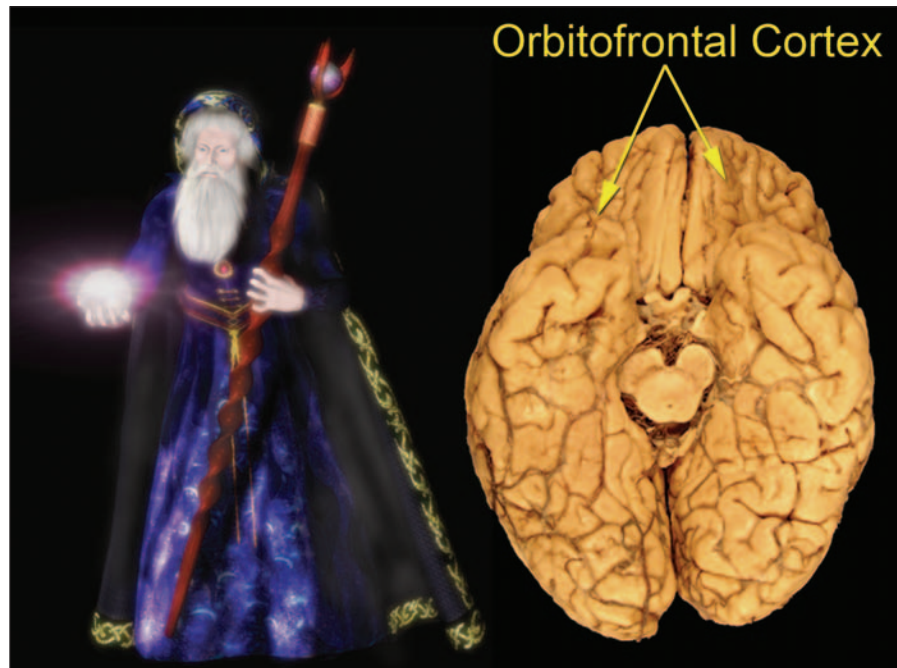


Figure 6. Metaphorical depiction of the superego, as well as the orbitofrontal cortex, which implements a number of superego functions. It generates emotional states that can temper the pursuit of reward and saliency with considerations of risk. Orbitofrontal circuitry provides the basis for modulating behavior on the basis of context. Individuals with orbitofrontal damage are impulsive and socially inappropriate. They are often indistinguishable from individuals with antisocial personality disorder.

therapeutic change, the patient’s neural infrastructure can begin to support adaptive behavioral responses and emotional states that are contextually appropriate and personally satisfying.

REFERENCES

1. Mesulam, MM. The human frontal lobes: transcending the default mode through contingent encoding. In: Stuss DT, Knight RT, eds. *Principles of Frontal Lobe Function*. New York, NY: Oxford University Press; 2000:[PAGE NUMBERS].
2. Mega MS, Cummings JL. Frontal subcortical circuits: anatomy and function. In: Salloway SP, Malloy PF, Duffy JD, eds. *The Frontal Lobes and Neuropsychiatric Illness*. Washington, DC: American Psychiatric Publishing; 2001:[PAGE NUMBERS].
3. Burruss JW, Hurley RA, Taber KH, et al. Functional neuroanatomy of the frontal lobe circuits. *Radiology*. 2000;214(1):227-230.
4. Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. *Trends Cogn Sci*. 2000;4(6):215-222.
5. Critchley HD, Mathias CJ, Josephs O, et al. Human cingulate cortex and autonomic control: converging neuroimaging and clinical evidence. *Brain*. 2003;126(Pt 10):2139-2152.
6. Barbas H, Saha S, Rempel-Clower N, Ghashghaei T. Serial pathways from primate prefrontal cortex to autonomic areas may influence emotional expression. *BMC Neurosci*. 2003;4:25-37.
7. Mayberg HS, Liotti M, Brannan SK, et al. Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. *Am J Psychiatry*. 1999;156(5):675-682.
8. Rolls ET. *The Brain and Emotion*. Oxford, England: Oxford University Press; 1999.
9. Viamontes GI, Beitman BD, Viamontes CT, Viamontes JA. Neural circuits for self-awareness. In: Beitman BD, Nair J, eds. *Self-Awareness Deficits in Psychiatric Patients*. New York, NY: WW Norton; 2005:24-111.
10. Phillips ML, Drevets WC, Rauch SL, Lane R. Neurobiology of emotion perception I: The neural basis of normal emotion perception. *Biol Psychiatry*. 2003;54(5):504-514.
11. Ochsner KN, Bunge SA, Gross JJ, Gabrieli JD. Rethinking feelings: an FMRI study of the cognitive regulation of emotion. *J Cogn Neurosci*. 2002;14(8):1215-1229.
12. Gabbard GO. *Psychodynamic Psychiatry in Clinical Practice*. 3rd ed. Washington, DC: American Psychiatric Publishing; 2000.
13. Anderson MC, Ochsner KN, Kuhl B, et al. Neural systems underlying the suppression of unwanted memories. *Science*. 2004;303(5655):232-235.
14. Sapolsky RM. *Stress, the Aging Brain, and the Mechanisms of Neuron Death*. Cambridge, MA: MIT Press; 2002.