Chapter 29

Brain Processes Informing Psychotherapy

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Successful psychotherapy is correlated with discrete brain changes (Etkin et al. 2005; Roffman et al. 2005) because psychotherapy, like medication, ultimately targets neuroanatomical structures and modulates their function. Early evidence suggests that concepts such as extinction, free association, cognitive restructuring, and repression can be mapped onto the brain (Roffman et al. 2005). Because of the direct correspondence of therapeutic processes to specific neural phenomena, and the power that knowing the details of these phenomena can provide, we argue that psychotherapists should learn the brain. The rationale that supports our opinion is presented in the first section of this chapter, "Reasons for Developing a Neurobiology of Psychotherapy."

Many psychotherapists challenge the need to learn neurobiology, claiming that knowledge of psychotherapeutic theory and technique is sufficient for successful outcomes. Clinicians sometimes argue that there is too much to learn about the brain while, at the same time, knowledge about psychotherapy theory and technique continues to expand. Fears of information overload are therefore not uncommon. To address these concerns, the field must attempt to define a cohesive set of neurobiological concepts that apply specifically to psychotherapy. In the second section of the chapter, we begin this process by presenting some of the basic neuroanatomy that underlies the brain-mind phenomena of engagement, self-awareness, pattern definition, and id-ego-superego constructs.

AUTHOR: Previous paragraph, last sentence: Note that second section of chapter, "Neural Correlates of Basic Psychotherapeutic Processes," seems to have these subsections: "Engagement," "Self-Observation," "Pattern Search," and "Brain Correlates of Classical Psychotherapeutic Concepts," three of which don't match the wording in previous sentence. OK?

More than these correlates, however, are needed for a successful adaptation of neurobiology to psychotherapy. Clinicians need practical concepts that bridge mind and brain—ideas that encourage them to seek greater knowledge of neurobiology so they can understand how their thoughts, words, and nonverbal behaviors can physically influence the brain of the other. In the third section, "Neurobiological Empathy," we engage in disciplined speculation from current knowledge with an eye toward clinical utility. The ideas presented are not restricted to either "mind" or "brain"; instead, they bridge the Cartesian dualism that isolates psychotherapy from its biological underpinnings by creating mind–brain conceptualizations for the targets of psychotherapeutic change. We use the term *neurobiological empathy* to describe these attempts to know the mind-brain of our patients. It is an objective process that provides special insight into a patient's mental processes through an understanding of the neural deficits that are causing the patient's psychopathology.

AUTHOR: Previous paragraph, next-to-last sentence: Note change from "We call these attempts to know the mind–brain of our patient's neurobiological empathy." OK?

In the chapter's next section we address *mirror neurons*, an exciting discovery in neurobiology that has direct applications to psychotherapy. Mirror neurons are specialized circuits in the brains of primates that map the perceived actions of others for the purpose of determining their meaning. Therapists affect the mirror neurons of patients, and vice versa; therefore, the meaning that each participant derives from therapeutic interactions is a synthesis of observations, internal representations, and innate pattern recognition. This complicates communication but at the same time provides an opportunity for uncovering problems in the representational and pattern-matching processes of patients. Mirror neurons provide a neurobiological explanation for a variety of psychotherapeutic phenomena, including some aspects of transference and countertransference.

We conclude the chapter with a review of functional imaging studies that define the neural activation patterns that characterize common psychiatric illnesses and the changes brought about by psychotherapy. It is clear that psychiatric illnesses affect a variety of neural circuits at both cortical and subcortical levels, and that psychotherapy has measurable effects on the functioning of these circuits. Although the complexity of neural circuitry and the lack of uniformity among studies have made it difficult to draw definitive conclusions, a number of trends have emerged that are helpful in understanding how psychotherapy restores the working capacity of malfunctioning neural circuits.

AUTHOR: 1) Note change of following heading from "Why Develop a Neurobiology of Psychotherapy?" because it was the only heading in chapter that was stated as a question. (Note also that this chapter heading is used at the end of the first paragraph of chapter, in case you alter the heading.)
2) Note also the addition of a brief paragraph after the heading to explain the numbering of paragraphs. OK?

Reasons for Developing a Neurobiology of Psychotherapy

As discussed at the opening of this chapter, we believe it is important for psychotherapists to learn the brain. We enumerate here six reasons why this knowledge is valuable:

1. *Psychotherapy theory is in conceptual disarray.* There are too many schools, too many theories, and too many strategies and techniques. A brain-based infrastructure promises to provide solid grounding for basic psychotherapeutic concepts. This conceptual solidity will help to organize the disparate orientations and allow nonpsychotherapists to grasp more firmly the unique and helpful mechanisms of psychotherapeutic action.
2. *Payers are confused.* Customers, including patients, businesses, the government, and managed care companies, want positive outcomes, not theoretical debates. They want empirically based descriptions of the interpersonal technology of psychotherapy, as well as clarity about the roles of the participants. They want to know more accurately what psychotherapy does.
3. *Brain circuitry is the final common pathway for the ever-expanding set of methods that can be used to alleviate psychological distress.* In addition to psychotherapy, these include such divergent processes as meditation, prayer, friendship, and psychoactive substances, both legal and illegal. It can be productive to visualize our role as therapists in a wider context and think of ourselves as change agents who rely primarily on psychotherapeutic methods. The development of an approach to psychotherapy informed by both mind and brain will sharpen technical, strategic, and theoretical foci by insisting that all theoretical constructs can be mapped onto discrete brain functions.
4. *Brain-informed psychotherapy will confirm the validity of many existing concepts and techniques, as well as disconfirm less empirically based ideas that may seem useful on the surface but actually have little connection to brain function.*

Eye movement desensitization and reprocessing (EMDR), for example, is a widely practiced treatment for posttraumatic stress disorder. Yet, the neurobiological underpinnings of EMDR remain unknown and continue to elicit wide debate. It is entirely possible that when the neurobiology of the process is clarified, the eye movements that characterize the technique might not actually be an essential therapeutic element. On the other hand, if the importance of eye movements in delivering the benefits of EMDR were scientifically proven, then the EMDR process could serve to clarify the function of important brain circuits.

5. *Brain-informed psychotherapy can help to simplify psychotherapeutic language.* For example, most therapies include instruction to keep doing that that seems helpful but use a variety of terms for this concept, including "practice," "working through," and "behavioral rehearsal." Psychotherapeutic change is actually based on increasing the probability of triggering adaptive rather than maladaptive pathways within the brain. When adaptive pathways do not exist, psychotherapy will be more difficult because these pathways will have to be created. To increase the probability of triggering adaptive pathways, they must be more firmly instantiated in the brain than less preferable ones. Here, the language of change could be simplified to describe the brain changes that maximize the probability of firing more adaptive circuits.
6. *By knowing how the phenomena that underlie core psychotherapeutic concepts and processes are generated in brain circuits, psychotherapists will become clearer about their psychotherapeutic intentions, more empirical in their understanding of illness, and more confident in their techniques.* It will eventually be possible to visualize the neurobiological targets for producing behavioral change, as well as the neural mechanisms by which psychotherapeutic interventions exert their effects.

The ultimate goal of this chapter is to introduce neurobiology that is relevant to psychotherapy, with the hope of encouraging therapists to learn more (for expansion of these ideas, see Viamontes et al. 2005). We would like to awaken interest in how the brain works during psychotherapy's basic processes, as outlined in the following section. With a deeper appreciation of the underlying neurobiology, therapists may be stimulated to put flesh on the bones of their own therapeutic processes in the context of functional neuroanatomy.

Neural Correlates of Basic Psychotherapeutic Processes

As was suggested in Chapter 26 ("Theory and Practice of Psychotherapy

Integration"), numerous reviews (Lambert and Bergin 1994; Lambert et al. 1986) and meta-analyses (Ahn and Wampold 2001; Prochaska and Norcross 2003) have demonstrated that no psychotherapy is inherently superior to any other, although all are superior to no treatment. These bodies of research also suggest that a core set of features shared by all therapies accounts for a significant portion of client symptomatic improvement.

Psychotherapy has a basic structure defined by a set of core processes (Beitman and Yue 2004), among which are engagement (the establishment of the working alliance), self-awareness, pattern search, change, termination, transference, countertransference, and resistance. This definition of core processes aids the task of mapping psychotherapy onto the brain by simplifying the wide variety of professional terms currently used to describe the psychotherapeutic process. We begin the task of linking core psychotherapeutic processes to specific circuits in the brain by describing some of the neural substrates that support the critical functions of engagement, self-observation, pattern search, and change.

AUTHOR: Previous paragraph: 1) Note that first and last sentences mention self-awareness, but the corresponding section below is called "Self-Observation." We changed to self-observation above. OK?

2) Last sentence mentions change, but the fourth section that follows has the heading "Brain Correlates of Classical Psychotherapeutic Concepts." Is that the subsection that represents "change"? Or is Change not represented in discussion at all, and "Brain Correlates of Classical Psychotherapeutic Concepts: not connected to that subject, which is what we assumed for now? Should subsection on Change be provided to follow Pattern Search?

Engagement

The strength of the working alliance has been the most studied process variable, and it has been shown to correlate positively with psychotherapeutic outcome (Krupnick et al. 1996; Wampold 2001). In fact, the working alliance—"the collaborative and affective bond between therapist and patient"—may be considered the therapeutic "quintessential integrative variable" (Wolfe and Goldfried 1988).

AUTHOR: Previous paragraph, last sentence: Please provide page number(s) for two quotes from Wolfe and Goldfried 1988.

When a therapist first encounters a patient, he or she immediately infers the patient's emotional state by observing facial expression, verbal output, and bodily demeanor. Work by Rizzolatti et al. (2001) showed that a critical neural processing step must occur prior to the transformation of observation to inference. Before the meaning of bodily movements and emotional expressions can be understood, these observations must be modeled in the therapist's brain (Rizzolatti et al. 2001). An array of mirror neurons found in the primate premotor region and in the parietal cortex become activated when the actions and expressions of others are modeled internally (Rizzolatti et al. 2001). The "meaning" of what the therapist senses both physically and emotionally when observing others is therefore an amalgam of actual observations and an internal transformation. The ability to be empathic and to accurately identify what a patient is "feeling" depends completely on the adequacy of the therapist's own limbic and cognitive circuitry. As such, the training of psychotherapists is, in great part, a tuning of brain circuitry to permit the accurate neural modeling of clinical observations and subsequent extraction of their "meaning."

As a therapist considers a patient's brain, the therapist can search for the neural source of the patient's emotional state. Imaging studies suggest that the patient's outward signs of anxiety—sweaty palms, quivering voice, motor agitation—are the result of activation of the neural circuits that detect risk and prepare the body to take appropriate action (Rolls 2005). Risk-detection circuitry is centered in the amygdala and orbitofrontal cortex (Rolls 1999, 2005). Both of these structures contain genetically preprogrammed information about natural "punishers"—that is, sensory perceptions (e.g., bitter tastes or pain) that throughout the evolutionary history of humans have been connected with unpleasant outcomes.

AUTHOR: Previous paragraph and other places in text: Rolls 2005 is cited but isn't in the references. Please add. Thanks!

AUTHOR: Paragraph below: Please note rephrasing in "These experiences are embodied in the form of synaptic linkages between . . ." Embodied accurate?

In addition, the amygdala and orbitofrontal cortex contain a record of the unpleasant experiences encountered throughout the person's lifetime. These experiences are embodied in the form of synaptic linkages between previously neutral stimuli associated with an unpleasant experience and the genetically determined collection of natural "punishers" that is already represented (Rolls 2005). For example, human infants quickly connect the sight of a syringe with pain and show signs of distress before immunizations. Many people with hypertension paradoxically increase their blood pressure just as it is about to be measured because the measurement process has become associated with unpleasant outcomes in the past. This phenomenon, which involves arousal as a response to cognitive information, requires activation of the dorsal anterior cingulate gyrus (Critchley et al. 2003), which in turn triggers autonomic centers.

The anxious patient in front of the therapist is focused intensely on his or her set of symptoms and wonders how the therapist could possibly "understand" this distress, given the therapist's privileged position of power and success. Instinctively, and without any knowledge of neurobiology, the patient senses that it will be difficult for the therapist to internally model the subjective components of his or her singularly unpleasant mental state. The cognitive uncertainties of the initial meeting with the therapist can cause even more autonomic arousal through the combined action of the dorsolateral prefrontal cortex, which represents current cognitive contents, and the cingulate gyrus, which generates autonomic tone consistent with those contents (Critchley et al. 2003).

As the therapist works toward successful therapeutic engagement, critical steps must include relief of this initial cognitive tension through an exchange of cognitive and emotional signals, until the therapist is indeed capable of "understanding," or internally modeling, the patient's situation. If engagement is successfully negotiated, then the therapeutic process can proceed. Eventually, previously neutral stimuli related to the therapist may become linked to experiences of reward in the patient's brain. This is also believed to involve synaptic modifications in the amygdala and orbitofrontal cortex, in a manner similar to what was described for unpleasant experiences (Rolls 2005).

As the patient begins to associate the therapist with symptom reduction and positive emotions, reward circuits and other areas in the patient's brain that represent gratifying social interactions are likely to be activated. For example, imaging studies have shown that internal representations of individuals perceived as "cooperative" in interactive situations elicit activation of the nucleus accumbens, which is at the center of reward circuitry (Viamontes and Beitman 2006), as well as the orbitofrontal cortex, fusiform gyrus, superior temporal sulcus, and insula (Ferris et al. 2004). We can hypothesize that excessive activation of reward circuitry may underlie the strong emotional attachments that patients can develop toward therapists.

AUTHOR: 1) Previous paragraph, next-to-last sentence: Should Viamontes and Beitman have the date 2006a and/or 2006b?

2) Next paragraph, near end of paragraph: Should Viamontes and Beitman have the date 2006a and/or 2006b?

Within the trusting, confiding psychotherapeutic relationship, patients can frequently reflect upon their emotionally laden difficulties in ways that would have been impossible outside therapy. Secure relationships such as can be achieved in therapy are associated with enhanced resiliency, as suggested by studies of traumatized children (Main 1991). In response to major losses such as the death of a parent, divorce, or major parental illness, children who were securely attached to their mothers were more resilient and less affected by the stressors than were other children. To be resilient is to be able to recognize that the "map is not the territory" or, in other words, that neural representations of the outside world, which incorporate both external and internal contents, are not equivalent to reality. Experimental evidence suggests that secure attachment, as extrapolated from imaging studies of romantic love (Bartels and Zeki 2000) and mother–child affection (Bartels and Zeki 2004), is associated with reduction in amygdala firing (lessening anxiety), increases in nucleus accumbens activity (possibly related to enhanced reward representations), and lessening of orbitofrontal firing (possibly reducing inhibitions). Within the secure attachment achieved through basic psychotherapeutic engagement techniques, circuits associated with negative emotions, social judgment, and "mentalizing" (Viamontes and Beitman 2006) can be activated safely through verbal means, and their consequences can be explored. This controlled activation of negative contents within the psychotherapeutic relationship helps liberate the patient from past constraints, permitting the exploration of new interpersonal concepts (Fonagy 2004). The common mechanism for such self-exploration is likely the activation of self-observation (Beitman and Soth

2006).

Self-Observation

Self-observation can produce knowledge about many internal states, such as intentions, expectations, feelings, thoughts, behaviors, and perceived effect on others. It can also enhance the capacity for introspection and anchor the person's understanding of his or her relationship with the environment (Stuss and Benson 1983). Self-observation increases the ability to "distinguish inner from outer reality, pretend from 'real' modes of functioning, and intrapersonal mental and emotional processes from interpersonal communications" (P. Fonagy et al., unpublished data). Psychotherapy, specifically the psychotherapeutic relationship, offers the opportunity to create and function within a "reflective space" that enhances the power to explore current maps of reality and alter them. Self-observation is a distinct process that can be distinguished from consciousness, awareness, and self-awareness.

AUTHOR: Is there an update for the status of Fonagy's unpublished data, mentioned in previous paragraph? If published, please provide page number. If from personal communication, please provide date of communication.

Consciousness, in the strictest neurological sense, refers simply to the waking state. This type of consciousness requires firing of the reticular activating system, as well as the integrity of basic homeostatic processes such as breathing, cardiac function, and autonomic tone. It represents the "general capacity that an individual possesses for particular kinds of mental representations and subjective experiences" that are "not directed at anything" (Wheeler et al. 1997). One must be conscious in order to be aware.

AUTHOR: Previous paragraph: Please provide page number for quote from Wheeler et al.

Awareness—the "particular manifestation or expression" that "always has an object" (Wheeler et al. 1997)—implies consciousness of content, such as a cloud, another person, or a painful experience. Self-awareness is a special type of awareness that is focused on the "object" of the self. The act of being self-aware encompasses the potential to observe the subjective neural representations of the self and to "model" internally an inferred representation of what others may think about the self (Beitman et al. 2005). Self-observation, in contrast, is an open-ended exploratory process that motivates the active scanning of one's inner world. In this context, observations can be made dispassionately, and without criticism or evaluation (Deikman 1982).

AUTHOR: 1) Previous paragraph, first sentence: Please provide page number for quote from Wheeler et al.

2) Previous paragraph, next-to-last sentence: Please specify Beitman et al. 2005a and/or 2005b. Thanks.

3) Next paragraph, last line: Please specify Beitman et al. 2005a and/or 2005b.

When observing oneself, one may focus attention on the totality of one's subjective reality, which includes representations of the self's experiences in the past, present, and future (Wheeler et al. 1997). The broad reflective potential of self-observation allows one to marshal the resources of self-awareness to alter prediction errors (Pally 2005). This capability provides a sense of agency, an "I" who is observing, planning, deciding, and evolving toward a future goal. Most psychotherapies help clients to activate their self-observational capacities, with the primary intention of altering faulty predictions and expectations (Beitman et al. 2005; Pally 2005).

The ability to observe the content of one's own mind depends on the healthy functioning of many different parts of the brain. To begin the process, one must be awake, with an intact brain stem and a functioning reticular activating system. Next, the objects of self-observation, which are neural representations in the various functional circuits that drive cognition, emotion, and behavior, must be accessed and integrated in working memory. The basic representation of the visceral self, along with a variety of internal states, can be obtained by accessing the insula; objects and space are represented in the temporal and parietal cortices; risk–reward considerations are continuously generated by the amygdala, orbitofrontal cortex, and nucleus accumbens; and episodic and semantic memories can be recalled by accessing the hippocampus and connected cortices. Cognitive considerations are generated in the lateral prefrontal cortices, and the strongest current focus of behavioral attention, whether internal or external, is represented by activity in the cingulate. Activity within regions along the border between the rostral anterior cingulate and the medial prefrontal cortex is associated with representations of mental states of the self (Frith and Frith 1999) and is consistently activated during self-reflective thought (Johnson et al. 2002). The top of this functioning pyramid of self-awareness appears to be the dorsolateral prefrontal cortex (DLPFC), which potentiates executive function and working memory (Wheeler et al. 1997) and is capable of integrating the full range of sensory, affective, and memory data.

The ability to generate a coherent self with temporal continuity depends on the power of the DLPFC to project individuals both backward and forward in time (Wheeler et al. 1997). People with damage to the DLPFC may lose the temporal sense of themselves. They may not recall episodic representations of past experiences and may be unable to project themselves into the future. The DLPFC and the right parietal lobe help to define the person in space and time by placing the body in the three physical dimensions, as well as in past, present, and future. Without this sense, the self erodes and merges with its environment. During meditation, the right parietal lobe may decrease its activity, which can induce dissolution of the sense of self in space and time (Newberg et al. 2002). Other studies have shown that disturbances of the temporoparietal region can generate "out of body" experiences, in which an individual has the sensation of floating above the ground and observing his or her body below (Blanke and Azry 2005).

As part of its integrating function, the DLPFC receives inputs from a variety of internal monitors. The insula, for example (Phillips et al. 2003), monitors visceral sensations as well as emotional body states, whereas the anterior cingulate can focus attention for the process of self-monitoring (Gusnard et al. 2001). In a clinical context, the dysfunction of prefrontal circuits that characterizes schizophrenia is thought to play an important role in the clinical finding that many patients with schizophrenia lack awareness of their disorder (Flashman 2005).

The current interest in the study of mindful awareness is likely to be supplemented by an expansion of knowledge about the neural circuitry that underlies self-observation. As researchers continue to acquire and integrate this information, self-observation will come to be viewed as another brain-based skill that can be developed not only in clients, but also in psychotherapists. In psychotherapy, the primary intent of self-observation is to uncover dysfunctional patterns that, if changed, will lead to relief of symptoms and improved functioning.

AUTHOR: Previous paragraph, 2nd sentence: Note change from "As we continue to acquire and integrate this information, we will come to view" to avoid "we," which could refer to you (the authors) or researchers. Correct interpretation?

Pattern Search

A major task of the central nervous system is to organize the linkage between internal representations of sensory information and adaptive responses (Mesulam 1998). The brain creates patterns from the huge array of sensory information that it processes to make sense of the environment in ways that optimize individual- and species-survival functions, including homeostasis, reproduction, and energy acquisition and conservation (Viamontes et al. 2005). Smaller brains cope with this challenge by developing inflexible bonds between sensation and action that are resistant to change. Larger brains have more flexible stimulus-response connections and therefore can have a wider range of alternative responses to specific environmental cues (Tanaka 2003). Smaller brains represent the world at a much coarser level of resolution because they have fewer cortical columns to devote to each aspect of represented reality. The simplification of the brain that can result from chronic stress or illness (Teicher et al. 2002) is relevant to this discussion. Although such simplification conserves energy and facilitates rapid responses, it can theoretically decrease the "richness" of experiences by limiting the amount of complexity that is represented.

An important component of habitual behavior is the formation of internal patterns that can be used to organize external stimuli, determine their "meaning," and respond to them. Humans are remarkably adept at inductive reasoning, which is the ability to infer complete patterns from perception of just a small number of their elements. Even advanced computers have difficulty matching the inductive power of the brain. People can recognize a song from a few notes, a person from a few words, and a concept from a single phrase. Effective psychotherapists induce patterns from nonverbal cues, key reported events, transference behaviors, and countertransference reactions (Beitman and Yue 2004). Psychotherapists can then help patients become aware of their internal patterns and drive therapeutic change by crystallizing awareness of maladaptive stimulus-response connections and ways in which these might be altered.

Understanding the brain's mechanisms for pattern recognition represents a major challenge for computational and neural sciences. Among the many perplexing questions is whether computational neuroscientists should attempt to mimic the brain with respect to pattern recognition, or develop an entirely different set of algorithms. Important clues about the brain's ability to recognize patterns have been gleaned from studies of visual pattern recognition. The following description of this process is quite simplified, and many of the described functions are not localized but rather widely distributed within the named area (Haxby et al. 2001). Nevertheless, it provides important insights into pattern recognition.

Visual inputs are first transmitted to the occipital cortex and then routed to the lateral inferior occipital lobe, where a "prepattern" is developed—an intelligent organization of the inputs. The data are sent to the fusiform gyrus in the ventral temporal lobe, where they are divided into at least two categories—namely, faces or objects. From the fusiform, the data continue to be transmitted rostrally. At the temporal pole, the object's identity is further clarified and integrated with limbic information. Data about the object are transmitted simultaneously to the parietal cortex, where the object is placed in three-dimensional space. Processed information about the object is sent to the entorhinal cortex, where its past significance is determined, and also to the dorsolateral prefrontal cortex, where its implications for the future are elaborated.

Our experiences are organized by the facilitated pathways for information processing that have been encoded in our brains throughout our lifetimes. These facilitated pathways organize our perceptions of reality and allow us to perform activities of daily living. These pathways or patterns in our brains create expectations: if this happens, then that will follow. A remarkable corollary of these experiential encodings is that they can induce the generation of expectations from neutral circumstances. We find what we seek because we expect it to be there. For example, the expectations of a person who believes that he or she will be rejected are inevitably fulfilled, in part because the expectation itself creates the circumstances for rejection.

Behavioral patterns are deeply ingrained and manifest themselves in many settings, from the therapist's office to the work environment, and certainly throughout the whole spectrum of personal relationships. Therapists also expect to find certain patterns: past–present connections, narcissistic injury, hidden anger, cognitive distortions, role-relationship conflicts, and many others. Some clinicians even have a "favorite" diagnosis, and a disproportionate number of their patients are identified as fitting its characteristic constellation of symptoms.

Patterns that organize perceptions and expectations in a maladaptive manner are at the core of many psychiatric disorders. In neurobiological terms, these faulty expectations are sometimes called pathological attractors, because input data are channeled toward them, and they invariably lead to maladaptive behavioral outputs. Angry, impulsive, passive, or anxious excesses are the products of inputs channeled through pathological attractors that connect to excessive outputs.

Consider the "black-and-white" thinking that is characteristic of many patients, especially those with borderline personality disorder. How might experience create black versus white attractors? One possible model involves the hippocampus, which may shrink in size with trauma (Teicher et al. 2002), although some controversy remains about this claim. The simplification of brain structures can have adaptive value in chronically stressful situations, as it conserves energy and shortens the stimulus-to-response interval. However, it also limits function.

AUTHOR: Previous paragraph: 1) Second sentence: Note change from "black/white attractors" to "black versus white attractors"—OK?

2)Note that "et al." was added to Teicher. OK?

If traumatic experiences do indeed cause hippocampal simplification, then when patients with borderline personality disorder suffer numerous traumatic events, the functions of their hippocampal circuitry are likely to be affected. Specifically, simplification of the cornu ammonis region 3 may reduce dendritic and axonal arborization, fostering excessive compression and simplification of information. In addition, damage to the dentate gyrus limits new cell production, which in turn may hinder the process of encoding new, differentiated memory patterns (Kemperman 2002).

AUTHOR: Note change from "simplification of CA3" to "simplification of the cornu ammonis region 3." OK?

Brain Correlates of Classical Psychotherapeutic Concepts

Sigmund Freud defined *ego*, *superego*, and *id* to segregate three functional modalities whose interplay, in his estimation, were 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 constant tension between unconscious appetitive urges and higher control that characterizes Freud's visualization has a definable origin in neural circuitry.

AUTHOR: Previous paragraph: Please provide reference for Freud. Thanks.

The development of the human brain included the evolution of circuits that can evaluate multiple variables before deciding on a course of action, including circuits that can postpone the motivational drive of appetitive urges to satisfy higher demands. These circuits transcend the narrow focus of the reward system and promote the pursuit of reward in a manner that is consistent with contextual considerations, learned rules, and a vision of the future. Often, the motivational elements of appetitive networks and higher circuits lead in opposite directions, and this generates emotions and bodily sensations that provide a somatic representation of the conflict. The manner in which such conflicts are represented and resolved is an important determinant of psychopathology and a focus of the psychotherapeutic process.

The higher circuits that determine human behavior have important components in the prefrontal cortex. The term *prefrontal cortex* refers to the region of the brain directly in front of the premotor and motor strips. In humans, the prefrontal cortex represents 30% of the neocortex and facilitates transcendence of simple reward-driven behavior by permitting the consideration of an expanded set of variables before the initiation of actions. It coordinates adaptable, goal-directed behavior that considers internal and external circumstances, memory, applicable rules, and projected consequences.

AUTHOR: Previous paragraph, last sentence: Is "behavior that considers" or "behavior by considering" correct wording?

Functional and anatomical considerations have demonstrated three distinct circuits in the prefrontal cortex that modulate complex behavior. These are the anterior cingulate, the orbitofrontal, and the dorsolateral circuits. The oculomotor circuit, which controls automatic eye movements, is a fourth prefrontal network, but it will not be discussed in this chapter. All the prefrontal circuits have nodes in the thalamus, cortex, basal ganglia, and globus pallidus and/or substantia nigra pars reticulata (Burruss et al. 2000; Mega and Cummings 2001). The circuits are somatotopically mapped and define numerous "channels" through each circuit component (Mega and

Cummings 2001).

The common functional element of all three circuits is modulation of the thalamus. Thalamic circuitry is tonically inhibited by the globus pallidus (Mega and Cummings 2001). 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 can therefore be selectively activated. Additional "indirect" loops pass through the subthalamic nucleus and external globus pallidus and complement the circuitry described above (Mega and Cummings 2001). Descriptions of the three major behavioral circuits in the prefrontal cortex follow (Burruss et al. 2000; Mega and Cummings 2001).

1. The anterior cingulate circuit has nodes in

    - Dorsomedial nucleus of the thalamus
    - Brodmann area 24 of the anterior cingulate gyrus
    - Ventromedial caudate, ventral putamen, nucleus accumbens, and olfactory tubercle
    - Rostromedial and ventral globus pallidus

2. The orbitofrontal circuit has nodes in

    - Ventral anterior and dorsomedial nuclei of the thalamus
    - Brodmann area 11 and inferomedial Brodmann area 10
    - Ventromedial caudate
    - Dorsomedial globus pallidus and substantia nigra pars reticulata

3. The dorsolateral circuit has nodes in

    - Ventral anterior and dorsomedial nuclei of the thalamus
    - Brodmann area 9 and dorsolateral Brodmann area 10
    - Dorsolateral caudate
    - Dorsomedial globus pallidus and substantia nigra pars reticulata

The anterior cingulate 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 (Bush et al. 2000). 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 (Bush et al. 2000).

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 (Critchley et al. 2003) and is an important component of reward circuitry. The cingulate receives cognitive data from the dorsolateral prefrontal cortex (Barbas et al. 2003) and facilitates emotional-cognitive integration by generating emotional states appropriate to cognitive contents (Critchley et al. 2003). 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 significantly diminished (Mega and Cummings 2001). At worst, severe cingulate damage results in "akinetic mutism," a state with little spontaneous movement or speech (Mega and Cummings 2001).

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 (Liu and Posner 2000). Cingulate gyrus–nucleus accumbens circuitry figures prominently in addictive states. The cingulate gyrus is also thought to generate the autonomic tone necessary to support many types of movement, and it signals behavioral conflicts by increasing arousal and autonomic tone (Critchley et al. 2003).

AUTHOR: Previous paragraph: Please provide reference for Liu and Posner 2000.

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 reciprocally connected 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. These define comprehensive views of both external and internal milieus. The inputs come primarily from downstream regions of the unimodal cortices, and therefore the information is probably at the whole object rather than the individual feature level (Barbas et al. 2003). 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, and this arrangement may allow the orbitofrontal cortex to extract the emotional significance of sensory events (Barbas et al. 2003). Both the amygdala and the 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 et al. 2003).

AUTHOR: Previous paragraph, sentence beginning "These define comprehensive views": Does "These" refer to inputs or cortices?

Barbas et al. (2003) 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, whereas the basolateral nucleus stimulates it.

The orbitofrontal cortex can suppress autonomic centers through stimulation of the amygdala's central nucleus (Barbas et al. 2003). Activation of this nucleus causes autonomic inhibition. The opposite result, autonomic activation, can be achieved by the orbitofrontal cortex through stimulation of the intercalated cell masses of the amygdala, which diminishes the default inhibition of hypothalamic nuclei by the amygdala's central nucleus (Barbas et al. 2003).

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 (Mega and Cummings 2001). 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 (Mega and Cummings 2001).

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 (Mega and Cummings 2001). The dorsolateral prefrontal cortex, like the orbitofrontal cortex, receives sensory inputs, although these are primarily from visual, auditory, and somatosensory cortices (Barbas et al. 2003). The frontal eye fields (Brodmann area 8) receive low-level visual information with a degree of detail that rivals what is found in the visual unimodal cortex (Barbas et al. 2003). Sensory information is less integrated in the dorsolateral cortex than in the orbitofrontal cortex, possibly facilitating more detailed analysis of specific stimuli (Barbas et al. 2003).

AUTHOR: Previous paragraph, sentence beginning "The frontal eye fields": Note change from BA 8 to "Brodmann area 8." Correct?

Individuals with damage to the dorsolateral prefrontal cortex have difficulty organizing behavior to meet internal or external demands, and tend to perseverate in their thoughts and speech. Their decision making is impaired, and they have a strong tendency to be drawn toward objects and situations with high salience, even if the interaction is contextually inappropriate. These individuals 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 (Mega and Cummings 2001).

The dorsolateral prefrontal cortex is the entry point for verbal psychotherapeutic interventions, because it is essential for advanced reasoning and for modulating behavior through the use of words. Mayberg et al. (1999) demonstrated increases in limbic-paralimbic blood flow in the subgenual cingulate (Brodmann area 25) and anterior insula in individuals experiencing sadness. Sad persons also demonstrated decreases in blood flow to the right dorsolateral prefrontal cortex and inferior parietal cortex (Mayberg et al. 1999). These imbalances can be corrected through psychotherapy (Mayberg et al. 1999).

AUTHOR: Previous paragraph: Note change from BA 25 to Brodmann area 25. Correct?

The dorsolateral prefrontal circuit has many of the attributes of the ego. It facilitates executive functions such as integration of perceptual information, problem solving, and decision making (Burruss et al. 2000; Mega and Cummings 2001). 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 (Anderson et al. 2004).

The manifestations of the id 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 are implemented through 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-functioning 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.

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. The dorsolateral prefrontal circuitry must be enlisted to use words as tools for shaping behavior. This circuit is also 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 (Critchley et al. 2003). 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 interactions (Ochsner et al. 2002).

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.

Neurobiological Empathy

Knowing the brain helps therapists to understand each patient's mind, which is, after all, a projection of the patient's brain processes into subjective and interpersonal space. A critical task for the therapist is to represent the minds of patients within his or her own. Through this process, the constellation of symptoms reported by the patient is categorized according to the structural elements stored in the therapist's neural circuits during psychotherapeutic training and practice. This representational effort is usually formalized in objective terms as a formulation, a diagnosis, or a case conceptualization. In subjective terms, the plight of the patient also arouses emotional activity within the therapist. In general, such activity is part of countertransference. More specifically, when the emotions and feelings generate a positive connection based on shared emotional experiences, the result is the subset of countertransference phenomena that we call empathy.

AUTHOR: Previous paragraph, sentence beginning "This representational effort": Please rephrase to avoid "formalized … as a formulation." Thanks.

In the context of a neural infrastructure for understanding behavior, a new kind of empathy becomes possible, which we call neurobiological empathy. Interpreting the actions and problems of patients requires the development of explanatory constructs that define a framework of imputed causality within the patient's sphere of interactions. These constructs can be experiential, rational, or both. In other words, the psychotherapist "understands" the nature and impact of the client's problem by accessing memories of similar experiences and/or applying theoretical knowledge about how the client's condition distorts normal rules of causality. In addition, the therapist can use neurobiological understanding to validate the patient's subjective experience and begin a dialogue about treatment. This dialogue can begin with an explanation of what is known about the neural basis of the patient's condition. For example, a psychotherapist treating a patient with severe phobia might have difficulty empathizing in a conventional way if he or she has never experienced a similar problem. In such a case, the psychotherapist must apply relevant knowledge acquired from previous treatment of similar patients and from having studied the neurobiology as well as the course and prognosis of the disorder.

The concept of neurobiological empathy asserts that the addition of focused neurobiological knowledge to this process can amplify the psychotherapist's ability to understand the patient and to communicate this understanding. If we return to the phobia example, recent neuroimaging work (Straub et al. 2006) has demonstrated a phobia-specific distortion of the cause-effect matrix that defines responses to environmental objects. During conscious identification of the feared object, phobic individuals showed activation of left and right amygdalas, the left insula, the left anterior cingulate gyrus, and the left dorsomedial prefrontal cortex. In addition, the right amygdala was strongly activated under conditions of attentional distraction, demonstrating amygdalar reactivity to the feared object even under conditions of subliminal perception. All of the regions that show activation have efferent projections that allow them to modulate autonomic arousal, and they represent critical nodes in the circuitry that turns previously neutral objects into perceived threats.

AUTHOR: Previous paragraph: Please add reference for Straub, Mentzel and Miltner, 2006.

An understanding of the neural mechanisms that underlie phobia can be important in planning its treatment. An important point to consider is that both conscious and unconscious representations of the feared object will cause activation of fear circuitry in the brain. Knowledge of the patient's neural reactions to the feared object is also the basis of neurobiological empathy. The therapist can explain to the patient the nature of the brain processes behind the behavioral problems that are the focus of therapy. This knowledge gives tangible reality to the patient's experiences and conveys to the patient a sense of informed concern and understanding by the therapist. Under these circumstances, both therapist and patient can begin their work from a concrete position that has both focus and objectivity. As knowledge of the neural basis of psychiatric disorders accumulates, this information can become an invaluable resource for those therapists who are prepared to use it.

Mirror Neuron Systems

Mirror neurons are groups of frontal and parietal neurons in the brains of primates that fire both during the execution of purposeful movements and during observation of other individuals performing similar actions (Iacoboni and Dapretto 2006). Mirror neurons were originally discovered in the brains of macaque monkeys by Rizzolatti and coworkers (Rizzolatti and Craighero 2004). These neurons are part of the brain's mechanisms for attributing meaning to the actions of others. In general, "meaning" in the brain is defined operationally and subjectively. In other words, the meaning of objects and movements are defined in terms of their functional significance to the individual. To encode this in the brain, some of the circuits involved in potential use of the object or movement in question are activated. In the case of mirror neurons, the meaning of observed actions is encoded by activating some of the neurons that would normally fire in the observer's brain if he or she were preparing to perform the same action.

AUTHOR: Previous paragraph: 1) Please add reference for Iacoboni and Dapretto 2006.
2) Please add reference for Rizzolatti and Craighero 2004.
3) Also, did Rizzolatti and Craighero 2004 discover the mirror neurons or report on the discovery by Rizzolatti and coworkers?

Mirror neurons in humans are located in two interconnected brain regions (Iacoboni and Dapretto 2006): 1) the pars opercularis of the inferior frontal gyrus (within Broca's area) in the frontal lobe and 2) the anterior area of the inferior parietal lobe. Frontoparietal circuits in general are thought to function in sensorimotor integration. In humans, these mirror neuron areas, together with the superior temporal sulcus, act as a key circuit that supports certain forms of motor imitation (Iacoboni and Dapretto 2006). The superior temporal sulcus provides a detailed visual description of the action to be imitated, the inferior parietal lobe defines its motoric components, and the pars opercularis defines its perceived goal.

AUTHOR: Next paragraph: Please add reference for Carr et al. 2003.

Mirror neurons also seem to be part of a system for understanding the intentions and emotional experiences of others. The system includes the following (Carr et al. 2003; Iacoboni and Dapretto 2006):

- Superior temporal cortex, which encodes a visual description of an observed action
- Posterior parietal mirror neurons, which encode the kinesthetics of the action's movement sequence
- Inferior frontal mirror neurons, which encode the perceived goal of the action
- Dysgranular field of the insula, which connects mirror neurons to limbic circuitry, and which facilitates the generation of a subjective body state related to the perceived action
- Limbic circuitry, including the amygdala, which can respond emotionally to the perceived goals

The ability to be empathic may depend on the functioning of these and related systems of circuits, although the actual mechanisms by which mirror neuron systems support empathy remain speculative (Carr et al. 2003).

These early findings can be tentatively extended to create brain-based explanations of a number of psychotherapeutic concepts. For example, patients with autism and autism spectrum disorders show markedly decreased activity in mirror neuron systems when viewing the emotional expressions of others (Iacoboni and Dapretto 2006). The well-known theory of mind deficit in autistic disorders can therefore be connected to actual brain dysfunction. Effective treatment may focus on enhancing mirror neuron activation to the degree that this might be possible, therefore optimizing the internal processes that lead to self- and other awareness.

Mirror neuron systems have become the cornerstone of an emerging neurobiological explanation of empathy. The highly social human brain may rely on these systems to navigate the complex universe of social interactions. As autism spectrum disorders suggest, people vary in their ability to register the emotional-cognitive states of others, including their psychotherapists.

Mirror neuron systems suggest an explanation of how a therapist's empathic resonance can affect a patient. Successful psychotherapy probably involves repeated "mirrorings" between the brains involved. The patient may mirror the therapist's empathic resonance by modeling the therapist's "attitude" within his or her neural circuits. Therefore, for a period of time of psychotherapeutic attunement, the therapist can give the patient a new set of experiences of the self. For example, the subjective experience of unbearable emotion and its therapeutic transformation in the mirrored environment of therapist calm may provide the patient access to a new set of circuits for emotional tolerance and management (Siegel 2006). On the other hand, overly empathic therapists may burn the internal experiences of emotionally difficult patients into their own brains through intense, repetitive mirroring, and may themselves sustain secondary trauma.

Functional Imaging Studies of the Effects of Psychotherapy on the Brain

The brain encodes experiences by altering neuronal connections, and prepares to meet perceived environmental challenges by modulating a variety of circuits, some of which have been discussed above. Before it was possible to visualize the activity of the brain as it addresses behavioral challenges, the neural correlates of psychotherapeutic change were unknown. At present, however, the visualization of functional changes in brain circuitry brought about by psychotherapy has become a reality. Because the field is relatively new and studies are not fully comparable in terms of methodology, hard conclusions cannot yet be drawn. However, important data are beginning to accumulate from which a theoretical framework that defines the neurobiology of psychotherapy can be built.

Goldapple et al. (2004) examined the effects of cognitive-behavioral therapy (CBT) on the brains of patients with depression, and compared the result with paroxetine treatment. Brain analysis involved positron emission tomography scanning, performed before the first and after the last treatment sessions. Patients in the psychotherapy group received 15–20 CBT sessions over a period of 19–33 weeks, and patients in the medication group received paroxetine for a similar period of time. All patients had equivalent scores (an average of 20 at the outset) on the Hamilton Rating Scale for Depression, and response was defined as at least a 50% reduction in the score.

AUTHOR: Previous paragraph: Please add reference for Goldapple et al. (2004).

In this study, responders to CBT showed significant increases in hippocampal and dorsal cingulate (Brodmann area [BA] 24) metabolism, as well as decreases in frontal cortex metabolism in dorsal (BA 9, 46), ventral (BA 47, 11), and medial (BA 9, 10, 11) regions. In contrast, responders to paroxetine showed increases in prefrontal metabolism, along with decreases in hippocampal and subgenual cingulate metabolism.

A study by Anderson et al. (2004) may be relevant to understanding the results of Goldapple et al. (2004). In Anderson et al.'s work, healthy volunteers were shown lists of words and asked to remember or forget certain ones. Successful forgetting was associated with increased activity of the prefrontal cortex, including the anterior cingulate, and decreased hippocampal activation during the initial word presentation. Conversely, the combination of increased cingulate and hippocampal activity was found to be important for successfully storing target words in memory.

In this context, the results reported by Goldapple et al. (2004) for the paroxetine group may represent decreased recall of dysphoric memories, combined with increased executive function. In the case of patients treated with CBT, increases in cingulate and hippocampal activity might have reflected the fact that CBT works by changing cognitive patterns, thus requiring cingulate and hippocampal effort, while at the same time other frontal regions that can recruit autonomic and emotional centers and which could have fueled the depressed state showed decreased activation.

Mayberg (2006), who was an investigator in the Goldapple et al. (2004) study, has reviewed imaging-based models of depression and its treatment, in light of her own work in the field. Mayberg conceptualizes the behavioral syndrome that we call depression as "a systems-level disorder affecting select cortical, subcortical, and limbic regions and their related neurotransmitter and molecular mediators" (Mayberg 2006, p. XX). She has analyzed brain responses to a variety of treatments for depression, including psychotherapy, medication, electroconvulsive therapy, and deep brain stimulation. According to Mayberg, "The best-replicated behavioral correlate of a resting state abnormality in depression is that of an inverse relationship between prefrontal activity and depression severity" (p. XX).

AUTHOR: Please provide reference for Mayberg 2006.
Also, please add page numbers for the two Mayberg quotes in previous paragraph.

Roffman et al. (2005) conducted a comprehensive review of neuroimaging studies in psychotherapy. In one of the reviewed studies (Ochsner et al. 2002), subjects were asked to reappraise mood cognitively. This technique resulted in improved mood, and the improvements correlated with increased metabolism in dorsolateral and dorsomedial prefrontal cortices, as well as decreased activity in the orbitofrontal cortex and amygdala.

In general, imaging studies of depressed patients have tended to show decreased activity in the dorsal prefrontal cortex (including the dorsolateral prefrontal cortex) and increased activity in ventral prefrontal regions (Roffman et al. 2005). Dorsal prefrontal areas tend to participate in cognitive circuits, whereas ventral prefrontal areas have significant links to emotional circuitry.

In addition to Goldapple et al.'s (2004) CBT results described above, studies comparing the treatment of depression with interpersonal psychotherapy and medication (paroxetine) have been reported. One such study (Brody et al. 2001) showed decreases in dorsal and ventral prefrontal activity in responders to interpersonal psychotherapy that were similar to those reported by Goldapple et al. (2004) with CBT. In contrast, however, Brody et al. (2001) also reported decreases in prefrontal metabolism in paroxetine responders.

AUTHOR: Previous paragraph, first sentence: Note change from "In addition to the CBT results described above." OK?

Roffman et al. (2005) also reviewed imaging studies of the treatment of obsessive-compulsive disorder with behavior therapy. In general, patients with symptomatic obsessive-compulsive disorder respond to either psychotherapy or medication by showing a reduction in caudate nucleus metabolism (especially on the right). This finding has been confirmed by several studies and is consistent with the theoretical conceptualization of obsessive-compulsive disorder as a disorder that affects thalamocorticostriatal circuitry.

Studies of the treatment of phobia with CBT and medication were also reviewed by Roffman et al. (2005). In one study (Furmark et al. 2002), individuals with social phobia were asked to read a speech about a personal experience to a small audience. At baseline, such patients exhibited activation of limbic regions, including the amygdala, the hippocampus, and the adjacent temporal cortex. After 8 weeks of treatment with either CBT or citalopram, the baseline pattern of limbic activation was greatly attenuated. CBT, but not citalopram, also resulted in decreased activation of the periaqueductal gray, an area involved in fear and defensive responses. Citalopram, but not CBT, also resulted in reduced activity of thalamic and ventral prefrontal cortex metabolism.

Functional neuroimaging of the psychotherapeutic process is in its infancy. As a result, there are currently no comprehensive models of psychotherapy's effects on the brain. Nevertheless, information is accumulating rapidly on the circuit-based changes in neural information processing that underlie psychotherapy's beneficial effects, as reviewed above.

Psychotherapy is clearly a top-down process. In other words, it relies on higher levels of communication, including verbal and emotional expressions, to access and modify the patient's neural circuitry. As the patient's brain processes the targeted communications of the therapist, dysfunctional representations and their emotional connections are modified. In this manner, the therapist is able to reshape the patient's internal representations and their subjective meaning, leading to more adaptive behavior.

AUTHOR: Please consider paring down the number of Key Points to 7–10 and adapting the extra material, which is excellent, in a Conclusion section, which has been included in most chapters in addition to Key Points. Thanks!

Key Points

- Psychiatric illness is associated with specific patterns of brain dysfunction, which are currently being defined with functional brain imaging.
- Successful psychotherapy brings about measurable changes in neurotransmission, which appear to be associated with its beneficial effects.
- As brain-based advances in the understanding and treatment of mental illness accumulate, it is important for psychotherapists to become conversant in basic neurobiology and to apply neurobiological knowledge to psychotherapeutic practice.
- Core psychotherapeutic concepts, such as engagement, self-awareness, pattern search, and behavioral change, can be tentatively associated with specific neural circuits that have been functionally defined.
- The following are some of the circuits that we believe to be of special interest to psychotherapists:
  - Mirror neuron circuits, first defined by Rizzolatti et al. (2001), which are groups of frontal and parietal neurons in the brains of primates that fire both during the execution of purposeful movements and during observation of other individuals performing similar actions; they are important in the attribution of meaning to the actions of others and in the development of empathy

- Circuits that contain basic representations of internal states and the visceral self, including representations in the brainstem and insula
- Risk–reward evaluation circuits with nodes in the amygdala, orbitofrontal cortex, cingulate gyrus, and nucleus accumbens
- Circuits that can generate discrete body states through autonomic and hormonal activation
- Memory circuits involving the hippocampus (explicit memory), dorsolateral prefrontal cortex (working memory), amygdala and orbitofrontal cortex (secondary rewards and punishers), and basal ganglia (implicit memory)
- Executive and evaluative circuits centered on the dorsolateral prefrontal cortex

- The Freudian concepts of ego, superego, and id can be functionally mapped to three thalamocorticostriatal circuits:
  - The *ego* as defined by Freud shares many functions with the cortical-subcortical circuit centered on the dorsolateral prefrontal cortex, including problem solving, working memory, self-direction, the ability to address novelty, and the use of language to guide behavior.
  - The *superego* as defined by Freud shares many functions with the cortical-subcortical circuit centered on the orbitofrontal cortex, including the ability to consider rules and potential consequences before acting, and to exert behavioral inhibition through the generation of aversive body states.
  - T*he id as* defined by Freud shares many functions with the cortical-subcortical circuit centered on the cingulate gyrus and nucleus accumbens, including the generation of motivational drive for the pursuit of pleasure. This circuit features prominently in addictive states.
- A concept called "neurobiological empathy" has been introduced. Knowing the neurobiological basis of a patient's behavioral complaints and sharing this knowledge with the patient can establish a concrete starting point for psychotherapeutic intervention, and can also validate the patient's subjective experience.
- Imaging studies of the successful treatment of a variety of psychiatric illnesses have appeared in the literature:
  - In depression, psychotherapy can alter the metabolic activity of the prefrontal cortex, hippocampus, and cingulate gyrus. Specific patterns of alteration have been variable across studies.
  - In obsessive-compulsive disorder, psychotherapy, like medication, has generally produced a reduction in caudate nucleus metabolism,

especially on the right.

- In specific phobia, psychotherapy has produced attenuation of metabolic activity in the amygdala, hippocampus, and periaqueductal gray.

- Psychotherapy is, by design, a top-down process. It relies on higher levels of communication, including verbal and emotional expressions, to access and modify a patient's neural circuitry. By producing beneficial changes in neurotransmission, psychotherapy can promote more adaptive patterns of behavior

References

Ahn H, Wampold BE: Where oh where are the specific ingredients? A meta-analysis of component studies in counseling and psychotherapy. J Couns Psychol 48:251–257, 2001

Anderson MC, Ochsner KN, Kuhl B, et al: Neural systems underlying the suppression of unwanted memories. Science 303:232–235, 2004

Barbas H, Saha S, Rempel-Clower N, et al: Serial pathways from primate prefrontal cortex to autonomic areas may influence emotional expression. BMC Neurosci 4:25–37, 2003

Bartels A, Zeki S: The neural basis of romantic love. Neuroreport 11:3829–3834, 2000

Bartels A, Zeki S: The neural correlates of maternal and romantic love. Neuroimage 21:1155–1166, 2004

Beitman BD, Soth AM: Activation of self-observation: a core process among the psychotherapies. Journal of Psychotherapy Integration 16:383–397, 2006

Beitman BD, Yue D: Learning Psychotherapy: A Time-Efficient, Research-Based, Outcome-Measured Psychotherapy Training Program, 4th Edition. New York, WW Norton, 2004

Beitman BD, Nair J, Viamontes GI: What is self-awareness? in Self-Awareness Deficits in Psychiatric Patients. Edited by Beitman BD, Nair J. New York, WW Norton, 2005a, pp 3–23

AUTHOR: Are both Beitman et al. 2005 references cited in text?

Beitman BD, Soth AM, Bumby NA: The future as an integrating force through the schools of psychotherapy, in Handbook of Psychotherapy Integration, 2nd Edition. Edited by Norcross J, Goldfried M. New York, Oxford University Press, 2005b, pp 65–83

Blanke O, Arzy S: The out-of-body experience: disturbed self-processing at the temporoparietal junction. Neuroscientist 11:16–24, 2005

Brody AL, Saxera S, Stoessel P, et al: Regional brain metabolic changes in patients with major depression treated with either paroxetine or interpersonal therapy: preliminary findings. Arch Gen Psychiatry 58:31–40, 2001

Burruss JW, Hurley RA, Taber KA, et al: Functional neuroanatomy of the frontal lobe circuits: Radiology 214:227–230, 2000

Bush G, Liu P, Posner MI: Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 214:227–230, 2000

Critchley HD, Mathias CJ, Josephs O, et al: Human cingulated cortex and autonomic control: converging neuroimaging and clinical evidence. Brain 126:1–14, 2003

Deikman AJ: The Observing Self. Boston, MA, Beacon, 1982

Etkin A, Pittenger C, Polan J, et al: Toward a neurobiology of psychotherapy: Basic science and clinical applications. J Neuropsychiatry Clin Neurosci 17:145–158, 2005

Ferris CF, Snowdon CT, King JA, et al: Activation of neural pathways associated with sexual arousal in non-human primates. J Magn Reson Imaging 19:168–175, 2004

Flashman LA: Disorders of insight, self-awareness, and attribution in schizophrenia, in Self-Awareness Deficits in Psychiatric Patients. Edited by Beitman BD, Nair J. New York, WW Norton, 2005, pp 129–158

Fonagy P: Psychotherapy: attachment and the brain. Paper presented at the annual meeting of the Society for Psychotherapy Research, Rome, Italy, June 2004

Frith CD, Frith U: Interacting minds: biological basis. Science 286:1692–1695, 1999

Furmark T, Tillfors M, Marteindottir I, et al: Common changes in cerebral blood flow in patients with social phobia treated with citalopram or cognitive-behavioral therapy. Arch Gen Psychiatry 59:425–433, 2002

Gusnard DA, Akbudak E, Sulman GL, et al: Medial prefrontal cortex and self referential mental activity: relation to a default mode of brain function. Proc Natl Acad Sci USA 98:4259–4264, 2001

Haxby JV, Gobini MI, Furey ML, et al: Distributed and overlapping representation of faces and objects in the ventral temporal lobe. Science 293:2425–2430, 2001

Johnson SC, Baxter LC, Wilder LS, et al: Neural correlates of self-reflection. Brain 125:1808–1814, 2002

Kemperman G: Why new neurons? Possible functions for adult hippocampal neurogenesis. J Neurosci 22:635–638, 2002

Krupnick JL, Sotsky SM, Simmens S, et al: The role of the therapeutic alliance in psychotherapy and pharmacotherapy outcome: findings in the National Institute of Mental Health Treatment of Depression Collaborative Research Program. J Consult Clin Psychol 64:532–539, 1996

Lambert MJ, Bergin AE: The effectiveness of psychotherapy, in Handbook of Psychotherapy and Behavior Change, 4th Edition. Edited by Bergin AE, Garfield SL. New York, Wiley, 1994, pp 143–199

Lambert MJ, Shapiro DA, Bergin AE: Evaluation of therapeutic outcomes and processes, in Handbook of Psychotherapy and Behavior Change, 3rd Edition. Edited by Garfield SL, Bergin AE. New York, Wiley, 1986, pp 157–212

Main M: Metacognitive knowledge, metacognitive monitoring, and singular (coherent) vs (incoherent) models of attachment: findings and directions for future research, in Attachment Across the Life Cycle. Edited by Harris P, Stevenson-Hinde J, Parkes C. New York, Routledge & Kegan Paul, 1991, pp 127–159

Mayberg HS, Liotti M, Brannon SK, et al: Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. Am J Psychiatry 156:675–683, 1999

Mega MS, Cummings JL: Frontal subcortical circuits: anatomy and function, in The Frontal Lobes and Neuropsychiatric Illness. Edited by Salloway SP, Mallory PF, Duffy JD. Washington, DC, American Psychiatric Press, 2001, pp 15–32

Mesulam M: From sensation to cognition. Brain 121:1013–1052, 1998

Newberg A, d'Aquili E, Rause V: Brain Machinery: Why God Won't Go Away. New York, Ballantine Books, 2002

Norcross JC: Psychotherapy Relationships That Work: Therapists' Contributions and Responsiveness to Patients. New York, Oxford University Press, 2002

AUTHOR: Please cite Norcross 2002 in chapter or delete the reference.

Ochsner KN, Bunge SA, Gross JJ, et al: Rethinking feelings: an FMRI study of the cognitive regulation of emotion. J Cogn Neurosci 14:1215–1222, 2002

Pally R: Non-conscious prediction and a role for consciousness in correcting prediction errors. Cortex 41:643–662, 2005

Phillips ML, Drevets WS, Rauch SL, et al: Neurobiology of emotion perception I: the neural basis of normal emotion perception. Biol Psychiatry 54:504–514, 2003

Prochaska JO, Norcross JC: Systems of Psychotherapy: A Transtheoretical Analysis, 5th Edition. Pacific Grove, CA, Brooks/Cole, 2003

Rizzolatti G, Fogassi L, Gallese V: Neurophysiological mechanisms underlying the understanding and imitation of action. Nat Rev Neurosci 2:661–670, 2001

Roffman JL, Marci CD, Glick DM, et al: Neuroimaging and the functional anatomy of psychotherapy. Psychol Med 35:1–15, 2005

Rolls ET: The Brain and Emotion. Oxford, England, Oxford University Press, 1999

Rolls ET: Hippocampo-cortical and cortico-cortical back projections. Hippocampus 10:380–388, 2000

AUTHOR: Please cite Rolls 2000 in text or delete reference. (Rolls 2005 is cited repeatedly–should that date be changed?)

Siegel DJ: An interpersonal neurobiology approach to psychotherapy. Psychiatr Ann 36:248–256, 2006

Stuss DT, Benson DF: Emotional concomitants of psychotherapy, in Advances in Neuropsychology and Behavioral Neurology. Edited by Heilman KM, Staz P. New York, Guilford, 1983, pp 11–40

Tanaka K: Columns for complex visual object features in the inferotemporal cortex: clustering of cells with similar but slightly different stimulus selectivities. Cereb Cortex 13:90–99, 2003

Teicher MH, Andersen SL, Polcari A, et al: Developmental neurobiology of childhood stress and trauma. Psychiatr Clin North Am 25:397–426, 2002

Viamontes GI, Beitman BD: Neural substrates of psychotherapeutic change, Part I: the default brain. Psychiatr Ann 36:225–237, 2006a

AUTHOR: Are both Viamontes & Beitman 2006 references cited in text?

Viamontes GI, Beitman BD: Neural substrates of psychotherapeutic change, Part II: beyond default mode. Psychiatr Ann 36:239–246, 2006b

Viamontes GI, Beitman BD, Viamontes CT, et al: Neural circuits for self-awareness: evolutionary origins and implementation in the human brain, in Self-Awareness Deficits in Psychiatric Patients. Edited by Beitman BD, Nair J. New York, WW Norton, 2005, pp 24–111

Wampold BE: The Great Psychotherapy Debate: Models, Methods, and Findings. Mahwah, NJ, Erlbaum, 2001

Wheeler MA, Stuss DT, Tulving E: Toward a theory of episodic memory: the frontal lobes and autonoetic consciousness. Psychol Bull 121:331–354, 1997

Wolfe BE, Goldfried MR: Research on psychotherapy integration: recommendations and conclusions from an NIMH workshop. J Consult Clin Psychol 56:448–451, 1988

Suggested Readings

Beitman BD, Yue D: Learning Psychotherapy: A Time-Efficient, Research-Based, Outcome-Measured Psychotherapy Training Program, 4th Edition. New York, WW Norton, 2004

Mega MS, Cummings JL: Frontal subcortical circuits: anatomy and function, in The Frontal Lobes and Neuropsychiatric Illness. Edited by Salloway SP, Mallory PF, Duffy JD. Washington, DC, American Psychiatric Press, 2001, pp 15–32

Mesulam M: From sensation to cognition. Brain 121:1013–1052, 1998

Rizzolatti G, Fogassi L, Gallese V: Neurophysiological mechanisms underlying the understanding and imitation of action. Nat Rev Neurosci 2:661–670, 2001

Roffman JL, Marci CD, Glick DM, et al: Neuroimaging and the functional anatomy of psychotherapy. Psychol Med 35:1–15, 2005

Rolls ET: The Brain and Emotion. Oxford, England, Oxford University Press, 1999

Viamontes GI, Beitman BD: Neural substrates of psychotherapeutic change, Part I: the default brain. Psychiatric Annals 36:225–237, 2006

Viamontes GI, Beitman BD: Neural substrates of psychotherapeutic change, Part II: beyond default mode. Psychiatr Ann 36:239–246, 2006

Viamontes GI, Beitman BD, Viamontes CT, et al: Neural circuits for self-awareness: evolutionary origins and implementation in the human brain, in Self-Awareness Deficits in Psychiatric Patients. Edited by Beitman BD, Nair J. New York, WW Norton, 2005, pp 24–111