THIS ISSUE:

The Neurobiology of Psychotherapy

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

The organizational hierarchy of the brain can be compared to a set of matryoshka, or nested Russian figures, each fitted precisely inside the other and hiding what awaits inside (see page 273). As each figure is uncovered, it invites further discovery until, at the very center, the smallest is revealed.

At this point, the dynamic nature of neural phenomena dictates a departure from our metaphor. Unlike a set of matryoshka, the "innermost" neural structures actually generate the outer reaches of the brain's functional sphere, namely behavior. Human actions are in fact direct "projections" of the neural mechanisms that cause them. In the recent past, it was not possible to define the nested structural and functional hierarchies that drive the progression from stimulus perception to behavior. Consequently, psychiatrists, psychologists, and other mental health professionals are trained primarily in the evaluation and management of the outer reaches of the brain's functional cascade. As a discipline, we have been limited historically to dealing with projections whose physical causes we can only guess. Advances in brain imaging and neurobiology, which provide the theoretical foundation for this issue of *Psychiatric Annals,* have made it possible to go deeper.

Knowledge of the brain by necessity constrains psychotherapeutic theorizing.[1] "Proof" of any theory's mental processes must be generated by correlating its higher order constructs with underlying brain phenomena. In the future, building on the explosion of findings in neurobiology, psychotherapists will be able to visualize the brain processes that underlie both psychopathology and psychotherapeutic change. Armed with this knowledge, psychotherapists will be able to define their patients' problems more precisely and focus their interventions more effectively.

A pragmatic look at the psychotherapeutic interaction suggests that it is a relationship between two brains and their bodies, with significant exchange of auditory, visual and other sensory inputs. These inputs convey cognitive and emotional information at both conscious and subconscious levels. Progress in psychotherapy depends on the ability of the therapist to analyze the totality of the patient's communications and devise effective strategies that will improve the patient's subjective sense of well-being and his or her capacity for behavioral adaptation.

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From a practical perspective, psychotherapists are trained to diagnose patients in a manner that emphasizes pathology rather than strengths. As much as therapists would like to think that they catalyze the emergence of new capabilities in their patients, more often than not, adaptive improvements are based on the activation of pre-existing but underused strengths. The National Institute of Mental Health collaborative study of depression found that patients with strong interpersonal skills responded better to interpersonal psychotherapy, while those who emphasized cognition responded better to cognitive therapy.[2] Therapists can sometimes help patients develop adaptive behavioral patterns de novo, but more frequently they assist patients in disinhibiting the expression of adaptive patterns that have already been developed but are rarely implemented.[3] These patterns, which are critical to both maladaptive behavior and psychotherapeutic change, are stored as synaptic connections within the brain.

Imaging research and advances in neurobiology are defining neural function in health and disease, and this work suggests three important reasons why psychotherapists should know the brain. First, a basic understanding of the brain is essential for approaching the current psychiatric literature. Second, many of the phenomena encountered in psychotherapy are being clarified through definition of their neural origins. Third, the next wave of progress in psychotherapy will be based on neurobiology.

Knowledge of the brain encompasses many levels. Most psychotherapists have at least a rudimentary knowledge of synapses, as the action of antidepressants and other psychotropic drugs has focused significant attention on this level. At or below the synapse are receptors, connectivity, signal transduction, and gene action. These biological processes and structures define exciting scientific fields whose concepts have relevance to psychotherapy, even though their levels of order are far removed from the behavioral phenomena that psychotherapists address. Much closer to behavior and essential to progress in psychotherapy is the information on functional neural circuits that is accumulating as a result of brain imaging research. Many of the concepts presented in this collection of articles are directly supported by such work.

Understanding brain function requires not only a knowledge of anatomy, neurobiology, and functional circuits but also familiarity with basic biological principles such as evolution and energy conservation. The human brain, with all its refinements, is built on a core of basic functionalities shared with lower species. Human brains can ask more questions, make better predictions, and drive more complex behaviors than the brains of mice; however, we are no more successful as a species because of this. Power-hungry brains such as those of humans are effective machines for obtaining energy from the environment, although the advantages of this capability depend strictly on external circumstances.

For example, in advanced societies, humans have continuous access to food, and the energy-acquisition mechanisms designed to ensure survival tend to drive weight gain instead. In adverse environments, such as situations of chronic abuse, war, and other types of unrelenting stress, the human brain simplifies. Stress hormones, or glucocorticoids, increase appetite and food-seeking behavior, and curtail many nonessential energy-using activities.[4] Adaptations to chronic stress include the simplification of brain connectivity and the suppression of neurogenesis and immune function.[4] Simplification of the brain can save energy and enhance response efficiency, but at the cost of sophisticated processing. The adaptations that help to preserve a person's life during war, for example, can be very maladaptive after a return to peaceful conditions. An important goal of psychotherapy is to optimize the brain's functional capacity within the specific context in which the brain must operate.

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IN THIS ISSUE

This issue provides a variety of resources for psychotherapists who are interested in exploring neurobiology. The first two articles provide an introduction to the basic neural substrates that drive behavior and support psychotherapeutic change. The articles describe the neural circuits that facilitate such processes as the generation of internal representations, memory, emotion, motivation, and cognition. The contribution of prefrontal circuitry to adaptive behavior and the relevance of these critical neural elements to psychotherapy are emphasized. The functional similarities of prefrontal circuits to Freud's concepts of ego, superego, and id are highlighted, and the neurobiology of unconscious mental processes is addressed.

The article by Dr. Siegel on the relevance of interpersonal neurobiology to psychotherapy highlights the value of creating a scientific infrastructure for the psychotherapeutic process. Siegel defines nine domains of integration that he believes are critical to well-being. He outlines some of the neurobiological processes that promote integration, including the "mirror neuron" system. Mirror neurons facilitate social communication by making it possible to understand the significance of the actions and expressions of others through representation, or "modeling," in the perceiver's own brain. By simple extension, mirror neurons can be hypothesized to provide "... the neural basis of mental attunement within and between ... patient and therapist." Siegel emphasizes the role of the psychotherapist in nurturing an integrative process that, once started, can have beneficial repercussions throughout the patient's life span.

Dr. Mayberg provides an integrative synthesis of her groundbreaking work in neuroimaging, as she defines the neural circuitry of depression and how that circuitry can be modulated by psychotherapy, psychotropic medications, and electrical stimulation. Depression is "conceptualized as a systems-level disorder affecting select cortical, subcortical, and limbic regions and their related neurotransmitter and molecular mediators." A depressive episode is the result of failed regulation of these circuits because of "cognitive, emotional, or somatic stress" in the context of such predisposing factors as "genetic vulnerability, affective temperament, and developmental insults."

Mayberg defines the major symptomatic manifestations of depression, namely motoric, mood, cognitive, and circadian disturbances, in terms of "working" compartments of associated neural elements that have been identified experimentally. According to Mayberg, the most robust and replicable findings in the functional imaging of depression have included decreased frontal lobe function (dorsolateral, orbital frontal and medial frontal cortices), as well as activity changes in the anterior dorsal cingulate. The best-replicated finding involves an inverse relationship between prefrontal activity and depression severity.

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The work of Mayberg and others has defined an array of neural targets for antidepressant treatments, including cortical, limbic-paralimbic and subcortical regions. The best replicated finding with respect to response to antidepressant treatments, including psychotherapy, antidepressants, electroconvulsive therapy, transcranial magnetic stimulation, sleep deprivation, ablative surgery, and deep brain stimulation, is normalization of frontal cortical abnormalities. Mayberg's own studies of successful pharmacotherapy using selective serotonin reuptake inhibitors have demonstrated increases in frontal, parietal, brainstem and posterior cingulate activity with treatment, with concomitant decreases in striatal, thalamic, hippocampal, and subgenual cingulate activity.

Mayberg also describes a variety of response predictors, including the fact that increased pretreatment activity in the subgenual cingulate predicts a positive response to medication and sleep deprivation. A predominantly cortical pattern of pretreatment abnormalities was found in patients who responded to cognitive behavioral therapy. Responders to selective serotonin reuptake inhibitors showed a limbic-cortical pattern, and treatment-resistant patients demonstrated a limbic-subcortical pattern. Deep brain stimulation of the subgenual cingulate in treatment-resistant patients relieved depressive symptoms and stabilized the entire network of depression-relevant circuits.

Next, we present a discussion of the core psychotherapeutic processes of engagement, self-observation, and pattern search (Beitman et al., see page 272). All successful psychotherapeutic systems contain these basic elements. The neural circuits that support engagement are important to social interactions in general. Mirror neurons are a key factor in the formation of a therapeutic alliance, as the patient wonders whether the therapist can understand his or her problems, and the therapist attempts to model the patient's brain states. The proper functioning of mirror neurons provides a sense of mutual understanding as psychotherapy progresses.

Self-observation is critical to the achievement of psychotherapeutic change, as it reveals the baseline behaviors that must be addressed, and signals whether progress is being made. The dorsolateral prefrontal cortex, which is a master integrator that also controls working memory, is essential for high-level self-observation. In addition, both synaptic and conscious access to the internal maps that represent the many aspects of the self are essential for the development of self-knowledge.

Pattern search is the final psychotherapeutic element discussed. Maladaptive behavior often results from faulty pattern recognition, including overgeneralization and inappropriate pattern completion. Simple recognition of inputs that have become associated with reward or punishment is mediated by the amygdala and orbitofrontal cortex, while the storage of more complex patterns, including verbal descriptions, is mediated by the hippocampus. The probability of a successful outcome in psychotherapy can be maximized through attention to the basic processes of engagement, self-observation, and pattern search.

Dr. Gabbard continues the discussion of core psychotherapeutic processes with a discussion of transference mechanisms in terms of neural networks. Transferences can be best understood as the activation of pre-existing synaptic patterns by the representations evoked during the psychotherapeutic process. "When something evokes a neural pattern that is similar to the configuration representing a previous encounter of a person, event, or feeling state, recognition occurs, a process known as 'pattern matching.'" Transference reactions are elicited as elements related to the psychotherapeutic process that activate pre-defined synaptic patterns that trigger emotions as well as cognitive expectations. Stimuli need not be conscious to trigger transference reactions. Gabbard discusses research that suggests amygdalar hyperactivity may underlie the exaggerated interpersonal responses of patients with borderline personality disorder by increasing vigilance and reactivity to signs of emotional expression in others.

Gabbard also explains how advances in cognitive neuroscience have made the concept of the "blank screen" analyst untenable, because "anonymity" is cognitively impossible. In addition, neuroscience suggests that analysis can be viewed, in part, "as a new attachment relationship that can be useful for many patients in restructuring attachment-related implicit memory." Neuroscience has provided solid scientific underpinnings for understanding how transference arises within psychotherapy and influences its outcome. It has also begun to clarify the neural mechanisms by which a significant proportion of mental life is unconscious.

SUMMARY

The work of Mayberg and others in the functional imaging of psychiatric disorders and their treatment is elucidating the biological substrates that underlie psychiatric interventions, and promises to revolutionize the future of psychiatry. With the emphasis on brain circuits as a common foundation for psychotherapeutic change, the idea of separate schools begins to give way to a new model of psychotherapy. For example, instead of simply thinking of transference as a strictly psychoanalytic concept, therapists can be confident that the emotions, cognitions and behaviors displayed in front of them have been programmed by a combination of genes and experience. Consequently, the signs and symptoms that the therapist observes are objective manifestations of the internal processing patterns that shape the patient's responses to the neural representations which the therapeutic relationship elicits.

The specific internal patterns whose maladaptive consequences have brought the patient to treatment are usually the result of many years of data processing by hippocampal-cortical circuits. Consequently, they can require significant time and effort to change. The psychotherapeutic process is an effective, structured, and neurobiologically definable method for decreasing the probability of the reactivation of old, maladaptive neural patterns, and catalyzing the creation and maintenance of a new set of adaptive synaptic patterns by which a patient can make sense of the world and respond effectively to its challenges.

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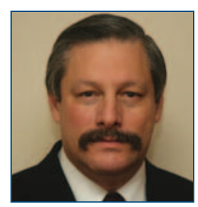
about the guest editors

Bernard D. Beitman, MD, is professor and chair of the Department of Psychiatry at the University of Missouri – Columbia. He is the author of the award winning *Learning Psychotherapy*, now in its second edition, *The Structure of Individual*, and *Integrating Psychotherapy and Pharmacotherapy*, and co-editor of *Self-Awareness Deficits in Psychiatric Patients*.

George I. Viamontes, MD, PhD, is regional medical director, United Behavioral Health Inc., St. Louis, MO, and assistant clinical professor, Department of Psychiatry, University of Missouri – Columbia. Dr. Viamontes was born in Cuba and came to the United States at age 11. He has a bachelor of science degree in biology from the University of Notre Dame, South Bend, IN, and a PhD in biology from Washington University, St. Louis. After he received his doctorate, he completed a fellowship in immunogenetics at the Sloan-Kettering Institute in New York, NY. He later obtained his medical degree from St. Louis University, where he also completed his residency in psychiatry.



Dr. Viamontes is currently preparing an illustrated book on the neurobiology of the self, to be published next year. His research interests include neural network predictive modeling for the identification of high-risk patients.