



## The Neurobiology of Psychotherapy – Clinical Insights

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### ABSTRACT

*Psychotherapy has existed as a therapeutic modality since over a century. The present review aims to look at a neurobiological basis for psychotherapy and therapist patient interactions and posit a biological theory of the mechanism of psychotherapy. Various neuroimaging techniques in the last decade have vastly improved our knowledge of brain function and dysfunction in the last decade. Various structures of the brain like the dorsolateral prefrontal cortex, the orbitofrontal cortex, the insula, the anterior cingulate cortex and the amygdala play a role in key psychotherapeutic processes. An emerging neurobiology of empathy from social affective neuroscience has greatly improved our understanding of therapist patient relationship and is explored. The role of mirror neurons in psychotherapy is highlighted and the need for further understanding in the neurobiology of psychotherapy is stressed.*

**KEYWORDS:** Neurobiology, psychotherapy

### INTRODUCTION

Successful psychotherapy is correlated with discrete brain changes because psychotherapy, like medication, ultimately targets neuro-anatomical 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 (1). Many psychotherapists challenge the need to learn neurobiology, claiming that knowledge of psychotherapeutic theory and technique is sufficient for successful outcomes. The present article thus tries to explore some of the brain correlates of classical psychotherapeutic concepts.

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 non-verbal behaviors can physically influence the brain of the other (2).

### THE NEED TO FORMULATE A NEUROBIOLOGY OF PSYCHOTHERAPY

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 non-psychotherapists to grasp more firmly the unique and helpful mechanisms of psychotherapeutic action (3). Patients 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. 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. 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. 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 (5).

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 (6).

### Neural Correlates of Basic Psychotherapeutic Processes

Psychotherapy has a basic structure defined by a set of core processes, 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 (7). 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. Research has shown that a critical neural processing step must occur prior to the transformation of observation to inference. 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 (8).

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 (9). 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. Risk-detection circuitry is centered in the amygdala and orbitofrontal cortex (10). In addition, the amygdala and orbitofrontal cortex contain a record of the unpleasant experiences encountered throughout the person's lifestyle.

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. 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 (DLPFC), which represents current cognitive contents, and the cingulate gyrus (CG), which generates autonomic tone consistent with those contents (11). 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 therapist

tic process can proceed. Eventually, previously neutral stimuli related to the therapist may become linked to experiences of reward in the patient's brain. This process is also believed to involve synaptic modifications in the amygdala and orbitofrontal cortex, in a manner similar to what was described for unpleasant experiences (12).

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 (13), as well as the orbitofrontal cortex, fusiform gyrus, superior temporal sulcus, and insula (14). Experimental evidence suggests that secure attachment, as extrapolated from imaging studies of romantic love and mother-child affection (15), is associated with reduction in amygdala firing (lessening anxiety) and increases in nucleus accumbens activity (possibly related to enhanced reward representations), and lessening of orbitofrontal firing (possibly reducing inhibitions) (16).

Observation can produce knowledge about many internal stages, such as intentions, expectations, feelings, thoughts, behaviors, and perceived effect on others. Observation of the self leads to the ability to distinguish inner from outer reality, pretend from real modes of functioning, and intrapersonal mental and emotional processes from interpersonal communications (17). 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. One must be conscious in order to be aware (18).

Awareness implies consciousness of contents, 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 (19). The ability to observe the content of one's own mind depends on the healthy functioning of many different parts of the brain. 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 (20).

Cognitive considerations are generated in the lateral prefrontal cortices (LPFC), 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 (MPFC) is associated with representations of mental states of the self and is consistently activated during self-reflective thoughts (21). The top of this functioning pyramid of self-awareness appears to be the DLPFC, which potentiates executive function and working memory and is capable of integrating the full range of sensory, affective and memory data (22).

The ability to generate and coherent self with temporal continuity depends on the power of the DLPFC to project individuals both backward and forward in time. 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 the past, present, and future (23). As part of its integrating function, the DLPFC receives inputs from a variety of internal monitors. The insula, for example, monitors visceral sensations as well as emotional body states, whereas the anterior cingulate gyrus can focus attention for the process of self-monitoring. 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 (24).

The current interest in the study of mindfulness based psychotherapies 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 (25).

A major task of the central nervous system is to organize the linkage between internal representations of sensory information and adaptive responses. 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, production, and energy acquisition and conservation (26).

Effective psychotherapists induce patterns from nonverbal cues, key reported events transference behaviors, and counter transference reactions. 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 (27). 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 (28).

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 (29). 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 patients are identified as fitting its characteristic constellation of symptoms (30).

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, 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 (31). 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 CA3 (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 (32).

### Brain Correlates of Classical Psychotherapeutic Concepts

Sigmund Freud (1923) 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 conceptualization. The constant tension between unconscious appetitive urges and higher control that characterizes Freud's visualization has a definable origin in neural circuitry (33).

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 (34).

### THE ROLE OF THE PREFRONTAL CORTEX

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 through the integration of internal and external circumstances, memory, applicable rules, and projected consequences (35). 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. The circuits are somato-topically mapped and define numerous "channels" through each circuit component (36).

The common functional element of all three circuits is modulation of the thalamus. Thalamic circuitry is tonically inhibited by the globus pallidus. 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 (37).

### THE ROLE OF THE ANTERIOR CINGULATE CORTEX

The anterior cingulate circuits, 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. 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 (38). 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 and is an important component of reward circuitry (39).

The cingulate receives cognitive data from the DLPFC and facilitates emotional cognitive integration by generating emotional states appropriate to cognitive contents. Conversely, it conveys emotional information to the DLPFC 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 (40). 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. Cingulate gyrus and nucleus accumbens circuitry figures prominently in addictive state. 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 (41).

### THE ROLE OF THE ORBITOFRONTAL CORTEX AND THE AMYGDALA

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 give sensory cortices, as well as from the insula. This information is integrated into comprehensive view of both external and internal milieu. 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 (42).

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 (43). The orbitofrontal cortex can suppress autonomic centers though stimulation of the amygdala's central nucleus. Activation of this nucleus causes autonomic inhibition. The opposite result, autonomic activation, can be achieved by the orbitofrontal cortex though stimulation of the intercalated cell masses of the amygdala, which diminished the default inhibition of hypothalamic nuclei by the amygdala's central nucleus (44). 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. The orbitofrontal cortex probably evolved to prevent injury in the pursuit of reward and to facilitate behavioral restraint by animals at lower levels of the social hierarchy. 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 (45).

### THE ROLE OF THE DORSOLATERAL PREFRONTAL CORTEX

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. The DLPFC, like the orbitofrontal cortex, receives sensory inputs, although these are primarily from visual, auditory and somatosensory cortices. Sensory information is less integrated in the dorsolateral cortex than in the orbitofrontal cortex, possibly facilitating more detailed analysis of specific stimuli (46). Individuals with damage to the DLPFC 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 (47).

The DLPFC is the entry point for verbal psychotherapeutic interventions, because it is essential for advanced reasoning and for modulating behavior through the use of words. Increases in limbic-paralimbic blood flow in the subgenual cingulate (Brodman area 25) and anterior insula in individuals experiencing sadness have been demonstrated. Sad people also demonstrated decreases in blood flow to the right DLPFC an inferior parietal cortex. These imbalances can be corrected through psychotherapy (48). 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. Imaging studies have also shown that the DLPFC, possibly in conjunction with the cingulate gyrus, plays a key role in the suppression of unwanted memories (49).

The manifestations of the id are very much a function of the 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 (50). The functions of the superego are implemented through orbitofrontal-amygdala circuitry. This functional network evolved to temper the pursuit of pleasure with considerations of context and risk. Orbitofrontal-amygdala 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 (51).

The prefrontal circuits described above, which support adaptive behavior by making it possible to consider many variable before responding to a stimulus, are important targets for the psychotherapist. The dorsolateral prefrontal circuit 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 (52).

### THE NEUROBIOLOGY OF 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 mind of patients within his or her own. More specifically, when the emotions and feelings generate a positive connection based on shared emotional experiences, the result is the subset of counter-transference phenomena that we call empathy (53). 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 has demonstrated a phobia-specific distortion of the cause-effect matrix that defines responses to environmental objects (54).

During conscious identification of the feared object, phobic individuals showed activation of left and right amygdala, 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 amygdala 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 (55).

#### **THE ROLE OF MIRROR NEURON SYSTEMS IN PSYCHOTHERAPY**

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. Mirror neurons were originally discovered in the brains of macaque monkeys. 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 is defined in terms of their functional significance to the individuals. To encode this in the brain, some of the circuits involved in potential use of the objects or movements 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 (56). Mirror neurons in humans are located in two interconnected brain regions i.e., the pars opercularis of the inferior frontal gyrus (within Broca's area) in the frontal lobe and the anterior area of the inferior parietal lobe. Fronto-parietal 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. 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 (57).

Mirror neurons also seem to be part of a system for understanding the intentions and emotional experiences of others. The system includes the following viz. the superior temporal cortex, which encodes visual description of observed action, the posterior parietal mirror neurons, which encode the kinesthetics of the action's movement sequence, the inferior frontal mirror neurons, which encode perceived goal of the action and the 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. The final point involves the limbic circuitry, including the amygdala, which can respond emotionally to the perceived goals (58-59).

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. 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 activa-

tion to the degree that this might be possible, therefore optimizing the internal processes that lead to self-and other awareness (60).

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 (61). Mirror neuron systems suggest an explanation of how a therapist's empathic resonance can affect a patient. Successful psychotherapy probably involves repeated mirroring 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 (62).

#### **FUNCTIONAL BRAIN IMAGING IN UNDERSTANDING THE NEUROBIOLOGY OF PSYCHOTHERAPY**

The brain encodes experience by altering neuronal connections, and prepares to meet perceived environmental challenges by modulation 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 (63). Studies have 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. In this study, responders to CBT showed significant increases in hippocampal and dorsal cingulate (Brodmann area 24) metabolism, as well as decreases in frontal cortex metabolism in dorsal (brodmann area 9, 46), ventral (Brodmann area 47,11), and medial (Brodmann area 9, 10,11) regions. In contrast, responders to paroxetine showed increases in prefrontal metabolism, along with decreases in hippocampal and subgenual cingulate metabolism (64).

Successful forgetting has been 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 (65). Researchers have conducted a comprehensive review of neuroimaging studies in psychotherapy. In one of the reviewed studies, 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 (66). In general, imaging studies of depressed patients have ended to show decreased activity in the dorsal prefrontal cortex (including the DLPFC) and increased activity in ventral prefrontal regions. Dorsal prefrontal areas tend to participate in cognitive circuits, whereas ventral prefrontal areas have significant links to emotional circuitry (67).

Researchers have 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 thalamocortico-striatal circuitry (68). 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 validate the patient's subjective experience (69). A scientific framework for psychotherapy is currently being de-

veloped, led by functional imaging studies of the successful treatment of a variety of psychiatric illnesses. 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 (70). In obsessive-compulsive disorder, psychotherapy, like medication, has generally produced a reduction in caudate nucleus metabolism, especially on the right (71). In specific phobia, psychotherapy has produced attenuation of metabolic activity in the amygdala, hippocampus, and periaqueductal gray (72).

## CONCLUSIONS

There have been studies on the neurobiology of various psychiatric disorders and with the advent of the imaging techniques like the fMRI

and SPECT studies, many more would follow. It is important that while we improve our knowledge of neurobiology, we also look at neurobiology and changes that interventions induce. This is where a need to understand completely the neurobiology of psychotherapy comes into play. Psychotherapy is a therapeutic technique that works and leads to improvement in psychiatric symptoms. It also has neurobiological ramifications and does not only act superficially or psychologically. Thus there is a felt need to further investigate and probe in this area.

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