### **REVIEW ARTICLE (INVITED)**

# **Rebuilding the brain with psychotherapy**

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# ABSTRACT

Brain has been the most fascinating and mysterious organ of the human body. Researchers have tried to explore into each and every function of different parts of the human brain linking it up with various mental and neural processes, some of which are phylogenetically shared and many are unshared. It has been hypothesized that brain is built during development and can be rebuilt during psychotherapy. Recent research in neuroscience of socioemotional cognition, developmental neuroscience, coupled with advances in investigative techniques of brain functions has provided tremendous opportunities for the study of brain and the mind. In this article, in the initial part, we have tried to explain the developmental processes involved in building of the human brain and what changes occur when an individual develops a psychiatric disorder. Later on, we have tried to postulate from different researches available that how psychotherapy can bring about a change in the neural mechanisms of the brain producing long-lasting effects. Several changes in the neural architecture of the brain occur during the process of psychotherapy. Further, we would like to elaborate on the hypothesis based on available literature that if psychiatric disorders can debuild the brain, then psychotherapy can help in rebuilding it again.

**Key words:** Brain, neuroscience, psychiatric disorders, psychotherapy

#### **INTRODUCTION**

Brain is the most complex and mysterious organ in the human body. Development of brain follows two interacting processes: (1) evolutionary influences carried through organizations and functioning of nervous system within a predetermined developmental timetable and (2) formation of neural architecture within the context of the environmental experience during evolution. There is tremendous increase in the size of neocortex in comparison to medulla size in *Homo sapiens* during evolution. Development of speech and language, self-awareness, and conscious thought

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represents an evolutionary leap in the development and potential of human brain. Mind comprises mental process that arises through the functioning brain. Thus, mind is a product of the working brain and all mental processes (such as memory, cognition, learning, emotions, behavior, love, and empathy) have a neural basis.

Historically, mental processes were studied by psychologists and brain and nervous system by neurologists. As psychotherapy tackles the mind and mental processes, it is prudent to believe that psychotherapy can influence neural architecture. Freud thought that talking cure could alter neural structures. Psychotherapy and neurosciences for almost one century developed as two independent parallel disciplines antithetical to one another. It is only recently that the two have started to converge, leading to emergence

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of a newer paradigm. Integration of psychotherapy and neuroscience has gained momentum only in the last two decades. Historically, neurologists concerned themselves with the study of the brain and psychologists were studying the mind and there was no meeting ground for the two. They used their own methods of study and a different language. Freud was a neurologist who wanted to understand the mind but could not find the principles or mechanisms or the methods to study mind–brain relationship. Hence, he changed the language and metaphor of his studies to psychodynamics and psychoanalysis.

Brain development, though under the influence of genetic programming through centuries of evolution, occurs as a result of environmental influences comprising interpersonal and social experiences and learning. Neural architecture is shaped and sculpted by encoding of the environmental experiences leading to the development of a unique human being, each one different from another in their personality and mental makeup.

#### THE TRIUNE BRAIN

Based on phylogenetic evolutionary theory, MacLean gave a model of the "Triune Brain" linking the evolutionary connection of human brain with lower animals.<sup>[1]</sup> According to him, there is the inner core, i.e., "reptilian brain" responsible for the activation, arousal, homeostasis, and reproduction functions. This is surrounded by the "paleomammalian brain" or the limbic system which is involved in learning, memory, and emotions. Then, there is the "neomammalian brain" comprising neocortex and corpus callosum that subserve the conscious thought and self-awareness. These systems of the brain are interconnected both vertically and horizontally but do not necessarily work in synchrony. Primitive brain is present at birth, whereas neocortical development is last to occur and is not complete until 20-25 years of age. Most of our interpersonal learning occurs in infancy and early childhood when the primitive brain is in command and higher brain is not yet developed. MacLean's description of nonverbal reptilian and paleo-mammalian brain influences the processing in the neomammalian brain unconsciously and serves as a neurological paradigm for Freud's unconscious and conscious brain mechanisms.

Brain is not a predetermined or unchanging organ; rather, it is the organ of adaptation; it adapts to the demands/characteristics of the environment. Developmental neuroscience helps us understand the process of how the brain is built and shaped by early experiences and how psychotherapy creates an interpersonal matrix capable of rebuilding it.<sup>[2,3]</sup>

#### THE FIVE PRINCIPLES OF KANDEL

Kandel, the famous American neuropsychiatrist and the recipient of the 2000 Nobel Prize in physiology/medicine for

his research on the physiological basis of memory storage in neurons, had laid down the basic foundations of neural basis of mental functions. He gave five main principles which have formed the backbone of our understanding of neurosciences in psychotherapy.<sup>[4]</sup> These are:

- All mental processes are neural, i.e., all mental processes, even the most complex psychological processes, derive from operations of the brain
- Genes and their proteins products determine neural connections, i.e., genes and their protein products are important determinants of the pattern of interconnections between neurons in the brain and the details of their functioning
- Experience alters gene expression, i.e., epigenetic influences alter the developmental trajectories. Altered genes do not, by themselves, explain all of the variances of a given major mental illness. Social or developmental factors significantly contribute to this process
- Learning changes neural connections: There are alterations in neural functions induced by experience and learning giving rise to changes in the patterns of neuronal connections as well as behavior
- Psychotherapy changes gene expression. Psychotherapy produces long-term changes in behavior, by producing changes in gene expression that alter the strength of synaptic connections and structural changes that alter the anatomical pattern of interconnections between nerve cells of the brain.

We would like to focus on the following fundamental questions:

- How the brain is built by experience during the period of development?
- Do Psychiatric disorders tend to debuild the brain?
- Can Psychotherapy help to rebuild the brain?

## **BUILDING OF THE BRAIN DURING DEVELOPMENT**

Brain is a self-organizing, self-adaptive, and a highly dynamic system capable of self-regulation, problem-solving, language/ communication, and social bonding. It is well known by now that there occurs most vigorous growth, interconnections of neurons, pruning, and all neuronal activity between  $1-1\frac{1}{2}$  years of age and 3–4 years of age – which is called "the sensitive period or critical period" of brain development. Brain can be divided grossly into four specific areas/lobes (frontal, parietal, temporal, and occipital) and each lobe specializes in specific functioning. There is also right to left lateralization and interhemispheric communication and coordination established during development. Experience is incorporated into the developmental process forming structural and functional neural networks.

#### **Role of experience**

Experience can change the actual structure of the brain. Brain development is basically an "activity-dependent" process. Every experience excites some neural circuits and leaves others alone. Neural circuits used over and over get strengthened and those that are not used are dropped resulting in "pruning," i.e., "*Neurons that fire together, wire together.*" Genes and environment also interact with each other through brain development, commonly called as gene–environment interaction (G x E). Genes form neurons which make connections among major brain regions. Environment and experience builds and refines these connections and thereby enhancing some connections while eliminating others during the process of development. Hence, in short, brain is an organ of adaptation and experience translates into neurobiology, making nature, and nurture into becoming one.

# Several neural processes that contribute to building of the brain have been understood

#### Epigenesis

Experience wires the brain through learning. A process that influences gene expression and strengthens the synaptic connections is called epigenesis. This leads to both biological and cultural evolution, of which the former is a slow process but later is a more rapid and a stronger process.

#### Neuronal plasticity

Experience transforms the brain through learning. It has been quite evident now that neuronal circuits change in response to environmental stimuli. There is long-term potentiation, which is the increase in efficacy of synapses as a result of high-frequency stimulus lasting from hours to days, resulting in alteration and creation of neuronal connections in response to experience. This can further explain conditioning, sensitization, and extinction of responses.

#### Neurogenesis

The capacity for neurogenesis is retained throughout the life span in humans.<sup>[5,6]</sup> Neurons generated as a result of experience are not only functional but also associated with better memory and plasticity.<sup>[7]</sup> The areas associated with emotions and memory, i.e., hippocampus, prefrontal cortex, amygdala, and temporal lobe are highly plastic and capable of regeneration.

#### Interactive memory, cognitive, and emotional systems

As postulated by MacLean, the mammalian brain has advantage over reptilian brain as it has emotional memory and explicit memory in addition to instinctual memory.<sup>[1]</sup> These systems interact with each other. Explicit memory requires hippocampus and medial temporal lobe and implicit memory requires specific sensory-motor system, cerebellum, basal ganglia, amygdala, hypothalamus, and prefrontal cortex. However, implicit memory systems are completely unconscious and are not available to conscious mind. It has also been postulated that "priming" is the neural basis of unconscious mental processes. Medial temporal cortex and prefrontal cortex process long-term memory and hippocampus processes learned information helping in consolidation and storage in the neocortex. Emotions, memories, and feelings are interconnected processes. Emotional arousal can activate amygdala which modulates storage of memories. Prefrontal cortex processes information after judging and evaluating them. Thus, memory is distributed throughout the brain; memory, cognitive, and emotional systems interact with one another and influence one another significantly.

#### Mirror neurons and attachment/bonding

It has been now well established that during infancy, attachment with caregiver/mother starts/modifies the areas which are associated with regulation of emotions and bodily arousal, i.e., the cortico-limbic and orbitofrontal circuitry, respectively.<sup>[8]</sup> Although these areas are not fully developed at birth, attachment gives these areas a template for future relationships. Here comes the role of mirror neurons. Mirror neurons are the neurons which fire both while watching someone performs an action and when performing the same action, i.e., the neuron "mirrors" the behavior of the other, as though the observer were itself acting. Such neurons have been directly observed in primates and are believed to occur in humans too.<sup>[9]</sup> These neurons are mostly located in the inferior parietal lobule, posterior parietal cortex, inferior frontal gyrus, Broca's area, cingulate cortex, and superior temporal sulcus. Mirror neurons through visual imagery allow people to make a brain-to-brain link with others. The review article on mirror neuron system (MNS) by Rajmohan and Mohandas illuminates in detail how this fascinating discovery has become the evidence base in cognitive neuroscience research explaining the neurobiology of socioemotional cognition, empathy, appreciation, and anticipation of other's emotions and intentions, relevant in explaining the socioemotional cognitive deficits in conditions such as autism spectrum disorders, schizophrenia, and personality disorders.<sup>[10]</sup> The MNS also has the potential to explain the brain changes occurring during the psychotherapeutic process.

#### Priming

Priming refers to an action or response elicited by a previously nonconsciously observed stimulus. Priming is an automatic and unintentional processing. Brain can process nonverbal and unconscious information. Unconscious perception depends on "priming" and is often seen in humans.

#### THE EMOTIONAL AND SOCIAL BRAIN

Social brain includes amygdala, anterior cingulate, and orbitofrontal areas of the prefrontal cortex and the frontal portions of the temporal lobes, which expand and interconnect in parallel with the social emotional and experiential information necessary for survival. Emotional processing may be dependent upon the functioning of two neural systems: (1) a ventral system (amygdala, ventral regions of anterior cingulate gyrus, prefrontal cortex) for identification of the emotional significance of environmental stimuli and the production of affective states and (2) a dorsal system (hippocampus, dorsal regions of anterior cingulate gyrus, prefrontal cortex) for the performance of executive functions and effortful regulation of affective states.<sup>[11]</sup> Networks of social and emotional brain dedicated to attachment and interaction are the primary components of neural substrate of emotions and form the core of the personality development of an individual.<sup>[12]</sup>

The building of the social brain between 18 and 24 months is driven by attunement between the right hemisphere of the mother and right hemisphere of the child,<sup>[8]</sup> and in this process, the unconscious of the mother is transferred to the unconscious of the child. Bonding initially is very primitive where smell and touch play the primary role. Physical contact with the mother sets the thermoregulation in the hypothalamus of the child. Infant's and mother's eye-to-eye contact establishes a lifelong relationship between nutritional and emotional nurturance and links their hearts, brains, and probably the souls too. Prolonged sharing of emotional gaze stimulates growth of networks of attachment in the entire brain.<sup>[2]</sup> During periods of mother and child separation and reunion, it has been seen that endorphin levels rise and fall leading to alternating rushes of wellbeing and distress in both of them. These mother-child interactions stimulate a cascade of neurohumoral and neurochemical changes such as secretion of oxytocin, prolactin, endorphin, and dopamine creating positive feelings in them. These biochemical changes stimulate structural maturation of the orbitofrontal cortex.<sup>[13]</sup>

The internalization of mother during childhood involves an intricate network of visceral, motor, sensory, and emotional memories. These memories get activated during adulthood during periods of stress and also have the capacity to support the ability to regulate affect in later life. Cozolino has proposed the role of endogenous opioids in this regard. Hence, early experiences of bonding and attachment become imprinted within the circuits of the social brain and continue in the adulthood.<sup>[14]</sup>

Early environments and experiences have an exceptionally strong influence on brain architecture. After most neural circuits in the brain have matured, their genetic plans and architecture can still be modified by experience, but the extent of these modifications tends to be far more limited. This means that what happens early has a unique advantage in shaping the architecture of developing brain circuits before they are fully mature and stabilized. The science of pediatrics relies upon not just biology but also various health and development factors – and increasingly, the role of "ecology," meaning the environments that child are raised in. These all influence each other's through the routes of neuroscience, life course sciences, and epigenetics.<sup>[15,16]</sup>

#### WHAT HAPPENS IN CASE OF NEGLECT?

Several studies have found that neglect in the form of physical/social/emotional (limited exposure to language, touch, or social interactions) during the critical periods of development bring about structural changes in the brain. As a result of neglect, there occurs lack of brain growth beyond effects of poor nutrition and neuronal death beyond "pruning." Toxic stress in early childhood also shapes the brain, but in a negative fashion. Toxic stress is associated with persistent effects on the nervous system and stress hormone systems that can damage developing brain architecture and lead to lifelong problems in learning, behavior, as well as physical and mental health. In addition, if there is repeated stress or neglect during early childhood, it can cause impairment in the normal neurodevelopmental trajectory leading to significant psychiatric morbidity in adulthood.

#### WHAT HAPPENS IN PSYCHIATRIC DISORDERS?

We know that the neural architecture depends on the following mutual and reciprocal influences.

#### Genetics

Genetics supply a basic blueprint or a plan for brain development. It provides the structure for the brain's architecture and supplies the means for interconnecting nerve cells within and across circuits. Genetic abnormalities lead to aberrant neurodevelopment and neuropsychiatric disorders.

#### Environment

The environment that the brain has to develop in has a profound influence in shaping the capacity of the brain. An adverse prenatal environment in the form of maternal stress/obstetric complications/prenatal infections can actually alter the genetic plans. Individual mental states are influenced by the individual's social environment. The social environment of an individual mediates the relationship between the genotype and phenotype. The environment forms the nongenetic etiological factor behind the development of neuropsychiatric disorders. It differs from experience in the way that it provides the basic arena, in which an individual interacts with its own species.

#### Experience

Experience refers to the interaction the child has with his or her environment. In normal development, it is the experience which molds the brain and behavior. Healthy and stimulating experience results in brain architecture that is able to operate at its full genetic potential. Even if one can have healthy genetics and healthy environment, but if interaction with that environment is prevented, still the brain is at risk, i.e., it will not develop properly. The nature of the environment and the individual's interaction with it determines much of the character of the brain.

Psychiatric disorders develop in an individual when any of the above-mentioned factors are impaired. More and more evidence is accumulating in favor of the "biological" nature of the psychiatric disorders. Symptoms of psychopathology from neurotic to psychotic disorders are based in the brain, specifically in the neural networks organizing conscious awareness, behavior, emotional/social cognition, learning and memory, and sensations. Psychopathology reflects the suboptimal integration and coordination of neural networks. Neural networks in psychiatric disorders are either underdeveloped, under-regulated, or under-integrated leading to various psychopathologies and symptomatologies. There can also be destabilization, disintegration, or dysregulation of previously well-formed neural networks due to any of the environmental causes such as stress as already described in literature, leading to genesis of psychiatric disorders. Psychotherapy attempts to modify or change these neural networks. It is based on the fact that human brain has the ability for neurogenesis in areas that are involved in new learning such as hippocampus and amygdala,<sup>[5]</sup> emotional bonding, epigenesis, and neural plasticity.

A recent voxel-based morphometry meta-analysis of 193 studies<sup>[17]</sup> has been done to identify common neurobiological substrate for mental illness, in which a total of 15,892 individuals with six diverse diagnostic groups (schizophrenia, bipolar disorder, depression, addiction, obsessive-compulsive disorder [OCD], and anxiety) were included. The results showed that findings of gray matter loss converged across diagnoses in three regions - dorsal anterior cingulate, right insula, and left insula. These common gray matter loss regions formed a tightly interconnected network during tasks and at rest and that the lower gray matter in this network was associated with poor executive functioning. Hence, from this study, we have concluded that areas linked with executive functions are the main neurocircuitry impairment seen in psychiatric disorders.<sup>[17]</sup>

In addition to all these, stress also plays a major role in development of psychiatric disorders. Stress in any form can directly have an impact on the hypothalamus, leading to activation of sympathetic nervous system and release of corticotropin release factor which through a series of effects can lead to production of cortisol or the stress hormone resulting in various bodily responses (physical and psychological) in an individual. Stress (basing upon the severity, nature, and cognitive schema of an individual) can lead to breakdown of an individual to psychiatric disorders. In short, psychiatric disorders indicate a state of destabilization of brain functions.

#### WHAT PSYCHOTHERAPY DOES TO THE BRAIN?

The process of psychotherapy involves:

- Verbal and nonverbal exchange and interactions between therapist and client
- Ventilation and catharsis
- Therapeutic alliance
- Empathy
- Transference
- Uncovering of the unconscious
- Resistance
- Working through
- Cognitive restructuring and new learning.

All the psychotherapeutic techniques and processes trigger/activate a series of functional alterations, wherein the conditions created by psychotherapy support neural integration, regeneration, and new learning. Fundamental principles and conditions created during the psychotherapy process cause the brain to change its structure and functions. The ingredients of psychotherapy governing such changes in the brain of an individual are therapeutic not only during the psychotherapy but also for long-term thereafter leading to a lasting impact. Some of these are discussed below.

#### **Enriched environment**

Psychotherapy provides an enriched environment. It has been well demonstrated in animal models of psychiatric disorders that animals raised in an enriched environment develop more neurons, more synaptic connections, greater number of capillaries, and more mitochondrial activity.<sup>[18-20]</sup> Research has shown that children raised in enriched environment characterized by higher levels of stimulation and complexity, learn and grow better than those who are raised in an impoverished environment. Human brain grows in response to challenge and new learning. Nurturing relationships facilitate formation and integration of neural networks. Psychotherapy recreates an enriched environment that promotes development of cognitive, emotional, and behavioral abilities. All these psychic functions though subserved by separate neural networks during the state of normal functioning are integrated. The environment created during the process of psychotherapy nurtures the brain of the client to understand and learn new abilities.

#### Positive therapeutic relationship

A key task in psychotherapy is creating and maintaining an optimal therapeutic relationship. The therapeutic relationship involves elements such as empathy, positive regard, and instilling hope. Positive emotional interaction, mutual eye gaze, acceptance of the client by the therapist

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gives rise to a bonding and attachment which can be comparable to early mother–child attachment. This process stimulates growth and organization of the brain. Interpersonal experience during psychotherapy impacts the neurobiology of brain in ways that stimulate neural plasticity and neurogenesis.

When a therapist speaks to a client and the client listens, he/she makes eye and voice contact with the therapist. During this entire period, the action of neuronal machinery in the therapist's brain is having an indirect and long-lasting effect on the neuronal machinery in the client's brain and vice versa. Words produce changes in the client's mind, and it is likely that these psychotherapeutic interventions produce changes in the client's brain. Thus, during the process of psychotherapy, both biological and sociopsychological approaches are joined/intermixed with each other.<sup>[4]</sup>

#### Safe and empathetic relationship

Empathy is the capacity for the imaginative transposing of oneself into the feeling and thinking of another individual.<sup>[21]</sup> The foundational aspects of empathy include affective sharing of others' problems, a sense of self, a sense of the other, and an embodied emotional regulation process between self and other at the same time. It has been postulated that the areas of brain such as anterior insula, amygdala, and anterior cingulate cortex are involved in the affective sharing between self and others.<sup>[22]</sup> Adopting the perspective of others is governed by frontoparietal cortex, ventromedial prefrontal cortex, and inferior parietal lobule. Self and emotion regulation is maintained by right temporoparietal junction and posterior cingulate. In brief, various brain areas get into activation during an empathetic relationship between the therapist and client, which is highly essential for perfect understanding of one's problems and other's (therapist) perspective in managing these problems.

#### Learning to mediate and modulate stress

During stress, biochemical environment of the brain shifts its focus to new learning.<sup>[23]</sup> Moderate stress triggers release of neurohormones that enhance cortical reorganization and new learning in animal studies.<sup>[24-26]</sup> Stressful and dangerous situations induce greater amount of alertness and attention conducive to learning. During stress, neural circuits are short chained to block conscious awareness/appraisal of the event or its emotional impact. During psychotherapy, there is controlled exposure to stress, under a highly supportive environment, where the individual is brought to recollect/rework the trauma. There is an effort to harness the interaction of stress and learning in such a manner that changes and integrates the brain functions, producing lasting benefits. New learning acquired through psychotherapy helps the individual handle stress better in future, consequently leading to enhanced neuronal growth

and interconnections. Indirect evidence of this phenomenon is available from the studies showing enhanced glucose metabolism and increase in neurotransmitter concentration in the brain blood flow.<sup>[27]</sup>

#### Change in gene expression during psychotherapy

It is known that 70% of our brain is added after birth.<sup>[2]</sup> Experience plays a vital role in gene expression through the activation of neural firing and cascade of biochemical processes. Genes serve as template as well as transcription function. The gene template forms the uniform structure of the brain which is unimpacted by the environment. Transcription genes depend upon environmental triggers for expression by activating neural firing and biochemical cascades. It is through the gene transcription that new neurons grow, existing neurons expand, and environmental stimulation continues to build the brain. It is the transcription function of the genes that provides the basis for the experiences like psychotherapy to build the brain.<sup>[28]</sup> As per Eric Kandel's Principles, psychotherapy produces long-term changes in behavior, by producing changes in gene expression that alter the strength of synaptic connections and structural changes further altering the anatomical pattern of interconnections between the nerve cells of the brain.

#### Promotion of neural integration

Healthy functioning requires proper development and functioning of neural networks organizing conscious awareness, behavior, emotions, and sensations. Dissociation following trauma reflects disconnection among networks of behavior, emotion, sensation, and cognition due to high levels of stress hormones and chemicals. Under stress, circuits of reptilian and paleomammalian brain get delinked from the conscious neomammalian cortex. Cortical networks serving memory, language, and cognitions are inhibited. Psychotherapy aims at psychological integration, i.e., cognitive functions of the executive brain to have increasing access to information across networks of sensation, behavior, and emotions. There occurs integration of neural networks of affect and cognition in psychotherapy.

#### Bringing unconscious to conscious awareness

In psychoanalytic thought, it is believed that much of our psyche operates at an unconscious level, which the conscious mind is unaware of. Bringing the unconscious mental process to conscious level is one of the important tasks in psychotherapy.

The current understanding of the neurobiology of unconscious is that it is equivalent to the implicit memory which has implicit representations as "potentials for reactivation."<sup>[29]</sup> Activation of one node of networks (including knowledge, feeling, or motives) can either "facilitate or inhibit activation of other nodes." The activation of a certain network may trigger a cascade of

cognitive, affective, motivational, and behavioral processes consciously or unconsciously recognized or expressed.

Stress and trauma in childhood and later life lead to dissociation. During psychotherapy, awareness of inhibited, repressed, and dissociated thoughts and emotions is attempted. Thereby, it leads to activation of normally inhibited cortical circuits to allow for descending cortical control of fear or anxiety. Psychotherapy helps bring out implicit memories and link them with explicit memories, and maladaptive learning is brought to the forefront.

#### Reflecting on right hemisphere

Brain functions are highly lateralized and these operate in an integrated manner. Left hemisphere is biased toward positive affect and prosocial behavior and helps to be more social and less anxious. Right hemisphere is biased toward anxiety, fear, and negative emotions. Dysregulation between the two hemispheres can lead to loss of balance between the positive and negative affect.<sup>[30]</sup> Any form of treatment requires rebalancing of these systems.

Psychotherapy attempts to integrate these functions through emotional expression, interpretation, logical reasoning, reality testing, and putting words to feelings. Right hemisphere functions are akin to Freud's unconscious mind which develops first and incorporates emotional, sensory, motor, preverbal experiences.<sup>[31]</sup> Thus, right hemisphere processing is similar to primary process thinking, whereas left hemisphere functions are conscious, verbal, logical, and akin to secondary process thinking. Cognitive therapies help to treat depression and anxiety by stimulation of rational thought process located in the left hemisphere. Similarly, relief can be obtained by downregulation of right hemisphere process through relaxation training.

Patients suffering from alexithymia have inability to consciously experience and describe feelings. Their emotional memories from right hemisphere do not have access to left hemisphere, thus losing verbal expression and awareness. Alexithymia patients have been described to have a "bidirectional interhemispheric transfer deficit."<sup>[32]</sup> Such patients are unable to benefit from psychotherapy.

# Use of verbal language and integration of left and right brain functions

Language located in left brain develops later than right brain functions and connects with right brain later. Left hemisphere communicates through verbal language, whereas right hemisphere communicates through facial expressions, body language, emotions, and attitudes. Many psychiatric disorders appear to correlate with disruption of integrated processing between right and left hemisphere. During psychotherapy, the patient has to learn to translate the right hemisphere language into the left hemisphere language and bring it to conscious awareness. The whole process incorporates hemispheric integration. Frontal lobe provides a sense of a sense of time, autobiographical memory, and a sense of identity and self-awareness. In psychotherapy, there occurs integration of three language systems – reflective social language, internal dialog, and self-reflection. Use of language in the emotionally meaningful psychotherapeutic relationship is the key to resculpting of neural networks.<sup>[14]</sup> Language helps us to combine in conscious memory, the knowledge, sensations, feelings, and behaviors supporting the underlying neural network integration.<sup>[3]</sup>

#### Activating fears, phobias, traumas, and release of emotions in an anxiety free controlled environment

Emotions are associated with subjective experiences of states of nervous system. Emotions involve primitive circuits which are basic and robust processing units that are conserved across evolution. Emotional memories last longer and may be more vivid than other types of memories. Traumatic experiences get submerged in the circuits of unconscious memory that control anxiety and fear and prevent them from coming to the consciousness. Brain also deploys various maladaptive coping mechanisms and defense mechanisms to control these traumatic emotions. Neural connections that result in defenses shape one's life by selecting what one approaches and what one avoids.

In psychotherapy, therapist attempts to activate the client's emotions and hidden fears/phobias and his defenses are examined. Therapist also attempts to revisit to the inner unconsciousness and thereby facilitates the release of fear and emotions in an anxiety free controlled environment. This results in integration of cortical linguistic processes with unconditional subcortical arousal leading to inhibition, regulation, and modification of maladaptive reactions.

#### Reevaluation and revalidation of childhood experiences

Fundamental goal of psychotherapy is to bring unconscious to conscious awareness which means increasing the interconnections and integration of neural networks dedicated to unconscious (implicit) and conscious (explicit) memory. Implicit or early childhood memory intrudes into adult consciousness in many ways that can determine the emergence of psychopathology and provide useful directions for psychotherapeutic interventions. Disturbed and insecure attachment or bonding with mother can lead to highly unstable and disturbed interpersonal relationships in adulthood. Overreaction to comments/criticism, etc., implies sensitization during early childhood with shame which is a primary socializing affect starting at about 12 months.<sup>[33]</sup> State of silence evokes anxiety as implicit memories get activated during such periods. Many people get uncomfortable when they try to relax because of the implicit memories of thoughts, emotions, and images that tend to gain expression in the conscious awareness. It is also known that memory is vulnerable to suggestion,

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distortion and fabrication, and falsification. This mental ability of memory is a manifestation of plasticity of the nervous system, which provides an opportunity to alter the nervous systems. During psychotherapy, when childhood experiences are revisited and reevaluated from an adult perspective, newer networks and interconnections are created to serve insights and newer memories, during therapy, altering the emotional reactions.

#### **Development of transference**

Transference is the unconscious act of assigning to another in the present environment, feelings and attitudes associated with someone of significance from one's past. Freud has mentioned that transference is a projection of one's feelings toward one person to another; essentially the second person becomes a surrogate for the first. Positive form of transference develops when a client trusts his or her therapist because the client is reminded of a trustworthy person from his or her past. From neurobiology point of view, it has been postulated that it is because of mirror neurons, the client develops transference toward his/her therapist.

Mirror neurons track the emotional flow, movement and even intentions of the person we are with, and replicate this sensed state in our own brain by stirring in our brain the same areas active in the other person. Mirror neurons allow people to make a brain-to-brain link with others. Mirror neurons provide the link up for the impact of early learning and the lifelong influence others have on our unconscious processing resulting in transference in therapy. When two minds feel connected, when they become integrated, the state of firing of each individual can be proposed to become more coherent. Literally, this may mean that the corresponding activations between the body-proper, limbic areas, and even cortical representations of intentional states between two individuals enter a state of "resonance," in which he matches the profiles of the other.<sup>[34]</sup>

#### Learning in psychotherapy

Learning within neural networks occurs as a result of trial and error, leading to a consistent adaptive pattern of behavior. One keeps trying till one learns to do what one wants to do. In this way, neural networks organize behavior, emotions, thoughts, and sensations that are built and rebuilt throughout life. In this way, all our behaviors and actions get patterned through previous learning into automatic actions to the extent that we become incapable of engaging in random actions. Neuronal growth, interconnectivity, neural connectivity, and neurogenesis are the basic mechanisms of all learning and adaptation. New neurons are generated in different areas of the brain, particularly those involved in ongoing learning, such as hippocampus, amygdala, and frontal and temporal lobes.<sup>[5,6]</sup> All psychotherapies involve learning. Learning is reflected in synaptic changes within the brain, mediated by changes in gene expression.

## EVIDENCE IN FAVOR OF THE REBUILDING PHENOMENON OF BRAIN THROUGH PSYCHOTHERAPY

Emerging evidence from the recent studies shows that psychotherapy leads to definitive and demonstrable changes in the brain. Functional magnetic resonance imaging studies on the cognitive behavior therapy (CBT) effects in OCD were consistent in showing decreased metabolism in the right caudate nucleus. CBT in phobia resulted in decreased activity in limbic and paralimbic areas. Similar effects were observed after successful intervention with selective serotonin reuptake inhibitors in both OCD and phobia, indicating commonalities in the biological mechanisms of psychotherapy and pharmacotherapy. Increased activity in the right caudate was the common finding of symptom provocation studies in OCD across imaging modalities. Correspondingly, all studies of the effects of CBT in OCD on resting-state glucose metabolism or blood flow so far reported a decrease in right caudate activity in treatment responders.<sup>[35]</sup> While symptom provocation and resting state studies produced fairly consistent signatures of pathological metabolism for OCD (right caudate hyperactivity) and phobias (limbic and paralimbic hyperactivity), the situation is more complicated for major depressive disorder (MDD). The functional imaging studies of therapy effects in MDD had yielded partly heterogeneous results across studies and also across treatment approaches. Not only in neurotic disorders but also in psychotic disorders, psychotherapy has been proved to be beneficial. Studies on cognitive enhancement therapy (CET) (which helps in enhancing cognitive tasks of attention and memory and social cognition) in patients with schizophrenia have demonstrated improvement in emotion recognition defects, social cognition, and neurocognition, following CET.<sup>[36]</sup> A recent study from India on facial emotion recognition defects (FERDs) in schizophrenia patients, before and after treatment with antipsychotics, demonstrated FERD during drug naïve state and improvement in FERD after treatment with antipsychotics.<sup>[37,38]</sup> Hence, all these studies demonstrate that psychotherapy can lead to structural and functional changes in the brain. In fact, psychiatry and neurology have come together to bring the advent of neuroscience of mental process.

#### CONCLUSIONS

In India, as early as 1959, Indian psychiatrist Nand had acknowledged the "split" of psychiatrists into biologically oriented and analytically oriented,<sup>[39]</sup> and by 1980, it was proposed that psychotherapy will gradually relegate into oblivion.<sup>[40]</sup> Indian research on psychotherapy is quite limited, but recent times had seen new research on family interventions,<sup>[41]</sup> empathy among mental health professionals and lay counselors,<sup>[42]</sup> concepts of Patanjali in the treatment of psychiatric disorders,<sup>[43]</sup> and many more.

#### Malhotra and Sahoo: Rebuilding brain with psychotherapy

Manickam in his review article<sup>[44]</sup> has very well proposed that psychiatrists should try to strike a balance between biological determinants of behavior and carry out more and more evidence-based psychotherapies.

However, after the extensive research on the neurobiology of psychiatric disorders, now, we have begun to understand the neurobiological basis of mental processes and mental illness. The growing research in the field of neuroscience of psychotherapy has established that psychotherapy allows and helps in bringing a change in the brain. Evidence of neurogenesis and neural plasticity has opened newer possibilities of interventions for increasing our ability to alter the brain. Psychotherapy that had long been dubbed as an unscientific and an invalidated dogma is beginning to find its neurobiological underpinnings and regaining its value as an immensely scientific method of intervention. This has led to the convergence between neuroscience and psychotherapy which earlier followed totally divergent paths opening a new era of research in this field.

Freud had postulated over a century ago that the mental processes are reflected in the neural architecture of the brain and nervous system, an idea whose time has come now in the 21<sup>st</sup> century. Freud was, thus, ahead of his times. There is renaissance of psychoanalytic thought within the realm of neural sciences.

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#### **Conflicts of interest**

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