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PSYCHOLOGICAL TREATMENTS AND BRAIN PLASTICITY

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SUMMARY

For number of years there existed two groups amongst those involved in treating mental disorders, the psychological and biological camps. Psychological camp recommending that "psychological disorders" require psychological treatments, whilst biological camp argued for biological treatment for "biological disorders". Here, I will provide emerging evidence that both forms of treatments have similar underlying neurobiological basis. Beginning at the molecular level, the fields of gene expression, functional genomics, epigenetics have become increasingly important in expanding our knowledge and providing an understanding of the mechanisms that are likely to be involved in changes that occur as result of psychological treatments. Understanding the biological basis of memory systems that include, the concepts of long-term potentiation (LTP) and long-term depression (LTD) through which synaptic plasticity is thought to occur go some way towards explaining how various psychotherapies modify memories and learning in a positive way. Finally various neuroimaging studies have provided a further insight in to the neural changes occurring as a result of psychological treatments.

Key words: *psychotherapies - gene expression - brain plasticity - neuroimaging*

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Neural plasticity can be described as the brain's ability to change its structure and function as a result of external influences. It is needed for the long lasting change in cognition, emotion and behaviour, which are considered to be abnormal in psychiatric disorders to varying degrees.

Whilst, huge strides have been made towards the understanding of effects of so- called biological treatments (medications, ECT, Light therapy, and repetitive transcranial magnetic stimulation (rTMS)) on brain's structure and functions, the research evidence on how psychological treatments exert their effects on the brain and lead to the desired therapeutic change is rather limited.

For number of years, psychiatric disorders have been explained through ever growing neuroscientific understanding of the brain's structure and functioning. Indeed, the psychiatric treatments, such as by medications or by other so- called biological methods have also tended to have been explained in terms of the knowledge acquired from neuroscience.

Most health professionals recognize that the psychiatric disorders can be treated using biological treatments and by various psychological treatments (talking therapies), either alone or in combination. Yet, amongst some, there still exits this erroneous idea that the psychological therapies are for "psychological disorders" and the biological therapies are for "biological disorders".

Here, I will argue why when dealing with treatment of psychiatric disorders, it may not be helpful to use terms such as "psychological disorders" and "biological disorders". I will also provide some emerging evidence, which suggests that this distinction is erroneous and indeed the two forms of treatments are likely to exert similar influences on the structure and functioning of the brain.

At molecular level, the current knowledge tells us that genes as encoded information in the sequence of nucleotides (DNA) are transcribed into messenger RNA (mRNA) and then translated in to amino acids and proteins. This process is called *gene expression.* Along with formation of the physical structure of the body and the brain, the proteins also act as messengers (enzymes, hormones and neurotransmitters), hence driving the physiological functions and providing the basis of mental and bodily experiences.

Functional genomics is dynamic and encompasses gene expression (gene transcription, translation and protein-protein interaction), whilst genomic information such as DNA sequence or structure are rather static.

Functional genomics attempts to answer questions about the function of DNA at the levels of genes, RNA transcripts, and protein products.

Most psychiatric disorders are not due to mutations in a single gene, but involve molecular disturbances entailing multiple genes and signals that control their expression. More recently, research has demonstrated that complex *'epigenetic*' mechanisms, which regulate gene activity without altering the DNA code, have long-lasting effects within mature neurons. It points to sustained epigenetic mechanisms of gene regulation in neurons that have been implicated in the regulation of complex behaviour, including those in number of psychiatric disorders (Tsankova et al. 2007).

It is clear that from the womb to the tomb, the brain remains flexible and responsive to the outside world.

It receives signals from the outside world, forms memories and allow us to learn from our experiences. At cellular level, changes in gene expression accompany many of brain functions. Histone modification and DNA methylation that constitute epigenetic mechanisms, stabilize gene expression, which is important for long-term storage of information. It can therefore be argued

that epigenetic changes are part of mental disorders and need to be understood, if we are to have better understanding of the causes and provide more effective treatments.

Eric Kandel (1998) in his highly cited paper eloquently described the relationship between psychotherapy, gene expression and brain plasticity.

He described a framework using number of principles, as outlined below:

1. All mental processes (from simple to most complex psychological processes) that lead to behaviour occur in the brain, including those in psychiatric disorders, what ever the origin of the causes.
2. Genes and resulting proteins determine inter-neuronal connections, hence exert influence over behaviour and therefore contribute to development of major mental illnesses.
3. Just as genes, through gene expression contribute to behaviour, "so can behavior and social factors effect the brain by feeding back upon it to modify the expression of genes and thus the function of nerve cells. Learning, including learning that results in dysfunctional behavior, produces alterations in gene expression. Thus all of "nurture" is ultimately expressed as "nature."'
4. "Alterations in gene expression induced by learning give rise to changes in patterns of neuronal connections. These changes not only contribute to the biological basis of individuality but presumably are responsible for initiating and maintaining abnormalities of behavior that are induced by social contingencies."
5. "Insofar as psychotherapy or counseling is effective and produces long-term changes in behavior, it presumably does so through learning, 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. As the resolution of brain imaging increases, it should eventually permit quantitative evaluation of the outcome of psychotherapy."

The role of learning and memory in various forms psychotherapies is clearly very important. Indeed, understanding the neural substrates of learning and memory and its link with neural plasticity is likely to help us understand how the psychotherapies affect the brain's structure and functions.

It is helpful to consider, two distinct memory systems, described as explicit and implicit memory. The research evidence (Squire et al. 1992, Paller 1992) suggests that these memory systems have different physiological properties and utilize different set of neural structures, which results in different brain functions. Explicit memory is described as conscious recollection of facts and events and involves medial temporal lobe and the hippocampus. Whilst implicit memory refers to heterogeneous collection of abilities and experiences which alters behavior non-consciously, without providing access to any memory content. The latter is thought to involve the basal ganglia as well as the cerebellum as suggested by the observable influence on emotional behaviors related to early attachment experiences.

The progress towards understanding the biological basis of memory and neural plasticity began with Cajal (1911) who suggested that information could be stored by modifying the connections between communicating nerve cells in order to form associations. Hebb (1952) further observed that modifications only takes place between the connected cells, if both neurons were simultaneously active. Information is encoded by strengthening the connections between neurons that are simultaneously activated "Neurons that fire together will wire together"; this is known as Hebb's rule, and it leads to 'Hebb - like synaptic plasticity'.

At an elementary level, three forms of CNS synaptic plasticity are described: 1) LTP (long-term potentiation) mediated by *N*-methyl-D-aspartate (NMDA) receptor activation; 2) LTP mediated by voltage-dependent calcium channel activation; and 3) LTD (long-term depression) mediated by the NMDA receptor (Bliss and Collingridge 1993).

It appears that the synaptic plasticity, primarily through LTP of excitatory synapses, following a Hebbian learning rule, is the basis of remodeling of what is represented at cortical level.

Evidence suggests that many synapses in the hippocampus and neocortex can be modified bidirectionaly (Bear 1996). Indeed these modifications persist long enough to contribute to long-term memory storage. Evidence of recent cortical activity and the amount of NMDA receptor activation are considered to be important variables that reflect the extent of synaptic plasticity.

Amini et al. (1996), has suggested that human infants during the neurodevelopmental stage are more capable of implicit learning, so that certain rules are extracted and stored from the large amount of complex information. These implicit rules lead to unconscious biased towards past experiences for interpretation of later experiences. It is argued that psychotherapy helps to reveal and reflect upon these set of implicit rules. Change is then brought about by learning new patterns, which are explicitly repeated then ingrained upon the implicit memory system.

Further evidence for the biological effects of psychotherapy has come from number of neuroimaging studies.

Baxter et al. (1992) used PET (positron emission tomography) scans to compare changes in cerebral metabolic rates for glucose in OCD patients receiving behavior therapy and those receiving fluoxetine. Interestingly they found a similar decrease in the head of the right caudate nucleus in the two treatment groups.

Also studying group of OCD patients, Schwartz et al. (1996) from their PET scans studies showed that responders to cognitive behaviour treatment had significantly greater bilateral decreases in caudate glucose metabolic rate when compared with poor responders.

Van der Kolk (1997) carried out single-photon emission computed tomography (SPECT) studies of patients with posttraumatic stress disorder (PTSD) who underwent treatment with eye movement desensitization and reprocessing (EMDR) and reported increased prefrontal metabolism and decreased limbic system activation in SPECT scans of these patients. This studies suggested EDMR to be not only effective, but actually having biological effect in the certain regions of the brain.

Paquette et al. (2003) using fMRI scans of patients with spider phobia, showed that effectively treated (with cognitive behaviour therapy-CBT) patients showed no significant of activation of dorsolateral prefrontal cortex (DLPFC) or the parahippocampal gyrus. The authors suggested that "CBT, has the potential to modify the dysfunctional neural circuitry associated with anxiety disorders" and "that the changes made at the mind level, within a psychotherapeutic context, are able to functionally "rewire" the brain."

Viinamaki et al. (1998) carried out SPECT imaging before and after one year of dynamic psychotherapy in a patient with borderline personality disorder and depression and compared with a patient who received no therapy and with 10 healthy control subjects. Their findings suggested that both patients initially had decreased serotonin uptake in prefrontal cortex and thalamus compared with the healthy control subjects. However, after one year, the patient who received psychotherapy had normal serotonin uptake, suggesting that dynamic psychotherapy can affect serotonin metabolism. Despite these interesting findings, it should be noted that this study has many methodological problems and has not yet been replicated.

Conclusion

The expanding knowledge of neuroscience towards understanding the neurobiological basis of various psychotherapies has brought the "psychological" and "biological" camps of psychiatry much closer. The number of studies are relatively small in comparison with those with biological treatments alone. In addition, some studies show different regions of the brain being modified by biological and psychological treatments and indeed in many cases the evidence for the neurobiological effects of psychotherapies is somewhat indirect. Never the less, there is enough evidence to suggest that time is ripe to assign the idea of psychological therapies for "psychological disorders" and "biological therapies" for biological disorders to the history books.

A greater understanding of functional genomics, epigenetics, memory and brain plasticity is useful in providing neurobiological explanations of psychological treatments. These, disciplines provide great opportunities for further understanding of how and why psychological treatments work.

Indeed, these disciplines can potentially provide scientific methods of identifying which patient would benefit from which psychotherapy, as well as, help to monitor and quantify the success of a particular psychotherapy. Many consider psychotherapies to be not only cheaper but also user (patient) friendly, therefore, from the economic and patient's perspective, it also makes sense to provide health providers with scientific rationale behind psychological treatments

The research in to the biological treatments has expanded our knowledge of scientific basis of mental disorders. The research evidence so far suggests that same is likely to be true for the research in the biological basis of psychological treatments.

An added advantage of further research in this field is that it is likely to provide us with better understanding of negative impact of environmental influences on vulnerable individuals and therefore, will help us to increase our knowledge of preventative psychiatry.

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