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PHARMA HIGHLIGHTS

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Long COVID: Prevalent Neurological and Neuropsychiatric Symptoms

Over the past two years, the COVID-19 virus has overwhelmed the healthcare system. As of 20 March 2022, over 6 million deaths have been reported globally (WHO epidemiological update on COVID-19) due to the virus. Beyond infection, scientists are now concerned with the long-term effects of COVID-19. According to the National Institute for Health and Care Excellence (NICE) guidelines, post-COVID-19-syndrome, also known as long COVID, refers to "Signs and symptoms that develop during or after an infection consistent with COVID19, continue for more than 12 weeks and are not explained by an alternative diagnosis". This means symptoms can persist for a long time or newly develop even 12 weeks or more after infection. Besides other symptoms, a wide range of neurological and neuropsychological symptoms have been reported by patients suffering from suspected long COVID.

A recent meta-analysis published in the Journal of Neurological Sciences, aimed to determine the pervasiveness of neurological and neuropsychiatric symptoms recorded 12 weeks or more after the onset of COVID-19. The study involved 11,324 patients. The most prevalent neurological symptoms among the patients were fatigue, memory loss, brain fog, difficulties with attention, myalgia, anosmia, dysgeusia, and headache. Sleep disturbances, anxiety and depression were the most prevalent neuropsychitaric symptoms. Interestingly, this study showed that hospitalized patients with acute COVID-19 infection had a lower frequency of anosmia, anxiety, depression, dysgeusia, fatigue, headache, myalgia, and sleep disturbance at three months post COVID-19 infection than non-hospitalized patients. The meta-analysis also found that some symptoms may appear for the first-time months after the onset of infection.

The data also shows that ICU patients are most likely to develop anxiety, depression, and sleep disturbances. These may overlap with post ICU neuropsychiatric symptoms. Overall, the study highlighted that fatigue, brain fog, memory issues, attention disorder, and insomnia are the critical symptoms found in certain subsets of COVID patients. Further randomized controlled clinical trials are necessary to develop a better understanding of long covid syndrome to identify risk factors and susceptible patient groups which will facilitate the design of therapeutic interventions for the prevention and management of these long COVID symptoms.

Some scientists have hypothesized the cause of long COVID syndrome. They believe that COVID-19 virus can hamper CNS neuronal mitochondrial functions by obstructing ATP production and oxidative phosphorylation (Medical Science Monitor).

There is no well-established medication to mitigate long COVID. It has become an obstacle for everyday life and a high burden for the healthcare system. Further research is needed to understand the pathophysiology of long COVID syndromes and mitigate potential neuronal damages.

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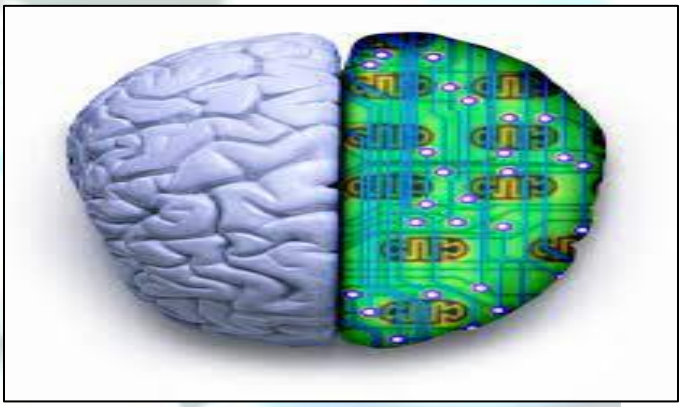
Computational Neuroscientific Approaches on Mental Disorders

According to WHO mental disorders are any psychological disorders that are characterized by a combination of abnormal thoughts, perceptions, emotions and behaviour. The dysfunctions that occur in the brain during mental disorder is still unknown. However, with computer simulation we can now look into the physical anatomy of the brain and attempt to understand it better.
Theoretical neuroscience is the quantitative analysis for determining neural functions and pathways. Whereas, computational neuroscience is a subfield of theoretical neuroscience where studies of the brain are done through mathematical tools and theories. In the last few decades, a lot of advancements have occurred in this sector which explains the brain's function in a concise manner. Various models are being utilized to link between mental disorders and neural activity. In schizophrenia, due to its complexity and heterogeneity, several techniques have been used. One of them is Functional Magnetic Resonance Imaging or fMRI. It measures brain activity through working memory performance by detecting the change in cerebral blood flow. Another technique is Genome-Wide Association Study or GWAS. This associates specific genetic variations in a single neuron with particular diseases. Another most common neurological aging disorder is Alzheimer's disease and the computational approach requires big data set. For this instance, The Virtual Brain or the TVB is the most useful technique as it combines structural and functional information of the brain acquired from various models. In case of pros and cons, fMRI can assess neurodevelopmental changes but sometimes reveal abnormalities in working memory. GWAS can study large samples but the widespread frequency of gene variants can create barriers. TVB finds out the rate of neuronal signaling but is not always validated. All these approaches are potentially important in psychiatric research to understand the underlying etiology and pathophysiology of various mental diseases. In the near future, these approaches offers technological advancements for developing new theories and models of neuroscience.



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Three-Dimensional Printing (3DP) Strategies to Induce Bone Regeneration

Three-Dimensional Printing (3DP) is a technology to produce complicated shapes of materials layer-by-layer process whereas bone tissue engineering is a procedure that replaces or improves bone by combining it with the surrounding tissues by introducing biomaterials to develop a cell scaffold. There are three elements in bone tissue engineering which are- cells, growth factors and bone scaffolds.
Cells give the bodily component its shape and these are obtained from postnatal and adult stem cells, embryonic stem cells etc. Growth factors such as- bone morphogenic

proteins, vascular endothelial growth factor etc. are needed for the successful regeneration by modifying cell signaling in the damaged region. Bone scaffolds are the construction of a physically stable bone which resembles human and helps the cell to bind and migrate. The clinical results of the present traditional methods which involves surgery or transplantation show that these cannot sufficiently treat bone injury, displacement or tissue regeneration but the recent advancements in tissue engineering have exhibited some beneficial means that can treat these conditions effectively.

Various 3DP methods are used in bone tissue engineering starting from the traditional SLA (Stereolithography), FDM (Fused Deposition modeling), Material Jetting, Powder Bed Fusion, Binder Jetting, Sheet Lamination, Directed Energy Deposition to modern method of Bioprinting.

These methods have both pros and cons for manufacturing scaffolds. But, FDM method is used widely for fabricating higher mechanical strength of the scaffold among these and bioprinting method still needs development as it lacks suitable biomaterials. Biomaterials play a significant part in this process by supporting regenerating cells and tissue regeneration. Some examples of these in use are - ceramics, metals, polymers, composites etc. The regeneration capability of natural polymers (collagen, chitosan etc.) and ceramics (calcium phosphate ceramics, bio-glass etc.) are very high. Besides, some recent progress that has been made in order to induce bone regeneration currently are by inducing conductive materials like polypyrrole, polyaniline etc. and by mechanical and electrical stimulation for inducing bone regeneration. Although 3D printing methods have proved to be a great exploration in the biomedical industry, more varieties of materials are needed considering both the structure and function of the scaffold and also to mimic the natural bone.

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