Applications of the Understanding of Neuroplasticity in the Advancement of the Treatment of Neurological Conditions.

Neuroplasticity concerns the brain's ability to change, reorganize and grow neural networks. This can be through the formation of new synapses or the formation of new neurons. Neuroplasticity plays a vital role in the learning of motor and cognitive functions; this raises thoughts over its potential applications in the treatment of various neurological conditions. Treatments that promote neuroplasticity have applications in both psychiatry and neurology. In paediatric cerebral palsy cases, treatments that promote neuroplasticity have been observed to have improved motor function. There is also an adult application to treatments that promote neuroplasticity: in the treatment of chronic depressive and anxiety disorders, talk therapies have been seen to be more effective when used in conjunction with treatments that promote neuroplasticity such as deep brain stimulation and transcranial magnetic stimulation. The application of neuroplasticity in the treatment of traumatic brain injuries and stroke rehabilitation has proved incredibly effective in the relearning of motor functions lost upon brain injury. Finally, the use of neuroplastic potential mapping allows for accurate prognosis and treatment plans for both brain injury and psychiatric cases. It is evident that neuroplasticity can have many positive impacts on the field of neurology by providing alternative, non-invasive treatments and diagnostic methods for both psychological and physiological conditions. By applying neuroplasticity to the treatment of neurological conditions in the future, we can improve treatments for a wide range of conditions, greatly improving patient outcomes.

Cerebral Palsy is a group of conditions in which an individual experiences brain damage to the cerebral motor cortex of their brain during early development, often before birth. Individuals with CP often have difficulty with balance, coordination of movements and difficulty with fine motor control. CP has many comorbidities, including hearing loss, vision impairment, seizure disorders and learning difficulties. The physical disability caused by CP, however, is primarily due to the loss of neurological function in the motor cortex leading to spasticity in muscles and a lack of control over muscles. The resulting poor motor control means difficulties carrying out daily tasks. The most common treatment for CP is physiotherapy, focussing on strengthening muscles through repeated exercises. However, there are also physical therapies that have been used to promote neuroplasticity by learning movements through repeated processes. The use of therapies like DBS or TMS in conjunction with such physical therapies could prove immensely beneficial in improving and prolonging positive treatment outcomes for children with CP.

Because the paediatric brain is so plastic, treatments that promote neuroplasticity are most effective in paediatric cases. A study on the effects of rTMS on paediatric cases of spastic CP showed improvements in gross motor function[1]. By utilizing treatments promoting neuroplasticity, the function of the damaged regions of the motor cortex can be done by other, undamaged regions of the brain (through compensatory masquerade), resulting in motor gain and, improvements in the quality and control of movements. The motor gain recorded by the study also reported an improvement in sitting functions. This is especially beneficial to children with CP because it lessens the need for restrictive seating systems in their wheelchairs and enables them to have much more independence throughout their lives: for example, toileting becomes much easier. The improvement in fine motor skills recorded by the study enables improvements in skills such as writing, personal hygiene and eating, meaning positive effects on the quality of life of the patients in the study.

A recently published[2] paper on the use of targeted radiofrequency therapy in the treatment of CP patients focussed on using specific wavelengths of radio waves to activate neural progenitor

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[1] Gupta, M, Rajak. B, Bhatia. D Mukhgerjee. A, (2016). "Transcranial Magnetic Stimulation Therapy in Spastic Cerebral Palsy Children Improves Motor Activity." *Journal of Neuroinfectious Diseases. 7. 1-4. 10.4172/2314-7326.1000231. [*online] Available at: https://www.researchgate.net/publication/311100101_Transcranial_Magnetic_Stimulation_Therapy_in_Spastic_Cerebral_Palsy_Children_Improves_Motor_Activity (Accessed 30th April 2024)

[2] GZ Module Pages. (n.d.). "NeuroCytonix Completes Clinical Trial of its NeuroCytotron Treatment of Cerebral Palsy." [online] Available at: https://members.mdtechcouncil.com/member-news/Details/neurocytonix-completes-clinical-trial-of-its-neurocytotron-treatment-of-cerebral-palsy-144904 (Accessed 30 Apr. 2024).

cells, which have the ability to divide a limited number of times to produce glial and neuronal cell types. This accelerates the process of neuroplasticity by providing new pathways for neural connections to form, enabling the goal of improving motor and speech function to be achieved through alternative pathways, bypassing the damaged region of the motor cortex.

Using treatments aimed at promoting neuroplasticity can be beneficial in treating CP, particularly at a paediatric level because the brain is in such a plastic state at this stage of development. By applying neuroplasticity to the treatment of brain damage, the process of learning motor function can be accelerated, especially when used in conjunction with physical therapy.

Though the applications of neuroplasticity are more evident in paediatric cases because of the brain's plastic state during childhood, the adult applications of neuroplasticity in treating neurological conditions are just as important. Treatments like TMS and DBS have been used in the treatment of chronic psychological conditions, proving especially effective when used in conjunction with talk therapies.

The psychological effects of anxiety, depression and other mental illnesses may be rooted in the physiological impacts of stress. In patients who faced chronic stress and depression, suppressed levels of neurogenesis (the formation of new neurons) and formation of glial cells (which have a role in synaptic transmission) has been observed[3]. Suppression of such processes can lead to a reduction in the formation of new synapses, resulting in reduced neuroplasticity. High and prolonged levels of stress have also been linked with reducing numbers of dendritic spines, reducing the numbers of synapses between neurons and therefore, neuroplasticity. Stress has

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[3] Patel. K, Kshirsagar. S. V, Deshmukh. A. H, (2023) "Neuroplasticity and Mental Health: Harnessing Brain Adaptability for Therapy", [online] *Journal for ReAttach Therapy and Developmental Diversities*, 6(1), pp. 756–761. Available at: https://jrtdd.com/index.php/journal/article/view/2016 (Accessed: 30th April 2024).

also been linked with excessive neural activity in the amygdala[4], the area of the brain responsible for emotional expression, this is caused by maladaptive plasticity. This causes intense responses to fear and stress, worsening the anxious behaviours exhibited by such patients. In chronic mental illness maladaptive plasticity can occur, resulting in the recurrence of symptoms, such is the case with excessive activity in the amygdala in anxiety patients. In patients with PTSD a reduction in the volume of hippocampi has been observed. This can lead to enhanced avoidance behaviours. 'Stress hormones' such as adrenocorticotropic hormone (ACTC) have also been linked with altering the function of the brain's neural network, resulting in behavioural changes. The long-term effect of acute stress includes dysregulating synaptic plasticity, which disrupts the normal neuroplastic mechanisms in the brain, possibly causing long term symptoms of chronic anxiety and depressive disorders. Seemingly, neuroplasticity and the disruption of mechanisms responsible for forming neuroplastic pathways are key factors in causing many mental illnesses. By applying knowledge of neuroplasticity to the development of new treatments for mental illnesses, we can effectively treat both causes and symptoms of such conditions.

Utilizing treatments that promote neuroplasticity could lead to the reversal of symptoms of some neurological conditions. Such treatments include Transcranial Magnetic Stimulation (TMS) and Deep Brain Stimulation (DBS). TMS causes an increase in the activity of neurons and promotes neurogenesis. In a study on DBS in the treatment of anxious behaviours in rats, dendritic plasticity was observed. Both treatments show an increase in neuroplasticity, leading to potential applications in the treatment of the neurological conditions outlined previously. By promoting neuroplasticity, TMS and DBS can restore normal neural function, reducing maladaptive plasticity by promoting the formation of new synapses and increasing neural

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[4] Wang. F, Pan. F, Shapiro. L. A., Huang. J. H, "Stress Induced Neuroplasticity and Mental Disorders", [online] *Neural Plasticity*, vol. 2017, Article ID 9634501, 3 pages, 2017. Available at: https://doi.org/10.1155/2017/9634501 (Accessed 30th April 2024)

activity, alleviating symptoms of mental illness. Harnessing the neuroplastic nature of the brain, particularly the amygdala, can help reduce the symptoms of stress, depression and anxiety and invoke more control in response to stressful stimuli from patients. Treatments promoting neuroplastic pathways in patients with PTSD can help to restore the normal function of the hippocampus[5], reducing avoidance behaviours and reducing symptoms of PTSD. This is an example of map expansion neuroplasticity.

The effectiveness of treatments for mental health disorders that target neuroplasticity is evident through the study of TMS in the treatment of major depressive disorders (MDD). TMS was found to be especially effective in treating treatment resistant depression. With fewer side effects and a shorter course of treatment than many antidepressant drugs, the effects of TMS on patients with MDD was overwhelmingly positive[6]. A study by the American Journal of Psychiatry concluded that 'TMS shows promise as a novel antidepressant treatment.' In the same study, TMS was seen to have increased the release of dopamine in the pre-frontal cortex, again, beneficial to reducing the symptoms of MDD. Low dopamine levels can lead to reduced synaptic activity, leading to low motivation and low mood. By using TMS as a treatment for chronic mental health conditions, treatment courses can be less aggressive, and recovery can be successful over a shorter period of time.

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[5] Thiel, E, (2019) "How to Promote Neuroplasticity Following Trauma" *Counsellor Education Capst ones. 113.* Available At: https://openriver.winona.edu/counseloreducationcapstones/113 (Accessed 30th April 2024)

[6] Albert PR. (2019) "Adult neuroplasticity: A new "cure" for major depression?" [online] *Journal of Psychiatry and Neuroscience*. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6488487/ (Accessed 30th April 2024)

By using treatments that promote neuroplasticity to treat chronic mental health conditions, patients are exposed to fewer side effects than faced when taking antidepressant drugs. Treatments are also non-invasive and highly effective, especially when used in conjunction with talk therapies or over a longer period, for example, repetitive TMS. By using rTMS, therapies are repeated over a longer course of time, improving treatment outcomes. It is evident that many common psychological issues have a physiological basis, rooted in the disruption of neuroplastic mechanisms. By utilizing treatments that promote neuroplasticity, the symptoms and impacts of such conditions on the patient can be decreased[7].

Following traumatic brain injury or a stroke, often a patient must relearn motor skills. This is a long, gruelling process and often involves intensive rehabilitation therapy. Neuroplasticity can improve motor and cognitive functions by forming new neural pathways around regions of damaged brain tissue. By applying knowledge of neuroplasticity to the treatment of such brain damage, the process of rehabilitation can be accelerated, and treatment outcomes improved.

In patients with traumatic brain injuries (TBIs) or in cases of brain damage, whole areas of the brain can be affected, causing disruption to motor and cognitive functions. By utilizing treatments that promote neuroplasticity, TBI patients can relearn neurological functions. During childhood, the brain is at its most plastic. In paediatric cerebral palsy cases TMS has been used to promote neuroplasticity so that patients can improve their motor function, despite their damaged motor cortex. Based on similar principles to TMS, a treatment based on using targeted radio frequency therapy to activate neural progenitor cells has recently been developed and has undergone its first clinical trial on CP patients. TBIs and CP are incurable, but

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[7] Falowski SM, Sharan A, Reyes BA, Sikkema C, Szot P, Van Bockstaele EJ. (2011) "An evaluation of neuroplasticity and behaviour after deep brain stimulation of the nucleus accumbens in an animal model of depression." [online] *Neurosurgery* Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707959/ (Accessed 30th April 2024)

what all of treatments have in common is the role neuroplasticity plays in the treatment and recovery from such conditions, by promoting the formation of new neural pathways some cognitive and motor function can be regained and improvements in the patient's condition are possible. The successful application of treatments promoting neuroplasticity in the treatment of paediatric CP, suggests its potential success in treating other forms of brain injury such as TBIs.

Traumatic Brain Injuries can result in many different symptoms depending on the location of the damage, but often results in cell death and gliotic scar formation which can result in the loss of speech and motor function. By using treatments like DBS and TMS to promote neuroplasticity, new neural pathways can form around the region damaged by the TBI, allowing patients to regain some motor and speech function. Similar principles are already commonly used in rehabilitation therapy, whereby relearning actions repeatedly means compensatory masquerade[8] can occur, forming a new neural pathway resulting in regaining some motor or speech function.

So, by utilising treatments promoting neuroplasticity in the treatment of adult brain injuries, especially when used as well as rehabilitation therapy, patient outcomes improve, and patients can relearn motor and cognitive skills more effectively.

By applying understanding of neuroplasticity to diagnostic methods, treatment plans can be effectively tailored to individual patients. The use of brain mapping of neuroplastic potential can offer accurate prognosis and tailored treatment following neurosurgery or brain injury.

Brain mapping has been used in many ways in the diagnosis of neurological conditions: for example, in allowing a doctor to understand the location of a seizure in the brain, as well as allowing neuroscientists to understand the function of distinct parts of the brain. By mapping

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[8] Levine. C. (2019) "Cross-modal plasticity". [online] *Encyclopaedia Britannica*, Available at: https://www.britannica.com/science/cross-modal-plasticity. (Accessed 30 April 2024.)

neuroplastic potential, areas with high and low plasticity can be identified, in turn, allowing the region of the brain worst affected by a specific psychological condition or brain damage to be identified. It can also allow for the investigation into how brain tumours affect their surrounding tissues. Neuroplastic Potential Mapping allows for a more accurate prognosis to be made, in turn leading to the development of more effective treatment plans.

Neuroplastic Potential Mapping has been used in the cases of glioma patients. Patients were mapped before and after surgery to remove the glioma to investigate neural reorganization after the tumour's removal. This increased the scientific understanding of how such a tumour had caused neurological change and the effects that such changes could have on the patient.

This method of mapping has also been utilized in predicting outcomes and giving accurate prognosis to TBI patients. Neuroplastic Potential Mapping revealed elevated levels of cortical plasticity in the cortex and low levels in the connective tracts. This allows for predictions of recovery time and the extent of recovery in TBI patients as well as improving the care of TBI patients, through specific care plans created by understanding the prognosis of the patient.

By using Neuroplastic Potential Mapping, accurate prognosis can be delivered to patients, also allowing for the caregiver to accurately make a care plan based off the prognosis. This can improve outcomes in the long term by leading to a much more effective treatment program for TBI patients. Furthermore, by understanding how gliomas and other brain tumours interact with the brain tissue surrounding them, we can better understand how to treat them with minimal neurological side effects in the future.

In conclusion, by applying our knowledge of neuroplasticity to the treatment of neurological conditions, both psychological and physiological, we can improve the prognosis and treatment outcomes of patients with such conditions. In the cases of patients with mental illnesses such as MDD or anxiety disorders the promotion of neuroplasticity using Transcranial Magnetic Stimulation and Deep Brain Stimulation can return normal neurological function where neural activity in the brain has been previously dampened. This allows the treatment of symptoms effectively and at an accelerated pace by promoting synaptic formation, thus, resulting in the restoration of normal behaviour sooner. In cases of Traumatic Brain Injuries, treatments promoting neuroplasticity allow the patient to regain motor and speech function much sooner than using rehabilitation therapy alone. Similarly, in cases of paediatric cerebral palsy TMS improved gross motor function when used in conjunction with physiotherapy. Finally, the mapping of neuroplastic potential across the brain allows for accurate prognosis and personalized treatment plans based off such prognosis. By utilizing therapies targeting the promotion of neuroplasticity and the restoration of normal neural activity by plastic pathways treatment is accelerated and more effective. TMS is non-invasive and DBS, though requiring surgical access, is minimally invasive. And both have far fewer side effects than traditional treatments such as antidepressants. The use of such treatments that are based around the principle of neuroplasticity offer an alternative treatment of neurological issues, through the medium of a minimally invasive, accelerated treatment program. Such applications of the understanding of neuroplasticity offer an exciting future to the treatment of neurological conditions.

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