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The Implementation of Memantine for Recovering Stroke Patients

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Introduction

Stroke is the fourth leading cause of death worldwide. It is caused by a blood clot or a ruptured artery in the brain. Following stroke onset, 70%-88% of patients have motor dysfunction. Rehabilitation programs aim to combat this motor deficit through repetitive tasks designed to guide the brain to adapt to new movements and gain muscle memory in those movements. Rehabilitation is strongly dependent on the brain's plasticity, which is enacted through increased levels of brain-derived neurotrophic factor (BDNF). BDNF has been proven to be increased through aerobic exercise, a common element found in rehabilitation programs. Memantine, an Alzheimer's drug tested in rats regarding motor function, is a viable drug to increase plasticity. In several rat models, Memantine was proven to increase cognitive function and BDNF levels in the brain, which is vital for the recovery of stroke patients. However, the drug is still only used to treat Alzheimer's patients. So, by understanding the relationship between time, exercise, plasticity, and recovery, Memantine can be introduced and implemented in recovery programs for stroke patients.

4th
Stroke is the fourth leading cause of death worldwide

70%-88%
The percentage of stroke patients that suffer from motor dysfunction post-stroke onset

87%
Cases of ischemic strokes in the US

13%
Cases of hemorrhagic strokes in the US

Objectives

The two main objectives of this study are:

1. To understand the relationship between factors such as time, exercise, and plasticity to refine existing rehabilitation treatments for recovering stroke patients
2. To introduce Memantine, a drug commonly used for Alzheimer's disease, as a new addition to stroke rehabilitation programs

Methods

A compilation of expert opinions on stroke recovery, rehabilitation programs, brain plasticity, and neuronal regrowth was examined, in addition to analyses of case studies relating factors such as time, and physical activity to neuronal regrowth and adaptation. The literature analyzed includes studies from the *Journal of Neuroscience, Journal of American Medical Association,* and the *Journal of the American Physical Therapy Association* .

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Results

Rehabilitation Programs

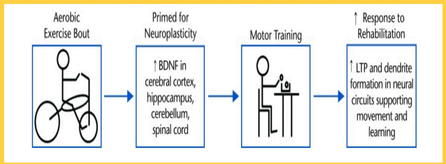
- Previous studies have proven that rehabilitation procedures increase cellular proliferation and dendritic growth. With the cellular proliferation comes the creation of new neurons and neuronal pathways. The new neurons allow the brain to be plastic and adapt to new environments and thus allow recovering patients to regain their lost motor functions and fix their motor impairment.
- The key to neurorehabilitation of the brain after a stroke is repetitive tasks that are similar to the patient's everyday movements. The tasks are designed in this method so that patients can concentrate and gain practice in the movements that are most important in their day-to-day life. The application of their rehabilitation training with practical tasks creates stronger muscle memory than if the training was done by itself.

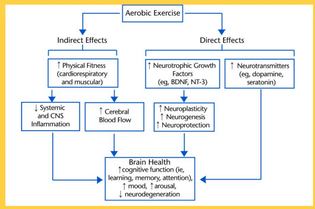
Time

- The length of time in which the brain is plastic differs slightly for every patient. However, there is an average period of time known as the critical period in which the adult brain's plasticity is at its highest.
- Certain studies state that the stroke recovery is at its highest in the first six-ten weeks after stroke onset. Others argue that programs started within the first 100 days produces the same results no matter when the patient began rehabilitation within the 100-day period.
- But, there is a consensus on the fact that the brain has a critical period within which treatment must be completed.

Physical Activity

- BDNF belongs to a family group of proteins that is responsible for neuroprotection, neurogenesis, and neuroplasticity. It has been noted as a key mediator for motor learning and rehabilitation after a stroke occurrence, and is essential for long term memory, learning, and memory formation.
- Physical activity has a positive effect on the brain regarding plasticity and cognitive functions. The manner in which aerobic exercise affects BDNF production is by indirectly altering molecular signaling pathways that act directly on the central nervous system, specifically, in the hippocampus, cerebellum, cerebral cortex, and spinal cord.
- To affect BDNF levels, aerobic exercise sessions should be more than 30 minutes at a maximum of 70% heart rate, four times a week, and there must be a combination of aerobic and resistance exercises
- In addition, the exercise must be done in close proximity with a rehabilitation task frequently in order to make the changes more permanent and effective.



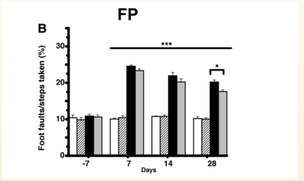


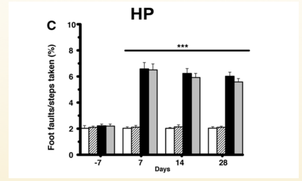
Combination Treatments

- Since neurological diseases and conditions have common factors underlying their symptoms and outcomes, combination therapies including exercise and drugs that affect growth factors for compounds such as BDNF provide a more successful recovery for patients
- Memantine has the capacity to improve and restore the levels of neurotrophins that affect motor functions, lower deficits and increase cognitive ability, while also increasing the synaptic plasticity of the brain.

Memantine

- In a beam crossing test, Memantine decreased the time it took for the rat to cross the beam when compared with the control group.
- In the same study, Memantine also increased the time during which the rats could hang on to a rod in the horizontal grid test when compared to the control group.
- In a grid walking test, the number of foot faults out of total steps was measured in a non-Memantine group of rats, and Memantine injected group of rats. The results showed that the Memantine injected group of rats had a lower number of foot faults out of total steps taken.





Further Studies

Before Memantine can be administered as an official treatment, further studies must be conducted regarding:

1. The critical period following stroke onset to better understand the relationship between time and brain plasticity
2. Physical activity and Memantine to establish a baseline combination therapy for the average stroke patient

Conclusions

- The checklist for the best chance of higher BDNF levels is a relatively simple list to complete. The tasks are simply aerobic exercise at a 70% heart rate for four days a week. By following this list, patients have higher BDNF levels. However, patients are not always capable of meeting these requirements due to emotional, mental, or physical capacity or ability. Without these requirements, their brain plasticity levels would not be high enough to train the brain to learn new skills.
- To counteract this, Memantine can be administered to the patient to increase their BDNF levels in order to promote plasticity and kick-start rehabilitation training. Memantine can be used as an alternative to the exercise prior to rehabilitation tasks, or if needed, in conjunction with the exercise.
- Patients that are able to perform some of the aerobic exercise can use Memantine as a booster to increase their BDNF levels to an adequate amount. Patients that are incapable of performing any exercise may take Memantine as an alternative treatment prior to their rehabilitation training.

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