Investigating Methods to Promote Neuroplasticity and Brain Regeneration following a Stroke

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Abstract

Stroke is one of the most common causes of physical and mental disability and is a ubiquitous neurological impairment throughout the world. In the United States, an individual is impacted by a stroke every 40 seconds. While there currently are FDA approved therapies, such as clot-dissolving anticoagulants and procedural thrombectomies, or the process to medically remove a clot, they only aim for restoring the proper blood flow to the affected area rather than providing an overall solution to prevent further damage.This highlights the necessity for therapies that not only restore blood flow, but also promote neuroplasticity, or the brain's ability to reorganize and recover itself by repairing broken connections. The medical field could improve stroke treatment by focusing on the promotion of neuroplasticity. This paper explores a multitude of therapies designed to promote neuroplasticity after a stroke from different categories: cognitive, physical, and pharmacological.

Keywords: stroke, neuroplasticity, ischemia, physical therapy, cognitive therapy, pharmacological therapy, synaptic plasticity

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STROKES

Ischemic strokes, which make up 87% of stroke cases, occur by an obstruction in a cerebral artery supplying blood flow to a particular region in the brain (Virani et al., 2021). This obstruction can be divided into two types, thrombotic and embolic. Thrombotic strokes occur from the emergence of a blood clot, or thrombus, in one of the arteries that supplies blood to the brain. Thrombotic strokes are frequently associated with atherosclerosis, a chronic inflammatory condition causing plaque buildup in the inner lining of the arteries, leading them to thicken and harden. Over a duration of time, this results in the restriction of blood flow and oxygen to the brain. Thrombotic strokes are primarily observed in older individuals, often those with higher cholesterol levels, causing them to have symptoms that develop over time. Thrombotic strokes are usually preceded by a series of transient ischemic attacks (TIA). These "mini strokes" serve as a precautionary harbinger of the increased stroke risk to follow. (Hui et al., 2024) Embolic strokes transpire when debris, or a sizable blood clot (i.e., embolus) forms in a location other than the brain and travels through the bloodstream to create a blockage in a cerebral artery. Embolic strokes often occur within patients associated with conditions such as atrial fibrillation, or an abnormality in the heart beat, leading to arrhythmia, causing the embolism to form. (Hui et al., 2024) When formed, they travel rapidly and suddenly to the brain, usually without any sort of warning. Embolic strokes are the most common in patients following heart surgery or with pre-existing conditions (Velez et al., 2020).

Hemorrhagic strokes occur when a blood vessel in the brain ruptures, causing it to bleed, or hemorrhage. The brain and the surrounding tissue do not receive the amount of oxygen that they need, which causes the cells to die. This type of stroke makes up the other 13%, making it less common than ischemic strokes, but is considered critical, and also divided into two subcategories ((Martin et al., 2024). Intracerebral hemorrhage (ICH) pertains to direct bleeding into the brain tissue. The main cause of ICH is hypertension, or the condition of incredibly high raised blood pressure. This extreme pressure on the blood vessel walls causes them to rupture, therefore causing a brain bleed (Tenny & Thorell, 2024). Hemorrhaging usually happens without any warning, with the patient experiencing a set of symptoms that deals with the expeditious deterioration of the brain function and movement. Subarachnoid hemorrhage is caused by bleeding in between the brain and the membranes in the meninges, the layers that cover and protect the brain and the spinal cord. This brain bleed is generally caused by an aneurysm, or another form of head trauma (Tenny & Thorell, 2024). Individuals who suffer from subarachnoid hemorrhage generally complain about a sudden, intense headache, followed by loss of upper body movement and sometimes their consciousness as well.

SYMPTOMS AND TREATMENTS

Symptoms and treatments vary by each individual case of stroke, but they can primarily be identified by the following common symptoms. Patients may experience difficulty speaking or understanding the speech of others. The Broca's area of the brain is responsible for language and speech production, so strokes affecting this area can cause the lack of speech production (Acharya & Wroten, 2023). Various parts of the body can suffer from paralysis, or the loss of movement in a body part, such as the arms or legs. Patients can suffer not only motor deficits, but sensory ones also, including the loss of touch or other sensations (Price et al., 2018). Along with the loss of mobility, stroke patients can have difficulty maintaining their balance and walking in a regular manner. Strokes can also cause changes in cognitive function in the brain, such as the loss of memory, difficulty following directions, and memory loss. Behavioral patterns can change from person to person, but studies have shown that there also can be immense personality shifts, due to damage in the frontal lobe (Price et al., 2018).

Treatment options for ischemic strokes include both pharmacological and surgical interventions. These involve a combination of medical therapies and medicine aimed to restore neural connections and create pathways for blood flow to continue again. The main treatment for an ischemic stroke is a drug called tissue plasminogen activator (tPA). tPA is a thrombolytic medicine given intravenously to eradicate and dissolve pre-existing blood clots in the brain that caused the stroke. The many contraindications of tPA make it difficult to work in the same manner for each individual. To achieve the best results, the medicine must be administered within a 4.5 hour time window after the stroke symptoms begin, and it cannot be given to patients with a history of excessive bleeding, uncontrolled diabetes, uncontrolled hypertension, or in patients that have an extremely large blood clot (Barthels & Das, 2020). In addition to tPA, there are other surgical procedures such as a mechanical thrombectomy, which involves the insertion of a catheter into the artery to physically remove the clot from the brain. These methods can drastically improve a stroke patient's life, but treatment is not universal. A plethora of factors, involving a patient's age, time to treatment after a stroke, and the severity of the stroke change the results and effectiveness of the treatment. Older patients, especially those who wait before seeking the treatment, are at higher risk for complications and for the medicine to not be able to help them (Szelenberger et al., 2019). tPA is currently the singular FDA approved drug administered to treat ischemic stroke, and while it can prove difficult at times for the individuals not meeting the criteria, it is effective at dissolving the blood clots and promoting healthy blood flow to the brain.

NEUROPLASTICITY

Neuroplasticity refers to the process by which the brain reorganizes and adapts to a new structure and function after the brain undergoes an injury, or as a response to stimulation (Szelenberger et al., 2019). The nervous system has the capability to change its activity and response by reorganizing its structure and function, allowing it to adapt and learn new information. The first 48 hours following a stroke is when the cells undergo death and deal with the loss of connections and neurons, but inflammatory mechanisms and the ischemic cascade can cause additional cell death for days to weeks post-stroke (Puderbaugh & Emmady, 2024). To compensate for this cell death, neuroplasticity can allow the brain to establish new neural connections and create new pathways for neurons to activate. Post-stroke, the cells can begin to form new connections and continue to reorganize during the subsequent weeks and months.

On a cellular level, neuroplasticity involves changes to dendrites and axons that form synaptic connections between neurons. Dendrites are structures of neurons that receive all the information from axonal signals. Axons are long fibers that transmit and send those signals, which the dendrites receive, and pass on to the next axon in a neuron. Dendritic sprouting and arborization involves the growth of dendrites attaching damaged neurons to more intact neurons to form a new pathway for a connection. This process helps to facilitate neuroplasticity through fostering and establishing new connections. Similar to dendritic sprouting, axonal sprouting occurs when finer nerve fibers grow out of already intact neurons, and those fibers connect to other neurons, forming another new connection. By creating new pathways, the brain can begin the process of rebuilding after a stroke (Benowitz & Carmichael, 2010). A third way in which the neurons exhibit neuroplasticity is in synaptic plasticity, which refers to the ability of the neurons to modify the strength of their connections. Post-stroke, neurons can strengthen their connections in reaction to the decreased neural activity, aiding in restoring the brain's neurological functions.

Beyond the cellular level, this neural activity can result in larger scale restructuring, strengthening, development, and recovery in the regions of the brain. In the cortical level of the brain, several regions of the brain can recover after a stroke. The somatosensory system, the region of the brain responsible for processing information about the body and its surroundings, can undergo several changes after a stroke. Post-stroke, the somatosensory system has been observed to strengthen its connections to other regions of the brain. Touch sensation improves due to these strengthened connections in the months following a stroke (Lv et al., 2022). The somatosensory system also reorganizes itself in order to promote the processing of sensory stimuli throughout the body, as this is often lost as a result of a stroke (Barthels & Das, 2020).

A significant aspect of neuroplasticity vital to recovering after a stroke is the improved structural integrity of the corticospinal tract. The corticospinal tract is the major neural pathway that transmits motor signals from the brain to the spinal cord. Therefore, damage to the corticospinal tract can significantly impact motor movements as well as result in paralysis (Velez et al., 2020). After the stroke, there can be significant strengthening and regrowth of the damages to the corticospinal tract. Also at the cortical level, interhemispheric functional connectivity can be restored post-stroke (Marín-Medina et al., 2024). Strokes often disrupt connections between the left and right hemispheres of the brain, which interrupts motor, cognitive, and sensory functions. A vital part of the brain's recovery after a stroke is the redevelopment of the cross-hemisphere connections. Altogether, neuroplasticity in the brain and its development after a stroke is crucial in restoring functions like motor control, and even walking and talking, that may have been lost during a stroke.

THERAPIES TO PROMOTE NEUROPLASTICITY

Neuroplasticity significantly helps the brain to reorganize and recover post-stroke, and there are various ways that healthcare providers can stimulate neuroplasticity. While there are many therapies that may promote neuroplasticity following injury or stroke, this review will discuss several interventions that fall into three categories: cognitive, physical and pharmacological.

COGNITIVE

Cognitive therapies, including cognitive behavioral therapy (CBT), and cognitive restructuring, are modeled to enhance and improve brain function by stimulating the mind via modifying thought patterns and behavioral changes. Cognitive therapies can lead to significant changes in a brain's structure or function. By investing in these therapies, a patient can increase connectivity in the regions in the brain that handle cognitive control, such as the prefrontal cortex and the anterior cingulate cortex, which then subsequently allows for positive changes throughout a person's cognitive thinking skills.

Brain computer interface (BCI), is a significant, computer-based innovation in the field of stroke recovery. It involves linking neural activity to a device that can acquire brain signals and convert them into commands which allow the interface to complete movements that are connected to the patient's brain. BCI can be categorized into two classifications, invasive, and non-invasive. Invasive means that the electrodes are placed directly onto the scalp to receive the signals from the neurotransmitters. Non-invasive BCI is conducted through electroencephalogram (EEG) signals. After the signals are passed from the brain through the computer, BCI allows robotic motorized parts to be able to move through the signals, and the patient can move their robotic hand or leg body part. Unlike the robot assisted therapies, BCI also allows patients to do self-directed movements based on the body part their mind is thinking of to move (Dobkin & Dorsch, 2013)

PHYSICAL

Physical therapies can play a crucial role in a patient's journey to rehabilitation. After a stroke, regaining muscle movement or relearning how to perform basic bodily functions can be a physically taxing task, but these therapies are specifically designed to promote neuroplasticity in the brain by improving a patient's motor functions (Dobkin & Dorsch, 2013). Aerobic exercises, such as biking or walking, specifically on an exercise bike or treadmill, can prove to be effective physical strategies for patients to regain motor strength and skills, while promoting neuroplasticity (Hill et al., 2023). These strategies offer lightly-paced exercises that are tailored towards rebuilding and working on regaining function in legs, arms, and other body parts that may have been impacted after suffering from a stroke. The neural circuits that are responsible for movements in the body are activated through repetitive and rhythmic exercises, such as walking and cycling. This furthers a patient's ability to regain motion, work on motor skills, and stimulate the brain to engage in cortical reorganization.

In the initial stages of this recovery, patients may not be able to keep up for long periods of time, enabling them to take shorter approaches with the help of physical therapists, mentors, and support groups. Group therapy with circuit training has been proven to be a reasonable approach in order for patients to regain their lost mobility (Stephan & Pérennou, 2021). These support groups can range from beginner workouts, to gradually increasing in intensity based on the initial benefits of neuroplasticity. Physical training can improve motor function over time by enabling neural synaptic connections and increasing intensity of the workouts (Hill et al., 2023). By participating in aerobic exercises, patients can promote and improve blood flow to the brain, which further promotes the release of neurotrophic factors. By completing these exercises, survivors of stroke can generate neuroplasticity and improve their motor ability (Dobkin & Dorsch, 2013).

Along with bodily motor functions, speech therapy can play a crucial role in improving a patient's ability to regain speech movement, especially those who are affected by aphasia, or a speech impediment. There are special speech-language pathologists that work with patients in order to stimulate the brain by working on language exercises that engage neural pathways. By performing these exercises, the pathologists can help patients target the affected and damaged areas in their brain involved in language and speech processing. One specific method that these pathologists use is melodic intonation, or the process of patients speaking through a series of rhythms and melodies. Melodic intonation enriches the left hemisphere of the brain, which is involved in speech production. By strengthening this side, the brain can now form new synaptic connections and neural pathways, thus helping the patients recover (Dobkin & Dorsch, 2013).

Robot assisted therapies (RAT) have also been proven to assist patients in their journey to recovery. RAT involves the use of robotic devices, such as a faux hand or body part exoskeletons to aid in repetitive, rhythmic patterns that help rebuild motor function in upper and lower limbs (Marín-Medina et al., 2024). Patients may struggle to move their limbs without assisted support, so the robotic aid helps them monitor the level of intensity and movement a patient can perform. Over a duration of time and practice, full function can be regained (Marín-Medina et al., 2024).

PHARMACOLOGICAL THERAPIES

Pharmacological therapies have proven to assist in the path to stroke recovery, specifically in the early stages. Tissue plasminogen activator (tPA), is an FDA approved drug which facilitates the process of internally breaking down blood clots. Within a 4.5 hour time window following a stroke, tPA helps to restore blood flow to brain regions affected by a stroke, thereby limiting the risk of damage and functional impairment (Hacke et al., 2008). By removing the blood clots, or thrombus, the blood flow is able to be restored, thus preventing expansion of the damage to the rest of the brain. By administering the medication in the span of 4.5 hours post-stroke, it increases the chance to fully repair the brain and promote the highest amount of neuroplasticity (Marín-Medina et al., 2024). There has yet to be pharmacological therapies to help stroke patients in long term recovery that are fully functional.

Following a stroke, these exercises and therapies work best to promote neuroplasticity when patients start doing them as soon as possible, maximizing efficiency. Everyone’s physical and mental capability differ, so the patients who regularly complete their therapies and are physically or mentally able to work on their progress show more signs of recovery than those who are limited by a number of factors influencing their decisions, such as age, reaction to the medicine, and both physical and mental capability (Yadav et al., 2022).

CONCLUSION

Stroke continues to be a leading cause of physical and mental disability in the United States, which calls for innovative and novel therapies in order to treat it, ranging from CBT, to physical therapy and melodic intonation. These therapies, varying in intensity and efficacy, can improve a patient’s motor and cognitive function. In the future, the field of stroke can improve through research on more innovative and creative approaches that center around neuroplasticity, and generation of neuroplasticity. Although current therapies seem to be having a positive effect on some individuals, researchers can focus on developing treatments that are beneficial to all ages and mental/physical capability. In time, as our understanding of stroke research and neuroplasticity expands, our options for treatment can also grow.

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