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BIOCHEMICAL MECHANISMS UNDERPINNING PHYSICAL THERAPY INTERVENTIONS IN STROKE RECOVERY

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ABSTRACT

This review explores motor function recovery after stroke, focusing on biochemical pathways and the role of physical therapy. Stroke, resulting from disrupted brain blood flow, causes cellular damage involving mitochondrial dysfunction, oxidative stress, and energy metabolism impairments. Topics include stroke types, risk factors, cardiac effects, and the gut-brain axis in recovery. Emphasis is placed on neuro-protective strategies, neuroplasticity, and physical therapy's role in enhancing recovery and brain function. Components of stroke rehabilitation, including the phases of recovery, rehabilitation modalities, and the influence of diet and nutrition, are discussed in the context of maximizing recovery. Furthermore, neuropsychiatric complications, patient engagement, and self-management strategies are highlighted. We also examine the role of neuroimaging in stroke rehabilitation and explore innovations and future trends in stroke recovery therapies.

INTRODUCTION:

According to the World Health Organization stroke is quickly emerging clinical symptoms caused by a disruption in brain function, persisting for twenty four hours or more or resulting in death, with no obvious cause other than a vascular origin (Ansong, *et al*., 2024). The World Stroke Organization currently aims to reduce the global impact of stroke by focusing on prevention, effective treatment, and comprehensive long-term care (Septianingrum *et al.,* 2024).

Stroke is one of the primary causes of death and disability globally, resulting from disrupted blood flow to a region of the central nervous system (Sahebi *et al.,* 2024). Notably, more than 50% of stroke survivors face difficulties with activities of daily living, as strokes impact individuals in various ways such as dressing, bathing or cooking, and up to 40% rely on manual instruments like wheelchairs after discharge from rehabilitation (Ansong, 2024).

Types of Stroke:

A cerebrovascular accident, commonly known as a stroke, is a neurological impairment caused by various vascular injuries that disrupt brain function (Kakarla, 2024). Stroke is classified into two types based on its pathophysiology, one of which is ischemic stroke, also referred to as a cerebral infarction, which is due to the obstruction of blockage of cerebral artery due to formation of embolus or thrombus and is the most common type of stroke, affecting around 80% of stroke patients (Sahebi *et al.,* 2024). The other type of stroke is a cerebral hemorrhage, which happens when blood vessels rupture, leading to bleeding either inside or outside the brain (Fig: 1).

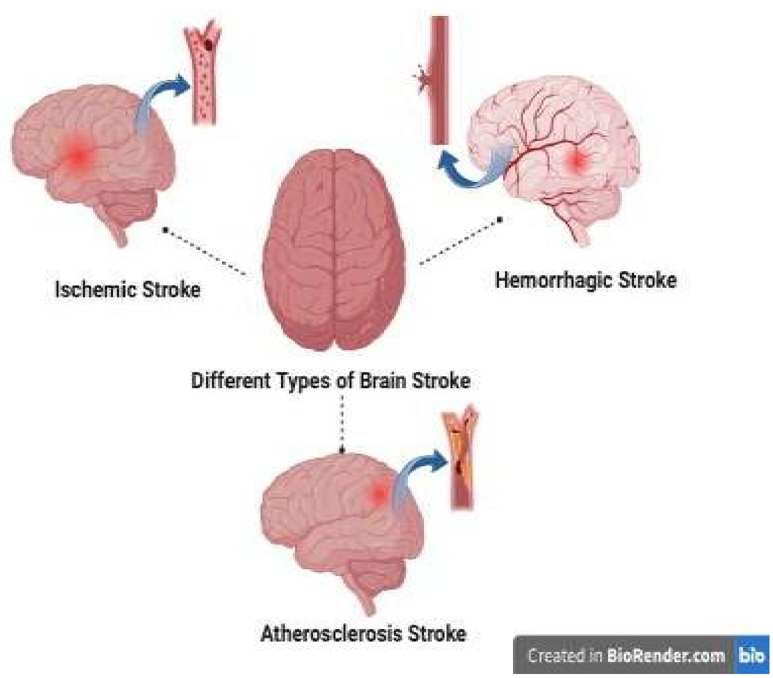

Fig. 1: Representation of two types of stroke based on its pathophysiology (Retrieved from biorender).

Table 1: Types of strokes , their main causes, symptoms and their treatments.

Stroke type	Main Cause	Symptoms	Treatment	References
Ischemic stroke	Large artery atherosclerosis, cardiac embolis	Weakness in arms and legs, blurred vision, dizziness	Fibrinolytic therapy, thrombolytic therapy, endovascular thrombectomy	(Kakarla *et al.,* 2024)
Hemorrhagic stroke	Cerebral amyloid angiopathy, subarachnoid hemorrhage	Severe headache, nausea, lack of consciousness, neck stiffness	AVM removal, Physical therapy	(Picard *et al.,* 2024)
TIA (mini stroke)	Thromboembolism, atherosclerosis	Initial symptoms indicating minor stroke, median pre- stroke, hypertension, vasospasm	TTE, TEE, ICM monitoring, cryptogenic TIA	(Pavan *et al.,* 2024)
Cryptogenic stroke	Atrial fibrillation	No clear symptoms	Same as others	(Lorenz *et al.,* 2024)

Epidemiology and Risk Factors

Nearly 800,000 people in the USA are affected by cerebrovascular accidents, or strokes, each year, making it the leading neurological disorder in terms of burden (Egan *et al.,* 2024). Stroke in young individuals carries significant socioeconomic costs, and patients often face long-term consequences throughout their lives thus quickly recognizing the signs, symptoms, and risk factors of ischemic stroke is crucial for effective treatment and preventing recurrence. Risk factors include non-modifiable factors such as age, sex, and race/ethnicity, as well as modifiable factors like high blood pressure, smoking, poor nutrition, and physical inactivity (Sahebi *et al.,* 2024). Additional risk factors include inflammatory conditions, infections, pollutants, and certain cardiac conditions (Fernandes *et al.,* 2024).

Biochemical Pathways of Injury and Repair

Numerous intricate genetic, molecular, and cellular pathways contribute to stroke (Sahebi *et al.,* 2024). In 'ischemic core', due to vascular occlusion, the ischemic brain tissue is completely cut off from the blood supply. Additionally, there is a significant depletion of ATP and a failure of aerobic glycolysis, which frequently result in irreversible brain tissue damage (Gao *et al.,* 2024). The ischemic penumbra, the area around the core, is distinguished by a marked drop in cerebral blood flow below the threshold (Garcia *et al.,* 2024). During an ischemic stroke, the brain produces free radicals due to a lack of oxygen and nutrients, leading to oxidative stress. Free radicals are highly reactive molecules containing oxygen that can damage cells, proteins, lipids, and DNA (Bernoud *et al.,* 2024). Endothelial cells (ECs), mural cells, astrocytes, immunological cells, and neurons make up the majority of the blood-brain barrier. The BBB serves as a unique microenvironment required for proper brain function and homeostasis. After a stroke, neutrophils are the first immune cells to infiltrate the brain, followed by monocytes and lymphocytes within 48 hours (Oestreich *et al.,* 2024). Blood-brain barrier disruption causes edema and potential hemorrhagic transformation. Macrophages and activated microglia clear debris, releasing proinflammatory substances and cytotoxic agents. Later, repair mechanisms like neuroplasticity and tissue remodeling attempt recovery (Bernoud *et al.,* 2024). The acute phase of stroke activates apoptotic pathways and releases proinflammatory cytokines, such as in caspase-dependent cell death brain (Fig: 2). Neuroplasticity, driven by pathways like BDNF and mTOR, is key for functional recovery after stroke (Taye *et al.,* 2024).

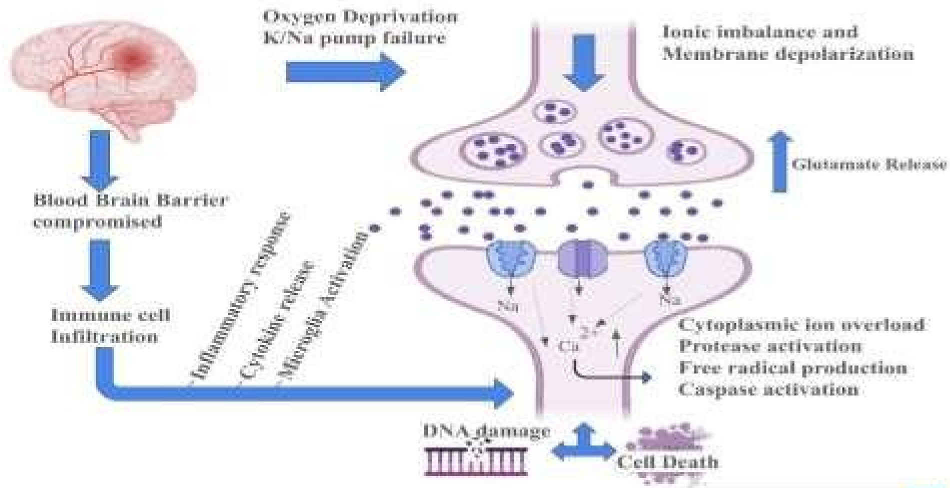

Fig. 2: Diagramatic illustration of the the cascade of events of stroke leading to cell death following oxygen deprivation (Retrieved from biorender).

Cardiac Damage as a Consequence of Stroke

After stroke, cardiovascular problems rank as the second most common cause of mortality (Fu *et al.,* 2024). Stroke-induced cardiac damage can vary from serious problems like heart failure to curable illnesses like NSC (Bernoud *et al.,* 2024). An 'invisible' connection between the brain and heart has been discovered by recent study. Cardiac dysfunctions worsen brain damage and contribute to new brain issues, creating a cycle of impairments. After acute ischemic stroke, stroke patients face a two-way interaction between the brain and heart, increasing the risk of severe cardiovascular complications (Zhang *et al.,* 2024). A study found that systolic dysfunction, linked to one-month mortality, occurred in 340 of 1,020 acute stroke patients. Additionally, 85% of stroke patients showed ECG abnormalities within 24 hours, including ST segment, T wave, or Q wave changes, and a prolonged corrected QT interval, indicating improper ventricular repolarization (Fu *et al.,* 2024).

Energy Metabolism and Recovery after Stroke

Neurological disorders like stroke, ischemia, and Parkinson's disease often disrupt central energy (Bernoud *et al.,* 2024). The brain, which makes up 2% of body weight, uses 20% of the body's total energy. This high energy demand makes the brain vulnerable to disruptions. Stroke-induced disruptions in energy metabolism hinder brain recovery (Gao *et al.,* 2024). Ischemic events reduce blood flow, limiting oxygen and glucose availability for ATP production. This energy shortage impacts neuronal and glial cells, causing dysfunction, injury, and cell death. Overcoming this energy deficit is crucial for restoring normal brain function and preventing further damage (Taye *et al.,* 2024).

Mitochondrial Dysfunction and Oxidative Stress

Mitochondrial dysfunction plays a key role in the energy crisis after a stroke. It produces excess reactive oxygen species (ROS), which reduces ATP synthesis and increases oxidative stress (Taye *et al.,* 2024). This ROS production worsens neuronal damage, triggering apoptosis and autophagy pathways. Oxidative damage and cellular dysfunction hinder stroke recovery. Mitochondrial stress impacts cerebral function and the link between mitochondria and neuro-inflammation are key in stroke pathophysiology (Bernoud *et al.,* 2024).

Impact of Physical Therapy on Energy Metabolism

Energy metabolism has been demonstrated to be positively impacted by physical therapy, which involves both aerobic and resistance training. Additionally, exercise improves cerebral blood flow, which helps oxygen and nutrients reach areas of the brain that are recuperating (Gao *et al.,* 2024). This reduces additional harm and enhances health by assisting in the generation of ATP and the removal of metabolic waste products. Exercise improves outcomes for stroke patients by promoting neuro repair processes that aid in the reconstruction of synaptic connections and hasten functional recovery (Taye *et al.,* 2024).

Electroacupuncture as an Adjunct to Physical Therapy

Electroacupuncture is a form of acupuncture that has demonstrated therapeutic effects in stroke patients. Electroacupuncture is a Korean medicine that combines acupoint stimulation and electro stimulation, allowing controlled, localized treatment with minimal side effects (Taye *et al.,* 2024). Studies show that electroacupuncture preconditioning boosts AMP-activated protein kinase expression and phosphorylated AMPK, reducing TUNEL-positive cells and neuronal apoptosis after stroke. When combined with physical exercise, it creates chronic metabolic stress, enhancing regional cerebral blood flow and metabolic function, which supports recovery (Gao *et al.,* 2024).

The Brain-Gut Relationship in Stroke Recovery

Most of the bacteria in the human body are found in the stomach. A vital component of the intestinal micro-ecosystem, intestinal flora is intimately related to both human health and the emergence of illnesses. Intestinal flora and the host mutually depend on and regulate each other to maintain the balance of intestinal microecology (Gao *et al.,* 2024). The micro biota-gut-brain axis connects the gut and brain through immune, hormonal, and neural signals. Gut micro biota produce molecules that influence brain function, while the brain regulates immune and gastrointestinal processes. The vagus nerve serves as the main communication link between the central nervous system and microbiota (Bernoud *et al.,* 2024).

Gut Microbiota and Disorders Associated with Strokes

Ischemic stroke increases the risk of vascular dementia and vascular cognitive impairment. VCI is linked to endothelial dysfunction, cerebrovascular issues, and atherosclerosis, all influenced by gut micro biota disruption. Components like lipopolysaccharides, trimethylamine N-oxide, and short-chain fatty acids can increase intestinal permeability and activate immune responses, contributing to VCI (Macoir, 2024). Disruption of intestinal flora significantly influences the pathophysiology of ischemic stroke, increasing the permeability of the intestinal and blood-brain barriers. It adds to consequences such as stroke-associated pneumonia in addition to its function in stroke pathology (Nayak *et al.,* 2024).

Physical Therapy Interventions Following Stroke

Strokes remain a leading cause of adult disability, with nearly four out of ten stroke patients requiring a manual wheelchair after rehabilitation discharge and five out of ten experiencing difficulties with daily tasks (Macoir, 2024). After a stroke, other challenges include loss of vision and dysphagia. Enhancing function, encouraging independence, and improving quality of life are the primary objectives of physical therapy in stroke rehabilitation (Sato *et al.,* 2024).

Components of Stroke Rehabilitation

Recovery from a stroke depends on a number of rehabilitation therapies. In order to assist stroke victims regain the ability to do daily activities such as eating, drinking, swallowing, dressing, bathing, reading, writing, and using the restroom, occupational therapy is crucial (Oestreich *et al.,* 2024). A common method used by therapists to assist stroke patients in managing their swallowing difficulties and regaining functional speech is speech therapy. For those with normal cognitive and reasoning abilities who struggle with voice formation or written word comprehension, voice therapy may be beneficial (Egan *et al.,* 2024). Exercises for rehabilitation can encourage oral intake and enhance swallowing skills. Strengthening exercises for the tongue and the muscles used in swallowing are the goals of indirect workouts. Direct exercises include swallowing and swallowing with effort (Macoir *et al.,* 2024).

REHABILITATION PHASES:

Acute Phase

After 3 days, low-intensity therapy was initiated in the ICU or stroke-specialized units. Patients are provided with an overview of the recovery process, encompassing the amount of time, treatment strategy, and expected disabilities (Gaviria *et al.,* 2024). The adverse consequences of extended bed rest and deconditioning can be avoided with early movement and appropriate monitoring. Early rehabilitation initiation during the acute phase has been linked to improved long-term results because it lowers the risk of complications and promotes neuroplasticity (Garcia *et al.,* 2024).

Subacute Phase

The subacute phase occurring after 1–3 weeks post-stroke targets motor, cognitive, and communication recovery, it prevents further complications. Physical and occupational therapy enhance mobility, strength, and daily living skills, while speech therapy addresses communication and swallowing challenges (Briones *et al.,* 2024). As well as preventative care, neuroplasticity therapies, psychosocial support, and caregiver education are vital for fostering recovery, enhancing independence, and improving quality of life (Garcia *et al.,* 2024).

Chronic Phase

Patients were given a home exercise program with instruction on exercise intensity, fall avoidance, posture adjustments, and general health about six months after their stroke. For functional improvement, water-based workouts and community fitness were emphasized (Zhang *et al.,* 2024). According to a study on stroke patients in the chronic stage, upper limb motor dysfunction decreased after 90 hours of physical therapy duration administered over three weeks at five sessions per week (Egan *et al.,* 2024).

PHYSICAL THERAPY MODALITIES IN STROKE REHABILITATION

Non-Invasive Brain Stimulation

While noninvasive brain stimulation targets different parts of the brain, post-stroke cognitive impairment is not well addressed by many treatments. By adjusting brain oscillations and neurotransmitter levels, transcranial alternating current stimulation, a kind of transcranial electrical stimulation, employs low-intensity alternating current to improve synaptic connection and plasticity (Williams *et al.,* 2024). Non-invasive brain stimulation has been shown to improve upper extremity motor disability and involvement in daily living activities (Garcia *et al.,* 2024). Cognitive training with sham or active stimulation targeting the ipsilesional dorsolateral prefrontal cortex using anodal tDCS or theta burst rTMS showed positive results in two 2022 trials with sub-acute stroke patients. This brain region is also a common target in effective depression treatments (Taye *et al.,* 2024).

Vagus Nerve Stimulation

For a person with persistent post-stroke mobility deficits, vagus nerve stimulation greatly increased gait speed and distance traveled within a predetermined time frame when combined with mobility training (Picard *et al.,* 2024). The vagus nerve passes through numerous structures that are essential to human bodily functioning as it travels from the brainstem to the colon. Vagus nerve stimulation uses an implanted or non-implantable device placed on the skin above the nerve. This approach is believed to create a brain environment that enhances experience-dependent plasticity. When paired with complete therapy, VNS showed both immediate and long-lasting benefits on motor function as measured by appropriate scales (Pavan *et al.,* 2024).

Robotic Therapy

Robotic systems have shown progress in helping stroke victims regain their motor and cognitive abilities. When given a comparable treatment dose, large randomized clinical trials have shown that they are equivalent to traditional rehabilitation (Pavan *et al.,* 2024). Robotics in stroke rehabilitation offers benefits like higher exercise intensity, precise recovery evaluations, and a stimulating environment to boost patient engagement (Zhang *et al.,* 2024). A study found robotic-assisted rehabilitation reduced spasticity, improved passive range of motion, and enhanced glenohumeral subluxation measures (Pavan *et al.,* 2024).

Nutrition and Diet's Effect

The basal energy need rises by 7–26% after a stroke, and ischemic stroke patients are most likely to have a hyper metabolic condition (Kakarla *et al.,* 2024). A healthy diet helps manage blood pressure, maintain weight, and lower stroke risk, making it a key preventive measure. Reducing saturated and trans fats, limiting salt, and increasing fruits, vegetables, whole grains, and lean proteins can improve health and reduce ischemic stroke risk. The Mediterranean diet lowers cholesterol, trans fats, and harmful animal fats and is advised for stroke prevention. It gives priority to vitamins, antioxidants, omega-3 fish oil, olive oil, canola oil, and balsamic vinegar. Oral nutrition should begin within seven days after an acute stroke for undernourished or at-risk patients (Pavan *et al.,* 2024).

Blood Glucose Regulation

Hyperglycemia after AIS can worsen outcomes by impairing recanalization, reducing reperfusion, increasing reperfusion injury, and raising the risk of intracranial hemorrhage. Hyperglycemia occurs early in up to two-thirds of ischemic stroke cases during hospitalization (Picard *et al.,* 2024). Since both hyperglycemia and diabetes mellitus are associated with a higher probability of both conditions, better blood sugar control is generally acknowledged as a way to avoid PSCI and dementia. RT combined with aerobic exercise can improve glucose-insulin homeostasis measures in an additive manner. In addition to improving hyperlipidemia and resting blood pressure, resistance exercise also enhances endothelial function (Kakarla *et al.,* 2024).

Omega-3 Fatty Acids and Neuroprotection

Dietary supplements containing PUFAs can be able to control thrombus formation and vascular occlusion. This might reduce the likelihood of stroke (Briones *et al.,* 2024). Additionally, it has been demonstrated that omega-3 promotes neurovascular healing dynamics and brain regeneration, which will eventually enhance neurological function after a stroke (Picard *et al.,* 2024).

Vitamins and Antioxidants

Vitamin C, Vitamin E, and polyphenols (found in tea, nuts, fruits, and vegetables) help reduce oxidative stress by neutralizing free radicals (Teng *et al.,* 2024). High-dose 1, 25-vitamin D3 supplements may reduce brain damage after a stroke. While the exact mechanism is unclear, vitamin D is believed to inhibit the NLRP3-mediated pyroptotic pathway and activate the Nrf2/HO-1 antioxidant pathway (Briones *et al.,* 2024).

Protein and Muscle Recovery

Sarcopenia in stroke patients can be triggered by factors like paralysis, stiffness, inflammation, and metabolic imbalances. Muscle weakening occurs on the non-paralyzed side within a week, while motor unit reduction on the paralyzed side happens around four hours post-stroke (Zheng *et al.,* 2024). Preventing sarcopenia requires targeted rehabilitation with stroke therapy, including intensive gait training, early mobilization, and nutritional therapy to ensure adequate protein and energy intake (Oestreich *et al.,* 2024).

Neuropsychiatric complications

Post-stroke neuropsychiatric complications (PSNCs) result from complex processes involving neuronal cytokines and neurotransmitter systems. Factors like inflammation, HPA axis dysfunction, and mitochondrial dysfunction affect nearly all PSNCs, Psychosis, a potential stroke side effect, is linked to disability and increased mortality (Zheng *et al.,* 2024). Though rare, recent estimates show 4.87% of acute stroke patients experience delusions or hallucinations with poor cognitive awareness. These complications can hinder rehabilitation and physical therapy progress, making it crucial to address them in comprehensive stroke care (Oestreich *et al.,* 2024).

Post-stroke Depression (PSD)

Post-stroke depression affects 18% to 61% of survivors and is linked to functional impairments, including cognitive, balance, walking, and overall independence. Post-stroke depression symptoms include feelings of inadequacy, suicidal thoughts, insomnia, poor focus, weight fluctuations, agitation, low energy, and exhaustion. Affected patients may withdraw from social interaction and rehabilitation. These symptoms often emerge within the first three months after a stroke (Butsing *et al.,* 2024). Mental pain from physical limitations is believed to be a primary cause of post-stroke depression (PSD). Research suggests that cerebral lesions following a stroke may significantly contribute to PSD, especially when compared to depression in patients with disabilities unrelated to the stroke. Recent clinical trials show that acupuncture aids nerve function recovery after stroke, improves quality of life, and reduces depression symptoms. It is safer and more cost-effective than medications (Oestreich *et al.,* 2024).

Patient Engagement and Self-Management in Rehabilitation

Adaptive strategies for enhancing engagement in important activities and social responsibilities after a stroke are practical attempts to assist individuals in leading fulfilling lives even in the face of ongoing disability (Egan *et al.,* 2024).Therapists also need to recognize the value of patient involvement in the rehabilitation process. One of the functional outcome factors in hospitalized patients has been identified as motivation. Effective self-management can improve patient well-being, reduce treatment costs, boost confidence, promote autonomy, and enhance satisfaction. Well-informed patients may also lower the risk of future strokes. The core principle of self-management is providing individuals with the information, skills, and confidence needed to enhance recovery and reintegration into society (Septianingrum *et al.,* 2024).

Long-Term Self-Management Support Strategy

Self-management support is a key element of stroke rehabilitation, tailored to each individual's needs. It helps patients gain the abilities, knowledge, and confidence required to manage daily life and live fully. All stroke patients who need it and are discharged from hospitals must have access to early, effective community-based rehabilitation and disability management through a specialized multidisciplinary team structure (Septianingrum *et al.,* 2024).

Healthcare providers support stroke survivors through home visits, phone calls, emails, and community resources. Self-management support involves collaboration among professionals, patients, caregivers, and families to manage symptoms, therapies, and post-discharge challenges. It includes planning, goal-setting, care coordination, and focuses on rehabilitation and reintegration to improve outcomes and quality of life (Ansong *et al.,* 2024).

The Role of Motivation

Adherence to a rehabilitation program reflects motivation, while noncompliance hinders post-stroke recovery. Using motivational strategies can improve health outcomes and patient adherence (Fernandes *et al.,* 2024). A study found that patients considered the reasons for lack of motivation when choosing motivational techniques. For example, anxiety prevented stroke survivors from resuming activities, hindering recovery. Participants helped address concerns about the future by educating patients on recovery potential and available rehabilitation programs. Sub-acute stroke patients are initially motivated by extrinsic rewards, like compliments from family, medical experts, or therapists (Septianingrum *et al.,* 2024).

Neuroimaging Techniques in Stroke Rehabilitation

Neuroimaging is vital not only for diagnosing cerebrovascular illness but also for ongoing care (Zheng *et al.,* 2024). Neuroimaging biomarkers can assess the structure and function of the sensorimotor network, including the nonprimary motor cortex, sensory cortex, and cerebellum. Combined results show that the ipsilesional motor cortex and CST are key to regaining motor function after a stroke (Gaviria *et al.,* 2024). CT and MRI are commonly used for stroke diagnosis. While MRI offers more accurate imaging for ischemic strokes, CT is preferred due to lower costs and faster imaging. Vascular imaging techniques like CT and MRI help determine the extent of ischemia and the site of artery obstruction (Zhao *et al.,* 2024).

Electroencephalography

Electroencephalography (EEG) is a non-invasive technique that uses electrodes on the scalp to capture brain electrical activity. It allows specialists to study brain impulses, providing valuable insights into neurological disorders and cognitive functions like comprehension, attention, and memory (Septianingrum *et al.,* 2024). Clinical evaluation and neuroimaging are important to identifying the ischemic core and salvageable penumbra in stroke patients (Bétrisey *et al.,* 2024) . EEG should be considered a supplemental tool for functional monitoring and diagnosis in stroke assessments (Zhao *et al.,* 2024).

Functional Near-Infrared Spectroscopy

Neuroplasticity responses may be dynamically monitored in both temporal and spatial dimensions by combining functional near infrared spectroscopy with cerebral neuromodulator. As a result, precise brain stimulation for neural rehabilitation and improving cognition is advanced through real-time evaluation, coaching, and input concerning neuromodulator outcomes (Huo *et al.,* 2024).

Prior research has evaluated upper limb movements and conditions, including cortical remodeling, focal upper limb dystonia, and grip strength (Septianingrum *et al.,* 2024).

The Future of Stroke Rehabilitation

Virtual Reality

Through the use of computer-based technology, virtual reality produces immersive simulations that provide users real-time performance feedback while emerging them in multisensory landscapes. It provides stroke victims with the opportunity to partake in activities that mimic actual situations, making their recuperation experience distinctive and captivating (Septianingrum *et al.,* 2024). With a focus on important motor learning elements including complexity, accuracy, intensity, practice salience, motivation, attention, performance proficiency, and results, virtual reality offers task-specific settings that may be tailored to a patient's demands. Furthermore, VR can enhance motor learning mechanisms that are crucial for motor recovery following a stroke by activating the mirror neuron system (Briones-Valdivieso *et al.,* 2024).

Artificial Intelligence in Rehabilitation

AI in clinical practice integrates medical, psychological, and technical expertise through algorithms that analyze data from digital devices (Macoir*,* 2024). Real-time patient data can be integrated with artificial intelligence, enabling computers to modify exercise length, intensity, and difficulty to increase engagement and encourage neuronal plasticity (Septianingrum *et al.,* 2024).

CONCLUSION

Physical therapy interventions in stroke rehabilitation are underpinned by biochemical mechanisms including recovery, inflammatory pathways and biochemical changes. Different techniques including aerobic and task-specific training exercises are used to improve vascular functions, reduce further damage and to compensate for the loss that occurred due to stroke. The duration and intensity of the interventions are critical, as the early and on time therapies maximize the biochemical benefits, and reduce the biochemical loss and changes occurring due to stroke. Further monitoring is needed to integrate the biochemical changes, to explore more techniques and therapies to rehab the stroke patients, and combining different fields for better results such as physical therapy with pharmacological treatments. Advancing this understanding will pave the way for more effective strategies, preventive measures and rehab techniques for stroke patients.

REFERENCES:

Ansong, R., & Gazarian, P. (2024). Healthcare self-management support of stroke patients after discharge: A conceptual analysis using Rodger's evolutionary approach. Journal of Advanced Nursing.

Bernoud-Hubac, N., Lo Van, A., Lazar, A. N., & Lagarde, M. (2024). Ischemic brain injury: involvement of lipids in the pathophysiology of stroke and therapeutic strategies. Antioxidants, 13(6), 634.

Bétrisey, S., Haller, M. L., Efthimiou, O., Speierer, A., Del Giovane, C., Moutzouri, E., ... & Gencer, B. (2024). Lipid-lowering therapy and risk of hemorrhagic stroke: a systematic review and meta-analysis of randomized controlled trials. Journal of the American Heart Association, 13(4), e030714.

Briones-Valdivieso, C., Briones, F., Orellana-Urzúa, S., Chiuchiarelli, S., Saso, L., & Rodrigo, R. (2024). Novel Multi-antioxidant Approach for ischemic stroke therapy targeting the role of oxidative stress. Biomedicines, 12(3), 501.

Butsing, N., Zauszniewski, J. A., Ruksakulpiwat, S., Griffin, M. T. Q., & Niyomyart, A. (2024). Association between post-stroke depression and functional outcomes: A systematic review. Plos one, 19(8), e0309158.

Egan, M., Kessler, D., Gurgel-Juarez, N., Chopra, A., Linkewich, E., Sikora, L., ... & Duong, P. (2024). Stroke rehabilitation adaptive approaches: A theory-focused scoping review. Scandinavian Journal of Occupational Therapy, 31(1), 1-13.

Fernandes, J. B., Fernandes, S., Domingos, J., Castro, C., Romão, A., Graúdo, S., ... & Godinho, C. (2024). Motivational strategies used by health care professionals in stroke survivors in rehabilitation: a scoping review of experimental studies. Frontiers in Medicine, 11, 1384414.

Fu, Z., Ma, X., Zhao, X., Du, X., & Wan, Y. (2024). Associations between Total Atherosclerosis Burden of Baroreceptor-Resident Arteries and ECG Abnormalities after Acute Ischemic Stroke. Brain Sciences, 14(5), 505.

Gao, L., Peng, L., Wang, J., Zhang, J. H., & Xia, Y. (2024). Mitochondrial stress: a key role of neuroinflammation in stroke. Journal of Neuroinflammation, 21(1), 44.

Garcia-Bonilla, L., Shahanoor, Z., Sciortino, R., Nazarzoda, O., Racchumi, G., Iadecola, C., & Anrather, J. (2024). Analysis of brain and blood single-cell transcriptomics in acute and subacute phases after experimental stroke. Nature Immunology, 25(2), 357-370.

Gaviria, E., & Eltayeb Hamid, A. H. (2024). Neuroimaging biomarkers for predicting stroke outcomes: A systematic review. Health Science Reports, 7(7), e2221.

Huo, C., Xu, G., Xie, H., Chen, T., Shao, G., Wang, J., ... & Li, Z. (2024). Functional near-infrared spectroscopy in non-invasive neuromodulation. Neural Regeneration Research, 19(7), 1517-1522.

Kakarla, R., Vinjavarapu, L. A., & Krishnamurthy, S. (2024). Diet and Nutraceuticals for treatment and prevention of primary and secondary stroke: emphasis on nutritional antiplatelet and antithrombotic agents. Neurochemistry International, 105823.

Lorenz, E. A., Su, X., & Skjaeret-Maroni, N. (2024). A review of combined functional neuroimaging and motion capture for motor rehabilitation. Journal of NeuroEngineering and Rehabilitation, 21(1), 3.

Macoir, J. (2024). Language impairment in vascular dementia: a clinical review. Journal of Geriatric Psychiatry and Neurology, 37(2), 87-95.

Nayak, K., Gopan, A., Muraleedharan, A., Varghese, A., Patil, A., & Manokaran, K. (2024). Gut microbiota and geriatric health. Reviews and Research in Medical Microbiology, 10-1097.

Oestreich, L. K., Lo, J. W., Di Biase, M. A., Sachdev, P. S., Mok, A. H., Wright, P., ... & Zalesky, A. (2024). Network analysis of neuropsychiatric, cognitive, and functional complications of stroke: implications for novel treatment targets. Psychiatry and Clinical Neurosciences, 78(4), 229-236.

Pavan, A., Fasano, A., Lattanzi, S., Cortellini, L., Cipollini, V., Insalaco, S., & Aprile, I. G. (2024). Effectiveness of Two Models of Telerehabilitation in Improving Recovery from Subacute Upper Limb Disability after Stroke: Robotic vs. Non-Robotic. Brain Sciences, 14(9), 941.

Picard-Fraser, M., Van de Winckel, A., Prudente, C., Bisson, T. A., Engineer, N., & Kimberley, T. J. (2024, February). Vagus Nerve Stimulation Paired with Mobility Training in Chronic Ischemic Stroke: A Single-Subject Design. In 2024 Combined Sections Meeting (CSM). APTA.

Sahebi, K., Foroozand, H., Amirsoleymani, M., Eslamzadeh, S., Negahdaripour, M., Tajbakhsh, A., & Savardashtaki, A. (2024). Advancing stroke recovery: unlocking the potential of cellular dynamics in stroke recovery. Cell Death Discovery, 10(1), 321.

Sato, Y., Yoshimura, Y., Abe, T., Nagano, F., & Matsumoto, A. (2023). Hospital-associated sarcopenia and the preventive effect of high energy intake along with intensive rehabilitation in patients with acute stroke. Nutrition, 116, 112181

Septianingrum, Y., Yusuf, A., Widyawati, I. Y., Purwanti, N., Hatmanti, N. M., Lestari, S. N., & Yuswanto, A. (2024). Individual and health care provider factors influencing stroke self-management behavior: A cross-sectional study. F1000Research, 13, 492.

Teng, T. Q., Liu, J., Hu, F. F., Li, Q. Q., Hu, Z. Z., & Shi, Y. (2024). Association of composite dietary antioxidant index with prevalence of stroke: insights from NHANES 1999-2018. Frontiers in immunology, 15, 1306059.

Williams, E. E., Sghirripa, S., Rogasch, N. C., Hordacre, B., & Attrill, S. (2024). Non-invasive brain stimulation in the treatment of post-stroke aphasia: a scoping review. Disability and Rehabilitation, 46(17), 3802-3826.

Xi, C., Zhang, J., Liu, H., Tao, S., Xie, Y., Liu, J., ... & Zhang, X. (2024). Can Omega-3 prevent the incidence of stroke: a mendelian randomization study. Hereditas, 161(1), 30.

Zhang, L., Chang, Y., Zhang, F., & Li, J. (2024). A Review on Combined Strategy of Non-invasive Brain Stimulation and Robotic Therapy. Chinese Journal of Mechanical Engineering, 37(1), 113.

Zheng, J. S., Steur, M., Imamura, F., Freisling, H., Johnson, L., van der Schouw, Y. T., ... & Forouhi, N. G. (2024). Dietary intake of plant-and animal-derived protein and incident cardiovascular diseases: the pan-European EPIC-CVD case–cohort study. The American journal of clinical nutrition, 119(5), 1164-1174.