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# STROKE: PATHOGENESIS, TRADITIONAL AND MODERN NEUROREHABILITATION STRATEGIES – A REVIEW OF CURRENT METHODS

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**ABSTRACT**

**Objectives:** Stroke remains one of the leading causes of mortality and long-term disability worldwide. The objective of this review was to synthesize current evidence on the biological mechanisms underlying ischemic and hemorrhagic stroke and to evaluate the effectiveness of traditional and emerging neurorehabilitation strategies.

**Methods:** A structured narrative review was conducted using major medical databases, including PubMed, Scopus, Web of Science, and Google Scholar. Additional sources were identified through manual reference screening. Studies examining pathophysiology and rehabilitation approaches in stroke were included and qualitatively analyzed.

**Results:** Findings indicate that acute energy failure, excitotoxicity, oxidative stress, and neuroinflammation are key pathophysiological drivers of early neuronal damage, while phases of neuroplastic reorganization strongly influence recovery potential. Traditional rehabilitation approaches remain central due to strong evidence supporting their effectiveness in motor relearning, however, limitations related to therapy intensity and patient engagement persist. Emerging modalities—such as robotic-assisted training, virtual reality-based interventions, telerehabilitation, non-invasive brain stimulation, and vagus nerve stimulation—show increasing evidence for enhancing training dosage, modulating cortical excitability, and enabling individualized therapy.

**Conclusions:** Integrating conventional rehabilitation with modern technological and neuromodulatory interventions appears to offer the most effective strategy for optimizing functional outcomes and supporting sustainable long-term recovery in stroke survivors.

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**KEYWORDS**

Stroke, Neurorehabilitation, Neuroplasticity, Robotic-Assisted Therapy, Virtual Reality, Non-Invasive Brain Stimulation

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**Introduction**

Stroke is an acute cerebrovascular event defined by the sudden loss of neurological function due to focal brain ischemia or hemorrhage, and it remains one of the principal causes of mortality and long-term disability worldwide (Campbell & Khatri, 2020). Historical epidemiological research, such as the landmark WHO Collaborative Study on stroke incidence, demonstrated considerable variation in stroke rates across countries and socioeconomic contexts while simultaneously underscoring its universal public-health importance (Aho et al., 1980). Contemporary population studies show that although age-standardized stroke mortality has declined in many regions due to improved prevention and acute care, the absolute number of cases and the overall disability burden continue to rise as a result of population aging and increased survival after the acute event (Feigin et al., 2010). In Poland, stroke remains a leading cause of adult disability and a major contributor to mortality, with national data emphasizing the substantial incidence and societal impact of cerebrovascular disease (NFZ, 2024).

The pathophysiology of ischemic stroke is characterized by an abrupt interruption of cerebral blood flow that initiates a complex and temporally evolving cascade of cellular and molecular events. Energy failure resulting from oxygen and glucose deprivation leads to membrane depolarization, excessive glutamate release, calcium overload, generation of reactive oxygen species, and activation of proteases and lipases that culminate in necrosis or apoptosis within the infarct core (Dirnagl, Iadecola, & Moskowitz, 1999). Surrounding the core lies the ischemic penumbra, a region of functionally impaired but potentially salvageable tissue in which delayed mechanisms such as spreading depolarizations, inflammation and programmed cell death determine ultimate tissue fate (Dirnagl et al., 1999). Hemorrhagic stroke produces additional injury mechanisms, including mass effect, hemoglobin-derived toxicity and secondary inflammation, each of which disrupts neural

networks and white-matter tracts and thereby produces focal motor, sensory or cognitive deficits corresponding to the lesioned territory (Campbell & Khatri, 2020).

Advances in acute stroke management, in particular the systematic use of neuroimaging to differentiate ischemic from hemorrhagic stroke and the development of reperfusion therapies such as intravenous thrombolysis and endovascular thrombectomy, have substantially altered early outcomes and expanded the number of patients who survive the acute phase (Campbell & Khatri, 2020). Nevertheless, a substantial proportion of survivors are left with persistent deficits that limit independence and quality of life, creating an expanding population with chronic stroke-related disability that poses clinical and socioeconomic challenges (Grefkes & Fink, 2014). Recovery after stroke is fundamentally dependent on neuroplasticity, the capacity of the brain to reorganize synaptic connections and functional networks. Experimental and clinical data indicate that a time-limited period of heightened plastic potential follows focal brain injury, during which intensive, activity-dependent training can induce synaptic remodelling and functional gains (Murphy & Corbett, 2009; Zeiler & Krakauer, 2013). This biological window provides the rationale for early, repetitive and task-specific rehabilitation aimed at driving adaptive reorganization rather than maladaptive compensation.

Because of the substantial burden of post-stroke impairment, structured neurorehabilitation is an essential and evidence-based component of the stroke care pathway. International guidelines and systematic reviews consistently recommend that rehabilitation be delivered in a coordinated, multidisciplinary fashion and with sufficient intensity and duration to achieve meaningful functional improvements (Winstein et al., 2016; Langhorne, Bernhardt, & Kwakkel, 2011; Pollock et al., 2014). Conventional rehabilitation interventions include physiotherapy focused on motor relearning and gait retraining, occupational therapy (OT) to restore independence in activities of daily living, and speech and language therapy for communication and swallowing disorders; these approaches rely principally on repeated, task-specific practice and progressive challenge to engage motor learning principles and promote cortical reorganization (Langhorne et al., 2011; Pollock et al., 2014). Despite clear benefit, access to high-dose therapy is often constrained by workforce, logistical and motivational factors, which has stimulated the investigation of adjunctive and technology-enabled strategies to increase the quantity, quality and specificity of rehabilitation practice. Over the past two decades, a broad array of modern, feedback-driven and neuromodulatory approaches has been introduced with the explicit aim of augmenting conventional therapy and targeting mechanisms of plasticity more effectively. Robotic devices for the upper and lower limbs provide reproducible, high-intensity, and objective training that can deliver thousands of task repetitions while recording kinematic performance (Veerbeek et al., 2017). Virtual reality (VR) and motion-controlled interactive gaming offer multimodal sensory feedback and immersive task contexts that enhance patient engagement and allow progressive task difficulty tailored to individual performance (Laver et al., 2017; Richards et al., 2018). Non-invasive brain stimulation (NIBS) techniques, including repetitive transcranial magnetic stimulation (rTMS), seek to modulate cortical excitability and interhemispheric balance to create a neurophysiological milieu favorable to relearning (Lefaucheur et al., 2020). Telerehabilitation and home-based digital platforms enable remote delivery and monitoring of therapy, which can increase practice dose and continuity of care particularly in regions or circumstances where in-person services are limited (Ciorcea et al., 2021; Straudi et al., 2025). Recent systematic reviews and meta-analyses indicate promising effects for many of these modalities, while also highlighting heterogeneity in study designs, outcome measures and dose parameters that complicates generalization to routine clinical practice (Saposnik & Levin, 2011; Dawson et al., 2021; Faralli et al., 2013).

The proliferation of technology-assisted interventions has encouraged integrative frameworks that combine conventional task practice with neuromodulatory priming, real-time feedback, and remote supervision to maximize intensity and specificity of training and to individualize rehabilitation trajectories (Kopalli et al., 2025; Ciorcea et al., 2021). At the same time, evidence syntheses emphasize the need for rigorous randomized trials, standardized outcome reporting and pragmatic implementation research to determine which patients benefit most from particular approaches and how best to integrate new technologies into established care pathways (Pollock et al., 2014; Velayati et al., 2020). These considerations are central to translational efforts that aim to move promising experimental therapies from research settings into scalable clinical practice.

This review aims to synthesize current understanding of stroke pathogenesis and to critically appraise both traditional and contemporary neurorehabilitation strategies with attention to biological rationale, clinical evidence and implementation considerations. The scope includes a concise overview of injury mechanisms that underpin recovery potential, an evaluation of established rehabilitative methods and guideline recommendations, and a detailed examination of modern, technology-driven and neuromodulatory interventions and their evidence base.

### **Materials and Methods**

This study is a structured narrative review. A literature search was conducted in PubMed, Scopus, Web of Science, and Google Scholar, covering the period from January 1999 to December 2024. The search strategy combined terms related to cerebrovascular disease and rehabilitation, including “stroke,” “ischemic stroke,” “hemorrhagic stroke,” “neuroplasticity,” “neurorehabilitation,” “physiotherapy,” “OT,” “robotic-assisted therapy,” “VR,” “telerehabilitation,” and “NIBS.” Additional relevant publications were identified by manually screening the reference lists of key articles to ensure that no major sources were overlooked.

Studies were included if they involved adult populations with ischemic or hemorrhagic stroke and addressed neural injury mechanisms, principles of neuroplasticity, conventional rehabilitation approaches, or emerging technology-assisted and neuromodulatory interventions. Eligible study designs encompassed randomized controlled trials, systematic reviews, meta-analyses, observational studies, and clinical guidelines. Publications were excluded if they focused on pediatric stroke, were unrelated to rehabilitation or neural recovery, were not peer-reviewed, or involved exclusively animal models without clear translational relevance.

For all included studies, data extraction focused on study objectives, methodological design, sample characteristics, intervention parameters, outcome measures, and key findings. The evidence was synthesized narratively and organized thematically to provide a coherent overview of stroke mechanisms, traditional rehabilitation methods, and modern technology-assisted approaches. This methodology ensured that the review remained comprehensive, clinically relevant, and aligned with current standards for evidence-based synthesis in neurorehabilitation research.

### **Mechanisms of Stroke and Pathobiology**

Understanding the biological mechanisms underlying stroke is essential for designing effective neurorehabilitation strategies.

#### **Ischemic Stroke Pathophysiology**

Ischemic stroke results from an abrupt reduction or complete cessation of cerebral blood flow, most frequently caused by thrombotic occlusion or embolism of major cerebral arteries. The resulting energy deficit initiates a complex cascade of cellular and molecular events that evolve within minutes. The core–penumbra concept remains central to understanding the spatial and temporal progression of ischemic injury. The ischemic core, where perfusion is critically reduced, undergoes rapid and irreversible necrosis as neurons lose membrane integrity due to severe ATP depletion and dysfunction of ionic pumps. Surrounding this core is the penumbra, a metabolically compromised yet structurally intact region maintained by partial collateral circulation, which represents the main target for interventions aiming to preserve tissue and function (Dirnagl, Iadecola, & Moskowitz, 1999).

Within the penumbra, excitotoxicity driven by excessive glutamate release leads to intracellular calcium overload and activation of proteolytic enzymes, further compromising cellular structures. Concurrently, mitochondrial dysfunction generates reactive oxygen species, amplifying oxidative stress and contributing to delayed neuronal death. Inflammatory mechanisms involving microglia and infiltrating immune cells release cytokines and chemokines, which both exacerbate tissue damage and participate in reparative processes during later stages. Apoptotic pathways are particularly relevant in penumbral zones, where neurons are partially viable, adding another dimension to the delayed evolution of ischemic injury (Murphy & Corbett, 2009; Dirnagl et al., 1999). These interconnected processes define the therapeutic window and highlight the need for timely reperfusion and appropriately timed rehabilitation to maximize tissue preservation (Campbell & Khatri, 2020).

#### **Hemorrhagic Stroke Pathophysiology**

Hemorrhagic stroke, although less common than ischemic stroke, frequently results in more severe clinical outcomes due to the combination of mechanical and biochemical injury mechanisms. Initial vessel rupture leads to accumulation of blood in the brain parenchyma, increasing intracranial pressure and compressing adjacent neural structures, which produces immediate neurological deficits. As the hematoma expands, it disrupts white matter tracts, distorts local microvascular architecture, and impairs perfusion to surrounding tissue (Campbell & Khatri, 2020; Błażejewska-Hyżorek et al., 2019).

In addition to mechanical effects, blood components themselves contribute to neurotoxicity. Hemoglobin degradation products, particularly iron, promote free radical generation and lipid peroxidation, driving oxidative stress. Breakdown of the blood–brain barrier allows peripheral immune cells and

inflammatory mediators to infiltrate the parenchyma, exacerbating secondary injury. Perihematomal edema develops over hours to days, further compromising tissue perfusion and contributing to delayed neurological deterioration. These dynamic pathophysiological processes shape the pattern and severity of functional deficits, particularly within motor, sensory, and higher-order cognitive domains.

### **Neuroplasticity and Recovery Mechanisms**

Neuroplasticity underlies the capacity of the post-stroke brain to reorganize structurally and functionally in response to injury. Surviving networks undergo extensive reorganization characterized by dendritic sprouting, synaptic strengthening, and recruitment of previously silent or latent pathways. The extent and pattern of these changes are influenced by lesion location and size, the intensity and timing of rehabilitation, and the type of interventions applied (Murphy & Corbett, 2009; Zeiler & Krakauer, 2013).

Post-stroke plasticity is temporally constrained and differs from developmental plasticity, opening a critical window during which rehabilitative interventions can yield maximal functional recovery. Behavioral experience and task-specific training interact with neural circuitry to guide adaptive changes, and principles of motor learning, including repetition, variability, and specificity, are essential for shaping recovery. Overstimulation or poorly timed interventions during early recovery may be counterproductive, underscoring the need for carefully calibrated therapy. Neuroplastic mechanisms provide the biological foundation for both spontaneous recovery and structured rehabilitation, highlighting the need to align clinical strategies with the dynamic processes governing neuronal reorganization (Grefkes & Fink, 2014).

### **Traditional Neurorehabilitation Methods**

Traditional rehabilitation forms the foundation of stroke recovery and remains central in clinical practice despite the emergence of modern technologies.

### **Physiotherapy and Motor Recovery**

Physiotherapy is the foundational element of stroke rehabilitation and encompasses a broad spectrum of interventions aimed at restoring sensorimotor function, improving mobility, and reducing disability. The central principle underlying physiotherapy is activity-dependent neuroplasticity, whereby repetitive and task-specific exercises drive reorganization within surviving neural circuits. After stroke, impairments in muscle strength, coordination, balance, and gait are common, and their recovery requires structured, high-dose motor practice. Conventional physiotherapy includes passive and active range-of-motion exercises to prevent contractures, progressive strengthening to rebuild muscle force, and targeted training to restore postural control. Early mobilization is particularly beneficial, provided it is safely implemented, as it prevents complications such as deconditioning, venous thromboembolism, and pressure injuries while simultaneously stimulating neural pathways involved in motor recovery (Langhorne et al., 2011).

Gait rehabilitation represents a central focus of physiotherapy. Stroke survivors often exhibit hemiparetic gait patterns characterized by reduced stride length, impaired limb coordination, circumduction, and diminished walking speed. Gait training may include treadmill-assisted walking, overground stepping exercises, balance retraining, proprioceptive neuromuscular facilitation, and use of external supports such as canes, orthoses, or body-weight support systems. Studies indicate that high-intensity, repetitive gait training improves mobility, endurance, and functional ambulation more effectively than low-intensity or unstructured practice (Pollock et al., 2014).

Balance training is another critical domain, as postural stability deficits not only limit mobility but also increase fall risk, which remains one of the major causes of injury in stroke survivors. Physiotherapists use a variety of balance exercises that challenge the center of mass, encourage weight shifting, and strengthen core musculature. Visual or auditory biofeedback may be integrated to enhance proprioceptive awareness and facilitate motor learning (Richards et al., 2018). The progression of exercises is carefully calibrated, beginning with stable positions and advancing to dynamic tasks that approximate real-life movement demands.

The effectiveness of physiotherapy is tightly linked to therapy intensity. Regular, high-frequency sessions, ideally multiple times per day in the early subacute phase, are consistently associated with better outcomes. However, logistical constraints such as staffing, cost, and patient fatigue often limit the achievable therapy dose in clinical settings, highlighting the need for complementary modern technologies designed to increase practice volume.

### **Occupational Therapy and Functional Integration**

OT focuses on improving the patient's ability to perform and participate in meaningful daily activities such as dressing, feeding, bathing, household tasks, and community engagement. Following stroke, impairments in upper limb function, visuospatial processing, executive function, and task sequencing commonly interfere with independence. OT aims to bridge the gap between isolated motor improvements and real-life functional performance.

Task-oriented training is a central OT principle. Instead of practicing isolated joint movements, patients engage in purposeful activities, such as handling utensils, buttoning clothing, writing, or reaching for objects, that mirror real-world tasks. This approach harnesses motor learning principles such as repetition, relevance, and specificity, which are known to enhance neuroplasticity (Coupar et al., 2012; Zeiler & Krakauer, 2013). The therapist may use strategies like task decomposition, environmental modification, or adaptive equipment to facilitate safe performance of activities while gradually increasing task complexity.

Home-based OT programs play a significant role in extending the dose of therapy beyond the clinical environment. Evidence indicates that home-based, repetitive, goal-oriented programs tailored to individual needs improve upper limb coordination, dexterity, and autonomy in daily tasks, especially when combined with regular therapist feedback (Langhorne et al., 2011; Pollock et al., 2014; Winstein et al., 2016). By working in natural environments, patients learn to generalize skills and develop compensatory strategies that support long-term functional integration.

### **Speech and Language Therapy**

Speech and language therapy addresses a range of post-stroke communication disorders, including aphasia, dysarthria, apraxia of speech, and difficulties with reading or writing. Aphasia, one of the most challenging sequelae of stroke, affects linguistic comprehension and expression and significantly impacts social participation and emotional well-being. Speech and language therapy employs structured exercises targeting phonological, semantic, syntactic, and pragmatic aspects of language. Intensive therapy, particularly approaches that emphasize high-repetition practice of meaningful language tasks, has been shown to promote measurable improvements even in chronic stages of recovery (Winstein et al., 2016; Dawson et al., 2021). In selected cases, neuromodulatory techniques such as rTMS may further enhance treatment effects by modulating cortical excitability within language networks (Lefaucheur et al., 2020).

In addition to restorative strategies, therapists frequently teach compensatory communication methods, including the use of gestures, communication boards, or alternative and augmentative communication tools. These methods are crucial for patients with severe aphasia or apraxia who require alternative pathways for expressing needs and engaging in social interaction. Group therapy and conversational practice help restore functional communication in real-world settings and reduce social isolation.

### **Constraint-Induced Movement Therapy and Upper Limb Rehabilitation**

Upper limb dysfunction is one of the most persistent and disabling consequences of stroke. Constraint-induced movement therapy (CIMT) is a prominent evidence-based intervention designed to counteract "learned non-use," a phenomenon in which patients over-rely on the unaffected limb while neglecting the paretic arm. CIMT involves restraining the unaffected limb for most of the day and engaging the affected limb in intensive, repetitive, task-specific practice. The combination of forced use and high training intensity stimulates neuroplastic reorganization in motor cortical regions and improves functional performance (Langhorne et al., 2011; Pollock et al., 2014; Winstein et al., 2016).

Modified versions of CIMT have been developed to increase feasibility and patient adherence, often involving shorter daily restraint periods but maintaining essential principles of frequent, task-oriented practice. Upper limb rehabilitation also includes bilateral arm training, fine motor exercises, sensory discrimination tasks, and functional strengthening. The integration of motor learning principles, such as variability, progressive challenge, and augmented feedback, is critical to achieving durable improvements.

### **Driving Retraining and Cognitive-Motor Integration**

Driving is a sophisticated activity requiring complex integration of motor, sensory, visuospatial, and executive functions. Post-stroke deficits in visual scanning, reaction time, divided attention, and motor coordination can significantly impair driving safety. Driving retraining programs, often delivered by OT in collaboration with rehabilitation specialists, incorporate cognitive-motor exercises, simulator-based training, and, when appropriate, on-road assessments.

Driving simulators allow patients to practice hazard perception, lane maintenance, and decision-making in controlled and progressively challenging scenarios. Studies have shown that simulator-based intervention improves visual scanning strategies, reaction times, and overall driving performance among stroke survivors (Akinwuntan et al., 2010; Akinwuntan et al., 2012; Ponsford et al., 2008). These programs not only help restore driving ability but also support broader cognitive recovery, as they challenge working memory, processing speed, and attention, domains critical for community reintegration.

### **Guidelines and Multidisciplinary Coordination**

Effective stroke rehabilitation relies on cohesive, interdisciplinary teamwork. International guidelines consistently emphasize the importance of early assessment, individualized goal-setting, structured therapy plans, and continuous monitoring of progress (Błażejewska-Hyżorek et al., 2019; Winstein et al., 2016). Rehabilitation is not the sum of isolated therapies; rather, it is an integrated process combining physiotherapy, OT, speech therapy, neuropsychology, nursing, and medical oversight.

Regular interdisciplinary meetings allow clinicians to tailor interventions, adjust goals, and address emerging needs. Patient-centered approaches promote autonomy and motivation, while family involvement enhances carryover of therapeutic strategies to home environments. The coordinated, holistic framework of multidisciplinary rehabilitation remains one of the most important predictors of functional recovery after stroke.

### **Modern and Technology-Assisted Neurorehabilitation**

Technological innovation has transformed the landscape of rehabilitation.

#### **Robotic-Assisted Rehabilitation**

Robotic-assisted rehabilitation has emerged as one of the most significant technological advancements in modern post-stroke therapy. Robotics provide patients with high-intensity, repeatable, and task-specific movements that are difficult to achieve consistently through conventional therapy alone. Devices targeting both upper and lower extremities can deliver hundreds or even thousands of repetitions per session, leveraging the principle that high-dose practice is a critical driver of neuroplasticity. Upper-limb robots, such as end-effector and exoskeleton devices, assist patients in performing reaching, grasping, and fine-motor tasks with adjustable levels of support, enabling engagement across a wide spectrum of impairment severity. These systems often incorporate interactive feedback, motivating patients and facilitating more precise motor relearning (Laver et al., 2017).

Lower-limb robotic systems, including treadmill-based exoskeletons and gait orthoses, allow reproducible gait cycles that help restore walking patterns and build endurance. Body weight-supported robotic gait training is particularly useful for patients with significant motor deficits, as it enables early mobilization and intensive practice without excessive physical strain on therapists. Meta-analytic evidence indicates that robotic rehabilitation improves upper limb function, enhances walking ability, and increases the likelihood of regaining independent ambulation when combined with conventional therapy, particularly in the subacute period (Veerbeek et al., 2017; Tollár et al., 2025).

Robotic systems also allow precise modulation of parameters such as resistance, assistance, movement range, and speed, enabling individualized training that can be progressively adjusted as recovery progresses. However, their benefits are maximized when robotics are not used as stand-alone interventions but integrated into personalized neurorehabilitation plans in combination with physiotherapy and task-oriented training. This integrated approach ensures that robotic gains translate into meaningful functional outcomes.

#### **Virtual Reality and Immersive Digital Environments**

Virtual reality (VR) has rapidly expanded as a complementary tool in stroke rehabilitation, offering immersive, engaging, and highly motivating therapy environments. VR systems range from fully immersive head-mounted displays to semi-immersive screen-based systems and interactive gaming platforms. Through gamified tasks, VR encourages high levels of repetition and provides immediate sensory feedback, which are essential components of motor relearning.

Systematic reviews demonstrate that VR-based interventions enhance upper limb function, balance, and gait performance, often outperforming or matching traditional therapies when used as an adjunct (Laver et al., 2017; Saposnik & Levin, 2011). The enriched environments provided by VR stimulate multisensory integration and may enhance cortical activation beyond what is achieved through conventional therapy alone.

VR tasks can be tailored to mimic real-world functional activities, such as reaching for objects, navigating virtual spaces, or performing bimanual tasks.

A key advantage of VR is its capacity to enhance motivation and sustained engagement through real-time feedback, goal-oriented tasks, and adaptive difficulty. These features are especially valuable in chronic stroke, where maintaining motivation can be challenging. VR can also support cognitive rehabilitation, as tasks involving attention, memory, visuospatial abilities, and executive function can be embedded within motor exercises. Studies show additional benefits in reducing learned non-use and improving patient satisfaction.

Emerging research explores augmented reality (AR) applications, which overlay virtual elements onto real-world environments. AR has the potential to bridge the gap between therapy exercises and daily tasks, although evidence remains preliminary compared with the more mature VR literature.

### **Telerehabilitation and Remote Therapy Delivery**

Telerehabilitation has become a pivotal tool for expanding access to therapy beyond the hospital or clinic setting. Remote rehabilitation platforms allow patients to engage in supervised or semi-supervised therapy from their homes, addressing barriers such as transportation difficulties, limited availability of specialists, or geographic constraints. Telerehabilitation typically integrates video consultations, remote monitoring, exercise instructions, and digital tools that enable therapists to track performance and adjust programs in real time.

Studies show that telerehabilitation produces functional outcomes comparable to in-person therapy for upper limb recovery, daily functioning, and mobility (Velayati et al., 2020; Ciortea et al., 2021). Self-management tools included in these platforms, such as home exercise programs, instructional videos, progress dashboards, and wearable sensors, promote autonomy and facilitate continuous practice between formal therapy sessions. Wearable sensors can provide data on movement quality, adherence, and activity levels, enabling personalized adjustments and increasing the overall therapy dose.

Importantly, telerehabilitation supports continuity of care during transitions from inpatient rehabilitation to home-based settings, allowing patients to maintain rehabilitation intensity during critical phases of neuroplasticity. Remote cognitive rehabilitation is also increasingly feasible, with structured digital tasks targeting attention, memory, and executive functions. For many patients, hybrid models combining in-person sessions with remote follow-up offer the most effective and flexible approach.

### **Non-Invasive Brain Stimulation**

NIBS techniques, primarily repetitive rTMS and transcranial direct current stimulation (tDCS), are increasingly integrated into post-stroke neurorehabilitation due to their potential to modulate cortical excitability and facilitate neuroplasticity. After stroke, imbalances in interhemispheric inhibition often develop, with the unaffected hemisphere exerting excessive inhibitory influence on the lesioned hemisphere. NIBS aims to restore excitatory–inhibitory balance by enhancing activity in the affected hemisphere or reducing maladaptive overactivity in the contralesional hemisphere (Lefaucheur et al., 2020).

rTMS delivers magnetic pulses that induce targeted neuronal depolarization. High-frequency stimulation typically increases excitability, while low-frequency stimulation decreases overactive regions. Numerous studies demonstrate that rTMS improves upper limb function, hand dexterity, motor strength, and even language outcomes in aphasia when paired with behavioral training (Grefkes & Fink, 2014; Veldema & Gharabaghi, 2022).

tDCS, in contrast, applies low-intensity electrical currents that modulate neuronal membrane potentials, subtly shifting the likelihood of firing during rehabilitation exercises. tDCS is portable, safe, and easily combinable with other therapies such as VR, robotics, or constraint-induced movement therapy. Evidence suggests that tDCS enhances motor learning, improves coordination, and supports gains achieved through conventional therapy (He et al., 2019; Faralli et al., 2013).

The synergy between NIBS and behavioral therapies is increasingly recognized, as stimulation appears most effective when administered immediately before or during rehabilitative training. Although optimal stimulation parameters, timing, and patient selection criteria require further refinement, NIBS represents one of the most promising adjuncts for enhancing plasticity-driven recovery.

### **Peripheral Neuromodulation and Vagus Nerve Stimulation**

Peripheral neuromodulation techniques, particularly vagus nerve stimulation (VNS), have gained growing interest as tools capable of boosting recovery after stroke. VNS stimulates the cervical branch of the vagus nerve, triggering widespread neuromodulatory effects mediated by cholinergic and noradrenergic pathways that enhance synaptic plasticity. When paired with rehabilitation exercises, VNS amplifies the effects of motor training by strengthening task-dependent cortical reorganization (Dawson et al., 2021).

Clinical studies report that rehabilitation coupled with VNS leads to greater improvements in upper limb motor function compared to therapy alone, with enhanced dexterity and functional independence. Benefits appear particularly robust in individuals with moderate upper limb impairments. Non-invasive VNS devices offer a lower-risk alternative to implanted systems and may broaden accessibility as evidence continues to grow.

In addition to VNS, peripheral neuromodulation also includes neuromuscular electrical stimulation (NMES), which is frequently used to reduce post-stroke spasticity and support motor recovery. NMES activates peripheral nerves through patterned electrical impulses, facilitating improved muscle recruitment and modulating spinal and supraspinal circuits involved in motor control. Evidence shows that NMES combined with conventional rehabilitation reduces limb spasticity and enhances motor performance more effectively than rehabilitation alone (He, Gao, & Fan, 2019). These findings position NMES as a practical, widely accessible adjunctive intervention that complements both traditional therapy and more advanced neuromodulatory methods.

### **Intelligent, AI-Assisted, and Personalized Rehabilitation Systems**

Recent research explores how artificial intelligence and machine learning can advance neurorehabilitation by personalizing therapy programs, optimizing training parameters, and improving monitoring. Intelligent systems can analyze movement patterns, detect compensatory strategies, and adapt exercise difficulty in real time. Early evidence shows that AI-supported rehabilitation improves adherence, enhances precision of movement correction, and allows therapists to identify subtle changes in progress more rapidly (Quattrocelli et al., 2024; Kopalli et al., 2025).

These technologies integrate data from motion sensors, robotic devices, VR environments, and neurophysiological signals to deliver individualized training plans. Personalized therapy, informed by objective metrics, extends the concept of precision medicine to neurorehabilitation and may become a central feature of future stroke care.

### **Integration of Traditional and Emerging Rehabilitation Approaches**

The increasing diversification of post-stroke rehabilitation methods has encouraged the development of integrated therapeutic frameworks that combine the strengths of traditional, clinician-delivered interventions with emerging technology-assisted strategies. Conventional rehabilitation, rooted in task-specific training, motor relearning principles, gait and balance retraining, upper limb practice, and functional task performance, continues to provide the core therapeutic foundation for most patients. However, evidence consistently demonstrates that functional recovery is strongly dose-dependent and that traditional therapy alone often cannot deliver the high repetition numbers required to optimize neuroplasticity (Pollock et al., 2014; Winstein et al., 2016). This gap has accelerated interest in complementing therapist-led interventions with technologies such as robotics, VR, telerehabilitation, NIBS, and neuromodulatory tools, each of which can increase the volume, intensity, or biological impact of therapy.

Integrating these approaches hinges on harmonizing several mechanistic and practical dimensions. Robotics, for example, offer reproducible, high-frequency motor practice and can supplement physiotherapy sessions by providing structured repetition and kinematic accuracy that are difficult to sustain manually. When used alongside conventional physiotherapy, robotic-assisted training supports motor relearning by pairing massed practice with therapist-guided functional transfer exercises, allowing gains achieved during robotic sessions to be consolidated through real-world tasks (Laver et al., 2017; Veerbeek et al., 2017). OT, which emphasizes meaningful and context-specific activity performance, plays a critical role in translating robotic improvements in proximal limb control into functional autonomy during daily tasks.

VR integrates naturally into both physiotherapy and OT by creating immersive environments that promote engagement through real-time feedback and gamified tasks. Studies show that VR enhances upper limb dexterity, balance, and gait when applied as an adjunct to standard therapy, particularly when therapists reinforce learned VR tasks with equivalent real-world functional activities (Laver et al., 2017; Saposnik &

Levin, 2011). VR thereby acts as an amplifier of traditional therapy principles, sustaining patient motivation and enabling higher therapy doses during the subacute and chronic stages.

The integration of telerehabilitation into the broader rehabilitation pathway addresses a different but equally important dimension of recovery: continuity of care. Remote rehabilitation platforms allow patients to maintain practice intensity after discharge, when access to face-to-face therapy declines sharply. Telerehabilitation complements traditional in-person therapy by allowing therapists to supervise, progress, and customize home-based programs while simultaneously increasing accessibility and adherence (Velayati et al., 2020; Ciortea et al., 2021). These hybrid models are particularly valuable in chronic stroke, where ongoing training is essential to prevent functional decline but healthcare utilization is typically lowest.

Neuromodulatory interventions, including rTMS, transcranial tDCS, and VNS, introduce a neurophysiological layer to integrated rehabilitation models. Their primary function is not to replace behavioral therapy but to prime cortical circuits, modulate interhemispheric balance, and create conditions favorable for motor learning. Evidence indicates that pairing stimulation with task-oriented practice produces larger functional gains than stimulation or training alone, reinforcing the concept that neuromodulation serves as an enhancer of traditional rehabilitation rather than a stand-alone therapy (Lefaucheur et al., 2020; Veldema & Gharabaghi, 2022; Dawson et al., 2021). This synergistic model reflects contemporary neuroscience research demonstrating that neuroplasticity is most effectively shaped when multiple modalities converge on the same functional domains.

Artificial intelligence based systems add yet another layer of integration by enabling personalized adaptation of exercise difficulty, detection of compensatory movement patterns, and real-time modification of therapy parameters. These systems expand the role of traditional rehabilitation by providing objective feedback that clinicians can use to refine clinical decision-making and therapy progression (Quattrocelli et al., 2024; Kopalli et al., 2025). Their incorporation into rehabilitation workflows represents a shift toward precision neurorehabilitation, in which therapy is continuously shaped by performance data rather than fixed schedules.

Overall, the integration of traditional and emerging rehabilitation approaches reflects a transition from single-modality therapy to multimodal, personalized rehabilitation ecosystems. Modern rehabilitation is increasingly defined not by isolated techniques but by coordinated combinations of interventions that target complementary aspects of recovery, repetition, engagement, biological priming, functional relevance, and continuity of care. As evidence from systematic reviews and clinical trials accumulates, a clearer picture is emerging of how these modalities interact, which patients benefit most, and how integrated rehabilitation can be implemented effectively within routine clinical practice.

## **Discussion**

The evolving landscape of stroke rehabilitation reflects a growing understanding of the complex neurobiological mechanisms underlying both injury and recovery, as well as the limitations of traditional therapy models in delivering the intensity and specificity required to maximize functional gains. Classical neurorehabilitation approaches, anchored in task-oriented training, motor relearning, and multidisciplinary care, remain the essential backbone of post-stroke treatment. However, evidence consistently shows that conventional therapy often falls short in providing sufficient repetition, progressive challenge, and continuous reinforcement to fully engage neuroplastic processes, particularly during the critical early window of heightened plasticity (Murphy & Corbett, 2009; Zeiler & Krakauer, 2013). This gap has motivated the increasing adoption of adjunctive methods designed to augment therapeutic dose, enhance motivation, or modulate neural circuitry to create conditions more conducive to recovery.

A central conclusion of recent research is that no single modality, traditional or novel, can adequately address the multifaceted nature of post-stroke impairment. Instead, optimal outcomes are achieved when interventions target complementary aspects of motor learning and neural reorganization. For example, robotic-assisted therapy provides high-repetition, kinematically precise practice, but its functional impact is maximized only when the gains achieved during robotic sessions are translated into meaningful tasks through guided physiotherapy and OT (Laver et al., 2017; Veerbeek et al., 2017). Similarly, VR enhances engagement and repetition by offering enriched, feedback-driven environments, yet improvements in virtual performance must be anchored to real-world functional exercises to avoid context-limited learning (Saposnik & Levin, 2011). Telerehabilitation extends practice beyond the clinic, providing a mechanism for long-term continuity of care, but its effectiveness depends on appropriate clinical supervision and integration with in-person assessment and goal-setting (Velayati et al., 2020; Ciortea et al., 2021).

Neuromodulatory therapies exemplify the more biologically targeted adjuncts that have entered the rehabilitation landscape. NIBS and VNS aim to modulate cortical excitability, influence interhemispheric balance, or enhance synaptic plasticity, thereby altering the responsiveness of neural networks to behavioral training (Lefaucheur et al., 2020; Veldema & Gharabaghi, 2022; Dawson et al., 2021). However, consistent across the literature is the understanding that these modalities are not standalone treatments; rather, they are most beneficial when paired with task-specific therapy that provides the behavioral substrate required for experience-dependent plasticity. This underscores a broader principle that neurobiological modulation and behavioral practice must converge to produce durable functional gains.

Despite the promise of emerging technologies, several challenges limit their integration into routine clinical pathways. One issue is heterogeneity in patient characteristics, including lesion location, severity of impairment, cognitive status, and comorbidities, all of which influence responsiveness to specific modalities. Tailoring therapy to individual recovery profiles remains a key challenge, although AI-assisted systems show potential to support more personalized, data-driven decision-making by adapting exercise difficulty, detecting compensatory strategies, and guiding therapist interventions (Quattrocchi et al., 2024). Nevertheless, the widespread implementation of such systems requires infrastructural investment, workforce training, and careful validation to ensure reliability and clinical applicability.

Another challenge is the variability in evidence quality across different modalities. While traditional therapies are supported by decades of research and remain universally recommended in guidelines (Langhorne et al., 2011; Pollock et al., 2014; Winstein et al., 2016), emerging technologies often show mixed or modest effect sizes in meta-analyses (Faralli et al., 2013; Straudi et al., 2025). These discrepancies may reflect methodological limitations, such as small sample sizes, heterogeneous protocols, inconsistent dosing, and inadequate long-term follow-up, rather than inherent ineffectiveness. Nonetheless, they highlight the need for more rigorous, standardized trials that assess not only functional outcomes but also mechanistic biomarkers capable of capturing subtle changes in neural plasticity and network reorganization.

A further consideration is the real-world feasibility of delivering intensive, multimodal rehabilitation. Stroke systems of care vary widely across regions and healthcare infrastructures, creating substantial disparities in access to high-dose therapy and advanced rehabilitation technologies. Telerehabilitation and home-based digital tools may partially mitigate these inequities by offering scalable, remote solutions, yet their effectiveness depends on digital literacy, sustained patient engagement, and reliable mechanisms for monitoring performance. Moreover, the long-term sustainability of technology-assisted rehabilitation remains uncertain, as many interventions demonstrate declining adherence over time when not supported by structured therapist or caregiver involvement.

Taken together, the available evidence supports a conceptual shift toward blended rehabilitation models that harness the strengths of both traditional and emerging approaches. The goal is not to replace established therapies, but to enhance them through methods that increase practice intensity, improve feedback precision, elevate patient motivation, or prime neural circuits to respond more effectively to training. This integrated perspective aligns closely with contemporary neurobiological frameworks and major clinical guidelines, which emphasize the importance of repeated, meaningful, and progressively challenging practice delivered within a physiologically receptive neural environment (Winstein et al., 2016).

Ultimately, the trajectory of stroke rehabilitation is moving toward greater precision, multimodality, and continuity across the recovery trajectory. Continued research is required to refine patient selection criteria, optimize dosing strategies, and determine how best to sequence or combine interventions at different stages of recovery. As technologies mature and become more widely accessible, the future of neurorehabilitation will likely be defined by dynamic, individualized treatment ecosystems that adapt continually to each patient's evolving neurological capacity and functional goals. In this context, the integration of traditional and emerging rehabilitation methods represents not a transitional phase but a sustainable and forward-looking model for maximizing recovery and improving long-term outcomes for stroke survivors.

### **Future Directions**

Future work in stroke rehabilitation must address the existing research gaps by strengthening both methodological rigor and translational relevance. Large-scale, multicenter trials with standardized dosing parameters, clearly defined intervention taxonomies, and long-term follow-up are essential to establish more definitive evidence regarding the relative and combined efficacy of traditional and emerging rehabilitation methods. Incorporating neurophysiological and imaging biomarkers into clinical studies may help identify

patient-specific predictors of treatment responsiveness, enabling precision rehabilitation strategies that align therapeutic selection and timing with neurobiological readiness for change.

Advances in artificial intelligence hold substantial promise for enhancing individualized therapy. AI-driven systems can dynamically adjust task difficulty, monitor performance in real time, detect compensatory movement patterns, and support therapist decision-making. These capabilities may help bridge the gap between high-intensity, structured therapy delivered in clinical environments and the variable conditions of home-based practice. Parallel progress in wearable sensors, remote monitoring technologies, and telerehabilitation infrastructure could further extend therapeutic intensity beyond the clinic, allowing patients to engage in meaningful, sustained training over longer time periods. However, achieving equitable access to these innovations will require coordinated efforts involving policy development, reimbursement frameworks, and specialized clinical training.

Neuromodulation represents another critical frontier for future research. Further studies are needed to refine stimulation parameters, establish biomarkers predictive of treatment responsiveness, and optimize the integration of stimulation with task-specific training. More broadly, next-generation rehabilitation paradigms will likely draw increasingly from theoretical models of motor learning, cognitive engagement, and motivational science, acknowledging that behavioral, cognitive, and emotional factors shape neuroplastic potential as much as biological interventions.

As the field continues to evolve, the development of hybrid rehabilitation models that strategically combine traditional therapies with targeted technological and neuromodulatory adjuncts will be central. Such integrative approaches should not merely increase training intensity, but also leverage neurobiological windows of opportunity, enhance patient engagement, and support personalized, adaptive trajectories of recovery. Ultimately, the future of stroke rehabilitation lies in sophisticated, multidimensional frameworks that align biological mechanisms with patient-centered functional goals to maximize long-term outcomes.

### **Conclusions**

Stroke rehabilitation is undergoing a profound transformation driven by advances in neuroscience, technological innovation, and evolving clinical practice. Traditional, therapist-guided neurorehabilitation remains the foundation of functional recovery, grounded in principles of task specificity, high-repetition practice, and coordinated multidisciplinary care. However, growing recognition that conventional therapy alone may not deliver sufficient intensity, adaptability, or long-term continuity has accelerated the development of complementary approaches aimed at enhancing neuroplasticity and expanding therapeutic opportunities beyond the limits of standard clinical schedules.

Emerging technologies, including robotic-assisted training, VR, telerehabilitation platforms, neuromodulation techniques, and AI-driven adaptive therapy, offer promising avenues to augment and refine established rehabilitation methods. Current evidence suggests that these modalities yield the greatest benefit when integrated into comprehensive, well-coordinated rehabilitation programs that align biological readiness for change, behavioral engagement, and functionally relevant practice. Rather than replacing traditional therapy, technological and neuromodulatory interventions serve to intensify practice, enrich sensory feedback, and optimize the neural conditions under which learning and recovery occur.

Despite encouraging progress, several challenges continue to impede widespread implementation. Heterogeneity in patient characteristics, variability in study methodologies, limited availability of advanced technologies, and the absence of validated biomarkers hamper efforts to deliver tailored, multimodal rehabilitation pathways. Overcoming these barriers will require rigorous and collaborative research, particularly multicenter trials with standardized intervention frameworks, as well as systemic adjustments in healthcare policy, reimbursement, and workforce training.

Ultimately, the future of stroke rehabilitation lies in dynamic, individualized care models that integrate biological, technological, and behavioral dimensions of recovery. Continued advances in understanding neural repair mechanisms, combined with broader access to high-quality, evidence-based interventions, will be essential for reducing long-term disability and improving quality of life for stroke survivors worldwide.

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