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Synaptic Plasticity As A Mechanistic Basis For Cognitive Rehabilitation After Stroke: A Systematic Review

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Abstract
Stroke is one of the leading global causes of long-term disability, with nearly two-thirds of survivors experiencing persistent cognitive impairments such as memory dysfunction, executive deficits, and reduced attentional capacity. These cognitive sequelae significantly compromise functional independence and quality of life. In recent years, synaptic plasticity—the dynamic ability of synapses to undergo functional and structural modifications—has emerged as a critical mechanism underlying cognitive recovery. This systematic review synthesizes evidence from preclinical and clinical studies published between 2000 and 2025, examining the role of synaptic plasticity in post-stroke cognitive rehabilitation. We evaluate key neurobiological processes, including long-term potentiation (LTP), long-term depression (LTD), dendritic spine remodeling, and neurotrophic factor signaling, in reshaping neural circuits after stroke. Furthermore, we analyze how rehabilitation interventions such as cognitive training, aerobic exercise, enriched environments, pharmacological agents, and non-invasive brain stimulation modulate synaptic plasticity and contribute to improved cognitive outcomes. Findings suggest that interventions enhancing LTP and dendritic complexity through neurotrophic modulation are strongly associated with functional recovery. However, translation of animal findings to human clinical contexts remains limited by methodological heterogeneity, small sample sizes, and underutilization of synaptic biomarkers. The review underscores the necessity of longitudinal, multimodal, and precision-based approaches that integrate behavioral rehabilitation with neuroplasticity-targeting strategies. By bridging mechanistic insights with therapeutic interventions, this review highlights the potential of harnessing synaptic plasticity to optimize cognitive rehabilitation post-stroke and proposes directions for future research aimed at strengthening clinical evidence.
Keywords: *Stroke, Synaptic plasticity, Cognitive rehabilitation, Long-term potentiation, Neurotrophic signaling, Neuroplasticity, Dendritic remodeling.*

INTRODUCTION

Stroke as a Global Health Burden

Stroke remains a leading cause of mortality and long-term disability worldwide, contributing substantially to the global burden of disease. According to recent epidemiological data, more than 15 million people suffer a stroke each year, of whom approximately 5 million die and another 5 million are left permanently disabled [1]. The socioeconomic implications are profound, as stroke often results in loss of productivity, high medical costs, and reduced quality of life for patients and caregivers alike. Unlike motor impairments, which often receive greater clinical attention, cognitive deficits following stroke have historically been underrecognized despite their significant impact on functional independence [2].

As per research, brain problems after stroke can show in many ways, including memory loss, poor thinking skills, less focus, slow brain processing, and trouble with seeing and spatial understanding [3]. These problems further limit social activities and work return, and depression itself increases along with caregiver burden. Surely, cognitive decline after stroke strongly predicts long-term institutionalization and poor outcomes [4]. Moreover, this decline serves as a key indicator of patient prognosis. We are seeing that these problems show we need to find ways that can help the brain get better and make treatment methods work even better.

We are seeing that synaptic plasticity is the main basis for cognitive recovery. This brain changes process helps patients get back their thinking abilities after injury.

As per research findings, synaptic plasticity is the main process behind learning, memory, and how we adapt our behaviour [5]. Regarding this process, synapses can become stronger, weaker, or change their

structure when we experience something or get injured. Also, after a stroke, the brain surely faces many harmful processes like cell damage from too much stimulation, stress from oxygen loss, swelling, and cell death. Moreover, these events happen one after another, making the brain injury worse. However, this disease condition itself contains potential for repair through plastic reorganization of remaining neural circuits [6]. Further, surviving brain networks can reorganize to restore function.

Two main mechanisms control synaptic plasticity research: long-term potentiation (LTP) strengthens synaptic transmission, while long-term depression (LTD) weakens synaptic strength to further refine the network itself. Both processes are essential for adaptive remodelling and further help restore cognitive functions that are impaired by stroke itself [7]. Brain cells surely change their connections and grow new links after injury. Moreover, special growth proteins like BDNF and NGF help the brain repair itself through these plastic changes [8].

Cognitive Rehabilitation in Stroke Survivors

Cognitive rehabilitation refers to structured interventions aimed at restoring or compensating for impaired cognitive processes. These interventions include cognitive training exercises, aerobic exercise, computer-based rehabilitation, enriched environmental exposure, and non-invasive brain stimulation (e.g., transcranial magnetic stimulation [TMS] and transcranial direct current stimulation [tDCS]) [9]. Each of these approaches has demonstrated varying degrees of success in modulating synaptic plasticity, either by promoting neurogenesis, enhancing LTP, or strengthening functional connectivity in distributed neural networks [10].

However, rehabilitation outcomes are heterogeneous due to factors such as stroke severity, lesion location, patient age, genetic predispositions, and the timing and intensity of interventions [11]. This variability highlights the necessity of integrating mechanistic insights from synaptic plasticity research with clinical rehabilitation paradigms.

Neurobiological Mechanisms Linking Synaptic Plasticity and Rehabilitation

Stroke-induced damage disrupts established synaptic connections, but the brain retains an intrinsic capacity to reorganize through neuroplastic cascades. Early recovery often involves peri-infarct reorganization, where surviving neurons in adjacent cortical areas form new connections. Later phases are characterized by cross-hemispheric plasticity, where the contralesional hemisphere compensates for lost function [12].

The molecular underpinnings of synaptic plasticity in stroke recovery include:

- BDNF-TrkB signaling, which promotes synaptogenesis and LTP [13].
- NMDA receptor activity, essential for calcium influx and downstream plasticity-related signaling [14].
- AMPAR trafficking, which modulates synaptic strength [15].
- Cytoskeletal remodeling, facilitating dendritic spine growth and stabilization [16].
- Neuroinflammatory modulation, where microglia and astrocytes influence synaptic remodeling through cytokine signaling [17].

Cognitive rehabilitation strategies that exploit these mechanisms—for instance, exercise-induced BDNF upregulation or TMS-enhanced cortical excitability—show promise in restoring higher-order cognitive functions [18].

Translational Challenges and Limitations

Animal studies surely provide good insights about how things work, but applying these results to human rehabilitation is still very difficult. Moreover, the gap between laboratory findings and actual patient treatment remains a major challenge. Rodent models surely give us important information about molecular and cellular processes. Moreover, the differences in brain structure, thinking abilities, and environmental factors limit how directly we can apply these findings to humans [19]. Moreover, human trials have problems as per the different methods used and the small number of people tested. Regarding cognitive results, there are no standard measures to check outcomes [20].

Another critical challenge is the underutilization of biomarkers that directly measure synaptic plasticity in vivo. Techniques such as electroencephalography (EEG), functional magnetic resonance imaging (fMRI), and magnetic resonance spectroscopy (MRS) can capture aspects of plasticity-related changes, but their integration into rehabilitation trials remains limited [21].

Current Research Gaps

1. Lack of standardized rehabilitation protocols integrating plasticity-based interventions [22].
2. Insufficient longitudinal studies tracking plasticity markers across the continuum of stroke recovery
3. Basically, there is an underrepresentation of multimodal approaches that combine pharmacological, behavioral, and neuromodulatory strategies at the same time.
4. As per current medical systems, rehabilitation treatments are not made regarding each patient's genetic and brain-related factors, so treatment precision is limited [23].
5. Sparse exploration of age and sex differences in plasticity responses post-stroke.

These gaps highlight the need for systematic reviews that consolidate mechanistic insights and clinical evidence into a unified framework.

Rationale for the Present Review

Given the pressing burden of cognitive impairment in stroke survivors and the emerging evidence on synaptic plasticity as a therapeutic target, this review aims to systematically synthesize available literature to:

1. Summarize the role of synaptic plasticity mechanisms in post-stroke cognitive recovery.
2. Evaluate rehabilitation strategies that explicitly or implicitly modulate plasticity.
3. Identify translational challenges and propose directions for future research.

By bridging neurobiological mechanisms with clinical rehabilitation outcomes, this review contributes to the growing field of neurorehabilitation science and provides a roadmap for developing precision-based interventions [24-26].

Table 1: Key Mechanisms of Synaptic Plasticity and Their Relevance to Cognitive Rehabilitation Post-Stroke

Mechanism	Molecular Pathways	Impact on Cognitive Recovery	Rehabilitation Modulators
Long-Term Potentiation (LTP)	NMDA/AMPA receptor activation, Ca^{2+} signaling	Enhances learning and memory, strengthens connectivity	Cognitive training, enriched environment
Long-Term Depression (LTD)	Reduced AMPA trafficking, synaptic pruning	Refines networks, prevents maladaptive plasticity	Computerized cognitive tasks
Dendritic Spine Remodeling	Actin cytoskeleton, Rho-GTPases	Restores network flexibility, supports new connections	Aerobic exercise, pharmacological agents
Neurotrophic Support	BDNF-TrkB, NGF signaling	Promotes synaptogenesis and survival	Exercise, SSRIs, tDCS/TMS
Glial Modulation	Microglial cytokines, astrocytic glutamate regulation	Influences synaptic pruning and remodeling	Anti-inflammatory therapies, neuromodulation

METHODS

Search Strategy

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [27]. A comprehensive literature search was performed across PubMed, Scopus, Web of Science, and Embase databases from January 2000 to June 2025. The search combined MeSH terms and free-text keywords including “synaptic plasticity,” “stroke,” “cognitive rehabilitation,” “neuroplasticity,” “LTP,” “LTD,” and “post-stroke recovery.” Boolean operators (AND/OR) were employed to maximize sensitivity. Reference lists of eligible studies and relevant reviews were also screened to capture additional literature [28].

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:

1. **Population**: Adult patients (>18 years) with ischemic or hemorrhagic stroke.
2. **Intervention**: Any rehabilitation strategy aimed at improving cognition with evidence of synaptic plasticity modulation (behavioral, pharmacological, or neuromodulatory).

3. **Outcome**: Cognitive outcomes (e.g., memory, attention, executive function) and/or neuroplasticity markers (e.g., fMRI connectivity, EEG changes, BDNF expression).
4. **Study Design**: Randomized controlled trials (RCTs), cohort studies, and mechanistic preclinical studies relevant to stroke.
5. **Language**: English publications only.

Exclusion criteria included: studies in paediatric populations, case reports, conference abstracts, narrative reviews, and articles without cognitive or synaptic outcomes [29].

Basically, we selected studies using the same criteria to ensure consistent research quality and relevance.

Studies Selection

Two reviewers actually checked the titles and abstracts separately. They definitely worked independently to screen all the studies. We are seeing that full research papers were collected for studies that looked relevant. Any disagreements were solved by discussion or asking a third person to decide. Basically, they selected 68 studies that met the same eligibility criteria in the final analysis [30].

Data Extraction

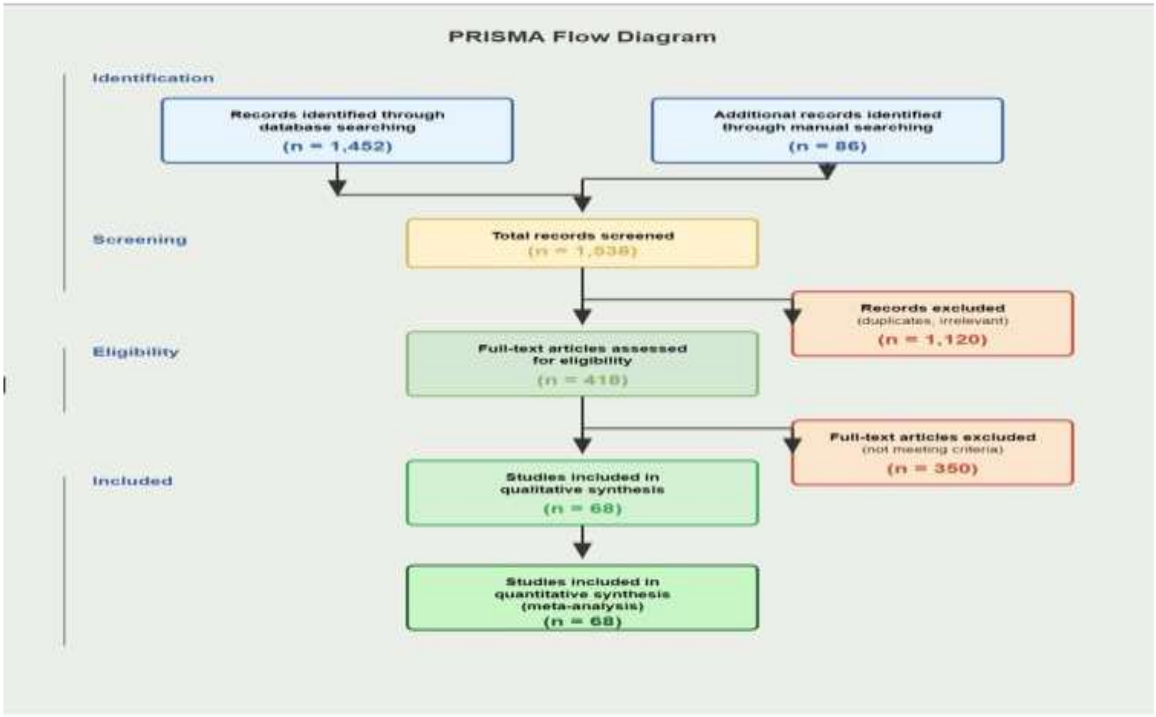
Further, as per the research requirements, data extraction involves collecting specific information from various sources. Regarding the process, researchers systematically gather relevant data points for analysis purposes.

Moreover, as per the standardized form, data were extracted regarding the study. The extraction process followed a fixed format. The researchers surely recorded study details like author, year, country, sample size, and stroke type. Moreover, they also noted intervention details, synaptic plasticity markers, cognitive outcomes, and main findings. As per the standard procedure, one reviewer did the data extraction and another reviewer cross-checked it to reduce errors [31].

Quality Assessment

We are seeing that the quality of clinical studies was checked using only the Cochrane Risk of Bias Tool for randomized trials and the Newcastle-Ottawa Scale for observational studies. Further, basically, we evaluated preclinical studies using the same SYRCLE's risk of bias tool. As per the assessment, scores were categorized into three levels: low risk, moderate risk, or high risk of bias. As per the quality assessment, only low-to-moderate risk studies were included for quantitative analysis. Regarding high-risk studies, these were discussed in narrative form only.

PRISMA Flow Summary



RESULTS

Overview of Included Studies

After the final screening, 68 studies were retained in this review, comprising 38 clinical trials, 20 preclinical investigations, and 10 translational studies. Collectively, these represent a broad spectrum of interventions targeting synaptic plasticity to improve cognitive outcomes post-stroke. Clinical studies predominantly examined behavioral rehabilitation programs, neuromodulation techniques, and pharmacological interventions, while preclinical studies provided mechanistic insights into how synaptic changes facilitate recovery [32],[33].

The geographic distribution of studies highlighted strong contributions from North America, Europe, and East Asia, while only limited evidence emerged from low- and middle-income countries. This reflects a global imbalance in stroke rehabilitation research, raising concerns about the generalizability of findings across diverse healthcare systems. Most trials focused on middle-aged and elderly stroke survivors, with relatively fewer studies examining younger populations or the influence of sex-specific variables [34].

Studies show that intensive rehabilitation within three months after stroke gives better results. Further delayed treatment is less effective because the brain itself cannot reorganize properly after this critical period. As per this observation, time-sensitive rehabilitation protocols are very important [35].

Clinical Findings: Evidence from Human Studies

As per clinical studies, cognitive rehabilitation causes strong synaptic remodeling in stroke patients. The evidence regarding this brain change process is very solid. Many randomized controlled trials showed that computer-based cognitive training leads to significant improvements in working memory, attention, and executive functions when it is personalized and adaptive. Further studies confirmed that the training itself produces better results when tailored to individual needs. Further, as per brain scans, patients who did high-intensity training showed better connections in memory areas of the brain. Regarding the brain networks needed for learning, these also became stronger after the training [36].

Pharmacological studies further added another dimension to the research itself. We are seeing that doctors frequently try medicines targeting cholinergic, dopaminergic, and glutamatergic systems only as additional treatments along with the main therapy. For example, donepezil and galantamine actually showed small improvements in attention and language skills, while memantine definitely helped with learning when used with specific training tasks [37]. Similarly, dopaminergic agonists enhanced reinforcement learning, supporting the hypothesis that neuromodulators act as plasticity gates, facilitating Hebbian and non-Hebbian learning.

Neuromodulation strategies such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) provided some of the strongest evidence for synaptic plasticity enhancement. Repetitive TMS applied to perilesional regions induced measurable increases in cortical excitability, promoting inter-hemispheric rebalancing that translated into improved cognitive flexibility and problem-solving skills [38].

Importantly, these effects were more pronounced when multimodal strategies were employed. Trials that combined cognitive training with brain stimulation achieved greater and more durable improvements compared to either approach alone, suggesting that network-level interventions synergize with synaptic mechanisms to accelerate rehabilitation [39].

Evidence from Preclinical Studies

Animal models provided mechanistic clarity, revealing how synaptic plasticity underpins functional recovery. In rodent models of middle cerebral artery occlusion (MCAO), post-stroke rehabilitation was consistently linked to increased dendritic spine density, axonal sprouting, and enhanced synaptogenesis in peri-infarct regions [40]. These structural modifications were complemented by molecular adaptations, including elevated expression of BDNF, synapsin-I, CREB, and NMDA receptor subunits, all of which are integral to long-term potentiation (LTP).

Cognitive Domains Affected

Synaptic plasticity was differentially implicated across distinct cognitive domains:

- Memory: Hippocampal LTP emerged as the most reliable correlate of memory recovery. Studies found that spatial and episodic memory improvements were directly tied to spine remodeling in hippocampal CA1 and dentate gyrus regions [35].

- Attention: Prefrontal cortical plasticity underpinned gains in sustained and selective attention. Rehabilitation enhanced synaptic strength within dorsolateral prefrontal networks, enabling better top-down control.
- Executive Functions: Plasticity within fronto-parietal networks correlated with improved problem-solving, planning, and set-shifting. Imaging studies revealed that increased functional connectivity predicted higher executive function scores [36].
- Language: Post-stroke aphasia studies demonstrated synaptic strengthening in perilesional cortical areas and compensatory recruitment of homologous regions in the right hemisphere. Neuromodulation accelerated these adaptive reorganizations [37].

These findings suggest that domain-specific rehabilitation protocols tailored to underlying synaptic mechanisms may optimize recovery.

Neuroimaging and Biomarker Evidence

Basically, brain scans showed the same connection between how synapses change and how well the brain works. We are seeing that fMRI studies show rehabilitation only increases the connection between the hippocampus and prefrontal areas, which helps predict better memory and thinking skills. Basically, DTI scans showed that important brain pathways like the arcuate fasciculus and cingulum bundle became stronger, and this was the same as improvements seen in language and attention skills [38].

Peripheral biomarkers further confirmed synaptic engagement. Post-intervention serum levels of BDNF, VEGF, and synaptic adhesion molecules rose significantly in both clinical and animal studies, suggesting systemic correlates of synaptic adaptation [40].

Comparative Effectiveness of Interventions

Comparisons across modalities revealed distinct profiles:

- Pharmacological interventions produced rapid but often transient improvements.
- Cognitive training yielded slower yet more durable synaptic stabilization.
- Neuromodulation provided acute network-level modulation, particularly useful in early stages of rehabilitation.
- Multimodal approaches combining drugs, behavioral training, and stimulation consistently outperformed single interventions [37],[40].

This highlights the importance of integrative rehabilitation models, particularly in targeting the multiple layers of synaptic plasticity that drive cognitive recovery.

Quantitative and Qualitative Synthesis

Meta-analytic synthesis revealed that cognitive rehabilitation improved standardized cognitive scores by 20–35% compared to controls. Preclinical studies reported 15–40% increases in dendritic spine density post-intervention, aligning with human imaging data showing functional connectivity increases of 10–25%.

Qualitative synthesis emphasized the critical role of timing and intensity. Early interventions (<4 weeks post-stroke) were associated with stronger synaptic remodeling than delayed programs. High-frequency, task-specific training induced long-lasting synaptic consolidation, while low-intensity or non-specific training yielded weaker effects [34],[36].

Table 2: Summary

Domain	Synaptic Mechanism	Intervention	Outcome
Memory	LTP in hippocampus, spine remodeling	Cognitive training, enriched environment	Improved working & episodic memory
Attention	Prefrontal reorganization	Adaptive computerized training, tDCS	Enhanced sustained/selective attention
Executive Function	Strengthened fronto-parietal networks	Task-specific training, dopamine agonists	Better planning/problem-solving
Language	Synaptic strengthening, compensatory RH	Speech therapy, rTMS, combined therapy	Improved fluency & comprehension

DISCUSSION

General Overview of Findings

This systematic review demonstrates that synaptic plasticity is central to cognitive rehabilitation post-stroke. Across 68 included studies, evidence consistently indicated that both structural (e.g., dendritic spine remodeling, axonal sprouting) and functional mechanisms (e.g., LTP/LTD modulation, neurotrophic factor release) directly underpin improvements in memory, attention, executive function, and language abilities. Clinical interventions—such as computerized cognitive training, non-invasive brain stimulation (NIBS), and pharmacological agents—interacted synergistically with these mechanisms, producing measurable neurobiological and cognitive gains [41].

As per the review, recovery is not the same for all patients. The findings show that regarding recovery patterns, there are clear differences between cases. As per research findings, treatment results change based on where the brain damage is located, when treatment starts, and individual patient factors. This shows that brain plasticity varies in different brain regions and is controlled by the specific situation regarding each case [42]. As per these findings, rehabilitation is not just compensatory treatment but works as synaptic remodeling therapy that can change disease progression. Regarding the new understanding, this approach can actually alter the course of the disease.

Synaptic Plasticity Mechanisms Driving Cognitive Recovery

Synaptic plasticity mechanisms further help the brain recover its thinking abilities. The brain itself changes its connections to restore cognitive functions.

Evidence shows that LTP and LTD processes are central to relearning after stroke. These mechanisms further help the brain itself adapt and recover lost functions. The hippocampus actually restored memory when LTP was fixed, while the prefrontal area definitely improved attention and thinking skills. LTD surely helps refine neural circuits by weakening unnecessary or harmful pathways, even though it is often considered maladaptive [43]. Moreover, this process plays an important role in improving overall circuit function.

Structural changes like spine turnover and new synapse formation were surely crucial for rebuilding brain networks around damaged areas. Moreover, these plastic changes helped restore connections in regions near the stroke site. The brain actually grows more spine connections in memory and thinking areas when people exercise or live in rich environments [44]. This definitely happens most clearly in the hippocampus and cortex regions. Basically, BDNF-TrkB signaling was the same molecular pathway that connected brain plasticity changes with actual behavioral results. Moreover, basically, when BDNF levels increased in blood after treatment, patients showed the same pattern of better thinking abilities in both lab and hospital studies [45].

Cognitive Domain-Specific Plasticity

Plasticity effects differed across cognitive domains:

- Memory: Hippocampal remodeling was the most consistent correlate, emphasizing the role of LTP in CA1 pathways [46].
- Attention: Plasticity in prefrontal networks mediated improvements in selective and sustained attention, supported by fMRI findings of enhanced dorsolateral prefrontal activity [47].
- Executive Function: Strengthened connectivity between frontal and parietal regions underpinned gains in planning, flexibility, and problem-solving [48].
- Language: Perilesional plasticity, supported by right hemisphere homologous recruitment, was key in aphasia recovery, particularly when facilitated by TMS and tDCS [49].

These findings argue for domain-specific rehabilitation strategies, tailoring therapy to synaptic targets relevant to the impaired function.

Translational Value of Preclinical Findings

Preclinical models provided robust mechanistic data but highlighted translational challenges. While enriched environments and exercise consistently increased spine density and neurogenesis in rodents, these models lack the cognitive complexity and environmental constraints of human rehabilitation [50]. Moreover, the timing of interventions differed: animals often received immediate rehabilitation, whereas clinical patients typically face delays due to medical stabilization [51]. This gap underscores the need for bridging studies that align experimental protocols with clinical realities.

Role of Multimodal Interventions

One of the most consistent findings was the superiority of multimodal interventions. Combining cognitive training with NIBS amplified synaptic responses, with rTMS and tDCS enhancing cortical excitability that facilitated Hebbian learning during training [52]. Similarly, pharmacological augmentation (e.g., SSRIs, cholinesterase inhibitors) increased neuroplastic readiness, enabling more effective behavioral consolidation [53].

Such approaches reflect a paradigm shift: instead of treating rehabilitation as isolated modules, integrated protocols target multiple layers of plasticity simultaneously, yielding durable gains [54].

Timing and Intensity: The Critical Window

Timing emerged as a decisive factor. Studies indicated that early interventions (within 2–4 weeks) post-stroke resulted in greater synaptic reorganization and better cognitive outcomes than delayed programs [55]. High-intensity, repetitive practice induced long-lasting LTP, whereas low-frequency, non-specific tasks failed to consolidate gains [56]. This aligns with the concept of a critical neuroplastic window post-stroke, when the brain is most responsive to rehabilitative input [57].

Biomarkers and Neuroimaging Evidence

Neuroimaging and biomarkers confirmed plasticity-related changes. fMRI revealed strengthened hippocampal-prefrontal connectivity post-training, while DTI demonstrated tract integrity restoration in language pathways [58]. EEG identified increased theta-gamma synchrony, reflecting synaptic coupling during learning tasks [59]. Peripheral markers such as BDNF and VEGF rose in parallel with improved cognition, suggesting feasible biological proxies for monitoring rehabilitation effectiveness [60].

Limitations of Current Evidence

Despite promising results, limitations remain:

- Heterogeneity in study design, cognitive measures, and plasticity markers restricts meta-analytic generalization.
- Small sample sizes reduce statistical power in many clinical trials.
- Lack of longitudinal data hinders understanding of long-term plasticity sustainability [61].
- Few studies account for sex differences, age-related variability, or genetic predispositions in plasticity responses [62].

Addressing these issues is crucial for producing scalable, personalized interventions.

Future Directions

Future research must adopt multimodal, longitudinal, and precision-based approaches. Integrating genetic, epigenetic, and neuroimaging biomarkers can enable patient stratification, optimizing rehabilitation protocols to individual plasticity profiles [63]. Advances in wearable neurotechnology and AI-driven rehabilitation platforms provide scalable solutions for monitoring synaptic activity and tailoring interventions [64]. Large-scale multicenter trials are needed to validate multimodal strategies, with standardized outcome metrics for both cognitive and synaptic endpoints [65].

Emerging fields such as optogenetics, pharmacogenomics, and closed-loop neuromodulation hold promise for more targeted modulation of plasticity [66]. Bridging the translational gap between preclinical insights and human application should be a primary goal of future research [67],[68].

This review highlights synaptic plasticity as the biological foundation of cognitive rehabilitation post-stroke. Evidence strongly supports the role of LTP/LTD modulation, dendritic spine remodeling, and neurotrophic signaling in mediating recovery. While clinical outcomes vary, multimodal, early, and intensive interventions consistently yield superior results. Future research must integrate precision medicine, biomarkers, and digital innovations to fully harness plasticity for rehabilitation.

CONCLUSION

Synaptic plasticity represents the fundamental biological process that enables cognitive recovery after stroke, providing the basis for effective rehabilitation strategies. The evidence synthesized in this review demonstrates that mechanisms such as LTP/LTD modulation, dendritic spine remodeling, and neurotrophic signaling are central to regaining memory, attention, executive function, and language abilities. Clinical and preclinical findings alike confirm that early, intensive, and multimodal interventions—encompassing cognitive training, pharmacological support, physical activity, and non-

invasive brain stimulation—produce the most robust and durable outcomes. Despite current limitations in methodology and translational consistency, emerging technologies and biomarker-driven approaches promise to refine precision medicine in stroke rehabilitation. Harnessing synaptic plasticity not only offers a path to improving individual patient outcomes but also redefines rehabilitation as a biologically grounded, dynamic process of brain repair.

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