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Assessing Functional Recovery and Neural Plasticity in Ischemic Stroke Rodent Models- A Systematic Review

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Abstract

Ischemic stroke is a pervasive and debilitating condition, ranking as a leading cause of disability worldwide. The aftermath of a stroke poses significant challenges for rehabilitation and recovery, emphasizing the need for effective interventions. Rodent models have emerged as indispensable tools in investigating post-stroke rehabilitation strategies, providing valuable insights into the complex mechanisms governing stroke recovery. This systematic review provides a comprehensive synthesis of evidence from 10 experimental studies, carefully selected through a rigorous literature search to investigate the efficacy of physical exercise in promoting functional recovery and neural plasticity in rodent models of ischemic stroke. Study quality was meticulously evaluated using the SYRCLE risk of bias tool, ensuring the precision and trustworthiness of the findings. The findings reveal that treadmill exercise leads to significant, long-lasting improvements in motor and cognitive function, decreases infarct volume, and boosts neurotrophic factors like BDNF, driving synaptic plasticity, neurogenesis, and myelin repair. Notably, the results indicate that exercise-induced neuroplasticity is facilitated by key signaling pathways, including CREB/BDNF and caveolin-1/VEGF mechanisms, offering crucial insights into the underlying mechanisms of exercise-mediated recovery. These findings have significant implications for developing effective rehabilitation strategies for stroke survivors, emphasizing the therapeutic benefits of physical exercise in enhancing functional outcomes and quality of life

Keywords: *Cerebral Ischemia, Functional Assessment, Histomorphometry Evaluation, Neuro Regeneration, Treadmill Exercise.*

Introduction

Stroke poses a formidable and growing global health threat, ranking as the primary cause of physical disability in adults and the second leading cause of mortality in middle- to high-income countries. A cluster of key risk factors contributes to stroke incidence, including hypertension, diabetes, cardiovascular disease, smoking, substance abuse, obesity, and sedentary lifestyle. The Trial of Organisation in Acute Stroke Treatment (TOAST) classification system stratifies cerebral ischemia into five distinct subtypes:

1. Atherosclerotic large artery disease.
2. Cardioembolic stroke.
3. 3.lacunar stroke.
4. Stroke from other identified causes.
5. Stroke of unknown or undetermined aetiology.

Inadequate blood supply to cerebral tissue results in a reversible loss of function, which, if prolonged, leads to infarction and neuronal loss

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[4]. Ischemic stroke initiates a cascade beginning with electrical function loss, progressing to membrane disturbance, calcium influx, excitotoxicity, reactive oxygen species generation, and cell membrane destruction. This causes irreversible damage, disrupting functional capabilities and significantly altering lifestyle [5].

Rodent models, particularly mice and rats, are widely used in stroke studies due to their cost-effectiveness, ease of monitoring, and ethical considerations [6]. Rats are favored because their cerebral vasculature and physiology closely resemble that of humans. Their moderate body size facilitates monitoring, and their small brain size is conducive to fixation procedures [7]. Furthermore, the resemblance between human limb movements and rodent arm movement patterns, observed during reaching behaviors, indicate that these models can be effectively translated to study human motor function and dysfunction [8-10, 15].

Functional recovery and neural plasticity are extensively discussed. Long-term potentiation in perilesional areas, observed seven days post-lesion induction, indicates enhanced plasticity potential [11]. Phasic and tonic GABAergic inhibition exhibit distinct regulatory patterns in peri-infarct regions, which is essential [12]. The reorganization of areas surrounding the lesion, measured through intracortical microstimulation, shows that motor output is produced by small neuronal groups around the infarct, aiding in functional recovery [13, 14].

There is a notable scarcity of literature on the impact of exercise and neural plasticity on brain recovery post-injury. This systematic review aims to synthesize and critically evaluate existing research, highlighting the benefits and drawbacks of various methodological approaches. By undertaking this comprehensive review, we aim to provide a valuable resource for researchers investigating the relationship between neural plasticity and functional recovery. This review seeks to advance the understanding of functional assessment and histomorphometry analysis in ischemic stroke rodent models.

Methodology

We conducted a qualitative systematic review using the Preferred. Systematic Reviews and Meta-Analysis were conducted following PRISMA guidelines. The search included electronic databases such as Google Scholar, PubMed, and ScienceDirect. The systematic literature search covers article ranging from the year 2015 to 2025 using a combination of keywords and MeSH terms such as Ischemic Stroke, Treadmill Exercises, Functional assessment, Neural Plasticity and Rodent models. A thorough search strategy was utilized to find pertinent studies. Various keyword combinations and permutations were used to ensure a comprehensive and thorough search.

Data Collection Criteria

Studies Using Rodents Animals (Rats or mice), Studies using surgical intervention to induce Ischemic stroke (Middle cerebral Artery Occlusion), Studies using Physical Exercises (treadmill Rehabilitation/exercises), Studies using various equipment's to perform exercises (Rota Rod). Studies which are using outcome measures as Functional assessment (such as mNSS (Modified Neurological Severity Scoring) which includes Motor Assessment, Sensory Assessment, Reflex Abnormality and balance test). Studies using methods to calculate total infarct value (Nissl staining, TSS staining). Studies evaluating Histomorphometry evaluation (H&E staining, Western Blot, Apoptic Cell death, Flow Cytometry Array). Only experimental studies are included. Recent studies (2015-2025) were selected to capture the most up-to-date findings to guarantee contemporary relevance.

Selection Process for Studies

Process for selecting studies (refer to Figure 1), details the step-by-step process of identifying and selecting studies for inclusion.

Initially, 388 records were identified through database searching (from 2015-2025). 90 Full text article is not available and were removed, leaving 298 records. Following the screening process, 131 records were excluded due to not meeting the disease or eligibility criteria, 10 were excluded because of article being in different language, 28 were excluded because of Human study. Another 102 articles are from conference papers. 27 records were selected for retrieval. However, 09 records couldn't be retrieved.

This resulted in 18 records being assessed for eligibility. The remaining records underwent further evaluation. Out of these reports, 8 were excluded for specific reasons: 2 studies using various animals for the intervention, 3 studies for incompletion of data, 2 for weak methodology and 1 for small sample size. Ultimately, this review included 10 relevant studies. (Table 1). The flow chart (Figure 1) visually represents the filtering process from initial identification to the final inclusion of studies.

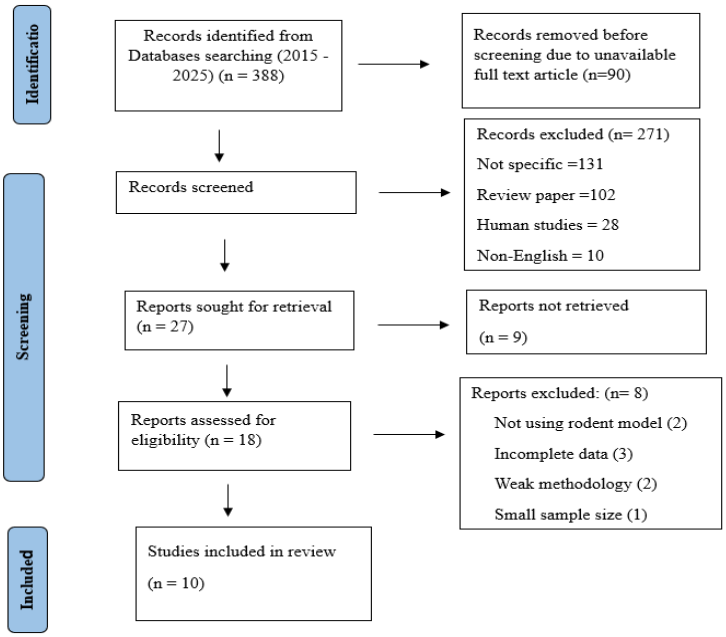

Figure 1. PRISMA Flow Diagram: A Systematic Literature Search of Studies Published Between 2015 and 2025

Methodological Quality

The SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) risk of bias tool, designed for use with Revman software, assesses bias in animal studies [16]. The evaluation tool includes 10 items that cover six categories of bias: selection, performance, detection, attrition, reporting, and other forms of bias. Each item is evaluated with a signaling question, with responses categorized Assessments were made using a three-tiered system: 'yes' (low risk of bias), 'no' (high risk of bias), and 'unclear' (ambiguous risk of bias). A response of 'no' signifies a high risk of bias for that particular item. Reviewers independently assessed key elements, such as the adequacy of randomization and allocation concealment, baseline characteristics, blinding of participants and outcomes, randomization of housing and outcome assessment, completeness of data, and selective reporting. Each aspect of bias was classified as low (green), high (red), or unclear (yellow).

Table 1. Review Of Literature

Author Name and year of publication	**Title of the study**	**Type of Paper**	**Rodents Model**	**Sample Size**	**Surgical Intervention**	**Type of Intervention**	**Treatment duration**	**Outcome measure**	**Reflection**
Qingfeng Xie, et al 2018	Treadmill exercise ameliorates focal cerebral ischemia/reperfusion-induced neurological deficit by promoting dendritic modification and synaptic plasticity via upregulating caveolin-1/VEGF signaling pathways	Experimental study	Sprague-Dawley male rats	191	Middle Cerebral Artery Occlusion (MCAO)	Treadmill Exercises	28 days	Functional Assessment Infarct volume assessment Histomorphometry Assessment	**Neurological function test:** Measured at 1 day, 7 days, and 28 days after MCAO, which assesses motor, sensory, reflex, and balance tests. **Infarct volume assessment:** Nissl staining is used to measure the infarct volume in the ipsilateral hemisphere. **Histomorphometric Assessment**: **HE staining:** HE staining uses hemalum, which stains cell nuclei blue. The study used an Olympus BH-2 microscope (Olympus Optical, London, UK) to capture the images. **Western blot analysis:** Densitometric analysis was conducted on coronal

									sections from the anterior of the frontal lobe, as well as the middle brain tissue block
Fengwu Li, et al 2020	In Search of a Dose: The Functional and Molecular Effects of Exercise on Post-stroke Rehabilitation in Rats	Research Article	male Sprague–Dawley rats	150	Middle Cerebral Artery Occlusion	Treadmill Exercise	28 Days	Functional Assessment Cerebral Infarct Volume Histomorphometry Assessment	**Functional Assessment:** Adhesive removal, beam balance, forelimb placing, grid walking, and Rota-rod performance assessed at days 1, 3, 7, 14, 21, and 28. **Cerebral Infarct Volume**: Brains were resected and cut into 2-mm-thick slices, which were then treated with 2,3,5-triphenyltetrazolium chloride for calculating infarct volume to minimize error caused by edema **Histomorphometry Assessment: Apoptotic Cell Death**: For quantification of apoptosis-related DNA fragmentation, a commercial enzyme immunoassay were used to determine cytoplasmic histone-associated DNA fragments.

									Neuron Isolation and Flow Cytometry Assay: an adult brain dissociation kit (Miltenyi Biotec, Bergisch Gladbach, Germany) was used for neuron isolation. **Western Blot Analysis**: Tissue samples from the ipsilesional ischemic cerebral hemispheres of all experimental groups were harvested, and total protein extraction was performed using cell lysis solutions. Protein concentration was then determined by the BCA method
JINGYAN CHENG, et al 2019	Treadmill exercise promotes neurogenesis and myelin repair via upregulating Wnt/β-catenin signaling pathways in the juvenile brain following focal cerebral ischemia/reperfusion	Experimental research	Sprague-Dawley male rats	171	Middle Cerebral Artery Occlusion	Treadmill Exercises	14 days	Functional Assessment Infarct volume assessment Histomorphometry Assessment Transmission electron microscopy (TEM)	**Functional Assessment**: **The modified neurological severity score (mNSS) test** at 1, 7 and 14 days after MCAO. **Infarct volume assessment:** For determination of the volume of cerebral infarction, TTC staining was performed.

									Histomorphometry Assessment: Bromodeoxyuridine injection: injected intraperitoneally into rats every day after MCAO for 7 or 14 days to label newly formed cells. **H&E staining**: H&E staining were performed at room temperature for 2 h, and observed under a light microscope (Olympus Corporation). Pathological changes in brain tissue were observed, images were captured. Toluidine blue. **Nissl staining**: To decolorized and dehydrated with ethanol and sealed with neutral resin. Under light microscopy (Olympus Corporation), the Nissl bodies of neurons were blue and purple. Western blot analysis: Total protein and nuclear protein were extracted respectively. The protein concentration

									was detected by a BCA protein detection kit. **Transmission electron microscopy (TEM):** The rats were sacrificed at 7 and 14 days after MCAO, and ultrastructural changes of neurons in the ischemic penumbra cortex was observed by TEM.
Juanjuan Lu, et al 2021	Treadmill Exercise Attenuates Cerebral Ischemia–Reperfusion Injury by Promoting Activation of M2 Microglia via Upregulation of Interleukin-4	Research Article	male Sprague Dawley Rats	117	Middle Cerebral Artery Occlusion	Treadmill Exercises	6 days	Functional Assessment Infarct Assessment Histomorphometry Assessment	**Functional Assessment: Modified Neurological Severity score**: 1, 4, and 7 days. mNSS is comprised of motor, sensory, reflex and balance tests. **Infarct Assessment:** 2,3,5-triphenyltetrazolium chloride (TTC) were used to estimate the volume of the brain infarct. **Histomorphometry Assessment: Quantitative Real-Time Polymerase Chain Reaction Analysis**: Total RNA was extracted from the penumbra and its concentration and purity

									examined using BioPhotometer plus. **Luminex Multiplex Assay**: To measure the concentrations of cytokines including IL-4, IL-10, IL-13, IL-1a, IL-1b, IL-6, and MCP-1 **Western Blotting**: To extract the protein of the penumbra was performed.
Min Cheol Chang, et al. 2019	Early treadmill exercise increases macrophage migration inhibitory factor expression after cerebral ischemia/reperfusion	Research Article	male Sprague-Dawley rats	40	Middle Cerebral Artery Occlusion	Treadmill Exercises	5 days	Functional Assessment Infarct Assessment Histomorphometry Assessment	**Functional Assessment: The wire hang and Garcia tests** were performed. The wire hang test: For the wire hang test, a wire mesh grid (15 cm × 25 cm) was used. The rats were placed on the wire mesh grid 40 cm above a foam cushion. Then, the mesh was inverted 180°, and the rats were forced to grasp the wire using their four limbs. The hanging time was recorded as the duration the rats remained hanging before falling on the cushion.

									The Garcia test: For evaluating neurological functions consisted of 6 subtests: spontaneous activity, symmetry of movements, symmetry of forelimbs, climbing wall of wire cage, reaction to touch on either side of trunk, and response to touch. The total scores ranged from 3 to 18, and higher scores corresponded to better functions. **Infarct Assessment: By using MRI, T2-weighted images** (T2WIs) were acquired. The degree of ischemic injury was evaluated by measuring the fractional anisotropy (FA) values on the FA map derived from diffusion MRI data. **Histomorphometry Assessment: Immunohistochemical analysis:** Primary antibodies against macrophage migration inhibitory factor

									(MIF) and BDNF (overnight at were detected with the HRP/DAB kit
Huixia Geng, et al 2022	Early Rehabilitation Exercise after Stroke Improves Neurological Recovery through Enhancing Angiogenesis in Patients and Cerebral Ischemia Rat Model	Research Article	Male adult Sprague–Dawley rats	Not Mentioned	Middle Cerebral Artery Occlusion (MCAO)	Treadmill Exercises	5 days	Functional Assessment Infarct Assessment Histomorphometry Assessment	**Functional Assessment: Modified Neurological Severity Scores** (mNSS) for assessing the state of rodents neurological function deficits **Infarct Assessment: TTC staining** were used to detect the cerebral infarction volume in each group after middle cerebral artery occlusion. The result shows that rehabilitation training at 24 h after MCAO can reduce the volume of cerebral infarction and reduce brain damage caused by cerebral ischemia-reperfusion **Histomorphometry Assessment:** **Western Blot analysis:**

									To extract the total protein. The total protein was quantified by BCA kit. **Immunofluorescence**: Slides were mounted with DAPI glycerol and observed under a fluorescence microscope and images were captured.
Li-Mei Cao, et al 2018	Treadmill training improves neurological deficits and suppresses neuronal apoptosis in cerebral ischemic stroke rats	Research article	Sprague-Dawley rat	120	Middle Cerebral Artery Occlusion (MCAO)	Treadmill Training	7 days	Functional Assessment Infarct Assessment Histomorphometry Assessment	**Functional Assessment: Locomotor function scoring:** Neurological deficit and locomotor function were assessed at 1, 3, and 7 days post the first training using a five-point scale (0–4) with the Bederson's test **Infarct Assessment: TTC (2,3,5-Triphenyltetrazolium chloride** (TTC) staining) staining was performed to evaluate the infarct volumes of the brain in MACO rats **Histomorphometry Assessment: Double immunofluorescence of terminal deoxynucleotidyl**

									transferase-mediated dUTP nick end labeling (TUNEL) staining and NeuN to visualize neuronal apoptosis. **Western blot assay** For the assessment of cAMP-PKA and Akt-GSK-3β activation, western blot assay was used to detect the expression of phosphor and PKA-Cα
Caroline Pin-Barre, et al 2025	Effects of High- Versus Moderate-Intensity Training on Neuroplasticity and Functional Recovery After Focal Ischemia	Research Article	Male Sprague-Dawley rats	108	Middle Cerebral Artery Occlusion (MCAO)	Treadmill Exercises	14 days	Functional Assessment Infarct Assessment Histomorphometry Assessment	**Functional Assessment**: **The elevated body swing test, the ladder-climbing test**, **and the forelimb grip force** were performed before (PRE) and after the surgery at day 1, 7, and 14. **Infarct Assessment:** Cresyl violet Were used to measure the infarct volume and the percentage of tissue loss (% tissue loss) **Histomorphometry Assessment: Immunohistochemistry Analysis:** To investigate the changes of p75NTR and microglia

									form, immunostaining with antibodies against the p75NTR and ionized calcium binding adaptor molecule 1 (Iba-1) **Western Blot Analysis**: To detect IL-10, IL-1β, IL-12p40, p75NTR, KCC2, and NKCC1 expression, the total protein extracted from each frozen hemisphere
Yamei Li, et al 2018	Learning-dependent LTP and synaptic ultrastructural modification after physical exercise in rats with middle cerebral artery occlusion: relevance for learning and memory	Research article	male Wistar rats	32	Middle Cerebral Artery Occlusion (MCAO)	Rolling-cage training, Balance training and screen training, to improve the walking, grabbing, and balancing functions	10 days	Functional Assessment Histomorphometry Assessment	**Functional Assessment:** **Y-maze:** contained three arms, a start arm and two choice arms. On the top of each arm there was a signal lamp, which was used as an indicator of dangerous region when the lamp lightened for 6 seconds. The rats were stimulated to run from the light arm to the dark arm by the energization of 36 V alternating current. If the rat ran from one light arm to another light one, it was recorded as wrong. Otherwise, if the rat ran to

									the dark one and it was recorded as correct. **One-trial passive avoidance response:** A multi-functional box for conditioned reflex training was put at the side of a table which was 60 cm high to make the box's diving board suspended in midair. Rats were put on the diving board with tails towards the gate. The normal reaction of the rats were panic and quickly finding the gate to enter the box. Once the rats entered the box, the gate was closed, and shocks with proper voltage were closely followed to apply to the rats' front paws for 5 to 10 seconds, so repeated for 3 times. **Histomorphometry Assessment:** **Quantitative measurements of synaptic ultrastructure:** With the QUANTIMENT-520 image analysis system, the width of

									synaptic cleft, the thickness of postsynaptic density (PSD), the chord length and the arc length of the postsynaptic membrane, the length of synapse's active zone, and percentage of perforated synapses were measured.
WEI LIU, et al 2018	Physical exercise promotes proliferation and differentiation of endogenous neural stem cells via ERK in rats with cerebral infarction	Research article	male Sprague Dawley rats	135	Middle cerebral artery occlusion (MCAO)	Treadmill exercises	21 days	Functional Assessment Infarct Assessment Histomorphometry Assessment	**Functional Assessment: Neurological severity scores. Modified neurological severity score (mNSS) tests** were used to assess the neurological function of the rats. **Infarct Assessment: TTC solution** were used to see the infarct volume **Histomorphometry Assessment: Hematoxylin and eosin (H&E) staining**: H&E staining was used to detect MCAO-induced lesions at the respective time point. **Immunofluorescence staining**

									Immunofluorescence staining was used to detect BrdU+/neuronal nuclei (NeuN)+ and BrdU+ /glial fibrillary acidic protein (GFAP)+ cells. **Western blot analysis:** Western blotting used to detect cyclin-dependent kinase 4 (CDK4), Cyclin D1, retinoblastoma protein (p-Rb), P-16, phosphorylated (p)-ERKl/2 and c-Fos protein expression in the hippocampus

Figure 2 offers a detailed breakdown of the risk of bias across various domains for each study. Each row represents an individual study, and each column represents a specific bias domain. Studies like Yameili et al. (2018) and Fengwu Li et al. exhibit high-risk domains, particularly in blinding, allocation concealment and random housing.

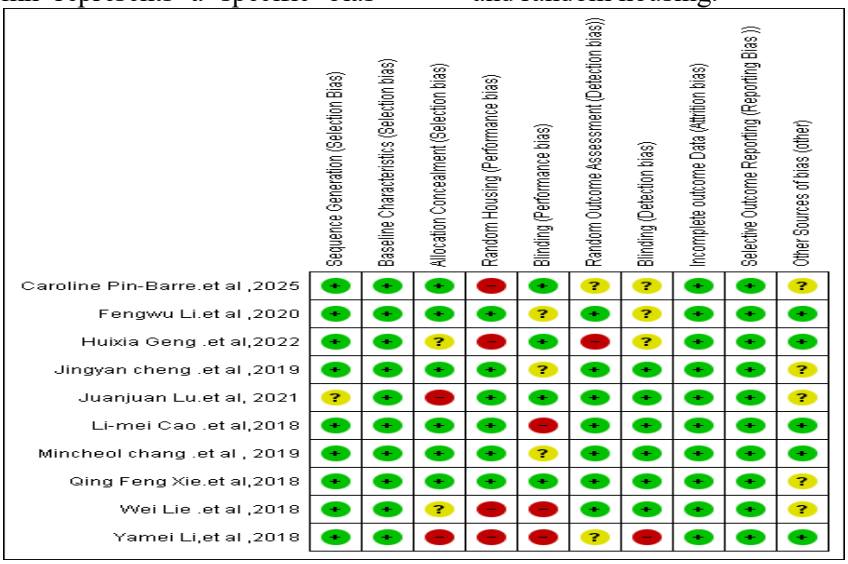

Figure 2. Study-Specific Risk of Bias

Figure 3 The chart provides a visual representation of the studies' risk of bias, grouping them into Low (green), Unclear (yellow), and High (red) risk categories for each domain. Low Risk (Green) dominates in most categories, such as Sequence generation, baseline characteristic, random housing, Incomplete Outcome Data and selective outcome reporting indicating that many studies followed rigorous methodology in these areas. Unclear Risk (Yellow) is prevalent in categories like blinding and other sources of bias assessment suggesting that some studies lacked sufficient information to make a clear judgment. High Risk (Red) is most noticeable in Blinding and Random Housing highlighting potential methodological flaws in these areas.

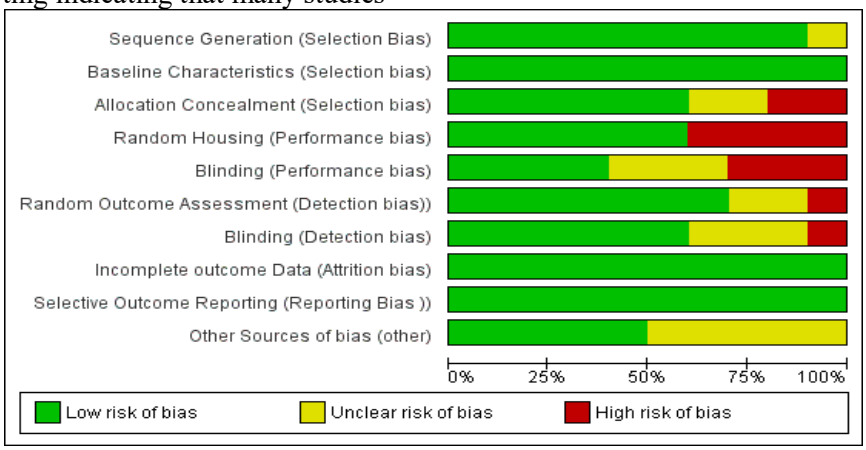

Figure 3. Summary of Risk of Bias of All Studies

Result

This systematic review analysed 10 studies on Neural Plasticity in Ischemic stroke in rodent models, highlighting the diverse methodologies employed to assess Neural Plasticity. The results are categorized into 3 main assessment types: Functional Assessment, Total Infarct Volume and Histomorphometry Analysis

Functional Assessments

Functional assessment methods include the Modified Neurological Severity Score (mNSS), adhesive removal, beam balance, forelimb placing, grid walking, Rota-rod performance, wire hang, Garcia tests, elevated body swing test, ladder-climbing test, forelimb grip force, and Y maze test. The mNSS scoring system was used in 7 of the 10 studies.

The mNSS is a multifaceted assessment tool used to evaluate neurological function, incorporating motor, sensory, and reflex components, with a maximum score of 14. The severity of neurological defects is classified based on scores: mild (1-4), moderate (5-9), and severe (10-14). Research has successfully employed the mNSS to assess long-term outcomes in stroke models, demonstrating its effectiveness in detecting neurological dysfunction.

Total Infarct Volume

Out of 10 studies, 9 studies have calculated Total infarct volume it calculates the sum of ischemic infarct in each slides. Various methods is being used to calculate the volume, the common method used are Nissl Staining and TTC staining. For total infarct volume assessment, brain sections from bregma +4.0 to +6.0 mm were cut into five coronal slices, each 2.0 mm thick. The sections were frozen at -20°C for 10 minutes, followed by immersion in 2% TTC solution at 37°C for 30 minutes. After fixation in 4% paraformaldehyde buffer at 4°C for 24 hours, the total infarct volume was calculated by summing the areas of infarction.

Histomorphometry Analysis

Many biomarkers are been used to study the plasticity of the brain and the effects exercises to the brain. The biomarkers which are used are BDNF and HE staining to know about the nulei, ribosomes and chromatin of brain. Out of 10 studies all 10 studies have Western Blot analysis to study about the protein and to extract the proteins of brain. 1 Study has done the analysis of Apoptic Cell Death to quatify the aptosis related DNA. The concentration and purity of total RNA extracted from the penumbra are evaluated using Quantitative Real-Time Polymerase Chain Reaction (qRT-PCR) analysis. Each study has employed different approaches to investigate the brain, indicating that diverse methods are required to understand brain plasticity. The absence of specific analyses makes it challenging to apply findings in clinical practice. These results underscore the importance of combining diverse techniques to better understand and evaluate the neural plasticity while addressing gaps in consistency and relevance for human applications.

Discussion

To summarize the finding of the study exercises helps to induce neural plasticity and this is proven by various Histomorphometry assessments. The systematic review underscores that exercise induces neural plasticity, demonstrated through various Histomorphometry assessments. The neuroprotective effects of exercise make it a crucial element in the treatment of ischemic stroke, as it fosters a conducive environment for neurogenesis and myelin regeneration within the penumbra. Enhancing complexity of dendrites and spine growth of dendrites are potential mechanisms for recovery after cerebral ischemia, supported by evidence of plasticity of dendrites which has relationship with the caveolin-1/VEGF signaling pathway. Expectedly, inhibitors suppressed these exercise effects post-MCAO [17, 28].

The combination of treadmill training and other interventions improves motor and cognitive functions in neonates after hypoxia-ischemia, potentially by stimulating oligodendroglial-mediated myelination, activating the CREB/BDNF signaling cascade, and enhancing myelin repair. Long-term exercise promotes BDNF expression, ameliorating ischemia-induced myelin damage

post-cerebral ischemia. Oligodendrocyte precursor cells (OPCs) play a crucial role in repairing damaged myelin sheaths by differentiating into mature oligodendrocytes. Treadmill exercise may augment this process, fostering neurogenesis and myelin repair, and potentially enhancing neural plasticity post-stroke. [18, 19].

BDNF expression is boosted during development, as evidenced by histomorphometric analysis, and is involved in the regulation of various cellular processes, including cell signaling, neuronal regeneration, synaptic plasticity, and higher-order cognitive functions like learning, memory, and sensorimotor recovery [20, 21, 27]. The review highlights that neuroplasticity is driven by growth factors like BDNF, IGF-I, and VEGF. BDNF is critical for synaptic plasticity, fundamental for learning and memory, facilitating long-term potentiation (LTP) [22].

Nonetheless, studies on exercise induced plasticity (learning) and cognitive function dysfunctions caused by stroke, as well as synaptogenesis and changes functional ability, remain limited. The systematic review's limitations include a lack of exact treadmill exercise intensity, duration, and frequency details, exclusive focus on rodent models without human study data, and evidence primarily limited to animal studies. The study's strength lies in Exercise consistently shows a positive effect on recovery and neural plasticity following an ischemic stroke.

Future research should prioritize neuroimaging techniques to better define neural plasticity, standardize histomorphometry assessments, and extend findings to human studies.

Conclusion

Based on the evidence collected with the limitations of the current systematic review, this systematic review highlights the significant role of physical exercise in inducing neural plasticity and promoting recovery post-ischemic stroke. Exercise-induced improvements in dendritic complexity and dendritic spine growth may be mediated by the caveolin-1/VEGF signaling pathway, according to the study's findings. Treadmill training shows promise in improving functional ability and cognitive function by enhancing the oligodendroglia involved in the CREB/BDNF signaling pathway, aiding in myelin repair.

Exercise has been shown to boost the expression of morphometric analysis, which is crucial for synaptic plasticity, learning and memory. The review underscores the neuroprotective effects of exercise, promoting neurogenesis and myelin repair, with histomorphometric analysis revealing significant improvements in neuronal regeneration and synaptic plasticity [29].

The review concludes that various assessment are available to assess plasticity of the brain which is not clearly defined and more studies should be done for further understanding. It provides a valuable summary of current knowledge, emphasizing the need for further research to improve understanding of nerve regeneration and develop more effective treatments.

Conflict of Interest

The authors declare that there are no conflict of interest regarding the publication of this study.

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