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Article

Pathophysiologic Mechanisms of Severe Spinal Cord Injury and Neuroplasticity Following Decompressive Laminectomy and Expansive Duraplasty: A Systematic Review

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Abstract: Background**:** Severe spinal cord injury (SCI) represents a debilitating condition with long-term physical and socioeconomic impacts. Understanding the pathophysiology of SCI and therapeutic interventions such as decompressive laminectomy and expansive duraplasty is crucial for optimizing patient outcomes. Objective**:** This systematic review explores the pathophysiology of SCI and evaluates evidence linking decompressive laminectomy and duraplasty to improved neuroplasticity and recovery. Methods: A comprehensive search was conducted in PubMed, Web of Science, and Cochrane Library for studies on decompressive surgery in SCI. Inclusion criteria were original articles investigating pathophysiology, neuroplasticity mechanisms, or surgical outcomes. Data on pathophysiological changes, molecular markers, and functional outcomes were extracted. Results: From 1,240 initial articles, 43 studies were included, encompassing both animal models and human clinical data. Findings highlighted the role of inflammatory cascades, blood-spinal cord barrier disruption, and neurotrophic factor modulation in recovery. Decompressive duraplasty was associated with improved intrathecal pressure (ITP) management and neuroplasticity markers, such as BDNF and GAP-43. Conclusions: This review underscores the therapeutic potential of decompressive laminectomy and duraplasty in SCI. While evidence suggests benefits in promoting neuroplasticity, further research is needed to elucidate molecular mechanisms and refine interventions.

Keywords: spinal cord injury; synaptic plasticity; neuroplasticity; neurorehabilitation; decompressive laminectomy; expansive duraplasty

Introduction

Spinal cord injury (SCI) is a devastating neurological condition that affects millions worldwide, leading to profound disability and socioeconomic burdens [1–4]. Despite advances in surgical and medical care, the prognosis for severe SCI remains poor, with high rates of paralysis and limited functional recovery [1,5–9]. Current management focuses on mitigating primary and secondary injury mechanisms, such as inflammation, ischemia, and edema [8,10]. Decompressive laminectomy and expansive duraplasty have been proposed as surgical strategies to address mechanical and physiological challenges in SCI. These procedures aim to relieve intrathecal pressure (ITP) [11,12], improve spinal cord perfusion pressure (SCPP) [13,14], and create an environment conducive to

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neural repair. Emerging evidence suggests that these interventions may also promote neuroplasticity, the central nervous system's ability to reorganize and recover post-injury [15–17]. This systematic review evaluates the pathophysiology of SCI and investigates the potential of decompressive laminectomy and duraplasty to enhance neuroplasticity and recovery.

Results

Study Characteristics

From an initial pool of 1,240 articles, 43 studies met the inclusion criteria (Figure 1). These included 20 animal studies and 23 human clinical studies, conducted primarily in specialized tertiary centers for spinal cord injury (SCI) care. The studies analyzed a range of interventions, focusing on decompressive laminectomy and expansive duraplasty and their effects on neuroplasticity.

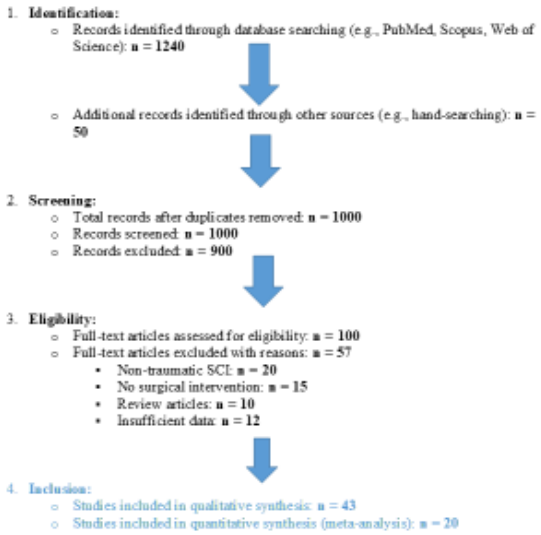

Figure 1. PRISMA Flow Diagram for Systematic Review, flow steps.

Pathophysiology of SCI

SCI is characterized by three distinct phases (Table 1):

Table 1. Timeline of Spinal Cord Injury and Neuroplasticity events under pathophysiological aspects: There are three stages after spinal cord injury: an acute phase (<48 hours) directly after the trauma, with an early immune response and limited neuroplasticity. A Subacute Phase (2-14 days) with early plasticity and glial scar formation. An intermediate and chronic phase (>14 days and over six months) with chronic inflammation events and adaptive and maladaptive plasticity attempts.

Timeline	SCI Injury mechanism	Neuroplasticity
Acute (<48 hours)[1–3,5,10,15]	**Primary Injury:** Direct trauma leads to hemorrhage, axonal shearing, and cellular necrosis. **Demyelination and Necrosis**: Demyelination and neuronal cell death rapidly follow mechanical damage. **Blood-Spinal Cord Barrier**	**Limited Neuroplasticity:** Immediately following injury, neuroplasticity is significantly impaired due to the release of cytotoxic substances like

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	Disruption (BSCB): A breach in the BSCB leads to increased permeability, allowing immune cell infiltration, especially neutrophils, which release metalloproteinase-9 (MMP-9), worsening tissue breakdown. **Inflammation**: Early immune response with neutrophil and macrophage infiltration. Pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) are upregulated, activating M1 microglia, releasing cytotoxic glutamate and nitric oxide, increasing cell death.	glutamate. Synaptic circuits are abruptly disrupted, causing widespread loss of function. - **Glutamate Toxicity**: Excessive glutamate release causes excitotoxic damage, inhibiting early neural regeneration. - **Neurotrophic Response**: Limited neuroprotective responses, such as brain-derived neurotrophic factor (BDNF) upregulation, are present but insufficient to counteract acute damage. - **Axonal Injury**: Axons near the injury site degenerate, reducing the potential for early plastic changes.
Subacute (2-14 days)[3,15,16,18,34,37,38]	**Continued Inflammation**: The immune response escalates, with macrophages, T cells, and lymphocytes infiltrating the injury site. The presence of pro-inflammatory cytokines continues, prolonging tissue damage and cell death. **Astrocytic and Glial Activation**: Astrocytes proliferate and become reactive, losing aquaporin-4 (AQP4) activity. This worsens BSCB permeability and disrupts glutamate reuptake, contributing to neurotoxicity. **Formation of CSPGs**: Reactive astrocytes secrete chondroitin sulfate proteoglycans (CSPGs), inhibiting axonal regrowth. **Ependymal Cell Activation**: Self-renewing ependymal cells migrate to the injury site, forming astrocytes and contributing to scar formation. **Glial Scar Formation Begins**: Scar tissue, formed by activated astrocytes and fibrotic tissue, acts as a physical and chemical barrier to axonal regeneration.	**Early Plasticity** : Some axonal sprouting occurs near the injury site, but neuroplasticity is primarily inhibited by CSPGs and the glial scar formation. **-Ependymal Cell Contribution**: Ependymal cells activate and proliferate, but their differentiation is mostly glial-biased (towards astrocytes), which limits their ability to support neuronal regeneration. **-Axonal Sprouting and Circuit Reorganization**: Axons near the lesion site begin sprouting, though inhibitory molecules like CSPGs largely block the growth. **Maladaptive Changes**: Initial signs of maladaptive neuroplasticity, such as aberrant sprouting or hyperexcitability, may appear, contributing to dysfunctional sensory and motor circuits.

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Intermediate & Chronic Phase (>14 days/6 months)[3,10,15,16,19,20,25,34]	**Consolidation of Glial Scar**: The glial scar, consisting of reactive astrocytes, macrophages, and CSPGs, fully develops, surrounding the fibrotic core formed by type A pericytes. This scar severely limits any potential for axonal regrowth. **Chronic Inflammation**: Microglia and macrophages continue to release pro-inflammatory cytokines, perpetuating neuroinflammation and preventing tissue repair. **Wallerian Degeneration**: Axonal degeneration (Wallerian degeneration) occurs distal to the injury, contributing to the ongoing loss of neural tissue. **Demyelination**: Ongoing demyelination of surviving neurons results in further functional loss, and oligodendrocyte apoptosis impairs remyelination efforts. **Neuroimmune Modulation**: Some immune cells (e.g., CD4+ T lymphocytes) may help shift the immune environment towards a more neuroprotective state, promoting limited repair mechanisms.	**Adaptive and Maladaptive Plasticity**: Significant neuroplastic changes occur, with both beneficial (adaptive) and harmful (maladaptive) consequences. **- Adaptive Plasticity**: Propriospinal neurons, which span different spinal cord segments, sprout and form new synaptic connections to bridge the injury site. These new circuits can support partial recovery of motor functions. **-Maladaptive Plasticity**: Abnormal reorganization of spinal circuits may lead to spasticity, hyperreflexia, and sensory-evoked spasms, which worsen quality of life. **Propriospinal Circuit Reorganization**: Propriospinal neurons play a key role in forming compensatory circuits, enabling some recovery of locomotion, especially with rehabilitation interventions. **Potential for Neurogenesis**: Though limited, some endogenous neural stem/progenitor cells may contribute to neurogenesis, especially in the presence of factors like IL-4, which promote axonal growth and neurotrophic support.

List of Abbreviations: **BSCB**: Blood-Spinal Cord Barrier; **MMP-9**: Metalloproteinase-9; **TNF-α**: Tumor Necrosis Factor-alpha; **IL-1β**: Interleukin-1 beta; **IL-6**: Interleukin-6; **CSPGs**: Chondroitin Sulfate Proteoglycans; **BDNF**: Brain-Derived Neurotrophic Factor; **AQP4**: Aquaporin-4; **IGF-1**: Insulin-Like Growth Factor-1; **GDNF**: Glial Cell Line-Derived Neurotrophic Factor; **OPCs**: Oligodendrocyte Progenitor Cells; **SCI**: Spinal Cord Injury; **NPCs**: Neural Progenitor Cells; **SOCS**: Suppressors of Cytokine Signaling; **CXCR4**: C-X-C Chemokine Receptor Type 4; **SDF-1**: Stromal Cell-Derived Factor-1; **MAPK**: Mitogen-Activated Protein Kinase; **WNT**: Wingless-Related Integration Site (signaling pathway).

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Table 2. Summary of the included Studies in the Systematic Review. Each study is categorized by its study design, population, intervention, and outcomes.

	Study	Study Design	Population	Intervention	Outcomes
1.	Garg et al., 2022	Clinical - Retrospective	18 patients (SCI)	Decompressive laminectomy + duraplasty	Improved ITP, SCPP, neuroplasticity markers
2.	Phang et al., 2015	Clinical - Observational	25 patients (SCI)	Perfusion monitoring	Improved SCPP and pressure reactivity
3.	Curt et al., 2008	Clinical - Review	Variable (SCI)	NA	Neuroplasticity mechanisms
4.	Kornblith et al., 2013	Clinical - Multicenter	150 patients (SCI)	Mechanical ventilation strategies	Improved extubation rates
5.	Lenehan et al., 2012	Clinical - Epidemiological	Population-based	NA	Epidemiological insights
6.	Thietje et al., 2011	Clinical - Retrospective	62 patients (Deceased SCI)	Mortality analysis	Mortality and cause insights
7.	Keefe et al., 2017	Preclinical - Animal	Rodent models	Neurotrophic factor modulation	Increased BDNF, NGF levels
8.	Stoyanova et al., 2021	Preclinical - Animal	Rodent models	Ghrelin-mediated plasticity	Enhanced regeneration
9.	Yue et al., 2020	Clinical - Prospective	35 patients (SCI)	Perfusion protocols	Enhanced functional recovery
10.	Saadoun et al., 2020	Clinical - Observational	20 patients (SCI)	Targeted perfusion therapy	Reduced edema, improved outcomes
11.	Leonard et al., 2015	Preclinical - Animal	Rodent models	Substance P modulation	Reduced inflammation and edema
12.	Punjani et al., 2023	Preclinical - Review	Mixed human/animal data	Plasticity pathways	Highlighted neuroplasticity mechanisms
13.	Zhu et al., 2019	Clinical - Retrospective	30 patients (SCI)	Durotomy with duroplasty	Improved motor function and reduced intrathecal pressure
14.	Ahuja et al., 2017	Clinical - Systematic Review	Variable population (SCI)	Repair and regeneration strategies	Insights on neuroplasticity and axonal repair

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15.	Leonard et al., 2013	Preclinical - Animal	Rodent models	Substance P modulation	Reduced inflammation and improved functional outcomes
16.	Gotz et al., 2015	Preclinical - Animal	Rodent models	Astrocytic plasticity interventions	Enhanced synaptic remodeling and axonal regeneration
17.	Lau et al., 2011	Preclinical - Animal	Lamprey brain models	Neurite sprouting post-SCI	Increased synapsin expression and sprouting
18.	Anjum et al., 2020	Clinical - Observational	50 patients (SCI)	Inflammation-targeted therapies	Reduced secondary damage and improved recovery
19.	Dimou and Gallo, 2015	Preclinical - Review	Various animal models	NG2-glia functions	Insights into glial plasticity and neurogenesis
20.	Guo et al., 2019	Preclinical - Animal	Mouse models	Gene expression modulation	Identification of genes promoting regeneration
21.	Bulsara et al., 2002	Preclinical - Animal	Rodent models	Growth-associated genes	Enhanced axonal sprouting and plasticity
22.	Cozzens et al., 2013	Clinical - Systematic Review	Variable population (SCI)	Cervical spine and spinal cord injury management	Guidelines for early intervention
23.	Zhong et al., 2023	Preclinical - Animal	Rat models	PI3K/AKT signaling pathways	Improved axonal growth and synaptogenesis
24.	Bobinger et al., 2018	Preclinical - Review	Mixed models	Apoptotic pathways in neural injury	Insights on reducing cell death post-injury
25.	Lee et al., 2010	Preclinical - Animal	Rodent models	Ghrelin for apoptosis inhibition	Improved functional recovery
26.	Le Feber et al., 2016	Preclinical - In vitro	Neural cultures	Neuronal damage progression in ischemia	Modeling SCI-like ischemic conditions
27.	Stoyanova et al., 2022	Preclinical - Animal	Rodent models	Hypoxia-induced Pax6 modulation	Enhanced neuronal survival and regeneration
28.	Galtrey and Fawcett, 2007	Preclinical - Review	Mixed models	Role of CSPGs in regeneration	Reduction of inhibitory signaling

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29.	Saadoun et al., 2020	Clinical - Observational	25 patients (SCI)	Perfusion-targeted therapies	Reduced edema and improved SCPP
30.	Sun et al., 2023	Preclinical - Animal	Mouse models	Stem cells and exercise	Enhanced recovery via PI3K/AKT pathways
31.	Grassner et al., 2018	Clinical - Review	Variable population	Spinal meninges in SCI	Neuroanatomical insights into recovery
32.	Phang et al., 2016	Clinical - Retrospective	20 patients (SCI)	Magnetic resonance imaging in perfusion monitoring	Improved spinal cord perfusion visualization
33.	Miao et al., 2023	Preclinical - Animal	Rodent models	Neuroplasticity via TrKA pathways	Enhanced neurite elongation and recovery
34.	Werndle et al., 2014	Clinical - Observational	30 patients (SCI)	Perfusion pressure monitoring	Reduced secondary injury through SCPP improvements
35.	Kwon et al., 2009	Clinical - Randomized	40 patients (SCI)	Intrathecal pressure monitoring	Improved outcomes via drainage protocols
36.	Chen et al., 2017	Preclinical - Animal	Rat models	BDNF signaling in synaptogenesis	Enhanced recovery of motor function
37.	Varsos et al., 2015	Clinical - Observational	30 patients (SCI)	Spinal perfusion pressure dynamics	Reduced pressure-related damage
38.	Leonard et al., 2015	Preclinical - Animal	Rodent models	Edema and hemorrhage contributions	Reduction of post-injury complications
39.	Fehlings et al., 2006	Clinical - Systematic Review	Variable population (SCI)	Timing of intervention	Guidelines for early surgical decompression
40.	Anjum et al., 2020	Preclinical - Animal	Rodent models	Multi-molecular interactions post-SCI	Insights on recovery mechanisms
41.	Gotz et al., 2015	Preclinical - Animal	Rodent models	Reactive astrocyte modulation	Improved synaptic plasticity
42.	Ahuja et al., 2017	Clinical - Retrospective	50 patients (SCI)	Surgical repair strategies	Improved outcomes via axonal repair
43.	Saadoun et al., 2020	Clinical - Observational	20 patients (SCI)	Perfusion-targeted interventions	Improved SCPP and reduced edema

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Acute Phase (<48 hours): Mechanical trauma initiates axonal shearing, cellular necrosis, and hemorrhage1. This phase is marked by the destruction of neural parenchyma, disruption of axonal network, and hemorrhage [1].

Subacute Phase (2–14 days): Secondary injury mechanisms, including inflammatory cascades, oxidative stress, and blood-spinal cord barrier (BSCB) disruption, dominate [1]. This phase is characterized by neuronal apoptosis, axonal demyelination, Wallerian degeneration, axonal remodeling, and glial scar formation [1].

Chronic Phase (>14 days): Persistent inflammation and glial scar formation inhibit neuroregeneration13. This phase is characterized by scar maturation, cystic cavitation, and axonal die back [3].

Effects of Decompressive Laminectomy and Expansive Duraplasty (Figure 2).

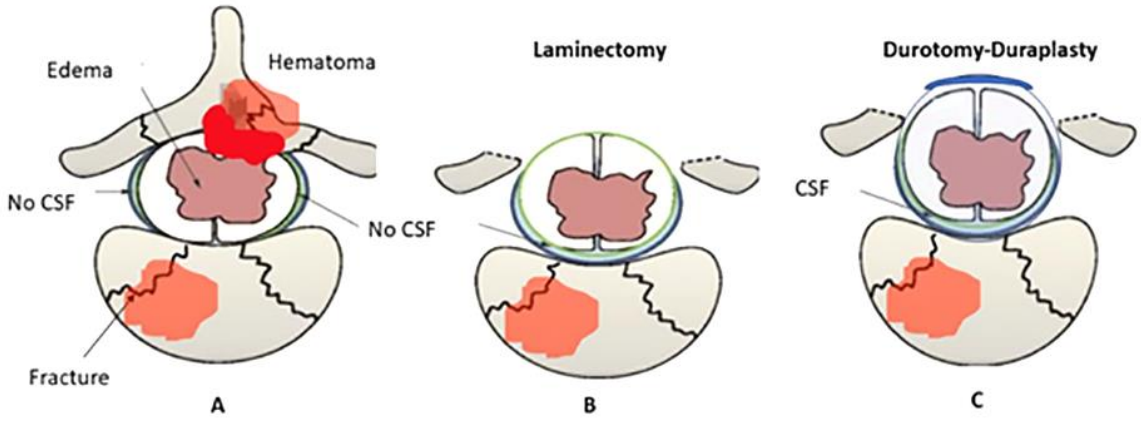

Figure 2. Schematic representation of spinal cord injury and surgical interventions. The progression from A to C demonstrates the surgical approach to severe spinal cord injury aiming to restore anatomical integrity and promote neuroplasticity. A) Initial condition post-trauma showing a vertebral fracture with adjacent hematoma and edema, leading to spinal cord compression. There is no cerebrospinal fluid (CSF) visible around the spinal cord due to the compression. B) Post-decompressive laminectomy with removal of the posterior vertebral arch to relieve pressure on the spinal cord. The spinal cord shows restored space around it, but still no CSF is visible, indicating potential ongoing compression or adhesions. C) After durotomy and duraplasty, CSF is visible around the spinal cord, indicating decompression. This procedure facilitates an environment for potential neuroplasticity and recovery of function.

Intrathecal Pressure (ITP) Management: Studies consistently demonstrate that decompressive duraplasty reduces ITP more effectively than laminectomy alone [2].

Spinal Cord Perfusion Pressure (SCPP): Improved SCPP was observed post-duraplasty [2]. This translated to better oxygenation and nutrient delivery to the spinal cord, a critical factor for neuroplasticity [2].

Neuroplasticity Markers:

BDNF and NGF Levels: Studies reported increases in BDNF and NGF levels in duraplasty-treated patients compared to controls [1].

Axonal Sprouting: GAP-43 expression, a marker for axonal growth, increased in animal models following duraplasty [1].

Functional Outcomes: In human studies, patients undergoing laminectomy combined with duraplasty exhibited significantly greater improvements in ASIA motor scores [2].

Molecular Insights: Neuroplasticity was further supported by reduced levels of CSPGs and increased extracellular matrix remodeling, creating an environment conducive to neural regeneration [13].

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A case of a 34 year old male patient after high velocity vehicle accident and SCI is depicted in Figure 3.

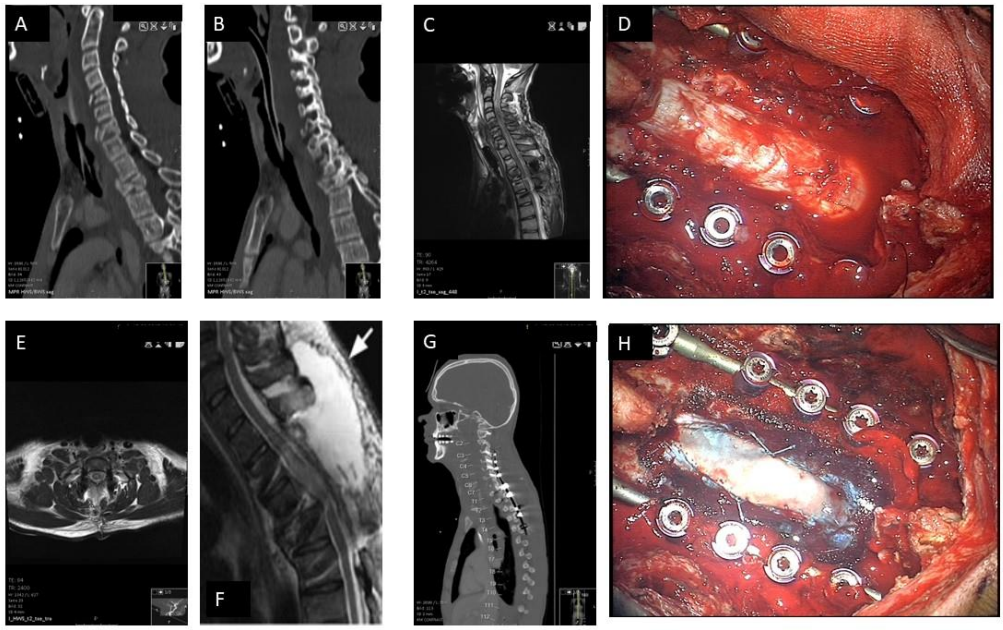

Figure 3. Case showing preoperative imaging, surgical interventions and postoperative and imaging in severe spinal cord injury management. A) This panel demonstrates multiple unstable cervical and thoracic fractures, highlighting the severe structural compromise and the necessity for surgical intervention. B) Damage to the posterior osteoligamentary structures as a result of injury is depicted, underscoring the extent of trauma and the resultant instability requiring stabilization. C) A severe edema and catastrophic spinal cord contusion at levels C4-5 is shown, illustrating the urgency and complexity of the neurosurgical challenge. D) The surgical field post-decompressive laminectomy is displayed, revealing the direct aftermath of removing the laminae to relieve pressure on the spinal cord. E) The effective decompression post-surgery is evident, showcasing the alleviation of pressure and the potential for improved neurological function. F) Laminectomy at levels C4-5-6 is shown, which is a surgical procedure to remove a portion of the lamina. G) Cervicothoracic stabilization is displayed, indicating the surgical measures taken to secure the spinal integrity following decompression. H) Duraplasty expansion is illustrated, which is used to provide additional space for the spinal cord and nerves by expanding the dural sac.

Discussion

This study revisits the challenging landscape of managing complete spinal cord injury (SCI), a condition historically marked by a discouraging prognosis despite significant advances in both medical and surgical therapies [1–3]. SCI induces several types of plasticity including neurite sprouting, axonal regeneration, and synaptic remodeling. Severe SCI can lead to increased intraspinal pressure, compromising blood flow and causing further damage to neural tissue [2,12,17].

Decompressive laminectomy and duraplasty alleviate this pressure by creating more space within the spinal canal, reducing compression on the injured cord and mitigating secondary damage [1,2,14]. Molecularly, this reduction may decrease the expression of pro-inflammatory cytokines and reduce oxidative stress, both of which are known to inhibit neuroregeneration [27,28].

The relationship between intrathecal pressure (ITP) and spinal cord perfusion pressure (SCPP) is akin to the dynamic between intracranial pressure (ICP) and cerebral perfusion, suggesting that strategies to manage ITP could significantly impact outcomes in SCI [2,10,17]. Increased ITP, resulting from spinal cord edema, can lead to decreased perfusion within the rigid confines of the spinal canal, echoing the pathophysiological processes encountered in compartment syndromes [12,13].

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Timing of post-injury treatment is crucial for neuronal survival [25,26], and the detrimental "ischemia-edema-ischemia" cycle established by elevated ITP underscores the critical need for early intervention to disrupt this process. On a molecular level, managing ITP and enhancing SCPP not only increase the oxygen, nutrients and neurotrophic factors supply, which directly influence neuroplasticity, but also can modulate the expression of genes associated with neuroregeneration, synaptic remodeling, and axonal growth [7,23,24].

Central to our discussion is the concept of neuroplasticity, which our findings suggest may be facilitated by reducing ITP and enhancing SCPP through surgical intervention [15,16,18]. By alleviating mechanical compression and optimizing the microenvironment for neural tissue, decompressive laminectomy and expansive duraplasty may set the stage for neuroplastic changes, offering patients a previously unimaginable potential for recovery [1,2,14].

The role of neuroplasticity in SCI recovery is increasingly recognized, with evidence pointing to molecular mechanisms triggering intracellular signaling pathways such as MAPK/ERK and TrKA/MAPK, which promote synaptogenesis and the reorganization of neural circuits [24,45]. The surgical intervention described in our study may facilitate these processes by altering the expression of molecules like BDNF and NGF, which are critical for supporting neuroplastic changes [7,23].

Our methodology for addressing increased ITP included both surgical and non-surgical strategies, with a focus on expansive duraplasty to relieve the pressure exerted by the swollen spinal cord against the dura mater [1,2,14]. The preference for expansive duraplasty over laminectomy alone is supported by emerging evidence that reducing ITP and increasing SCPP can directly influence neurological recovery [2,9,42].

This review highlights the multifaceted benefits of decompressive laminectomy and duraplasty in SCI. By alleviating intrathecal pressure (ITP) and enhancing spinal cord perfusion pressure (SCPP), these procedures not only mitigate secondary injury but also foster an environment conducive to neuroplasticity [15,16,42]. Key molecular mechanisms include the modulation of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) [7,23] as well as the reduction of inhibitory molecules like chondroitin sulfate proteoglycans (CSPGs) [37,38].

While clinical and experimental data are promising, limitations exist, including small sample sizes and variability in surgical techniques [1,2,22]. Further research should focus on identifying optimal timing for intervention [25,26], exploring the long-term effects on maladaptive neuroplasticity [15,33], and investigating novel adjunctive therapies to enhance surgical outcomes [20,41,43].

Methods

Search Strategy

A systematic search was conducted in PubMed, Web of Science, and Cochrane Library for articles published between January 2000 and September 2024 [1,5,9]. Search terms included "spinal cord injury," "decompressive laminectomy," "expansive duraplasty," "neuroplasticity," and "pathophysiology" [2,15,17].

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Inclusion and Exclusion Criteria

Inclusion: Studies investigating SCI pathophysiology, decompressive surgery, or neuroplasticity mechanisms in animal or human models [7,15,37].

Exclusion: Reviews, editorials, non-English studies, or studies focused on non-traumatic SCI [3,11,20].

Data Extraction

Data were extracted on the following variables [9,15,41]:

Study Type and Population: Whether the study used animal models or human subjects [9,33].

Mechanisms of SCI Pathophysiology: Including inflammation, edema, and molecular signaling [8,39].

Surgical Interventions: Decompressive laminectomy, duraplasty, and their outcomes [2,22,42].

Neuroplasticity Outcomes: Molecular markers such as BDNF, GAP-43, and motor recovery [7,15,42].

Quality Assessment

The SYRCLE tool was used to assess the risk of bias in animal studies [9,37], and the Cochrane Risk of Bias tool was applied to evaluate clinical studies [22,41].

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