Spinal cord injury pathophysiology

- Challenges in Pulmonary Management after Traumatic Brain and Spinal Cord Injury
- Diffusion Tensor Imaging Findings in Cerebral Sensorimotor Areas in Patients After Spinal Cord Injury Correlate With Neurophysiological Deficits
- Advanced Therapeutic Approaches Based on Small Extracellular Vehicles (sEVs) For the Regeneration of Spinal Cord Injuries
- Microglial pruning of glycinergic synapses disinhibits spinal PKCgamma interneurons to drive pain hypersensitivity in mice
- Role of MS4A7 in Regulating Microglial Polarization and Neuroinflammation in Spinal Cord Injury via the cGAS-STING-NLRP3 Axis
- Traumatic Spinal Cord Injury: Review of the Literature
- Mechanisms of Different Motor Neurons in the Occurrence of Spasticity After Spinal Cord Injury: A Narrative Review
- Spinal cord injury models: Advantages and disadvantages in the view of pathophysiology and clinical significance

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Spinal cord injury is a **dynamic process** that evolves through two main phases: **Primary injury** and **Secondary injury**.

1. Primary Injury

- Occurs at the **moment of trauma**. - Mechanical forces directly cause:

- Neuronal and axonal damage
- Hemorrhage
- Vascular disruption
- Cell membrane rupture

- Mechanisms: compression, contusion, laceration, stretch, or transection.

2. Secondary Injury

- Initiates within **minutes to hours** after trauma and can continue for **days to weeks**. - Complex cascade involving:

a) Vascular Dysfunction

- Disruption of blood-spinal cord barrier (BSCB) - Ischemia and hypoxia - Vasospasm, thrombosis

b) Inflammatory Response

- Activation of microglia and astrocytes - Infiltration of neutrophils, macrophages, T-cells - Release of cytokines (IL-1β, TNF-α, IL-6)

c) Excitotoxicity

- Excessive release of glutamate - Overactivation of NMDA and AMPA receptors - Calcium influx leading to neuronal death

d) Oxidative Stress

- Accumulation of free radicals (ROS/RNS) - Lipid peroxidation - Mitochondrial dysfunction

e) Apoptosis and Necrosis

- Programmed cell death of neurons and oligodendrocytes - Progressive demyelination

f) Glial Scar Formation

- Reactive astrocytes produce a **glial scar**. - Both **protective** (limits spread of injury) and **inhibitory** (blocks axonal regeneration).

3. Chronic Phase (Weeks to Months)

- Persistent inflammation - Cystic cavity formation - Loss of neural circuits - Limited endogenous neuroplasticity - Potential for functional reorganization through rehabilitation

Summary

Spinal cord injury pathophysiology is a **multistep, multiphase process** where primary mechanical damage triggers complex biological cascades leading to progressive neurological deterioration. Effective therapies aim to minimize **secondary injury** and promote **regeneration and plasticity**.

Severe spinal cord injury leads to hemorrhage, edema and elevated tissue pressures that propagate ischemia. Liquefactive necrosis of damaged tissue eventually results in chronic cavities due to a wound healing process lacking adhesive contractile cells.

Spinal cord injury induces the disruption of blood-spinal cord barrier and triggers a complex array of

tissue responses, including endoplasmic reticulum (ER) stress and autophagy. However, the roles of ER stress and autophagy in blood-spinal cord barrier disruption have not been discussed in acute spinal cord trauma.

The pathophysiology of spinal cord injury (SCI) related processes of axonal degeneration and demyelination are poorly understood. The present systematic review and meta-analysis were performed such to establish quantitative results of animal studies regarding the role of injury severity, SCI models and level of injury on the pathophysiology of axon and myelin sheath degeneration. 39 related articles were included in the analysis. The compiled data showed that the total number of axons, number of myelinated axons, myelin sheath thickness, axonal conduction velocity, and internode length steadily decreased as time elapsed from the injury (Pfor trend<0.0001). The rate of axonal retrograde degeneration was affected by SCI model and severity of the injury. Axonal degeneration was higher in injuries of the thoracic region. The SCI model and the site of the injury also affected axonal retrograde degeneration. The number of myelinated axons in the caudal region of the injury was significantly higher than the lesion site and the rostral region. The findings of the present meta-analysis show that the pathophysiology of axons and myelin sheath differ in various phases of SCI and are affected by multiple factors related to the injury [1].

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Hassannejad Z, Yousefifard M, Azizi Y, Zadegan SA, Sajadi K, Sharif-Alhoseini M, Shakouri-Motlagh A, Mokhatab M, Rezvan M, Shokraneh F, Hosseini M, Vaccaro AR, Harrop JS, Rahimi-Movaghar V. Axonal Degeneration and Demyelination Following Traumatic Spinal Cord Injury; A Systematic Review and Meta-analysis. J Chem Neuroanat. 2019 Feb 3. pii: S0891-0618(18)30164-9. doi: 10.1016/j.jchemneu.2019.01.009. [Epub ahead of print] Review. PubMed PMID: 30726717.