









Implementing Omics Technologies to Analyze Rehabilitation Strategies in Spinal Cord Injury

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pinal cord injury (SCI) can disrupt sensory, motor, and autonomic functions, significantly affecting recovery and quality of life. Despite these advancements, rehabilitation remains limited due to the complexity of neuronal regeneration and plasticity.² Omics-based (genomics, approaches epigenomics, metagenomics, transcriptomics, proteomics, and metabolomics) can provide insights into the molecular mechanisms, such as:

- neuroinflammation (increase in proinflammatory cytokines,
- metabolic shifts/ disorders,
- (🔅) gut microbiota imbalance (increase of harmful taxa),
- urinary tract infections,
- loss of muscle mass (muscular atrophy),
- loss of bone density (osteoporosis),

influencing rehabilitation outcomes.³

- Give a comprehensive overview of omics technologies used in analyzing rehabilitation interventions
- Effectiveness of different interventions in SCI rehabilitation, where omics technologies are used to assess biological changes triggered by rehabilitation strategies and assess molecular outcomes.

Methods

Three databases (Embase, Medline, Web of Science) were searched. Two reviewers independently screened, extracted data and assessed risk of bias (RoB) (National Heart Lung and Blood Institute Quality Assessment Tool).

Inclusion criteria:

✓ Age ≥18 years; traumatic SCI; assessed outcomes through omics; published in peer-reviewed journal

Exclusion criteria:

Animal studies, reviews, commentaries, and conference abstracts

Literature research:

Main Results [圖] 6,021 references retrieved, 🖹 136 full-text articles reviewed, 🗸 23 trials included (文8 RCTs, 式 5 non-RCTs, 🛣 10 pre-post trials); 🗥 96% moderate RoB.

Study characteristics: Molecular outcomes **Clinical outcomes** Intervention **Omics** Transcriptomics **Muscle Function** 1 muscle oxidative capacity and 1 mitochondrial biogenesis and oxidative 48% resistance fatigue regulation (PGC-1α, NR4A3) 1 muscle small molecule transport (FNDC5) ↑ cardiorespiratory fitness (VO₂ max) Exercise and electrical stimulation 1 muscle regenreation (Myogenin) 65% ↑ insulin sensitivity (HOMA2-IR), ↓ markers of muscle atrophy (MSTN) Matsuda Index) Circadian Regulation @ expression patterns ↑ body clock genes (PER1,PER2) **Neurological Recovery** ↑ neuronal plasticity (ERK1) ↑ motor index score (ASIA, ISNCSCI) 1 metabolic support for nerve regeneration (Acetone, Sucinate, Isoleucine) ↑ AIS grade conversion 13% ↓ uninhibited muscle contraction ❖ Restoration of voluntary control **Epigenomics** (Glycine) 4% Immune/ Inflammatry Function ↓ systemic inflammation **Proteomics** 1 imune balance 9% Diet 13% ↑ sperm motility (WHO criteria) ↓ reduced inflammation (25/30 inflammatory) ↓ urinary symptoms markers) Metagenomics **Metabolic Improvement** 17% `oxidative stress balance (AOPP, GPx) disuse-induced downregulation of metabolic genes energy metabolism (UCP2, UCP3) Medi hormor the **Altering Microbiome** 9% Gastrointestinal Quality of Life Index `Coprococcus, Bacteroides thetaiotaomicron Akkermansia, Escherichia-Shigella ↓ urogenital symptoms

Conclusion

- Omics technologies are increasingly used (2012: n = 2; 2025: n = 14)
 - Enable monitoring of biological adaptations
 - Transcriptomics & metagenomics most used
- Exercise & electrical stimulation drive muscle gene adaptation
- Microbiome shifts reduce inflammation
 - Linked to better bowel and metabolic outcomes

Suggests sustained adaptation potential

Epigenomics shows lasting molecular effects

- Proteomics & metabolomics detect systemic changes
 - Hormones & cell therapies → signature proteins/metabolites
- Early molecular shifts can guide rehabilitation
 - May forecast recovery ahead of clinical signs
 - Enable real-time intervention tuning
- Current evidence is promising but limited
 - Need for standardized (multi)-omics clinical trials

Most studies small, short, and high variability

References: ¹Ahuja, C.S., et al., Traumatic spinal cord injury. Nature Reviews Disease Primers, 2017. 3(1): p. 17018 DOI: 10.1038/nrdp.2017.18. ²Nagappan, P.G., H. Chen, and D.-Y. Wang, Neuroregeneration and plasticity: a review of the physiological mechanisms for achieving functional recovery postinjury. Military Medical Research, 2020. 7(1): p. 30 DOI: 10.1186/s40779-020-00259-3. 3 Martínez-Torija, M., Esteban, P. F., Santos-De-La-Mata, A., Castillo-Hermoso, M., Molina-Holgado, E., & Moreno-Luna, R. (2025). Multifaceted Pathophysiology and Secondary Complications of Chronic Spinal Cord Injury: Focus on Pressure Injury. Journal of Clinical Medicine, 14(5), 1556. https://doi.org/10.3390/jcm14051556