







Implementing Omics Technologies to Analyze Rehabilitation Strategies in Spinal Cord Injury

Alexander Stacul^{1,2}, Ezra Valido¹, Nicole Nyfeler¹, Alessandro Bertolo^{1,3}, Ramona Maria Zeh¹, Andrea Fontana⁴, Carla Sabariego^{1,5,6}, Jürgen Pannek^{4,7}, Jörg Krebs⁴, Margaret Hund⁸, Xavier Jordan⁹, Onur Boyman^{10,11}, Alexander Leichtle¹², Marija Glisic^{1,3} and Jivko Stoyanov^{1,3}

¹Swiss Paraplegic Research, Nottwil, Switzerland; ²Graduate School for Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland, ³Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, ⁴Swiss Paraplegic Center, Nottwil, Switzerland, Clinical Trial Unit, Swiss Paraplegic Center, Nottwil, Switzerland, ⁵Faculty of Health Sciences, University of Lucerne, Switzerland, Clinical Trial Unit, Swiss Paraplegic Center, Nottwil, Switzerland, Switzerland, Clinical Trial Unit, Swiss Paraplegic Center, Nottwil, Switzerland, Clinical Trial Unit, Swiss Paraplegic Center, Nottwil, Switzerland, Clinical Trial Unit, Swiss Paraplegic Center, Nottwil, Switzerland, Clinical Trial Unit, Switzerland, Clinical Trial Unit, Switzerland, Clinical Trial Unit, Switzerland, Clinical Chemistry, Inselspital Center, Nottwil, Switzerland, Clinical Chemistry, Inselspital, Bern University of Bern, Switzerland, Switzerland, Clinical Chemistry, Inselspital, Bern University of Bern, Switzerland, Clinical Chemistry, Inselspital, Switzerland, Clinical Chemistry, Inselspital, Bern University of Bern, Switzerland, Clinical Chemistry, Inselspital, Switzerland, Clinical Chemistry, Inselspital

Background

pinal cord injury (SCI) can disrupt sensory, motor, and autonomic functions, significantly affecting recovery and quality of life. Despite advancements made, rehabilitation remains limited due to the complexity of neuronal regeneration and plasticity. Omics-based approaches (genomics, 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

Objectives

- 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:

Exclusion criteria:

Animal studies, reviews, commentaries, and conference abstracts

Literature research:

[6,021 references retrieved, 136 full-text articles reviewed, ✓ 23 trials included (ズ38 RCTs, 式 5 non-RCTs, 10 pre-post trials); 1 96% moderate RoB.

Main Results

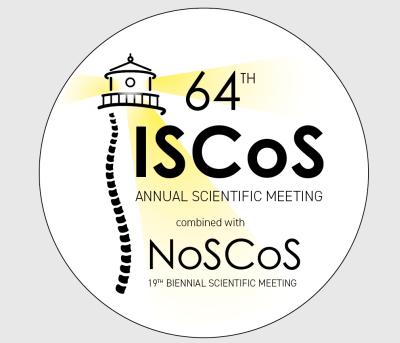
Study characteristics: Molecular outcomes **Clinical outcomes** Intervention **Omics** Transcriptomics **Muscle Function** 1 muscle oxidative capacity and 1 mitochondrial biogenesis and oxidative 48% resistance fatigue regulation (PGC-1α, NR4A3) 1 muscle small molecule transport (FNDC5) ↑ cardiorespiratory 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

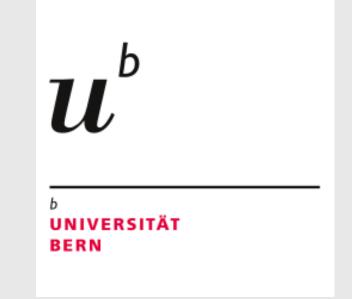
Conclusion

- 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
- Epigenomics shows lasting molecular effects
 - Suggests sustained adaptation potential

- 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











Implementing Omics Technologies to Analyze Rehabilitation Strategies in Spinal Cord Injury

Alexander Stacul^{1,2}, Ezra Valido¹, Nicole Nyfeler¹, Alessandro Bertolo^{1,3}, Ramona Maria Zeh¹, Andrea Fontana⁴, Carla Sabariego^{1,5,6}, Jürgen Pannek^{4,7}, Jörg Krebs⁴, Margaret Hund⁸, Xavier Jordan⁹, Onur Boyman^{10,11}, Alexander Leichtle¹², Marija Glisic^{1,3} and Jivko Stoyanov^{1,3}

¹Swiss Paraplegic Research, Nottwil, Switzerland; ²Graduate School for Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland, ³Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, ⁴Swiss Paraplegic Center, Nottwil, Switzerland, Clinical Trial Unit, Swiss Paraplegic Center, Nottwil, Switzerland, ⁵Faculty of Lucerne, Lucerne, Switzerland, ⁶Center for Rehabilitation in Global Health Systems, WHO Collaborating Center, University of Lucerne, Lucerne, Switzerland, ⁷Department of Urology, Inselspital, Bern, Switzerland, ⁸REHAB Basel, Clinic for Neurorehabilitation and Paraplegiology, Basel, Switzerland, ⁹Clinique Romande de Réadaptation, Sion, Switzerland, ¹⁰Department of Immunology, University of Zurich, Zurich, Switzerland, ¹¹Faculty of Medicine and Faculty of Science, University of Zurich, Zurich, Zurich, Switzerland, ¹²University Institute of Clinical Chemistry, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

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 approaches (genomics, 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 (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

Main Results

Literature research:

Study characteristics:

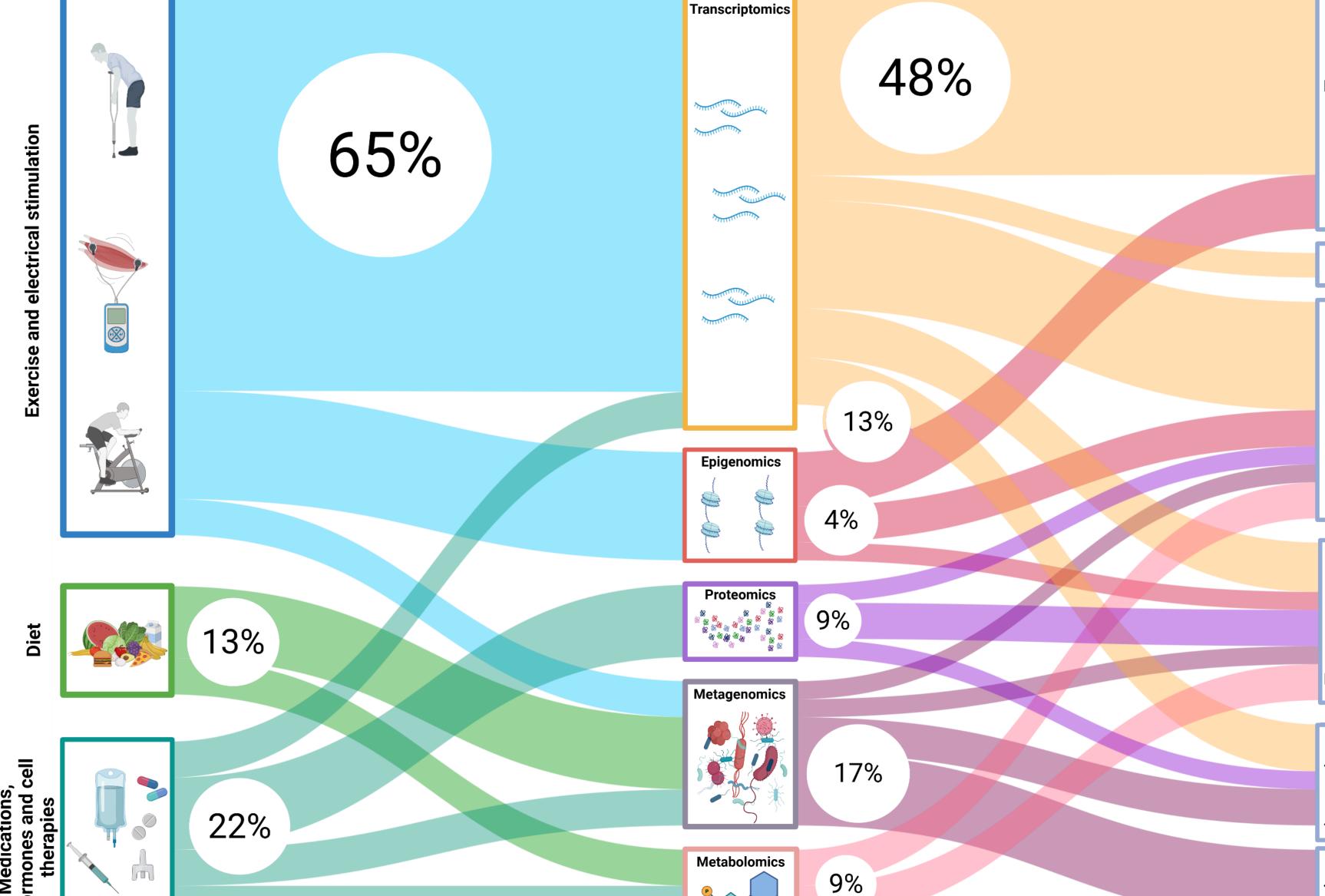
Intervention

6,021 references retrieved, 136 full-text articles reviewed, 23 trials included

Omics

> 8 randomized controlled trials (RCTs)

10 pre-post trials



Molecular outcomes **Clinical outcomes Muscle Function** 1 muscle oxidative capacity and 1 mitochondrial biogenesis and oxidative resistance fatigue regulation (PGC-1α, NR4A3) 1 muscle small molecule transport (FNDC5) ↑ cardiorespiratory fitness (VO₂ max) 1 muscle regenreation (Myogenin) 1 insulin sensitivity (HOMA2-IR), ↓ markers of muscle atrophy (MSTN) Matsuda Index) Circadian Regulation @ expression patterns 1 body clock genes (PER1,PER2) **Neurological Recovery** ↑ neuronal plasticity (ERK1) ↑ motor index score (ASIA, ISNCSCI) 1 metabolic support for nerve regeneration (Acetone, Sucinate, Isoleucine) 1 AIS grade conversion ↓ uninhibited muscle contraction ❖ Restoration of voluntary control (Glycine) **Immune/ Inflammatry Function** ↓ systemic inflammation 1 imune balance 1 sperm motility (WHO criteria) ↓ reduced inflammation (25/30 inflammatory) markers) ↓ urinary symptoms **Metabolic Improvement** 1 oxidative stress balance (AOPP, GPx) 🔅 📜 condition of the disuse-induced downregulation of metabolic genes lenergy metabolism (UCP2, UCP3) **Altering Microbiome** Coprococcus, Bacteroides thetaiotaomicron ↑ Gastrointestinal Quality of Life Index

Conclusion

Omics technologies are increasingly applied in research trials, investigating molecular adaptations of rehabilitation interventions after SCI. These methods enable the early identification of molecular changes and have shown relevance in analyzing processes related to metabolism, endocrine function, and inflammation. While not yet part of clinical routine, omics approaches provide valuable insights in the rehabilitation setting and hold potential for informing the design and monitoring of future strategies

References

↓ urogenital symptoms

Akkermansia, Escherichia-Shigella

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.

³Martínez-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