BMJ Open

Central and peripheral neuroplasticity in cervical spinal cord injury following intensive upper limb motor training: a randomised controlled trial protocol

Imke Jana Hrycyk ,[1] Nele Bertels,[1] Hatice Tankisi,[2] Joanne Valentina Glinsky,[3] Kristine Oostra,[4] Charlotte van Laake-Geelen,[5,6] Lisa Tedesco Triccas,[1,7] Annemie Spooren[1]

To cite: Hrycyk IJ, Bertels N, Tankisi H, *et al*. Central and peripheral neuroplasticity in cervical spinal cord injury following intensive upper limb motor training: a randomised controlled trial protocol. *BMJ Open* 2026;**16**:e107352. doi:10.1136/bmjopen-2025-107352

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2025-107352).

Received 02 July 2025
Accepted 26 February 2026

For numbered affiliations see end of article.

Correspondence to
Imke Jana Hrycyk;
imke.hrycyk@uhasselt.be

ABSTRACT

Introduction This multi-centre, randomised controlled trial (RCT) investigates the effects of intensive upper limb (UL) motor training on neurophysiological and functional recovery in individuals with cervical spinal cord injury (c-SCI) during the sub-acute phase. The study aims first to assess neurophysiological adaptations in the central and peripheral nervous systems and functional changes to evaluate the impact of intensive UL motor training on recovery. Second, it determines dose dimensions and their correlation with neural and functional improvements.

Methods and analysis A total of 44 individuals with c-SCI within 13 weeks post-injury will be recruited from five rehabilitation centres in Belgium and the Netherlands. They will be randomised into an intervention group, receiving six additional hours of goal-directed UL training per week for 8 weeks, or a control group receiving standard care. Primary outcomes are changes in resting motor threshold, a proxy for corticospinal tract integrity; compound muscle action potential amplitude, indicating peripheral nerve excitability and functionality; and assessments of strength, sensory function and prehension, with the primary comparison between groups at baseline and after the intervention period. Secondary outcomes cover additional neurophysiological assessments and motor function. Dose dimensions will be quantified and related to primary and secondary outcomes.

Ethics and dissemination The central medical ethics committees, METC Máxima MC (NL84212.015.23) and MEC Gent (B6702023000227), as well as local ethics committees, reviewed and approved this trial. The protocol is registered (ClinicalTrials.gov; NCT06065384). The findings of this RCT will be disseminated through articles in peer-reviewed journals and at neurological rehabilitation conferences.

Trial registration number NCT06065384.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study is a prospective randomised controlled trial to comprehensively investigate central and peripheral neuroplasticity concomitantly with a training intervention in people with a sub-acute cervical spinal cord injury (c-SCI).
⇒ Rigorous documentation of the provided care and longitudinal assessment offers a crucial insight into motor training and recovery in sub-acute rehabilitation.
⇒ Lack of blinding of participants and therapists due to the nature of the intervention introduces potential biases.
⇒ Same assessment protocol for an expected heterogeneous study population, including all levels of incomplete c-SCI.

INTRODUCTION

Impairment of arm and hand function heavily impacts independence and quality of life in people with cervical spinal cord injury (c-SCI), making its restoration a key rehabilitation goal.[1] Following an SCI, the central and peripheral nervous systems undergo changes triggered by disruptions of descending and ascending neural pathways and direct damage to upper and lower motor neurons. Functional and structural reorganisation occurs, first in the form of an inflammatory response, demyelination and neuronal and glial cell death. Subsequently, compensatory mechanisms are initiated, such as the unmasking of latent connections in spared motor pathways or the promotion of axonal sprouting.[2] Damage to lower motor neurons, dependent on their proximity to the lesion, can result in absent or abnormal function.[3] Motor neurons farther from the lesion are initially spared but experience altered supraspinal input and, over time, can be subjected to transsynaptic degeneration.[4] Subsequently, regeneration and reinnervation within the peripheral nervous system can occur, leading to a redistribution of the motor unit activation.[5]

Rehabilitation, particularly active motor training, can potentiate adaptive neuroplastic

changes by stimulating latent connections and triggering beneficial neural adaptations following exercise, for example, releasing plasticity-stimulating neuromodulators.[6 7] Especially in motor-incomplete SCIs, motor training can strengthen the spared connections to enhance function.[8] This proposed underlying mechanism for an activity-based improvement is hypothesised to increase further during intensive training,[9 10] but functional recovery, especially in people with c-SCI, remains limited.[11] Potential explanations could be that the optimal dosage for recovery is not established or that intensive training schemes, which should further incorporate task-specific and goal-directed practices,[12–14] are not sufficiently implemented in rehabilitation practice. Ongoing research, such as the SCI-MT trial, investigates early, intensive motor training in SCI rehabilitation,[15] emphasising the current need to assess the impact of intensive motor training in people with c-SCI, whereby the measurement of neurophysiological changes can uncover potential recovery mechanisms.

Transcranial magnetic stimulation (TMS) is an established method for assessing corticospinal tract (CST) neuroplasticity via motor-evoked potentials (MEPs).[16] Large-scale studies highlight the importance of neurophysiological assessments, like TMS, during recovery following SCI and revealed associations between measures of CST integrity and functional recovery.[17 18] Prior research has demonstrated neuroplastic changes following upper limb (UL) motor training in people with chronic SCI, such as increased cortical representation of motor areas[19] and increased MEP amplitudes of trunk muscles after arm exercise.[20] Currently, no randomised controlled trials (RCTs) have assessed the effect of intensive UL motor training on cortical excitability in people with c-SCI in the sub-acute stage.

Concerning the neuroplasticity in the peripheral nervous system, Van de Meent *et al*[4] found that the compound muscle action potential (CMAP) measured in the upper and lower limbs of people with an SCI following nerve stimulation displayed severe degradation within the first 6 months after the injury. Importantly, they noted that such a decrease negatively affects the muscle power and functional abilities of people with SCI. In people with incomplete SCI, recovery of CMAP amplitude has been observed, potentially due to peripheral reinnervation.[18 21] However, analysing only the absolute CMAP amplitude fails to capture essential information, as reinnervation could mask motor unit loss.[22 23] Newer measurement protocols for peripheral nerve stimulation can provide details on underlying de- or regenerative processes, such as the degree of axonal loss, and identify signs of reinnervation.[24 25] However, no such assessments have been done in people with c-SCI in sub-acute stages, and neither has the effect of training interventions on longitudinal measures been investigated.

To summarise, this research aims to investigate intensive UL motor training on arm- and hand function in early-stage c-SCI rehabilitation with measures of central and peripheral neuroplasticity and functional assessments. The primary objective is to assess training-induced neurophysiological changes using TMS (CST integrity) and peripheral nerve assessment (nerve excitability), as well as functional changes in strength and prehension, which serve as mediators of motor recovery. A secondary objective of this study is to determine the training intensity and dose parameters associated with neural and functional recovery. We hypothesise that participants receiving additional UL motor training will show steeper recovery, with increases in measures of neuronal excitability, reflected in a reduced activation threshold, increased CMAP and greater improvements in functional outcomes. Connected, we propose that higher training intensity and dose will be associated with greater neural and functional recovery. Lastly, a third objective is to explore additional central and peripheral excitability and functional measures to analyse subtle effects and potential associations between different outcome measures.

METHODS

This international, multicentric, prospective investigator-initiated trial entails two randomised-controlled 1:1 parallel branches with assessor-blinded repeated-measures.

Study population

Forty-four subjects with c-SCI will be recruited from five centres across Belgium and the Netherlands. Eligible participants must have a traumatic or non-traumatic c-SCI in the preceding 13 weeks, classified as motor incomplete by the American Spinal Injuries Association Impairment Scale (AIS), that is, AIS C or D, or complete AIS A with zones of partial preservation (ZPP) as defined by the International Standards for Neurological Classification of SCI (ISNCSCI). The participants must be medically stable and provide consent. Exclusion criteria are classification AIS A without ZPP, AIS B, or other significant medical conditions that could prevent participation in the measures or intervention. Participants are excluded from TMS measures if they exhibit any of the following contraindications: epilepsy, metal implants in the brain, a defibrillator, a pacemaker or pregnancy.[26] Each cooperating rehabilitation centre will have a team of rehabilitation physicians who will continuously identify and approach eligible patients in the spinal cord ward. Their consent will be collected by a medical doctor or medical staff, using the informed consent form for the Belgian or Dutch sites (see online supplemental material 1). Subsequently, a medical doctor with full access to the participant's medical file and history, will conduct a screening for TMS eligibility.

Intervention

The present research implements a goal-directed, intensive UL motor training programme for people with c-SCI within 13 weeks of their injury. This programme is adapted from the SCI-MT programme developed by

Harvey *et al*,[15 27] with a specific focus on promoting neural recovery through repeated muscle activation at and below the injury level.

Unlike the original SCI-MT programme, which includes upper- and lower-limb training, our adapted version focuses solely on UL training. As part of this adjustment, we reduced the overall intervention time to 8 weeks, which is the required timeframe to achieve at least moderate improvements in arm and hand function,[12] and to 6 hours per week, thereby improving the feasibility of clinical implementation. These changes were made in response to difficulties reported in implementing 12 additional hours of training as initially planned. More importantly, we limited the additional UL training hours to prevent overtraining, as standard care is already comprehensive in Belgian and Dutch rehabilitation programmes, with roughly 3 hours of daily UL training in sub-acute c-SCI.[28]

In alignment with the SCI-MT trial, all participants will continue to receive standard care, whereby the therapy hours and content for both upper and lower limbs are consistent with those of non-participants. Participants in the intervention group will receive an additional 6 hours of UL motor training per week provided by trained physiotherapists and occupational therapists. The training will focus on goal-directed, targeted and functional activities aimed at muscles at and below the lesion level, particularly in tasks related to UL activities, such as reaching and grasping.

Goal-setting will be client-centred, using the Canadian Occupational Performance Measure to establish four goals: two to be addressed within 8 weeks and two within 6 months. Additionally, weekly goals will be set to guide the additional training.

Following the protocol of the SCI-MT trial, each centre will assign a therapist to plan the additional training using a workbook that includes targeted exercises, dose parameters and weekly reflections. This will allow for adjustments to the programme as needed. Training intensity can be modified through high volumes of task repetitions and progressive adjustments in resistance, speed or range of motion. Optional supplements such as neuromuscular electrical stimulation may also be used to enhance the programme.

Therapists will document the content and duration (in minutes) of the standard care (usual training) and the additional training's content, duration and repetitions on specified practice sheets to ensure consistency and track progress.

Outcome measures

Outcome measures will be collected at baseline, 8 weeks and 6 months after randomisation (table 1). A shortened measurement protocol will be assessed at the end of the fourth week of training. A researcher blinded to the group assignment will undertake all measurements on-site at the rehabilitation clinic, where participants are inpatients for the duration of the trial.

Neurophysiological outcomes

CST excitability will be measured with TMS over the primary motor cortex. The stimulation target is a distal muscle of the primarily trained side, as determined by the treating therapists and the participant's goals. The abductor pollicis brevis (APB) will be the first muscle to test for a measurable MEP, that is, a peak-to-peak amplitude of 200 µV. If no MEP can be elicited, this finding will be noted as 'MEP negative'. For the outcome collection, the researchers will pragmatically assess suitable stimulation targets based on muscles that exhibit muscle activity. All the following measures will be repeated in the same muscle.

The primary endpoint is the resting motor threshold (RMT), which will be assessed using the threshold-tracking technique, an adaptive method in which a continuous target MEP of 200 µV is tracked by an automated logarithmic adjustment of stimulation intensity to reach the target threshold.[29] RMT 200 µV is defined as the percentage of maximum stimulation output (%MSO) needed to elicit an MEP 200 µV. Motor threshold will be taken as a direct measure of corticomotor excitability, with higher reliability in SCI populations and faster acquisition compared with other measures.[30 31] Secondary endpoints concerning cortical excitability will be assessed through measures of a stimulus-response function,[32] short- and long-intracortical inhibition,[33] and neuronavigated motor mapping with the RMT 50 µV, centre of gravity and map size[19] as outcome variables.

The peripheral nerve assessments will be collected by stimulating the median nerve at the distal wrist crease on the primarily trained side using an isolated constant-current stimulator (DS5) with a maximum output of 50 mV. The elicited CMAP will be measured at the APB, and CMAP amplitude will serve as the primary endpoint for the peripheral assessment. Secondary endpoints will be collected using the nerve excitability testing protocol, consisting of five subtests that assess axonal excitability through stimulation paradigms, allowing assessment of axonal membrane polarisation and ion channel function. This detailed assessment elucidates the mechanisms underlying the described pathophysiology in the peripheral nervous system. The MScanFit Motor Unit Number Estimation (MUNE) test measures CMAP activation from supramaximal to subthreshold activation. A subsequently fitted model (MScanFit-2) estimates the number of motor units, motor unit sizes and the corresponding activation profile. The outcome measures of MUNE thereby provide information about motor unit distribution and recruitment, which are prerequisites for motor activation during motor training and voluntary movement. This quantification of the extent of axonal loss and damage to lower motor neurons can therefore serve as a biomarker of peripheral denervation and adaptation following SCI.[34]

Functional outcomes

Motor recovery, specifically arm and hand function, will be assessed using the Graded Redefined Assessment of

Table 1 Participant timeline: schedule of enrolment, interventions and assessments

		Trial period						
	Enrolment	Post-randomisation						Follow-up
TIMEPOINT **Assessments (T)**	0	*T1*		*T2*			*T3*	*T4*
Continuous measures (CM)			*CM1*		*CM2*	*CM3*		
	>13 post-injury	**Study visit 1 (baseline)**	**On-site data collection (week 2)**	**Study visit 2 (4 weeks after baseline)**	**On-site data collection (week 5)**	**On-site data collection (week 8)**	**Study visit 3 (8 weeks after baseline)**	**Study visit 4 (6 months after baseline)**
ENROLMENT:								
Eligibility screening	X							
Informed consent	X							
ISNCSCI assessment	X						X	
Randomisation	X							
INTERVENTION/COMPARATOR:								
Additional active UL training		X	→	→	→	→	X	
Usual care	X	→	→	→	→	→	X	
ASSESSMENTS:								
Demographic information (date of birth, gender, date of injury)		X						
RMT (50 mV and 200 mV)		X		X			X	X
SRF		X		X			X	X
Motor mapping (centre of gravity, map size)		X					X	X
SICI/LICI		X					X	X
NET		X		X			X	X
MUNE		X		X			X	X
GRASSP		X					X	X
VLT		X					X	X
Muscle strength		X		X			X	X
SCIM-SR		X					X	X
Goals		X					X	X
Therapy documentation		X	→	→	→	→	X	
Accelerometer measurement			X		X	X		
Perceived difficulty			X		X	X		
Perceived exertion			X		X	X		

GRASSP, Graded Redefined Assessment of Strength, Sensibility, and Prehension; ISNCSCI, International Standards for Neurological Classification of SCI; MUNE, Motor Unit Number Estimation; NET, Nerve Excitability Testing; RMT, Resting motor threshold; SCIM-SR, Spinal Cord Independence Measure Version III—Self Report; SICI/LICI, Short-/Long intracortical inhibition; SRF, Stimulus-Response Function; UL, Upper Limb; VLT, Van Lieshout Test.

Strength, Sensibility and Prehension (GRASSP).[35 36] As secondary endpoints, the upper extremity motor scores of the ISNCSCI and muscle strength will be measured using hand-held dynamometers to indicate motor recovery.[15 37] The Van-Lieshout test provides information on arm and hand movement quality during performance of basic activities.[38] Two patient-reported outcomes will be collected, namely, patients will rate their independence with the Spinal Cord Independence Measure Version III—Self Report using the self-care sub-score,[39 40] and participants will rate their satisfaction and performance for each of the four goals on a 0–10 scale.

Dose dimension outcomes

The dose dimensions (duration and intensity) will be assessed during three designated weeks of the intervention period (weeks 2, 5 and 8). During all training sessions of these weeks, active and inactive time will be measured using accelerometers (ActiGraph wGT3X-BT) worn on both wrists by participants. A MATLAB analysis script will be used to determine both arms' active time in minutes.

Additionally, within these weeks, the patients will rate the subjective training intensity and subjective difficulty with the visual analogue scale (0–10) as well as perceived exertion with a BORG scale (0–10) after each training session.[41] The total session length and length of UL training will be derived from the therapists' practice sheets and workbooks. Following Bertels *et al*, therapy dose will be categorised in the dimensions: UL session length, objective active time, subjectively perceived session intensity and subjectively perceived session difficulty.[28]

Proposed analysis and expected results

Descriptive statistics on participants' baseline characteristics will be obtained. Continuous variables will be presented as mean±SD, while categorical variables will be reported as absolute numbers and percentages.

Objective 1

The primary analysis evaluates the effects of the intervention on neurophysiological and functional outcomes. Changes in primary neurophysiological (RMT 200 µV expressed in % MSO and maximum CMAP amplitude expressed in mV) and functional (GRASSP total score) outcomes between groups will be analysed using separate linear mixed effects approaches with fixed effects (*group* and *time*) and random effects accounting for participant-specific intercepts and slopes. The linear mixed effects models are well-suited as they can be fitted to account for repeated measures over time, handle unbalanced and missing data, and account for potential confounders by adjusting for baseline covariates (eg, age, AIS grade, injury level) and individual variability.

A secondary analysis will use a joint multivariate repeated-measures mixed model for RMT, CMAP and GRASSP to account for potential correlations among the measures. An unstructured covariance matrix will account for within-subject dependencies across outcomes and time points using Bayesian or frequentist methods, depending on convergence. The main effects, beta coefficients (β), 95% CI and p values will be calculated and reported. Post hoc comparisons will be conducted to obtain estimated marginal means using Tukey's Honestly Significant Difference (HSD) adjustment for multiple comparisons.

Objective 2

The analysis aims to assess the correlation between training dosage and neural and functional recovery. It will be examined using linear or nonlinear regression models, with different dose dimensions (UL session length, objective active time, subjectively session intensity, subjectively session difficulty) as independent variables and neurophysiological and functional outcomes as the dependent variables.

Objective 3 (exploratory analysis)

Correlational analysis using Pearson correlation (for normally distributed variables) or Spearman correlation (for non-normally distributed variables) will be used to explore the correlations between the delta scores of secondary endpoints, such as the additional measures of central and peripheral plasticity, to investigate subtle changes. The size and significance of the correlation will be evaluated. Separate regression models will be used to identify baseline factors (AIS grade, injury level, age, baseline functional and neurophysiological outcomes) associated with increased recovery in functional scores. This allows exploration of distinct intervention effects within subgroups, for example, by AIS grade.

Trial monitoring

To ensure intervention adherence and treatment fidelity, all involved therapists received online educational materials that provide instructions and guidelines for the implementation and documentation of the additional motor training. Moreover, adherence will be monitored at week four. A researcher with clinical expertise will review the therapy documentation and accelerometer data, and therapists will receive feedback if necessary. As a final point, the researchers with clinical expertise meet regularly with the coordinating therapists at each centre to provide guidance on interventions and ongoing support. Our proposed analysis can handle missing data, allowing for the inclusion of incomplete cases and accounting for within-subject correlations. If deemed necessary due to substantial data loss and/or a small dataset, Bayesian models for integration will be explored. A steering committee meets annually to oversee the trial.

Safety and adverse events

Participants will be in inpatient care throughout the intervention period and thereby in close contact with their treating physicians and care team. All measures will be conducted on-site. In case of concerns about a participant's condition, the continuation of the trial will be discussed within the care team, and a senior member of

the research team who is unblinded to the allocation. Mild and serious adverse events (AEs) will be recorded by the treating physicians and clinical care team and reported. Specifically, we will record measurement-related AEs (specifically TMS-related events), SCI-related AEs (eg, spasticity), rehabilitation-related AEs (eg, musculoskeletal injuries, fatigue) and general unanticipated AEs (eg, falls or infections). These AEs will be reported to and reviewed by the yearly steering committee, which may determine the continuation, modification or ending of the trial.

Randomisation

Participants will be recruited and selected by rehabilitation physicians not involved in randomisation, data collection and analysis. Randomisation is done by a set member of the research team through MATLAB using a permuted block design, with a 1:1 ratio in blocks of four, stratified by site, and occurs after baseline assessments. The involved therapists and rehabilitation physicians are subsequently informed about the allocation. All measurements are conducted by an assessor blinded to group allocation.

Sample size

Our primary analysis is a group comparison, comparing the differences in scores between the baseline and postintervention assessment. Comparable prior research using UL motor training and RMT as an outcome measure is limited to chronic SCI, although suggesting large effect sizes.[42] A comparable preliminary study using an arm-and-leg training programme[43] similarly reports significant MEP changes. In earlier phases after an SCI, most neurological recovery occurs at the lesion site, that is, the spinal cord, and such adaptations are expected to be present in both the intervention and control group. Neuroplastic changes in the cortex following an intensive training intervention are expected to be more pronounced in the intervention group. Taking this into account and considering that in sub-acute phases following an SCI, our control group is also hypothesised to display some degree of delta changes, we propose a moderate effect size. Power analysis ('effect size 0.45', 'alpha 0.05' and 'power 0.8', R-package 'pwr') suggests 41 participants are required. Assuming a 10% dropout, we aim to recruit 22 participants per group.

Patient and public involvement

Patients and members of the public were involved at several stages of the trial, including its design, management and execution. The study design was elaborated in a consortium of rehabilitation physicians and researchers. As described in section 2.2, the intervention was adjusted based on patient input and involved therapists and clinicians. Relevant outcome measures, specifically concerning training dose, were selected in collaboration with physio- and occupational therapists working in neurological rehabilitation.

ETHICS AND DISSEMINATION

Ethical approval has been granted from the medical ethics committees, namely METC Máxima MC (NL84212.015.23) and MEC Gent (B6702023000227), as well as local ethics committees, including CME Hasselt, UZ Gent, UZ Leuven, RZ RevArte, De Hoogstraat Revalidatie and Adelante Zorggroep. The trial has been registered on ClinicalTrials.gov (initial release: 2 October 2023; latest update: 5 December 2025; NCT06065384).

Recruitment began in October 2024, with completion anticipated by early 2027. Data will be handled in compliance with the European General Data Protection Regulation and will be pseudonymised for publication. The findings of this RCT will be disseminated through articles in scientific, peer-reviewed journals and at national and international neurological rehabilitation conferences.

Author affiliations
[1]REVAL, Faculty of Rehabilitation Sciences, Hasselt University, Diepenbeek, Belgium
[2]Department of Neurophysiology, Aarhus University Hospital, Aarhus, Denmark
[3]Kolling Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia
[4]Department of Physical Medicine and Rehabilitation, Universitair Ziekenhuis Gent, Gent, Belgium
[5]Adelante Centre of Expertise in Rehabilitation and Audiology, Adelante, Hoensbroek, The Netherlands
[6]CAPHRI, Maastricht University, Maastricht, the Netherlands
[7]Queen Square Institute of Neurology, University College London, London, UK

Acknowledgements The authors thank Dr Lisa Harvey for her advice and resources for the motor training programme and Dr Alexander Kristensen for his support regarding the peripheral neurophysiological measurements. Further, the authors thank all cooperating rehabilitation physicians and therapists for their input in the project formulation and active involvement in the study execution.

Contributors AS, NB, HT, KO, CL-G, JVG and LTT were involved in the conceptualisation of the project. AS is responsible for funding acquisition, supervision and guarantor. IJH is responsible for data collection and primary analysis. All authors are members of a yearly steering committee overseeing study management and quality assessment. IJH drafted the manuscript. All co-authors approved and critically revised the final manuscript. During the preparation of this work, the authors used Grammarly (Grammarly, San Francisco, CA, USA) to spell-check and Chat Generative Pre-Trained Transformer (ChatGPT; OpenAI, San Francisco, CA, USA) to aid in structuring content and enhance readability. After using these tools, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

Funding This work was supported by Research Foundation – Flanders (FWO; grant number G076623N).

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Imke Jana Hrycyk https://orcid.org/0009-0003-1315-7648

REFERENCES

1 Snoek GJ, IJzerman MJ, Hermens HJ, *et al*. Survey of the needs of patients with spinal cord injury: impact and priority for improvement in hand function in tetraplegics. *Spinal Cord* 2004;42:526–32.
2 Calderone A, Cardile D, De Luca R, *et al*. Brain Plasticity in Patients with Spinal Cord Injuries: A Systematic Review. *Int J Mol Sci* 2024;25:2224.
3 Grumbles RM, Thomas CK. Motoneuron Death after Human Spinal Cord Injury. *J Neurotrauma* 2017;34:581–90.
4 Van De Meent H, Hosman AJ, Hendriks J, *et al*. Severe degeneration of peripheral motor axons after spinal cord injury: a European multicenter study in 345 patients. *Neurorehabil Neural Repair* 2010;24:657–65.
5 Oliveira DSD, Carbonaro M, Raiteri BJ, *et al*. The discharge characteristics of motor units innervating functionally paralyzed muscles. *J Neurophysiol* 2025;133:343–57.
6 Del Vecchio A, Casolo A, Negro F, *et al*. The increase in muscle force after 4 weeks of strength training is mediated by adaptations in motor unit recruitment and rate coding. *J Physiol (Lond)* 2019;597:1873–87.
7 He L-W, Guo X-J, Zhao C, *et al*. Rehabilitation Training after Spinal Cord Injury Affects Brain Structure and Function: From Mechanisms to Methods. *Biomedicines* 2023;12:41.
8 Rank MM, Flynn JR, Battistuzzo CR, *et al*. Functional changes in deep dorsal horn interneurons following spinal cord injury are enhanced with different durations of exercise training. *J Physiol (Lond)* 2015;593:331–45.
9 Dunlop SA. Activity-dependent plasticity: implications for recovery after spinal cord injury. *Trends Neurosci* 2008;31:410–8.
10 Walker JR, Detloff MR. Plasticity in Cervical Motor Circuits following Spinal Cord Injury and Rehabilitation. *Biology (Basel)* 2021;10:976.
11 Scivoletto G, Bonavita J, Torre M, *et al*. Observational study of the effectiveness of spinal cord injury rehabilitation using the Spinal Cord Injury-Ability Realization Measurement Index. *Spinal Cord* 2016;54:467–72.
12 Bertels N, Seelen H, Dembele J, *et al*. Essential training variables of arm-hand training in people with cervical spinal cord injury: a systematic review. *J Rehabil Med* 2023;55:jrm7147.
13 Lotter JK, Henderson CE, Plawecki A, *et al*. Task-Specific Versus Impairment-Based Training on Locomotor Performance in Individuals With Chronic Spinal Cord Injury: A Randomized Crossover Study. *Neurorehabil Neural Repair* 2020;34:627–39.
14 Bertels N, Piškur B, Janssen-Potten Y, *et al*. Therapists' perspectives on an interdisciplinary approach of arm-hand rehabilitation in cervical spinal cord injury: a qualitative study. *Disabil Rehabil* 2025;47:5260–7.
15 Harvey LA, Glinsky JV, Chu J, *et al*. Early and intensive motor training to enhance neurological recovery in people with spinal cord injury: trial protocol. *Spinal Cord* 2023;61:521–7.
16 Arora T, Desai N, Kirshblum S, *et al*. Utility of transcranial magnetic stimulation in the assessment of spinal cord injury: Current status and future directions. *Front Rehabilit Sci* 2022;3:1005111.
17 Balbinot G, Li G, Kalsi-Ryan S, *et al*. Segmental motor recovery after cervical spinal cord injury relates to density and integrity of corticospinal tract projections. *Nat Commun* 2023;14:723.
18 Schuch CP, Jovanovic LI, Balbinot G. Corticospinal Tract Sparing in Cervical Spinal Cord Injury. *J Clin Med* 2024;13:6489.
19 Hoffman L, Field-Fote E. Effects of practice combined with somatosensory or motor stimulation on hand function in persons with spinal cord injury. *Top Spinal Cord Inj Rehabil* 2013;19:288–99.
20 van Helden JFL, Alexander E, Cabral HV, *et al*. Home-based arm cycling exercise improves trunk control in persons with incomplete spinal cord injury: an observational study. *Sci Rep* 2023;13:22120.
21 Franz S, Eck U, Schuld C, *et al*. Lower Motoneuron Dysfunction Impacts Spontaneous Motor Recovery in Acute Cervical Spinal Cord Injury. *J Neurotrauma* 2023;40:862–75.
22 Berger MJ, Dengler J, Westman A, *et al*. Nerve Transfer After Cervical Spinal Cord Injury: Who Has a "Time Sensitive" Injury Based on Electrodiagnostic Findings? *Arch Phys Med Rehabil* 2024;105:682–9.
23 Sørensen DM, Tankisi H. Reliability of MScanFit Motor Unit Number Estimation in the Trapezius Muscle. *Muscle Nerve* 2025;71:166–70.
24 Witt A, Fuglsang-Frederiksen A, Finnerup NB, *et al*. Detecting peripheral motor nervous system involvement in chronic spinal cord injury using two novel methods: MScanFit MUNE and muscle velocity recovery cycles. *Clin Neurophysiol* 2020;131:2383–92.
25 Hrycyk I, Triccas LT, Tankisi H, *et al*. Assessment of neuroplastic changes in the peripheral nervous system following cervical spinal cord injury using nerve excitability testing and mscanfit motor unit number estimation. In: Pons JL, Tornero J, Akay M, eds. *Converging clinical and engineering research on neurorehabilitation V*. 2024. . Cham: Springer Nature Switzerland, 2024: 291–5.
26 Rossi S, Hallett M, Rossini PM, *et al*. Screening questionnaire before TMS: an update. *Clin Neurophysiol* 2011;122:1686.
27 Ben M, Glinsky JV, Chu J, *et al*. Early and intensive Motor Training for people with spinal cord injuries (the SCI-MT Trial): description of the intervention. *Spinal Cord* 2023;61:600–7.
28 Bertels N, Janssen-Potten Y, van Laake-Geelen C, *et al*. Arm-hand training strategies and therapy dose dimensions during the subacute rehabilitation of people with cervical spinal cord injury: a longitudinal observational study. *Spinal Cord* 2025;63:557–65.
29 Fisher RJ, Nakamura Y, Bestmann S, *et al*. Two phases of intracortical inhibition revealed by transcranial magnetic threshold tracking. *Exp Brain Res* 2002;143:240–8.
30 Hrycyk IJ, Tankisi H, Tedesco Triccas L, *et al*. Test-Retest Reliability of Threshold-Tracking TMS and Peripheral Nerve Testing in Healthy Adults and Individuals with Chronic Cervical Spinal Cord Injury. *Manuscript in Preparation* 2025.
31 Arora T, Potter-Baker K, O'Laughlin K, *et al*. Measurement error and reliability of TMS metrics collected from biceps and triceps in individuals with chronic incomplete tetraplegia. *Exp Brain Res* 2021;239:3077–89.
32 Nardone R, Höller Y, Thomschewski A, *et al*. Assessment of corticospinal excitability after traumatic spinal cord injury using MEP recruitment curves: a preliminary TMS study. *Spinal Cord* 2015;53:534–8.
33 Mi YP, Bailey AZ, Nelson AJ. Short- and Long-Intracortical Inhibition in Incomplete Spinal Cord Injury. *Can J Neurol Sci* 2016;43:183–91.
34 Debenham MIB, Franz CK, Berger MJ. Neuromuscular consequences of spinal cord injury: New mechanistic insights and clinical considerations. *Muscle Nerve* 2024;70:12–27.
35 Poutanen J, Savolainen S, Shulga A, *et al*. ICF-linking and psychometric properties of upper extremity mobility outcome measures in spinal cord injury – a scoping review. *J Spinal Cord Med* 2024;47:201–13.
36 Velstra I-M, Fellinghauer C, Abel R, *et al*. The Graded and Redefined Assessment of Strength, Sensibility, and Prehension Version 2 Provides Interval Measure Properties. *J Neurotrauma* 2018;35:854–63.
37 ASIA and ISCoS International Standards Committee. The 2019 revision of the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)—What's new? *Spinal Cord* 2019;57:815–7.
38 Spooren AIF, Janssen-Potten YJM, Snoek GJ, *et al*. Rehabilitation outcome of upper extremity skilled performance in persons with cervical spinal cord injuries. *J Rehabil Med* 2008;40:637–44.
39 Anderson K, Aito S, Atkins M, *et al*. Functional Recovery Measures for Spinal Cord Injury: An Evidence-Based Review for Clinical Practice and Research: Report of the National Institute on Disability and Rehabilitation Research Spinal Cord Injury Measures Meeting. *J Spinal Cord Med* 2008;31:133–44.
40 Fekete C, Eriks-Hoogland I, Baumberger M, *et al*. Development and validation of a self-report version of the Spinal Cord Independence Measure (SCIM III). *Spinal Cord* 2013;51:40–7.
41 Hutchinson MJ, Kouwijzer I, de Groot S, *et al*. Comparison of two Borg exertion scales for monitoring exercise intensity in able-bodied participants, and those with paraplegia and tetraplegia. *Spinal Cord* 2021;59:1162–9.
42 Beekhuizen KS, Field-Fote EC. Sensory stimulation augments the effects of massed practice training in persons with tetraplegia. *Arch Phys Med Rehabil* 2008;89:602–8.
43 Hassanlouei H, Kurukuti N, Miller L, *et al*. Changes in corticospinal plasticity following 12 weeks of arm and leg cycling in incomplete spinal cord injury. In: Pons JL, Tornero J, Akay M, eds. *Converging clinical and engineering research on neurorehabilitation V*. Cham: Springer Nature Switzerland, 2024: 25–9.