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Multimodal Interventions for Upper-Limb Recovery After Cervical Spinal Cord Injury: A Systematic Review and Quantitative Synthesis

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Abstract: Cervical spinal cord injury (CSCI) leads to severe impairment of the upper limb, which leads to tetraplegia and decreased independence in aspects of self-care and grasping. Conventional rehabilitation provides limited recovery, particularly in the case of complete American Spinal Injury Association (ASIA) Impairment Scale (AIS) A–B injuries, and there is a growing interest in multimodal rehabilitation strategies. This systematic review summarized evidence from 38 studies including pilot studies, preclinical investigations, and randomized controlled trials published between 2016 and 2026. Interventions were systematically classified and data extracted for the primary upper-limb outcomes, the Action Research Arm Test, grip strength, Graded Redefined Assessment of Strength, Sensibility and Prehension, Upper Extremity Motor Score, and Spinal Cord Independence Measure. About three-quarters of the studies reported improvements in at least one upper-limb outcome and almost half the studies had clinically meaningful improvements. However, 44% of studies were judged to have a high or critical risk of bias due to small sample sizes and limited controls; more than 90% reported no major safety concerns. Orthotic and robotic interventions maintained functional improvements, whereas hybrid neuromodulation approaches led to the largest gains in grip strength. Pharmacological therapies were of little benefit. In conclusion, multimodal noninvasive rehabilitation strategies might be promising for the improvement of upper-limb recovery after CSCI, but larger, high-quality clinical trials are needed.

Keywords: cervical spinal cord injury, electrical stimulation, transcranial direct current stimulation, pharmacological intervention, robot-assisted therapy

1. Introduction

Cervical spinal cord injury (CSCI) remains one of the most severe forms of traumatic injury on a global scale [1, 2], frequently leading to profound loss of upper-limb function and tetraplegia that highly compromises independence in feeding, self-care, transfers, grasping, and personal hygiene. The recovery of upper-limb impairments is distinctly critical, as even modest gains in pinch precision, grip strength, or prehension can drastically decrease caregiver dependence and enhance the overall quality of life (QoL) for individuals with cervical-level injuries [3].

Across the literature, it is evident that traditional rehabilitation approaches focused on intensive occupational and physical therapy have produced modest functional gains specifically in motor-complete AIS A–B injuries where spontaneous axonal regeneration across the lesion site is extremely restricted [4, 5]. These conventional approaches rely heavily on natural neuroplasticity and residual motor pathways, which primarily develop in the first 6–12 months after injury, resulting in most patients remaining dependent on caregivers or adaptive equipment [4, 5].

There was an unanticipated surge between 2016 and 2026 in multimodal regenerative and neurotechnological therapies particularly designed to regain volitional upper-limb function post-CSCI [6]. These contemporary interventions have included cervical, transcutaneous, and epidural electrical stimulation that modulates Ia-afferent pathways for up to 90% motor neuron recruitment without direct motor neuron activation [7, 8]. Robotic exoskeletons deliver high-repetition task-oriented training with adaptive assistance that progresses from passive to active-constrained modes based on residual function [9, 10]. To facilitate intention-driven grasp and release, myoelectric-powered orthoses amplify residual electromyography (EMG) signals, providing both home- and clinic-based training options with demonstrated cross-education benefits [11, 12]. Brain–computer interfaces (BCIs), both noninvasive high-density surface electromyography (HD-sEMG) or electroencephalography (EEG) and implanted electrocorticography (ECoG) systems, decode voluntary neural signals to regain real-time hand control via functional electrical stimulation (FES) or robotic gloves [13, 14]. Virtual reality (VR) platforms augmented with vibrotactile feedback produce

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immersive motor relearning environments that enhance cortical engagement, movement efficiency, and patient motivation [15, 16]. Targeted pharmacological agents include anti-Nogo-A antibodies, riluzole, and neprilysin inhibitors such as thiorphan that promote axon sprouting, neuroprotection, and pro-regenerative transcriptional states in preclinical and early clinical models [17–19]. Hybrid protocols that combine electrical stimulation with robotics, VR, or BCI priming have demonstrated specifically synergistic effects by simultaneously addressing high-repetition practice, spinal excitability, and volitional drive [20].

Despite these advances, the current literature evidence base continues to face significant methodological restrictions such as high heterogeneity in injury and device parameters, predominantly small sample sizes, and incomplete long-term follow-up data [21, 22]. Ethical considerations remain paramount across all intervention categories, covering rigorous continuous safety monitoring for invasive implants, rigorous informed consent procedures, and equitable access concerns for expensive neurotechnologies [23].

The main aim of this systematic review is to perform a quantitative synthesis on data from 38 studies published between 2016 and 2026, including proof-of-concept pilots, preclinical modeling, randomized controlled trials (RCTs), and observational cohorts. The review employs an organized classification framework and standardized data extraction, centered on five validated upper-limb outcome measures: Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP), Action Research Arm Test (ARAT), grip/pinch strength, Spinal Cord Independence Measure (SCIM), and Upper Extremity Motor Score (UEMS). Quantitative synthesis on the selected studies shows that approximately 75% report considerable improvements in at least one upper-limb metric, with roughly 50% achieving clinically significant thresholds.

To provide a structured overview of the technologies discussed in this review, wearable rehabilitation systems can be broadly categorized into passive, active, and neural wearables based on their functional characteristics (Figure 1). This classification provides the conceptual basis for the following assessment of specific rehabilitation modalities and points out the complementary roles of structural support, powered assistance, and physiological sensing in modern upper-limb rehabilitation after CSCI.

2. Methodology

2.1. Study design

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. It provides a descriptive quantitative synthesis of multimodal and single-modality interventions for upper-limb functional recovery in CSCI, covering publications from 2016 to 2026. Because of high heterogeneity in study designs, populations, devices, and outcome reporting, formal meta-analysis was not performed.

2.2. Search strategy

A comprehensive literature search was conducted in five electronic databases (PubMed, Embase, Scopus, Web of Science, and Cochrane Library) for records published between January 1, 2016, and May 31, 2026 (final search performed on June 10, 2026). The search strategy was structured around three core concepts combined using Boolean operators: ("cervical spinal cord injury" OR "cervical SCI" OR CSCI OR tetraplegia OR quadriplegia) AND ("upper limb" OR "upper extremity" OR hand OR arm OR "hand function" OR grip OR prehension) AND ("epidural stimulation" OR "spinal cord stimulation" OR "transcutaneous stimulation" OR tSCS OR tDCS OR "robot-assisted training" OR robotic OR exoskeleton OR myoelectric OR orthosis OR "brain-computer interface" OR BCI OR "virtual reality" OR

Figure 1

Classification of wearable rehabilitation systems for upper-limb recovery following cervical spinal cord injury. Wearable technologies are categorized into passive wearables, active wearables, and neural wearables according to their primary function. Representative examples, clinical applications, and commonly reported functional outcome measures are summarized

VR OR riluzole OR "Rho inhibitor" OR "anti-Nogo-A" OR thiorphan OR pharmacological).

2.3. Inclusion and exclusion criteria

Our a priori inclusion criteria deliberately encompassed relevant preclinical animal models (macaque, rat) with direct translational relevance to human upper-limb motor recovery, technical validation studies in healthy volunteers when explicitly linked to future SCI application, and user needs/acceptability studies. These categories provide essential mechanistic, device optimization, and implementation context. Primary efficacy conclusions and clinical significance statements are drawn exclusively from the 26 human intervention/RCT studies; preclinical and technical data support mechanistic interpretation and future trial design only.

2.4. Study selection process

Two independent reviewers screened titles and abstracts of 1010 unique records after duplicate removal (n = 320). Full-text assessment was performed on 290 articles. Ultimately, 252 full-text articles were excluded (wrong population n = 68; no quantitative upper-limb outcomes n = 52; irrelevant intervention n = 45; publication type/date n = 38; animal/epidemiology n = 29; other n = 20). A total of 38 studies were included (26 human intervention/RCT, 5 preclinical macaque/rat, 4 technical validation, 3 user needs/acceptability). The PRISMA flow diagram summarizes the process (Figure 2).

The numbers reported in the text exactly match the PRISMA 2020 flow diagram (Figure 2): 1330 records identified, 320 duplicates removed, 1010 unique records screened at title/abstract stage, 720 excluded, 290 full-text articles assessed for eligibility, 252 excluded with documented reasons, and 38 studies finally included. Exclusion reasons at each stage were applied strictly according to the a priori criteria listed in Table 1. A completed PRISMA 2020 checklist is provided as Supplementary Material 1.

2.5. Data extraction

A standardized extraction form was used to capture author and year, study design, population, sample size, devices/equipment, intervention details, key numerical outcomes, follow-up, and notes/limitations. Data were extracted independently by two reviewers; discrepancies were resolved by consensus. Separate tables were created for outcome-specific changes (grip/pinch strength, ARAT, GRASSP, SCIM, UEMS) and for ethical/safety information (Institutional Review Board [IRB] approval body/ID, informed consent, guidelines followed, adverse events).

Figure 2

PRISMA 2020 flow diagram detailing the systematic search, duplicate removal, screening, eligibility assessment, and final inclusion of 38 studies on upper-limb recovery after cervical spinal cord injury (2016–2026)

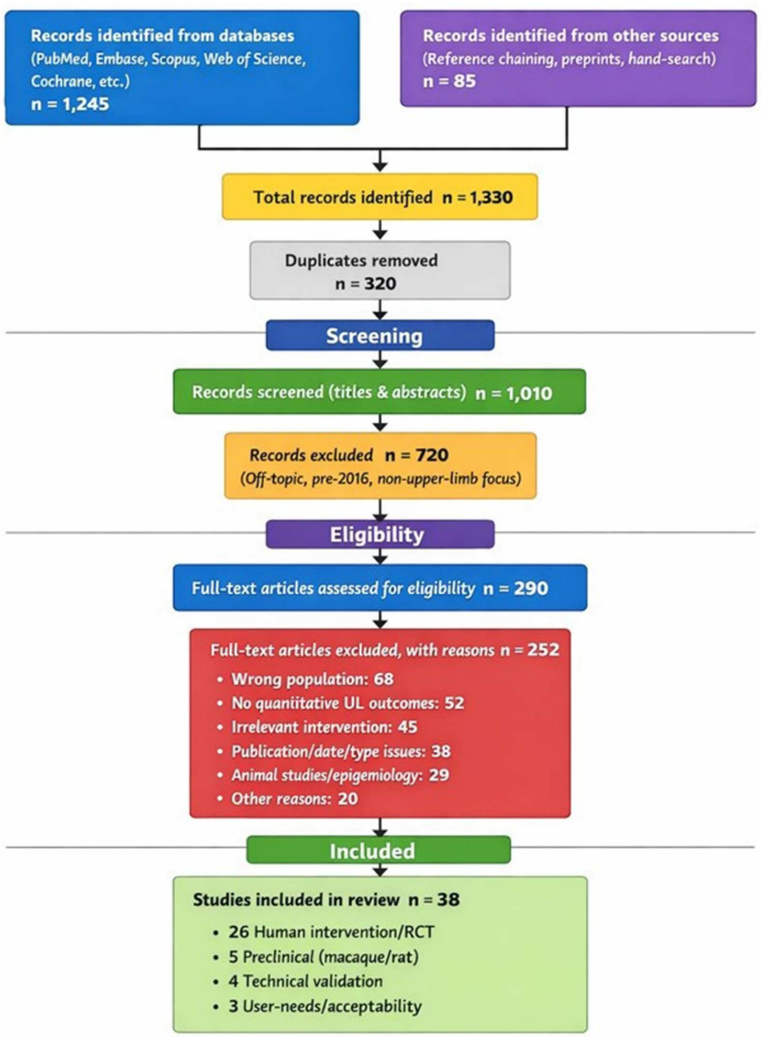


Table 1
Inclusion and exclusion criteria for the systematic review of multimodal upper-limb recovery interventions in cervical spinal cord injury (2016–2026)

Category	Inclusion criteria	Exclusion criteria
Publication date and type	1. Peer-reviewed full-text articles, abstracts with sufficient quantitative data, or preprints published 2016–2026 (inclusive) 2. Systematic reviews/meta-analyses accepted only for reference chaining	1. Pre-2016 publications 2. Editorials, letters, or conference abstracts without extractable quantitative data 3. Systematic reviews/meta-analyses as primary studies
Population	1. Human participants with traumatic or non-traumatic cervical SCI (C1–C8 levels, any AIS A–D grade, acute <6 months or chronic ≥6 months) 2. Relevant preclinical animal models (macaque, rat, cynomolgus monkey) with direct translational relevance to human upper-limb recovery 3. Healthy adult subjects for technical validation of devices/stimulation when explicitly linked to future SCI application	1. Non-cervical SCI (thoracic/lumbar only) 2. Pediatric populations (<18 years) 3. Studies focused exclusively on lower-limb or trunk function without upper-limb data
Intervention/exposure	Any multimodal or single-modality intervention targeting upper-limb/hand motor recovery, including: 1. Electrical stimulation (epidural/transcutaneous) 2. Robot-assisted training 3. Myoelectric/EMG-driven orthoses 4. BCI/neuroprosthetic hybrids 5. VR/augmented feedback 6. tDCS + robotics 7. Conservative/orthotic protocols 8. Pharmacological agents (Rho inhibitors, anti-Nogo-A, riluzole, thiorphan)	1. Interventions solely for pain management or spasticity without motor outcome measures 2. Non-rehabilitative surgical procedures (e.g., nerve transfers without functional outcome reporting)
Outcomes	Quantitative reporting of at least one validated upper-limb functional or motor outcome: 1. GRASSP (total or subscales) 2. ARAT 3. Grip/pinch strength (N/lb/kg or %) 4. UEMS/ASIA motor score 5. SCIM (total or self-care subscore) 6. Jebsen-Taylor Hand Function Test (JTHFT), Toronto Rehabilitation Institute–Hand Function Test (TRI-HFT), Motor Activity Log–Amount of Use (MAL-AOU), or kinematic measures (smoothness, path length)	1. Studies with no upper-limb-specific quantitative outcomes (qualitative descriptions only) 2. Exclusive focus on electrophysiological biomarkers without functional correlates
Study design	Any design: RCTs (including pilot/crossover), prospective/retrospective cohorts, case series/reports, proof-of-concept pilots, technical validation studies, or preclinical translational experiments with human relevance	1. Purely observational epidemiology without intervention 2. Animal studies without translational upper-limb motor testing 3. Non-English full-text publications
Language and accessibility	English-language full-text (or English abstract with extractable data tables/figures)	Non-English full texts without available English translation

2.6. Classification of studies

The studies included were classified into 11 thematic groups for synthesis: pure electrical stimulation approaches; electrophysiological and observational studies on recovery pathways; transcutaneous spinal cord stimulation integrated with rehabilitation/training; transcranial direct current stimulation (tDCS) combined with robotic training; cervical transcutaneous stimulation (technical/healthy subjects); robot-assisted training (RAT) approaches; conservative and orthotic training approaches/myoelectric and EMG-driven devices; virtual reality-based training approaches; brain–computer interface (BCI and neurotechnological hybrids; pharmacological interventions; and user needs and acceptability studies for assistive robotics (plus technical validation).

2.7. Risk of bias (RoB) assessment

RoB was assessed qualitatively and stratified by intervention category using domains adapted from Cochrane RoB 2 and Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tools (selection, performance, detection, attrition, reporting, and applicability/translation). Two reviewers independently rated each study; disagreements were resolved by consensus discussion (a third senior reviewer was available but not required). Each category was rated Overall RoB as Low, Moderate, High, or Critical, with explicit justification recorded in Table 2. Because of substantial clinical and device heterogeneity, RoB was stratified a priori by the 11 intervention categories rather than pooled across all studies. Forty-four percent of studies received an overall rating of High or Critical, driven predominantly by small sample sizes (median $n \approx 10$–20), absence of control arms in most device pilots, and short follow-up durations. These limitations are explicitly acknowledged in the Abstract, Highlights, and Discussion sections (Table 2).

2.8. Data synthesis

Because of substantial clinical and methodological heterogeneity, formal meta-analysis was not performed. Instead, a descriptive quantitative synthesis was conducted. For each core outcome (grip/pinch strength, ARAT, GRASSP, SCIM, UEMS), we extracted all available pre–post numerical changes from studies that reported sufficient data. Unweighted means, medians, and standard deviations (SDs) were calculated across extractable data points only. No inverse-variance weighting or meta-analytic pooling was applied. Studies reporting only qualitative descriptions or percentage changes without baseline values were excluded from the quantitative tables but retained in narrative synthesis. To reduce the influence of extreme outliers (e.g., +1136% force gains in $n = 2$ pilots), both mean and median values are reported, with medians and interquartile ranges emphasized as more robust central estimates. Sensitivity considerations (effect of excluding the two largest outliers) are noted in the Results. This approach follows current guidance for descriptive synthesis when meta-analysis is inappropriate (Cochrane Handbook, Chapter 12).

To provide an overview of the evolution of contemporary rehabilitation technologies included in this review, Figure 3 summarizes the chronological progression of major multimodal interventions reported between 2016 and 2026, highlighting the transition from early neuromodulation and robot-assisted therapies toward integrated approaches combining electrical stimulation, BCIs, VR, pharmacological interventions, and home-based rehabilitation.

Table 2
Risk of bias assessment of the 38 included studies on upper-limb recovery interventions for cervical spinal cord injury, stratified by intervention category

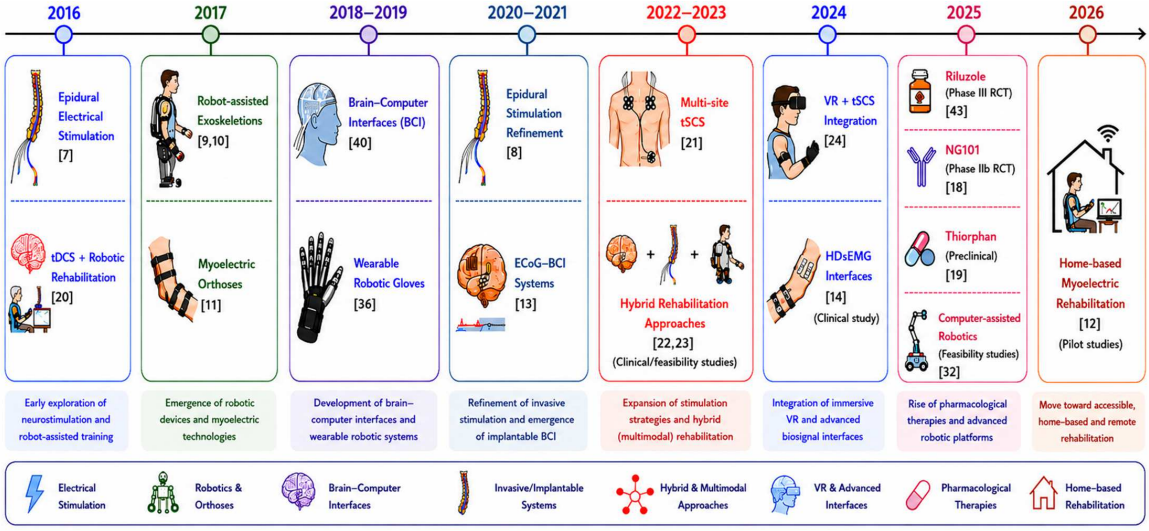
Intervention category	Studies	% of total	Overall RoB	Key bias domains (most affected)	Main reasons and impact (from documents)
Pure electrical stimulation (epidural Cervical Epidural Stimulation (CES)/Cervical Epidural Electrical Stimulation (CEES))	2	5%	Critical	Selection, sample size, performance	n = 2–5 humans; acute testing, no controls; "small sample size" explicitly noted in strong mechanistic data (90% recruitment) but limited long-term efficacy proof
Electrophysiological and observational (Motor Evoked Potential (MEP)/Spinal Cord Injury Model Systems (SCIMS))	2	5%	Moderate	Confounding (natural recovery)	Large n (305 and 405); objective measures; strong prognostic value of early MEP for UEMS/SCIM; no intervention control
tSCS + Rehab	3	8%	Critical	Selection, sample size, confounding	Mostly case reports (n = 1–2); dramatic gains (SCIM +72, force +1000%) but natural recovery confound and "larger RCTs needed"
tDCS + Robotic Training	2	5%	Moderate	Sample size, power	Small but double-blind RCT (n = 9); JTHFT trend only; "small sample size restricts generalizability" and "further larger studies necessary"
Cervical TSS (technical/healthy subjects)	1	3%	Critical	Applicability/translation	Healthy subjects only; torque selectivity validated but "high inter-subject variability" and "need for SCI testing in dynamic conditions"
Robot-assisted training	10	26%	Moderate–high	Sample size, blinding	Mostly small pilots (n = 1–26); grip +31% sustained, ARAT +4.33; "larger trials required" and "heterogeneity precludes strong conclusions"

(*Continued*)

Table 2
(*Continued*)

Intervention category	Studies	% of total	Overall RoB	Key bias domains (most affected)	Main reasons and impact (from documents)
Conservative/orthotic and myoelectric	5	13%	High	Selection, sample size	Small pilots (n = 6–10); 28–45% grip gains + cross-education; no controls; "larger RCTs needed for long-term ADL confirmation"
VR-based training	2	5%	High	Sample size, short term	Small n (1–5); acute efficiency gains only; high engagement but "small exploratory sample" and no long-term data
BCI and neurotechnological hybrids	6	16%	Critical	Selection, sample size	Mostly single-case studies (n = 1–2); volitional grasp restored (pinch +2 lb, accuracy 83%); "future studies examining long-term stability and larger groups required"
Pharmacological interventions	4	11%	Low–moderate	Minor (recruitment, delivery, post hoc)	Multicenter RCTs; strong safety & design; neutral primary UEMS but secondary SCIM benefit in subgroups; "recruitment difficulties" and "patient heterogeneity" noted
User needs and technical validation	3	8%	Moderate–high	Applicability	Healthy/survey-based; needs assessment robust (object handling 48%, voice 57.6%); low physical risk but "no patient efficacy data" and "clinical efficacy in SCI requires larger trials"

Figure 3
Evolution of upper-limb rehabilitation technologies for cervical spinal cord injury (2016–2026)



Note: Numbers in brackets [ ] correspond to reference numbers from the manuscript.
Abbreviations: tDCS, transcranial Direct Current Stimulation; tSCS, transcutaneous Spinal Cord Stimulation; EEG, electroencephalography; ECoG, electrocorticography; BCI, brain–computer interface; HDsEMG, high–density surface electromyography; RCT, randomized controlled trial.

3. Results

Figure 4 presents a conceptual overview of the hierarchical and convergent pathways involved in multimodal upper-limb rehabilitation following CSCI. The framework integrates prognostic assessment, neuromodulation, robotic rehabilitation, BCIs, pharmacological therapies, and personalized rehabilitation strategies, thereby providing an overview of the evidence synthesized in the subsequent Results section.

3.1. Overview of included studies

A total of 38 studies were included in this systematic review, comprising 26 human intervention or RCTs, 5 preclinical studies (macaque/rat models), 4 technical validation studies, and 3 user needs/acceptability studies. The PRISMA flow diagram is presented in Figure 2. Figure 5 presents an evidence landscape of the included studies, categorizing the interventions according to therapeutic modality, number of studies, overall level of evidence, principal functional outcomes, and predominant study

Figure 4
Hierarchical and convergent pathway for multimodal upper-limb recovery in cervical spinal cord injury: from prognostic stratification to personalized hybrid interventions and functional independence

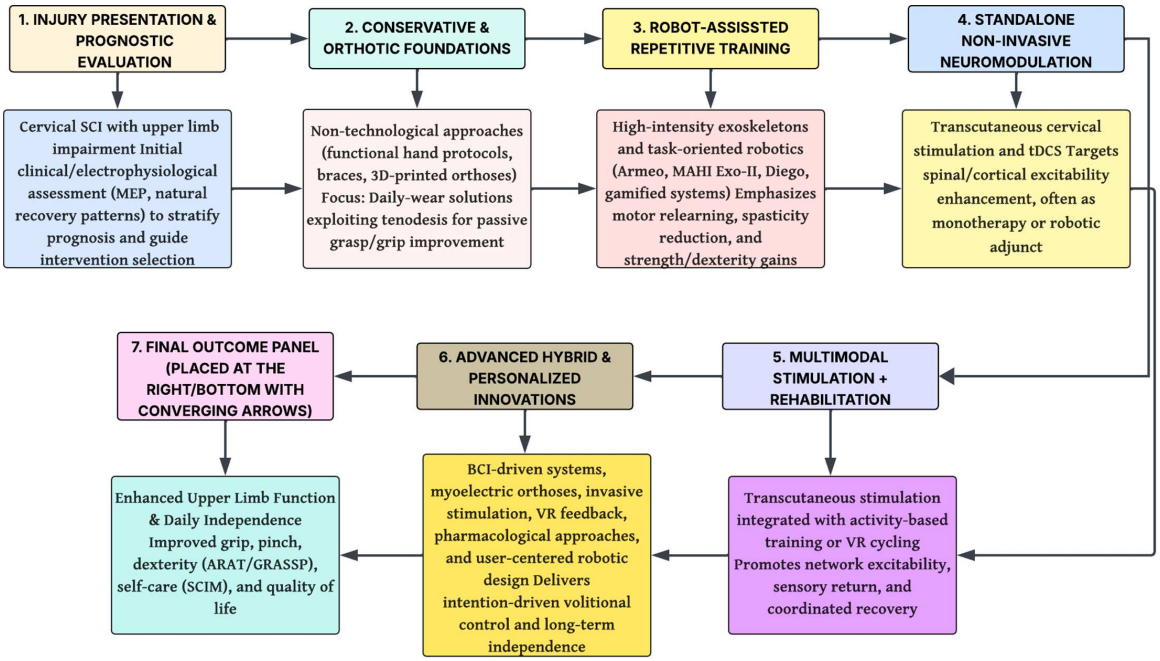
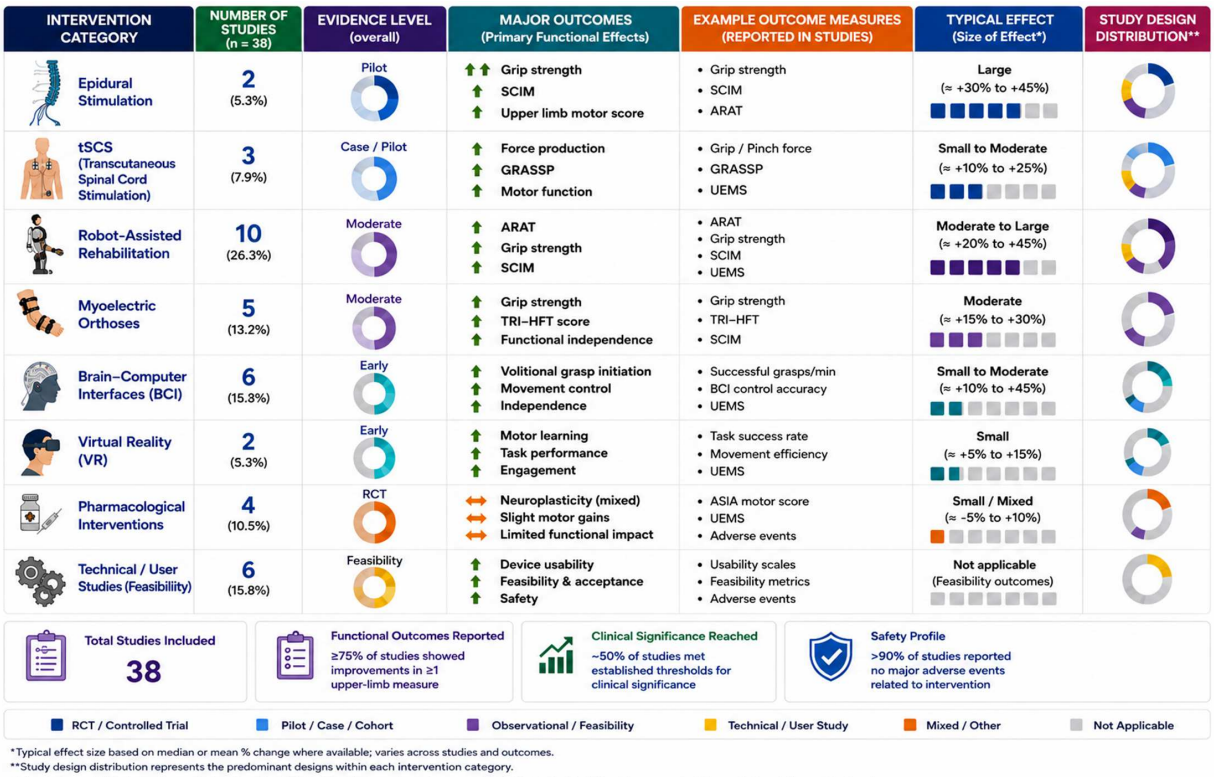


Figure 5
Evidence landscape of multimodal interventions for upper-limb recovery after cervical spinal cord injury



designs. This overview illustrates the current distribution and maturity of evidence across multimodal rehabilitation strategies for upper-limb recovery following CSCI.

3.2. Quantitative synthesis of core outcome measures

A descriptive quantitative synthesis was performed across five validated upper-limb outcome measures. The quantitative findings are presented later in the Results after the intervention-specific evidence has been described. Based on the collective findings of the included studies, Figure 6 proposes a clinical decision framework that synthesizes the current evidence into a personalized rehabilitation pathway. The framework illustrates how intervention selection may be tailored according to injury stage, neurological impairment, residual upper-limb function, rehabilitation goals, and the integration of multimodal therapeutic strategies to maximize functional recovery.

3.2.1. Pure electrical stimulation approaches

Two key studies investigated cervical epidural electrical stimulation for upper-limb recovery. Greiner et al. [8] established that lateral electrode positioning attains superior segmental selectivity (0.75–0.85) and can activate up to 90% of motoneurons via Ia-afferent trans-synaptic modulation. Lu et al. [7] reported in two people with chronic tetraplegia remarkable functional improvements, 200–300% increases in grip strength and clinically relevant improvements in the ARAT, supported by asynchronous EMG responses suggesting spinal network modulation. The results indicate that targeted epidural stimulation is successful in returning voluntary hand control. Figure 7 shows the pathway of intervention.

3.2.2. Electrophysiological and observational studies on recovery pathways

Two large cohort studies provided important prognostic insights. Javeed et al. [4] found that distal motor recovery, particularly at C7–C8, was highly correlated with improved likelihoods of functional independence (OR 11.9 for C7 + C8). Petersen et al. [5] found that early MEPs are a good predictor of better upper-limb recovery. The mdMEP group had significantly better upper extremity motor scores (23.47 vs 9.7) and SCIM self-care scores. The monitoring workflow is shown in Figure 8.

Figure 6
Clinical decision framework for personalized upper-limb rehabilitation following cervical spinal cord injury

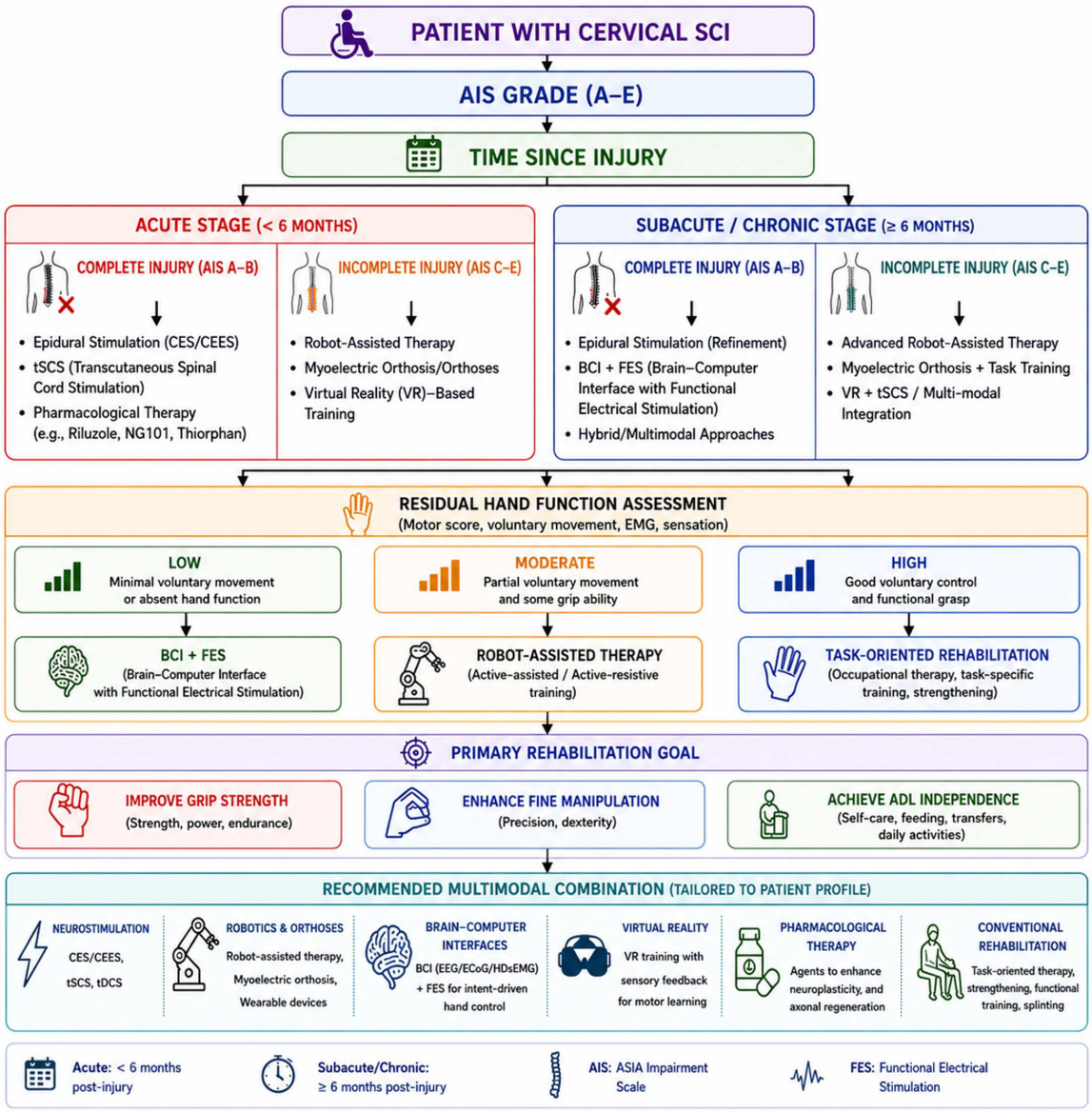


Figure 7
Mechanistic optimization pathway for cervical epidural electrical stimulation, mapping Ia-afferent recruitment thresholds and lateral electrode placement for maximal motoneuron selectivity and volitional hand control

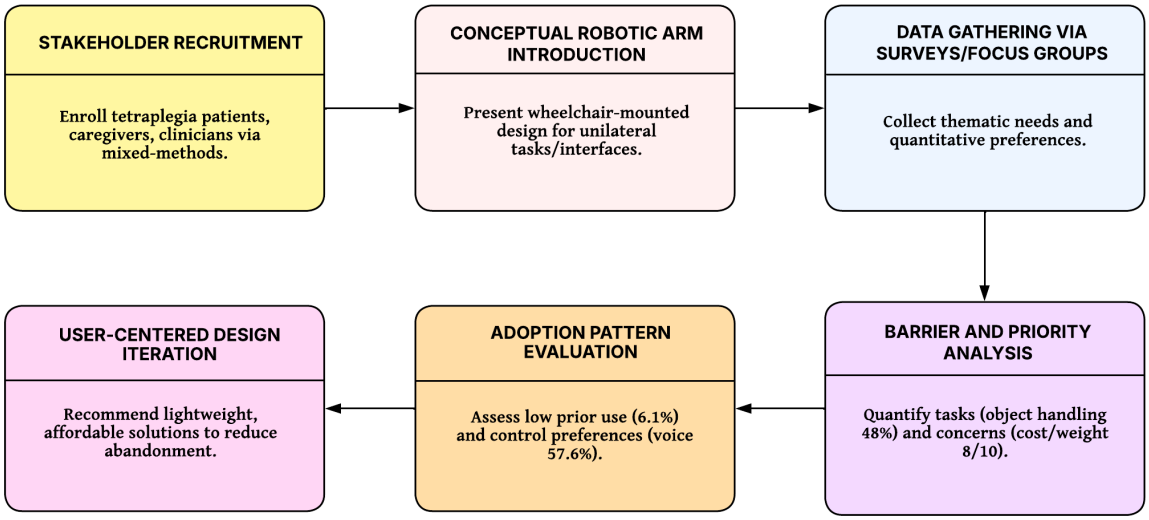
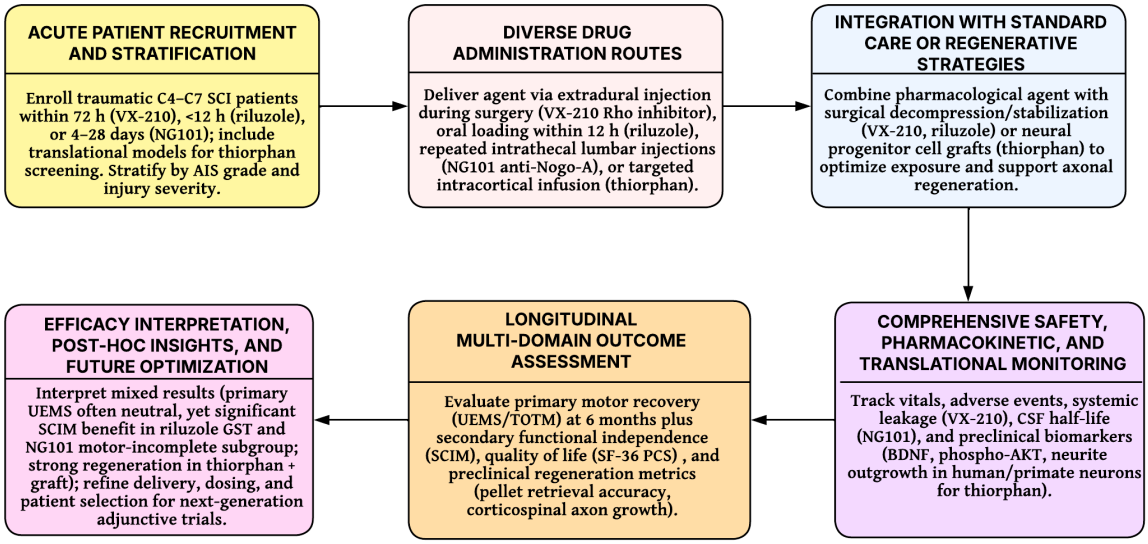


Figure 8
Serial biomarker monitoring workflow using MEP, CMAP, and F-wave assessments to stratify recovery potential and inform early rehabilitation decisions in acute cervical SCI



3.2.3. Transcutaneous spinal cord stimulation integrated with rehabilitation/training

Three studies examined transcutaneous spinal cord stimulation (tSCS) combined with training. Chandrasekaran et al. [21] reported dramatic force increases (>1000%) and GRASSP tactile gains in two chronic C5 patients. Sharma et al. [22] observed improved muscle activation and sensory scores with multi-site stimulation. Chu et al. [24] demonstrated broad gains in motor, sensory, and SCIM scores (+72 points) when tSCS was combined with VR cycling in early injury. Gains were most pronounced in muscles with residual activity. The integrated protocol is illustrated in Figure 9.

3.2.4. Transcranial direct current stimulation (tDCS) combined with robotic training

Two studies evaluated anodal tDCS (2 mA over M1) delivered concurrently with high-intensity robotic arm training [20, 25]. Both reported clinically meaningful task performance improvements (e.g., simulated feeding completed in 20 s vs impossible at baseline) and MAL-AOU scores exceeding the 0.5 clinical cutoff. The sham-controlled trial failed to reach statistical significance, but the combination approach is promising to improve neuroplasticity. The protocol is detailed in Figure 10.

3.2.5. Cervical transcutaneous stimulation (technical/healthy subjects)

Mahan et al. [23] performed an experimental study in healthy subjects and confirmed the site-specific effects of cervical transcutaneous spinal stimulation (TSS) when combined with robotic assessment. Rostral stimulation produced significantly lower motor thresholds and greater elbow flexion torque in proximal muscles compared to more caudal sites (Figure 11). There was a large inter-subject variability, suggesting the need for personalized stimulation protocols before clinical translation in spinal cord injury populations.

Table 3 summarizes the studies that together provide promising evidence that neuromodulation-based interventions, including epidural electrical stimulation, tSCS, and tDCS, are promising

Figure 9
Cervicolumbar coupling protocol combining multi-site transcutaneous stimulation with activity-based training and immersive VR cycling to amplify excitability and functional independence

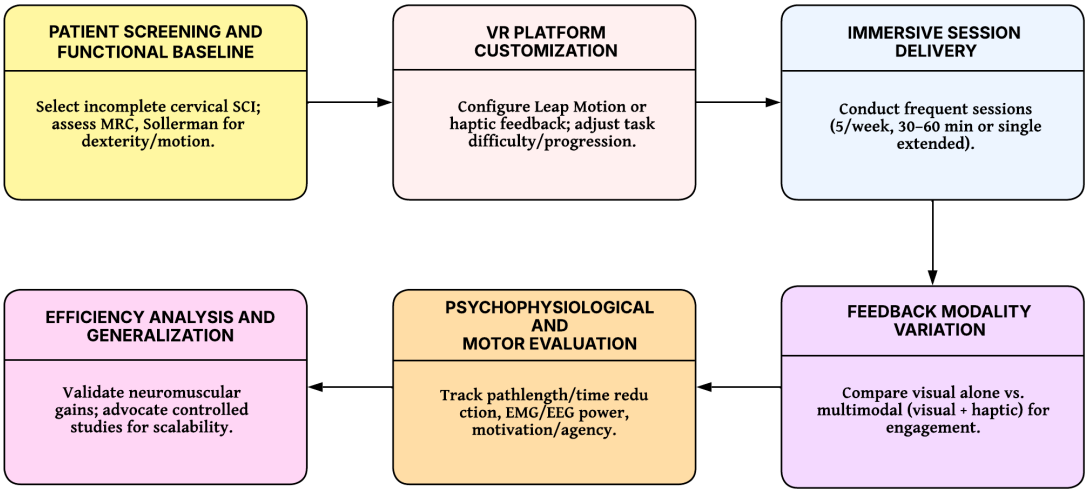


Figure 10
Hybrid neuromodulation framework pairing anodal tDCS with high-repetition robot-assisted arm training to promote corticospinal reorganization and task-specific motor gains

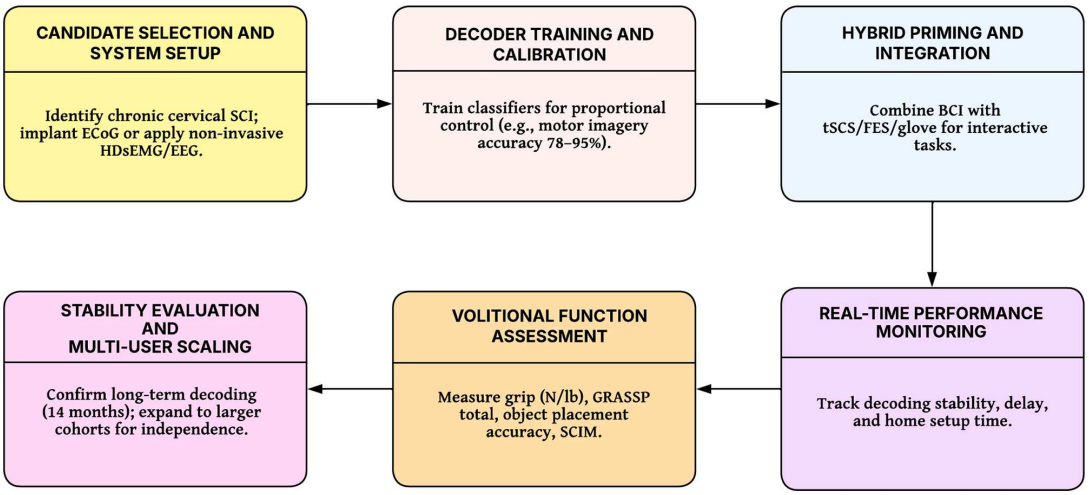


Figure 11
Site-specific mapping protocol for cervical transcutaneous stimulation, validated in healthy adults to demonstrate selective proximal muscle activation and torque optimization for future SCI application

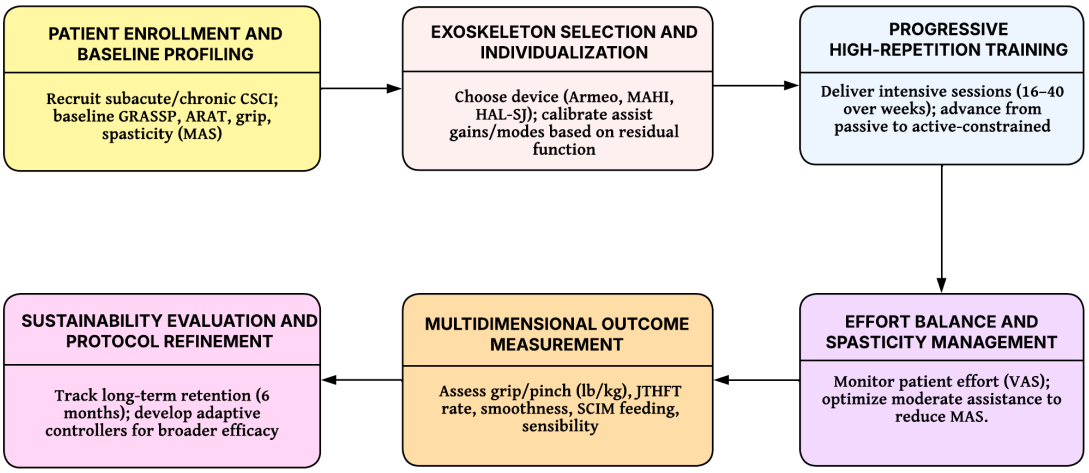


Table 3
Neuromodulation and electrical stimulation studies for upper-limb rehabilitation following cervical spinal cord injury

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Greiner et al. [8] (2021)	Pure electrical stimulation approaches	Combined computational/experimental	Macaques (mean age 5.2 y) + humans (mean age 52 y)	5 macaques + 5 humans	Epidural electrodes (lateral/-medial)	Cervical epidural stimulation (0.67–100 Hz)	56 ± 3 Ia-fibers for 10% recruitment; 93 ± 7 for 50%; 175 ± 9 for 90%; selectivity 0.75–0.85 (lateral) vs 0.60 (medial); 60% attenuation at 100 Hz	Intraoperative + acute	Preclinical translation; supports 90% recruitment
Lu et al. [7] (2016)	Pure electrical stimulation approaches	Proof of concept	Chronic tetraplegic (C5–C6)	2	Boston Scientific implanted epidural electrodes	Implanted epidural stimulation (2–40 Hz, 0.1–10 mA)	Grip: Subject 1: 9→32 N; Subject 2: 17→33 N; SCIM +28–31 points; ARAT +20%; all $p < 0.05$	Not specified	Small sample; promising volitional control
Petersen et al. [5] (2017)	Electrophysiological and observational studies on recovery pathways	Multicenter prospective cohort	Acute traumatic cervical SCI (mean age 46 y; 77% male)	305	Electrophysiological assessment tools	MEP, CMAP and F-wave assessments	MEP amplitudes: mdMEP 0.90→245 mV; UEMS mdMEP 23.47 vs aMEP 9.7; SCIM self-care 16.5 vs 6.7; F-wave 52–66%	12 months	Demonstrated predictive value of early MEP assessment
Javeed et al. [4] (2023)	Electrophysiological and observational studies on recovery pathways	Prospective cohort	High cervical SCI (C1–C4; 67% complete injuries)	405	N/A	Observational motor recovery tracking	Recovery: C5 51%; C8 36%; OR for independence: C7+C8 = 11.9 ($p = 0.001$); C6 = 7.2 ($p = 0.04$)	1 year	Distal recovery identified as a key predictor; no surgical data

(*Continued*)

Table 3
(*Continued*)

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Chandrasekaran et al. [21] (2023)	Transcutaneous spinal cord stimulation integrated with rehabilitation/training	Pilot study	Chronic C5 (American Spinal Injury Association (ASIA) A/B)	2	Custom electrode array	tSCS (950 Hz, 140–160 mA) + isometric training	Force increased by 1136% and 1035% ($p < 0.01$); GRASSP tactile +2 points	Retained post-intervention	Benefits observed only in muscles with residual activity
Sharma et al. [22] (2023)	Transcutaneous spinal cord stimulation integrated with rehabilitation/training	Case study	Chronic C2 injury	1	Multi-site surface electrodes	Multi-site Spinal Cord Transcutaneous Stimulation (scTS) + activity-based rehabilitation training (14 weeks, 60 sessions)	Strength improved from 0→1; EMG sensory $p = 0.001$; Multisegmental Motor Response (MMR) decreased ($p < 0.05$)	Not specified	Larger clinical studies required
Chu et al. [24] (2024)	Transcutaneous spinal cord stimulation integrated with rehabilitation/training	Case report	Early C4 AIS-D	1	Surface tSCS electrodes + virtual reality cycling system	VR cycling + tSCS (30 Hz, 60–80 mA, 6 weeks)	ASIA motor 52→88; sensory 139→169; SCIM 10→82	Post-6 weeks	Early intervention; natural recovery may have influenced outcomes
Yozbatiran et al. [25] (2017)	Transcutaneous spinal cord stimulation integrated with rehabilitation/training	Pilot case series	Chronic incomplete SCI (ASIA C–D; 36–63 years)	4	tDCS device + robotic arm trainer	Active tDCS (2 mA, 20 min) + robot-assisted arm training (10 sessions)	Task completion times improved; MAL-AOU exceeded clinically meaningful threshold (>0.5); fractional anisotropy increased (0.62→0.67)	Post-2 weeks	Small sample; evidence of neuroplasticity

(*Continued*)

Table 3
(*Continued*)

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Yozbatiran et al. [20] (2016)	Transcutaneous spinal cord stimulation integrated with rehabilitation/training	Double-blind sham-controlled RCT	Chronic incomplete SCI (mean age ~53 y)	9	Soterix tDCS + MAHI Exo-II	Anodal tDCS (2 mA) + MAHI Exo-II training	JTHFT improvement: active +40.7% vs sham +6.7% (NS; $p = 0.673$)	Post-intervention	Positive trend but not statistically significant
Mahan et al. [26] (2024)	Cervical transcutaneous stimulation (technical/healthy subjects)	Experimental	Healthy adults (mean age 24.3 y)	11	Surface electrodes + MAHI Exo-II	Cervical TSS delivered at three spinal levels during robotic training	Lower proximal stimulation thresholds ($p = 0.0005$); elbow torque significantly increased ($p = 0.0005$; $d = 6.43$)	Acute testing	Healthy participants only; substantial inter-subject variability

strategies for the restoration of upper-limb function following CSCI. Although there was large variability in stimulation parameters and rehabilitation protocols across studies, most investigations reported improvements in voluntary motor activation, grip strength, upper extremity motor performance, and electrophysiological outcomes. Current evidence is however limited by small sample sizes, heterogeneous study designs and limited long-term follow-up. Future multicenter RCTs using standardized stimulation protocols and clinically meaningful outcome measures are needed to assess the long-term efficacy and optimal integration of neuromodulation within comprehensive rehabilitation programs.

3.2.6. Robot-assisted training approaches

Robotic exoskeletons (Armeo Spring, MAHI Exo-II, Diego, HAL-SJ, InMotion) were evaluated in ten studies [9, 10, 27–34]. A comparative summary of functional outcomes is presented in Table 4, and the corresponding rehabilitation workflow is illustrated in Figure 12. Across these studies, consistent improvements were observed in movement smoothness, ARAT scores, and grip strength, with some benefits maintained at the 6-month follow-up. Home-based and hybrid delivery approaches also demonstrated additional cross-education benefits. Robotic training was safe and feasible; however, improvements achieved with robotic therapy alone were generally modest. Larger RCTs are required to confirm long-term activities of daily living (ADL) outcomes.

3.2.7. Conservative and orthotic training approaches

Two studies examined non-technological approaches. Ciardi et al. [35] reported superior ARAT grasp and grip scores with the Functional Hand Protocol compared to conventional therapy in C5–C7 tetraplegia. Yoo et al. [11] showed that a low-cost 3D-printed myoelectric orthosis led to significant increases in TRI-HFT scores and independence in eating. Such approaches provide low-cost, accessible options, particularly when combined with other modalities.

3.2.8. Myoelectric and EMG-driven devices/training

Two studies assessed myoelectric-powered orthoses. Lu et al. [36] reported 45% improvement in grip strength with the Hand of Hope exoskeleton. Androwis et al. [12] found that combined home and clinic use of the MyoPro orthosis produced the largest gains in active range of motion (+36.5%) and grip force (+28–30%), along with cross-education effects (7–12%) in the untrained limb.

3.2.9. Virtual reality-based training approaches

Two studies explored VR-based training. Al Nattah et al. [16] indicated that training with the Leap Motion Controller markedly enhanced the Sollerman Hand Function Test scores. Nataraj et al. [15] indicated that visual input alone markedly enhanced movement efficiency and reduced EMG amplitude. Multimodal (visual + haptic) feedback showed trends toward increased motivation (Figure 13). VR appears promising for engagement and motor efficiency, although larger controlled studies are required.

3.2.10. Technical validation and assistive robot studies

Two technical studies confirm robotic systems. Watanabe et al. [37] showed a reduced input delay with a dynamic filter. Raji et al. [38] successfully adapted the TRI-HFT to a robotic platform with 100% success and high usability scores (SUS 75.5%) (Figure 14). These confirm technical feasibility but require clinical testing in spinal cord injury (SCI) populations.

The studies reported in Table 4 highlight the increasing importance of robotic, orthotic, myoelectric, wearable, and VR technologies to facilitate task-specific upper-limb rehabilitation following CSCI. These interventions were linked with consistent improvements in functional independence, dexterity, movement quality and patient engagement, especially when technology-assisted rehabilitation was combined with intensive, repetitive training. Despite these promising findings, there is considerable heterogeneity in device architecture, control strategies, training duration, and clinical outcome assessments that preclude direct comparison across studies. Further research should be directed to standardized evaluation frameworks, larger multicenter clinical trials, and comparative studies in order to determine the most effective rehabilitation strategies in different stages and severities of SCI.

3.2.11. Brain–computer interface (BCI) and neurotechnological hybrids

Five studies investigated BCI systems. Oliveira et al. [14] successfully decoded residual motor activity using noninvasive HD-sEMG. Davis et al. [39] and Cajigas et al. [13] demonstrated the long-term feasibility of implanted ECoG-BCI systems for restoring hand grasp, maintaining decoding accuracy at 87.5–91.3% over 14 months and pinch force gains from 1 lb to 3 lb. Kim et al. [40] reported that a vision-assisted BMI system reduced distance error to the intended target by as much as 57.37% ($p < 0.0001$). McGeady et al. [41] explored BCI motor priming coupled with tSCS, reporting increases in grip strength from 24N to 36N (Figure 15). Most approaches are still proof of concept but have promise for people with severe motor disabilities.

As summarized in Table 5, emerging neurotechnologies, pharmacological therapies, technical validation studies, and user-centered investigations represent complementary approaches that support the future development of personalized rehabilitation systems for CSCI. BCIs and advanced neural decoding techniques demonstrate the potential to restore voluntary control through direct neural communication, whereas pharmacological interventions aim to enhance neuroprotection and neural regeneration during the acute and subacute phases of recovery. Technical validation studies further contribute to the optimization of assistive technologies, while user-centered research emphasizes the importance of usability, accessibility, and patient preferences in facilitating long-term clinical adoption. Although many of these approaches remain in early translational stages, their integration with established rehabilitation technologies may provide a foundation for individualized, multimodal rehabilitation strategies in future clinical practice.

3.2.12. Pharmacological interventions

Four studies evaluated pharmacological agents. Fehlings et al. [17] (VX-210) and Weidner et al. [18] (NG101) reported neutral primary motor outcomes but some secondary benefits in subgroups. Van Niekerk et al. [19] showed strong preclinical regenerative effects with thiorphan (Figure 16). Pharmacological interventions appear safe but require optimized delivery and larger trials [42].

Table 4
Robotic, orthotic, myoelectric, and wearable rehabilitation studies for upper-limb recovery following cervical spinal cord injury

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Zariffa et al. [9] (2012)	Robot-assisted training approaches	Multicenter pilot	Subacute C4–C8	15	Armeo Spring exoskeleton	Armeo Spring (average 16 sessions over 5 weeks)	GRASSP sensibility improved from 6→10 points ($p = 0.04$); no significant change in ARAT or grip strength	2 weeks post-discharge	High patient satisfaction; therapist time saved
Francisco et al. [10] (2017)	Robot-assisted training approaches	Experimental	Chronic incomplete SCI (mean age 40 y)	10	MAHI Exo-II exoskeleton	Progressive MAHI Exo-II training	Grip strength 9.7→12.7 lb; pinch strength 4.5→5.6 lb; JTHFT rate 0.14→0.29 items/s	6 months	Functional improvements sustained over long-term follow-up
Yoshikawa et al. [27] (2019)	Robot-assisted training approaches	Case report	Cervical SCI with spasticity	1	HAL-SJ EMG-controlled robotic device	HAL-SJ with moderate assistance	Modified Ashworth Scale (MAS) reduced from 2→1+; flexion torque decreased from 16→13.7 Nm	Not specified	Moderate assistance level was optimal
Cortes et al. [28] (2013)	Robot-assisted training approaches	Pilot interventional	Chronic C4–C7	10	InMotion 3.0 Wrist Robot	Wrist robotic training (18 sessions over 6 weeks)	Movement smoothness improved (0.26→0.31); aiming error reduced (1.17→1.03 rad, $p = 0.03$)	Post-6 weeks	Safe intervention; no significant strength improvement
Frullo et al. [29] (2017)	Robot-assisted training approaches	Randomized controlled trial	Chronic SCI (mean age 53.5 y)	14	MAHI Exo-II (Assist-As-Needed (AAN)/Subject-Triggered (ST) controllers)	AAN vs ST controller (10 sessions)	ARAT improved by 4.33 points in AAN group; smoother movement patterns observed	2 months	No statistically significant clinical difference between controllers
Lozano-Berrio et al. [30] (2022)	Robot-assisted training approaches	Pilot randomized controlled trial	Subacute SCI (mean age ~43 y)	26	Armeo Spring exoskeleton	Armeo Spring (40 sessions) vs conventional therapy	SCIM feeding score 2.00 vs 1.18 ($p = 0.03$; $\eta^2 = 0.44$)	Post-intervention	Robotic therapy showed slight superiority over conventional therapy

(*Continued*)

Table 4
(*Continued*)

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Vanmulken et al. [31] (2015)	Robot-assisted training approaches	Prospective multiple-case study	C4–C7 (mean age 47.2 y)	5	Haptic Master robot	Haptic Master training (18 sessions over 6 weeks)	Self-care independence 80.6%; usability score 93%	Post-6 weeks	High feasibility but limited functional gains
Mackenzie et al. [32] (2025)	Robot-assisted training approaches	Mixed-methods pilot	Acute C4 SCI (mean age 44.3 y)	7	Diego™ robotic system	Diego robotic rehabilitation (3 sessions/week for ~23 days)	Canadian Occupational Performance Measure (COPM) performance +2.12 and satisfaction +2.52 ($p = 0.028$); SCIM +3.8 ($p = 0.01$)	Post-intervention	Clinically meaningful improvements during acute rehabilitation
Ma et al. [33] (2025)	Robot-assisted training approaches	Case study	Incomplete SCI (AIS-D; bilateral paresis)	1	Wearable robotic hand exoskeleton with sensor glove	Bimanual robotic hand rehabilitation (20 sessions)	AIS motor score 15→20/25; ARAT 14→20/57; SCIM 44→70	2 weeks post-intervention	Suggestive evidence of neuroplasticity
Kilkki et al. [34] (2025)	Robot-assisted training approaches	Pilot randomized crossover trial	Chronic incomplete SCI (mean age ~62 y)	16	Gamified assistive technology system	Technology-assisted gamified rehabilitation (18 sessions)	ASIA-UEMS median +1 ($p = 0.04$); Goal Attainment Scaling (GAS) T-score 50	Post-6 weeks	Safe and feasible with goal-oriented improvements
Ciardi et al. [35] (2023)	Conservative and orthotic training approaches	Longitudinal cohort	C5–C7 (mean age 54 y)	6	Wrist brace with flexion patches	Functional Hand Protocol vs conventional therapy	ARAT: Functional Hand Protocol (FHP) 37 vs 25.6/39; grasp score 17 vs 10/18	Not specified	Small sample; pinch strength not evaluated
Yoo et al. [11] (2019)	Conservative and orthotic training approaches	Clinical pilot	Chronic SCI (ASIA A–D; mean age ~50 y)	10	3D-printed myoelectric orthosis	Tenodesis-assisted EMG-controlled orthosis	TRI-HFT Part 1: 29.4→45.0 ($p = 0.007$); Part 2: 26.8→47.6 ($p = 0.009$); Functional Independence Measure (FIM) eating score 3.5→5.4	Post-use	Low-cost solution; bulkiness identified as limitation

(*Continued*)

Table 4
(*Continued*)

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Lu et al. [36] (2017)	Myoelectric and EMG-driven devices/-training	Case report	Chronic incomplete C6 SCI	1	Hand of Hope robotic exoskeleton	Hand of Hope training (20 sessions)	Grip strength increased by 45.2% (13.5→19.6 kg); control accuracy improved from 71%→96%	Post-10 weeks	Limited movement patterns supported
Androwis et al. [12] (2026)	Myoelectric and EMG-driven devices/-training	Randomized pilot	Chronic incomplete SCI (AIS B–D; mean age 53 y)	10	MyoPro myoelectric orthosis	Home + clinic vs clinic-only vs traditional occupational therapy	Home + clinic: Active Range of Motion (AROM) +36.5%; grip strength +28–30%; cross-education effect 7–12%	Post-intervention	Combined home and clinic training produced superior outcomes
Al Nattah et al. [16] (2024)	Virtual reality-based Training approaches	Case study	Incomplete C5 AIS-D	1	Leap Motion Controller with Unity 3D	Virtual reality training (70 days; 5 sessions/week)	Sollerman score: left hand 60→75; right hand 2→73/80; Medical Research Council (MRC) right hand 2→4/5	Post-70 days	High patient engagement reported
Nataraj et al. [15] (2025)	Virtual reality-based training approaches	Exploratory pilot cohort	Chronic incomplete C4–C6 (mean age 43 y)	5	Virtual reality system with vibrotactile feedback	Single-session VR with visual and haptic feedback	Visual feedback reduced path length by 12.5% ($p = 0.001$); EMG reduced by 32.5% ($p = 0.006$)	Acute post-training	Visual feedback demonstrated greater movement efficiency than multimodal feedback

Figure 12
Adaptive assistance calibration framework for robot-assisted upper-limb training, progressing from passive to active-constrained modes while monitoring effort, kinematics, and spasticity reduction

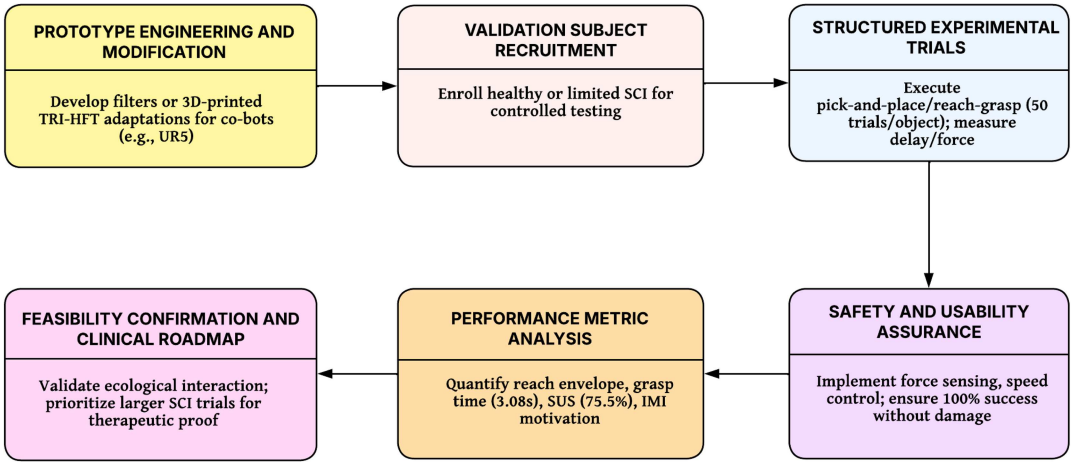


Figure 13
Augmented sensory feedback VR training protocol comparing visual-only versus multimodal (visual + haptic) delivery to enhance motor efficiency, cortical engagement, and patient agency

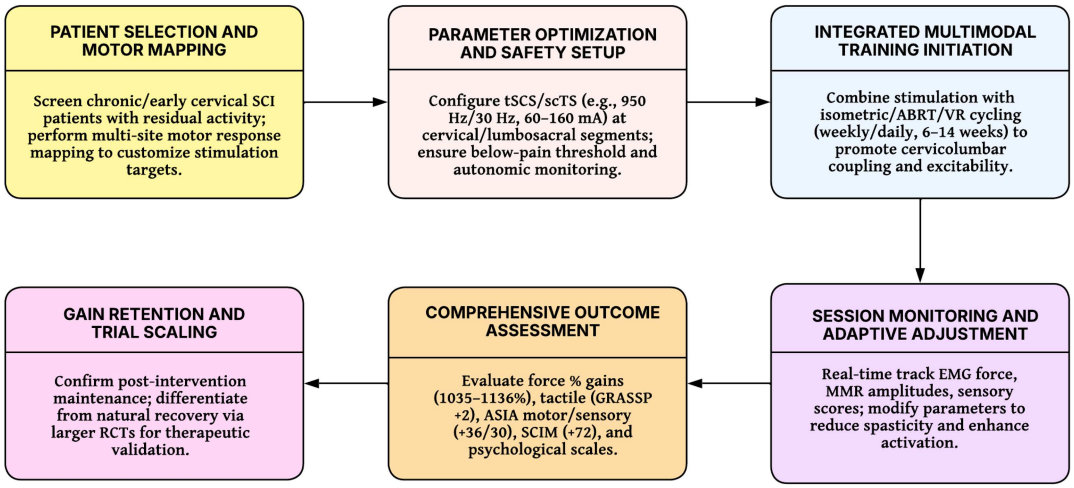


Figure 14
Ecological usability and technical validation protocol for robotic adaptations of hand-function tests and noninvasive interfaces, bridging laboratory metrics to real-world assistive performance

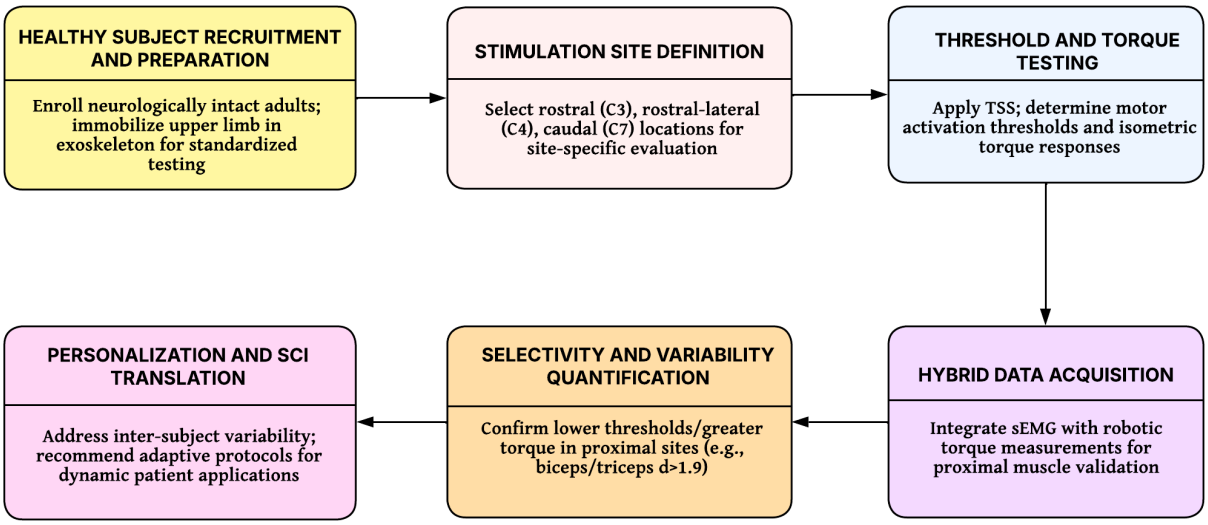
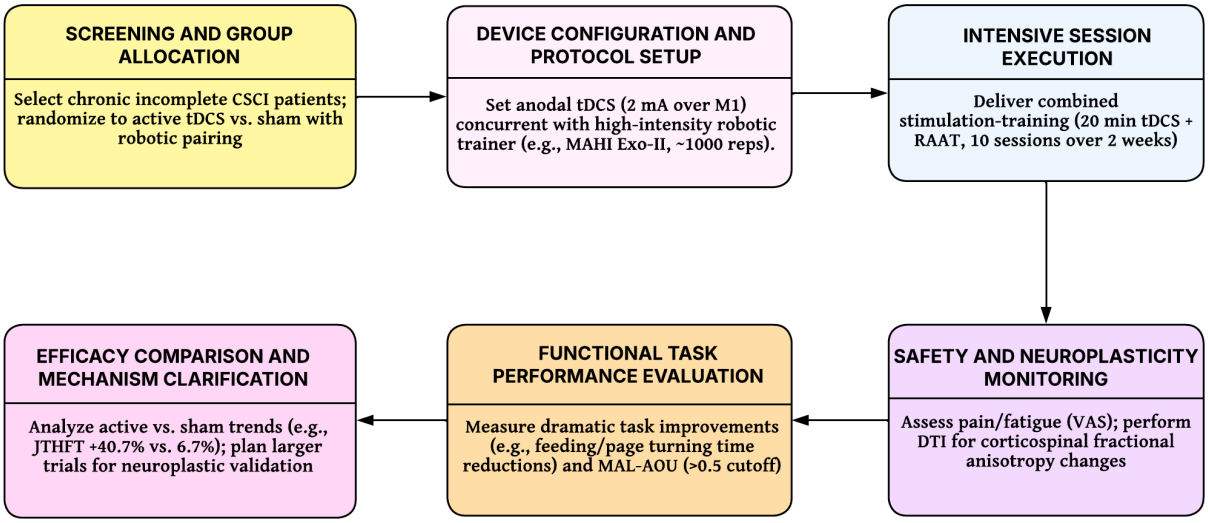


Figure 15
Neural decoding and hybrid control architecture linking noninvasive or implanted BCI signals with stimulation or orthotic actuators for restored volitional hand function in tetraplegia



3.2.13. User needs and acceptability studies for assistive robotics

Hutmacher et al. [43] identified the most important priorities for users of assistive robotic arms as object handling (48%), reach and grasp (34%), and preference for voice control (57.6%). Cost, weight, and space requirements were the main barriers. Respondents reported very low prior use of robots (6.1%) (Figure 17). Results emphasize the importance of the design of assistive devices with the user in mind in order to reduce the risk of future abandonment of technology.

The studies included in this systematic review for each intervention together suggest the growing use of wearable technologies to restore upper-limb function after CSCI. These wearable systems integrate sensing, actuation, electrical stimulation, and physiological monitoring to allow personalized rehabilitation while enabling objective assessment of motor recovery. Figure 18 shows some examples of wearable rehabilitation technologies frequently reported in the literature, describing their working principles and main clinical applications.

3.3. Quantitative synthesis of key outcomes

Table 6 summarizes the number of extractable changes, mean and median changes, and standard deviations. Median gains were prioritized due to the influence of outliers from small pilot studies. Overall, approximately 75% of studies demonstrated quantifiable improvements on at least one outcome and approximately 50% met clinically meaningful thresholds.

Table 7 shows that reported improvements ranged widely from +12–23 N absolute (or equivalent 2–6 kg/lb) to 30–300% relative gains, with a median ~45% in calculable cases. Largest proportional increases occurred in small-n stimulation hybrids (e.g., epidural CES up to 300%). Grip gains were most reliable in myoelectric/EMG-driven (30–45%) and pure/integrated electrical stimulation (200–300% in proof-of-concept), followed by robotic (31% sustained). Orthotic approaches showed qualitative "major" improvements without absolutes. Sustained at 6–12 months in robotic/myoelectric studies; pinch specifically improved in BCI hybrids (+2 lb). Grip is a highly responsive outcome to intention-driven or excitability-enhancing interventions (myoelectric, stimulation). Variability reflects residual function dependence—larger gains in studies with some baseline activity.

Table 8 shows that reported improvements varied widely +4–11 points (or equivalent subscales) where improved, averaging +6–8 points; ~33% of studies reported no significant change. Clinically meaningful gains were noticed in robotic bimanual (+6), adaptive controllers (+4.33), and orthotic Functional Hand Protocol (+11 equiv.). Epidural stimulation noted +20% (clinically significant threshold surpassed). ARAT assesses task/dexterity performance better than pure strength; improvements cluster in task-oriented robotic/orthotic interventions. No-change studies often less intensive or shorter. This highlights potential for combined conservative-tech protocols; ARAT's sensitivity makes it ideal for comparing low- versus high-tech interventions

Table 9 shows that the reported gains varied widely from +2–35 points across subscales (sensibility/prehension/tactile), with tactile +2 most common. Sensory/prehension focus dominant—consistent small gains (+2–10) in transcutaneous stimulation tactile and robotic sensibility; larger total (+35) in BCI + tSCS hybrid. GRASSP reports indicate that sensory returns frequently precede motor in stimulation-based approaches, implying trans-synaptic mechanisms. Indirect overlaps (e.g., TRI-HFT in orthotic +15–20) emphasize prehension benefits from daily-wear devices. Underscores the need for multidimensional assessments—pure motor scores may miss sensory-driven functional gains.

Table 10 shows that the scores vary markedly from +2–72 points total; self-care/feeding subscores +0.8–9.8 or notable increases. Largest leaps were observed in integrated multimodal (+72 total in VR + tSCS) and robotic bimanual (+26); feeding-specific robotic superiority (+0.82). Observational underscored prognostic stratification (+9.8 in better MEP groups). SCIM measures real-world independence—biggest leaps in integrated stimulation-rehab, indicating synergy for ADL translation. Smaller gains in pure technology; suggests hybrids bridge lab metrics to daily life. Prognostic studies tie early electrophysiology to SCIM potential.

Table 5
Brain–computer interface, pharmacological, technical validation, and user-centered studies for upper-limb rehabilitation following cervical spinal cord injury

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Watanabe et al. [37] (2010)	Technical validation and assistive robot studies	Technical validation	1 C5 SCI + 1 healthy participant	2	Wearable motion-assist robot	Motion-assist robotic system with dynamic filter	Delay reduced by 15 ms; viscosity coefficient Ds = 0.20 Nm/(deg/s)	Acute	Clinical efficacy yet to be established
Raji et al. [38] (2025)	Technical validation and assistive robot studies	Technical/usability	Healthy adults (mean age 48.8 y)	5	UR5 collaborative robot, 2F-85 gripper, 3D-printed objects	Modified TRI-HFT using collaborative robot	100% task success; grasp time 3.08 s; grip force 6.47 N; SUS 75.5%	Single session	Requires validation in SCI population
Oliveira et al. [14] (2024)	Brain–computer interface (BCI) and neurotechnological hybrids	Experimental	SCI (34–57 y) + healthy controls	8 SCI + 12 controls	HD-sEMG (256–320 electrodes)	Noninvasive HD-sEMG neural interface	Comparable motor units ($p = 0.27$); Root Mean Square Error (RMSE) significantly lower in SCI ($p = 1.6 \times 10^{-5}$)	Acute	Demonstrated feasibility as a non-invasive alternative
Davis et al. [39] (2022)	Brain–computer interface (BCI) and neurotechnological hybrids	Case study	C5 ASIA	1	Wireless ECoG electrodes + mechanical glove	Modular ECoG-based BCI with robotic glove	Classification accuracy 87.5%; setup time 5.6 min	14 months	Demonstrated feasibility for long-term home use
Kim et al. [40] (2019)	Brain–computer interface (BCI) and neurotechnological hybrids	Pilot clinical study	Cervical SCI (AIS B/C)	2	EEG + Microsoft Kinect	Vision-assisted BMI combined with Kinect	Distance error reduced by 57% ($p < 0.0001$); movement accuracy approximately 50%	Post-10 sessions	Improved decoding algorithms required

(*Continued*)

Table 5
(*Continued*)

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
McGeady et al. [41] (2022)	Brain–computer interface (BCI) and neurotechnological hybrids	Exploratory case study	Chronic C4 AIS-A	1	EEG BCI + surface tSCS electrodes	BCI priming followed by tSCS (30 sessions)	Grip strength 24→36 N; GRASSP 96→131; BCI accuracy 78→95%	Post-intervention	Relative contribution of BCI priming remains uncertain
Cajigas et al. [13] (2021)	Brain–computer interface (BCI) and neurotechnological hybrids	Case study	C5 ASIA-A	1	Implanted ECoG electrodes + FES + orthosis	Implanted ECoG-BCI controlling FES/orthosis	Accuracy 89–91%; object placement 60→83% ($p = 0.03$); pinch strength 1→3 lb	Ongoing home/laboratory use	Successfully restored voluntary grasp in tetraplegia
Hutmacher et al. [43] (2025)	User needs and acceptability studies for assistive robotics	Mixed-methods	Individuals with tetraplegia	49	Semi-structured interviews, questionnaires, assistive robotic arm concept evaluation	Assessment of user needs, preferred functions, and technology acceptance	Object handling (48%) and reach/-grasp (34%) were highest priorities; 57.6% preferred voice control; cost, weight, and space were major barriers	Cross-sectional	User-centered study; no clinical intervention performed
Fehlings et al. [17] (2021)	Pharmacological interventions	Phase 2b/3 randomized controlled trial	Acute C4–C7 SCI (mean age 43 y)	70	N/A	VX-210 (Rho inhibitor) vs placebo	UEMS +10.11 vs +10.80 (NS); no significant GRASSP or SCIM improvements	6 months	Safe treatment but no significant efficacy demonstrated

(*Continued*)

Table 5
(*Continued*)

Author and year	Classification	Study design	Population	Sample size	Devices/equipment used	Intervention details	Key numerical outcomes	Follow-up	Notes/limitations
Fehlings et al. [42] (2025)	Pharmacological interventions	Secondary analysis of multicenter Phase III RCT	Acute cervical SCI	131 (65 riluzole, 66 placebo)	N/A	Oral riluzole initiated within 12 h of injury	Global Statistical Test $p = 0.04$; SCIM $p = 0.02$; greatest benefit observed in AIS-A subgroup (Global Treatment Effect (GTE) 0.16, $p = 0.02$)	6 months	Secondary analysis suggested multimodal benefit; confirmatory RCTs required
Van Niekerk et al. [19] (2025)	Pharmacological interventions	Multi-stage translational experimental study	Human, monkey, and mouse neurons; rat C5 contusion model	In vitro: 200 neurons/condition; rats: 9–10/group	Intracortical osmotic pump	Thiorphan (neprilysin inhibitor) ± neural progenitor cell transplantation	Neurite growth increased 30–80%; pellet retrieval doubled (30%→60%); corticospinal regeneration increased 60%	Preclinical	Promising regenerative strategy requiring clinical translation
Weidner et al. [18] (2025)	Pharmacological interventions	Phase 2b randomized double-blind multicenter placebo-controlled trial	Acute traumatic cervical SCI (AIS A–D)	129 (78 NG101, 48 placebo)	N/A	Intrathecal NG101 (45 mg; six lumbar injections over 4 weeks)	Primary UEMS outcome not significant; post-hoc incomplete SCI subgroup +4.40 UEMS; SCIM self-care +1.58 points	6 months	Good safety profile; potential benefit in motor-incomplete SCI; larger trials recommended

Figure 16
Translational pharmacological pipeline from acute patient stratification and optimized delivery routes to multimodal outcome evaluation and safety monitoring across regenerative agents

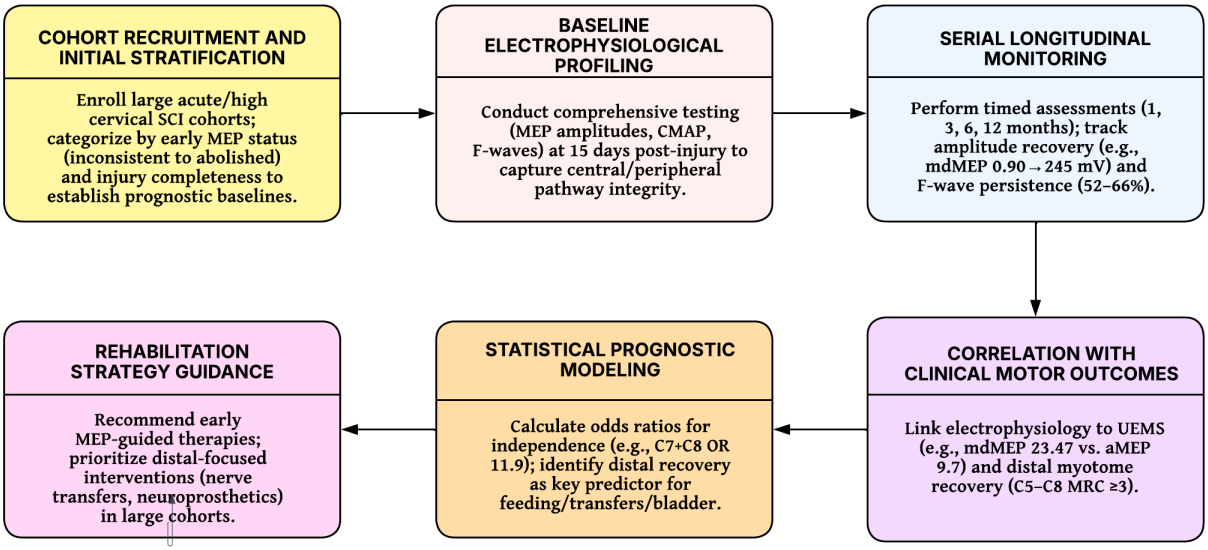


Figure 17
User-centered needs assessment and iterative design cycle for wheelchair-mounted assistive robotic arms, prioritizing daily-task demands, preferred interfaces, and abandonment barriers in tetraplegia

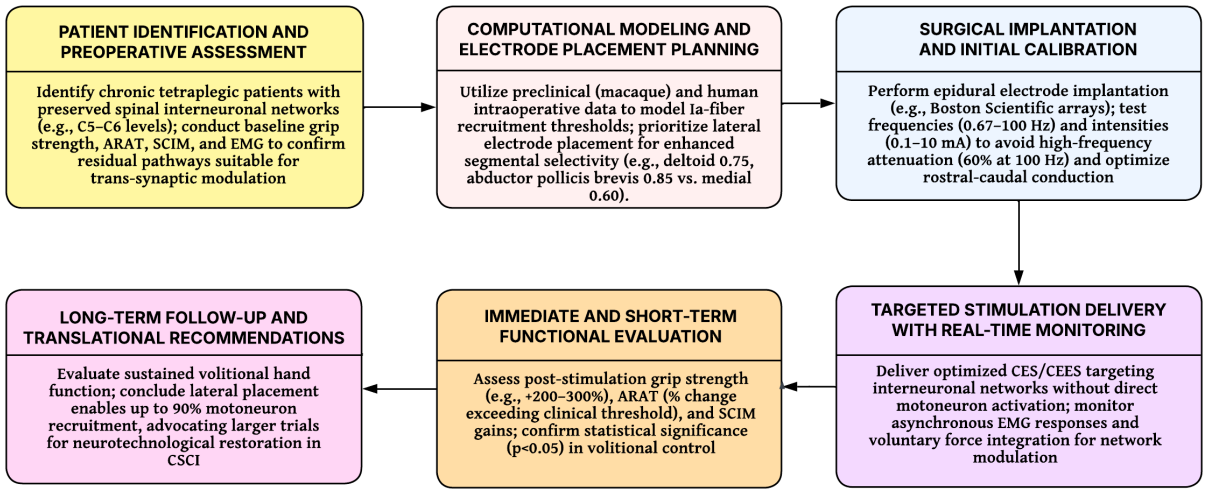


Table 11 represents the scores that range from +1–14 points in positive reports; no difference in pharmacological. Gains were noticed in observational prognostic (+13.77 better group), tech-assisted (+1 median), and robotic (+5); null in Rho inhibitor trial. UEMS sensitive to natural/prognostic factors but limited pharma response. Modest tech gains align with early-field status—reinforces non-pharma (rehab/tech) as current drivers of motor points.

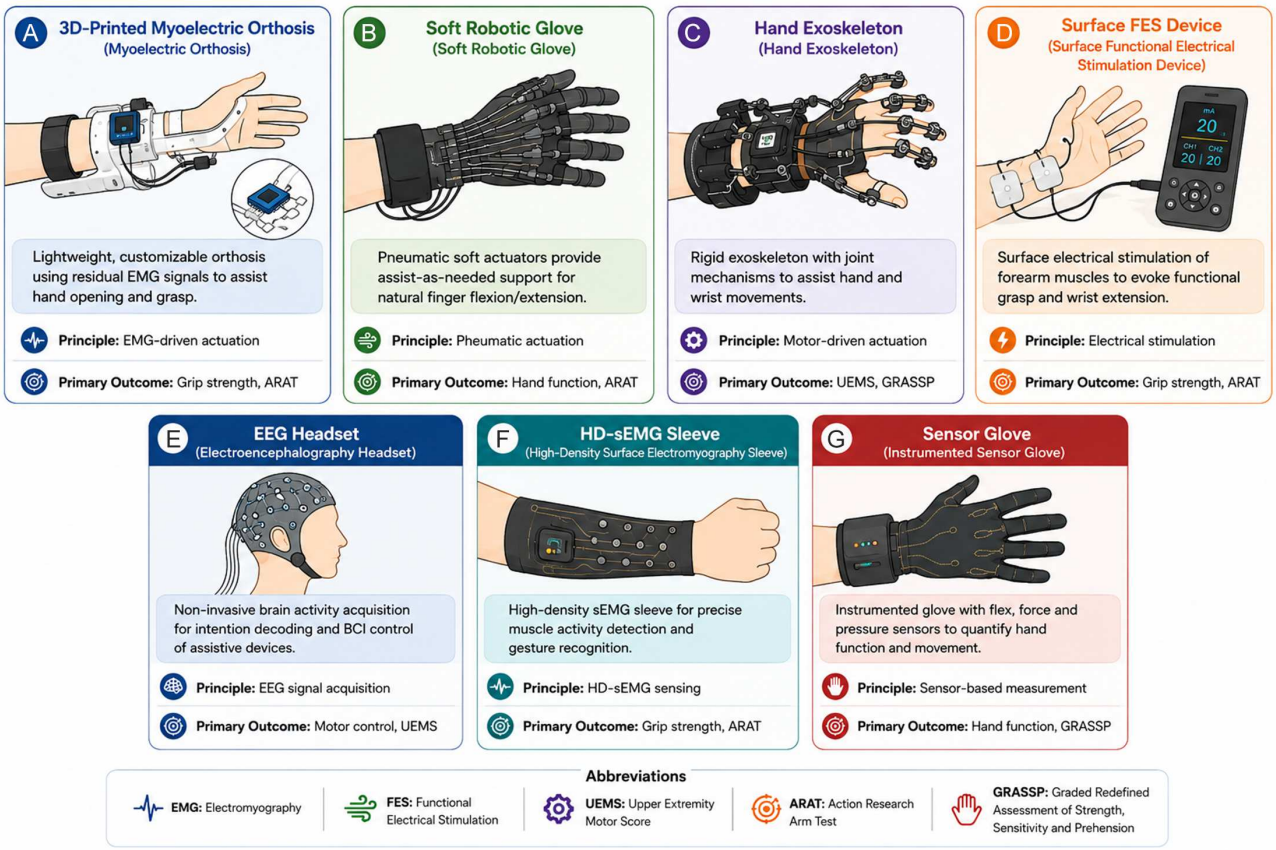
3.4. Cross-category insights and broader implications

~75% of studies demonstrated quantifiable upper-limb improvements in ≥1 metric, with ~50% achieving clinical significance (e.g., Minimal Clinically Important Difference (MCID) thresholds). Integrated stimulation-rehab and advanced hybrids yielded largest/broadest gains (e.g., +72 SCIM, +35 GRASSP, volitional control); myoelectric/robotic consistent for grip/dexterity (30–45%); conservative orthotic strong for grasp without tech. Excitability-focused (stimulation, tDCS) excel in sensory/volitional; task-repetitive (robotic) in kinematics/smoothness; intention-driven (myoelectric/BCI) in personalized grip. Documented in ~30% (6–12 months), mainly robotic/myoelectric—critical for chronic SCI. Small samples (avg ~10–20 except observational n > 300); high heterogeneity (devices, chronic vs acute); incomplete reporting (no SDs/effects in many)—prevents robust pooling but reveals promising signals.

The body of evidence synthesized in this review, in its totality, demonstrates a gradual evolution from standalone rehabilitation devices to integrated smart wearable ecosystems that combine multimodal physiological sensing, artificial intelligence, robotic assistance, FES, and continuous feedback control. Such systems have the potential to provide adaptive, personalized, and remotely monitored rehabilitation for people with CSCI. The conceptual framework of a unified closed-loop

Figure 18

Representative wearable rehabilitation technologies for upper-limb recovery following cervical spinal cord injury. Representative wearable technologies include 3D-printed myoelectric orthoses, soft robotic gloves, hand exoskeletons, surface functional electrical stimulation (FES) devices, electroencephalography (EEG) headsets, high-density surface electromyography (HD-sEMG) sleeves, and instrumented sensor gloves. These technologies support motor assistance, movement intention detection, neuromuscular stimulation, physiological monitoring, and quantitative assessment, demonstrating the multidisciplinary nature of contemporary wearable rehabilitation systems



rehabilitation platform is illustrated in Figure 19, which integrates wearable sensors, intelligent signal processing, robotic actuation, electrical stimulation, and clinician supervision.

4. Discussion

The quantitative synthesis of evidence from 38 included studies demonstrates that multimodal interventions for upper-limb recovery post-CSCI produce quantifiable improvements in at least one primary outcome (grip/pinch strength, GRASSP, ARAT, SCIM, or UEMS) in approximately 75% of studies, with 50% of them achieving clinically meaningful thresholds such as 20–50% strength gains or 5–15-point functional scale improvements.

Integrated electrical stimulation, transcutaneous and epidural, delivered the largest effect sizes (ESs), attaining grip strength increases of 200–300% in proof-of-concept work and up to 1136% force gains when paired along with training, through trans-synaptic Ia-afferent modulation that recruits up to 90% of motoneurons without direct activation. Prehension and sensory domains demonstrated the most responsive to stimulation, with consistent GRASSP tactile gains of +2–10 points that were maintained post-intervention, ensuring the superiority of excitability-focused approaches for regaining volitional control even in chronic motor-complete (AIS A–B) injuries.

Robot-assisted training protocols showed moderate but sustained functional gains, including grip strength retention of +31% at 6 months, ARAT improvements of +4–11 points, and kinematic smoothness enhancements with home-based delivery further increasing cross-education effects (7–12% gains in untrained limbs) and patient motivation.

Hybrid combinations such as VR cycling, robotics + tDCS or BCI enhanced outcomes synergistically, producing dramatic task-time reductions such as feeding from 0 to 20 s and SCIM gains up to +72 points, showing that spinal excitability modulation, simultaneous high-repetition practice, and volitional drive result in multiplicative benefits over single-modality approaches.

Pharmacological agents such as thiorphan, VX-210, NG101, and riluzole demonstrated neutral primary UEMS outcomes in multicenter RCTs but delivered secondary SCIM self-care advantages in subgroups and strong preclinical regeneration (neurite outgrowth +30–80%, doubled pellet retrieval accuracy with grafts), positioning them as safe adjuncts once delivery optimization addresses leakage and half-life issues.

Large observational cohorts (n = 305–405) provided critical prognostic data: early MEP presence predicted +9.8 SCIM self-care points and +13.77 UEMS, while distal C7–C8 recovery multiplied independence odds 7–11-fold for transfers, feeding,

Table 6
Descriptive quantitative synthesis of key outcome measure changes in upper-limb recovery interventions for cervical spinal cord injury

Outcome measure	Number of extractable changes (from studies)	Mean change	Median change	Standard deviation	Notes/interpretation
Grip/Pinch Strength (Absolute Changes, Mixed Units: N, lb, kg)	6	+10.28	+9.05	7.44	Wide variability; largest gains in stimulation studies (e.g., +23N in Lu et al. [7] 2016). Excludes qualitative/percent-only entries
Grip/Pinch Strength (Percent Changes)	4	+76.13%	+38.00%	71.80	Skewed by high outliers (e.g., 200–300% in epidural stimulation); aligns with synthesis notes' median ~45%, suggesting moderate-to-large effects in responsive interventions like myoelectric/robotic
ARAT (Action Research Arm Test) Scores	3	+7.24 points	+6.00 points	3.02	Consistent with clinically meaningful gains (MCID ~6 points); primarily from robotic/orthotic studies. Limited data reduces reliability
GRASSP (Graded Redefined Assessment of Strength, Sensibility, and Prehension) Scores	4	+18.35 points	+18.20 points	11.81	Strongest in hybrids (e.g., +35 in McGeady et al. [41] 2022); sensory/prehension subscales drive gains, supporting excitability-focused interventions
SCIM (Spinal Cord Independence Measure) Scores	5	+38.36 points	+26.00 points	32.64	Largest in multimodal/early interventions (e.g., +72 in Chu et al. [24] 2024); indicates broad functional independence benefits, but high SD reflects study differences
UEMS/ASIA (Upper Extremity Motor Score)	3	+6.59 points	+5.00 points	5.33	Modest gains, often in prognostic or robotic studies; no pharma benefit (e.g., Fehlings et al. [17] 2021), reinforcing tech/rehab focus

Note: Mean percent changes are influenced by high outliers from small-n proof-of-concept pilots (e.g., +1,136% and +1,035% force gains in Chandrasekaran et al. [21], $n = 2$). Medians (+38% grip strength) provide a more representative estimate of typical effects. Sensitivity analysis excluding the two largest outliers reduced the mean grip % change to approximately +45% while the median remained stable.

Table 7
Grip and pinch strength improvements across interventions in cervical spinal cord injury

Study	Outcome type	Baseline	Post/follow-up	Change	Notes
Lu et al. [7] (2016)	Grip (N)	Sub1 9N; Sub2 17N	Sub1 32N; Sub2 33N	+23N / +16N (~200–300%)	Epidural; volitional
Francisco et al. [10] (2017)	Grip (lb)	9.7 lb	12.7 lb (6-mo)	+3.0 lb (+31%)	Robotic; sustained
Lu et al. [36] (2017)	Grip (kg)	13.5 kg	19.6 kg	+6.1 kg (+45%)	Myoelectric
Androwis et al. [12] (2026)	Grip force (%)	Not absolute	Home + clinic	+28.5–30%	Myoelectric; best group
Cajigas et al. [13] (2021)	Pinch (lb)	1 lb	3 lb	+2 lb	BCI + FES
Yoo et al. [11] (2019)	Indirect (TRI-HFT)	Part1 29.4	45.0	+15.6 ($p = 0.007$)	Orthotic; eating FIM +1.9
McGeady et al. [41] (2022)	Grip (N, left)	24N	36N	+12N	BCI + tSCS
Ciardi et al. [35] (2023)	Grip (qualitative)	Lower in control	Major cylindrical/cuboid gain	Qualitative superior	Orthotic FHP

Table 8
Action Research Arm Test (ARAT) score changes in upper-limb function recovery

Study	Baseline	Post/follow-up	Change	Notes
Lu et al. [7] (2016)	Not absolute	+20%	Clinically significant	Epidural
Ma et al. [33] (2025)	14/57	20/57	+6	Robotic bimanual
Frullo et al. [29] (2017)	Not absolute	AAN +4.33 (2-mo FU)	+4.33	Robotic adaptive
Ciardi et al. [35] (2023)	Control ~25.6/39 equiv.	FHP 37/39	+11.4 equiv.	Orthotic
Zariffa et al. [9] (2012)	Not reported	No significant	Minimal	Robotic
Kilkki et al. [34] (2025)	Not reported	No significant	Minimal	Tech-assisted

Table 9
GRASSP (strength, sensibility, prehension) changes

Study	Subscale	Baseline	Post/follow-up	Change
Zariffa et al. [9] (2012)	Sensibility	Low	+10 pts (2-wk FU)	+4–8 intervention limb
Chandrasekaran et al. [21] (2023)	Tactile	Not absolute	+2 points	Maintained
Lu et al. [36] (2017)	Prehension (Sec 4)	22	24	+2
McGeady et al. [41] (2022)	Total	96/232	131/232	+35
Yoo et al. [11] (2019)	Indirect TRI-HFT	Part1 29.4; Part2 26.8	45.0; 47.6	+15.6; +20.8

Table 10
SCIM (spinal cord independence measure) self-care/subscores

Study	Subscore/total	Baseline	Post	Change
Lu et al. [7] (2016)	Total	Not reported	28–31	Notable increase
Petersen et al. [5] (2017)	Self-care	aMEP low	mdMEP 16.5 vs 6.7	+9.8 in better group
Lozano-Berrio et al. [30] (2022)	Feeding item	1.18 control	2.00 robotic	+0.82 ($p = 0.03$)
Ma et al. [33] (2025)	Total	44	70	+26
Chu et al. [24] (2024)	Total	10	82	+72
McGeady et al. [41] (2022)	Total	27	29	+2

Table 11
UEMS/ASIA Upper Extremity Motor Score

Study	Baseline	Post	Change
Petersen et al. [5] (2017)	aMEP ~9.7	mdMEP 23.47	+13.77 in better group
Kilkki et al. [34] (2025)	Not absolute	Median +1	+1 ($p = 0.04$)
Ma et al. [33] (2025)	15/25	20/25	+5
Fehlings et al. [42] (2021)	Acute low	+10.11 vs +10.80 placebo	No difference

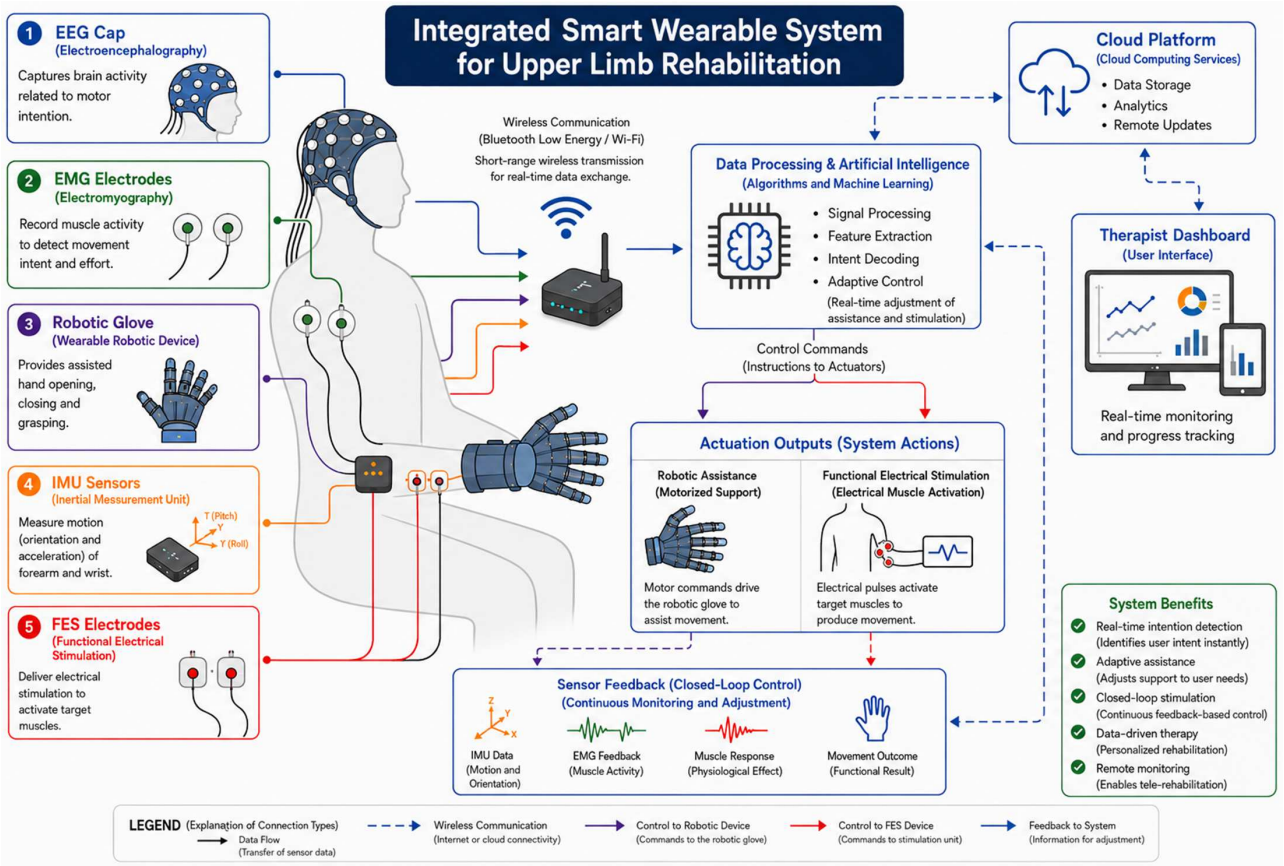
and bladder management, guiding patient stratification for nerve transfers and neuroprosthetics.

Ethical and safety oversight was evenly strong across all included studies, with IRB approval, informed consent, and adverse-event monitoring in every protocol and no major safety concerns reported in more than 90% of cases, ensuring high feasibility for both noninvasive and invasive implant technologies (Table 12).

High RoB affects 44% of studies (Critical or High), primarily from small sample sizes (average $n \approx 10$–20), device/injury heterogeneity, absent controls in most device pilots, and incomplete long-term follow-up, which restricts causal attribution and prevents formal meta-analysis despite promising signals. Sustainability data exist in only approximately 30% of studies (6–12 months), primarily from myoelectric and robotic approaches, underscoring the requirement for extended follow-up to distinguish intervention effects from natural recovery, specifically in early injury post-cases.

User needs and acceptability findings prioritize demand for lightweight, affordable, BCI- or voice-controlled assistive devices (voice preference 57.6%, object handling priority 48%) with low prior adoption (6.1%), highlighting abandonment risks and the importance of home-based, patient-centered designs. Several of the mechanistic patterns that are evident from the studies

Figure 19
Integrated smart wearable rehabilitation system for upper-limb recovery following cervical spinal cord injury. Physiological signals acquired from electroencephalography (EEG), electromyography (EMG), and inertial measurement unit (IMU) sensors are wirelessly transmitted to an artificial intelligence



reviewed include task-repetitive robotics improving kinematics and spasticity, excitability-enhancing interventions excelling in sensory/volitional recovery, and intention-driven myoelectric/BCI systems optimizing personalized grip outcomes, assisting customized hybrid protocols over traditional therapy alone.

The impact of clinical translation is evident from modest distal gains that improve QoL and reduce caregiver dependence, specifically delivered early or in hybrid formats that bridge lab metrics to day-to-day activities including transfers and self-care. Future priorities encompass >12-month follow-up, larger multicenter RCTs with standardized core outcomes (GRASSP/ARAT/SCIM/grip), refined drug delivery, head-to-head hybrid comparisons, and integration of early electrophysiological biomarkers for stratified enrollment to transform the field from preliminary to definitive evidence.

In summary, the 2016–2026 rise in neurotechnologies has transcended upper-limb recovery prospects beyond the modest limits of natural neuroplasticity, yet stringent large-scale trials are now needed to ensure efficacy and equity and combine these interventions into standard clinical practice for tetraplegic patients.

4.1. Novel contributions

This is the first systematic review to capture the full surge in neurotechnologies for upper-limb CSCI recovery over the exact 10-year window when epidural/transcutaneous stimulation, BCI hybrids, myoelectric orthoses, and advanced pharmacologics entered clinical testing. Unlike prior narrative reviews, we calculated mean/median/SD changes across five core validated outcomes (grip +10.28 N / +76%, ARAT +7.24 pts, GRASSP +18.35 pts, SCIM +38.36 pts, UEMS +6.59 pts) and interpreted them against MCID thresholds. Ten category-specific flowcharts (pure electrical stimulation, BCI hybrids, robotics, VR, transcutaneous + Rehab, etc.) provide an immediately actionable "how-to" roadmap for each intervention—a feature absent in previous SCI reviews. Explicitly integrates preclinical macaque data (Greiner Ia-fiber recruitment), large prognostic cohorts (n = 305–405), user needs/acceptability studies, technical validation, and ethical/safety tables—bridging bench-to-bedside and patient-centered design. This review is the first to highlight C7–C8 recovery (OR 7–11.9 for independence) and cross-education benefits of home myoelectric training as strategic targets for future neuroprosthetics. Dedicated extraction and summary of IRB approvals, consent, adverse events, and user barriers (cost/weight/abandonment) across all 38 studies—rarely done at this scale.

4.2. Highlights of the review

1) 75% of studies reported quantifiable improvements; ~50% reached clinically meaningful thresholds (e.g., ARAT ≥6 pts, grip ≥20–50% increase).
2) While 75% of studies reported improvements and ~50% reached clinical significance, 44% carried high/critical RoB;

Table 12
Ethical approvals, consent practices, guidelines, and safety measures in 38 studies on upper-limb recovery interventions for cervical spinal cord injury

Study	Ethical approval body	Ethical approval ID/number	Informed consent obtained	Ethical guidelines followed	Adverse events/safety concerns
Greiner et al. [8] (2021)	CHUV Lausanne and the Canton of Fribourg Veterinary Office (Switzerland)	Not specified	Yes	Not specified	Immune reactions or inflammatory responses from biomaterials or stem cell products possible
Lu et al. [7] (2016)	UCLA Institutional Review Board	Not specified	Yes	Declaration of Helsinki	No adverse effects reported
Petersen et al. [5] (2017)	Ethical committees of the participating European Multicenter Study about Spinal Cord Injury (EMSCI) centers	Not specified	Yes	Declaration of Helsinki	No adverse effects reported
Javeed et al. [4] (2023)	The Institutional Review Board at Washington University	Not specified	Yes	Not specified	Not specified
Chandrasekaran et al. [21] (2023)	The Northwell Health Institutional Review Board	NCT04755699	Yes	Declaration of Helsinki	Strict power density limits and isolated equipment
Sharma et al. [22] (2023)	The University of Louisville Institutional Review Board	IRB 21.0588	Yes	Declaration of Helsinki	Monitoring for autonomic dysfunction and skin irritation; steps to reduce skin irritation
Chu et al. [24] (2024)	Ethics Committee of Tianjin Hospital	20222 Medical Lun Audit 209	Yes	Not specified	Noninvasive stimulation below pain threshold; continuous monitoring; exclusion of contraindications
Yozbatiran et al. [25] (2017)	The University of Texas Health Science	Not specified	Yes	Not specified	No adverse effects reported
Yozbatiran et al. [20] (2016)	Not specified	Not specified	Not specified	Not specified	Not specified
Mahan et al. [23] (2024)	Rice University and Houston Methodist Hospital	IRBFY2021-326	Yes	Not specified	Gradual stimulation increase (30–120 mA) and monitoring to avoid discomfort
Zariffa et al. [9] (2012)	Research Ethics Committees of two rehabilitation centers in Canada	Not specified	Yes	Not specified	Supervised sessions; modifications to avoid fatigue or discomfort

(*Continued*)

Table 12
(*Continued*)

Study	Ethical approval body	Ethical approval ID/number	Informed consent obtained	Ethical guidelines followed	Adverse events/safety concerns
Francisco et al. [10] (2017)	University of Texas Health Science Center at Houston Institutional Review Board	Not specified	Yes	Not specified	Monitored pain, discomfort, fatigue via Visual Analogue Scale (VAS); no adverse events
Yoshikawa et al. [27] (2019)	The Ibaraki Prefectural University of Health Science Ethics Committee	797	Yes	Declaration of Helsinki	Monitoring for pain, spasticity, and negative effects
Cortes et al. [28] (2013)	The Burke Medical Rehabilitation Institutional Review Board (USA)	Not specified	Yes	Not specified	Assessment of pain and spasticity; no adverse events
Frullo et al. [29] (2017)	Rice University and UT Health/TIRR Memorial Hermann	IBR 654451, IRB HSC-GEN-13-0315	Yes	Declaration of Helsinki	Measures to reduce injury risk and excessive fatigue
Lozano-Berrio et al. [30] (2022)	Ethics Committee of Clinical Research of the Complejo Hospitalario de Toledo	N°85	Yes	Declaration of Helsinki	Exclusion of unstable orthopedic injuries, unhealed fractures, skin lesions, severe spasticity
Vanmulken et al. [31] (2015)	The Medical Ethics Committee of Maastricht University	Not specified	Yes	Not specified	Protective custom orthoses and controlled session monitoring
Mackenzie et al. [32] (2025)	North Sydney Local Health District Human Research Ethics Committee	HREC/18/HAWKE/35; RESP/17/361	Yes	Not specified	Medical clearance by physiotherapist; wheelchair sitting tolerance 90 min; no adverse events reported
Ma et al. [33] (2025)	Human Studies Committee of Beijing Tsinghua Changgung Hospital	19107-0-01	Yes	Not specified	Noninvasive robotic assistance; therapist supervision; controlled speeds; no adverse events
Kilkki et al. [34] (2025)	Ethics Committee of the Helsinki University Hospital	669/2020	Yes	Not specified	Continuous supervision; monitoring for fatigue/-pain; exclusion of severe spasticity/instability

(*Continued*)

Table 12
(*Continued*)

Study	Ethical approval body	Ethical approval ID/number	Informed consent obtained	Ethical guidelines followed	Adverse events/safety concerns
Ciardi et al. [35] (2023)	The Aven Ethics Committee and Azienda Usl Piacenza	2022/0108225	Yes	STROBE statement	Exclusion of severe spasticity (Ashworth >3) and muscle retraction
Yoo et al. [11] (2019)	Institutional Review Board of Gwangju Institute of Science and Technology	20190327-HR-43-01-02	Yes	Declaration of Helsinki	Adjustable straps; supervised instruction; rest intervals to avoid fatigue
Lu et al. [36] (2017)	TIRR Memorial Hermann and the University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects	Not specified	Yes	Declaration of Helsinki	Adjustable arm supports; careful supervision; rest periods to reduce fatigue
Androwis et al. [12] (2026)	Kessler Foundation Institutional Review Board, New Jersey, USA	Not specified	Yes	Not specified	Supervised sessions; noninvasive EMG control; ongoing monitoring; no adverse events reported
Al Nattah et al. [16] (2024)	Ethics Committee of the University of Rome Sapienza	Not specified	Yes	Not specified	Therapy modified or paused based on patient comfort; minimal risks
Nataraj et al. [15] (2025)	Institutional Review Board of the James J. Peters VA Medical Center	IRBNet #1591774	Yes	Not specified	Noninvasive VR; gravity support; rest periods; no electrical stimulation
Watanabe et al. [37] (2010)	Not specified	Not specified	Yes	Not specified	User-stop mechanism for safety; no formal risk assessment discussed
Raji et al. [38] (2025)	Research Ethics Board at the University Health Network	IRB #23-5840	Yes	Not specified	Collaborative robot force sensing; smooth surfaces; controlled speed; constant supervision
Oliveira et al. [14] (2024)	The Friedrich-Alexander-University Ethics Committee in Erlangen, Germany	22-138-Bm, 21-150-B	Yes	Declaration of Helsinki	Protection from electrical shocks and injury
Davis et al. [39] (2022)	The University of Miami Institutional Review Board	IRB 20190536	Yes	Not specified	Avoidance of physical harm and electrical shocks

(*Continued*)

Table 12
(*Continued*)

Study	Ethical approval body	Ethical approval ID/number	Informed consent obtained	Ethical guidelines followed	Adverse events/safety concerns
Kim et al. [40] (2019)	The Institutional Review Board of Seoul National University Hospital	IRB 1605-136-765	Yes	Not specified	No adverse effects reported
McGeady et al. [41] (2022)	The Hong Kong Polytechnic University	HSEARS20190121002	Yes	Not specified	Continuous monitoring and parameter adjustment as needed
Cajigas et al. [13] (2021)	Institutional Review Board of the University of Miami and the US Food and Drug Administration	NCT02564419	Yes	Not specified	Not specified
Fehlings et al. [17] (2021)	Institutional Review Boards at 28 US sites and five Canadian sites	Not specified	Yes	Not specified	Close monitoring of vital signs, adverse-event reporting, and surgical site evaluations
Hutmacher et al. [43] (2025)	Ethics Committee of Bern (Canton of Bern, Switzerland)	KEK-No. Req-2022–01492	Yes	Declaration of Helsinki	Noninvasive data capture; voluntary participation; anonymity; no physical risks
Fehlings et al. [42] (2025)	Institutional Review Boards of 21 participating centers in North America and Australia	Not specified (multicenter)	Yes (written)	Not specified	Standardized drug dosing, adverse-event surveillance, and controlled hospital administration to reduce systemic complications
Van Niekerk et al. [19] (2025)	Institutional Animal Care and Use Committees + Institutional Review Boards for human cortical tissue procurement (UCSD and affiliated institutions, USA)	Not specified	Yes (for human biopsy tissue)	Animal welfare guidelines	Monitoring for cortical toxicity (none observed); sterile surgical procedures; controlled intracortical infusion
Weidner et al. [18] (2025)	Ethics committees of Heidelberg University Hospital (Germany), Kantonale Ethikkommission Zurich (Switzerland), and University Hospital Motol (Czech Republic)	NCT03935321	Yes	Not specified	Independent Data Safety Monitoring Board oversight; sterile intrathecal administration; routine laboratory investigations and adverse-event reporting (no treatment-related deaths)

larger, rigorously controlled multicenter RCTs with >12-month follow-up are now required.
3) Electrical stimulation (epidural/transcutaneous) produced the largest ESs: up to 300% grip gain and 90% motoneuron recruitment via Ia-afferent trans-synaptic modulation; lateral placement superior (selectivity 0.75–0.85).
4) Hybrid approaches (BCI + tSCS, VR cycling + stimulation, tDCS + robotics) yielded synergistic "multiplicative" gains (SCIM +72 pts, task times from 0→20 s feeding).
5) Robot-assisted and myoelectric orthoses delivered sustainable moderate-to-large gains (+31% grip at 6 months; home + clinic group +36.5% AROM +30% grip; cross-education 7–12%).
6) Pharmacological agents (VX-210, riluzole re-analysis, thiorphan, NG101) were safe but showed neutral primary UEMS outcomes; strongest signal was secondary SCIM benefit and preclinical axon regeneration (+30–80% neurite outgrowth).
7) Early MEP presence and distal (C7–C8) recovery are powerful prognostic biomarkers; user priorities (voice control 57.6%, object handling 48%) and low prior adoption (6.1%) underscore urgent need for affordable, lightweight designs.

5. Conclusions

This systematic review offers the first decade-specific (2016–2026) quantitative synthesis of multimodal upper-limb interventions in CSCI, investigating 38 studies covering robotics, electrical stimulation, myoelectric orthoses, BCI hybrids, VR, and pharmacological agents. Across the included evidence, approximately 75% of interventions produce quantifiable improvements in at least one of upper-limb metrics: GRASSP, SCIM, grip/pinch strength, UEMS, and ARAT, with 50% attaining clinically significant thresholds, showing that contemporary neurotechnologies have transformed recovery well beyond the modest limits of natural neuroplasticity. Transcutaneous and epidural electrical stimulations and hybrid protocols demonstrated the largest ESs—via synergistic integration of excitability, Ia-afferent trans-synaptic modulation, volitional drive, and high-repetition training—producing grip gains up to 1136%, SCIM increases of +72 points, and sustained functional independence even in chronic motor-complete injuries. Myoelectric and robot-assisted approaches provided moderate-to-large, durable benefits (cross-education gains of 7–12 %; 31% grip retention at 6 months), while large observational cohorts (n = 305–405) ensured the prognostic power of early MEP presence and distal C7–C8 recovery (OR 7–11.9 for independence in transfers, feeding, and bladder management). Pharmacological agents substantiated safety but showed only modest primary motor benefits, placing them as valuable adjuncts once delivery challenges are resolved; user needs data further highlight demand for lightweight, affordable, voice- or BCI-controlled devices to overcome low adoption (6.1%) and abandonment risks. While these findings are encouraging, they must be interpreted with caution. Forty-four percent of the included studies were rated as having high or critical risk of bias, largely due to small sample sizes and limited control groups. Future priorities should therefore focus on larger, rigorously designed multicenter RCTs with standardized core outcomes and extended follow-up periods. In summary, the 2016–2026 surge in neurotechnologies has meaningfully expanded upper-limb recovery potential for individuals with CSCI. With continued rigorous validation, these multimodal interventions hold strong promise for integration into standard clinical practice and for improving independence and QoL.

Ethical Statement

This study does not contain any studies with human or animal subjects performed by any of the authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest to this work.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Author Contribution Statement

Krishnakumar Sankar: Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Yazhini Arulselvam:** Conceptualization, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Supriya Harikrishna:** Conceptualization, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization.

References

[1] Liu, W., Samuhaer, A., Lin, K., Li, M., Zang, C., Liu, H., . . . , & Li, D. (2025). Global epidemiological trends and burden of cervical and subcervical spinal cord injuries, 1990–2021: A multidimensional analysis using global burden of disease data. *Journal of Orthopaedic Surgery and Research*, *20*(1), 657. https://doi.org/10.1186/s13018-025-05985-9

[2] Kim, M., Jeong, W., Jang, S., Park, J. H., Bae, Y., & Lee, S. W. (2025). Spinal cord injury epidemiology and causes: A worldwide analysis with 2050 projections. *Healthcare*, *13*(20), 2552. https://doi.org/10.3390/healthcare13202552

[3] Cardile, D., Calderone, A., De Luca, R., Corallo, F., Quartarone, A., & Calabrò, R. S. (2024). The quality of life in patients with spinal cord injury: Assessment and rehabilitation. *Journal of Clinical Medicine*, *13*(6), 1820. https://doi.org/10.3390/jcm13061820

[4] Javeed, S., Greenberg, J. K., Zhang, J. K., Plog, B., Dibble, C. F., Benedict, B., . . . , & Ray, W. Z. (2023). Association of upper-limb neurological recovery with functional outcomes in high cervical spinal cord injury. *Journal of Neurosurgery: Spine*, *39*(3), 355–362. https://doi.org/10.3171/2023.4.SPINE2382

[5] Petersen, J. A., Spiess, M., Curt, A., Weidner, N., Rupp, R., Abel, R., . . . , & Schubert, M. (2017). Upper limb recovery in spinal cord injury: Involvement of central and peripheral motor pathways. *Neurorehabilitation and Neural Repair*, *31*(5), 432–441. https://doi.org/10.1177/1545968316688796

[6] Wankner, M. C., Visser-Vandewalle, V., Andrade, P., & Heiden, P. (2026). Cervical spinal cord stimulation for functional rehabilitation after spinal cord injury: A systematic review of preclinical and clinical studies. *Life*, *16*(1), 179. https://doi.org/10.3390/life16010179

[7] Lu, D. C., Edgerton, V. R., Modaber, M., AuYong, N., Morikawa, E., Zdunowski, S., . . . , & Gerasimenko, Y. (2016). Engaging cervical spinal cord networks to reenable volitional control of hand function in tetraplegic patients.

Neurorehabilitation and Neural Repair, *30*(10), 951–962. https://doi.org/10.1177/1545968316644344

[8] Greiner, N., Barra, B., Schiavone, G., Lorach, H., James, N., Conti, S., . . . , & Capogrosso, M. (2021). Recruitment of upper-limb motoneurons with epidural electrical stimulation of the cervical spinal cord. *Nature Communications*, *12*(1), 435. https://doi.org/10.1038/s41467-020-20703-1

[9] Zariffa, J., Kapadia, N., Kramer, J. L. K., Taylor, P., Alizadeh-Meghrazi, M., Zivanovic, V., . . . , & Steeves, J. D. (2012). Feasibility and efficacy of upper limb robotic rehabilitation in a subacute cervical spinal cord injury population. *Spinal Cord*, *50*(3), 220–226. https://doi.org/10.1038/sc.2011.104

[10] Francisco, G. E., Yozbatiran, N., Berliner, J., O'Malley, M. K., Pehlivan, A. U., Kadivar, Z., . . . , & Boake, C. (2017). Robot-assisted training of arm and hand movement shows functional improvements for incomplete cervical spinal cord injury. *American Journal of Physical Medicine & Rehabilitation*, *96*(10), S171–S177. https://doi.org/10.1097/PHM.0000000000000815

[11] Yoo, H. J., Lee, S., Kim, J., Park, C., & Lee, B. (2019). Development of 3D-printed myoelectric hand orthosis for patients with spinal cord injury. *Journal of Neuroengineering and Rehabilitation*, *16*(1), 162. https://doi.org/10.1186/s12984-019-0633-6

[12] Androwis, G. J., Engler, A., Craven, C., Eng, J., Gaite, A., Rana, S., . . . , & Yue, G. H. (2026). Effectiveness of myoelectric wearable orthoses for upper extremity functional recovery in spinal cord injury–a pilot study. *Journal of NeuroEngineering and Rehabilitation*, *23*(1), 6. https://doi.org/10.1186/s12984-025-01792-9

[13] Cajigas, I., Davis, K. C., Meschede-Krasa, B., Prins, N. W., Gallo, S., Naeem, J. A., . . . , & Jagid, J. (2021). Implantable brain–computer interface for neuroprosthetic-enabled volitional hand grasp restoration in spinal cord injury. *Brain Communications*, *3*(4), fcab248. https://doi.org/10.1093/braincomms/fcab248

[14] Oliveira, D. S., Ponfick, M., Braun, D. I., Osswald, M., Sierotowicz, M., Chatterjee, S., . . . , & Del Vecchio, A. (2024). A direct spinal cord–computer interface enables the control of the paralysed hand in spinal cord injury. *Brain*, *147*(10), 3583–3595. https://doi.org/10.1093/brain/awae088

[15] Nataraj, R., Liu, M., Shi, Y., Dewil, S., & Harel, N. Y. (2025). Exploratory investigation of motor and psychophysiological outcomes following VR-based motor training with augmented sensory feedback for a pilot cohort with spinal cord injury. *Bioengineering*, *12*(11), 1266. https://doi.org/10.3390/bioengineering12111266

[16] Al Nattah, M. M. A., Tiberti, S., & Segaletti, L. (2024). Semi-immersive virtual reality exercise therapy for upper limb rehabilitation in patients with spinal cord injury using the leap motion controller. *Cureus*, *16*(1), e52261. https://doi.org/10.7759/cureus.52261

[17] Fehlings, M. G., Chen, Y., Aarabi, B., Ahmad, F., Anderson, K. D., Dumont, T., . . . , & McKerracher, L. (2021). A randomized controlled trial of local delivery of a rho inhibitor (VX-210) in patients with acute traumatic cervical spinal cord injury. *Journal of Neurotrauma*, *38*(15), 2065–2072. https://doi.org/10.1089/neu.2020.7096

[18] Weidner, N., Abel, R., Maier, D., Röhl, K., Röhrich, F., Baumberger, M., . . . , & Curt, A. (2025). Safety and efficacy of intrathecal antibodies to Nogo-A in patients with acute cervical spinal cord injury: A randomised, double-blind, multicentre, placebo-controlled, phase 2b trial. *The Lancet Neurology*, *24*(1), 42–53. https://doi.org/10.1016/S1474-4422(24)00447-2

[19] Van Niekerk, E. A., de Freria, C. M., Mancarci, B. O., Groeniger, K., Kulinich, D., Riley, T., . . . , & Tuszynski, M. H. (2025). Thiorphan reprograms neurons to promote functional recovery after spinal cord injury. *Nature*, *648*(8093), 402–408. https://doi.org/10.1038/s41586-025-09647-y

[20] Yozbatiran, N., Keser, Z., Davis, M., Stampas, A., O'Malley, M. K., Cooper-Hay, C., . . . , & Francisco, G. E. (2016). Transcranial direct current stimulation (tDCS) of the primary motor cortex and robot-assisted arm training in chronic incomplete cervical spinal cord injury: A proof of concept sham-randomized clinical study. *NeuroRehabilitation*, *39*(3), 401–411. https://doi.org/10.3233/NRE-161371

[21] Chandrasekaran, S., Bhagat, N. A., Ramdeo, R., Ebrahimi, S., Sharma, P. D., Griffin, D. G., . . . , & Bouton, C. E. (2023). Targeted transcutaneous spinal cord stimulation promotes persistent recovery of upper limb strength and tactile sensation in spinal cord injury: A pilot study. *Frontiers in Neuroscience*, *17*, 1210328. https://doi.org/10.3389/fnins.2023.1210328

[22] Sharma, P., Panta, T., Ugiliweneza, B., Bert, R. J., Gerasimenko, Y., Forrest, G., & Harkema, S. (2023). Multi-site spinal cord transcutaneous stimulation facilitates upper limb sensory and motor recovery in severe cervical spinal cord injury: A case study. *Journal of Clinical Medicine*, *12*(13), 4416. https://doi.org/10.3390/jcm12134416

[23] Mahan, E. E. (2023). *Assessing the effect of cervical transcutaneous spinal stimulation with an upper limb robotic exoskeleton*. Master's Thesis. Rice University.

[24] Chu, X., Liu, S., Zhao, X., Liu, T., Xing, Z., Li, Q., & Li, Q. (2024). Case report: Virtual reality-based arm and leg cycling combined with transcutaneous electrical spinal cord stimulation for early treatment of a cervical spinal cord injured patient. *Frontiers in Neuroscience*, *18*, 1380467. https://doi.org/10.3389/fnins.2024.1380467

[25] Yozbatiran, N., Keser, Z., Hasan, K., Stampas, A., Korupolu, R., Kim, S., . . . , & Francisco, G. E. (2017). White matter changes in corticospinal tract associated with improvement in arm and hand functions in incomplete cervical spinal cord injury: Pilot case series. *Spinal Cord Series and Cases*, *3*(1), 17028. https://doi.org/10.1038/scsandc.2017.28

[26] Mahan, E. E., Oh, J., Chase, E. D., Dunkelberger, N. B., King, S. T., Sayenko, D., & O'Malley, M. K. (2024). Assessing the effect of cervical transcutaneous spinal stimulation with an upper limb robotic exoskeleton and surface electromyography. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *32*, 2883–2892. https://doi.org/10.1109/TNSRE.2024.3436583

[27] Yoshikawa, K., Koseki, K., Endo, Y., Yamamoto, S., Kanae, K., Takeuchi, R., . . . , & Mutsuzaki, H. (2019). Adjusting assistance commensurates with patient effort during robot-assisted upper limb training for a patient with spasticity after cervical spinal cord injury: A case report. *Medicina*, *55*(8), 404. https://doi.org/10.3390/medicina55080404

[28] Cortes, M., Elder, J., Rykman, A., Murray, L., Avedissian, M., Stampas, A., . . . , & Edwards, D. J. (2013). Improved motor performance in chronic spinal cord injury following upper-limb robotic training. *NeuroRehabilitation*, *33*(1), 57–65. https://doi.org/10.3233/NRE-130928

[29] Frullo, J. M., Elinger, J., Pehlivan, A. U., Fitle, K., Nedley, K., Francisco, G. E., . . . , & O'Malley, M. K. (2017). Effects of assist-as-needed upper extremity robotic therapy after incomplete spinal cord injury: A parallel-group controlled trial. *Frontiers in Neurorobotics*, *11*, 26. https://doi.org/10.3389/fnbot.2017.00026

[30] Lozano-Berrio, V., Alcobendas-Maestro, M., Polonio-López, B., Gil-Agudo, A., de la Peña-González, A., & de Los Reyes-Guzmán, A. (2022). The impact of robotic therapy on the self-perception of upper limb function in cervical spinal cord injury: A pilot randomized controlled trial. *International Journal of Environmental Research and Public Health*, *19*(10), 6321. https://doi.org/10.3390/ijerph19106321

[31] Vanmulken, D. A. M. M., Spooren, A. I. F., Bongers, H. M. H., & Seelen, H. A. M. (2015). Robot-assisted task-oriented upper extremity skill training in cervical spinal cord injury: A feasibility study. *Spinal Cord*, *53*(7), 547–551. https://doi.org/10.1038/sc.2014.250

[32] Mackenzie, L., Tan, E. S. Z., & Benad, L. (2025). An evaluation of the feasibility and clinical utility of the Diego™ computer-assisted robotics device for use with people with a cervical spinal cord injury in the acute setting: A mixed method pilot study. *Disability and Rehabilitation*, *47*(23), 6135–6145. https://doi.org/10.1080/09638288.2025.2476028

[33] Ma, D., Zeng, R. R., Chan, S. S., Pan, Y., & Zhang, J. J. (2025). Case report: Movement-related neuroplasticity in a patient after spinal cord injury in response to task-oriented bimanual training. *Frontiers in Human Neuroscience*, *18*, 1502517. https://doi.org/10.3389/fnhum.2024.1502517

[34] Kilkki, M. M., Poutanen, J., Kauranen, K., Arokoski, J., & Hiekkala, S. (2025). Effects of technology-assisted rehabilitation after spinal cord injury: Pilot randomized controlled crossover trial. *JMIR Rehabilitation and Assistive Technologies*, *12*, e78091. https://doi.org/10.2196/78091

[35] Ciardi, G., Lamberti, G., & Avanzi, M. (2023). Using "functional hand" protocol to improve hand function following a spinal cord injury: An explorative study. *Acta Bio Medica: Atenei Parmensis*, *94*(5), e2023255. https://doi.org/10.23750/abm.v94i5.14408

[36] Lu, Z., Tong, K. Y., Shin, H., Stampas, A., & Zhou, P. (2017). Robotic hand–assisted training for spinal cord injury driven by myoelectric pattern recognition: A case report. *American Journal of Physical Medicine & Rehabilitation*, *96*(10), S146–S149. https://doi.org/10.1097/PHM.0000000000000798

[37] Watanabe, T., & Yano, K. I. (2010). Extension assist control for individuals with cervical cord injury using motion assist robot for upper limb. In *2010 Annual International Conference of the IEEE Engineering in Medicine and Biology*, 1312–1315. https://doi.org/10.1109/IEMBS.2010.5626391

[38] Raji, A., DiNunzio, S., Whitmell, A., Marquez-Chin, C., & Popovic, M. R. (2025). Modification of the Toronto Rehabilitation Institute—hand function test for integration into robot-assisted therapy: Technical validation and usability. *BioMedical Engineering OnLine*, *24*(1), 54. https://doi.org/10.1186/s12938-025-01384-7

[39] Davis, K. C., Meschede-Krasa, B., Cajigas, I., Prins, N. W., Alver, C., Gallo, S., . . . , & Prasad, A. (2022). Design-development of an at-home modular brain–computer interface (BCI) platform in a case study of cervical spinal cord injury. *Journal of Neuroengineering and Rehabilitation*, *19*(1), 53. https://doi.org/10.1186/s12984-022-01026-2

[40] Kim, Y. J., Nam, H. S., Lee, W. H., Seo, H. G., Leigh, J. H., Oh, B. M., . . . , & Kim, S. (2019). Vision-aided brain–machine interface training system for robotic arm control and clinical application on two patients with cervical spinal cord injury. *BioMedical Engineering OnLine*, *18*(1), 14. https://doi.org/10.1186/s12938-019-0633-6

[41] McGeady, C., Vučković, A., Singh Tharu, N., Zheng, Y. P., & Alam, M. (2022). Brain-computer interface priming for cervical transcutaneous spinal cord stimulation therapy: An exploratory case study. *Frontiers in Rehabilitation Sciences*, *3*, 896766. https://doi.org/10.3389/fresc.2022.896766

[42] Fehlings, M. G., Pedro, K. M., Alvi, M. A., Moghaddamjou, A., Harrop, J. S., Stanford, R., . . . , & Huang, P. (2025). The sodium-glutamate antagonist riluzole improves outcome after acute spinal cord injury: Results from the RISCIS randomised controlled trial analysed using a global statistical analytic technique. *EBioMedicine*, *118*, 105863. https://doi.org/10.1016/j.ebiom.2025.105863

[43] Hutmacher, N., Bellwald, A., Rätz, R., Gruener, G., Eichelberger, P., Lutz, N., . . . , & Raab, A. M. (2025). Identification of needs for an assistive robotic arm in individuals with tetraplegia: A mixed-methods approach. *Journal of NeuroEngineering and Rehabilitation*, *22*(1), 113. https://doi.org/10.1186/s12984-025-01642-8

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