EFFECTIVENESS OF CORTICOSPINAL ACTIVATION PROTOCOL ON CENTRAL PATTERN GENERATOR OF LOCOMOTION IN INDIVIDUALS WITH INCOMPLETE SPINAL CORD INJURY

Kaur S[1*], Arumugam N[1], Chhabra HS[2]
1Department of Physiotherapy, Punjabi University, Patiala, Punjab, India
2Sri Balaji Action Spine Medical Institute, New Delhi, India
*Corresponding author

ABSTRACT
Background: Incomplete spinal cord injury (SCI) disrupts the functional coupling between descending corticospinal inputs and spinal central pattern generator (CPG) circuits that underlie rhythmic locomotor output. The Corticospinal Activation Protocol (CAP) is a seven-domain, multimodal rehabilitation intervention designed to re-couple corticospinal drive with CPG activity in order to restore locomotion after incomplete SCI.
Objective: To evaluate the effectiveness of the CAP, delivered in conjunction with conventional physiotherapy, on CPG-linked neurophysiological and functional locomotor outcomes in individuals with incomplete SCI, relative to conventional physiotherapy alone.
Methods: In this randomised controlled trial (CTRI/2023/02/049536), 56 individuals with traumatic or non-traumatic incomplete SCI (AIS grade B-D) were randomised, stratified by AIS grade, to an experimental group (Group A, n=28; CAP plus conventional physiotherapy) or a control group (Group B, n=28; conventional physiotherapy alone) for 20 sessions over four weeks. Motor Evoked Potentials (MEPs), Somatosensory Evoked Potentials (SEPs), ASIA Impairment Scale (AIS) motor and sensory scores, Walking Index for Spinal Cord Injury-II (WISCI-II), Spinal Cord Independence Measure-III (SCIM-III), and General and Sacral Autonomic Function (ISAFSCI) were assessed at baseline (Day 0), mid-intervention (Day 15), and post-intervention (Day 30). Within-group change was analysed using one-way repeated-measures ANOVA and between-group differences using independent-samples t-tests ($p \leq 0.05$).
Results: Group A showed statistically significant within-group improvement across all outcome measures from Day 0 to Day 30 ($p \leq 0.05$). At post-intervention, Group A demonstrated significantly greater improvement than Group B in WISCI-II (12.69±4.09 vs 6.39±4.37, p=0.001), SCIM-III (76.11±13.10 vs 58.64±18.13, p=0.001), ASIA lower-limb motor score (22.54±10.93 vs 11.25±9.42, p=0.001), ASIA light touch and pin-prick scores (p=0.001), General and Sacral Autonomic Function (p=0.001), MEP latency of tibialis anterior (41.53±7.04 vs 39.58±7.40 ms), and SEP P37 latency (44.08±3.64 vs 45.73±3.38 ms, p=0.043). ASIA upper-limb motor score did not differ significantly between groups at any time point ($p > 0.05$), consistent with the CAP's targeted action on lower-limb CPG circuitry.
Conclusion: The Corticospinal Activation Protocol, delivered alongside conventional physiotherapy, produced significantly greater CPG-linked neurophysiological and functional locomotor recovery than conventional physiotherapy alone in individuals with incomplete SCI, supporting its use as a targeted adjunct in neurorestorative rehabilitation.
Keywords: Spinal cord injury; Central pattern generator; Corticospinal activation protocol; Neurorehabilitation; Motor evoked potentials; Locomotion; Randomised controlled trial
How to cite this article: Kaur S, Arumugam N, Chhabra HS. Effectiveness of Corticospinal Activation Protocol on Central Pattern Generator of Locomotion in Individuals with Incomplete Spinal Cord Injury. Int J Drug Deliv Technol. 2026;16(70s): 1377-1384. DOI: 10.25258/ijddt.16.70s.148

INTRODUCTION

Spinal cord injury (SCI) interrupts the continuity of descending corticospinal, propriospinal, and reticulospinal pathways, thereby disconnecting supraspinal motor commands from the spinal central pattern generator (CPG) networks that generate the rhythmic, alternating muscle activation underlying stepping and locomotion. Substantial experimental and clinical evidence, including epidural stimulation studies demonstrating stepping-like electromyographic activity in individuals with motor-complete SCI, confirms that the human lumbosacral spinal cord retains dedicated CPG circuitry capable of generating locomotor rhythm independent of supraspinal drive[1,2]. Even when injury is incomplete and residual axonal continuity persists across the lesion, the strength and timing of corticospinal drive onto these CPG circuits is frequently insufficient to produce functional, coordinated gait. Restoring this corticospinal-CPG coupling, rather than the CPG circuitry alone, has therefore emerged as a key neurorehabilitative target in incomplete SCI.

This rationale is grounded in the principle of activity-dependent spinal cord plasticity, whereby repetitive, patterned afferent and efferent activity

reorganises synaptic efficacy within residual corticospinal, propriospinal, and spinal interneuronal circuits in a manner that can be harnessed therapeutically[3,4]. The Corticospinal Activation Protocol (CAP) was developed and content- and construct-validated through a modified Delphi consensus process involving an eleven-member expert panel of SCI neurorehabilitation specialists and a biostatistician, prior to its evaluation in a pilot randomised controlled trial conducted in accordance with recommended pilot and feasibility trial methodology[5,6,7]. The CAP integrates seven training domains-cognitive-motor integration, autonomic activation, central pattern generator activation, task-specific trunk control, sensorimotor integration and balance, ambulation and locomotion training, and vocational/social participation-into a single, sequenced rehabilitation programme intended to simultaneously engage cortical drive, autonomic regulation, and spinal rhythmogenic circuitry.

While the pilot phase of this research programme established the feasibility, safety, and preliminary effectiveness of the CAP, the effect of the full protocol on objective neurophysiological indices of corticospinal-CPG coupling-namely motor and somatosensory evoked potentials-alongside functional locomotor and independence outcomes, has not previously been evaluated in an adequately powered randomised controlled trial. The present study, therefore, examined the effectiveness of the CAP, delivered alongside conventional physiotherapy, on CPG-linked neurophysiological and functional locomotor recovery in individuals with incomplete SCI, in comparison with conventional physiotherapy alone.

MATERIALS AND METHODS

Study Design, Registration, and Ethical Approval

This was a two-arm, parallel-group, randomised controlled trial constituting Phase II of a multi-phase research programme (systematic review, Delphi expert consensus, pilot RCT, and definitive RCT). The trial was prospectively registered with the Clinical Trials Registry of India (CTRI/2023/02/049536) and approved by the Institutional Ethics Committee, Punjabi University, Patiala (Ref. No. 28/55/IEC/PUP/2022). Written informed consent was obtained from all participants prior to enrolment, in accordance with the Declaration of Helsinki.

Participants

Individuals of either sex, aged 20-80 years, with a clinical diagnosis of traumatic or non-traumatic incomplete SCI (American Spinal Injury Association Impairment Scale [AIS] grade B, C, or D) and intact cognitive function (Mini-Mental State Examination score ≥26)[8] were recruited by purposive sampling. Individuals with cognitive or neurodegenerative deficits, epilepsy or head injury, implanted electronic devices incompatible with neurophysiological testing, severe cardiorespiratory or metabolic comorbidity, active pressure injuries, pregnancy, active malignancy, or concurrent medications known to alter neuromuscular excitability were excluded.

Sample Size

Sample size was calculated using G*Power software assuming a small effect size (0.25), power of 0.80, and α of 0.05, yielding a requirement of 84 participants; adjusting for an anticipated 10% attrition rate produced a target and final enrolled sample of 56 participants.

Randomisation and Group Allocation

Following baseline assessment, eligible participants were allocated in a 1:1 ratio to Group A or Group B using a computer-generated random number sequence, stratified by baseline AIS grade (B, C, or D) to balance injury severity across arms. Group A (n=28) received the CAP in conjunction with conventional physiotherapy; Group B (n=28) received conventional physiotherapy alone, serving as an active control. Both groups received matched treatment dosage (45-60 minutes/session, 5 sessions/week, 20 sessions over 4 weeks) to control for non-specific effects of therapist contact time.

Interventions

The CAP comprised seven integrated training domains: (1) cognitive-motor integration training, engaging higher cortical motor centres and the reticular activating system; (2) autonomic nervous system activation training, targeting sympathetic-parasympathetic balance; (3) central pattern generator activation, using automaticity- and rhythmicity-based exercises to facilitate lumbosacral locomotor networks[1,2]; (4) task-trunk control with developmental task-specific training; (5) sensorimotor integration, balance, and proprioception training; (6) ambulation and locomotion training; and (7) vocational and social participation training. Conventional physiotherapy, delivered to both groups, comprised standard evidence-based SCI rehabilitation components: upper- and lower-extremity strengthening, trunk stabilisation, body-weight-supported treadmill training where appropriate, functional electrical stimulation, balance and proprioception training, transfer and mobility training, flexibility exercises, and respiratory/postural training.

Outcome Measures

Primary neurophysiological outcomes were Motor Evoked Potential (MEP) latency and amplitude of the tibialis anterior, recorded via transcranial magnetic stimulation and surface electromyography[13,14], and Somatosensory Evoked Potential (SEP) P37 and N45 latencies and N45-P37 amplitude of the posterior tibial nerve[15], recorded at Day 0 and Day 30. Secondary outcomes-AIS upper- and lower-limb motor scores and AIS light touch and pin-prick sensory scores[9], the Walking Index for Spinal Cord Injury-II (WISCI-II)[10], the Spinal Cord

Independence Measure-III (SCIM-III)[11], and General and Sacral Autonomic Function (International Standards to document remaining Autonomic Function after SCI, ISAFSCI)[12]-were assessed at Day 0, Day 15, and Day 30 by assessors following standardised protocols consistent with recommended measurement standards for patient-reported and clinician-administered outcome instruments[16].

Statistical Analysis

Data were analysed using IBM SPSS Statistics (Version 20.0). Within-group change across the three (or two, for MEP/SEP) assessment time points was evaluated using one-way repeated-measures analysis of variance (ANOVA), with pairwise post-hoc comparisons. Between-group differences at each time point were evaluated using independent-samples t-tests. Statistical significance was set at $p \leq 0.05$ throughout.

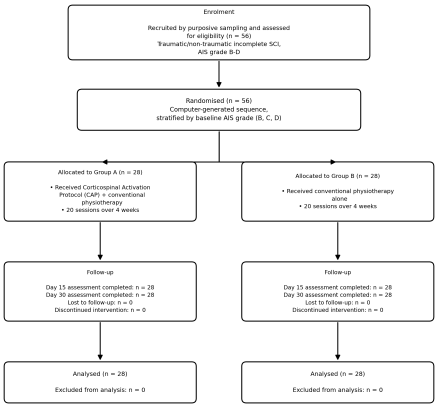

Figure 1. CONSORT flow diagram of participant enrolment, randomisation, allocation, follow-up, and analysis.

RESULTS

A total of 56 participants with incomplete SCI completed the study, 28 in each group. Baseline demographic and clinical characteristics are summarised in Table 1. The mean age of participants was 38±11.99 years in Group A and 45±15.35 years in Group B; 86% of the overall sample was male. Groups were broadly comparable at baseline for injury level, cause, chronicity, and AIS grade distribution.

Table 1. Baseline demographic and clinical characteristics of participants (Group A and Group B)

Characteristic	Group A (n=28)	Group B (n=28)	Total (n=56)
Age, years (Mean±SD)	38±11.99	45±15.35	42±14.12
Male, n (%)	25 (89%)	23 (82%)	48 (86%)
Female, n (%)	3 (11%)	5 (18%)	8 (14%)
Married, n (%)	19 (68%)	22 (79%)	41 (73%)
Traumatic SCI, n	17	23	40
Non-traumatic SCI, n	11	5	16
Cervical level (C1-C7), n	7	7	14
Upper thoracic (D1-D6), n	3	1	4
Lower thoracic (D7-D12), n	15	13	28
Lumbar (L1-L5), n	3	7	10
AIS Grade B, n	17	19	36
AIS Grade C, n	6	5	11
AIS Grade D, n	5	4	9
Acute (0-6 mo), n	8	5	13
Sub-acute (6-18 mo), n	6	10	16
Chronic (≥18 mo), n	14	13	27

Table 2. Within-group comparison of outcome measures across Day 0, Day 15, and Day 30 (one-way repeated-measures ANOVA)

Outcome measure	Group A (CAP + conventional PT)					Group B (Conventional PT alone)				
	Day 0	Day 15	Day 30	F	p	Day 0	Day 15	Day 30	F	p
ASIA-UL Motor	45.68±9.22	46.36±8.28	47.32±6.76	9.491	0.001*	44.21±10.42	44.68±9.59	45.07±8.77	4.417	0.017*
ASIA-LL Motor	16.39±10.39	19.25±10.77	22.54±10.94	79.036	0.001*	9.33±8.40	10.04±9.33	11.25±9.40	36.45	0.001*
ASIA Light Touch	84.25±16.62	88.18±15.28	93.14±15.15	79.036	0.001*	77.54±17.49	79.18±16.79	80.43±17.23	23.61	0.001*

ASIA Pin-Prick	83.50±17.84	87.43±17.65	92.71±16.13	68.537	0.001*	77.21±17.78	78.75±17.22	80.14±17.23	21.00	0.001*
WISCI-II	6.75±4.88	8.68±4.11	12.69±4.09	165.89	0.001*	4.61±4.41	5.61±4.53	6.39±4.37	30.42	0.001*
SCIM-III	60.71±17.04	68.64±14.27	76.11±13.10	119.10	0.001*	50.39±20.22	54.50±19.21	58.64±18.13	71.50	0.001*
General Autonomic Function	9.71±1.24	10.64±0.95	11.32±0.72	49.482	0.001*	9.82±1.38	10.04±1.42	10.18±1.36	6.494	0.003*
Sacral Autonomic Function	7.82±3.56	9.61±3.47	12.46±3.97	51.50	0.001*	7.86±4.03	8.29±3.98	8.50±3.91	9.00	0.001*

Table 2 (contd). Within-group comparison of neurophysiological outcomes, Day 0 vs Day 30 (paired t-test)

Neurophysiological measure	Group A, Mean±SD				Group B, Mean±SD			
	Day 0	Day 30	t	p	Day 0	Day 30	t	p
MEP Latency, ms (TA)	44.62±6.68	41.53±7.04	2.022	0.024*	40.89±7.13	39.58±7.40	4.280	0.000*
MEP Amplitude, mV (TA)	0.16±0.10	0.22±0.20	1.009	0.364	0.10±0.05	0.20±0.10	1.986	0.057
SEP P37 Latency, ms	45.74±3.66	44.08±3.64	1.754	0.043*	46.35±3.30	45.73±3.38	3.300	0.003*
SEP N45 Latency, ms	38.02±5.48	36.57±5.65	1.373	0.080	38.73±2.22	38.15±2.25	5.214	0.000*
SEP N45-P37 Amplitude, µV	1.23±0.52	1.62±0.64	1.710	0.046*	1.44±0.38	1.62±0.29	5.475	0.000*

Table 3. Between-group comparison of functional and clinical outcome measures at Day 0, Day 15, and Day 30 (independent-samples t-test)

Outcome measure	Day 0				Day 15				Day 30			
	A	B	t	p	A	B	t	p	A	B	t	p
ASIA-ULMotor	45.68±9.22	44.21±10.42	0.557	0.290	46.36±8.28	44.68±9.59	0.701	0.243	47.32±6.76	45.07±8.77	1.075	0.144
ASIA-LLMotor	16.39±10.39	9.33±8.40	2.670	0.005*	19.25±10.77	10.04±9.33	3.419	0.001*	22.54±10.93	11.25±9.42	4.137	0.001*
ASIA Light Touch	84.25±16.62	77.54±17.49	1.472	0.072	88.18±15.28	79.18±16.79	2.098	0.020*	93.14±15.15	80.43±16.64	2.989	0.001*
ASIA Pin-Prick	83.50±17.84	77.21±17.78	1.320	0.096	87.43±17.65	78.75±17.22	1.862	0.034*	92.71±16.13	80.14±17.23	2.818	0.003*
WISCI-II	6.75±4.88	4.61±3.84	1.6	0.0	8.68±4.11	5.61±4.53	2.6	0.00	12.61±4.09	6.39±4.37	5.4	0.00

			49	52			54	5*			88	1*
SCIM-III	60.71±17.04	50.39±20.22	2.065	0.022*	68.64±14.27	54.50±19.21	3.126	0.001*	76.11±13.10	58.64±18.13	4.130	0.001*
General Autonomic Function	9.71±1.24	9.82±1.38	0.304	0.381	10.64±0.95	10.04±1.42	1.874	0.033*	11.32±0.72	10.18±1.36	3.921	0.001*
Sacral Autonomic Function	7.82±3.56	7.86±4.03	0.035	0.486	9.61±3.47	8.29±3.98	1.321	0.096	12.46±3.97	8.50±3.91	3.761	0.001*

Table 4. Between-group comparison of neurophysiological outcomes at Day 0 and Day 30 (independent-samples t-test)

Neurophysiological measure	Day 0				Day 30			
	Group A	Group B	t	p	Group A	Group B	t	p
MEP Latency, ms (TA)	44.62±6.68	40.89±7.13	2.022	0.054	41.53±7.04	39.58±7.40	1.009	0.159
MEP Amplitude, mV (TA)	0.16±0.15	0.10±0.05	1.171	0.123	0.22±0.20	0.20±0.19	0.350	0.364
SEP P37 Latency, ms	45.74±3.66	46.35±3.30	0.658	0.257	44.08±3.64	45.73±3.38	1.754	0.043*
SEP N45	38.02±5.48	38.73±2.22	0.6	0.2	36.57±5.65	38.15±2.25	1.3	0.088
Latency, ms			34	64			73	
SEP N45-P37 Amplitude, μV	1.23±0.52	1.44±0.38	1.718	0.0092	1.62±0.64	1.62±0.29	0.0400	0.968

Values expressed as Mean±Standard Deviation. TA = Tibialis Anterior. *Significant at p≤0.05. AIS = ASIA Impairment Scale; UL = upper limb; LL = lower limb; WISCI-II = Walking Index for Spinal Cord Injury-II; SCIM-III = Spinal Cord Independence Measure-III; MEP = Motor Evoked Potential; SEP = Somatosensory Evoked Potential.

Within-group analysis (Table 2) revealed statistically significant improvement across all outcome measures from Day 0 to Day 30 in both groups (p≤0.05), with the exception of MEP amplitude and SEP N45 latency in Group A and MEP amplitude in Group B, which did not reach significance. Between-group comparison (Table 3) showed no significant baseline differences for ASIA-UL motor score, ASIA light touch, ASIA pin-prick, WISCI-II, GAF, and SAF (p>0.05), indicating adequate baseline equivalence for these CPG-relevant measures; a significant baseline difference was present for ASIA-LL motor score and SCIM-III, reflecting the stratified-but-imperfect balance inherent to a 56-participant sample.

By post-intervention (Day 30), Group A showed significantly greater improvement than Group B in ASIA-LL motor function, ASIA light touch, ASIA pin-prick, WISCI-II, SCIM-III, General Autonomic Function, and Sacral Autonomic Function (all p≤0.05). ASIA-UL motor score, reflecting a region outside the primary locomotor CPG target of the protocol, did not differ significantly between groups at any time point, consistent with the anatomical specificity of CAP's action on lumbosacral, rather than cervical, motor output.

Neurophysiological indices of corticospinal-CPG coupling (Table 4) mirrored the functional findings. At Day 30, SEP P37 latency of the posterior tibial nerve was significantly shorter in Group A than Group B (44.08±3.64 ms vs 45.73±3.38 ms, p=0.043), consistent with enhanced ascending somatosensory conduction. MEP latency of tibialis anterior showed a similar directional reduction in Group A (41.53±7.04 ms) relative to Group B (39.58±7.40 ms), though the between-group difference did not reach significance (p=0.159); a near-significant baseline imbalance in MEP latency (p=0.054) should be considered when interpreting this comparison. SEP N45 latency and MEP/SEP amplitude measures showed favourable within-group trends in Group A but did not differ significantly between groups.

DISCUSSION

The present trial demonstrates that a four-week programme of the Corticospinal Activation Protocol,

delivered alongside conventional physiotherapy, produces significantly greater improvement than conventional physiotherapy alone in CPG-linked locomotor outcomes-WISCI-II and ASIA lower-limb motor and sensory scores-together with greater gains in functional independence (SCIM-III) and autonomic function in individuals with incomplete SCI. These functional gains were accompanied by a significant reduction in SEP P37 latency and a favourable, though not statistically significant, trend toward shorter MEP latency in the experimental group, providing neurophysiological corroboration that the observed functional improvement reflects, at least in part, enhanced conduction along corticospinal and ascending somatosensory pathways rather than compensatory strategy alone.

Neurophysiological Basis of the Observed Improvements

The WISCI-II and SCIM-III gains observed in Group A are consistent with the theoretical target of the CAP's central pattern generator activation domain: the lumbosacral rhythmogenic interneuronal networks that generate the basic alternating flexor-extensor pattern of stepping. Epidural stimulation studies in individuals with motor-complete SCI have shown that this spinal circuitry can produce locomotor-like electromyographic output even when isolated from supraspinal control[1], and subsequent work has confirmed that these networks remain modifiable by patterned afferent input in humans[2]. In incomplete SCI, where some corticospinal continuity is preserved, automaticity- and rhythmicity-based training of the type embedded in the CAP is theorised to strengthen the residual corticoreticulospinal and corticospinal projections that drive these circuits, thereby improving the gain and reliability of supraspinal-to-CPG transmission rather than creating new locomotor circuitry.

This mechanism is supported by the principle of activity-dependent spinal cord plasticity, whereby repetitive, task-specific afferent and efferent activity produces lasting changes in synaptic efficacy, motoneuron excitability, and axonal conduction properties within spinal and corticospinal circuits[3], and by demonstrations that such plasticity can be therapeutically directed through structured rehabilitative training after SCI[4]. Direct neurophysiological support for this mechanism in incomplete SCI comes from studies showing that sustained treadmill and locomotor training increases corticospinal tract conduction efficiency, evidenced by increased MEP amplitude and reduced MEP threshold in previously paretic muscles, with the magnitude of neurophysiological change correlating with the degree of locomotor recovery[18]. Longitudinal cohort data further show that the evolution of MEP integrity over the first year after SCI tracks recovery of leg motor function, underscoring MEPs as a sensitive marker of corticospinal reorganisation rather than a static injury descriptor[19]. The directional reduction in MEP latency observed in Group A in the present study (44.62 to 41.53 ms) is consistent with this reorganisational process, although the between-group comparison did not reach significance, likely reflecting the shorter four-week training window relative to the several months typically required for maximal corticospinal adaptation.

The significant reduction in SEP P37 latency in Group A relative to Group B indicates enhanced conduction efficiency along the dorsal column-medial lemniscal pathway and more efficient thalamocortical relay of ascending somatosensory input. Because ascending somatosensory feedback is a principal source of afferent drive that shapes and entrains CPG output during stepping[2], improved SEP conduction is mechanistically compatible with-and may partly explain-the parallel gains in ASIA light touch, pin-prick, and locomotor scores, since more accurate and rapid proprioceptive and cutaneous feedback would be expected to improve the timing and amplitude modulation of CPG-driven muscle activation during gait.

The concurrent improvement in General and Sacral Autonomic Function in Group A is compatible with the anatomical proximity and functional interconnection between lumbosacral somatic CPG circuits and sacral autonomic (parasympathetic and pudendal) nuclei, such that repetitive activation of adjacent somatic networks may produce a degree of trans-synaptic facilitation of autonomic pathways-a phenomenon broadly consistent with the non-selective, activity-dependent nature of spinal plasticity described after SCI[3,4]. Electrophysiological evidence that residual corticospinal conduction can be tracked and modified in parallel with functional recovery[17] lends further plausibility to this interpretation, although the present study did not directly measure autonomic-specific conduction pathways, and this explanation should be regarded as hypothesis-generating rather than confirmed.

The dissociation between the ASIA upper-limb result (non-significant between groups) and the consistently significant lower-limb, locomotor, and autonomic findings further supports the anatomical specificity of the CAP's action: the protocol's central pattern generator and ambulation-training domains are directed at lumbosacral, not cervical, motor output, and the absence of an upper-limb effect argues against a generalised placebo or attention-related explanation for the lower-limb and autonomic gains.

The improvement observed in the conventional physiotherapy (control) group across nearly all measures indicates that standard rehabilitation alone produces meaningful, though generally smaller, gains over four weeks-an expected finding given the inclusion of task-specific and weight-supported

locomotor components in the standard-of-care comparator. The magnitude of between-group separation, evident by Day 15 for several measures and widening by Day 30, suggests a dose-response or cumulative neuroplastic effect of the additional CAP domains rather than an immediate ceiling effect.

Several limitations warrant consideration. First, the four-week intervention window, while sufficient to demonstrate early neurophysiological change, precludes conclusions about long-term retention of corticospinal-CPG coupling gains; longer-term follow-up is required, particularly as corticospinal adaptation after incomplete SCI has been shown to continue evolving over several months to a year. Second, the baseline imbalance observed for ASIA lower-limb motor score, SCIM-III, and the borderline imbalance in MEP latency, despite AIS-grade-stratified randomisation, should be considered when interpreting the magnitude of the treatment effect, and future analyses may benefit from baseline-adjusted (ANCOVA) modelling. Third, therapists delivering the intervention could not be blinded to group allocation given the nature of the protocol, though outcome assessment used objective neurophysiological and standardised clinical instruments. Fourth, the proposed mechanistic links between somatic CPG activation and autonomic improvement, and between SEP conduction and locomotor gain, are inferential rather than directly demonstrated by the present electrophysiological protocol and warrant dedicated mechanistic study. Finally, as a single-centre trial, generalisability to other rehabilitation settings and injury profiles should be confirmed in multi-centre studies.

CONCLUSION

The Corticospinal Activation Protocol, delivered in conjunction with conventional physiotherapy, produced significantly greater improvement in central pattern generator-linked locomotor function (WISCI-II), lower-limb motor and sensory recovery, functional independence, and autonomic function than conventional physiotherapy alone in individuals with incomplete spinal cord injury, with corroborating neurophysiological evidence of enhanced somatosensory pathway conduction. These findings support the CAP as an effective, targeted adjunct to standard rehabilitation for promoting corticospinal-CPG coupling and locomotor recovery after incomplete SCI.

ACKNOWLEDGEMENT

The authors acknowledge the Department of Physiotherapy, Punjabi University, Patiala, and Sri Balaji Action Spine Medical Institute, New Delhi, for institutional and clinical support during this research.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Dimitrijevic MR, Gerasimenko Y, Pinter MM. Evidence for a spinal central pattern generator in humans. Ann N Y Acad Sci. 1998;860:360-376.
2. Minassian K, Hofstoetter US, Dzeladini F, Guertin PA, Ijspeert A. The human central pattern generator for locomotion: does it exist and contribute to walking? Neuroscientist. 2017;23(6):649-663.
3. Wolpaw JR, Tennissen AM. Activity-dependent spinal cord plasticity in health and disease. Annu Rev Neurosci. 2001;24:807-843.
4. Edgerton VR, Tillakaratne NJ, Bigbee AJ, de Leon RD, Roy RR. Plasticity of the spinal neural circuitry after injury. Annu Rev Neurosci. 2004;27:145-167.
5. Thabane L, Ma J, Chu R, et al. A tutorial on pilot studies: the what, why and how. BMC Med Res Methodol. 2010;10:1.
6. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. Pilot Feasibility Stud. 2016;2:64.
7. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655.
8. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189-198.
9. Kirshblum SC, Burns SP, Biering-Sorensen F, et al. International standards for neurological classification of spinal cord injury (revised 2011). J Spinal Cord Med. 2011;34(6):535-546.
10. Ditunno JF, Ditunno PL, Graziani V, et al. Walking index for spinal cord injury (WISCI): an international multicenter validity and reliability study. Spinal Cord. 2000;38(4):234-243.
11. Catz A, Itzkovich M, Agranov E, Ring H, Tamir A. SCIM - spinal cord independence measure: a new disability scale for patients with spinal cord lesions. Spinal Cord. 1997;35(12):850-856.
12. Krassioukov A, Biering-Sorensen F, Donovan W, et al. International standards to document remaining autonomic function after spinal cord injury. J Spinal Cord Med. 2012;35(4):201-210.
13. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. Lancet. 1985;1(8437):1106-1107.
14. Rossini PM, Burke D, Chen R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. Clin Neurophysiol. 2015;126(6):1071-1107.

15. Nuwer MR, Aminoff M, Desmedt J, et al. IFCN recommended standards for short latency somatosensory evoked potentials. Electroencephalogr Clin Neurophysiol. 1994;91(1):6-11.
16. Mokkink LB, Prinsen CAC, Patrick DL, et al. COSMIN study design checklist for patient-reported outcome measurement instruments. Amsterdam: COSMIN; 2018.
17. Curt A, Dietz V. Electrophysiological recordings in patients with spinal cord injury: significance for predicting outcome. Spinal Cord. 1999;37(3):157-165.
18. Thomas SL, Gorassini MA. Increases in corticospinal tract function by treadmill training after incomplete spinal cord injury. J Neurophysiol. 2005;94(4):2844-2855.
19. Petersen JA, Spiess M, Curt A, Dietz V, Schubert M; EM-SCI Study Group. Spinal cord injury: one-year evolution of motor-evoked potentials and recovery of leg motor function in 255 patients. Neurorehabil Neural Repair. 2012;26(8):939-948.