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CASE REPORT

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Trans-spinal magnetic stimulation combined with kinesiotherapy as a new method for enhancing functional recovery in patients with spinal cord injury due to neuromyelitis optica: a case report

Rodrigo Brito[1,2], Bárbara Marroquim[1], Lívia Shirahige[1,2], Adriana Baltar[1,2], Sérgio Rocha[1], Alexia Perruci[1] and Katia Monte-Silva[1,2*]

Abstract

Background Experimental studies have shown that repetitive trans-spinal magnetic stimulation (TsMS) decreases demyelination and enables recovery after spinal cord injury (SCI). However, the usefulness of TsMS in humans with SCI remains unclear. Therefore, the main objective of this study is to evaluate the effects of TsMS combined with kinesiotherapy on SCI symptoms. We describe a protocol treatment with TsMS and kinesiotherapy in a patient with SCI due to neuromyelitis optica (NMO)-associated transverse myelitis.

Case presentation A 23-year-old white male with NMO spectrum disorders started symptoms in 2014 and included lumbar pain evolving into a mild loss of strength and sensitivity in both lower limbs. Five months later, the symptoms improved spontaneously, and there were no sensorimotor deficits. Two years later, in 2016, the symptoms recurred with a total loss of strength and sensitivity in both lower limbs. Initially, physiotherapy was provided in 15 sessions with goals of motor-sensory recovery and improving balance and functional mobility. Subsequently, TsMS (10 Hz, 600 pulses, 20-seconds inter-trains interval, at 90% of resting motor threshold of the paravertebral muscle) was applied at the 10th thoracic vertebral spinous process before physiotherapy in 12 sessions. Outcomes were assessed at three time points: prior to physiotherapy alone (T-1), before the first session of TsMS combined with kinesiotherapy (T0), and after 12 sessions of TsMS combined with kinesiotherapy (T1). The patient showed a 25% improvement in walking independence, a 125% improvement in balance, and an 18.8% improvement in functional mobility. The Patient Global Impression of Change Scale assessed the patient's global impression of change as 'much improved'.

Conclusion TsMS combined with kinesiotherapy may safely and effectively improve balance, walking independence, and functional mobility of patients with SCI due to NMO-associated transverse myelitis.

Keywords Spinal cord injury, Transverse myelitis, Transcranial magnetic stimulation, Balance, Walking independence

*Correspondence:
Katia Monte-Silva
monte.silva@ufpe.br
Full list of author information is available at the end of the article

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Introduction

Neuromyelitis optica (NMO) is an autoimmune astrocytopathic disease of the central nervous system with a predilection for the spinal cord and optic nerves and may cause transverse myelitis and optic neuritis, respectively, if these regions are affected [47, 49]. The symptoms associated with transverse myelitis are similar to those of spinal cord injury (SCI), including sensorimotor symptoms, pain, cardiovascular symptoms, and symptoms of bladder, bowel, and sexual dysfunction [22].

Regarding recovery from NMO-associated transverse myelitis, physiotherapy does not seem to result in the deterioration of symptoms in most patients [38]; however, few cases with poor functional recovery have been reported [43, 45]. Despite the proposal of a variety of treatment approaches, such as surgery, physiotherapy, and cell-based therapy, either individually or in combination, their limited efficacy in fully restoring functionality for many patients underscores the need for exploring innovative interventions [12, 15]. Non-invasive brain stimulation (NIBS) is a promising tool for altering cortical and spinal excitability safely and painlessly [42]. Experimental studies in mice with SCI have shown a reduction in demyelination and axonal and walking recovery after trans-spinal magnetic stimulation (TsMS) [8, 31].

These studies provide evidence that TsMS induces therapeutic effects in an experimental animal model and suggest a possible translation of the results to clinical application in humans [8]. The usefulness of TsMS in human patients with SCI has not been documented. In this case report, we describe the usefulness and safety of repetitive TsMS combined with physiotherapy provided to improve mobility of a patient with chronic incomplete SCI due to NMO-associated transverse myelitis.

Case description

Publication of this case report was approved by the local ethics committee (4.755.012), and all study procedures were conducted following the principles stated in the Declaration of Helsinki. The patient underwent physiotherapy at the Applied Neuroscience Laboratory (LANA) at Universidade Federal de Pernambuco (Recife, Pernambuco, Brazil).

The patient was a 23-year-old white male diagnosed with NMO spectrum disorders, presenting no relevant family history. The symptoms started in 2014, when the patient was 18 years old, initially manifesting as lumbar pain evolving into a mild loss of strength and sensitivity in both lower limbs. Five months later, the symptoms improved spontaneously, and there were no sensorimotor deficits. However, 2 years later, in 2016, the symptoms recurred with a total loss of strength and sensitivity in both lower limbs. During this period, the patient did not exhibit any visual symptoms. Over the past 3 years, the patient underwent physiotherapy twice a week, each lasting 35 min, but reported only minimal improvement in their functional sensory-motor symptoms. Consequently, the patient contacted our research group seeking further treatment options.

According to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) by the American Spinal Injuries Association (ASIA) [24], the patient had ASIA Impairment Scale (AIS) grade D (motor function is preserved below the neurological level, and at least half of the key muscles below the neurological level have a muscle grade of 3 or more) with sensory level at T5 and motor level at L2 in both right and left sides, and the neurological level was at T5. The patient was independent in activities of daily living such as self-care, dressing, feeding, and movement. Based on the Walking Index for Spinal Cord Injury II (WISCI II) scale [14], the patient ambulated with two crutches both indoor and outdoor, with no braces and physical assistance.

Initially, we opted for an exclusive kinesiotherapy-based treatment for the patient, conducting 15 sessions. Unfortunately, this strategy failed to produce any noticeable gains in motor function. Given the insights from emerging studies, such as those by Ainhoa Insausti-Delgado *et al.* [21], which highlighted TsMS capacity to promote neuroplasticity in the motor cortex, we decided to integrate TsMS into our kinesiotherapy protocol [21]. After checking the safety criteria for transcranial magnetic stimulation [42] and obtaining written informed consent for participation in the research, the patient underwent 12 sessions of trans-spinal magnetic stimulation (TsMS) in conjunction with kinesiotherapy, tailored to the patient's specific functional requirements.

Interventions

The initial plan of rehabilitation

The patient underwent 15 sessions of physiotherapy; each session lasted for approximately 2 hours, and the therapy was provided two times a week. Each treatment session had the following goals: (i) to regain muscle strength in lower limbs, (ii) to achieve sensory recovery, (iii) to achieve balance, and (iv) to achieve functional mobility. All proposed exercises were performed considering principles of motor learning theory and principles of neuroplasticity [25]. The physiotherapy protocol is shown in Table 1.

Trans-spinal magnetic stimulation protocol

The patient was asked to lie prone on a stretcher during the TsMS session. The resting motor threshold (rMT) of the paraspinal muscle at the 10th thoracic vertebral

Table 1 Protocol of physical therapy during the initial plan of rehabilitation and with trans-spinal magnetic stimulation

Goals	Procedures
Foot mobility	Myofascial release of plantar fascia
Sensory stimulation	Sensory peripheral stimulation
	Vibratory stimulation
	Tactile and proprioceptive stimulation
Muscle strength	Progressive resistive exercises for:
	(i) Core and trunk muscles
	(ii) Abdominal muscles
	(iii) Gluteus muscles
	(iv) Lower limb muscles (hip flexors and extensors; knee flexors and extensors; dorsiflexors and plantar flexors)
Transfer training	Sitting down on knees to standing
	Sitting to standing
Trunk stability training	PNF combination of isotonic muscles in different positions (on knees, semi-kneeling, sitting, and standing)
	Postural stability on Biodex Balance System sd
Limits of stability training	Limits of stability on Biodex Balance System sd
	Reach task
Balance training	Random control and maze control on Biodex Balance System sd
Specific gait training	Focus on mid-balance and midstance phases
Gait training	Moderate-intensity treadmill training without body weight support (15 to 20 minutes)

PNF proprioceptive neuromuscular facilitation

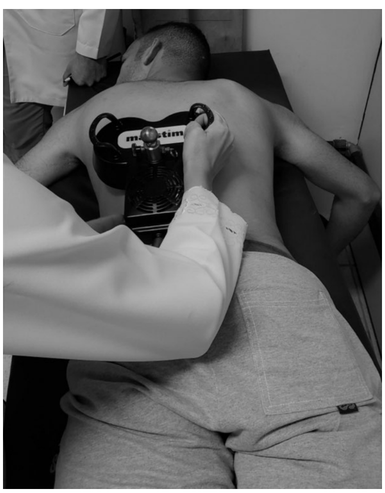

Fig. 1 Positioning of the figure-of-eight coil for assessing the resting motor threshold of the paraspinal muscle at the level of the 10th thoracic vertebra

level was assessed (Fig. 1). rMT was defined as the lowest intensity of TsMS output that was able to produce visible muscular contraction in the target muscle in more than 5 of 10 trials. TsMS was performed using a figure-of-eight coil attached to a MagStim Super Rapid magnetic stimulator (MagStim Company, Whitland, UK) and placed over the spinous process of the 10th thoracic vertebra. A 10-Hz stimulus was delivered with 600 pulses (60 pulses, 10 trains) and 20-seconds inter-trains intervals at 90% rMT.

Physiotherapy was conducted immediately after TsMS in another 12 sessions (10 sessions were held daily for five times a week [induction phase], and two sessions were performed with a 48-hours interval between them [maintenance phase]). The protocol and main goals of the physiotherapy were the same as those of the initial plan of rehabilitation.

Outcomes

Except for the ISNCSCI grading, all evaluations were performed at the baseline (T-1), before starting TsMS (T0), and immediately after the completion of the 12th TsMS session (T1). The outcome measures were chosen based on the body structure, body function, and activity domains of the International Classification of Functioning, Disability, and Health (ICF) framework.

The activity was assessed using the WISCI II scale for walking independence. The WISCI II scale assesses the extent of physical assistance and devices required for walking following paralysis that results from SCI. There are 20 levels of assessment; higher levels indicate more independent mobility [13], and a change of one WISCI level can be considered a substantial difference in the clinical context (minimal detectable change [MDC]) [6]. At baseline, the patient had a WISCI II score of 16

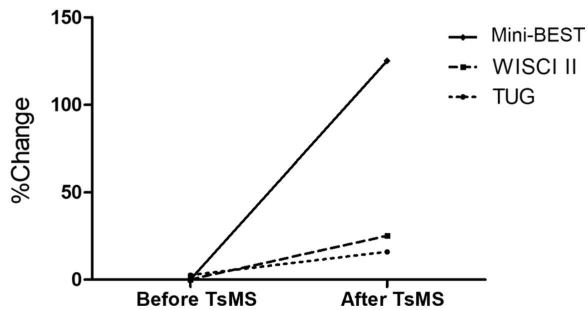

Fig. 2 Graphical representation of quantitative assessment before and after 12 sessions of repetitive trans-spinal magnetic stimulation combined with physical therapy. Mini-BEST: short version of the Balance Evaluation Systems test; WISCI II: Walking Index for Spinal Cord Injury scale; TUG: timed get up and go test, before TsMS represent the "T0: before starting TsMS", after TsMS represent the "T1: after TsMS"; % Change: [(value after TsMS – value before TsMS)/value before TsMS] × 100; TsMS: trans-spinal magnetic stimulation

(ambulation with two crutches with no braces and physical assistance), and the score remained the same during the initial rehabilitation period. The WISCI II score changed only after initiating TsMS treatment, reaching the maximum level (20; ambulation with no device, braces, and physical assistance). The patient achieved four times the MDC in the WISCI II scale assessment (Fig. 2, Table 2).

In addition, the activity was assessed using the timed get up and go (TUG) test [41] for functional mobility. The TUG test requires the patient to get up from a chair, walk a distance of 3 m, turn around, and return to the chair. During this activity, the time is measured, and a shorter time indicates better functional mobility [41]. The MDC is 10.8 s or a reduction of 30% [29]. The time required by the patient to perform the TUG test was reduced by 18% after TsMS. Although the MDC was not attained, a substantial reduction was possible after TsMS (Fig. 2, Table 2).

Body function was assessed using the short version of the Balance Evaluation Systems Test (Mini-BEST) [20]. The Mini-BEST is a 14-item test scored on a 3-level ordinal scale, where higher scores indicate better balance, and aims to target and identify six different balance control systems [17, 20]. Therefore, it assesses the activity as well as ICF domains. There is no MDC suggested for SCI, however, the score for Parkinson's disease is 5.52 points [30] and for vestibular disorders is 3.5 points [18]. Even though the MDC for SCI was not available, we observed that the patient achieved a score comparable with those for the other patient populations (10 points) (Fig. 2, Table 2). This improvement was scored based on anticipatory adjustment (2 to 5 points), reactive postural control (1 to 5 points), sensory orientation (2 to 3 points), and dynamic gait (3 to 5 points).

Finally, the Patient Global Impression of Change Scale (PGICS) that assesses a patient's belief about the efficacy of treatment was used at the end of the TsMS sessions [16]. The patient reported "an improvement that has made a real and worthwhile difference" (level 6). The presence of adverse effects was also assessed after the end of each TsMS session. No adverse effects were reported. Thus, TsMS may be considered a safe and non-invasive tool.

Discussion

The present case demonstrated that improvement in balance, walking independence, and functional mobility occurred after adding TsMS protocol in a physiotherapy program for a patient with SCI. The use of repetitive transcranial magnetic stimulation (rTMS) of the motor cortex to improve functional recovery in patients with chronic incomplete SCI is well-established [2, 7, 28, 34, 39]. However, to the best of our knowledge, this is the first case report on the trans-spinal application of magnetic field for improving functional recovery in a patient with SCI.

Table 2 Quantitative assessment before and after 12 sessions of repetitive trans-spinal spinal magnetic stimulation combined with physical therapy

Assessment	Baseline (T-1)	Before TsMS (T0)	After TsMS (T1)	% Change (T0–T-1)	% Change (T1–T0)	MDC
WISCI II scale (0–20 points)	16	16	20	5	25	Yes
Mini-BEST (0–32 points)	8	8	18	0	125	Yes
TUG test (s)	15″ 40	15″	12″ 62	2.6%	18.8%	No
PGICS (0–7 points)	6 (much improved)					

TsMS: trans-spinal magnetic stimulation; WISCI II: Walking Index for Spinal Cord Injury; Mini-BEST: short version of the Balance Evaluation Systems Test; TUG: timed get up and go; PGICS: Patient Global Impression of Change Scale; % Change: (value after TsMS – value before TsMS)/value before TsMS × 100; MDC: minimal detectable change

We hypothesized that TsMS could augment the effects of physiotherapy by causing changes in spinal reflexes, especially a decrease in the amplitude of H-reflex [26, 27, 36]. H-reflex is a control measure of spinal motoneuronal excitability. An increase in the amplitude of H-reflex reflects a clinical sign of spasticity [11, 33]. There is high variability in the observed effects of rTMS on H-reflex (a decrease, increase, or no change in the amplitude of H-reflex) [40], depending on the intensity, frequency, and duration of the stimuli used [46, 48] as well as the time since SCI [3]. Consequently, we preferred to use TsMS in the present case.

Only a few studies have assessed the modulatory effects of TsMS on spinal cord functions. Nielsen *et al.* [35] performed the first investigation using TsMS for modifying spasticity in patients with multiple sclerosis. Later, clinical trials were performed to confirm the modulatory effects of TsMS on multiple sclerosis [36, 37], SCI, and healthy subjects [26]. However, these studies only evaluated bodily functions and structures (spasticity) and electrophysiological assessment (stretch reflex), whereas our study evaluated functional and activity recovery and the priming effect of TsMS, since motor recovery improved after the addition of TsMS to the physiotherapy program.

rTMS can augment motor training and enhance the sensitivity of the brain to physiotherapy by increasing cortical excitability [5, 44]. Although no study has proved the relationship between spinal and cortical excitability after TsMS, studies on trans-spinal direct current stimulation (tsDCS) have suggested this relationship [1, 4]. Consequently, we assumed that TsMS also might be a tool for priming the brain to learn. The patient had a history of non-improvement in motor functions with physiotherapy, which could be noted in T-1 and T0 assessments. TsMS could improve balance, allowing the patient to progress from walking with two crutches to walking with no device, braces, and physical assistance. This improvement was reported as “an improvement that has made a real and worthwhile difference” in the PGICS assessment.

From a clinical perspective, we hypothesize that functional recovery could be achieved through improvement in balance. Maintenance of balance is a complex task that requires coordination among somatosensory/proprioceptive, visual, and vestibular systems [19]. It is necessary to activate the muscular fuse through stretch reflex that is directly related to the spinal interneurons for activating the somatosensory system [32]. Previous studies with tsDCS had shown that excitatory stimulation of the spinal cord could modulate polysynaptic and multisegmental spinal reflexes in the case of a nociceptive stimulus [1, 9, 10]. As high-frequency TsMS is also an excitatory stimulation, it may have positively influenced these reflexes and supported the balance recovery in the patient.

Additionally, the patient had improvement in walking independence and functional mobility assessed using the WISCI II scale and TUG test, respectively. In a similar situation such as traumatic SCI, rTMS of the motor cortex area [2] combined with locomotor training [28] was not able to improve walking independence. These researchers chose the technique of transcranial application because of its ability to modify corticospinal projections and change cortical and spinal excitability [2]. However, studies on rTMS for modifying H-reflex have reported uncertain results [40]. H-reflex depends on the intensity, frequency, and duration of rTMS [46, 48] and the time since SCI [3]. Therefore, we chose trans-spinal instead of transcranial application in the present case.

An experimental study with TsMS had shown a decrease in demyelination, an increase in axonal plasticity, and locomotor recovery after SCI in a rodent model [8]. Additionally, there may be a relevant center called Central Pattern Generator (CPG) in the thoracolumbar region that regulates locomotor behavior [23]. During walking, descending commands from neurons of the midbrain and brain stem provide feedback to the CPG, which then generates the walking rhythm and coordinates muscle activation [23]. Thus, in the present case, TsMS applied in combination with a rhythmic locomotor training program, such as a treadmill training program, might have activated the CPG, which, in turn, might have played a very important role in achieving the results of the treatment.

It’s important to highlight the relapsing–remitting nature of NMO, characterized by phases of acute exacerbations followed by spontaneous remissions. Given this cycling pattern of NMO, we must approach the observed therapeutic benefits of combining TsMS with kinesiotherapy with caution. The improvements seen in patient outcomes could coincide with natural fluctuation of the disease, making it challenging to attribute changes directly to the treatment. Therefore, further studies are necessary to explore the efficacy of these interventions, considering the cyclic dynamics of NMO. However, this case report contributes to the body of knowledge on TsMS and also opens avenues for future investigations into its application in neurorehabilitation.

Conclusion

TsMS in combination with kinesiotherapy could improve the balance and walking independence of a patient with NMO-associated transverse myelitis. The patient showed an improvement of 10 points in balance, assessed using

Mini-BEST, and an increase of four levels in the WISCI-II scale for walking independence. This recovery implies an MDC and a patient global impression of "much improved." Therefore, the present case suggests that TsMS is a safe and promising tool for enabling functional recovery in patients with SCI due to NMO-associated transverse myelitis. However, randomized, sham-controlled clinical trials are required to confirm the results of this study and strengthen the evidence regarding the usefulness of TsMS for motor recovery in patients with SCI.

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Author contributions
RB, LS, AB, SR and KMS were responsible for planning the treatment; RB, BM, LS and SR conducted the physiotherapy; BM was responsible for data assessment; RB and AP participated in design and organization of the data in this manuscript; RB and KMS analyzed and interpreted the patient data and were a major contributor in writing and the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Approved by the local ethics committee (Universidade Federal de Pernambuco—Brazil: 4.755.012). Informed written consent to participate was obtained from the patient.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors report there are no competing interests to declare.

Author details
[1]Applied Neuroscience Laboratory, Department of Physical Therapy, Universidade Federal de Pernambuco, Jornalista Aníbal Fernandes Avenue, Recife, PE 50740-560, Brazil. [2]NAPeN Network (Núcleo de Assistência e Pesquisa em Neuromodulação), Recife, Brazil.

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References

1. Albuquerque PL, Campêlo M, Mendonça T, Fontes LA, Brito RD, Monte-Silva K. Effects of repetitive transcranial magnetic stimulation and trans-spinal direct current stimulation associated with treadmill exercise in spinal cord and cortical excitability of healthy subjects: a triple-blind, randomized and sham-controlled study. PLoS ONE. 2018;13(3): e0195276.
2. Benito J, Kumru H, Murillo N, Costa U, Medina J, Tormos JM, Pascual-Leone A, Vidal J. Motor and gait improvement in patients with incomplete spinal cord injury induced by high-frequency repetitive transcranial magnetic stimulation. Top Spinal Cord Injury Rehabil. 2012;18(2):106–12.
3. Benito Penalva J, Opisso E, Medina J, Corrons M, Kumru H, Vidal J, Valls-Solé J. H reflex modulation by transcranial magnetic stimulation in spinal cord injury subjects after gait training with electromechanical systems. Spinal Cord. 2010;48(5):400–6.
4. Bocci T, Barloscio D, Vergari M, Di Rollo A, Rossi S, Priori A, Sartucci F. Spinal direct current stimulation modulates short intracortical inhibition. Neuromodul J Int Neuromodul Soc. 2015;18(8):686–93.
5. Bolognini N, Pascual-Leone A, Fregni F. Using non-invasive brain stimulation to augment motor training-induced plasticity. J Neuroeng Rehabil. 2009;6(March):8.
6. Burns AS, Delparte JJ, Patrick M, Marino RJ, Ditunno JF. The reproducibility and convergent validity of the walking index for spinal cord injury (WISCI) in chronic spinal cord injury. Neurorehabil Neural Repair. 2011;25(2):149–57.
7. Calabrò RS, Naro A, Leo A, Bramanti P. Usefulness of robotic gait training plus neuromodulation in chronic spinal cord injury: a case report. J Spinal Cord Med. 2017;40(1):118–21.
8. Chalfouh C, Guillou C, Hardouin J, Delarue Q, Li X, Duclos C, Schapman D, Marie J-P, Cosette P, Guérout N. The regenerative effect of trans-spinal magnetic stimulation after spinal cord injury: mechanisms and pathways underlying the effect. Neurotherapeutics. 2020;17(4):2069–88.
9. Cogiamanian F, Vergari M, Pulecchi F, Marceglia S, Priori A. Effect of spinal transcutaneous direct current stimulation on somatosensory evoked potentials in humans. Clin Neurophysiol. 2008;119(11):2636–40.
10. Cogiamanian F, Vergari M, Schiaffi E, Marceglia S, Ardolino G, Barbieri S, Priori A. Transcutaneous spinal cord direct current stimulation inhibits the lower limb nociceptive flexion reflex in human beings. Pain. 2011;152(2):370–5.
11. Crone C, Johnsen LL, Biering-Sørensen F, Nielsen JB. Appearance of reciprocal facilitation of ankle extensors from ankle flexors in patients with stroke or spinal cord injury. Brain J Neurol. 2003;126(Pt 2):495–507.
12. Davletshin E, Sabirov D, Rizvanov A, Mukhamedshina Y. Combined approaches leading to synergistic therapeutic effects in spinal cord injury: state of the art. Front Biosci. 2022;27(12):334.
13. Dittuno PL, Ditunno JF Jr. Walking index for spinal cord injury (WISCI II): scale revision. Spinal Cord. 2001;39(12):654–6.
14. Ditunno JF Jr, Ditunno PL, Graziani V, Scivoletto G, Bernardi M, Castellano V, Marchetti M, *et al*. Walking index for spinal cord injury (WISCI): an international multicenter validity and reliability study. Spinal Cord. 2000;38(4):234–43.
15. Fawcett JW, Curt A, Steeves JD, Coleman WP, Tuszynski MH, Lammertse D, Bartlett PF, *et al*. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. Spinal Cord. 2007;45(3):190–205.
16. Ferguson L, Scheman J. Patient global impression of change scores within the context of a chronic pain rehabilitation program. J Pain. 2009;10(4):S73.
17. Franchignoni F, Godi M, Guglielmetti S, Nardone A, Giordano A. Enhancing the usefulness of the mini-BESTest for measuring dynamic balance: a Rasch validation study. Eur J Phys Rehabil Med. 2015;51(4):429–37.
18. Godi M, Franchignoni F, Caligari M, Giordano A, Turcato AM, Nardone A. Comparison of reliability, validity, and responsiveness of the mini-BESTest and Berg balance scale in patients with balance disorders. Phys Ther. 2013;93(2):158–67.
19. Horak FB. Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? Age Ageing. 2006;35(Suppl 2):ii7–11.
20. Horak FB, Wrisley DM, Frank J. The balance evaluation systems test (BESTest) to differentiate balance deficits. Phys Ther. 2009;89(5):484–98.
21. Insausti-Delgado A, López-Larraz E, Nishimura Y, Birbaumer N, Ziemann U, Ramos-Murguialday A. Quantifying the effect of trans-spinal magnetic stimulation on spinal excitability. In: 2019 9th international IEEE/EMBS conference on neural engineering (NER). IEEE; 2019. p. 279–82.
22. Jarius S, Paul F, Weinshenker BG, Levy M, Kim HJ, Wildemann B. Neuromyelitis optica. Nat Rev Dis Prim. 2020;6(1):85.
23. Kiehn O. Locomotor circuits in the mammalian spinal cord. Annu Rev Neurosci. 2006;29:279–306.

24. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, Johansen M, *et al*. International standards for neurological classification of spinal cord injury (revised 2011). J Spinal Cord Med. 2011;34(6):535–46.
25. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. J Speech Lang Hear Res. 2008;51(1):S225–39.
26. Krause P, Edrich T, Straube A. Lumbar repetitive magnetic stimulation reduces spastic tone increase of the lower limbs. Spinal Cord. 2004;42(2):67–72.
27. Krause P, Straube A. Reduction of spastic tone increase induced by peripheral repetitive magnetic stimulation is frequency-independent. NeuroRehabilitation. 2005;20(1):63–5.
28. Kumru H, Benito-Penalva J, Valls-Sole J, Murillo N, Tormos JM, Flores C, Vidal J. Placebo-controlled study of rTMS combined with Lokomat® gait training for treatment in subjects with motor incomplete spinal cord injury. Exp Brain Res Experimentelle Hirnforschung Experimentation Cerebrale. 2016;234(12):3447–55.
29. Lam T, Noonan VK, Eng JJ, SCIRE Research Team. A systematic review of functional ambulation outcome measures in spinal cord injury. Spinal Cord. 2008;46(4):246–54.
30. Leddy AL, Crowner BE, Earhart GM. Utility of the mini-BESTest, BESTest, and BESTest sections for balance assessments in individuals with parkinson disease. J Neurol Phys Ther. 2011;35(2):90–7.
31. Leydeker M, Delva S, Tserlyuk I, Yau J, Wagdy M, Hawash A, Bendaoud S, Mohamed S, Wieraszko A, Ahmed Z. The effects of 15 Hz trans-spinal magnetic stimulation on locomotor control in mice with chronic contusive spinal cord injury. Electromagn Biol Med. 2013;32(2):155–64.
32. MacKinnon CD. Sensorimotor anatomy of gait, balance, and falls. Handb Clin Neurol. 2018;159:3–26.
33. Morita H, Crone C, Christenhuis D, Petersen NT, Nielsen JB. Modulation of presynaptic inhibition and disynaptic reciprocal Ia inhibition during voluntary movement in spasticity. Brain J Neurol. 2001;124(Pt 4):826–37.
34. Nardone R, Höller Y, Thomschewski A, Brigo F, Orioli A, Höller P, Golaszewski S, Trinka E. rTMS modulates reciprocal inhibition in patients with traumatic spinal cord injury. Spinal Cord. 2014;52(11):831–5.
35. Nielsen JF, Klemar B, Hansen HJ, Sinkjaer T. A new treatment of spasticity with repetitive magnetic stimulation in multiple sclerosis. J Neurol Neurosurg Psychiatry. 1995;58(2):254–5.
36. Nielsen JF, Sinkjaer T. Long-lasting depression of soleus motoneurons excitability following repetitive magnetic stimuli of the spinal cord in multiple sclerosis patients. Mult Scler. 1997;3(1):18–30.
37. Nielsen JF, Sinkjaer T, Jakobsen J. Treatment of spasticity with repetitive magnetic stimulation; a double-blind placebo-controlled study. Mult Scler. 1996;2(5):227–32.
38. Nishikawa Y, Maeda N, Kimura H. Physical therapy for a patient with neuromyelitis optica during the acute phase: a case report. SAGE Open Med Case Rep. 2021. https://doi.org/10.1177/2050313X211013679.
39. Nogueira F, Shirahige L, Brito R, Monte-Silva K. Independent community walking after a short protocol of repetitive transcranial magnetic stimulation associated with body weight-support treadmill training in a patient with chronic spinal cord injury: a case report. Physiother Theory Pract. 2020;38(6):839–45.
40. Perez MA, Lungholt BKS, Nielsen JB. Short-term adaptations in spinal cord circuits evoked by repetitive transcranial magnetic stimulation: possible underlying mechanisms. Exp Brain Res Experimentelle Hirnforschung Experimentation Cerebrale. 2005;162(2):202–12.
41. Podsiadlo D, Richardson S. The timed 'up & go': a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–8.
42. Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol. 2009;120(12):2008–39.
43. Sato M, Sugiyama K, Kondo T, Izumi S-I. Rehabilitation for paraplegia caused by neuromyelitis optica: a case report. Spinal Cord. 2014;52(Suppl 3):S14–5.
44. Schabrun SM, Chipchase LS. Priming the brain to learn: the future of therapy? Man Ther. 2012;17(2):184–6.
45. Schreiber AL, Fried GW, Formal CS, DeSouza BX. Rehabilitation of neuromyelitis optica (devic syndrome). Am J Phys Med Rehabil. 2008. https://doi.org/10.1097/phm.0b013e31815b5e1a.
46. Touge T, Gerschlager W, Brown P, Rothwell JC. Are the after-effects of low-frequency rTMS on motor cortex excitability due to changes in the efficacy of cortical synapses? Clin Neurophysiol. 2001;112(11):2138–45.
47. Uzawa A, Mori M, Kuwabara S. Neuromyelitis optica: concept, immunology and treatment. J Clin Neurosci. 2014;21(1):12–21.
48. Valero-Cabré A, Oliveri M, Gangitano M, Pascual-Leone A. Modulation of spinal cord excitability by subthreshold repetitive transcranial magnetic stimulation of the primary motor cortex in humans. NeuroReport. 2001;12(17):3845–8.
49. Wu Y, Zhong L, Geng J. Neuromyelitis optica spectrum disorder: pathogenesis, treatment, and experimental models. Mult Scler Relat Disord. 2019. https://doi.org/10.1016/j.msard.2018.12.002.

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