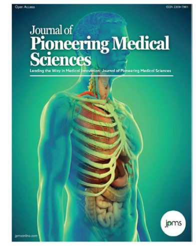

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Effect of Repetitive Transcranial Magnetic Stimulations on Spasticity in Stroke patients: A Randomized Controlled Trial

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Abstract Background & Objectives: Spasticity is a common motor impairment following stroke, significantly impacting patient functionality and quality of life. Repetitive transcranial magnetic stimulation (r-TMS) has gained attention as a non-invasive neuromodulation technique potentially beneficial for reducing spasticity. However, evidence regarding its impact on spinal motor neuron excitability remains inconclusive. This study aimed to investigate the effects of r-TMS combined with conventional physiotherapy on spasticity and spinal motor neuron excitability in stroke patients. Improving understanding of these interventions may help stroke patients achieve better movement control and enhance their overall rehabilitation outcomes. **Methods:** A randomized controlled trial was conducted involving 30 chronic stroke patients divided into two groups: Group-A (experimental; r-TMS with conventional physiotherapy) and Group-B (control; conventional physiotherapy alone). Intervention lasted 4 weeks, with 12 sessions administered (3 sessions/week). Clinical assessment of spasticity (Modified Ashworth Scale, MAS) and electrophysiological evaluations (H-reflex latency and amplitude) were measured pre- and post-intervention. **Results:** Post-intervention, Group-A demonstrated significant reductions in spasticity (MAS scores decreased from 2.4±0.6 to 1.2±0.5, p<0.001) compared to Group-B (2.3±0.7 to 1.9±0.6, p=0.02). Electrophysiological outcomes revealed significantly increased H-reflex latency (30.2±1.9ms to 32.8±1.6ms, p<0.001) and decreased amplitude (2.9±0.6mV to 1.7±0.5mV, p<0.001) in Group-A, indicating reduced spinal excitability, with minimal changes observed in Group-B. **Conclusions:** Integrating r-TMS with conventional physiotherapy effectively reduces spasticity and modulates spinal motor neuron excitability post-stroke. These findings support r-TMS as a valuable adjunct intervention in stroke rehabilitation protocols.

Key Words Stroke, Spasticity, Repetitive Transcranial Magnetic Stimulation, H-reflex, Physiotherapy, Rehabilitation

INTRODUCTION

Stroke remains one of the most prevalent neurological disorders and a leading cause of disability globally, affecting millions annually [1]. It significantly impacts individuals' physical, cognitive, emotional and social functions, posing substantial burdens on healthcare systems [2]. Motor impairments such as muscle weakness, impaired coordination and particularly spasticity represent prominent consequences of stroke, substantially influencing functional independence and quality of life [3,4].

Spasticity is characterized clinically by a velocity-dependent increase in muscle tone and exaggerated stretch reflexes due to disrupted supraspinal control and spinal hyperexcitability [5,6]. Approximately 30-80% of stroke survivors experience spasticity, highlighting its importance as a target for rehabilitation interventions [7]. Left unmanaged, spasticity can lead to contractures, pain and functional limitations that impede recovery [8]. Current management strategies include pharmacological treatments, such as baclofen and botulinum toxin injections and non-pharmacological interventions like physiotherapy and neuromodulation techniques [9,10]. However, these treatments possess limitations, including side effects, invasive nature, or inconsistent efficacy. Therefore, exploring safe, effective and non-invasive rehabilitation modalities remains crucial.

Repetitive Transcranial Magnetic Stimulation(r-TMS) has emerged as an increasingly popular intervention in stroke rehabilitation due to its non-invasiveness, minimal side-effects, ease of application and cost-effectiveness [11,12]. r-TMS involves delivering low-voltage electrical currents via surface electrodes on the skin, stimulating peripheral nerves to modulate neural activity. Studies suggest that r-TMS can decrease spasticity by altering spinal reflex activity and promoting cortical reorganization, ultimately enhancing functional recovery post-stroke [13,14].

Several systematic reviews have reported beneficial effects of r-TMS in stroke rehabilitation, including reductions in muscle spasticity and improvements in functional tasks such as gait and upper limb function [15,16]. Nonetheless, the precise neural mechanisms through which r-TMS exerts its therapeutic effects remain inadequately understood, limiting the ability to optimize treatment parameters and clinical application.

The Hoffmann reflex (H-reflex), an electrophysiological measure of spinal motor neuron excitability, has been widely employed in clinical research to evaluate neural changes post-stroke [17]. The H-reflex represents a monosynaptic reflex elicited by electrically stimulating IA sensory afferent fibers, providing insights into spinal motor neuron pool excitability and reflex circuit function [18]. Following stroke, increased H-reflex amplitudes and decreased latencies commonly occur, indicating enhanced spinal excitability and disrupted inhibitory control. Therefore, H-reflex assessments can objectively quantify spinal reflex modulation, offering valuable insights into r-TMS induced neurophysiological changes.

Recent studies investigating the effects of r-TMS on spinal excitability post-stroke have demonstrated promising but varied results. Some researchers reported significant reductions in H-reflex amplitude and increases in latency, suggesting decreased spinal excitability following r-TMS interventions [19,20]. In contrast, others have found minimal or inconsistent changes in H-reflex parameters, underscoring the need for further research to clarify these discrepancies [21,22].

Despite extensive research exploring r-TMS for stroke-related motor deficits, gaps in knowledge persist regarding optimal stimulation parameters (frequency, duration, intensity, electrode placement) and precise neural mechanisms [23,24]. Understanding these factors is critical for developing evidence-based guidelines to maximize clinical efficacy. Recent reviews advocate for individualized parameter selection based on patient-specific clinical presentations and electrophysiological profiles, highlighting the complexity and heterogeneity of stroke populations [25].

Moreover, current literature emphasizes combining r-TMS with conventional rehabilitation modalities, such as physiotherapy exercises and task-specific training, to exploit potential synergistic effects in promoting neuroplasticity and enhancing motor recovery [26]. However, standardized clinical protocols integrating r-TMS into routine stroke rehabilitation practices remain lacking, necessitating further investigation to substantiate integrated therapeutic approaches.

Identifying affordable, accessible and non-invasive treatments such as r-TMS could significantly improve stroke recovery outcomes for patients in local healthcare settings.

The primary objective of this study is to evaluate the effectiveness of repetitive transcranial magnetic stimulation (r-TMS) combined with conventional physiotherapy in reducing spasticity among chronic stroke patients. Specifically, the study aims to (1) assess changes in clinical spasticity levels using the Modified Ashworth Scale (MAS) and (2) measure neurophysiological changes in spinal motor neuron excitability through H-reflex parameters, including latency and amplitude.

Additionally, the study seeks to compare the outcomes between patients receiving combined r-TMS and physiotherapy versus those undergoing physiotherapy alone. Through these evaluations, the research aims to clarify the therapeutic mechanisms of r-TMS and its potential integration into routine stroke rehabilitation practices, particularly to enhance recovery outcomes in local healthcare settings.

METHODS

This study was designed as an experimental, randomized controlled trial aimed at evaluating the effect of Repetitive Transcranial Magnetic Stimulation(r-TMS) on spinal motor neuron excitability in patients with stroke. Ethical approval for the study was obtained from the institutional review board and informed consent was obtained from all participants prior to initiation. This study was conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines to ensure transparency, completeness and methodological rigor in the design, implementation and reporting of randomized controlled trials.

Participants

Thirty participants diagnosed with stroke (ischemic or haemorrhagic), confirmed by medical imaging (CT or MRI), were recruited from a neurology rehabilitation unit. The inclusion criteria included chronic stroke (>6 months post-onset), age between 40 and 70 years, clinically evident spasticity (Modified Ashworth Scale [MAS] ≥ 1+) and the ability to follow simple commands. Participants with severe cognitive deficits, sensory loss, recent fractures or skin lesions near the treatment site, epilepsy, pacemakers, or severe cardiovascular comorbidities were excluded. Following the CONSORT guidelines ensured that all critical aspects of the study-including participant selection, randomization process, intervention details, outcome measures and statistical analyses-were systematically and transparently reported.

The sample size was calculated based on an expected moderate effect size (Cohen's d = 0.6) for differences in MAS scores between groups, with a power of 80% ($\beta = 0.20$) and a significance level of 5% ($\alpha = 0.05$). Using these parameters and accounting for a potential 10% dropout rate, a minimum of 15 participants per group (total n = 30) was determined to be sufficient to detect statistically significant differences between interventions. The calculation was performed using G*Power software (version 3.1.9.7).

Participants were randomly allocated into two equal groups (Group A: Experimental group, receiving r-TMS plus conventional physiotherapy and Group B: Control group, receiving conventional physiotherapy only), using computerized block randomization.

Intervention Protocol

The experimental group (Group A) received r-TMS in addition to a standard physiotherapy protocol, while the control group (Group B) received only standard physiotherapy. The intervention lasted for 4 weeks, comprising 12 sessions of therapy (3 sessions per week).

Repetitive Transcranial Magnetic Stimulation (r-TMS) is administered using a figure-8 coil positioned over the ipsilesional or contralesional motor cortex, depending on the targeted modulation. Stimulation frequency ranges from 1 Hz (inhibitory) to 10 Hz (excitatory). Intensity is set at 80-110% of the resting motor threshold (RMT), determined via motor evoked potentials. Sessions last 20-30 minutes, delivering 1,000-3,000 pulses daily over 4 weeks. Coil placement follows the 10-20 EEG system, commonly over M1. Patients are monitored for adverse effects. This protocol enhances neuroplasticity and functional recovery post-stroke.

Each r-TMS session lasted 30 minutes, administered prior to conventional physiotherapy exercises. The standard physiotherapy exercises included passive and active-assisted range-of-motion exercises, stretching and task-specific functional training aimed at improving motor control and mobility.

Outcome Measures

The changes were assessed using clinical spasticity scores (Modified Ashworth Scale, MAS) and electrophysiological parameters (H-reflex latency and amplitude). Clinical evaluation of spasticity was performed using the Modified Ashworth Scale (MAS) for the affected lower extremity muscles at baseline and post-intervention. Assessments were conducted by an independent blinded assessor to ensure objectivity.

Likewise, Spinal motor neuron excitability was quantitatively assessed using the Hoffmann reflex (H-reflex). Electromyographic (EMG) recordings were captured using surface EMG electrodes placed over the soleus muscle, with participants in a relaxed supine position. The tibial nerve was stimulated electrically at the popliteal fossa using a monophasic square-wave pulse of 1 ms duration. The H-reflex latency and amplitude were recorded at baseline (pre-intervention), immediately after completion of the 4-week intervention and analyzed for intra-group and inter-group comparisons (Figure 1).

Data Analysis

Statistical analyses were conducted using SPSS software (version 25.0). Descriptive statistics (Mean±standard deviation) were utilized to summarize demographic characteristics and outcomes. Paired t-tests were conducted for intra-group comparisons (pre- and post-intervention) to assess changes in spinal motor neuron excitability (H-reflex latency and amplitude) and MAS scores. Independent t-tests were used for inter-group comparisons to evaluate differences in outcomes between the experimental and control groups. Statistical significance was set at a p-value of less than 0.05.

RESULTS

This study investigated the effects of repetitive transcranial magnetic stimulation (r-TMS) on spinal motor neuron excitability in patients with stroke by assessing changes in clinical spasticity scores (Modified Ashworth Scale, MAS) and electrophysiological parameters (H-reflex latency and amplitude). A comparative analysis was performed between Group-A (experimental, r-TMS plus conventional physiotherapy) and Group-B (control, conventional physiotherapy only).

Participant Demographics

A total of 30 stroke patients participated in this study, with 15 allocated to each group. Group-A (experimental, r-TMS plus conventional physiotherapy) and Group-B (control, conventional physiotherapy only). The demographic data indicated no significant differences between the groups regarding age, gender, or baseline clinical characteristics, confirming homogeneity across both groups.

Clinical Assessment (MAS scores)

Both groups exhibited reductions in MAS scores post-intervention. However, the experimental group (Group-A) demonstrated a significantly greater improvement in spasticity compared to the control group (Group-B), as shown in Table 1.

Electrophysiological Assessment (H-reflex Latency)

At baseline, H-reflex latency values were similar between the groups, indicating comparable spinal motor neuron excitability prior to intervention. Following intervention, Group-A demonstrated a significant increase in H-reflex latency, reflecting a reduction in spinal excitability. In contrast, Group-B showed minimal, non-significant changes (Table 2).

Inter-group comparison of post-intervention latencies revealed significant differences favoring Group-A ($p<0.01$, Table 4).

Electrophysiological Assessment (H-reflex Amplitude)

H-reflex amplitude, indicative of spinal motor neuron excitability, decreased significantly in Group-A after intervention. The control group (Group-B) experienced only slight and statistically insignificant changes, as illustrated in Table 3.

Inter-group comparison of post-intervention amplitudes showed statistically significant improvements in Group-A compared to Group-B ($p<0.01$). An overall summary of post-intervention intergroup comparisons showed significant differences favouring Group-A across all measured parameters.

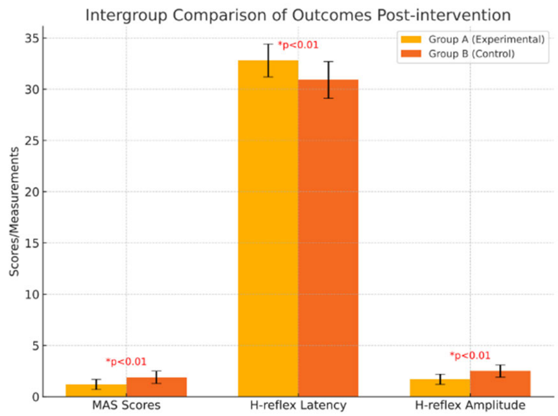

Figure 1: Intergroup comparison of outcomes Post-intervention

Table 1: Modified Ashworth Scale (MAS) Scores-intragroup comparison

Group	Baseline MAS (Mean±SD)	Post-Intervention MAS (Mean±SD)	p-value
Group-A (Experimental)	2.4±0.6	1.2±0.5	<0.001*
Group-B (Control)	2.3±0.7	1.9±0.6	0.02*

*Significant at p<0.05

Table 2: H-reflex latency (ms)-intragroup comparison

Group	Baseline Latency (Mean±SD)	Post-Intervention Latency (Mean±SD)	p-value
Group-A (Experimental)	30.2±1.9	32.8±1.6	<0.001*
Group-B (Control)	30.4±2.0	30.9±1.8	0.09

*Significant at p<0.05

Table 3: H-reflex amplitude (mV)-intragroup comparison

Group	Baseline Amplitude (Mean±SD)	Post-Intervention Amplitude (Mean±SD)	p-value
Group-A (Experimental)	2.9±0.6	1.7±0.5	<0.001*
Group-B (Control)	2.8±0.7	2.5±0.6	0.15

*Significant at p<0.05

Table 4: Intergroup comparison of outcomes post-intervention

Outcome Measure	Group-A (Mean±SD)	Group-B (Mean±SD)	p-value
MAS scores	1.2±0.5	1.9±0.6	<0.01*
H-reflex latency (ms)	32.8±1.6	30.9±1.8	<0.01*
H-reflex amplitude (mV)	1.7±0.5	2.5±0.6	<0.01*

*Significant at p<0.05

DISCUSSION

This study demonstrated that combining repetitive transcranial magnetic stimulation (r-TMS) with conventional physiotherapy was significantly more effective than physiotherapy alone in improving stroke-related spasticity and reducing spinal motor neuron excitability. Patients in the r-TMS group (Group-A) showed greater reductions in spasticity scores (MAS), significant increases in H-reflex latency and significant decreases in H-reflex amplitude compared to the control group (Group-B). These findings suggest that r-TMS, when integrated with physiotherapy, offers superior benefits in enhancing motor recovery and reducing neural hyperexcitability after stroke.

These results are consistent with and expand upon existing literature, providing a comprehensive understanding of r-TMS's therapeutic potential in stroke rehabilitation. For instance, a systematic review and meta-analysis by Xu *et al.* [27] concluded that r-TMS, particularly when applied for more than 30 minutes over motor cortex, effectively reduces lower limb spasticity in chronic stroke survivors. Similarly, Fan *et al.* [28] also buttressed this point that r-TMS application led to significant improvements in spasticity and motor function in hemiplegic stroke patients, suggesting that r-TMS may facilitate neural plasticity and functional recovery.

In earlier randomized controlled trial, Yan and Hui-Chan [20] found that combining r-TMS with task-related training significantly improved lower limb functions in chronic stroke patients, further supporting the adjunctive use of r-TMS in rehabilitation programs. A decade later, another study by Şan, Yılmaz and Kesikburun [29] reported that r-TMS applied to acupuncture points improved muscle function in multiple sclerosis, indicating the versatility of r-TMS application methods in spasticity management.

However, on the contrary there are few studies that have reported minimal or no significant effects of repetitive transcranial magnetic stimulation (r-TMS) on spasticity [30-32]. The study by Wang *et al.* [30] found that while r-TMS improved balance, its effect on spasticity was not statistically significant. These discrepancies may be attributed to variations in study design, r-TMS parameters, duration of intervention and patient characteristics. Therefore, standardizing r-TMS protocols and tailoring interventions to individual patient needs are crucial for optimizing therapeutic outcomes.

The increase in H-reflex latency and decrease in amplitude observed in this study indicate a reduction in spinal motor neuron excitability following r-TMS intervention. These electrophysiological changes are consistent with findings from previous research. For instance, a study by Chen *et al.* [21] demonstrated that r-TMS application resulted in prolonged H-reflex latency and reduced amplitude in stroke patients, suggesting enhanced presynaptic inhibition and modulation of spinal reflex pathways.

Similarly, Aydın *et al.* [33] reported that r-TMS application led to significant decreases in H-reflex amplitude in patients with spasticity, indicating reduced excitability of the monosynaptic reflex arc. These findings are corroborated by Hui-Chan and Levin [34], who observed prolonged stretch reflex latencies following r-TMS application in spastic hemiparetic subjects, suggesting that r-TMS may enhance inhibitory mechanisms within the spinal cord.

In contrast, some studies have reported no significant changes in H-reflex parameters following r-TMS intervention. For example, a study by Abdelkader *et al.* [35] found that r-TMS did not significantly alter H-reflex or F-wave parameters in healthy subjects. These inconsistencies highlight the need for further research to elucidate the mechanisms underlying r-TMS induced modulation of spinal excitability and to identify factors influencing individual responses to r-TMS therapy.

The exact mechanisms by which r-TMS reduces spasticity are not fully understood; however, several hypotheses have been proposed. One plausible mechanism is the activation of inhibitory interneurons within the spinal cord, leading to enhanced presynaptic inhibition of Ia afferent fibers and subsequent reduction in motor neuron excitability [36]. This mechanism is supported by the observed decreases in H-reflex amplitude following r –TMS application, indicating reduced excitability of the monosynaptic reflex pathway.

Another proposed mechanism involves the modulation of supraspinal structures. r-TMS may influence cortical excitability and promote neuroplastic changes in the central nervous system, thereby improving motor control and reducing spasticity [37,38]. Functional neuroimaging studies have shown that r-TMS can modulate activity in brain regions associated with motor control, suggesting a central mechanism of action.

Additionally, r-TMS may exert its effects through sensory gating mechanisms, wherein the stimulation of large-diameter afferent fibers inhibits the transmission of nociceptive and non-nociceptive inputs at the spinal level, leading to reduced spasticity [11]. This hypothesis is supported by studies demonstrating that r-TMS application reduces hyperactive stretch reflexes and passive resistive torque in spastic muscles [20].

The findings of this study have important clinical implications for stroke rehabilitation. The significant reduction in spasticity and modulation of spinal excitability observed with r-TMS application suggest that r-TMS can be an effective adjunct to conventional physiotherapy in managing post-stroke spasticity. Clinicians should consider incorporating r-TMS into rehabilitation programs, particularly for patients with significant spasticity that impairs functional performance.

A major strength of this study is its focused investigation on chronic stroke patients, a population often underrepresented in neuromodulation research. By specifically targeting individuals in the chronic phase, the study provides valuable insights into long-term neuroplastic potential beyond the acute recovery window.

To optimize therapeutic outcomes, it is essential to individualize r-TMS parameters, including frequency, intensity, pulse duration and electrode placement, based on patient-specific factors such as the severity of spasticity, muscle groups affected and overall health status [12]. Additionally, combining r-TMS with other rehabilitation modalities, such as task-oriented training and functional electrical stimulation, may yield synergistic effects and further enhance motor recovery.

However, it is crucial to be aware of the limitations and contraindications of r-TMS therapy. Patients with pacemakers or other implanted electronic devices should avoid r-TMS due to the risk of interference. Moreover, clinicians should monitor patients for potential adverse effects, such as skin irritation or discomfort at the electrode sites and adjust treatment parameters accordingly.

CONCLUSIONS

This study demonstrates that combining repetitive transcranial magnetic stimulation (r-TMS) with conventional physiotherapy significantly improves spasticity and reduces spinal motor neuron excitability in chronic stroke patients, compared to physiotherapy alone. The findings highlight the potential of r-TMS as an effective, non-invasive adjunct to enhance stroke rehabilitation outcomes. Continued research aimed at optimizing protocols, understanding underlying neural mechanisms and personalizing treatment strategies promises to enhance recovery trajectories and substantially improve the quality of rehabilitation care for stroke survivors.

Limitations

Despite the promising findings, this study has several limitations that warrant consideration. The relatively small sample size may limit the generalizability of the results. Future studies with larger, more diverse populations are needed to confirm these findings and establish standardized r-TMS protocols for spasticity management.

Additionally, the short duration of the intervention period in this study precludes conclusions about the long-term effects of r-TMS on spasticity and motor function. Longitudinal studies are necessary to assess the sustainability of r-TMS induced improvements and to determine the optimal duration and frequency of r-TMS application for long-term management of spasticity.

Furthermore, while this study focused on lower limb spasticity, future research should explore the effects of r-TMS on upper limb spasticity and functional outcomes. Given the functional importance of upper limb movements in daily activities, understanding the potential benefits of r-TMS in this context is crucial.

Lastly, mechanistic studies using advanced neuroimaging and electrophysiological techniques are needed to elucidate the central and peripheral mechanisms underlying r-TMS induced spasticity reduction. Such studies could inform the development of targeted interventions and enhance our understanding of neural plasticity in response to r-TMS therapy.

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Conflicts of Interest

The author declares that there are no conflicts of interest.

REFERENCES

[1] Benjamin, Emelia J. *et al.* "Heart disease and stroke statistics-2019 update: a report from the American Heart Association." *Circulation,* vol. 139, no. 10, January 2019, pp. e56-e528. https://www.ahajournals.org/doi/full/10.1161/CIR.0000000000000659.

[2] Feigin, Valery L. *et al.* "Global, regional and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019." *The Lancet Neurology,* vol. 20, no. 10, October 2021, pp. 795-820. https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(21)00252-0/fulltext?%20dgcid=raven_jbs_etoc_email.

[3] Li, Sheng and Gerard E. Francisco. "New insights into the pathophysiology of post-stroke spasticity." *Frontiers in Human Neuroscience,* vol. 9, April 2015. https://www.frontiersin.org/articles/10.3389/fnhum.2015.00192/full.

[4] Pandyan, Anand *et al.* "Spasticity: clinical perceptions, neurological realities and meaningful measurement." *Disability and Rehabilitation,* vol. 27, no. 1, 2005, pp. 2-6. https://www.tandfonline.com/doi/pdf/10.1080/09638280400014576.

[5] Lance, J.W. "Immunostimulating influence of herbal biomedicines on nonspecific immunity in grouper *Epinephelus tauvina* juvenile against *Vibrio harveyi* infection.." Spasticity: Disordered Motor Control, edited by Lance, J.W., Feldman, R.G., Young, R.R. and Koella, W.P., Chicago, CiNii Research,, 1980,, pp. 185-204. https://cir.nii.ac.jp/crid/1571980076255259520.

[6] Nielsen, Jens Bo *et al.* "The spinal pathophysiology of spasticity–from a basic science point of view." *Acta physiologica,* vol. 189, no. 2, January 2007, pp. 171-180. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1748-1716.2006.01652.x.

[7] Wissel, Jörg *et al.* "Toward an epidemiology of poststroke spasticity." *Neurology,* vol. 80, no. 3, January 2013, pp. S13-S19. https://www.neurology.org/doi/abs/10.1212/WNL.0b013e3182762448.

[8] Barnes, Michael P. "Medical management of spasticity in stroke." *Age and Ageing,* vol. 30, 2001, pp. 13-17.

[9] Francisco, Gerard E. *et al.* "Clinical pathways in stroke rehabilitation: Evidence-based clinical practice recommendations." Post-Stroke spasticity, edited by Gerard E. Francisco, United states, Springer, 2021, pp. 149-173. https://www.ncbi.nlm.nih.gov/books/NBK585580/.

[10] Chang, Eric Y. *et al.* "Immunostimulating influence of herbal biomedicines on nonspecific immunity in grouper *Epinephelus tauvina* juvenile against *Vibrio harveyi* infection.." Physical and Rehabilitation Medicine, edited by Markad Kamath, United states, Critical Reviews™, 2015, pp. 1-2. https://www.dl.begellhouse.com/journals/757fcb0219d89390,4ad21a6e021863fa,14fc2ebd541aeead.html.

[11] Sluka, Kathleen A. and Deirdre Walsh. "Transcutaneous electrical nerve stimulation: basic science mechanisms and clinical effectiveness." *The Journal of Pain,* vol. 4, no. 3, April 2003, pp. 109-121. https://www.sciencedirect.com/science/article/pii/S152659000300484X.

[12] Johnson, Mark I. and Jan M. Bjordal. "Transcutaneous electrical nerve stimulation for the management of painful conditions: focus on neuropathic pain." *Expert Review of Neurotherapeutics,* vol. 11, no. 5, January 2014, pp. 735-753. https://www.tandfonline.com/doi/abs/10.1586/ern.11.48.

[13] Sabut, Sukanta K. *et al.* "Functional electrical stimulation of dorsiflexor muscle: effects on dorsiflexor strength, plantarflexor spasticity and motor recovery in stroke patients." *NeuroRehabilitation,* vol. 29, no. 4, December 2011, pp. 393-400. https://journals.sagepub.com/doi/abs/10.3233/NRE-2011-0717.

[14] Levin, Mindy F. and Christina WY Hui-Chan. "Relief of hemiparetic spasticity by TENS is associated with improvement in reflex and voluntary motor functions." *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section,* vol. 85, no. 2, April 1992, pp. 131-142. https://www.sciencedirect.com/science/article/pii/016855979290079Q.

[15] Mahmood, Amreen *et al.* "Effect of transcutaneous electrical nerve stimulation on spasticity in adults with stroke: a systematic review and meta-analysis." *Archives of Physical Medicine and Rehabilitation,* vol. 100, no. 4, April 2019, pp. 751-768. https://www.sciencedirect.com/science/article/pii/S0003999318314552.

[16] Mills, Patricia Branco and Farhana Dossa. "Transcutaneous electrical nerve stimulation for management of limb spasticity: a systematic review." *American Journal of Physical Medicine & Rehabilitation,* vol. 95, no. 4, April 2016, pp. 309-318. https://journals.lww.com/ajpmr/fulltext/2016/04000/Transcutaneous_Electrical_Nerve_Stimulation_for.9.aspx.

[17] Misiaszek, John E. “The H-reflex as a tool in neurophysiology: Its limitations and uses in understanding nervous system function.” *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine,* vol. 28, no. 2, May 2003, pp. 144-160. https://onlinelibrary.wiley.com/doi/abs/10.1002/mus.10372.

[18] Knikou, Maria. “The H-reflex as a probe: pathways and pitfalls.” *Journal of neuroscience methodsm,* vol. 171, no. 1, June 2008, pp. 1-12. https://www.sciencedirect.com/science/article/pii/S0165027008001192.

[19] Ng, Shamay S.M. and Christina WY Hui-Chan. “Transcutaneous electrical nerve stimulation combined with task-related training improves lower limb functions in subjects with chronic stroke.” *Stroke,* vol. 38, no. 11, September 2007, pp. 2953-2959. https://www.ahajournals.org/doi/full/10.1161/STROKEAHA.107.490318.

[20] Yan, Tiebin and Christina WY Hui-Chan. “Transcutaneous electrical stimulation on acupuncture points improves muscle function in subjects after acute stroke: a randomized controlled trial.” *Journal of rehabilitation medicine,* vol. 41, no. 5, 2009, pp. 312-316. https://ira.lib.polyu.edu.hk/handle/ 10397/5754.

[21] Chen, Xiao *et al.* “Effects of repetitive transcranial magnetic stimulation in multiple sclerosis: a systematic review and meta-analysis.” *Multiple sclerosis and related disorders,* vol. 59, March 2022. https://www.sciencedirect.com/science/article/pii/S2211034822000797.

[22] Etoh, Seiji *et al.* “Effects of repetitive trascranial magnetic stimulation on repetitive facilitation exercises of the hemiplegic hand in chronic stroke patients.” *Journal of rehabilitation medicine,* vol. 45, no. 9, September 2013, pp. 843-847. https://europepmc.org/ article/med/23817976.

[23] Bjordal, Jan Magnus *et al.* “Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain.” *European Journal of Pain,* vol. 7, no. 2, April 2003, pp. 181-188. https://www.sciencedirect.com/science/article/pii/S1090380102000988.

[24] Johnson, Mark I. *et al.* “Transcutaneous electrical nerve stimulation for acute pain.” *Cochrane Database of Systematic Reviews,* vol. 6, June 2015. https://www. cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006142.pub3/abstract.

[25] Gladstone, David J. *et al.* “The Fugl-Meyer assessment of motor recovery after stroke: a critical review of its measurement properties.” *Neurorehabilitation and neural repair,* vol. 16, no. 3, September 2002, pp. 232-240. https://journals.sagepub.com/doi/abs/10.1177/154596802401105171.

[26] Kesar, Trisha M. *et al.* “Combined effects of fast treadmill walking and functional electrical stimulation on post-stroke gait.” *Gait & posture,* vol. 33, no. 2, February 2011, pp. 309-313. https://www.sciencedirect.com/science/article/pii/ S0966 636210004078.

[27] Xu, Peng *et al.* “Repetitive transcranial magnetic stimulation as an alternative therapy for stroke with spasticity: a systematic review and meta-analysis.” *Journal of Neurology,* vol. 268, July 2020, pp. 4013-4022. https://link.springer.com/article/10.1007/s00415-020-10058-4.

[28] Fan, Huiliu *et al.* “The effect of repetitive transcranial magnetic stimulation on lower-limb motor ability in stroke patients: a systematic review.” *Frontiers in Human Neuroscience,* vol. 15, September 2021. https://www.frontiersin.org/articles/10.3389/fnhum.2021.620573/full.

[29] Şan, Ayça Uran *et al.* “The effect of repetitive transcranial magnetic stimulation on spasticity in patients with multiple sclerosis.” *Journal of Clinical Neurology,* vol. 15, no. 4, October 2019, pp. 461-467. https://pubmed.ncbi.nlm. nih.gov/31591833/.

[30] Wang, Xiaohan *et al.* “Effects of non-invasive brain stimulation on post-stroke spasticity: a systematic review and meta-analysis of randomized controlled trials.” *Brain sciences,* vol. 12, no. 7, June 2022. https://www.mdpi. com/2076-3425/12/7/836.

[31] Naghdi, Soofia *et al.* “A pilot study on the effects of low frequency repetitive transcranial magnetic stimulation on lower extremity spasticity and motor neuron excitability in patients after stroke.” *Journal of bodywork and movement therapies,* vol. 19, no. 4, October 2015, pp. 616-623. https:// www.sciencedirect.com/science/article/pii/S1360859214001831.

[32] Mori, Francesco *et al.* “The use of repetitive transcranial magnetic stimulation (rTMS) for the treatment of spasticity.” *Progress in brain research,* vol. 175, 2009, pp. 429-439. https://www.sciencedirect.com/science/article/pii/S0079 612309175283.

[33] Aydn, Gülümser *et al.* “Transcutaneous Electrical Nerve Stimulation Versus Baclofen in Spasticity: Clinical and Electrophysiologic Comparison.” *American Journal of Physical Medicine & Rehabilitation,* vol. 84, no. 8, August 2005, pp. 584-592.

[34] Hui-Chan, Christina W.Y. and Mindy F. Levin. “Stretch reflex latencies in spastic hemiparetic subjects are prolonged after transcutaneous electrical nerve stimulation.” *Canadian Journal of Neurological Sciences,* vol. 20, no. 2, September 2015, pp. 97-106.

[35] Abdelkader, Ann A. *et al.* “Repetitive transcranial magnetic stimulation effect in multiple sclerosis spasticity (clinical and electrophysiological evaluation): A preliminary Egyptian study.” *Egyptian J Neurol Psychiatry Neurosurg,* vol. 50, no. 2, April 2013, pp. 157-162.

[36] Hiraoka, K. “Neural mechanisms underlying the effect of transcutaneous electrical nerve stimulation in humans.” *Electromyography and Clinical Neurophysiology,* vol. 42, no. 6, September 2002, pp. 359-366. https://europepmc.org/article/med/1222 4473.

[37] Şan, Ayça Uran *et al.* “The effect of repetitive transcranial magnetic stimulation on spasticity in patients with multiple sclerosis.” *Journal of Clinical Neurology*, vol. 15, no. 4, October 2019, pp. 461-467. https://pubmed.ncbi.nlm.nih.gov/31591833/.

[38] Liu, Yu *et al.* “A Meta-Analysis: Whether Repetitive Transcranial Magnetic Stimulation Improves Dysfunction Caused by Stroke with Lower Limb Spasticity.” *Evidence-Based Complementary and Alternative Medicine,* vol. 1, November 2021. https://onlinelibrary.wiley. com/ doi/abs/10.1155/2021/7219293.