Retrospective Review

Transcranial and Transcutaneous Stimulation for Pain: What Have We Learned From the COVID-19 Pandemic Shutdown?

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Background: Transcranial magnetic stimulation (TMS) and transcutaneous magnetic stimulation (tMS) offer a novel noninvasive treatment option for chronic pain. While the recent COVID-19 pandemic caused by the SARS-CoV-2 virus resulted in a temporary interruption of the treatments for patients, it provided an excellent opportunity to assess the long-term sustainability of the treatment, and the feasibility of resuming the treatments after a brief period of interruption as no such data are available in current literature.

Methods: First, a list of patients whose pain/headache conditions have been stably controlled with either treatment for at least 6 months prior to the 3-month pandemic-related shutdown was generated. Those who returned for treatments after the shutdown were identified and their underlying pain diagnoses, pre- and posttreatment Mechanical Visual Analog Scale (M-VAS) pain scores, 3-item Pain, Enjoyment, and General Activity (PEG-3), and Patient Health Questionnaire-9 scores were assessed in 3 phases: Phase I (P1) consisted of a 6-month pre-COVID-19 period in which pain conditions were stably managed with either treatment modality; Phase II (P2) consisted of the first treatment visit period immediately after COVID-19 shutdown; and Phase III (P3) consisted of a 3-4 month post-COVID-19 shutdown period patients received up to 3 sessions of either treatment modality after the P2 treatment.

Results: For pre- and posttreatment M-VAS pain scores, mixed-effect analyses for both treatment groups demonstrated significant ($P < 0.01$) time interactions across all phases. For pretreatment M-VAS pain scores, TMS (n = 27) between-phase analyses indicated a significant (F = 13.572, $P = 0.002$) increase from 37.7 ± 27.6 at P1 to 49.6 ± 25.9 at P2, which then decreased significantly (F = 12.752, $P = 0.001$) back to an average score of 37.1 ± 24.7 at P3. Similarly, tMS (n = 25) between-phase analyses indicated the mean pretreatment pain score (mean ± standard deviation [SD]) increased significantly (F = 13.383, $P = 0.003$) from 34.9 ± 25.1 at P1 to 56.3 ± 27.0 at P2, which then decreased significantly (F = 5.464, $P = 0.027$) back to an average score of 41.9 ± 26.4 at P3. For posttreatment pain scores, the TMS group between-phase analysis indicated the mean posttreatment pain score (mean ± SD) increased significantly (F = 14.206, $P = 0.002$) from 25.6 ± 22.9 at P1 to 36.2 ± 23.4 at P2, which then significantly decreased (F = 16.063, $P < 0.001$) back to an average score of 23.2 ± 21.3 at P3. The tMS group between-phase analysis indicates a significant (F = 8.324, $P = 0.012$) interaction between P1 and P2 only with the mean posttreatment pain score (mean ± SD) increased from 24.9 ± 25.7 at P1 to 36.9 ± 26.7 at P2. The combined PEG-3 score between-phase analyses demonstrated similar significant ($P < 0.001$) changes across the phases in both treatment groups.

Conclusions: Both TMS and tMS treatment interruptions resulted in an increase of pain/headache severity and interference of quality of life and functions. However, the pain/headache symptoms, patients' quality of life, or function can quickly be improved once the maintenance treatments were restarted.

Key words: Pain, headache, transcranial magnetic stimulation (TMS), transcutaneous magnetic stimulation (tMS), COVID_19 pandemic

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Transcranial magnetic stimulation (TMS) and transcutaneous magnetic stimulation (tMS) offer a means of noninvasive and nonpharmalogical intervention for pain and headaches (1,2). Both treatments, which can be delivered via a figure-of-8 magnetic coil, have been an integral component of pain interventions. However, due to the recent COVID-19 pandemic caused by the SARS-CoV-2 virus and the subsequent shutdown of elective pain interventional procedures, which include both TMS and tMS treatments, patients whose pain or headache were previously under stable control with the treatments lost the therapeutic access. While the shutdown transiently interrupted the treatments for the patients, it provided a unique opportunity to assess the long-term sustainability of the treatments, the requirement of ongoing maintenance treatments, and the feasibility of resuming the treatments after a brief period of treatment interruption as no such data have been reported in the current literature. This current study consisting of a combination of retrospective and prospective record review intends to illustrate how the temporary interruption of treatments may adversely affect their pain and quality of life and how resumption of treatments may help reverse these negative impacts. More specifically, the study aimed to:

1) demonstrate patients' conditions were stably managed with the treatments prior to the shutdown;
2) assess the impact of COVID-19 when treatments for patients, who have been stable on TMS maintenance protocol for pain treatment, were interrupted by the pandemic; and
3) assess the sessions of treatment required to reestablish prior clinical efficacy once the treatment was resumed.

Methods

Under a standing Institutional Review Board-approved protocol for tracking patients who have been receiving the treatments, a list of patients whose pain/headaches have been stably controlled with a maintenance treatment protocol for at least 6 months prior to the COVID-19 shutdown was generated. Those who returned for evaluation prior to resuming the treatment after the shutdown were identified. In addition, those who did not return were also identified. Patients' records in the Computer Patient Record System were then reviewed for their underlying pain diagnoses, pain assessment with Mechanical Visual Analog Scale (M-VAS) scores (3), treatment settings and durations, the 3-item Pain, Enjoyment, and General Activity (PEG-3), and Patient Health Questionnaire-9 (PHQ-9) scores in 3 phases (4,5): Phase I (P1) consisted of a 6-month pre-COVID-19 period in which pain conditions were stably managed with either treatment modality; Phase II (P2) consisted of the first treatment visit period immediately after the COVID-19 shutdown; and Phase III (P3) consisted of a 3-4 month post-COVID-19 shutdown period patients received up to 3 sessions of either treatment modality after the P2 treatment (Fig. 1).

Statistical Analyses

Study data were collected and input into an existing data management system using Microsoft Access software (Microsoft Corporation, Redmond, WA). The system provided a stable and secure platform for study data input, validation, edit and query, tracking of individual patient treatments, and data export to SPSS for analysis. Descriptive statistics and graphs were used to assess the normality and homogeneity of the data. Randomness of missing data were also examined (6). No significant violation was found. All statistical tests were 2-tailed. Differences were considered statistically significant provided a *P* value of 0.05 or less is obtained using SPSS Version 26 (IBM Corporation, Armonk, NY).

Averages of the different data categories from the 3 defined study phases were computed to provide a stable measurement of treatment effect before and after the shutdown. Data were analyzed using the mixed-effect model with one within the factor of the phase (3 levels) using average scores for the 3 phases. Additional analyses were conducted to ascertain the efficacy of reestablishing treatment effect by comparing data from P2 with data from each subsequent (a total of 3 treatments) treatment in P3.

Results

Study Cohort

A total of 52 patients were identified as receiving the treatments with stable pain/headache control in P1 with 27 and 25 patients received TMS and tMS, respectively. In the TMS cohort, 16 patients (Table 1) returned in P2 and completed treatments in P3. In the tMS cohort, 15 patients (Table 2) returned in P2 and completed treatments in P3. There were no significant differences in age, gender, and underlying pain condi-

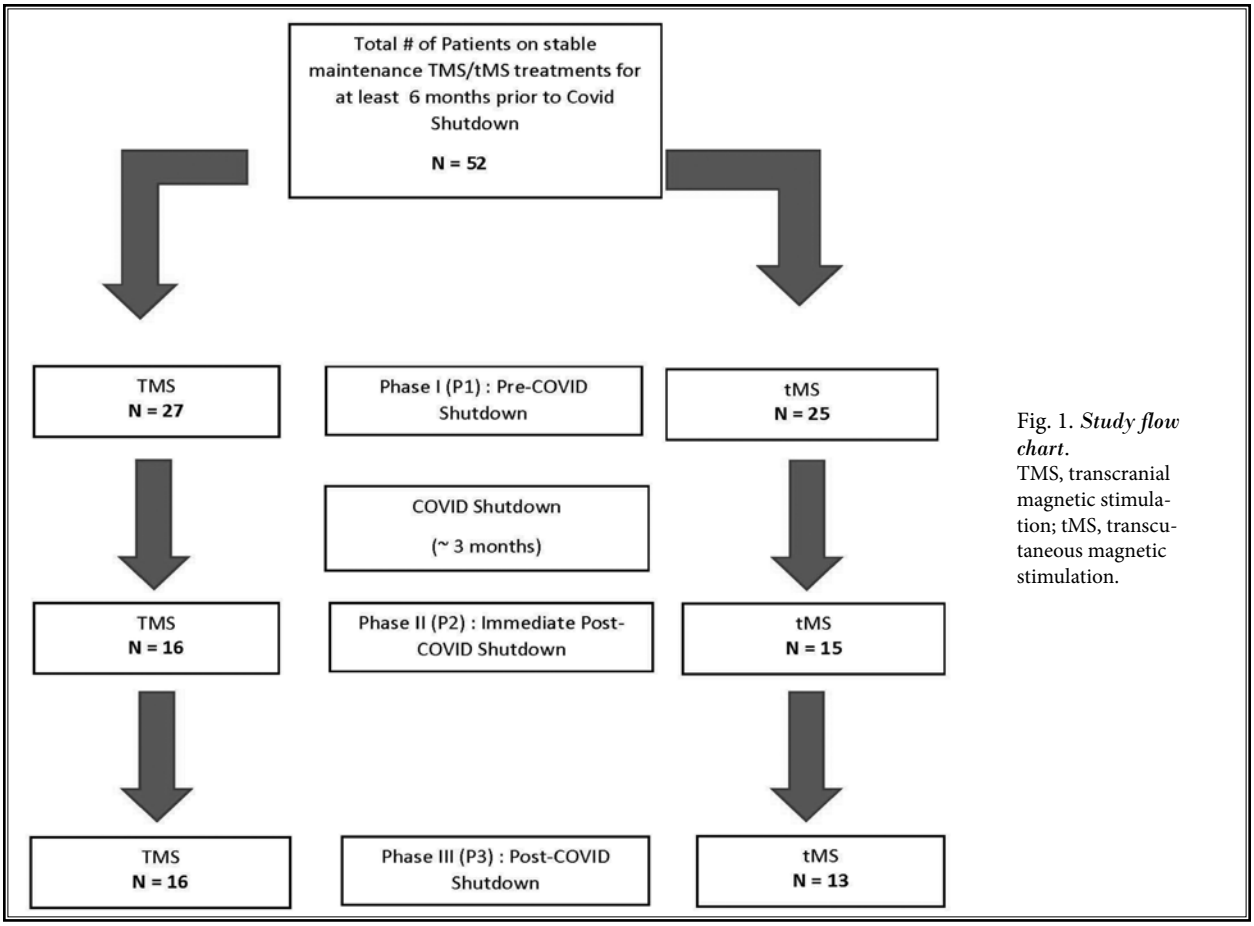

Fig. 1. *Study flow chart*.
TMS, transcranial magnetic stimulation; tMS, transcutaneous magnetic stimulation.

tions between return and nonreturn cohorts in both treatment groups. No significant difference between the return and nonreturn cohorts in both treatment groups for all assessment parameters, including pre-post treatment pain/headache intensity M-VAS, PEG-3, and PHQ-9 scores in P1 was found. While there is a treatment effect with significant difference between pre- and post-pain M-VAS scores, no significant interaction between return and nonreturn cohorts in both treatment groups was found. The main reasons for patients who received treatments in P1 but did not return in P2 or P3 were due to safety concern for the pandemic, and some no longer perceived the treatments as effective because the efficacy had subsided during the shutdown period. No significant ($P = 0.616$) difference in between-treatment duration (weeks ± standard deviation [SD]) was found between P1 (4.7 ± 1.8) and P3 (4.4 ± 1.7) for the TMS cohort. Likewise, no significant ($P = 0.0.157$) difference in between-treatment duration (weeks ± SD) was found comparing P1 (7.1 ± 2.9) and P3 (5.5 ± 3.5) for the tMS cohort.

Table 1. *Demographics and diagnosis: for the TMS cohort.*

Patient #	Age	Gender	Primary Treatment Indication
1	51	M	Chronic Cluster HA
2	51	M	Chronic Migraine HA
3	44	M	Chronic Migraine HA
4	50	W	Chronic Migraine HA With Diffuse Body Pain
5	50	W	Chronic Migraine Headache
6	56	M	PTBI HA
7	49	W	PTBI HA
8	72	M	PTBI HA
9	42	M	HA
10	37	M	PTBI HA
11	55	M	PTBI HA
12	38	M	PTBI HA
13	33	M	PTBI HA
14	47	W	PTBI HA
15	43	W	PTBI HA
16	74	M	PTBI-HA and PHN

Abbreviations: HA: Headache; PTBI: Posttraumatic Brain Injury; PHN: Postherpetic Neuralgia.

Table 2. *Demographics and diagnosis for the tMS cohort.*

Patient #	Age	Gender	Primary Treatment Indication
1	52	M	R Genitofemoral posttraumatic injury neuralgia
2	50	W	R Foot plantar nerve entrapment
3	40	M	R Genitofemoral posttraumatic injury neuralgia
4	82	M	R Ilioinguinal posttraumatic injury neuralgia
5	72	M	R Supraorbital posttraumatic injury neuralgia
6	49	M	L Genitofemoral posttraumatic injury neuralgia
7	73	M	L Genitofemoral posttraumatic injury neuralgia
8	37	M	R Ulnar posttraumatic neuralgia
9	52	M	L Genitofemoral posttraumatic injury neuralgia
10	71	M	R Superficial peroneal posttraumatic injury neuralgia
11	62	M	R Genitofemoral posttraumatic injury neuralgia
12	45	M	R Genitofemoral posttraumatic injury neuralgia
13	47	M	L Superficial peroneal posttraumatic injury neuralgia
14	69	M	L Genitofemoral posttraumatic injury neuralgia
15	69	M	L Radial nerve posttraumatic injury neuralgia

Abbreviations: R: Right; L: Left.

Pretreatment Pain Scores

For the TMS treatment group, the mixed effect analysis demonstrated a significant (F = 9.442; *P* = 0.001) time interaction across all phases. Between-phase analysis indicates a significant (F = 13.572, *P* = 0.002; F = 12.752, *P* = 0.001) interaction between P1 and P2, and P2 and P3 with the mean pretreatment pain score (mean ± SD) increases from 37.7 ± 27.6 at P1 to 49.6 ± 25.9 at P2, which then decreases back to an average score of 37.1 ± 24.7 at P3. No significant interaction between P1 and P3 was detected (Fig. 2a). P3 treatment-based subanalyses indicated significant interactions between P2 and all 3 subsequent P3 treatments (P3 first [Tx1]: F = 4.269, *P* = 0.048; P3 second [Tx2]: F = 12.491, *P* = 0.001; and P3 third [Tx3]: F = 7.219, *P* = 0.012) with a decrease of the mean pretreatment pain score from 49.6 ± 25.9 to 38.7 ± 25.6, 36.7 ± 29.5, and 36.0 ± 30.3, respectively (Fig. 2b).

For the tMS treatment group, the mixed effect analysis demonstrated a significant (F = 8.062, *P* = 0.002) time interaction across all phases (Fig. 2c). Between-phase analysis indicates a significant (F = 13.383, *P* = 0.003; F = 5.464, *P* = 0.027) interaction between P1 and P2, and P2 and P3 with the mean pretreatment pain score (mean ± SD) increases from 34.9 ± 25.1 at P1 to 56.3 ± 27.0 at P2, which then decreases back to an average score of 41.9 ± 26.4 at P3. No significant interaction between P1 and P3 was detected. P3 treatment-based subanalyses indicated significant interactions between P2 and P3 Tx1 treatment with a close to statistically significant decrease trend at P3 Tx2 (P3 Tx1: F = 4.337, *P* = 0.047; F = 3.962, *P* = 0.057). The mean pretreatment pain score decreases from 56.3 ± 27.0 at P2 to 43.2 ± 30.1, 44.0 ± 26.5, and 44.7 ± 25.2 for P3 Tx1, Tx2, and Tx3, respectively (Fig. 2d).

Posttreatment Pain Scores

For the TMS treatment group, the mixed effect analysis demonstrated a significant (F= 11.429; *P* < 0.001) time interaction across all phases. Between-phase analysis indicates a significant (F = 14.206, *P* = 0.002; F = 16.063, *P* < 0.001, respectively), interaction between P1 and P2, and P2 and P3 with the mean posttreatment pain score (mean ± SD) increases from 25.6 ± 22.9 at P1 to 36.2 ± 23.4 at P2, which then decreases back to an average score of 23.3 ± 21.3 at P3. No significant (*P* = 0.896) interaction between P1 and P3 was detected (Fig. 3a). P3 treatment-based subanalyses indicated significant interactions between P2 and Tx2 and Tx3 subsequent P3 treatments (P3 Tx1: F = 2.456, *P* = 0.128; P3 Tx2: F = 16.592, *P* < 0.001; P3 Tx3: F = 16.151, *P* < 0.001) with a decrease of the mean posttreatment pain score from 36.2 ± 23.4 at P2 to 22.4 ± 22.3 and19.1 ± 23.0 at P3 Tx2 and Tx3, respectively (Fig. 3b).

For tMS, the mixed effect analysis demonstrated no overall statistically significant time interaction across all phases. However, a between-phase analysis indicates a significant (F = 8.324, *P* = 0.012) interaction between P1 and P2 only with the mean pretreatment pain score (mean ± SD) increases from 24.9 ± 25.7 at P1 to 36.9 ± 26.7 at P2, which then decreases (although not statistically significant) back to an average score of 25.8 ± 21.6 at P3. No significant interaction between P1 and P3 was detected (Fig.3c). P3 treatment-based subanalyses indicated no significant interactions between P2 and all P3 treatment sessions (Fig. 3d).

Combined PEG-3 Scores

For TMS, the mixed effect analysis demonstrated a significant (F = 12.156, *P* < 0.001) time interaction

across all phases. Between-phase analysis indicates a significant (F = 14.966, *P* = 0.002; F = 21.044, *P* < 0.001) interaction between P1 and P2, and P2 and P3 with the mean PEG-3 combined score (mean ± SD) increases from 16.4 ± 7.0 at P1 to 20.3 ± 6.1 at P2, which then decreases back to an average score of 15.2 ± 8.0 at P3. No significant (F = 0.713, *P* = 0.405) interaction between P1 and P3 was detected (Fig. 4a). P3 treatment-based subanalyses indicated significant interactions between P2 and all 3 subsequent P3 treatments (P3 Tx1: F = 19.127, *P* < 0.001; P3 Tx2: F = 21.033, *P* < 0.001; P3 Tx3: F = 14.283, *P* < 0.001) with a decrease of the mean PEG-3 sum score from 20.3 ± 6.1 to 15.5 ± 7.6, 14.6 ± 9.0 and 15.3 ± 8.3, respectively (Fig. 4b).

For tMS, the mixed effect analysis demonstrated a significant (F = 5.431; *P* = 0.015) time interaction across all phases. Between-phase analysis indicates a significant (F = 7.4604, *P* = 0.014) interaction between P2 and P3 with the mean PEG-3 combined score (mean ± SD) decreases from 17.0 ± 7.4 at P2 to an average score of 13.3 ± 7.4 at P3 (Fig. 4c). P3 treatment-based subanalyses indicated significant interactions between P2 and 2 subsequent P3 treatments (P3 Tx1: F = 7.391, *P* = 0.015; P3 Tx3: F = 6.276, *P* = 0.024) with a decrease of the mean PEG-3 sum score from 17.0 ± 7.4 to 13.1 ± 7.8 and 12.5 ± 7.5, respectively. No significant interaction (F = 3.148, *P* + 0.094) interaction between P2 and P3 Tx2 was found (Fig. 4d).

PHQ-9 Scores

For TMS treatment, the mean (± SD) combined PHQ-9 score at P1 was 9.5 ± 6.8, which suggested mild depressive symptoms were present in this cohort. The mixed effect analysis demonstrated no significant (F = 1.714; *P* = 0.198) time interaction across all phases. Between-phase analysis indicated no significant interactions between P1 and P2, and P2 and P3. P3 treatment-based subanalyses also indicated no significant interactions among all phases.

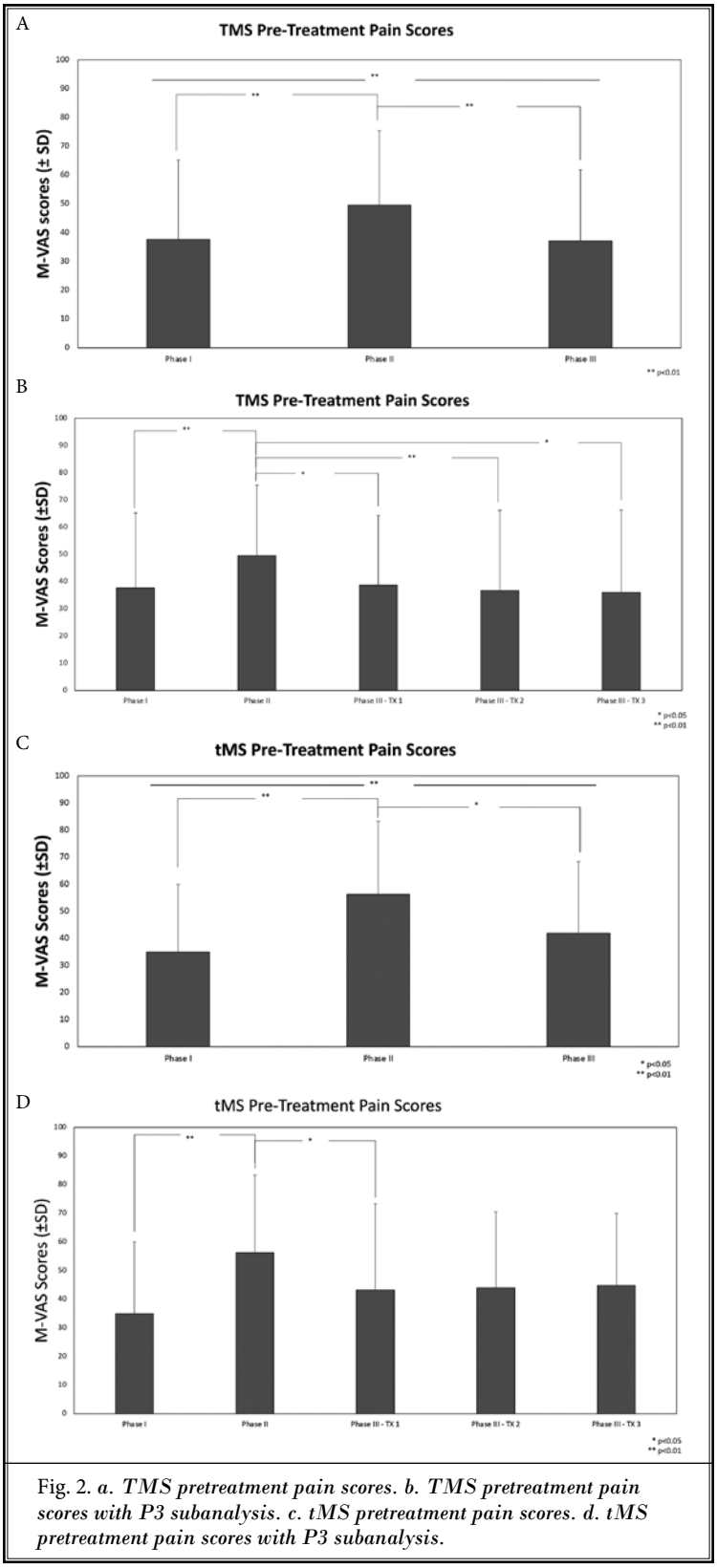

Fig. 2. *a. TMS pretreatment pain scores. b. TMS pretreatment pain scores with P3 subanalysis. c. tMS pretreatment pain scores. d. tMS pretreatment pain scores with P3 subanalysis.*

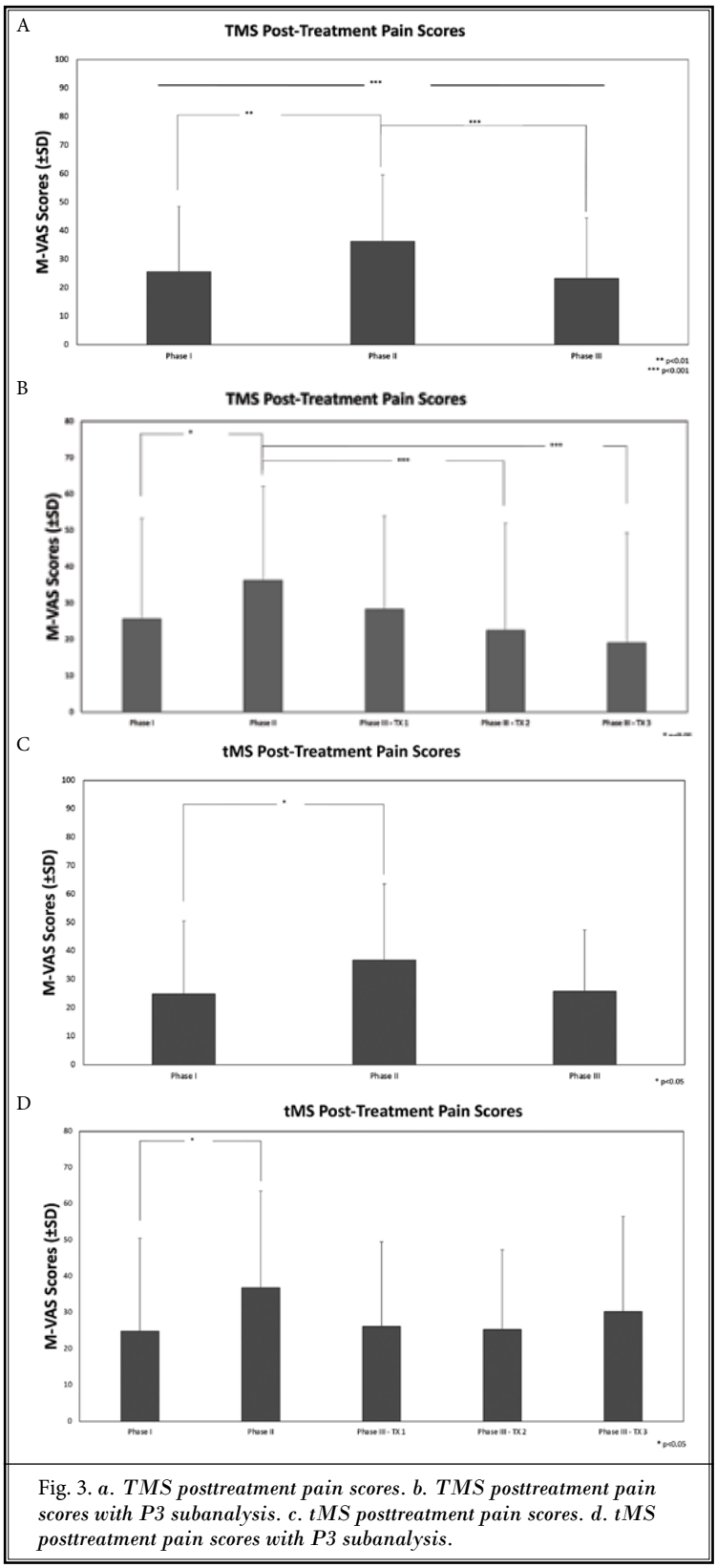

Fig. 3. *a. TMS posttreatment pain scores. b. TMS posttreatment pain scores with P3 subanalysis. c. tMS posttreatment pain scores. d. tMS posttreatment pain scores with P3 subanalysis.*

For the tMS treatment group, the mean (± SD) combined PHQ-9 score at P1 was 8.1 ± 6.1, which also suggested mild depressive symptoms were present in this cohort. The mixed effect analysis demonstrated no significant (F = 0.136; *P* = 0.874) time interaction across all phases. Between-phase analysis indicates no significant interactions between P1 and P2, and P2 and P3. P3 treatment-based subanalyses also indicated no significant interactions among all phases.

Discussion

Emerging evidence supports the use of neuromodulatory modalities, particularly noninvasive therapies for pain management. Both TMS and tMS are some of the most promising noninvasive treatment modalities for pain management (7-11). However, as in most neuromodulatory pain treatment modalities, previously published study durations were in the range of 1 to 3 months and long-term outcome data for the treatment modalities are scarce with the longest study duration of TMS in alleviating posttraumatic brain injury headache at about 6 months (8,9,12-14), while our adaptive protocol of tMS showed sustainable pain relief (> 50%) benefit for many patients with peripheral neuropathic pain (NP) for over a decade. For TMS, high frequency (> 5Hz) TMS on either the left dorsolateral prefrontal cortex (DLPFC), or the primary motor cortex (M1), are the preferred treatment targets and settings for analgesic benefit. With stimulations at the M1, a strong focal activation was observed in the thalamus, insula, cingulate-orbitofrontal junction, and the brainstem periaqueductal gray area in the brain stem, suggesting that a direct "top-down" activation of the descending pain control system mediated via a motor-thalamus and/or motor-brainstem functional linkage (15,16). On the other hand, repetitive TMS of the left DLPFC applied at the F3 site (according to "The International 10-20 System of Electrode Placement" [15,16]) exerts a diffuse "top-down" inhibitory effect along the

descending midbrain-thalamic-cingulate pathway through the descending fibers from the prefrontal cortex. Thus, the widespread effect of DLPFC stimulation can potentiate the motor cortex and modulate the affective circuits relevant to both pain and depression (14-16). For long-term outcome benefit, the recent international expert consensus panel recommend for patients with NP but no severe comorbid depression, an initial 5-10 induction sessions (at > 24 and < 72 hours intervals) at 10-20 Hz, 2,000 to 3,000 pulses per session, and an intensity of stimulation corresponding to 80% to 90% of the resting motor threshold (RMT) at the contralateral M1 for unilateral NP or left DLPFC for diffuse NP conditions. For patients with NP and comorbid severe depression, the task group recommends at least 10 induction sessions (at > 24 and < 72 hours intervals) at 10-20 Hz, 2,000 to 3,000 pulses per session and an intensity of stimulation corresponding to 80% to 90% of the RMT at the left DLPFC, followed by biweekly-to-monthly maintenance treatment sessions with similar settings based on the duration of the treatment benefits. In the current study, all patients have undergone the initial induction sessions as recommended and demonstrated sustainable treatment before they were placed on a stable maintenance treatment schedule in P1.

tMS treatment can be delivered with any conventional figure-of-8 TMS coils and low frequency stimulation (± 5 Hz) is the preferred setting for its inhibitory effect (2,17,18). While the tMS treatment protocol is less developed and fixed treatment intensity based on previously published case series has not been shown to have long-term effect in a randomized controlled trial, an adaptive protocol developed by the lead author (AL) (US Provisional Patent application #63/402,602 and 63/410,290) does appear to have sustainable benefit for treated patients in the current study cohort (19,20).

While the recent shutdown of elective procedures due to the COVID-19 pandemic has created much inconvenience and suffering for many chronic pain patients, it did

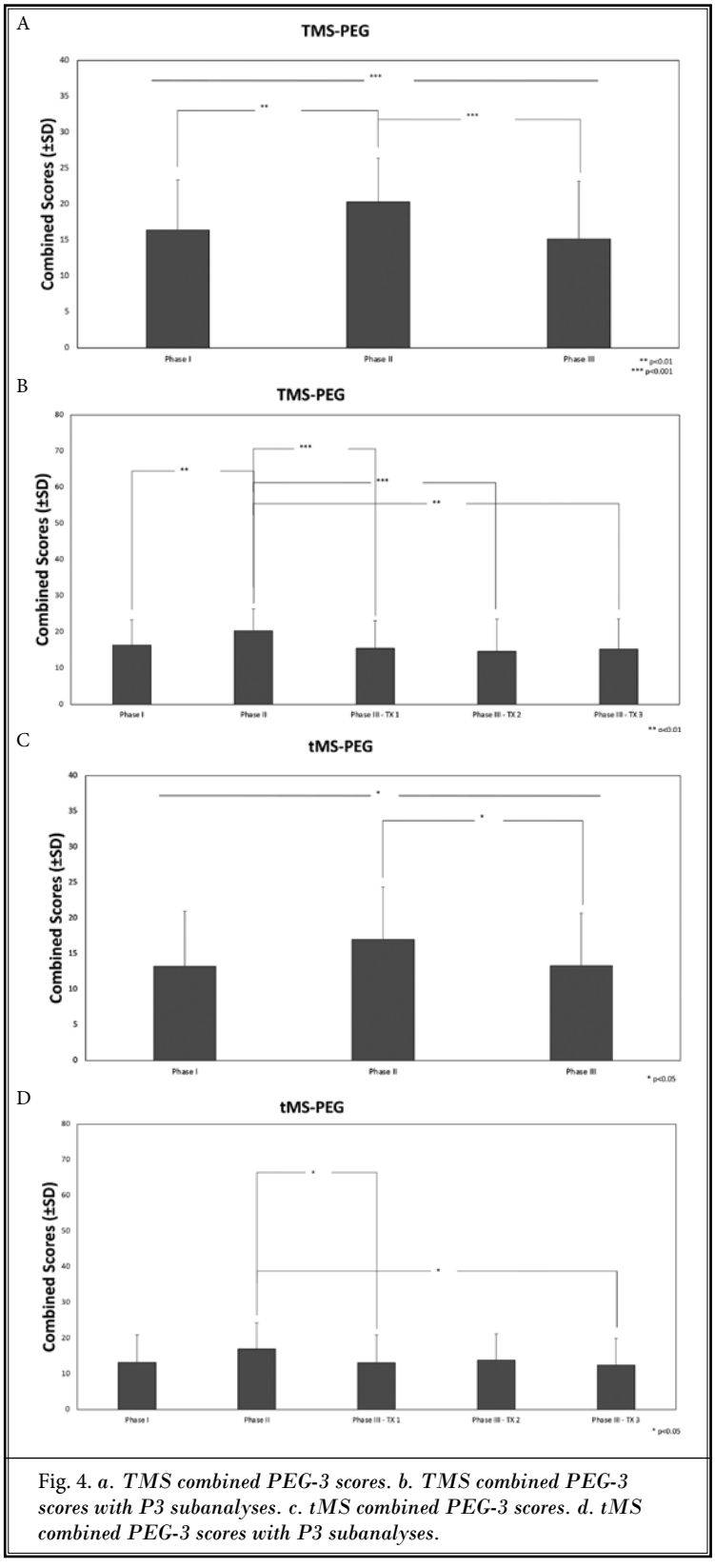

Fig. 4. *a. TMS combined PEG-3 scores. b. TMS combined PEG-3 scores with P3 subanalyses. c. tMS combined PEG-3 scores. d. tMS combined PEG-3 scores with P3 subanalyses.*

provide an unusual opportunity for assessing the feasibility of resuming the treatment after a brief period of treatment interruption. In the current case series, most patients' pain conditions were under stable control for at least 3-6 months prior to the shutdown. Their pain/headache conditions were under well control while they were on a monthly-to-bimonthly maintenance treatment schedule with either treatment modality. The result of the current study confirms these patients' pain/headache conditions were under stable control prior to the shutdown. While the 3-month pandemic-related shutdown did cause an increase of pain/headache levels and diminished quality of life for these patients, resuming the TMS treatments in 1 to 2 sessions can quickly reestablish preshutdown level of pain control with corresponding improvement in quality of life.

For tMS, while the pretreatment average pain scores suggest the reestablishment of the preshutdown treatment benefit, its overall effect has not been as robust as with TMS. Thus, perhaps a more frequent tMS treatment paradigm is required for reestablishing the treatment effect after a brief period on interruption.

Limitations

Some limitations of the study are worthy of discussion. The return to treatment after the shutdown was a voluntary decision based on the patient's preference, which could inadvertently create a treatment preference bias. Likewise, the nonreturn to treatment after the shutdown was also a voluntary decision based on the patient's preference and due to their concern for the ongoing pandemic. Thus, future studies may consider various durations of controlled treatment cessation based on a controlled randomized study design allowing prospective outcome assessment for both return and nonreturn groups.

In addition, due to exploratory nature of the study, and limited number of available but highly relevant outcome parameters (Pain, PEG-3, and PHQ-9), no adjustment for multiple comparison was performed. However, all follow-up pairwise comparisons between pre- and post-phases were done using a contrast method within each main analyses and controlling for the error terms in the model.

Conclusions

In short, the current result supports the notion that while both treatment modalities can provide sustainable pain relief benefit, maintenance treatment is required to sustain the analgesic benefit of the therapies. In the event that a brief period of treatment interruption occurs for up to 3 months, the analgesic benefit can be restored with resuming prior maintenance protocol with the requirement of a repetition of a more intense induction treatment protocol for tMS. While the current study serves as preliminary outcome evidence for the long-term efficacy of the treatment modalities, randomized controlled studies are required to adequately validate observed outcome.

References

1. Leung A, Shirvalkar P, Chen R, et al. Transcranial magnetic stimulation for pain, headache, and comorbid depression: INS-NANS expert consensus panel review and recommendation. *Neuromodulation* 2020; 23:267-290.
2. Leung A, Fallah A, Shukla S. Transcutaneous magnetic stimulation (TMS) in alleviating post-traumatic peripheral neuropathic pain states: A case series. *Pain Med* 2014; 15:1196-1199.
3. Price DD, Bush FM, Long S, et al. A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales. *Pain* 1994; 56:217-226.
4. Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med* 2009; 24:733-738.
5. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16:606-613.
6. Ridout MS. Testing for random dropouts in repeated measurement data. *Biometrics* 1991; 47:1617-1619; discussion 1619-1621.
7. Lefaucheur JP, Andre-Obadia N, Antal A, et al. Evidence-Based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clinical Neurophysiology* 2014; 125:2150-2206.
8. Boldt I, Eriks-Hoogland I, Brinkhof MW, et al. Non-Pharmacological interventions for chronic pain in people with spinal cord injury. *Cochrane Database Syst Rev* 2014; 11:CD009177.
9. Jin Y, Xing G, Li G, et al. High frequency repetitive transcranial magnetic stimulation therapy for chronic neuropathic pain: A meta-analysis. *Pain Physician* 2015; 18:E1029-E1046.
10. Gao F, Chu H, Li J, et al. Repetitive transcranial magnetic stimulation for pain after spinal cord injury: A systematic review and meta-analysis. *J Neurosurg Sci* 2017; 61:514-522.
11. Leung A, Donohue M, Xu R, et al. rTMS for suppressing neuropathic pain: A meta-analysis. *The Journal of Pain* 2009; 10:1205-1216.
12. Stilling J, Paxman E, Mercier L, et al. Treatment of persistent post-traumatic headache and post-concussion symptoms using repetitive transcranial magnetic stimulation: A pilot, double-blind, randomized controlled trial. *J*

Neurotrauma 2020; 37:312-323.

13. Koski L, Kolivakis T, Yu C, et al. Noninvasive brain stimulation for persistent postconcussion symptoms in mild traumatic brain injury. *J Neurotrauma* 2014; 32.
14. Leung A, Metzger-Smith V, He Y, et al. Left dorsolateral prefrontal cortex rTMS in alleviating MTBI related headaches and depressive symptoms. *Neuromodulation* 2018; 21:390-401.
15. Garcia-Larrea L, Peyron R, Mertens P, et al. Electrical stimulation of motor cortex for pain control: A combined PET-scan and electrophysiological study. *Pain* 1999; 83:259-273.
16. Peyron R, Garcia-Larrea L, Deiber MP, et al. Electrical stimulation of precentral cortical area in the treatment of central pain: Electrophysiological and PET study. *Pain* 1995; 62:275-286.
17. Leung A, Shukla S, Lee J, et al. Effect of low frequency transcutaneous magnetic stimulation on sensory and motor transmission. *Bioelectromagnetics* 2015; 36:410-419.
18. Leung A (ed). *Peripheral Nerve Injury and Pain: Epidemiology, Mechanisms, Rehabilitation and Treatment Guidelines.* NOVA Science Publishers, Hauppauge, NY 2019.
19. Leung A. Improving functions in veterans with post-traumatic peripheral neuropathic pain (PTP-NP), 2021. https://clinicaltrials.gov/ct2/show/results/NCT02979925?cond=post+traumatic+peripheral&draw=2&rank=3
20. Leung A. Adaptive transcutaneous magnetic stimulation therapy. VA, USA, 2022.