Received: 20 April 2022 | Revised: 10 January 2023 | Accepted: 1 February 2023

DOI: 10.1111/ijun.12351

ORIGINAL ARTICLE

BAUN BRITISH ASSOCIATION OF UROLOGICAL NURSES WILEY

Transcutaneous sacral neuromodulation for pelvic pain and non-relaxing pelvic floor: Findings from a pilot study

Stefano Terzoni PhD, MSN, RN[1] | Cristina Mora RN[2] | Maria Chiara Sighinolfi PhD, MD[3] | Giorgia Gaia MD[3] | Barbara Pinna MSN, RN[4] | Bernardo Rocco MD[5] | Anne Destrebecq MSC, RN[6]

[1]San Paolo Bachelor School of Nursing, San Paolo Teaching Hospital, Milan, Italy

[2]Pelvic Unit, ASST Santi Paolo e Carlo, Milan, Italy

[3]Department of Urology, ASST Santi Paolo e Carlo, Milan, Italy

[4]Nursing Management Office, ASST Santi Paolo e Carlo, Milan, Italy

[5]Department of Health Sciences, University of Milan, Milan, Italy

[6]Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

Correspondence
Stefano Terzoni, San Paolo Bachelor School of Nursing, University of Milan, San Paolo Teaching Hospital. Via Ovada 26, 20142 Milan, Italy.
Email: stefano.terzoni@asst-santipaolocarlo.it

Abstract

We sought to evaluate the effectiveness and acceptability by patients of transcutaneous sacral roots neuromodulation (TSRN) by paravertebral placement of surface electrodes to treat pelvic pain and pelvic muscle stiffness. Pelvic pain is a disabling condition, often related to non-relaxing pelvic muscles. Causes for the onset are often unclear; noninvasive treatment targeted at maintenance factors can be administered by nurses in some countries. previous studies have investigated the role of invasive stimulation for pelvic pain; TSRN has proved successful in other pelvic disorders. We conducted a pilot study on a sample of consecutive patients of both genders, reporting pelvic pain (chronic or not). Weekly sessions of TSRN with surface electrodes were performed; pain was recorded with the numeric rating scale (NRS) at baseline and after the end of the rehabilitation plan. Therapeutic success was defined as a reduction of 50% in pain scores. Twenty patients were enrolled, most complaining multiple symptoms apart from pain. Seven males had primary prostate pain syndrome, one had history of orthopaedic surgery, and eight had muscle stiffness (Median = 3 out of 4, IQR = [3;3], range [2;4]). Sixteen patients (12 males and 4 females) had chronic pelvic pain. The median NRS values in the sample at baseline was 4[5.5–7.5] with no significant differences between genders ($p = 0.144$) and decreased significantly (Me = 0.5, IQR[0.0–1.0], $p < 0.001$) after a median of 20 weekly sessions (range [10–30]). The results indicated clinically relevant benefit for all patients ($\omega^2 = 0.689$, 95%IC[0.505–0.793]) Decrease in pelvic muscle stiffness was significant (from Me = 3, IQR [3] to Me = 0, IQR[0–1], $p < 0.0001$) without differences between the genders ($p = 0.711$). No significant difference was found in the number of sessions required by males and females to achieve therapeutic success ($p = 0.282$). TSRN seems a promising treatment for pelvic pain and can be performed in outpatients' clinics with low costs and no invasivity. Further studies on larger, randomized samples are required to confirm these results.

Registration: Open Science Framework no. osf.io/m85rn

KEYWORDS
pelvic pain, rehabilitation, sacral neuromodulation

What is known about this topic?

- Pelvic pain is a disabling condition, not always localized to a single organ or clearly referable to a specific underlying condition or disease.
- Invasive neuromodulation has been proposed for some forms of pelvic pain, but it can be administered noninvasively as well.
- No authors have studied the effects of noninvasive neuromodulation for pelvic pain.

What this paper adds?

- Transcutaneous neuromodulation for pelvic pain is a noninvasive and promising option.
- In this pilot study, this treatment proved effective for reducing pain in males and females.
- This treatment can be administered by nurses in some countries and deserves further investigation.

1 | BACKGROUND

Pelvic pain is a disabling condition, not always localized to a single organ or clearly referable to a specific underlying condition or disease.[1] The most bothersome aspects are duration and intensity, this latter depending mainly on the anatomy of the pudendal nerve. This mixed nerve (sensory-motor) conveys sexual pleasure under normal conditions, as its numerous branches carry the sensory stimulus from the surface of the skin and mucous membranes of the genital region to the deeper anatomical fascia. In the presence of a painful stimulus, the pudendal nerve becomes a vehicle for pain in a vast anatomical region, deep down to innermost structures. In some cases (e.g., some forms of vulvodynia) the rubbing of clothes is often enough to exacerbate a symptom that remains latent and often does not disappear. The pain spike is immediately conveyed by the pudendal nerve, which turns on other 'triggers' (painful and stiff points in the pelvic muscles) in all the regions reached by pudendal branches.

Chronic pelvic pain (CPP) is a persistent pain (continuous or recurrent for at least 6 months) perceived in anatomical structures related to the pelvis of either men or women.[1] Chronic pelvic pain syndromes (CPPS) are defined as the presence of chronic pelvic pain, in the absence of proven infection or other obvious local pathology to which the symptom can be related.[2] The European guidelines emphasize that the period of 6 months is arbitrary, but was chosen because a period of 3 months would not be sufficient to declare the pain chronic, in case of cyclic symptoms.[1] In the presence of clear pathologies (infections, neuropathies, chronic inflammation) pain can be a consequence of a different clinical problem, and even lead to the onset of depression,[3] a major psychiatric condition which can sometimes become refractory to common treatments and difficult to cure.[4] In CPPS pain is the main symptom and is neither well localized nor related to other primary problems. Several forms of pelvic pain exist in men as well, with anatomical irradiation showing similar characteristics of intensity and depth to those found in women.[5] Pelvic pain has cognitive, behavioural, sexual, and emotional consequences; the European guidelines describe a wide range of signs and symptoms, which accounts for more than 25 different clinical conditions.[6]

It is often difficult to identify trigger conditions which cause the onset of pelvic pain, as they can be very numerous[1] (e.g., trauma, physical abuse, complications during delivery, consequences of surgical complications, and neurological diseases). Some triggers can be transient and remote in time, so that even the patient can find it hard to remember them and associate a precise episode to the onset of pain, which can sometimes occur months later. For this reason, several authors have suggested to focus on maintenance factors instead of triggers.[2] Based on these considerations, pain is a complex problem requiring multidisciplinary management by physicians, nurses, physiotherapists, midwives, and other professionals.[7]

Some authors[8–10] have reviewed the role of invasive neuromodulation in chronic pelvic pain, including anal pain[11] and concluded that further investigation is needed to elucidate the most effective treatment modality among the many proposed by the literature, as well as to identify the patients who would benefit most from this therapy. However, neuromodulation can be administered noninvasively, through self-adhesive electrodes placed at the level of sacral roots, as proposed by some nursing authors for refractory urinary incontinence.[8] This lays the foundation for nurses to investigate the effects of noninvasive neuromodulation, which could have practical advantages for patients over the invasive approach such as avoiding implanted electrodes.

2 | AIM

In this paper we report the results of a preliminary study aimed at evaluating the effectiveness and acceptability by patients of sacral roots neuromodulation by paravertebral placement of surface electrodes (TSRN, Transcutaneous Sacral Roots Neuromodulation).

TABLE 1 Characteristics of the stimulation

Parameter	Value
Type of electric current	Alternated asymmetric
Intensity range (mA)	4–20
Frequency range (Hz)	2–5
Impulse duration range (mSec)	150–200

3 | MATERIALS AND METHODS

3.1 | Participants

This was a pilot study on a non-randomized convenience sample of consecutive patients of both genders, reporting pelvic pain (whether chronic or not) for any reason. No control group was enrolled, as the aim of this investigation was to explore potential benefit of this treatment in patients who had already underwent evidence-based therapy without satisfactory results[12] (e.g., alpha-blockers for primary prostate pain syndrome, biofeedback for pain related to non-relaxing pelvic floor, physical therapy for vestibulodynia and vulvodynia). Our patients refer to the rehabilitation clinic for several types of pain: some have CPPS, others CPP or even non-chronic pain related to trigger points, complicated surgical history, and other algogenic conditions that do not necessarily chronicize. For this reason, we chose not to concentrate on a specific subgroup, in order to represent the real population we see in clinical practice.

3.2 | Procedures

TSRN was performed on a weekly basis by using an electrical stimulator already in use (ENRAF-Nonius® 6) in the nurse-led clinic for pelvic rehabilitation. Two square sticky patches sized 4 × 4 cm were placed at both sides of sacral vertebrae, to stimulate the roots at S3-S5 level. The stimulation programme was based on literature criteria[10,11,13] and was compliant with the settings offered by the electrical stimulator (Table 1).

3.3 | Outcome measures

The numeric rating scale (NRS) ranging from 0 to 10 was used, similarly to other studies in this field[12] to record pain before the beginning and after the end of the rehabilitation plan; pelvic muscle stiffness was assessed by palpation by the same nurse specialist for all patients, compliant with the objective criteria described in the so-called PERFECT scheme and other relevant literature[14,15] on a scale from 0 (relaxed muscle) to 3 (maximum stiffness). Relevant data regarding anamnesis, comorbidities, and previous therapies were recorded as described in previous works[16,17] by nurses according to their framework of competence.[18]

Data were analysed as median and interquartile range (IQR) after normality checking with Shapiro–Wilk's test; A generalized linear model with random effects was used to estimate the effect size of the treatment (partial omega-squared); homogeneity of variances was assessed with Levene's test and analysis of residuals was performed with Shapiro–Wilk's test. Kaplan–Meyer's survival tables and log-rank test were used to compare time-to-success between males and females. Success was defined as an improvement in NRS scores of at least 50% compared to baseline, similarly to other studies on pelvic pain.[19] Given the small sample size obtained, resampling was performed with 600 repetitions[20] to increase precision of the measures and improve generalizability of the results. The significance threshold was set at 0.05 for all calculation. Analysis was performed with SAS® 9 (SAS Inc., Cay, NY).

Acceptability was evaluated qualitatively, by asking the question 'Have you experienced any feelings of discomfort during the sessions, or have you found acceptable this form of treatment?'. Satisfaction was also evaluated as a response to a question ('Are you satisfied with the treatment and the results obtained?').

This study was conducted in compliance with the Declaration of Helsinki and the Italian law on data protection in force. Approval from the hospital board and written informed consent from all the participants were obtained. The study received no funding.

4 | RESULTS

Twenty consecutive patients, 10 males and 10 females (median age 36 years, IQR [29–58]) underwent TSRN. The median number of sessions was 20, range [10–30]. Most patients reported multiple symptoms apart from pain: among males, 7 patients out of 10 had primary prostate pain syndrome, one had history of orthopaedic surgery, and 8 had muscle stiffness (Median = 3.0 out of 4, IQR = [3.0;3.0], range [2; 4]). Among women, one had stiffness (with a value of 3 out of 4), three had vulvodynia (two of whom also presented vestibulitis). Overall, sixteen patients (12 males and 4 females) had chronic pelvic pain according to the abovementioned definitions.

The median NRS values in the sample at baseline was 4.0 [5.5–7.5] with no significant differences between males and females ($p = 0.144$). A statistically significant decrease in NRS values was observed in the sample at the end of the treatment (Me = 0.0, IQR[0.0–1.0], $p < 0.0001$; R-squared = 0.803, normality test of residuals distribution $p > 0.05$) as shown in Figure 1. The effect size measure (partial omega-squared = 0.689, 95% IC [0.505–0.793]) was very high, indicating clinically relevant benefits for most patients. The lower limit of the confidence interval suggest that this finding can be considered valid also in the population from which the sample was drawn. Of note, the final NRS scores did not differ significantly between males and females ($p > 0.05$) indicating a significant reduction in pain in both genders.

As regards pelvic muscle stiffness, a significant decrease was observed from baseline (Me = 3.0, IQR [3.0–3.0]) to the end of the treatment (Me = 0.5. IQR [0.0–1.0], $p < 0.0001$) still without significant differences between the two genders ($p = 0.711$) indicating a clinically relevant advantage for both males and females. Kaplan-Meyer analysis adjusted for age (Figure 2) revealed no significant difference in the number of sessions required by males and females to

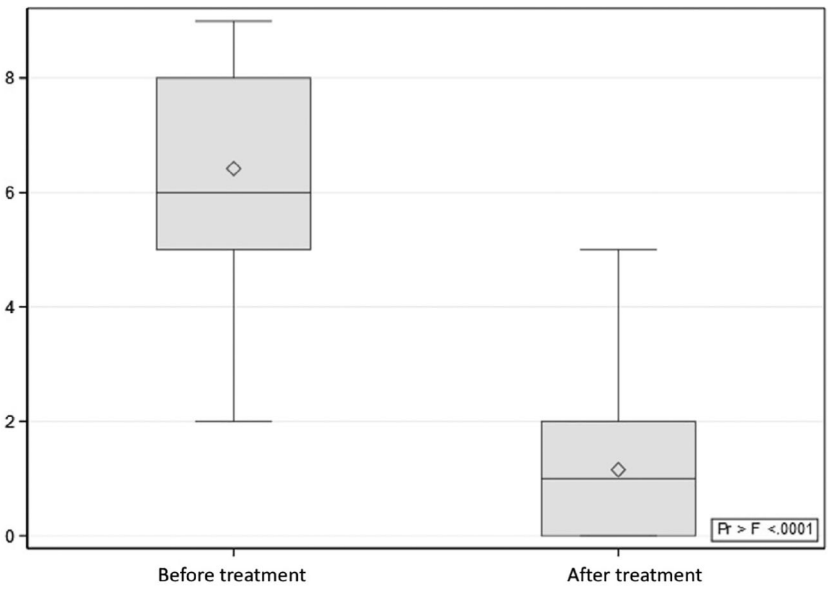

FIGURE 1 Median NRS scores of the whole sample before and after treatment

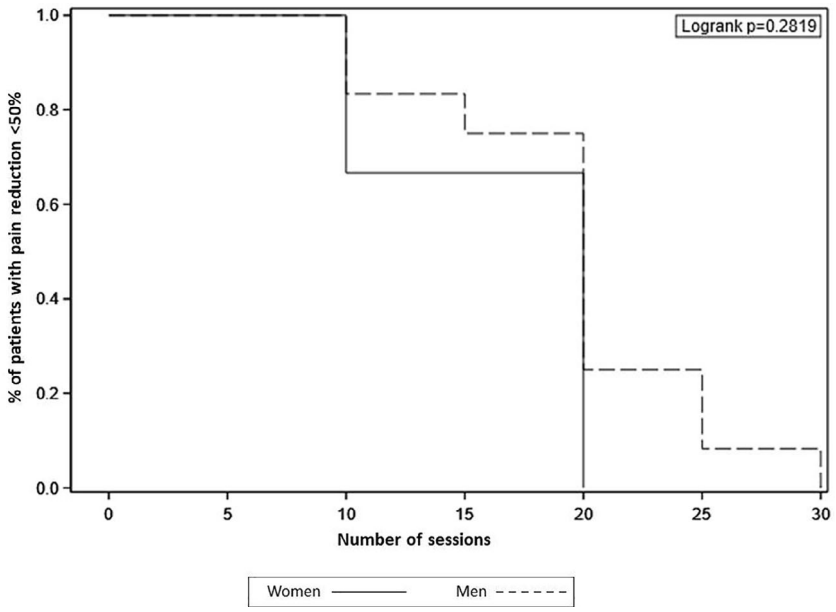

FIGURE 2 Time to success in men and women

achieve a clinically relevant result, defined as a reduction of pain of at least 50% compared to baseline (log-rank test $p = 0.282$).

As regards the perceptions of the patients, all of them claimed they were 'satisfied' or 'very satisfied' with this type of treatment. No-one reported discomfort or pain during the sessions, and all of them could sit comfortably in the armchair of the outpatients' and read a magazine, work out their mobile phones, or listen to music during the therapy sessions.

5 | CONCLUSIONS

Other than proving effective in reducing both pain and pelvic muscle stiffness, TSRN was well received by patients. All of them reported high levels of satisfaction with this treatment, as therapy was noninvasive and painless. No patient reported discomfort or annoyance related to the electrodes or the stimulation.

Although small in sample size, this appears to be the only study investigating both pain and muscular stiffness, this latter being a potential source of additional pain.[2] The resampling techniques used in the analysis partially mitigate this issue and foster generalizability of our results by increasing precision of our estimates. Other authors[12] have studied neuromodulation on larger cohorts of patients, but their study only enrolled patients with neuropathic pain. Neuromodulation is a well-established treatment for chronic pain, and transcutaneous treatment has been studied in some papers for body districts (e.g., limbs)[21] but not for the pelvic floor. Stimulation of sacral nerves has been investigated in multiple studies regarding subcutaneous implantation of permanent devices[22] but evidence regarding transcutaneous approach is still lacking. The rationale behind the

treatment of chronic pain lies in the fact that peripheral afferents sensitize in response to a variety of molecules secreted by immune cells, keratinocytes, and blood vessels cells. Such molecules include inflammatory cytokines and growth factors, which lead to reorganization of peripheral afferents and their connectivity.[23] These molecular alterations have been described at the level of the spinal cord, with consequences on modulators of synaptic transmission and the glial mechanisms which lead to the onset and maintenance of sensitization.[24] This is the reason why stimulation of sacral roots, and particularly the pudendal nerve with its many ramifications in the pelvic floor, makes sense in case of chronic pelvic pain, as the abovementioned mechanisms are the pathophysiological foundation of allodynia.[25]

Implanting a neuromodulator exposes the patient to the risk of infection[26] and electrode displacement.[27] Subcutaneous electrical stimulators require surgery to be implanted, and patients need a period of preliminary testing with an external stimulator and a pair of temporarily implanted electrodes to verify if such treatment is going to work for them. Hence the interest for the transcutaneous approach, which can be managed by non-medical personnel (e.g., nurse specialists, like in this pilot study) without the costs, discomfort and risk of complications for patients.

The possibility of combining biofeedback (suggested by the European guidelines for non-relaxing pelvic floor) and transcutaneous neuromodulation in the same session should be explored with the clinical rationale of modulating the neurological signals after relieving muscle stiffness.

As a final consideration, it should be noted that this treatment requires specific training: it is not possible to simply apply the electrodes and proceed to treat the symptoms, because a thorough assessment of the patient is required before undertaking any procedure. This assessment must be evidence-based and requires several steps, as described in the literature.[16] The use of the electrical stimulator requires knowledge of the electrical parameters, all of which have a specific clinical meaning and purpose (e.g. the frequency of the current must be within the optimal range of 2–5 Hz to promote endorphin release[28]). Therefore, prior to using this type of sacral neuromodulation, dedicated education and appropriate training under the supervision of a specialist is recommended.

AUTHOR CONTRIBUTIONS

Cristina Mora conceived the study and collected the data. Stefano Terzoni performed statistical analysis and drafted the manuscript. Maria Chiara Sighinolfi and Bernardo Rocco finalized the manuscript. Anne Destrebecq and Bernardo Rocco supervised the methodological process and provided insights for discussion and relevant literature.

ACKNOWLEDGMENT

Open Access Funding provided by Universita degli Studi di Milano within the CRUI-CARE Agreement.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests.

ORCID

Stefano Terzoni https://orcid.org/0000-0002-0716-5663

REFERENCES

1. Engeler D, Baranowski AP, Berghmans B, Borovicka J, Cottrell AM, Dinis-Oliveira P et al. EAU Guidelines on Chronic Pelvic Pain 2021. Retrieved on Oct 25, 2021 from https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Chronic-Pelvic-Pain-2021.pdf
2. Chaitow L, Lovegrove JR. *Chronic Pelvic Pain and Dysfunction*. Elsevier; 2016 ISBN 9780702035326.
3. Dydyk AM, Gupta N. Chronic pelvic pain 2021 Nov 11. *StatPearls [Internet]*. StatPearls Publishing; 2022 Jan–. PMID: 32119472.
4. D'Agostino A, Ferrara P, Terzoni S, et al. Efficacy of triple chronotherapy in unipolar and bipolar depression: a systematic review of the available evidence. *J Affect Disord*. 2020 Nov;1(276):297-304. doi:10.1016/j.jad.2020.07.026 Epub 2020 Jul 15. PMID: 32697712.
5. Franco JV, Turk T, Jung JH, et al. Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. *Cochrane Database Syst Rev*. 2018;5(5):CD012551. Published 2018 May 12. doi:10.1002/14651858.CD012551.pub3
6. Cornu JN, Ahyai S, Bachmann A, et al. A systematic review and meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic obstruction: an update. *Eur Urol*. 2015;67(6):1066-1096. doi:10.1016/j.eururo.2014.06.017
7. Doggweiler R, Whitmore KE, Meijlink JM, et al. A standard for terminology in chronic pelvic pain syndromes: a report from the chronic pelvic pain working group of the international continence society. *NeurourolUrodyn*. 2017;36(4):984-1008. doi:10.1002/nau.23072
8. Hunter CW, Falowski S. Neuromodulation in treating pelvic pain. *Curr Pain Headache Rep*. 2021;25(2):9. doi:10.1007/s11916-020-00927-y
9. Speer LM, Mushkbar S, Erbele T. Chronic pelvic pain in women. *Am Fam Physician*. 2016;93(5):380-387.
10. Tam J, Loeb C, Grajower D, Kim J, Weissbart S. Neuromodulation for chronic pelvic pain. *Curr Urol Rep*. 2018;19(5):32. Published 2018 Mar 26. doi:10.1007/s11934-018-0783-2
11. Dudding TC, Thomas GP, Hollingshead JR, George AT, Stern J, Vaizey CJ. Sacral nerve stimulation: an effective treatment for chronic functional anal pain? *Colorectal Dis*. 2013;15(9):1140-1144. doi:10.1111/codi.12277
12. Bridger C, Prabhala T, Dawson R, et al. Neuromodulation for chronic pelvic pain: a single-institution experience with a collaborative team. *Neurosurgery*. 2021;88(4):819-827. doi:10.1093/neuros/nyaa537
13. Terzoni S, Ferrara P, Mora C, et al. Transcutaneous pudendal nerve stimulation for refractory urinary incontinence: a viable option? *Int J Urol Nurs*. 2021;16:1-6. doi:10.1111/ijun.12293
14. Davidson MJ, Nielsen PMF, Taberner AJ, Kruger JA. Is it time to rethink using digital palpation for assessment of muscle stiffness? *NeurourolUrodyn*. 2020;39(1):279-285. doi:10.1002/nau.24192
15. da Silva JB, de Godoi Fernandes JG, Caracciolo BR, Zanello SC, de Oliveira ST, Driusso P. Reliability of the perfect scheme assessed by unidigital and bidigital vaginal palpation. *Int Urogynecol J*. 2021;32(12):3199-3207. doi:10.1007/s00192-020-04629-2
16. Terzoni S, Arianna F, Ferrara P, Mora C, Wallace E, Destrebecq A. Assessing the patient undergoing pelvic rehabilitation for urinary incontinence: from theory to practice. *Int J Urol Nurs*. 2021;15(2):59-69. doi:10.1111/ijun.12271
17. Prendergast SA. Pelvic floor physical therapy for vulvodynia: a Clinician's guide. *Obstet Gynecol Clin North Am*. 2017;44(3):509-522. doi:10.1016/j.ogc.2017.05.006
18. Terzoni S, Montanari E, Mora C, Ricci C, Destrebecq A. Reducing urine leakage after radical retropubic prostatectomy: pelvic floor exercises, magnetic innervation or no treatment? A quasi-experimental study. *Rehabil Nurs*. 2013;38(3):153-160. doi:10.1002/rnj.72

19. Nezhat CH, Seidman DS, Nezhat FR, Nezhat CR. Long-term outcome of laparoscopic presacral neurectomy for the treatment of central pelvic pain attributed to endometriosis. *Obstet Gynecol*. 1998;91(5 Pt 1):701-704. doi:10.1016/s0029-7844(98)00047-7
20. He J, Li F, Gao Y, Rothmann M. Resampling-based stepwise multiple testing procedures with applications to clinical trial data. *Pharm Stat*. 2021;20(2):297-313. doi:10.1002/pst.2076
21. Knotkova H, Hamani C, Sivanesan E, et al. Neuromodulation for chronic pain. *Lancet*. 2021;397(10289):2111-2124. doi:10.1016/S0140-6736(21)00794-7
22. De Wachter S, Knowles CH, Elterman DS, et al. New technologies and applications in sacral neuromodulation: an update. *Adv Ther*. 2020;37(2):637-643. doi:10.1007/s12325-019-01205-z
23. Kuner R, Kuner T. Cellular circuits in the brain and their modulation in acute and chronic pain. *Physiol Rev*. 2021;101(1):213-258. doi:10.1152/physrev.00040.2019
24. Chen G, Zhang YQ, Qadri YJ, Serhan CN, Ji RR. Microglia in pain: detrimental and protective roles in pathogenesis and resolution of pain. *Neuron*. 2018;100(6):1292-1311. doi:10.1016/j.neuron.2018.11.009
25. Koch SC, Acton D, Goulding M. Spinal circuits for touch, pain, and itch. *Annu Rev Physiol*. 2018;80:189-217. doi:10.1146/annurev-physiol-022516-034303
26. Lee C, Pizarro-Berdichevsky J, Clifton MM, Vasavada SP. Sacral neuromodulation implant infection: risk factors and prevention. *Curr Urol Rep*. 2017;18(2):16. doi:10.1007/s11934-017-0663-1
27. Zhang P, Zhang JZ, Wu LY, Zhang XD. Effects of appropriate prolonged sacral neuromodulation testing in improving implantation rate of a permanent implantable pulse generator in patients with refractory lower urinary tract dysfunctions in mainland China. *Chin Med J (Engl)*. 2017;130(4):439-444. doi:10.4103/0366-6999.199831
28. Martellucci J, ed. *Electrical Stimulation for Pelvic Floor Disorders*. Springer; 2015. doi:10.1007/978-3-319-06947-0. ISBN: 978-3-319-06946-3.

How to cite this article: Terzoni S, Mora C, Sighinolfi MC, et al. Transcutaneous sacral neuromodulation for pelvic pain and non-relaxing pelvic floor: Findings from a pilot study. *Int J Urol Nurs*. 2023;17(2):123-128. doi:10.1111/ijun.12351