Pain Medicine, 2024, **25**, 252–254
https://doi.org/10.1093/pm/pnad145
Advance access publication 31 October 2023
Research Letter

Pain relief in refractory fibromyalgia after vestibulocortical stimulation: an open-label pilot trial

Michael H. Kaplan, MD*[,1], Celine H. Zhou, MD[2], Emily Carroll, MD[1], Alan D. Weinberg, MS[3], Daniel J. Clauw, MD[4], Trung Thành Ngô, PhD*[,5], Ioannis Tassiulas, MD[1]

[1]Division of Rheumatology, Mount Sinai Hospital, New York, NY 10019, United States
[2]Division of Rheumatology & Clinical Immunology, Department of Medicine, University of Pittsburgh, PA 15232, United States
[3]Population Health Science & Policy, Mount Sinai Hospital, New York, NY 10019, United States
[4]Chronic Pain & Fatigue Research Center, University of Michigan, Ann Arbor, MI 48106-5737, United States
[5]RECOVER Injury Research Centre, The University of Queensland and Surgical, Treatment & Rehabilitation Service (STARS), Queensland 4029, Australia

**Corresponding author:* Division of Rheumatology, Department of Medicine, Mount Sinai Faculty Practice, 425 West 59th St, New York, NY 10019, USA. Email: Michael.Kaplan@mountsinai.org; RECOVER Injury Research Centre, The University of Queensland and Surgical, Treatment & Rehabilitation Service (STARS), Level 7, 296 Herston Road, Herston, Brisbane, Queensland 4029, Australia. Email: Trung.Ngo@uq.edu.au

T.T.N. and I.T. contributed equally.

Trial registration: ClinicalTrials.gov ID: NCT05004194.

Keywords: fibromyalgia; chronic pain; intractable pain; vestibular system; caloric test; noninvasive neuromodulation; pain management.

Dear Editor,

Fibromyalgia is a common debilitating disorder of widespread pain, affecting roughly 2% to 3% of the population, yet effective treatments are still lacking.[1] Novel interventions that are safe, affordable, effective, and readily translatable into clinical practice remain an urgent and unmet need.

Although traditionally used as a routine neurodiagnostic technique, the caloric test over recent decades has also demonstrated therapeutic benefits in centralized pain syndromes, such as post-stroke thalamic pain, transverse myelitis, migraine, and phantom limb pain, along with other wide-ranging multimodal effects (eg, improving mood, attention, perception, cognition/insight, and mobility).[2–5] The technique involves irrigating the external ear canal with cold/warm water to incite the vestibulo-ocular reflex, and it has been shown to consistently activate an endogenous restorative-function brain circuit. This vestibulocortical stimulation (VCS) procedure, unlike noninvasive neuromodulation modalities such as vagus nerve stimulation and repetitive transcranial magnetic stimulation,[6,7] is a low-cost, easy-to-administer, and widely accessible intervention with a long-standing safety profile since its development more than a century ago. In the present study, we therefore sought to examine whether VCS can also provide pain relief and improve quality-of-life measures in patients with refractory fibromyalgia.

Methods

This nonrandomized open-label effectiveness trial (data collection) was conducted between February and July 2021. All patients provided written, informed consent for participation in this trial and were recruited from a single rheumatology practice according to a study protocol approved by the Mount Sinai Hospital System Institutional Review Board (STUDY-20-01350M-CR001; ClinicalTrials.gov identifier: NCT05004194). Twenty-one patients (≥18 years of age) who satisfied the 2016 American College of Rheumatology diagnostic criteria for fibromyalgia (all refractory according to clinical assessment) participated in the trial (mean age = 46.5 years; 20 female). Of these, 10 had primary fibromyalgia, 11 had an underlying inflammatory disorder, and 18 were receiving at least one pharmacotherapy for fibromyalgia. There were several exclusion criteria.[8]

Each participant completed baseline surveys and pain intensity numeric pain scales daily (0= "no pain" to 10= "worst pain of my life") for 1 week before VCS. Each participant then underwent one VCS treatment session with 50 cc of right-ear cold-water irrigation (4°C) at 1–2 cc/second. VCS was confirmed by observing postprocedural nystagmus and patient-reported vertigo. Pain intensity scores were recorded before VCS and at 5 minutes, 15 minutes, and 30 minutes after VCS. Overall subjective well-being (0= "worst I've ever felt" to 10= "best I've ever felt") was also assessed at baseline and 30 minutes after the procedure. After VCS, each participant was asked to complete secondary surveys at 24 hours, 1 week, 2 weeks, and 4 weeks out. All participants' pain medications continued throughout this period. The primary outcome measure was change in pain intensity at 1 week after VCS, relative to baseline. Secondary outcomes included immediate change in pain and subjective well-being, improved quality of life, and assessment of VCS technique tolerability.

Results

There was rapid pain relief at 5 minutes after the procedure, and at 30 minutes after VCS, pain decreased in 17/21 participants

Received: 17 August 2023. **Revised:** 24 October 2023. **Accepted:** 28 October 2023

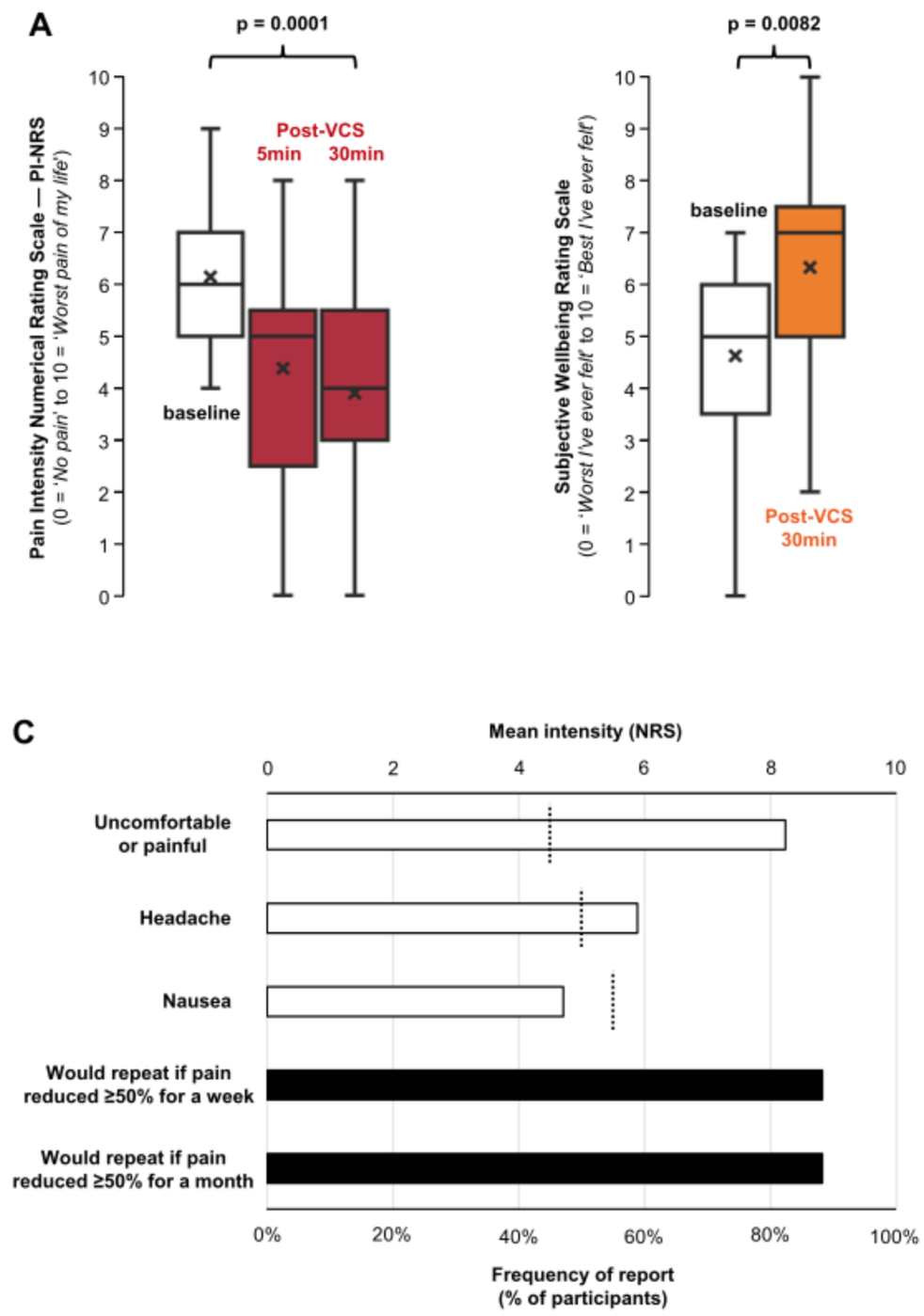

Figure 1. (A) Pain reduction and improved well-being ratings at 30 minutes after vestibulocortical stimulation (VCS). Left panel shows distributions of pain intensity ratings ($n = 21$) at baseline, 5 minutes, and 30 minutes after VCS. Right panel shows distributions of overall subjective well-being rating scores at baseline and 30 minutes after VCS. Boxes show the interquartile range (IQR), median (midline), and mean (×). Whiskers show the range of values beyond the box limits within a distance of 1.5 × IQR (ie, 12.5% and 87.5%). *P* values are from Wilcoxon signed-rank tests of baseline and post-VCS 30-minute data. **(B) Pain relief sustained for 7 days after VCS treatment.** After a single VCS administration on Day 7, mean pain ratings across Days 8–14 were significantly different from the baseline mean (ie, 7.29 from daily pre-VCS pain ratings averaged across Days 0–6; $P = .0172$). Mixed modelling methodology was used to perform this repeated pain measures analysis (PROC MIXED, SAS system software) and generate a mathematical equation expressing the trajectory of pain intensity over time while accounting for correlation between measures within participants, missing data points in a small trial (assumed to be missing at random), and irregularly spaced time between participant measures: $y = 7.59 + (0.26 \times day) - (0.11 \times day^2) + (0.0054 \times day^3)$; $P < .0001$. These analytical methods enable estimation of the shape that best fits the pattern of measures over time (eg, linear, parabolic, or cubic).[9] For the present trial data ($n = 17$), a nonlinear relationship (cubic function) provided the best fit, which suggests a gradual curvilinear decrease in pain over time (after VCS) for most participants and a slight increase toward the end of the follow-up period. Four participants out of $n = 21$ (panel A) had no pre-VCS (Days 0–6) or post-VCS (Days 8–14) data and thus were not included in the mixed modelling analysis. **(C) VCS technique tolerability, side effects, and participants' willingness to repeat intervention for pain relief.** The 3 white horizontal bars depict the percentages of participants (from total $n = 17$) reporting each of the VCS side effects (ie, 82% uncomfortable or painful; 59% headache; 47% nausea). The short vertical dotted lines indicate the mean intensity (0–10 numeric rating scale) for each of the respective side effects (ie, 4.5, 4.9, and 5.3, respectively). Their duration was not formally measured, but they resolved rapidly. The solid black horizontal bars depict the percentages of participants (from total $n = 17$) who indicated they would have repeat VCS sessions if VCS reduced their pain by 50% or more for 1 week or for 1 month (ie, 88% and 88%, respectively). These tolerability results overall are consistent with a recent VCS study in persistent pain disorders,[10] such as most participants' (ie, 15/17) willingness to have repeat VCS sessions for pain relief. Of the remaining 2 participants who would not have it repeated, one found the procedure too uncomfortable (ie, 10/10 score), whereas the other participant did not find it uncomfortable (ie, 3/10) but reported strong nausea (10/10) and had a single episode of small-volume emesis with no further issues. There were no major adverse events in the present study.

(81%), increased in 1/21 (4.8%), and was unchanged in 3/21 (14.3%) ($P < .0001$; Wilcoxon signed-rank tests; Figure 1A). In those who reported a pain reduction at 30 minutes after the procedure, 7/17 (41%) reported at least a 50% improvement. Subjective well-being ratings improved at 30 minutes after VCS in 11/21 participants (52.4%), worsened in 3/21 (14.3%), and were unchanged in 7/21 (33.3%) ($P = .0082$; Wilcoxon signed-rank tests; Figure 1A). Twenty-four hours after VCS and over the following week, a significant decrease in pain was maintained relative to baseline, as shown in a mixed modeling analysis ($P = .0172$; Figure 1B).[9] Decreases in average pain interference (7.2 to 3.4; Brief Pain Inventory Pain Interference subscale; $n = 12$) and fatigue (38.3 to 32.3; Global Fatigue Index; $n = 11$) were also observed a week after VCS treatment in a subsample of participants (ie, 12 and 11 patients completed these respective scales). The two subgroups of participants—primary fibromyalgia and comorbid inflammatory disease—had similar pain reductions. However, there was no statistically significant difference in pain reduction between the subgroups, and it should be noted that the present pilot trial was also not designed or sufficiently powered to detect such a difference. There were no major adverse effects in the present study. VCS was well tolerated, with the large majority of participants (88%) indicating that they would have the procedure again if it reduced

their pain by ≥50% for 1 week or for 1 month (Figure 1C). This finding is consistent with a recent VCS study in persistent pain disorders.[10] One patient in the present trial also reported that she felt "a curtain was lifted" after VCS with respect to overall mood and global improvement, and 3 participants requested a repeat treatment session.

Discussion

In the present pilot trial, VCS was found to be a safe and effective intervention for short-term pain relief and improving subjective well-being in patients with refractory fibromyalgia. The effects were quick in onset and lasted up to 7 days after the procedure for most participants. However, interpretation of these results is limited, as a sham intervention was not included and postprocedural data were incomplete for assessing the quality and longer-term duration of VCS treatment. As such, these findings require further investigation in large, randomized, placebo-controlled trials. The trials should be designed to assess the comparative efficacy, durability, tolerability, and health economics of VCS as a potential first-line and/or adjuvant therapy in the clinical management of fibromyalgia.

Acknowledgments

We were granted permission to use the Multidimensional Assessment of Fatigue (MAF) Scale in this study by the MAPI Research Trust (Lyon, France).

Funding

There is no funding to report for this study.

Conflicts of interest: There are no conflicts of interest to report.

References

1. Sarzi-Puttini P, Giorgi V, Marotto D, Atzeni F. Fibromyalgia: an update on clinical characteristics, aetiopathogenesis and treatment. Nat Rev Rheumatol. 2020; 16 (11):645-660.
2. Miller SM, Ngo TT. Studies of caloric vestibular stimulation: implications for the cognitive neurosciences, clinical neurosciences and neurophilosophy. Acta Neuropsychiatr. 2007; 19 (3):183-203.
3. McGeoch PD, Williams LE, Lee RR, Ramachandran VS. Behavioral evidence for vestibular stimulation as a treatment for central post-stroke pain. J Neurol Neurosurg Psychiatry. 2008; 79 (11):1298-1301.
4. McGeoch PD, Ramachandran VS. Caloric vestibular stimulation can relieve pain of spinal origin. Spinal Cord. 2008; 46 (11):756-757.
5. Aranda-Moreno C, Jáuregui-Renaud K, Reyes-Espinosa J, et al. Stimulation of the semicircular canals or the utricles by clinical tests can modify the intensity of phantom limb pain. Front Neurol. 2019; 10:117.
6. Martins DF, Viseux FJF, Salm DC, et al. The role of the vagus nerve in fibromyalgia syndrome. Neurosci Biobehav Rev. 2021; 131:1136-1149.
7. Choo YJ, Kwak SG, Chang MC. Effectiveness of repetitive transcranial magnetic stimulation on managing fibromyalgia: a systematic meta-analysis. Pain Med. 2022; 23 (7):1272-1282.
8. Tassiulas I. Vestibular Caloric Stimulation and the Modulation of Pain in Fibromyalgia. Accessed August 12, 2021. https://clinicaltrials.gov/ct2/show/NCT05004194.
9. Bayman EO, Oleson JJ, Rabbitts JA. AAAPT: assessment of the acute pain trajectory. Pain Med. 2021; 22 (3):533-547.
10. Ngo TT, Barsdell WN, Law PCF, et al. Tolerability of caloric vestibular stimulation in a persistent pain cohort. Brain Stim. 2020; 13 (5):1446-1448.