


## BRIEF COMMUNICATION

## Pain Reprocessing Therapy for migraine: A case series

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## Abstract

Pain Reprocessing Therapy (PRT) is a behavioral intervention that aims to remediate learned threat associations underlying chronic pain. It has shown efficacy in treating chronic low back pain and was explicitly developed to address a broader range of centrally mediated pain conditions. The focus of PRT on learned threat associations dovetails with emerging neurobiological models of migraine, which highlight learned threat associations—nonharmful internal (e.g., hunger, fatigue) or external (e.g., weather changes) cues that are persistently misinterpreted as danger signals—as a modifiable contributor to migraine pathophysiology. Despite its conceptual relevance, PRT has not yet been studied for migraine, a leading cause of disability with an ongoing need for more effective treatments, especially for patients who are refractory to evidence-based treatments. Addressing this gap, we present the first case series on PRT for migraine. We describe three individuals with chronic migraine who engaged in PRT delivered by a physician. All three patients had inadequate response to standard-of-care preventive and acute migraine treatments and presented with complex clinical histories, including non-headache pain comorbidities. PRT sessions (initial visit 60 min; follow-ups 30 min) focused on two key components: (1) education about neuroplastic pain and its relevance to migraine, and (2) guided instruction and daily practice of somatic tracking. Across all three cases, patients experienced large reductions in headache frequency and clinically meaningful improvements in pain intensity and functional outcomes. Case 1 improved from 18 to 25 headache days/month to 3, discontinued cannabis use, and canceled planned interventional treatments. Case 2 improved from 30 headache days/month to 5 and reported greater effectiveness and decreased use of acute medication. Case 3 improved from 30 migraine days/month to 3-4, remained off preventive medication, and reported improvement in migraine and comorbid pelvic and abdominal pain. In all cases, the most substantial gains appeared to follow a shift in pain attribution toward a learned threat association model and daily engagement in somatic tracking, consistent with prior literature on PRT in low back pain. This case series is the first to document the use of PRT for migraine and suggests its potential relevance as a mechanistically informed behavioral intervention for migraine. There is now a need to systematically evaluate PRT for migraine in controlled studies.

## KEYWORDS

case series, migraine, neuroplastic pain, nociplastic pain, pain reprocessing therapy, somatic tracking

## INTRODUCTION

Behavioral therapies are an evidence-based component of migraine care,<sup>1</sup> but meta-analyses show that the frontline behavior therapies yield only modest effects.<sup>2,3</sup> As such, the American Headache Society has recognized the development of more effective behavioral treatments as a pressing research priority.<sup>4</sup>

One promising new behavioral treatment direction is targeting dysregulated threat processing. Recent neurobiological models of migraine<sup>5,6</sup> propose that nonharmful interoceptive and environmental cues (e.g., hunger, weather changes, physical activity) can become conditioned as threats, triggering top-down activation of headache and other migraine symptoms that in turn cue safety-seeking responses (e.g., lying down in a dark room). Neuroplasticity-driven processes are thought to underlie the coupling of nonthreatening cues with pain and other symptoms,<sup>7</sup> a phenomenon increasingly recognized as *neuroplastic pain*.<sup>10,11</sup>

Pain Reprocessing Therapy (PRT) is a behavioral intervention designed to treat neuroplastic pain by reversing these learned threat associations.<sup>12–14</sup> PRT combines pain neuroscience education with somatic tracking, a technique intended to help patients reduce threat reactivity associated with bodily sensations. In a randomized controlled trial, PRT demonstrated large effect sizes in reducing low back pain by targeting pain-related threat responding.<sup>14,15</sup> PRT and related approaches stand apart from frontline behavioral therapies for headache disorders, such as cognitive behavioral and mindfulness-based interventions, which instead conceptualize migraine as a condition to be managed indefinitely with strategies such as lifestyle modifications or acceptance.<sup>16–18</sup>

To our knowledge, PRT has not been previously applied to migraine. This case series describes three individuals with chronic migraine who had poor responses to standard-of-care migraine treatments before achieving substantial clinical improvement following a short course of PRT.

## METHODS

### Case selection

A key purpose of case reports and case series in headache medicine<sup>19</sup> and similar areas<sup>20,21</sup> is to describe innovative, promising new therapeutic approaches. Accordingly, we selected three cases of patients who responded favorably to PRT after poor responses to standard-of-care treatments, including calcitonin gene-related peptide (CGRP) targeting therapies; PREEMPT protocol onabotulinumtoxinA; and, in some cases, interventional pain treatments, noninvasive neuromodulation, and implantable neuromodulation.

<sup>\*</sup>Related concepts include centralized<sup>8</sup> and nociplastic pain<sup>9</sup>; following the novel treatment model, we use the term *neuroplastic* here.

## Patients

Three patients (two female, one male; see [Table 1](#)) were treated in an integrative medicine clinic at an academic center. All were considered suitable PRT candidates based on inadequate response to standard-of-care migraine treatments, including pharmacotherapy and botulinumtoxin injections.

## Treatment

Treatment was delivered by a physician (A.M.P.) during a 60-min initial visit, followed by 30-min follow-up visits spaced 1–4 weeks apart. Following published PRT materials,<sup>12–14</sup> patients first received education about how learned threat associations engender neuroplastic pain, including migraine. Patients were encouraged to engage with PRT-aligned books and apps between visits to advance their understanding of neuroplastic pain. Next, patients learned and practiced *somatic tracking*: focusing on sensations combined with reminding oneself that painful sensations are due to the brain incorrectly perceiving a threat. They practiced this technique at treatment visits and multiple times daily between visits.

To avoid reinforcing symptom hypervigilance, patients were not asked to maintain a daily headache diary. Instead, the physician asked patients to estimate the number of headache or migraine days in the past month at treatment visits.

## Data extraction

The data reported here were obtained via review of the medical chart.

## Ethics

Written informed consent was obtained from the patients to publish their cases. Institutional review board review was determined not to be required at our institution for this project, given its scope as a case series.

## RESULTS

### Case 1

A 55-year-old woman with chronic migraine (18–25 headache days/month) and chronic thoracic pain presented after inadequate response to CGRP monoclonal antibodies, PREEMPT-protocol onabotulinumtoxinA injections, nerve blocks, neuromodulation, and cannabis (see further details in [Table 1](#)). The patient reported having sought out PRT previously in a community treatment setting but was unable to complete the treatment at that time because treatment would have been self-pay. She attended five PRT visits over 3 months.

TABLE 1 Summary of case characteristics and PRT course.

Case (age and sex)	Migraine history	Pre-PRT headache frequency	Response to 5–6 sessions of PRT
1 (55F)	<ul style="list-style-type: none"> <li>• First migraine early adulthood, worsening at age 40 years, had recently undergone prophylactic bilateral salpingo-oophorectomy at time of onset</li> <li>• Headaches lasting 6+ h and up to 3–4 days, localized to right orbital to temple to occiput with radiation down the neck into her body but not exclusively on the right side</li> <li>• Associated nausea, vomiting, photophobia, and phonophobia</li> <li>• Changes in barometric pressure a reliable migraine trigger</li> <li>• Preventive treatments: galcanezumab, eptinezumab, erenumab, PREEMPT protocol onabotulinumtoxinA, topiramate, propranolol, memantine, cervical trigger point injections, bilateral pericranial peripheral nerve blocks (greater and lesser occipital occipital, supraorbital, supratrochlear, and auriculotemporal nerve blocks), right cervical C3–5 medial branch blocks and radiofrequency ablation, transcutaneous supraorbital nerve stimulation, 60-day percutaneous right occipital nerve stimulator</li> <li>• Acute treatments: sumatriptan, acetaminophen, ketorolac oral and injection, cannabis</li> </ul>	18–25/30	<ul style="list-style-type: none"> <li>• Reduction in headache days to 3/ month</li> <li>• Eliminate use of cannabis as a migraine treatment</li> <li>• Somatic tracking reduces headache pain intensity</li> <li>• Canceled future trigger point injections and pain medicine follow-ups because she had sufficiently improved with PRT</li> </ul>
2 (36F)	<ul style="list-style-type: none"> <li>• Migraine with aura onset in adolescence</li> <li>• Headaches had worsened to daily frequency over year prior to PRT initiation; patient attributed frequency increase to heightened work-related stress</li> <li>• Throbbing headaches constant, daily, and localized to bilateral frontal and temporal regions</li> <li>• Associated nausea, phonophobia, photophobia, and blurred vision</li> <li>• Beginning of menstrual cycle, oral contraceptives, hormonal intrauterine device, and alcohol reliably worsened headache</li> <li>• Preventive treatments: erenumab, botulinum toxin injections to frontalis, procerus, corrugators, and masseters via dermatologist (one session per location), magnesium, acupuncture, physical therapy</li> <li>• Acute treatments: ubrogepant, sumatriptan, eletriptan, acetaminophen-aspirin-caffeine, over-the-counter nonsteroidal anti-inflammatory drugs</li> <li>• Ubrogapant at maximum frequency for acute or prodromal treatment at PRT initiation; drug delayed but did not reliably abort or prevent migraine attack</li> </ul>	30/30	<ul style="list-style-type: none"> <li>• Reduction in headache days to 5/ month</li> <li>• Decrease in average headache intensity from 9–10/10 to 6–7/10</li> <li>• Decreased ubrogepant dose frequency, increased perceived benefit from ubrogepant</li> <li>• No worsening of migraine frequency despite experiencing a previous migraine trigger (major employment-related stressor) during PRT treatment</li> <li>• Somatic tracking alleviates headache intensity</li> </ul>
3 (48 M)	<ul style="list-style-type: none"> <li>• Migraine onset age 40, concurrent with onset of pelvic floor dysfunction and ulcerative colitis-related pain</li> <li>• Holocephalic headaches worst in morning, improved throughout the day, and returned in the evening; associated with photophobia, phonophobia, nausea, dizziness, and fatigue</li> <li>• Headache severity mirrored severity of his pelvic floor symptoms</li> <li>• Psychosocial triggers</li> <li>• Preventive treatments: erenumab, galcanezumab, PREEMPT protocol onabotulinumtoxinA, propranolol, topiramate, valproic acid, amitriptyline, nortriptyline, venlafaxine, duloxetine, gabapentin, physical therapy and osteopathic manipulative treatment</li> <li>• Acute treatments: ubrogepant, sumatriptan, eletriptan, naratriptan, nonsteroidal anti-inflammatory drugs, acetaminophen, tetrahydrocannabinol</li> <li>• Taking galcanezumab at PRT initiation; stated would have severe headache with missed doses</li> </ul>	30/30	<ul style="list-style-type: none"> <li>• Reduction in migraine days to 3–4/ month while remaining off migraine preventive medications</li> <li>• No worsening of migraine frequency despite experiencing a previous migraine trigger (upper respiratory infection) during PRT treatment</li> <li>• Somatic tracking alleviates pain during migraine attacks</li> <li>• Continued to have daily headaches after six PRT sessions</li> </ul>

Abbreviations: C, cervical; F, female; M, male; PRT, Pain Reprocessing Therapy.

At the first visit, she received education on neuroplastic pain and engaged in a physician-guided somatic tracking exercise, which led to immediate relief of her thoracic and headache pain. In follow-up sessions, she practiced somatic tracking for both headache and thoracic symptoms and reported gradual improvements. By the third treatment visit, the patient attributed 50% of her pain to neuroplastic processes; and by the fourth, she had begun intentionally increasing physical activity and replacing cannabis use with somatic tracking and breathing practices.

At 1-month follow-up, she reported only 3 mild headache days managed with a single over-the-counter pain reliever dose. Furthermore, she reported no migraine or thoracic pain despite encountering previously triggering conditions on a vacation (e.g., vigorous physical activity, hot weather). She attributed her improvement to understanding her pain as neuroplastic and daily practice of PRT techniques. The patient canceled future trigger point injections and pain medicine follow-ups, stating that she no longer needed these treatments.

## Case 2

A 36-year-old woman with chronic migraine (30 headache days/month; pain severity rated 9–10/10) and neck pain presented after trying erenumab, onabotulinumtoxinA via a dermatologist, acupuncture, and physical therapy for prevention; and over-the-counter medications, triptans, and ubrogepant for acute treatment (see Table 1). She reported that ubrogepant during the prodromal phase delayed but did not prevent or abort migraine attacks. Approximately 3 weeks before starting PRT, the patient had received onabotulinumtoxinA injections to the procerus, corrugators, and frontalis, her first such treatment to date. She had read extensively about neuroplastic pain prior to treatment and was referred for PRT.

At her first PRT visit, the patient received education on neuroplastic pain and learned somatic tracking, resulting in immediate pain relief during the visit. She reported 4 headache-free days afterward. Between the first and second visit, she received onabotulinumtoxinA injections from her dermatologist to the bilateral masseter muscles, her first such treatment to the masseters.

Over the next three PRT sessions, spaced 1–2 weeks apart, she continued to experience immediate symptom relief during in-session somatic tracking and began daily somatic tracking practice at home. By the fourth visit, she fully endorsed a neuroplastic pain attribution and reported resolving migraine and neck pain episodes through somatic tracking alone. She additionally reported that she was able to fully resolve episodes of headache and neck pain using somatic tracking.

By the sixth visit (3 weeks after the fifth visit), her headache frequency decreased to 5 days/month. When migraine attacks occurred, pain severity was reduced from 9–10/10 before PRT to 6–7/10 after PRT. She reported that ubrogepant now provided pain freedom and most bothersome symptom freedom by 2 hours, and that she was taking it less frequently. Notably, she maintained these

improvements despite experiencing a major employment-related life stressor between the fifth and sixth visits—an event that previously would have triggered migraine worsening. She subsequently canceled her planned onabotulinumtoxinA injections.

## Case 3

A 48-year-old man with chronic migraine (30 migraine and 30 headache days/month; pain severity rated 7–10/10) and comorbid ulcerative colitis and pelvic pain presented for PRT. Prior preventive treatments included propranolol, antiseizure medications, tricyclics, serotonin–norepinephrine reuptake inhibitors, erenumab, and PREEMPT-protocol onabotulinumtoxinA (see Table 1). He had also tried triptans, ubrogepant, nonsteroidal anti-inflammatory drugs, acetaminophen, prochlorperazine, triptans, and tetrahydrocannabinol for acute treatment. At initiation of PRT, he was taking galcanezumab for migraine prevention and stated that he would have more severe headaches without it. He reported that his migraine and pelvic symptoms onset during a period of significant psychosocial stress and mirrored one another in severity. The patient reported having previously read a book about mind–body connections in pain (although it was not about PRT) before starting PRT.

At the first PRT visit, his presentation was conceptualized as neuroplastic due to chronic overlapping pain conditions, stress-linked onset, and lack of response to standard treatments. He accepted this explanation and began practicing somatic tracking multiple times daily.

By the second visit, the patient reported a reduction in migraine severity to 5/10 and described that using somatic tracking partially relieved both headache and abdominal pain. Over the next 2 months, with monthly PRT visits, his migraine frequency dropped to 5 days/month. He self-discontinued his preventive medications and reported no migraine flare during an upper respiratory infection, previously a reliable trigger. As of his 1-month neurology follow-up after his sixth PRT visit, he reported sustained improvement in migraine (3–4 migraine days/month) with ongoing PRT and daily practice, although he continued to report daily headaches. He continued PRT visits at 8–12 week follow-ups while remaining off preventive medications.

## DISCUSSION

This case series is the first to report on PRT as a treatment for migraine. Across three patients with chronic migraine who had not responded adequately to standard care (including traditional oral preventive medications, triptans, CGRP targeted therapies, and botulinumtoxin injections), we observed substantial reductions in headache and/or migraine frequency—from daily or chronic frequency to 3–5 days/month—and clinically meaningful improvements in pain severity. Furthermore, although not the focus of this case series, these patients also reported improvements in non-headache pain with PRT.

Consistent with the PRT model,<sup>12,13</sup> clinical improvement in these cases appeared to follow patients' attribution of their migraine to

learned threat associations and their daily practice of somatic tracking. This pattern aligns with mechanistic findings from a prior PRT trial in chronic low back pain, where changes in attribution and reductions in fear mediated treatment effects.<sup>14,15</sup> Systematic investigation is needed to clarify the relationship between PRT techniques, mechanisms, and outcomes in migraine and chronic pain conditions.

Several aspects of this case series warrant attention. The patients were highly receptive to the treatment rationale and readily began daily somatic tracking, and PRT was delivered in a medical setting by a physician. The combination of patients' readiness and a physician provider (which may overcome reluctance in patients with skepticism toward behavioral interventionist treatment<sup>22</sup>) explaining symptoms as neuroplastic may have enhanced treatment impact over just 5–6 sessions. These factors underscore the importance of evaluating optimal PRT formats and candidates.

This case series was primarily intended to describe the therapeutic techniques and potential clinical potency of PRT, a 5–6 visit behavioral intervention, for chronic migraine refractory to CGRP-targeted therapies and onabotulinumtoxinA. As such, this study fits into existing behavioral intervention development frameworks,<sup>23,24</sup> including in headache disorders.<sup>19</sup> It provides critical proof-of-concept data in a small sample that supports and informs future, larger investigations and, ultimately, methodologically rigorous, resource-intensive clinical trials. Logical next steps consistent with these intervention development frameworks would be (1) a trial to evaluate whether recruitment, randomization, and treatment completion are feasible; and (2) if feasibility is confirmed, an efficacy-focused randomized trial, potentially with sequential and multiple assignment elements,<sup>25</sup> to evaluate whether, when, and for whom PRT is most effective. These studies will be positioned to address the natural limitations<sup>20,21,26</sup> of this case series design, including its small size, lack of control condition, single provider and site, and nonconsecutive cases.

Other limitations of this case series include that medical records lacked complete documentation of both headache and migraine days per month and headache diary data; however, prior research supports the validity of monthly recall relative to prospective diaries.<sup>27,28</sup> This case series supports conducting future research with prospective collection of International Headache Society-recommended outcomes.<sup>29</sup> We focused on people with refractory chronic migraine, a population in need of new, effective treatments,<sup>30</sup> but did not examine treatment-naïve or episodic presentations. Further research is needed to understand which people with migraine may be most likely to benefit from PRT, and when. Finally, the cases described here were selected to explore the application and clinical potency of PRT for migraine, underscoring the need for future studies with systematic recruitment efforts to further evaluate PRT efficacy.

## CONCLUSIONS

This case series suggests that PRT may be a promising behavioral intervention for individuals with chronic migraine who have not benefited from standard treatments.

## AUTHOR CONTRIBUTIONS

**Joel N. Fishbein:** Writing – original draft; conceptualization; methodology; writing – review and editing; investigation. **Nathaniel M. Schuster:** Writing – review and editing; supervision; methodology; investigation; conceptualization. **Alpha Anders:** Writing – review and editing; investigation. **Ariel M. Portera:** Conceptualization; investigation; writing – review and editing; methodology. **Matthew S. Herbert:** Conceptualization; investigation; writing – review and editing; supervision; methodology.

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## CONFLICT OF INTEREST STATEMENT

**Joel N. Fishbein, Nathaniel M. Schuster, Alpha Anders, Ariel M. Portera, and Matthew S. Herbert** declare no conflicts of interest.

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