

PSYCHOLOGICAL AND BEHAVIORAL ASPECTS OF HEADACHE AND PAIN (D BUSE, SECTION EDITOR)

Behavioral Treatments for Post-Traumatic Headache

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Abstract

Purpose of Review Post-traumatic headache (PTH) is a common headache type after traumatic brain injury (TBI). There are no FDA approved medications for PTH, and it is unknown how medications can affect the brain's ability to recover from TBI. Thus, we sought to examine the biopsychosocial factors that influence PTH and the non-pharmacologic treatments studied for headache treatment. We also sought to determine if there is literature examining whether the non-pharmacologic treatments influence the biopsychosocial factors. The nonpharmacologic treatments assessed included cognitive behavioral therapy (CBT), biofeedback, progressive muscle relaxation therapy (PMR), acupuncture, and physical therapy (PT).

Recent Findings Factors associated with prognosis in PTH may include the following: severity of TBI, stress, post-traumatic stress disorder, other psychiatric comorbidities, so-ciocultural and psychosocial factors, litigation, base rate mis-attribution, expectation as etiology, and chronic pain. There are few high quality studies on the non-pharmacologic treatments for PTH. Thermal and EMG biofeedback appear to have been examined the most followed by CBT. Studies did not have secondary outcomes examining the psychosocial factors related to PTH.

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Mia Minen minenmd@gmail.com *Summary* Most of the behavioral studies involved a multimodality intervention limiting the ability to assess the individual non-pharmacologic interventions we sought to study. There were very few randomized clinical trials evaluating the efficacy of non-pharmacologic interventions. Therefore, future research, which considers the noted biopsychosocial factors, is needed in the field to determine if these interventions reduce PTH.

Keywords Post-traumatic headache · Traumatic brain injury · Behavioral treatment · Cognitive behavioral therapy · Biofeedback · Relaxation therapy

Introduction

Post-traumatic headache (PTH) is a common headache type, occurring in 30 to 90% of patients after traumatic brain injury (TBI) and lasting for more than a year in up to one-third of patients [1]. According to the International Classification of Headache Disorders (ICHD)-3 beta, PTH is defined as a headache caused by traumatic injury to the head that occurred within 7 days after one of the following: (1) injury to the head, (2) regaining of consciousness following injury to the head, or (3) discontinuation of medication(s) that impair ability to sense or report headache following the injury to the head [2]. There is difficulty in studying PTH given the numerous variables that cannot be controlled for in PTH study designs, e.g., patients have different mechanisms of injury, and patients may present for care at different time points-from the day of injury to year of post-injury. The accompanying cognitive symptoms can also make symptom reporting somewhat unreliable.

Research on PTH is limited; more studies assess factors related to prognosis, and fewer investigations are well-

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designed studies assessing which treatments might be effective for these patients [3...]. Factors related to prognosis include severity of the TBI, psychological comorbidities, base rate misattribution, litigation, and more, and they are discussed below. In terms of treatment, there are no FDA approved pharmacologic treatments for PTH. Physicians tend to consider the "phenotype" of the PTH and then prescribe medications traditionally used to treat the primary headache disorders of that corresponding "phenotype." Given the limited research on the pharmacologic treatment of migraine, and the fact that we do not know about the long-term effects of the pharmacologic treatments on the brain injury recovery process, non-pharmacologic treatments seem very appealing. Non-pharmacologic treatments have been used for various headache disorders for over 30 years, and they are essentially free of adverse effects [4].

Similarly to post-concussion syndrome (PCS), the etiology of PTH is likely diverse, multifactorial, and with individual variability. A perspective incorporating biological, social, cognitive, affective, and behavioral factors within the context of a biopsychosocial framework, proposed as useful for conceptualizing recovery trajectory of individuals with PCS [5–7], may also be relevant for PTH. Furthermore, treatment for PTH has often targeted various factors within the biopsychosocial framework suggesting the importance of considering a complex etiology and multifactorial approach to treatment.

Herein, using the biopsychosocial model, we review the factors related to PTH as well as possible non-pharmacologic treatment options for patients suffering from PTH. Given that the treatment of PTH may be provided by professionals across various disciplines, we review the literature on the nonpharmacologic treatments previously found to have grade A evidence for the treatment of migraine [8]: cognitive behavioral therapy (CBT), biofeedback and relaxation therapy, as well as common non-behavioral treatments such as acupuncture and physical therapy (PT). A review of the literature revealed that researchers have investigated the efficacy of combined treatments due to consensus that multimodal treatment is most effective in this population [4, 9]. As discussed below, our review of the PTH literature found a paucity of evidence supporting PTHspecific interventions [10, 11., 12., 13.]. Many PTH nonpharmacologic treatment studies used multimodal treatments, making it difficult to discern which components of multimodality behavioral therapy are most effective.

Related Factors

Given the multifactorial contributions to PTH, consideration of the following factors is paramount to inform treatment planning and minimize frequency, chronicity, and intensity of symptoms.

Severity of TBI

Review of extant literature suggests an inconsistent and unclear relationship between severity of TBI and PTH. Several studies have found an inverse relationship between severity of brain injury and frequency of chronic daily headache [14, 15], while other studies have found no differences between mild TBI and moderate/severe TBI populations [16, 17•, 18]. Two studies that mainly used loss of consciousness (LOC) to examine this association found that LOC was positively related to PTH intensity among individuals with mild TBI [19•, 20]. Contradictory and indistinct findings may have been impacted by various factors such as study design, use of different classifications of TBI, the difference between acute and chronic PTH, the nature of study populations (e.g., civilian vs. military personal, unawareness/cognitive issues that lead to underreporting for moderate-severe TBI populations), using different study time point for recruitment, and the impact of mediating factors (e.g., depression or PTSD) between mild TBI and PTH [14, 17•, 19•, 20, 21].

Psychological Considerations

Stress

Although no specific studies have examined the impact of general stress on PTH populations, the functional model of primary headache can be used to understand the multifactorial relationship between stress and headaches [22]. Stress can act as an immediate trigger for headaches, as well as worsen and exacerbate pre-existing headaches [23]. The mechanism of stress on headaches can be associated with the heightening of the hypothalamic-pituitary-adrenal axis (HPA axis) and stress responses, including β -endorphin and cortisol [23]. Physiologically, chronic stress also can impact the central pain control system, which can increase the likelihood of chronic pain or intensify pain responses [23]. Additionally, as head-aches may interrupt the sleep cycle and sleep deprivation is a common trigger for headaches, high levels of stress along with poor sleep can aggravate headaches [24].

Post-Traumatic Stress Disorder (PTSD)

Evidence has indicated that there are strong associations between PTSD and PTH, with PTSD being highly co-morbid with pain and complicating PTH treatment. Overall, increased PTSD symptoms have been found to be significantly related to increased frequency and severity of PTH rates among military personnel and veteran population with TBI [19•, 20, 25, 26••, 27•, 28••, 29•, 30, 31]. PTSD is predictive of PTH and is specifically related to migraine and tension-type headaches [25]. In addition to the aforementioned stress arousal model (i.e., please review the above section), researchers have proffered multiple theories to explain associations between PTSD and PTH. The triple vulnerability model proposed by Keane and Barlow posits that generalized biological and psychological factors, as well as one's perception of control, may contribute to PTSD and pain such as PTH [32]. The mutual maintenance model also suggests that factors such as attentional biases, anxiety sensitivity, and an avoidant coping style may lead to mutual maintenance between PTSD and pain [33].

Other Psychiatric Comorbidities

In addition to PTSD, studies have found associations between psychiatric comorbidities such as depression and anxiety and increased endorsement of PTH [34•]. For instance, in one investigation, nearly 30% of participants with PTH had PTSD, and more than 40% of those with PTSD also experienced severe depression [35]. In addition, a study found that compared to those without PTH, the severe PTH population scored higher on hypochondriasis, depression, hysteria, and schizophrenia scales on the Minnesota Multiphasic Personality Inventory [36]. A prospective study found higher levels of depression and anxiety in individuals with acute PTH compared to individuals without acute PTH [37•]. A separate investigation revealed that veterans with PTH reported higher levels of neuropsychiatric symptoms relative to veterans with TBI without PTH and controls [38..]. Among individuals with various pain conditions, one group of investigators found that those with PTH generally exhibited the highest levels of psychopathology, including anxiety and depression [39]. Relative to individuals with chronic primary headache, patients with PTH had a lower rate of depression, though the rate of depression among individuals with PTH was still high (33.3%) [40••].

Sociocultural and Psychosocial

Evans posited that low or even nonexistent rates of PCS in some countries indicate that sociocultural and psychosocial variables are linked to development of PCS symptoms, including PTH [41••]. There is evidence of significant ethnic disparities in pain prevalence and outcome across a variety of pain conditions [42, 43]. Solomon posited that social, cultural, and ethnic factors modulate pain appraisals and responses, thereby contributing to varying prevalence of PTH across countries and cultures [44]. For instance, in a sample of 180 individuals involved in motor vehicle accidents in Patras, Greece, over 90% demonstrated full resolution of pain and other symptoms at 4 weeks, and there were no cases of chronic disability [45]. Consistently, in a prospective study of 210 individuals involved in motor vehicle accidents in Kaunas, Lithuania, pain was self-limiting [46]. In terms of PTH, median duration was 4.5 h and maximum duration was 20 days. Relative to the control group, there were no significant differences in frequency and severity of PTH and other symptoms at 1-year follow-up. A separate investigation of 100 individuals with mild head injury in Austria found median duration of PTH was 3 days, and all individuals exhibited symptom resolution by 100 days [37•]. In his recent review paper, Evans noted that inadequate social support and increased social adversity have been observed among individuals with protracted PCS compared to those who have experienced symptom resolution [41••].

Base Rate Misattribution

Base rate misattribution refers to the tendency to misattribute pre-existing or common symptoms to an injury. As PTH and other PCS symptoms are non-specific, researchers have theorized that individuals tend to underestimate the frequency of symptoms in the pre-injury period, overestimate the frequency of symptoms post-injury, and subsequently attribute symptoms to the injury [44, 47, 48]. Indeed, one study found high rates of PCS symptoms among non-TBI participants and low pre-injury estimates of headache and other PCS symptoms among headache patients and non-athletes with head injury [49]. Another study found high base rates of PCS symptoms among 104 healthy participants, with over 50% endorsing headaches within the prior 2 weeks [50]. A separate study of 102 individuals with mild brain injury, 69 individuals with non-head injury trauma, and 115 controls found that retrospective endorsement of pre-injury symptoms, including headache, was significantly lower in the injury groups relative to the control group, indicating misattribution [51].

Expectation as Etiology

The concept of self-fulfilling prophecy, or a prediction that becomes realized because one acts as if it is true, has been applied to explanatory models of PTH pathogenesis. For example, authors have suggested that anticipating poor prognosis may lead to a self-fulfilling nocebo effect [52, 53]. A study comparing 100 participants with PCS compared to 223 volunteers with no history of brain injury found no differences between patients' symptom report and volunteers' imagined symptoms [54]. In fact, headache was the most commonly expected PCS symptom. Moreover, investigations have found low incidence of PTH in samples with absent or minimal expectations such as children [55], though other investigations have found elevated rates of PTH and other PCS symptoms in children with a history of mild head injury [56].

Chronic Pain

Individuals with chronic PTH have been found to have higher degrees of psychopathology in comparison to individuals with other types of chronic pain [39]. At this time, it is unclear whether this may be reflective of shared prevalence of psychiatric disorders among sufferers of PCS and chronic pain syndromes [41••]. There is also interplay between chronic pain, mood, and physical activity. Namely, pain can provoke anxiety and depression, which may in turn exacerbate pain intensity [57]. Additionally, chronic pain may result in decreased engagement in physical and social activities, which can lead to further psychological consequences [58].

Litigation

The relationship between chronic PTH and external factors such as psychosocial and legal circumstances surrounding the injury has been an area of debate [59]. While some studies have not found an effect of litigation on symptoms [60-62], in one study, 97 litigating individuals with mild head injury were found to have greater levels of anxiety, social dysfunction, and poorer outcome [63] in comparison to non-litigators. Often, litigation occurs in the context of an adversarial environment when the other party involved (employer, driver, etc.) may not acknowledge that the person was injured; this lack of acknowledgment often modulates the need for revenge [64]. Furthermore, litigants may experience increased anger when having to undergo the litigation process wherein they must counter the assumption about being non-injured or malingering [64]. This may result in psychological reactions exacerbating the frequency of symptoms, including PTH [65].

Behavioral Treatment

Despite a large body of literature on psychological treatment outcome studies for various types of headaches [66], studies on treatment for PTH are sparse. The complex interdependence of psychological, cognitive, and physiological symptoms [4, 67] requires various treatment components such as psychological interventions to manage depression and anxiety and psychoeducation regarding the role of emotional factors, the function of the autonomic nervous system, and the raised tension and pain levels associated with head trauma [68]. As such, many non-pharmacological treatment studies for PTH combine CBT and other modalities such as relaxation techniques, biofeedback, and psychoeducation.

CBT Treatments for PTH

Among the few studies that addressed behavioral interventions for PTH, there was one randomized controlled trial (RCT) the authors are aware of in which 90 participants with chronic PTH were provided CBT as well as relaxation techniques, including progressive muscle relaxation, breathing techniques, and visualization [69••]. Results indicated only a minor impact on quality of life, psychological distress, and non-headache symptoms, and no effect on headache itself [69••]. Interestingly, fewer somatic and cognitive symptoms in the waitlist control group were found post treatment. This was thought to be related to spontaneous remission over time while lack of remission of such symptoms in the treatment group was believed to be related to increased awareness of symptoms and disability [69••].

In addition to the RCT, a case series study [70] examined 12 participants with PTH who received 8–50 sessions of relaxation training and supportive psychotherapy within a cognitive behavioral framework. Seven participants also received biofeedback training. Eight of the 12 participants showed at least a 50% reduction in headache frequency and severity, as assessed by a headache diary measure. Of note, eight of the 12 participants met criteria for PTSD, and although this did not affect treatment outcome, those with PTSD required significantly more treatment sessions [70].

In another study, 20 participants with chronic PTH after mild, moderate, or severe TBI, who served as their own controls, were provided three weekly relaxation group sessions, six 30-min individual therapy sessions every 2 weeks, and a follow-up session [68]. Treatment content included PMR combined with the use of imagery, psychoeducation, cognitive behavioral strategies, lifestyle management, and maintenance and relapse prevention. Thirteen subjects completed the final outcome assessment, and findings showed significantly decreased headache symptoms, headache associated-disability, intensity, and frequency. Notably, emotional well-being significantly improved as well.

Biofeedback and Neurofeedback

Although a number of studies have indicated the efficacy of biofeedback on migraine, tension-type, or mixed-type headaches, biofeedback alone has been less studied among the PTH population [9]. Biofeedback, a self-regulation technique, utilizes physiologic markers such as muscle activity, skin temperature, respiration, blood flow, and brain activity to reduce sympathetic arousal. Individuals are attached to specific devices and receive feedback on selected parameters to acquire ways to control or refine their physiological response.

Electromyography (EMG) biofeedback—the method of muscle retraining involving conversion of myoelectrical signals into visual and auditory signals—has been studied most frequently. Ham and Packard conducted a retrospective study examining 40 subjects with PTH following mild head injury who had completed at least four biofeedback-treatment sessions in conjunction with relaxation training [71]. Participants received both EMG and thermal biofeedback with the electrodes being placed on the forehead, trapezii, frontal–posterior neck, or neck and thermistors on the second finger. Relaxation training encompassed PMR, deep muscle relaxation, autogenic phrases, and/or diaphragmatic breathing. Results showed that 53% of the subjects reported at least moderate improvement in PTH, with treatment outcomes being negatively associated with chronicity of the PTH and positively associated with dosage of treatment. Moreover, 80% of participants reported that biofeedback assisted relaxation treatment resulted in improved ability to relax and cope with pain. Consistently, McGrady et al. found that 12 participants who received EMG biofeedback with concurrent autogenic and PMR training and psychotherapy showed significant reductions in pain and muscle tension [72]. Notably, participants with higher pretreatment forehead tension levels and mild to moderate pain showed greater decreases in pain relative to participants with low tension and severe pain. Similarly, Onorato and Tsushima utilized forehead EMG biofeedback and found that EMG levels were significantly lower for both tension headache (n = 14) and PTH patient groups (n = 39), although the success rate was stronger for the tension headache group [73]. Additionally, results from a case study of a 23-year-old soldier with PTH indicated that three-modality feedback (i.e., surface EMG, temperature, and skin conduction), in conjunction with implementation of relaxation techniques (i.e., PMR and autogenic relaxation), were effective in managing and minimizing headache following four biofeedback treatment sessions [74]. Medina used a combined treatment approach that consisted of EMG and thermal biofeedback, which also showed positive results, as 70% of the 20 participants reported marked improvement in PTH, regardless of whether they had other medical complications [75]. Notably, the latter treatment program was tailored based on individualized needs, with some participants receiving concurrent education, pharmacological treatment, stress management, and physical therapy. A study investigating the effectiveness of either EMG or thermal biofeedback, PMR, education, and cognitive therapy on 14 participants with PTH found decreases in headache frequency and severity, though no significant differences were found between the waitlist group and treatment group [76]. The authors designed two phases of treatment with the first phase consisting of thermal biofeedback, PMR, education, and cognitive therapy, and the second phase consisting of ongoing cognitive therapy with concurrent exposure techniques for those participants with elevated levels of depressive and PTSD symptomatology. The treatment group showed decreases in post-concussive symptoms and state anxiety, and participants who completed the second phase showed reductions in state anxiety. An additional intervention termed heart rate variability biofeedback (HRV BFB) involving cardiorespiratory regulation of the autonomic nervous system has been used recently to manage PCS, including PTH. Specifically, a case study of a 42-year-old athlete who suffered a concussion reported significant reduction in impact of her headaches after the completion of a 10-week HRV BFB program [77].

The effects of EEG biofeedback or neurofeedback (NF) on PTH have also been examined. Nelson and Esty examined the

efficacy of the Flexyx Neurotherapy System (FNS), a variant of EEG biofeedback, on nine veterans with moderate to severe headaches post-TBI [78]. FNS is a type of passive neurofeedback, which does not require participants' active effort to control their EEG patterns. Instead, feedback is directly sent to the sensors to offset the amplitude of the lower frequency activity. In this study, sensors were placed all over the cerebral cortex. Participants attended a total of 20 sessions, with 2-3 sessions taking place per week. Findings suggested substantial reduction in selfreported PTH pain across various treatment time points. No significant side effects were reported, although a few participants initially reported experiencing minor symptoms. Kubik and Biedron also found that 15 headache patients with post-craniocerebral trauma had good and likely long-term effect following the completion of 40-60 sessions of neurofeedback [79]. Similarly, a brief report focusing on the use of quantitative electroencephalogram (QEEG)-guided NF also indicated promising results in reducing incidence and severity of PTH for a 17-yearold female athlete [80].

Although the above results appear promising, interpretation of the benefits of biofeedback on PTH needs to be approached with caution. The studies had a small N and were not randomized-controlled trials. In addition, some of the studies combined the use of other treatment modalities, such as medications, relaxation techniques, physical therapy, and stress management to examine outcomes. Moreover, not all of the above studies ruled out or excluded confounding factors or examined how specific factors (e.g., severity of brain injury, dosage of treatment, and location of the electrodes, etc.) impacted results. Other studies have suggested that specific types of biofeedback may be more beneficial for certain types of headaches. Specifically, EMG biofeedback is more effective for treating tension-type headache while thermal and blood volume pulse-biofeedback are more appropriate for individuals with migraine [74]. Still, it is unknown what types of biofeedback are more efficacious for the treatment of PTH.

PMR and Other Relaxation Therapies

PMR involves systematically tensing and relaxing various muscle groups in order to increase awareness of distinctions between tension and relaxation and ultimately the relaxation response over time. While PMR and other relaxation therapies have been studied extensively for treatment of primary headache and migraine [81] to our knowledge, no extant, published studies have examined the effectiveness of PMR alone for treatment of PTH. Relaxation therapies, including PMR, have been commonly examined in conjunction with biofeedback assisted relaxation [82].

Acupuncture

Few studies have examined the efficacy of acupuncture for PTH, though one recent randomized, controlled, prospective investigation explored the effectiveness of traditional Chinese acupuncture, auricular acupuncture, and usual care on previously deployed service members with PTH [83]. Twenty-nine of the 45 participants enrolled completed the outcome measure following 6 weeks of treatment. Relative to usual care, acupuncture was associated with decreased headache burden and pain. Although there is a paucity of studies examining acupuncture for treatment of PTH, many studies have demonstrated the efficacy of acupuncture for primary headaches and other headache types [12•]. However, there is some concern that the evidence for acupuncture as opposed to sham is not strong enough to recommend it as a therapy. A 2016 Cochrane review showed that acupuncture is efficacious in migraine prophylaxis, with evidence of moderate reduction in migraine frequency compared to no treatment and small though statistically significant reduction in migraine frequency compared to sham treatment [84]. Relative to prophylactic drug treatment, acupuncture was associated with a significantly increased reduction in migraine frequency, though at 3 and 6month-follow-up significance was not sustained. Similarly, a recent Cochrane review of acupuncture for episodic and chronic tension headaches showed evidence of benefit, with a significantly higher proportion of participants demonstrating at least 50% reduction in headache frequency when treatment groups were compared to control groups who received routine care [85]. Similarly, a significantly higher proportion of participants showed at least 50% reduction in headache frequency when treatment groups were compared to sham acupuncture, with acupuncture showing sustained effects at 6-monthfollow-up. Compared to physiotherapy, massage, or exercise, acupuncture demonstrated either comparable or slightly less efficacy, though available data was extremely limited and of moderate to low quality. Additionally, the preponderance of available evidence suggests that acupuncture is associated with improved well-being and quality of life [86, 87]. Overall, researchers suggest that acupuncture should be considered for management of posttraumatic headache, though future investigations are needed to evaluate efficacy [12•].

Physical Therapy

A paucity of studies has examined physical therapy as an intervention for PTH, though some authors suggest utilizing concomitant physical interventions, especially for headaches with musculoskeletal involvement [88]. Jensen conducted a randomized trial to compare manual therapy to cold packs among 19 PTH participants [89]. Results indicated that relative to the cold packs group, the pain index of the manual therapy group significantly declined. By the final session

(week 6), pain index reduced to 84% compared to the pretreatment level among the manual therapy group. Nine out of 10 participants who received manual therapy at the thoracic and cervical facet joints reported receiving prolonged benefits following 2 weeks of post-treatment. A case study of a 38year-old woman with PTH also indicated benefits from a combination of medication and osteopathic techniques consisting of low-amplitude techniques, cranial sacral techniques, and progressive inhibition of neuromuscular structure [90]. Additionally, aerobic exercise therapy was found to be beneficial for athletes and non-athletes for recovery from refractory post-concussion symptoms, including PTH [91].

Limitations and Future Directions

Altogether, the paucity of literature on psychological interventions for individuals with PTH highlights the need for randomized controlled studies to assess treatment efficacy. Limitations include studies using various forms of treatment simultaneously with poor description of the dosage of each component. Moreover, as studies have varied inclusion and exclusion criteria, making comparisons between investigations is challenging. For example, one study [69...] excluded individuals with medication-overuse headaches, while other studies [68, 70] did not specify. Furthermore, individuals with PTSD were included in one study [70], but psychiatric conditions were an exclusion criteria in other studies [68, 69...]. As noted, there is a higher prevalence of psychiatric comorbidities such as depression, anxiety, and PTSD among patients with PTH compared to head-injured individuals who do not develop PTH, and higher levels of psychopathology are associated with increased PTH frequency and intensity [17•, 23, 32, 33]. As such, including individuals with psychiatric comorbidities in studies is crucial in order to provide a better understanding of treatment efficacy and generalizability to a significant subset of PTH patients. Additionally, investigating predictors for therapy participation and adherence would provide insight as to who would be likely to benefit. Also, future investigations should include a clear description of TBI severity given findings of an inverse relationship between TBI severity and PTH. Variability in pain outcome measures and absence of associated outcomes such as functional impact and quality of life are additional limitations to be addressed when designing future investigations. As individuals with acute vs. chronic PTH sometimes have distinct clinical needs, studies targeting both PTH populations is crucial. Further, headache typology and phenotype should be clearly noted in studies to allow better understanding of treatment efficacy for various headache characteristics. Finally, it has also been proposed that psychological group treatment may be more effective in earlier states of PTH [68], which warrants further examination. Addressing the noted limitations may further our understanding of treating PTH, a complex inter-dependent manifestation of psychological, cognitive, and physiological symptoms [4, 67].

Conclusions

Amidst limited findings, the current review suggests the benefits of using a biopsychosocial model to treat the PTH population. Investigations of the multidisciplinary approach have provided encouraging outcomes. However, it is uncertain how each modality has individually contributed to the efficacy and effectiveness of PTH treatment. In order to better inform treatment recommendations, including efficacy and optimal dosage, future researchers should conduct randomized clinical trials to examine the strength of each modality in comparison to a combined intervention. There is growing awareness that multiple factors, including psychiatric comorbidities, chronic pain, and attributional biases, have implications for outcome. Accordingly, additional research which considers these potentially confounding factors is needed in order to aid development of more effective interventions.

Compliance with Ethical Standards

Conflict of Interest Felicia Fraser, Yuka Matsuzawa, and Yuen Shan Christine Lee declare that they have no conflict of interest.

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