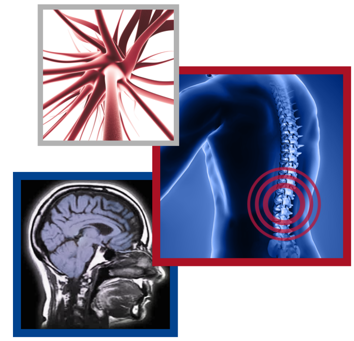
Research Article

Pain Management



User experiences of pre-sleep sensory alpha brainwave entrainment for people with chronic pain and sleep disturbance

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Aim: To explore the user experiences of pre-sleep alpha entrainment via a smartphone-enabled audio or visual stimulation program for people with chronic pain and sleep disturbance. **Materials & methods:** Semi-structured interviews were held with 27 participants completing a feasibility study of pre-sleep entrainment use for 4 weeks. Transcriptions were subject to template analysis. **Results:** Five top-level themes generated from this analysis are presented. These report on participants' impressions of the pain–sleep relationship, their previous experiences of strategies for these symptoms, their expectations and their experience of use and perceived impact on symptoms of audiovisual alpha entrainment. **Conclusion:** Pre-sleep audiovisual alpha entrainment was acceptable to individuals with chronic pain and sleep disturbance and perceived to have symptomatic benefits.

Plain language summary: In this study, people who had used an experimental treatment for chronic pain called alpha entrainment, which was delivered by audio (tones through headphones) or visual (flickering light) stimulation just before sleep each night for 4 weeks, were interviewed about their experiences. Analysis of the interview transcripts generated findings in five large areas: participants' impressions of the relationship between pain and sleep, previous strategies they had tried, expectations of using this intervention and their experiences of using it and how it affected their symptoms. Overall, participants found using this type of sensory stimulation last thing at night to be acceptable in a real-life setting, consistent with prior understanding, and many felt it to have benefits for sleep and pain symptoms with few side effects. Comfort of the equipment and having the choice of different types of stimulation were important. Further development should be guided by these user experiences.

First draft submitted: 25 October 2022; Accepted for publication: 17 May 2023; Published online: 10 July 2023

Keywords: alpha entrainment • brainwave entrainment • neuromodulation • pain • qualitative • sleep • template analysis

Chronic pain conditions are among the greatest contributors to disability globally [1]. Prevalence rates of one-fifth of adults in the USA [2] and between one-third and half of those in the UK [3] demonstrate that the current treatment approach is ineffective. 40% of those living with chronic pain in Europe regard their pain as not adequately controlled [4], and the poor efficacy and considerable side effect profile of conventional analgesic medications when used for chronic pain are well known [5,6]. In the search for treatments for chronic pain that are safe, well tolerated, effective and affordable and can also be personalized and self-managed by individuals without repeated healthcare consultations, sleep may represent an important avenue for innovation.

Sleep problems are experienced by over 70% of those with chronic painful conditions [7,8], rising to 96% of those with fibromyalgia, where the severity of sleep problems predicts the level of pain [9]. The relationship

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between chronic pain and sleep disturbance is bidirectional [10] and operates in terms of day-to-day symptom fluctuation [11] and likelihood of new symptomatology developing over a period of years [12,13], with nonrestorative sleep found to be a strong independent predictor of new-onset widespread pain [14]. Experimental sleep deprivation and fragmentation increase pain [15], whereas nonpharmacological treatment for insomnia in those with chronic pain improves not only insomnia but also pain, at least temporarily [16,17]. In recognition of this close relationship, sleep problems have been highlighted in recent research prioritization exercises [18,19].

Brain entrainment has received interest in recent years as a potential neuromodulatory approach to chronic pain. Entrainment refers to an oscillatory system becoming phase synchronized (falling in step) with an external input, which could be anything from a repeated direct physical force to, as in this case, rhythmic sensory stimulation. Alpha entrainment refers to modulation of cortical electrical oscillations ('brainwaves') in the alpha band (8–12 Hz) and can be achieved with rhythmic stimulation, which can be sensory or direct electric or magnetic stimulation [20]. Since alpha rhythm is involved in pain expectation [21], attention to pain [22] and expectation of pain relief [23], its modulation has been explored as a potential treatment for pain. Both healthy volunteers and individuals with chronic pain have used alpha entrainment in laboratory settings [24–27] and in more realistic home-based settings [28]. Alpha entrainment has not previously been used pre-sleep in those with chronic pain, but other forms of noninvasive brainwave entrainment have been investigated for this use. Audiovisual stimulation decreasing in frequency from 8 to 2 Hz was applied to participants with chronic pain and insomnia, aiming to aid sleep onset. In a pilot randomized controlled trial, adherence to the intervention was 99% and participants reported high ease of use on a Likert scale [29], but no more detailed qualitative exploration of user experience of this type of neuromodulation is available in the current literature.

This sparsity of user experience must be addressed for this field to move forward. Health systems (including in the UK) are responding to the immense challenge presented by long-term conditions such as chronic pain by prioritizing community- and home-based management and digitally enabled care [30]. Simultaneously, the medical technology sector is seeing rapid growth [31]. However, medical devices for use in the home environment require particular attention to usability [32], without which safety can be compromised and the benefits of the technology will fail to be realized. Although research into neuromodulation for chronic pain has increased dramatically in recent years [33], the detailed experiences of users are often neglected. Since chronic pain is a condition best understood through a biopsychosocial perspective [34], these experiences are likely to be crucial to our understanding of how interventions operate and why response differs between individuals. Furthermore, the Evidence Standards Framework for Digital Health Technologies required by the UK's National Institute for Health and Care Excellence states that user acceptability must be incorporated into the design of digital health technologies [35]. Our feasibility study of pre-sleep alpha entrainment for those with chronic pain and sleep disturbance found pre–post improvements in participant-reported measures of pain and sleep parameters, which should stimulate the controlled studies needed for further investigation [36]. This study builds on those results by providing rare detail regarding the experiences of individuals interacting with this home-based technology, offering insights of relevance both within and beyond this specific intervention.

The intervention used in this study, known as home-based Brainwave Entrainment Technology (hBET), uses visual or auditory stimulation at 10 Hz to increase the power of alpha brainwave activity. The stimulation is delivered via a smartphone application using either flickering light displayed in front of the user's closed eyes or binaural beats [37]. In the case of visual stimulation, the phone is placed over the eyes in a virtual reality phone-holding headset. The user sees a flickering light effect through their closed eyelids. In the case of audio stimulation, headphones are used and slightly different pure tones played in each ear, creating a humming effect. Screen brightness and volume are under the user's control. A 10-Hz repetitive stimulus is created in both cases. Applying alpha entrainment at bedtime aims to improve night pain and interrupt the dysfunctional relationship between pain and sleep and is a potential treatment for chronic pain and coexistent sleep disturbance. To be developed further following best co-design practice, it requires in-depth investigation of acceptability and usability by the target population.

The aim of the present study was to explore user experiences of hBET to inform future development of the technology and its evaluation. Specifically, we aimed to explore participants' existing attitudes, behaviors and expectations pertaining to sleep and pain; identify research feasibility and process issues; and elicit experiences of using hBET in terms of acceptability, effect on symptoms and adverse effects.

Materials & methods

Since pain is not a simple sensory experience, but rather a dynamic interaction between sensory and contextual (affective, motivation, cognitive) factors [38], it is crucial that the exploration of novel treatments encompass the perceptions and experiences of users. For this reason, qualitative methods were prioritized within the design of this feasibility study of hBET and considered to be the primary outcome measure. This article reports on these qualitative findings, whereas the results of before-and-after quantitative measures are published elsewhere [36].

Study design

Semi-structured interviews were conducted with individuals with chronic pain and sleep disturbance who had used hBET alpha brainwave entrainment for 4 weeks in the context of a feasibility study. Paradigmatically, the design was informed by a 'subtle realist' approach [39], in that the researcher's influence was acknowledged while still assuming the existence of a shared and accessible external reality. Specifically, the role of the primary researcher (SJ Halpin) as a rehabilitation physician situated him in a particular way socially to the participants, which was acknowledged as relevant to the findings and interpretation. However, the researcher had no role in the clinical care of participants. Ethical and regulatory approval of the study was granted by the Health Research Authority and National Health Service Research Ethics Committee (reference no. 19/YH/0313) and the procedures followed were in accordance with the Helsinki Declaration. The parent study was preregistered at ClinicalTrials.gov with the identifier NCT04176861.

Participants

A convenience sample of individuals with chronic pain and sleep disturbance was recruited from across the north of England. They primarily heard about the study through National Health Service musculoskeletal and rehabilitation clinics. Details of the study were also available via online publicity such as the National Institute for Health and Care Research website, which was the route for a minority of participants, but in both cases they were people who had long-term contact with health services because of chronic pain. Study processes were entirely separate from their usual clinical care, which continued in parallel. No stipulation was made on recency of medication changes prior to the start of the study, but timing of involvement in the study was planned to avoid any periods where significant interventions or medication regime changes were planned.

Inclusion criteria were age 18–80 years, chronic non-cancer pain (recurring pain of $\geq$3 months duration), nocturnal pain (worst pain $\geq$4 on a numeric rating scale of 0–10) and self-reported sleep difficulties (trouble falling asleep, difficulty staying asleep, waking up too early or waking up unrefreshed) three or more nights per week during the past month. Exclusion criteria were having a planned pain intervention during the 4-week hBET use period, seizure disorder, photosensitivity, hearing or sight problems causing inability to use hBET or cognitive problems or dementia or a mental health condition causing inability to consent or participate in the study.

Initial contact with the research team was by either email or telephone. Eligibility screening against the aforementioned inclusion and exclusion criteria was done by telephone. Participants were given the study information sheet and had the opportunity to ask questions before providing written informed consent. The protocol for the feasibility study involved participants being familiarized with the hBET application on a supplied smartphone during a one-to-one session with the researcher followed by a 1-week baseline period during which their sleep and pain levels were monitored. They then used hBET each evening just before sleep for 20–30 min and could choose whether to use the audio or visual programs on any given night. The equipment used by participants is shown in Figure 1.

Sleep and pain levels and hBET usage were monitored with daily diary and actigraphy, and standardized questionnaires assessing pain, fatigue, mood, sleep quality and health-related quality of life were completed before and after the hBET use period. The results of these quantitative measures are published separately [36]. EEG was not measured in this study. Therefore, although the mechanism of action supported by previous studies is alpha entrainment, we did not directly measure spectral power in the alpha band in this experiment.

Interviews

Within 5 days of completion of the hBET use period, a final meeting with the researcher was held, usually remotely over a video link in light of the COVID-19 pandemic, at which a semi-structured interview was conducted. Some participants had a family member present in the room, but only the participant contributed to the interview. Interviews were conducted by one male researcher (SJ Halpin) with experience and training in

Figure 1. Equipment used by participants. Headband with integrated Bluetooth speakers for audio stimulation mode, headset to hold phone for visual stimulation mode, smartphone displaying home-based Brainwave Entrainment Technology application menu and MotionWatch 8 actigraph watch.
Reproduced with permission from [36] Halpin © (2023).

qualitative interviewing and a professional background in rehabilitation medicine. The interviewer had no prior clinical relationship with any of the participants and was not known to them outside of the context of the study. Participants' knowledge of the interviewer was therefore primarily as a researcher motivated to investigate potential novel treatments for pain and desiring to understand the real-life experience of users. The interview schedule was designed to facilitate exploration of how participants approached hBET in the context of their experience of chronic pain and sleep disturbance and previous treatments, their experience of using hBET, its effect on their symptoms and usability. Interviews lasted between 30 and 60 min and were audio recorded and transcribed verbatim.

Data analysis

Transcripts were analyzed using template analysis, which is an approach to thematic analysis that emphasizes the hierarchical arrangement of themes in a template [40]. Template analysis is compatible with a range of epistemological stances and has been successfully used in combination with a subtle realist approach in the exploration of chronic pain previously [41]. Template analysis allows the identification of *a priori* themes, which suited this study, in that it helped structure the template to meet its several key aims. However, these *a priori* themes were tentative and subject to reconsideration as the analysis progressed. Following reading and re-reading of the data, a subset of ten interviews was coded to the initial template, which was then modified in discussion with the whole research team. The remaining interviews were then coded by one researcher (SJ Halpin), with resultant codes scrutinized and modified by a senior coauthor (RJ O'Connor), with divergences discussed to revise the template. The template was then further refined to best represent the most relevant findings with critical input from all authors. The target sample size was set in advance to meet the aims of all aspects of the feasibility study rather than by assessment of data saturation. However, it is judged that analysis of this relatively large sample of 27 interviews has adequately generated the themes of importance to the research question. Analysis was conducted using NVivo 12 Plus software (QSR International, MA, USA).

The final template contained six top-level themes: impressions of the pain and sleep relationship, previous experiences of therapies and strategies tried, expectations of hBET, experience of use and impact of symptoms of audio hBET, experience of use and impact of symptoms of visual hBET and research processes. The final template is presented in Supplementary File 1. Here we report findings from the first five themes, which have the greatest relevance for readers with regard to user experiences of hBET.

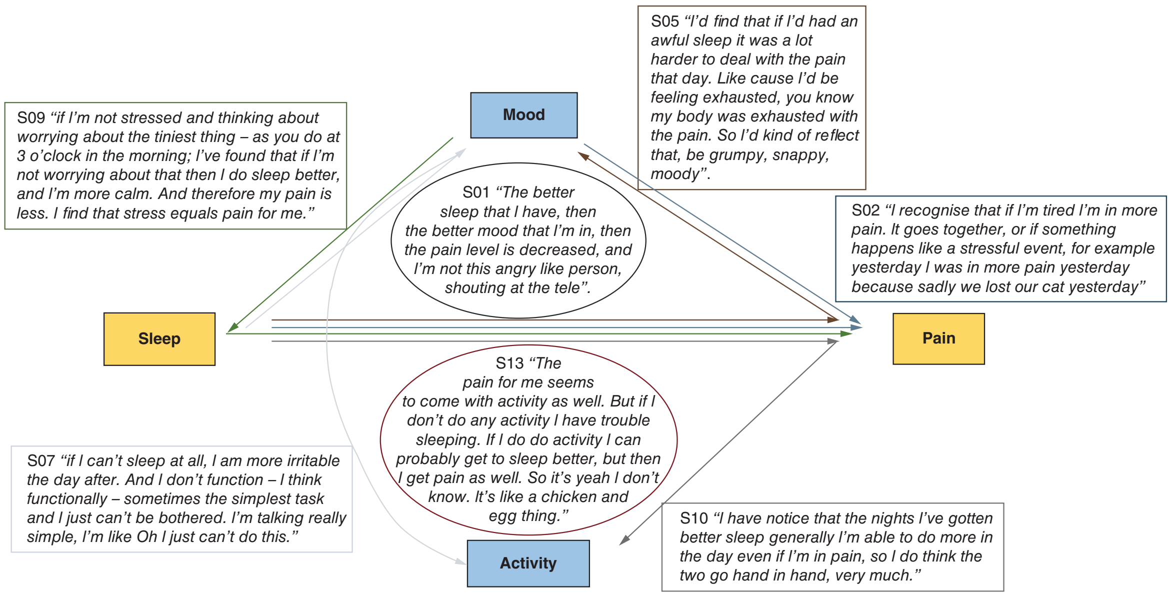

Figure 2. Reported web of relationships between sleep, pain, mood and activity with illustrative quotes.

Results

Participants

Of the 28 participants who completed the hBET feasibility study [36], 27 took part in an interview, with one choosing not to because of their personal time commitments. Participants had a mean age of 45 years (standard deviation: 12.4) and 21 (78%) were female. 14 were unemployed and four were retired, with three of these being under 60. The remaining nine were in full- or part-time work. These individuals had experienced chronic pain for between 1.2 and 40 years (median: 8). In the majority, the onset of pain and sleep problems was simultaneous, with reported sleep disturbance also having a median duration of 8 years. Diagnoses, as reported by the participants, included fibromyalgia in 24 cases, chronic widespread pain in two and trigeminal neuralgia in one. This last case represents a different category of chronic pain but was not excluded from the analysis, as retaining a range of participants was felt to be beneficial for meeting the aims of the current study regarding user experiences. Three participants were currently taking no pain medications, with others taking between one and five (median: two). The classes of medications being taken for pain were the following: opioids (16), gabapentinoids (14), paracetamol (14), NSAIDs (seven), tricyclic antidepressants (six), serotonin and norepinephrine reuptake inhibitors (four), benzodiazepines (three), triptans (two) and others (two).

Impressions of the pain & sleep relationship

The close and complex interrelation of sleep and pain was endorsed and expanded on in many responses. The concept of a bidirectional relationship was identified by many (often described as 'cyclical', 'intertwined', 'hand-in-hand') and was embellished with personal examples.

The most straightforward facet of the relationship, and often the first identified, was the impact of pain on sleep, which was experienced as the dominant direction by some respondents. One respondent related this to the greater tendency to attend to pain at night: "*I think, obviously I've got pain throughout the day, but at night, because there's nothing else to focus on, I feel it more. So when I'm actually trying to fall asleep I just feel it a lot more than throughout the day, when I'm actually busy with something else*" (P23). Another described this dominance of pain as making other solutions less relevant: "*I think because the pain was disturbing my sleep so much that the sleep hygiene routine would never break through that*" (P16).

Mood and activity levels were implicated by participants as factors in the sleep–pain relationship. Anxiety, including anxiety about sleep itself, was a reason for poor sleep and, equally, low mood and motivation were also experienced as consequences of poor sleep. Activity was implicated with a rich complexity of interactions proposed by interviewees. This web of relationships is described with example quotes in Figure 2.

Participants drew a distinction between pain 'level' and their ability to 'cope' or 'deal' with the pain. The benefits of good sleep are considered not only in terms of reducing the pain level but also in terms of making the same level more tolerable. This relates to insightful comments about the difficulties of judging pain in the context of a study that included a daily pain diary using a simple numeric rating scale (0–10). One respondent described a day with particularly upsetting and stressful circumstances: "*I think if I were to just solely judge the pain, it probably would have been similar to a different day. But if I were to judge everything else, I would give it a higher score*" (P23). Similarly, another reported that "*the* [pain] *is just there anyway, but sometimes it's amazing how it's there but you can cope with it. It's kind of you can push it to the background sometimes*" (P27). For multiple participants, sleep difficulties were related to a sense of their bodily state being out of step with their mental state, with the body being tired but the mind racing: "*I can feel dog tired, body is aching, but I get in bed and my mind is just racing, going*" (P08), and "*As much as you are desperate for sleep, you can't do it. Your body's sort of said no! Because you're in so much pain or just not tired enough or you're restless or your mind's working at a million miles an hour*" (P09).

Previous experiences of therapies & strategies

All participants had tried medications for their symptoms, and all but three were currently taking pain medications. The relationship with medications ranged from appreciative of the benefit some felt they had gained from medications to serious concern about tolerance, harm and side effects, and a common desire to reduce medications was expressed. Several respondents indicated a change over time in their relationship with and reliance on medications, captured in the subtheme of 'journey of realization that medications alone won't work'. Held alongside this was the common reality that medications are in fact the mainstay of management offered.

Expectations of hBET

The dominant sentiment around expectations was positive, with many respondents understandably hopeful that their symptoms would improve. This was often framed in terms of experience of comparable interventions or belief that the rationale was credible or consistent with their prior understanding of their pain experience: "*I was like 'well, it makes sense!' . . . All sorts of sensory stimuli affect the brain in certain ways, like you can have migraines triggered by sounds. So if a migraine could be triggered by a sound, surely sounds that you purposefully input can do things as well*" (P16).

Despite this positivity, participants were also cautious about having overly high expectations and referred to trying to keep an open mind: "*I had an open mind because I didn't want to have that in the back of my head that this was going to work, you know?*" (P09) and "*I wasn't expecting a cure or expecting it to be placebo either, just expecting to see what happens*" (P22). Others were more skeptical, having tried many things in the past unsuccessfully. Several respondents expressed being 'willing to try anything' which, in context, was an expression of openness rather than desperation: "*I'll try anything as long as it's, like, not drug-related. You know, if it's something that involves not taking drugs, that's better for you. So I'll go into anything open-minded and try it*" (P18). This narrative is in keeping with participants who have been through many years of chronic pain refractory to previous treatment attempts and who have learned from experience that pain may be something they have to manage long term rather than expecting a 'cure'.

Audio hBET: experience of use & impact on symptoms

The dominant sentiment expressed regarding the impact of audio hBET was that it had a positive effect on sleep difficulties. This was most often described as helping with sleep onset, being quicker and easier and giving confidence that the participant would be able to get to sleep, thereby reducing anxiety about sleep. Sleep onset improvement was closely followed by comments about improvement in consolidation of sleep, waking fewer times and perceiving sleep to have been deeper: "*I found the audio really, really helpful! I found that I was going to sleep a lot faster. I was waking up less during the night. And I just felt generally better rested*" (P15); "*There's more nights when I've slept through than I would have normally. It's a long time since I've not had broken sleep . . . so, for me, that's a positive, a big positive*" (P29); "*It was nice! My partner commented as well and said I've not tossed around anywhere near as much as usual. And I've been a lot more settled and, like, I've been in a lot deeper sleep than usual*" (P18); and "*All the anxiety around going to sleep seems to have been taken away because for some reason I do manage to get to sleep quite easily*" (P27).

Four participants gave potentially convergent opinions on how they felt the audio stimulation achieved this perceived positive effect, which relates to the aforementioned theme of the body being tired but the mind racing.

They described it blocking out other thoughts: "*For me, it blocks everything going on in my head. It blocks me thinking 'oh, God, what are we going to have for tea tomorrow?' and things like that. So it concentrated my mind and stopped me thinking about other things*" (P02), and "*If you relax and listen, it does kind of clear your mind 'cause you can't think about anything else. You can't think 'oh, we need bread' or 'oh, that bill needs paying'; you can't do any of that. Which is reminiscent to me of riding my motorbike – you can't be thinking about other things because you've got to concentrate on the mechanics of riding*" (P08).

Other benefits were described as being more refreshed in the morning, experiencing increased total sleep time and requiring less of other treatments to aid sleep, including alcohol and strong opiates. There were no negative effects on sleep reported, although two participants felt it offered no discernible benefit to their sleep.

Improvement in pain was also a common theme, though not affirmed by as many participants as reported a benefit to sleep. As well as generally reduced pain, this was put in terms of reduced pain compared with what would have been expected in stressful circumstances or around a symptom flare, reflecting the day-to-day fluctuation of fibromyalgia-type pain: "*There's days where, if my little boy's played all day, I'll think I'm going to suffer for it tomorrow. [But] I've had a really good sleep and then been fine*" (P18), and "*The thing that I noticed most that's different is that even if I've had a pain flare during the day, my night time pain was a lot less than it would have been previously*" (P16).

Some insights from users also distinguished a specific effect on widespread 'fibro' pain: "*Most of the time you get like the all-over pain. . . . But then, over the weeks [of using hBET], although I've still had pain, it's almost been isolated, so you can kind of deal with it*" (P21), and "*The fibro pain, after a couple of weeks, had lessened, like the shoulder pain and the upper back pain – those sort of went, pretty much. I mean, my shoulder was still giving a sort of niggle, but for the most part, after a couple of weeks, they sort of disappeared*" (P02). Other, wider effects were being able to be more active during the day (hitting the 'fibro wall' later in the day or not at all) and experiencing a positive psychological impact, with hBET frequently being described as relaxing, specifically despite stressful circumstances.

Audio hBET was described as easy to use and incorporate into the pre-sleep routine, with no major usability issues identified. Eight participants found the audio tones unpleasant or distracting: "*I only used it a few nights because I found it irritating! I just didn't like it*" (P07), and "*It's just this annoying buzz, and I just wanted it gone, the sooner the better!*" (P22). When asked about side effects, only four participants reported any, and these were all occasional or transient (occasional increase in pre-existing tinnitus, transient dizziness, transient restlessness, transient sick feeling).

Visual hBET: experience of use & impact on symptoms

During the study, participants could choose whether to use audio or visual stimulation on any given night. Across all participants, fewer chose to use the visual option, and there were two and a half times as many nights recorded in total using audio hBET compared with visual hBET. The prevailing reason for this was clearly expressed by participants as relating to usability issues. Those who struggled with the visual option chiefly found wearing the headset uncomfortable and cumbersome. The headset itself is not integral to visual hBET use but simply holds the smartphone in the required position to display visual flicker stimulation through closed eyelids. Thus, several participants suggested alternative delivery methods, such as a screen or light suspended above their head, to avoid the need for a headset. Although this was the dominant reason for visual stimulation being less popular, visual stimulation was also less commonly preferred in itself, with some users finding it unpleasant or not relaxing: "*How can I describe it? Like strobe lights, just there pulsing away . . . I didn't like it at all*" (P06). By contrast, others liked the 'trance-like' feeling of using visual stimulation, as one user vividly described: "*It was relaxing to use it. It was like being a passenger in a car and driving through a woodland or something like that, where you get the light coming through the trees and the shadow is flashing over the car the whole time and you end up nodding off in the back of the car. It reminded me of being a kid and, you know, sleeping on long journeys. That's what it reminded me of*" (P26).

Thus, there is an element of personal preference to the choice of stimulation modality. More side effects involving headaches were described with visual stimulation, with headaches being reported by five participants, two of whom experienced a severe migrainous type of headache. This did not require medical intervention but did result in these participants preferring to use the audio option.

Participants who used the visual hBET option reported improvement in sleep more readily than improvement in pain. With regard to audio hBET, improvement in sleep onset was most often commented on, as were fewer awakenings during the night: "*My sleep pattern is still all over the place, but at least I was getting some sleep with it! A couple of times I woke up and I still had the equipment on my head after 4 or 5 hours' sleep . . . that's really unusual. I'm normally waking up, tossing and turning or shaking to try to get rid of the pain or I just give up on it altogether. . . . But* *a few nights of using the visual stuff, it was just great. And even my partner noticed. In fact, they said this morning it's a shame that equipment's going back 'cause you've had better sleep with that equipment than you have for years!*" (P26).

Less predominant but still important was the report of some participants noting no marked effect on sleep despite tolerating the equipment. The overall sentiment of the visual experience varied quite widely between users, from very positive to immediately rejecting. As one participant put it, "*It's trial and error, I think*" (P08).

Reports on effect on pain were more balanced, with participants finding it more difficult to discern whether changes were attributable to visual hBET or other circumstantial factors, even when they had experienced improved sleep: "*I didn't seem to wake up half as much compared to normal. Pain-wise, [my scores] were still quite high*" (P19), and "*It has been a little bit different, but part of me wonders whether that was 'cause, with my husband being home, I don't do as much*" (P07). Wider effects described were improvement in mood, including a sense of hope that their chronic symptoms can be modulated, and a desire to keep using the equipment.

Discussion

Individuals with chronic pain and sleep disturbance who had used noninvasive alpha entrainment by audio or visual stimulation for 4 weeks took part in semi-structured interviews to elicit their experiences, which were transcribed and subjected to template analysis. This demonstrated that audiovisual stimulation at bedtime was acceptable to this cohort and its rationale was consistent with prior understanding of their pain experience. The comfort and practicality of equipment were a key consideration. Positive impacts on chronic sleep and pain symptoms were described, and there were few side effects. The audio modality was more popular in terms of both usability and impact on symptoms, but having a choice of options available accommodated individual preferences.

Pain and sleep were interrelated in a web of interactions that included mood and activity, endorsing the premise that sleep is important in the experience of chronic pain. The concept of a bidirectional link between chronic pain and sleep disturbance is core to the rationale of the feasibility study and therefore was a known idea introduced in discussions about participating in the study. Nevertheless, it was notable that the concept was easily recognized and endorsed by participants with colorful personal examples. The fact that the influence of pain on sleep was the strongest identified relationship by this group supports the rationale for an intervention on pain at night to intervene in this web of symptoms. Although neither mood nor activity levels featured in the interview schedule, respondents frequently detailed the role of these factors in the sleep–pain relationship, and they were incorporated into the model. An implication of this is that measurement of sleep, pain, mood and activity should be considered when hoping to intervene with respect to these related symptoms. Relatedly, participants engaged with the complexity of assessing pain, which is an inherently subjective experience [42]. By highlighting the relevance of fluctuating disease-related factors (e.g., fibromyalgia flares), activity levels and contextual factors, this analysis points to the value of measuring outcomes across the dimensions of impairment, activity, participation and context, as modeled by the International Classification of Functioning, Disability and Health [43].

The analysis brought out intriguing descriptions of a feeling of dyssynchrony between the body and mind, with a breakdown of the easy, natural sequence of sleep onset, and correspondingly, a suggestion that the benefit of hBET with regard to sleep onset was via calming the mind to align with the body's tiredness. This could be conceived to support the notion that thoughts were calmer in line with alpha entrainment, corresponding to the proposed inhibitory function the alpha rhythm on attention and other cognitive processes [44,45]. Indeed, increased occipital and parietal alpha power has been found in response to meditation [46]. However, this is speculative, as EEG was not measured in this study. It also opens an avenue of inquiry regarding the role of interoception and metacognition in the generation of symptoms that could respond to alpha entrainment and the selection of individuals most likely to benefit. This requires further careful research.

In terms of the impact of hBET on symptoms of pain and sleep disturbance, key findings were that although both improved, the positive sentiment around sleep improvement surpassed that around pain, which is interesting in light of the hypothesis that alpha entrainment improves pain and thereby sleep. Possible explanations are that pain improvement was sufficient to benefit sleep but not to impact the retrospective assessment of pain, which is known to be affected by recency, salience and assimilation effects [47] and is further complicated by impaired memory of the period immediately pre-sleep. Another possibility is that hBET benefits sleep via an independent mechanism, such as inhibiting attention to stimuli or perceptions other than pain. Future research should seek to understand the immediate and accumulating impacts of this intervention from the user's perspective to refine how it might best be incorporated into real-life use.

A limitation of this study is the possibility of reporting bias resulting from the interviewer being the researcher who guided the participants into the study, potentially leading to participants feeling a preference for reporting positively on the experience. This was mitigated against by encouragement to be honest and framing the value of their experience, whether positive or negative. The finding that many negative impressions were reported – for example, about the comfort of particular equipment – indicates that the participants did feel able to share these experiences. This aligns with participants' descriptions of their own expectations, which were open-minded and informed by previous experiences of diverse treatment modalities, many of which had been ineffective (potentially even to the point of inducing a nocebo effect). The cohort in this study had a mean age of 45 and was majority female, which mirrors population-level studies of chronic pain prevalence [3]. The cohort consisted of a majority with fibromyalgia and chronic widespread pain and one outlying participant with neuropathic pain (trigeminal neuralgia). This reflects the broad eligibility criteria chosen for this early stage of exploration of the treatment modality, but future studies with a more mechanistic focus will benefit from a less heterogeneous population.

This study demonstrated that use of a noninvasive sensory stimulation technology pre-sleep was acceptable to users with chronic pain and sleep disturbance, with encouraging reports of benefit to symptoms for many and few side effects. This should stimulate further rigorous investigation into this treatment modality, incorporating user insights, especially regarding comfort and ease of equipment use and further modification, particularly of the visual stimulation headset design.

Conclusion

Pre-sleep alpha entrainment by audio or visual stimulation was an acceptable intervention to people with chronic pain and sleep disturbance and was perceived to be associated with improvements in sleep and pain symptoms.

Summary points

- Alpha entrainment is a promising neuromodulatory treatment for chronic pain, and the perspectives of users are crucial to its development.
- This study reports on the experiences of 27 individuals with chronic pain who used alpha entrainment by audio or visual stimulation pre-sleep for 4 weeks.
- Using alpha entrainment pre-sleep at home was found to be acceptable and relevant from the perspective of users. Comfort was a key factor and having a choice of sensory modalities helped account for individual preferences.
- Participants vividly described a close relationship between sleep problems and pain experience, and the interaction also involved mood and activity levels.
- Overall, a positive impact on pain and sleep symptoms was described, with variation between participants and a preference for audio stimulation.
- These user perspectives should guide and stimulate development of noninvasive neuromodulatory approaches for chronic pain and sleep disturbance.

Supplementary data

To view the supplementary data that accompany this paper, please visit the journal website at www.futuremedicine.com/doi/suppl/10.2217/pmt-2022-0083

Author contributions

SJ Halpin prepared the study, conducted data collection and analysis and drafted the manuscript. NKY Tang contributed to methodology and analysis techniques and edited the manuscript. AJ Casson contributed to devising the study, oversaw development of the intervention, supervised the project and edited the manuscript. AKP Jones conceptualized the study, supervised the project and edited the manuscript. RJ O'Connor supervised the project and edited the manuscript. M Sivan conceived of the study, developed the methodology, supervised the project and edited the manuscript. All authors approved the final draft.

Acknowledgments

NK Jacob performed the technical development and testing of the audiovisual stimulation in the smartphone application described in this article.

Financial & competing interests disclosure

A joint Rosetrees Trust/Royal College of Physicians Research Fellowship awarded to SJ Halpin supported the completion of this study. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

References

1. Vos T, Abajobir AA, Abbafati C *et al.* Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 390(10100), 1211–1259 (2017).
2. Dahlhamer J, Lucas J, Zelaya C *et al.* Prevalence of chronic pain and high-impact chronic pain among adults – United States, 2016. *MMWR Morb. Mortal. Wkly Rep.* 67(36), 1001–1006 (2018).
3. Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open* 6(6), e010364 (2016).
4. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur. J. Pain* 10(4), 287 (2006).
5. Chou R, Turner JA, Devine EB *et al.* The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a national institutes of health pathways to prevention workshop. *Ann. Intern. Med.* 162(4), 276–286 (2015).
6. Wehling M. Non-steroidal anti-inflammatory drug use in chronic pain conditions with special emphasis on the elderly and patients with relevant comorbidities: management and mitigation of risks and adverse effects. *Eur. J. Clin. Pharmacol.* 70(10), 1159–1172 (2014).
7. Drewes AM. Pain and sleep disturbances with special reference to fibromyalgia and rheumatoid arthritis. *Rheumatology (Oxford)* 38(11), 1035–1038 (1999).
8. Abad VC, Sarinas PSA, Guilleminault C. Sleep and rheumatologic disorders. *Sleep Med. Rev.* 12(3), 211–228 (2008).
9. Bigatti SM, Hernandez AM, Cronan TA, Rand KL. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. *Arthritis Rheum.* 59(7), 961–967 (2008).
10. Affleck G, Urrows S, Tennen H, Higgins P, Abeles M. Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. *Pain* 68(2–3), 363–368 (1996).
11. Tang NKY, Goodchild CE, Sanborn AN, Howard J, Salkovskis PM. Deciphering the temporal link between pain and sleep in a heterogeneous chronic pain patient sample: a multilevel daily process study. *Sleep* 35(5), 675–687 (2012).
12. Stocks J, Tang NK, Walsh DA *et al.* Bidirectional association between disturbed sleep and neuropathic pain symptoms: a prospective cohort study in post-total joint replacement participants. *J. Pain Res.* 11, 1087–1093 (2018).
13. Gupta A, Silman AJ, Ray D *et al.* The role of psychosocial factors in predicting the onset of chronic widespread pain: results from a prospective population-based study. *Rheumatology (Oxford)* 46(4), 666–671 (2007).
14. McBeth J, Lacey RJ, Wilkie R. Predictors of new-onset widespread pain in older adults: results from a population-based prospective cohort study in the UK. *Arthritis Rheumatol.* 66(3), 757–767 (2014).
15. Smith MT, Edwards RR, McCann UD, Haythornthwaite JA. The effects of sleep deprivation on pain inhibition and spontaneous pain in women. *Sleep* 30(4), 494–505 (2007).
16. Tang NKY, Lereya ST, Boulton H, Miller MA, Wolke D, Cappuccio FP. Nonpharmacological treatments of insomnia for long-term painful conditions: a systematic review and meta-analysis of patient-reported outcomes in randomized controlled trials. *Sleep* 38(11), 1751–1764 (2015).
17. Selvanathan J, Pham C, Nagappa M *et al.* Cognitive behavioral therapy for insomnia in patients with chronic pain – a systematic review and meta-analysis of randomized controlled trials. *Sleep Med. Rev.* 60, 101460 (2021).
18. James Lind Alliance. Fibromyalgia (Canada) top 10 (2022). www.jla.nihr.ac.uk/priority-setting-partnerships/fibromyalgia-canada/top-10-priorities.htm

19. Fitzcharles M-A, Brachaniec M, Cooper L *et al.* A paradigm change to inform fibromyalgia research priorities by engaging patients and health care professionals. *Can. J. Pain* 1(1), 137–147 (2017).

20. Thut G, Schyns PG, Gross J. Entrainment of perceptually relevant brain oscillations by non-invasive rhythmic stimulation of the human brain. *Front. Psychol.* 2, 170 (2011).

21. Babiloni C, Brancucci A, Del Percio C *et al.* Anticipatory electroencephalography alpha rhythm predicts subjective perception of pain intensity. *J. Pain* 7(10), 709–717 (2006).

22. Hauck M, Lorenz J, Domnick C, Gerloff C, Engel AK. Top-down and bottom-up modulation of pain-induced oscillations. *Front. Hum. Neurosci.* 9, 375 (2015).

23. Huneke NTM, Brown CA, Burford E *et al.* Experimental placebo analgesia changes resting-state alpha oscillations. *PLOS ONE* 8(10), e78278 (2013).

24. Ecsy K, Jones AKP, Brown CA. Alpha-range visual and auditory stimulation reduces the perception of pain. *Eur. J. Pain* 21(3), 562–572 (2017).

25. Ecsy K, Brown CA, Jones AKP. Cortical nociceptive processes are reduced by visual alpha-band entrainment in the human brain. *Eur. J. Pain* 22(3), 538–550 (2018).

26. Arendsen LJ, Henshaw J, Brown CA *et al.* Entraining alpha activity using visual stimulation in patients with chronic musculoskeletal pain: a feasibility study. *Front. Neurosci.* 14, 828 (2020).

27. Lopez-Diaz K, Henshaw J, Casson AJ *et al.* Alpha entrainment drives pain relief using visual stimulation in a sample of chronic pain patients: a proof-of-concept controlled study. *Neuroreport* 32(5), 394–398 (2021).

28. Locke HN, Brooks J, Arendsen LJ *et al.* Acceptability and usability of smartphone-based brainwave entrainment technology used by individuals with chronic pain in a home setting. *Br. J. Pain* 14(3), 161–170 (2020).

29. Tang HY, McCurry SM, Pike KC, Riegel B, Vitiello MV. Open-loop audio–visual stimulation for sleep promotion in older adults with comorbid insomnia and osteoarthritis pain: results of a pilot randomized controlled trial. *Sleep Med.* 82, 37–42 (2021).

30. National Health Service. Online version of the NHS long term plan (2019). www.longtermplan.nhs.uk/online-version/

31. UK Government. Bioscience and health technology sector statistics 2021 (2022). www.gov.uk/government/statistics/bioscience-and-health-technology-sector-statistics-2021/bioscience-and-health-technology-sector-statistics-2021#trends-in-the-shape-and-size-of-the-life-sciences-sector

32. Tase A, Vadhwana B, Buckle P, Hanna GB. Usability challenges in the use of medical devices in the home environment: a systematic review of literature. *Appl. Ergon.* 103, 103769 (2022).

33. Knotkova H, Hamani C, Sivanesan E *et al.* Neuromodulation for chronic pain. *Lancet* 397 (10289), 2111–2124 (2021).

34. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol. Bull.* 133(4), 581–624 (2007).

35. National Institute for Health and Care Excellence. Evidence standards framework for digital health technologies (2022). www.nice.org.uk/corporate/ecd7

36. Halpin SJ, Casson AJ, Tang NKY, Jones AKP, O'Connor RJ, Sivan M. A feasibility study of pre-sleep audio and visual alpha brain entrainment for people with chronic pain and sleep disturbance. *Front. Pain Res. (Lausanne)* 4, 1096084 (2023).

37. Jacob NK, Kings HO, Casson AJ. A smartphone based platform for portable non-invasive light and sound neuromodulation. In: *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC).* Institute of Electrical and Electronics Engineers, Montreal, QC, Canada, 5228–5231 (2020).

38. Melzack R, Casey K. Sensory, motivational and central control determinants of chronic pain: a new conceptual model. In: *The Skin Senses* Kenshalo DR (Ed.). Thomas, IL, USA, 423–443 (1968).

39. Brooks J, McCluskey S, Turley E, King N. The utility of template analysis in qualitative psychology research. *Qual. Res. Psychol.* 12(2), 202–222 (2015).

40. King N. Doing template analysis. In: *Qualitative Organizational Research: Core Methods and Current Challenges*. SAGE Publications, Inc., London, UK, 426–450 (2017).

41. McCluskey S, Brooks J, King N, Burton K. The influence of 'significant others' on persistent back pain and work participation: a qualitative exploration of illness perceptions. *BMC Musculoskelet. Disord.* 12(1), 1–7 (2011).

42. Turk DC, Melzack R. *Handbook of Pain Assessment (3rd Edition).* Guilford Press, NY, USA (2011).

43. WHO. International classification of functioning, disability and health (ICF) (2019). www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health

44. Klimesch W. Alpha-band oscillations, attention, and controlled access to stored information. *Trends Cogn. Sci.* 16(12), 606–617 (2012).

45. Jensen O, Mazaheri A. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. *Front. Hum. Neurosci.* 4, 186 (2010).

46. Stapleton P, Dispenza J, McGill S, Sabot D, Peach M, Raynor D. Large effects of brief meditation intervention on EEG spectra in meditation novices. *IBRO Rep.* 9, 290–301 (2020).

47. Mason S, Fauerbach J, Haythornthwaite JA. Assessment of acute pain, pain relief, and patient satisfaction. In: *Handbook of Pain Assessment (3rd Edition).* Turk DC, Melzack R (Eds). Guilford Press, NY, USA, 283–293 (2011).