We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

5,000
Open access books available

125,000
International authors and editors

140M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Neurofeedback for Chronic Pain

Kajal Patel, Manoj Sivan, James Henshaw and Anthony Jones

Abstract

Neurofeedback is a novel neuromodulatory therapy where individuals are given real-time feedback regarding their brain neurophysiological signals in order to increase volitional control over their brain activity. Such biofeedback platform can be used to increase an individual's resilience to pain as chronic pain has been associated with abnormal central processing of ascending pain signals. Neurofeedback can be provided based on electroencephalogram (EEG) or functional magnetic resonance imaging (fMRI) recordings of an individual. Target brain rhythms commonly used in EEG neurofeedback for chronic pain include theta, alpha, beta and sensorimotor rhythms. Such training has not only been shown to improve pain in a variety of pain conditions such as central neuropathic pain, fibromyalgia, traumatic brain injury and chemotherapy induced peripheral neuropathy, but has also been shown to improve pain associated symptoms such as sleep, fatigue, depression and anxiety. Adverse events associated with neurofeedback training are often self-limited and resolve with decreased frequency of training. Provision of such training has also been explored in the home setting whereby individuals have been encouraged to practice this as and when required with promising results. Therefore, neurofeedback has the potential to provide low-cost yet holistic approach to the management of chronic pain.

Keywords: neurofeedback, EEG biofeedback, fMRI biofeedback, chronic pain, pain, fatigue, depression, anxiety, sleep

1. Introduction

Neurofeedback [1, 2] is a smart biofeedback platform which provides real-time feedback to individuals about their neurophysiological signals in order to achieve brain activity associated with therapeutic benefit. Brain activity of an individual is measured continuously using an EEG system during the course of neurofeedback training and parameters describing neurophysiological signals such as alpha power or peak alpha frequency are calculated in real-time [3]. These calculated features of ongoing brain activity are then presented to the individual either in an audio or visual form [3]. The idea behind this is that through repeated provision of such feedback, the individual gains an awareness of their current brain state and can identify different mental strategies which help them achieve the desired brain state [4]. Once the individual identifies strategies which work for them, they can keep practicing them over the course of multiple sessions with the final aim of being able to implement these strategies independent of a neurofeedback session.

Neurofeedback has already been investigated extensively for the management of several neuropsychiatric conditions [5] such as Attention Deficit Hyperactivity Disorder (ADHD) [6], depression and anxiety [7], cognition [8] and stroke

rehabilitation [9] for example. Being able to target brain signals through neurofeedback can be of great benefit in conditions such as chronic pain. This is because the perception of chronic pain depends on how multiple regions of the brain process the ascending pain signals [10, 11]. Such central processing of incoming pain signals has been shown to be different in chronic pain patients compared to healthy participants by a number of studies [12–14]. Considering the brain plays such an important in the development and maintenance of chronic pain state, being able to target changes in the neurophysiological signal which reflect such brain activity using a novel therapy such as neurofeedback is of great interest.

The field of neurofeedback therapy for chronic pain is rapidly developing. Several studies have been performed on a range of medical conditions over the last decade [15]. The current studies are highly heterogenous with a number of variations in neurofeedback protocol and delivery [15, 16]. This chapter aims to give an overview of the neurophysiological changes observed in chronic pain and how these have been targeted by different neurofeedback studies. We also discuss the different aspects of neurofeedback protocols which have been used so far and the outcomes of these studies in terms of reduction in pain and pain associated symptoms.

2. Neural pathways underlying pain perception

Our understanding of the neuroscience underlying pain has evolved significantly over time. Neural pathways involved in pain perception have been shown in **Figure 1**. One of the earliest theories explaining pain was the "specificity theory" (**Figure 1**: Red pathway). According to this theory, pain is experienced when an injury to a particular part of the body leads to signals being relayed via nociceptive neurons to the "pain center" [17]. The brain was considered to be a "passive recipient of sensory information" [17].

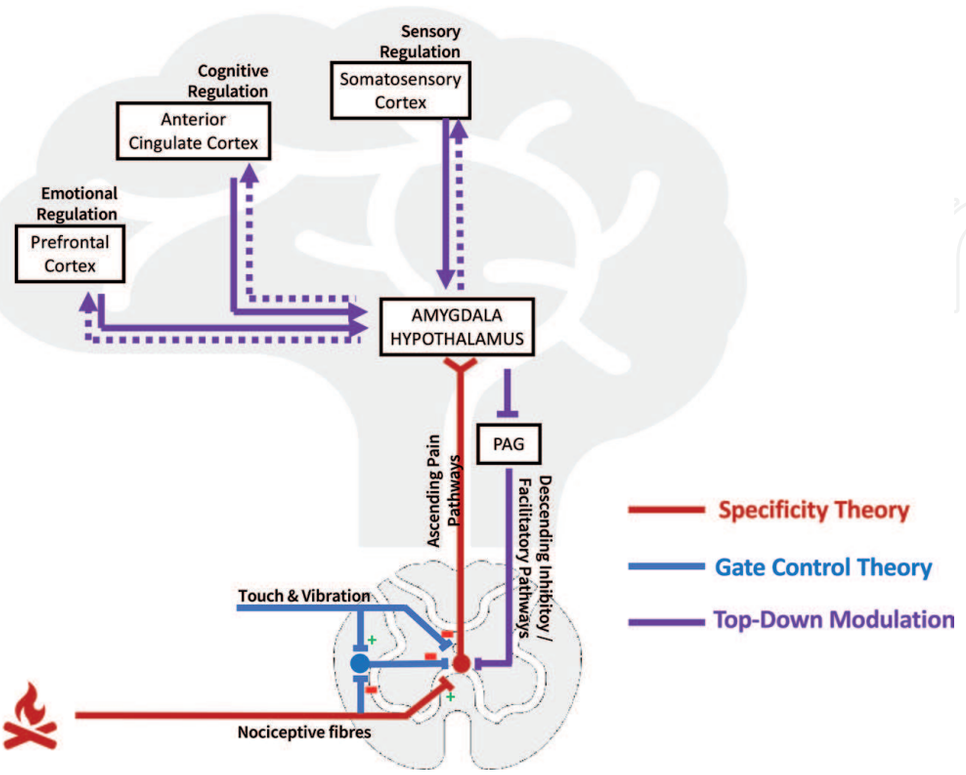

Figure 1.
Neural pathways underlying pain perception proposed by different pain theories.

One of the landmark theories which was highly influential in changing this prior understanding of pain was the Gate Control Theory by Melzack and Wall (1965) [18] (**Figure 1**: Blue pathway). This theory proposed that several neurons in the spinal cord, such as large fibers carrying touch and vibration sensations as well as interneurons in substantia gelatinosa of the dorsal horn, modulate the incoming signals from the site of pain, thereby influencing the final signal which is transmitted to the brain for processing.

Since then, advances in neuroimaging has revealed that in addition to neural pathways in the spinal cord, several cortical structures are also involved in modulating pain perception [19, 20] (**Figure 1**: Purple pathway). Some of the areas which have been reported to be involved include anterior cingulate gyrus, somatosensory cortex, insular cortex, thalamus and prefrontal cortex [19]. These findings suggest that there is not a single "pain centre". Instead, pain is processed by a "pain matrix" connecting different parts of the brain, thereby, reinforcing the idea that pain perception is a result of several sensory, affective and cognitive processes [10, 11]. Therefore, pain experienced by an individual is an integration of the current information about the painful sensory stimulation and prior information from previous experiences which influence the emotions, anxiety, attention and expectations of the individual about the pain [21].

Different areas of the cortex constituting the pain matrix project onto the hypothalamus and amygdala, which then give rise to both descending inhibitory pathways and descending facilitatory pathways [21, 22]. These descending pathways directly project onto the dorsal horn of the spinal cord where gating of pain is occurring, therefore, influence the signals which are relayed up the ascending pathways [21, 22]. This process is known as top-down modulation of pain [23].

In summary, the pain perceived by an individual is an integration of how different parts of the cortex process the ascending pain signals as well as how the activity of these cortical and subcortical structures influence the ascending pain signals via descending pathways [17, 21, 24]. With the discovery of these higher-order processes which influence pain perception, several neuromodulatory therapies such as neurofeedback (NFB), hypnosis and meditation, have been explored with the potential of controlling pain by influencing this supraspinal cortical processing of pain [25].

3. Brain rhythms associated with chronic pain

Generally, the EEG oscillations are categorized based on their frequency into theta (4–7 Hz), alpha (8–12 Hz), low beta or $beta_1$ (15–20 Hz) and high beta or $beta_2$ (22–30 Hz) [26–29]. Another oscillation which is widely investigated in the field of neuromodulation is sensorimotor rhythm (SMR). SMR refers to oscillations in the 12–15 Hz range which appear in spindle-like pattern over the sensorimotor cortex during idling of the motor cortex [30, 31]. Motor execution or motor imagery which activates the motor cortex leads to a decrease in the SMR activity [31].

Each of these brain rhythms is associated with a specific cognitive state. For instance, whilst alpha waves have been associated with a relaxed state, beta waves are associated with wakefulness and a state of engagement in task. Theta waves have been associated with drowsiness [27, 32].

Patients with chronic pain have differences in their resting-state brain (EEG) oscillations from healthy individuals. An example of a chronic pain condition which has been extensively investigated for identification of EEG correlates of chronic pain has been spinal cord injury (SCI). A study by Sarnthein et al. [12] showed that SCI patients with central neuropathic pain had increased activity of theta and beta

oscillations compared to healthy individuals. These findings were confirmed by another study [13] which observed similar increases in theta and beta activity, but in addition, also identified lower levels of alpha activity in this patient population. This association between chronic pain and EEG changes was further strengthened when Jensen et al. [33] demonstrated that even within a group of patients with spinal cord injury, individuals with central neuropathic pain had higher theta and lower alpha activity than patients with spinal cord injury but no chronic pain.

These patterns of EEG have also been reported in other chronic pain conditions. For instance, patients with migraine have higher theta and delta power compared to healthy controls [14]. Patients with fibromyalgia have been shown to have higher theta activity with sources estimated to be in the left dorsolateral prefrontal and orbitofrontal cortex, higher beta and gamma activity with sources estimated to be in the insular, primary motor and primary and secondary somatosensory cortices and slowing of the dominant alpha peak [34].

Identification of such neurophysiological correlates of chronic pain is important as it not only provides the necessary feedback signal to increase voluntary control in therapies such as neurofeedback, but also allows monitoring the efficacy of the therapy in modulating the neurophysiological processes targeted by the therapy.

4. Neurofeedback training protocols

There are two key modalities which have been used to provide neurofeedback – EEG neurofeedback and fMRI neurofeedback. Whilst EEG neurofeedback provides feedback based on the neurophysiological signals recorded through an EEG system, fMRI neurofeedback provides feedback based on the degree of activation of a particular region of the brain detected using fMRI imaging in real time [35]. Hence it is inevitable that there is some lag between the activation and signal detection in fMRI neurofeedback which happens almost instantaneously in EEG neurofeedback [35].

Evidence regarding efficacy of fMRI neurofeedback in pain is limited understandably due to the increased difficulties and expenses associated with this form. The common region of interest which has been targeted in fMRI studies has been rostral anterior cingulate gyrus (rACC), whereby increased activity of rACC, measured through detecting an increase in blood oxygen level dependent signal from the region, has been associated with pain reduction [36, 37]. However, these studies have been severely limited in terms of number of sessions [37, 38], therefore the full benefit of the neurofeedback which occurs over the course of several sessions has not been explored yet in fMRI neurofeedback for chronic pain.

A number of brain rhythms have been targeted by EEG neurofeedback in order to increase resilience to pain (**Table 1**). The commonly targeted rhythms include theta (4–7 Hz), alpha (8–13 Hz), beta (14–30 Hz) and sensorimotor (12–15 Hz over the sensorimotor area) [17]. However, the change desired in each of these rhythms varies. Whilst pain reduction has been associated with an increase in the power of alpha and sensorimotor rhythms, contrastingly, a decrease in theta and beta rhythms have been associated with pain relief [17]. However, very few studies target these signals in isolation [20, 39]. More often studies target multiple signals at the same time, whereby patients are either shown each rhythm individually at the same time or they are shown feedback based on the ratio of two such signals [40–43].

In general, neurofeedback sessions tend to be 30–45 minutes long and patients are offered 20–40 sessions [15]. The frequency of these sessions ranges from one to five times a week, but studies which administered more frequent sessions have reported greater pain relief. Commonly used electrodes for providing feedback include C3, C4, Cz, T3, T4, FP1, P3 and P4 [15].

Brain rhythm	Frequency	Desired change
Theta	4–7 Hz	Decrease in power
Alpha	8–13 Hz	Increase in power
Beta	14–30 Hz	Decrease in power
Sensorimotor rhythm	12–15 Hz Over sensorimotor cortex	Increase in power

Table 1.
Neurofeedback targets [17].

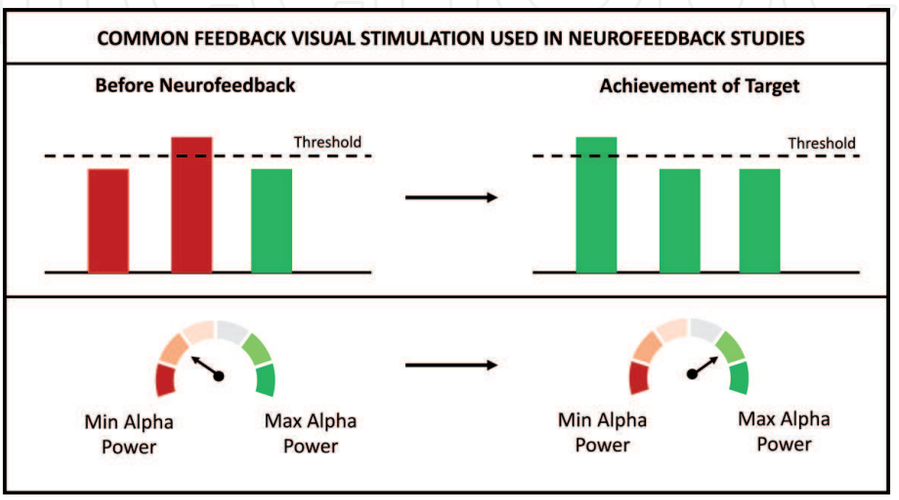

Figure 2.
Schematic representation of visual stimulus provided in different neurofeedback studies.

Feedback has been provided in a range of ways. Auditory feedback has been mainly in the form of changing volume of sound, whereby, achievement of signal has been associated with an increase in the volume heard [44]. Visual feedback used has been more varied (**Figure 2**). Some studies use simple bars to show the feedback, whereby the height of the bar is proportional to the intensity of the signal [45]. Other studies have changed the color of the bar on achievement of signal such that when the threshold is met, the color turns green, otherwise it remains red [43]. Some studies have tried to engage the users through the idea of games whereby the width of a river increases as the intensity of signal increases for instance [41, 46]. Therefore, feedback has been provided in a range of ways. Another form of stimulation which can be explored in the context of neurofeedback is tactile stimulation. Some studies have even combined two forms of stimuli such as visual and auditory whereby patient is shown an angry and shouting patient [36]. In order to calm the patient, the individual has to achieve the desired changes in the brain rhythms.

5. Efficacy of neurofeedback in management of chronic pain

Several neurofeedback studies have shown pain reduction following neurofeedback. Key randomized controlled trials in the field have been summarized in **Table 2**. Reduction in pain has been reported across several pain conditions such as Fibromyalgia [27, 29, 36, 41], Central Neuropathic Pain in Paraplegic patients [28, 43, 47–49], Traumatic Brain Injury [39, 50], Chemotherapy-Induced Peripheral Neuropathy [51], Primary Headache [52], Complex Regional Pain Syndrome Type I [53], Post-Herpetic Neuralgia [37] and chronic lower back pain [54]. There is a wide

range of pain reduction reported which can range from an average of 6–82% reduction in pain intensity [15]. A recent systematic review published showed that ten out of twenty-one studies published in the field reported a pain reduction of greater than 30% which is considered to be clinically significant reduction [15].

Such variability in the degree of pain reduction could be due to a number of aspects of the neurofeedback protocol ranging from number of sessions, frequency of sessions, target frequencies and electrodes used for feedback, for example. The neurofeedback studies conducted so far have been highly variable on more than one of these aspects [15, 16], making comparison of results across studies impossible. Therefore, it is difficult to determine which of these parameters is responsible for the difference or how to best optimize each of these aspects of the training.

Most of the neurofeedback studies have measured changes in pain immediately following neurofeedback [39, 43, 52, 55, 56]. Furthermore, pain reduction has been reported to be sustained even at follow up of 3–6 months after completion of neurofeedback training [28, 36, 41, 49–51, 54]. However, these studies do not report whether the corresponding change in brain rhythm which were measured following completion of training were also sustained at long-term follow-up. We do not know the length of time for which the effect of neurofeedback on brain rhythms is sustained. Interestingly, one study reported that although pain reduction did not occur immediately following completion of the training course, there was improvement in pain at follow-up [36]. This could suggest that perhaps NFB could lead to changes in the underlying brain networks which occurs over a longer period of time but can be sustained for longer duration. These results provide the preliminary evidence for potential of neurofeedback for providing analgesia in chronic pain.

It has been shown that neurofeedback not only leads to reduction in pain but leads to improvement in a number of pain associated symptoms such as depression

Study	**Chronic pain condition**	**Target brain oscillation**	**% Pain reduction**	**Pain associated symptoms reported to improve following NFB**
Goldway et al. (2019) [36]	Fibromyalgia	↓Amygdala activation (fMRI)	7%	REM latency Sleep quality
Prinsloo et al. (2018) [50]	Chemotherapy-induced peripheral neuropathy	↑Alpha ↓Beta	45%	Fatigue Cancer-related symptoms Physical functioning Quality of life
Guan et al. (2015) [37]	Post-herpetic Neuralgia	↓rACC activity (fMRI)	64%	None studied
Farahani et al. (2014) [45]	Primary headache	↑SMR ↓Theta ↓Beta	19%	None studied
Caro et al. (2011) [29]	Fibromyalgia	↑SMR ↓Theta ↓Beta	39%	Fatigue
Kayiran et al. (2010) [40]	Fibromyalgia	↑SMR ↓Theta ↓Beta	82%	Fatigue Depression Anxiety Social functioning Physical functioning

Table 2.
Randomized controlled trials investigating role of neurofeedback in chronic pain conditions.

[27, 39, 41, 54, 57–60], anxiety [27, 41, 54, 57, 59], fatigue [27, 29, 41, 49, 51], and sleep [36, 39, 49–51, 57]. These symptoms have been known to co-exist with pain in chronic pain conditions and also known to exacerbate the individual's pain on a day-to-day basis [61–63]. Therefore, by being able to target these symptoms along with pain, neurofeedback has the potential to holistically improve the well-being of these individuals. A summary of different symptoms which have been shown to improve following neurofeedback have been shown in **Figure 3**.

Current neurofeedback studies have a number of limitations. There are currently only seven controlled trials in the field [29, 41, 47, 51, 52, 64, 65], of which only one trial is of high quality [65]. Most of the trials lack appropriate blinding as the control group are often patients on other pain medications [29, 66]. This makes the blinding of patient difficult and could lead to patient's belief in treatment affecting the results. Only two studies have implemented sham neurofeedback [36, 37].

The best sham treatment to offer is debatable. One would argue that patients could be shown the feedback signal from another region of the brain. But this might not be best as it might be the case that another region which is used for feedback might be the undiscovered part of the pain matrix. Another way to provide sham feedback would be to show the individual the recording from another participant or their own recording in a reverse order. Whilst this might be a true sham condition as the feedback shown to the individual would be independent of the individual's brain activity, it might mean that the patients find no relief of symptoms and discover that it is a sham treatment. Either way, such sham neurofeedback needs to be implemented by more studies in order to truly understand whether the pain reduction reported in these individuals is due to underlying changes in neuronal networks.

Whilst we have learnt a lot about neurofeedback over the past decade, there is still a lot which is unknown about this technique. Neurofeedback differs from other neuromodulatory techniques such entrainment and transcranial magnetic stimulation in that neurofeedback involves active involvement of the individuals in changing

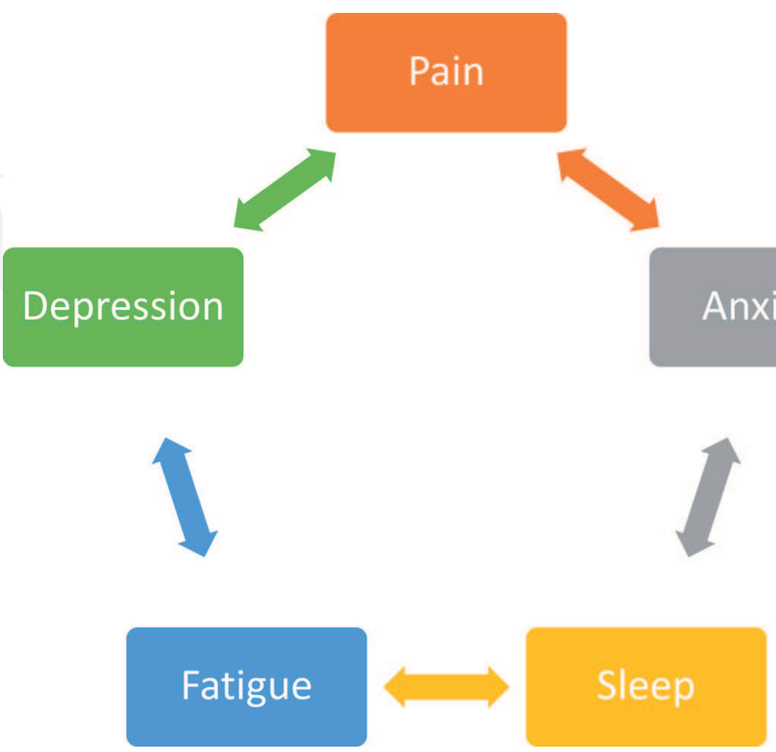

Figure 3.
Schematic representation of pain and pain associated symptoms in chronic pain syndromes.

the brain oscillations, as opposed to passive reception of stimulation [5]. We do not know which of these is a more efficient technique to alter brain oscillations yet. Furthermore, it is also unknown what mental strategies in particular are associated with changes in brain oscillations seen in the studies so far. Some of the common instructions given to patients undergoing training involve asking them to stay relaxed, imagining happy moments, revisiting happy memories and thinking about favorite family member or friends. However, none of the studies so far document which of these strategies actual work for the patients. Therefore, further qualitative studies are required to see what patients have been using to actively change their brain oscillations during neurofeedback in order to provide more focused instructions to patients undergoing training. Furthermore, studies should aim to analyze the correlation between neurophysiological signal and pain reduction rather than solely focusing on the behavioral outcomes [29, 41, 47, 51, 52, 64, 65]. Establishing such correlation between behavioral change and changes in neurophysiological signal is key to understanding whether the pain relief is truly due to neurofeedback.

In addition to this, there is also a possibility that once the patients have been able to identify the mental strategy which allows them to achieve the desired brain state and practice in the neurofeedback setting for a number a sessions, they might be able to implement such mental strategies without the ongoing EEG signal feedback. It is not clear if this possible or how long it might take for an individual to become independent of the EEG feedback and still receive pain relief.

The current neurofeedback studies are highly heterogenous. It is unclear which brain regions, oscillations, feedback form or training length is required to optimize the improvement in pain. More studies are required comparing one aspect of the neurofeedback training program at once in order to determine which of these parameters provide the most therapeutic benefit.

Another area of uncertainty is the efficacy of neurofeedback in different pain conditions. Studies so far have shown that all chronic pain condition report pain reduction to some degree following neurofeedback. However, it is not known whether neurofeedback is better for some chronic pain conditions than others. It might be the case that neuronal changes seen following neurofeedback is linked to central sensitization only, in which case several chronic pain conditions may benefit from it equally as many pain conditions have this as the underlying pathology. However, we do not know whether it is equally as good at treating nociceptive pain as seen in conditions such as arthritis.

Furthermore, the role that neurofeedback will play in pain management in the future is not clear [16]. It is not clear whether it has the true potential to substitute pharmacological agents completely. It might be the case that it might reduce the escalation of opioid usage in this patient cohort. Hence further studies are needed to determine the maximum potential of this form of therapy.

6. Adverse effects associated with Neurofeedback

In general, neurofeedback is well tolerated with a minority of patients experiencing mild adverse events. These adverse events are often self-limiting and tend to be controlled by decreasing the frequency of training [43, 48]. Adverse events seen in neurofeedback studies seem to be more common in certain patient groups than others. For instance, some individuals with spinal cord injury and central neuropathic pain have reported some hypersensitivity of soles of the feet due to recovery of proprioception or spasms of the lower limb, [28, 48]. Patients with traumatic brain injury have reported an increase in nausea and the intensity of their headaches [39, 67]. It is difficult to confirm that these side-effects are due to NFB as these reported symptoms

are often seen in these conditions irrespective of provision of neurofeedback therapy. Overall, NFB is safe and well-tolerated in majority of patients in most clinical studies.

7. Delivery of home-based neurofeedback therapy

Neurofeedback has also been delivered in the home setting by a few recent studies [43, 48]. This can be achieved through the use of a headset which records activity from one single electrode, such as C4 [43, 48] or FP1 [39] and makes use of an app on tablets to analyze and showcase feedback to the individual [28, 48]. Such systems have been implemented in patients with central neuropathic pain [43, 48] as well as traumatic brain injury [39]. Patients could practice neurofeedback for 5- or 10-minutes sessions as and when they wanted.

These studies have shown some promising results. With further expansion of this technology, it might be possible for individuals to benefit from neurofeedback at their home as and when required as patients have on average used neurofeedback 3–40 times over the course of 2–3 months in these studies [43, 48]. Two of these studies have reported around 33% reduction in pain [43, 48] whereas one of them reported 16% reduction in pain [39] on average in participants who tried these home-based systems.

One of these studies also performed qualitative research on user experience following such home-based systems [43]. Overall, it was reported that the patient satisfaction score was high when measured using QUESB (Quebec User Evaluation of Satisfaction Questionnaire). According to the patients, the key factors which affected the frequency of their use of the home-based device were their health state, availability of free time and their intensity of pain. Patients also put effectiveness, ease of use and comfort as their main priority when using any such home-based device. Hence whilst the current home-based technology used in this study showed that it could record the data with decent quality, it also highlighted that patients wanted technology which was able to provide neurofeedback wirelessly using headset and smart device as well as collect information from the scalp without the use of gel to connect electrodes.

Being able to do this on a regular basis would also increase the efficacy of the therapy and patients might be able to use neurofeedback in addition to or instead of commonly used pharmacological agents which are associated with significant adverse effect profiles. Therefore, home-based neurofeedback can act as a novel treatment option to provide pain relief to patients with much fewer side effects than current pharmacological agents [68].

8. Conclusions

Neurofeedback is a newly emerging technique which can be used to achieve brain states associated with increased resilience to pain. The results so far have been very promising not only in terms of improvement in chronic pain, where as many as half of the studies in the field have shown clinically significant reduction in clinical pain following neurofeedback, but also in terms of improvement in pain associated symptoms such as fatigue, depression, anxiety and sleep which have also been reported to improve with neurofeedback. Being able to target all of these co-morbidities holistically using neurofeedback is key for the overall improvement in the well-being of chronic pain patients because these factors are often interlinked and aggravate each other.

There is still a lot of work that needs to be done. Different aspects of training protocols, such as target signal, number of sessions, length of sessions and scalp region of interest, need to be optimized in order to identify parameters which lead not only to successful modulation of the brain activity but also a corresponding

change in pain signals. Currently, it is not clear what neurofeedback protocol brings about maximum pain relief for patients.

Furthermore, identification of mental strategies which enable individuals to reach therapeutic brain states is also required, with the aim being that eventually individuals will be able to practice these strategies independent of the feedback system after an initial course of training sessions. Whilst, there is a lot of work to do, the results so far have been promising, opening window of opportunity to manage a number of chronic pain conditions at low cost and without the side effects associated with the currently available pharmacological agents.

Conflict of interest

The authors have no conflict of interest to declare.

Author details

Kajal Patel[1*], Manoj Sivan[2,3], James Henshaw[2] and Anthony Jones[2]

1 School of Medicine, University of Manchester, Manchester, UK

2 The Human Pain Research Group, Division of Neuroscience and Experimental Psychology, University of Manchester, Manchester, UK

3 Academic Department of Rehabilitation Medicine, University of Leeds, Leeds, UK

*Address all correspondence to: kj.patel1020@gmail.com

References

[1] Evans JR. Handbook of neurofeedback: dynamics and clinical applications. CRC Press. 2007;

[2] Marzbani H, Marateb HR, Mansourian M. Methodological note: Neurofeedback: A comprehensive review on system design, methodology and clinical applications. Basic Clin Neurosci. 2016 Mar 1;7(2):143-58.

[3] Bagdasaryan J, Le Van Quyen M. Experiencing your brain: Neurofeedback as a new bridge between neuroscience and phenomenology. Front Hum Neurosci. 2013;7(OCT):1-10.

[4] Alkoby O, Abu-Rmileh A, Shriki O, Todder D. Can We Predict Who Will Respond to Neurofeedback? A Review of the Inefficacy Problem and Existing Predictors for Successful EEG Neurofeedback Learning. Vol. 378, Neuroscience. Elsevier Ltd; 2018. p. 155-64.

[5] Budzynski TH, Budzynski HK, Evans JR, Abarbanel A. Introduction to quantitative EEG and neurofeedback: Advanced theory and applications. Acad Press. 2009;

[6] Van Doren J, Arns M, Heinrich H, Vollebregt MA, Strehl U, K. Loo S. Sustained effects of neurofeedback in ADHD: a systematic review and meta-analysis. European Child and Adolescent Psychiatry. 2019.

[7] Schoenberg PLA, David AS. Biofeedback for psychiatric disorders: A systematic review. Appl Psychophysiol Biofeedback. 2014;39(2):109-35.

[8] Gruzelier JH. EEG-neurofeedback for optimising performance. I: a review of cognitive and affective outcome in healthy participants. Neuroscience and Biobehavioral Reviews. 2014. p. 124-41.

[9] Carvalho R, Dias N, Cerqueira JJ. Brain-machine interface of upper limb recovery in stroke patients rehabilitation: A systematic review. Physiotherapy Research International. 2019.

[10] Katz WA, Rothenberg R. The nature of pain: Pathophysiology. J Clin Rheumatol. 2005;11(2):11-5.

[11] Reddan MC, Wager TD, M.C. R. Brain systems at the intersection of chronic pain and self-regulation. Neurosci Lett [Internet]. 2019;702:24-33. Available from: http://www.elsevier.com/locate/neulet

[12] Sarnthein J, Stern J, Aufenberg C, Rousson V, Jeanmonod D. Increased EEG power and slowed dominant frequency in patients with neurogenic pain. Brain. 2006;129(1):55-64.

[13] Boord P, Siddall PJ, Tran Y, Herbert D, Middleton J, Craig A. Electroencephalographic slowing and reduced reactivity in neuropathic pain following spinal cord injury. Spinal Cord. 2008;

[14] Dos Santos Pinheiro ES, De Queirós FC, Montoya P, Santos CL, Do Nascimento MA, Ito CH, et al. Electroencephalographic patterns in chronic pain: A systematic review of the literature. PLoS One. 2016;11(2):1-26.

[15] Patel K, Sutherland H, Henshaw J, Taylor JR, Brown CA, Casson AJ, et al. Effects of neurofeedback in the management of chronic pain: A systematic review and meta-analysis of clinical trials. Eur J Pain (United Kingdom) [Internet]. 2020 Jun 5 [cited 2020 Jun 8];24:1440-1457. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/ejp.1612

[16] Roy R, de la Vega R, Jensen MP, Miró J. Neurofeedback for Pain Management: A Systematic Review. Frontiers in Neuroscience. 2020.

[17] Jensen MP, Sherlin LH, Hakimian S, Fregni F. Neuromodulatory approaches for chronic pain management: Research findings and clinical implications. J Neurother. 2009;13(4):196-213.

[18] Melzack R, Wall PD. Pain Mechanisms : A New Theory. Science (80-) [Internet]. 1965 [cited 2019 Sep 29];150:971-8. Available from: https://science-sciencemag-org.manchester.idm.oclc.org/content/sci/150/3699/971.full.pdf

[19] Apkarian AV, Bushnell MC, Treede R-D, Zubieta J-K. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain [Internet]. 2005 [cited 2019 Sep 29];9:463-84. Available from: www.EuropeanJournalPain.com

[20] Mayaud L, Wu H, Barthélemy Q, Favennec P, Delpierre Y, Congedo M, et al. Alpha-phase synchrony EEG training for multi-resistant chronic low back pain patients: an open-label pilot study. Eur Spine J. 2019;

[21] Ossipov MH, Dussor GO, Porreca F. Central modulation of pain. J Clin Invest [Internet]. 2010 [cited 2019 Sep 30];120(11):3779-87. Available from: http://www.jci.org

[22] DeLeo JA. Basic science of pain. J Bone Jt Surg. 2006;88(2):58-62.

[23] Donaldson LF, Lumb BM. Top-down control of pain [Internet]. Vol. 595, Journal of Physiology. 2017 [cited 2020 Jan 12]. p. 4139-40. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491874/

[24] Apkarian A V, Hashmi JA, Baliki MN. Pain and the brain: Specificity and plasticity of the brain in clinical chronic pain. [cited 2019 Nov 9]; Available from: http://www.iasp-pain.org/

[25] Jensen MP, Day MA, Miro J. Neuromodulatory treatments for chronic pain: efficacy and mechanisms. Nat Rev Neurol [Internet]. 2014;10(3):167-78. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med10&NEWS=N&AN=24535464

[26] Kropotov JD. Rhythms of the Healthy Brain. In: Functional Neuromarkers for Psychiatry [Internet]. 2016 [cited 2020 Jan 10]. p. 403-5. Available from: http://dx.doi.org/10.1016/B978-0-12-410513-3.00038-3

[27] Kayiran S, Dursun E, Ermutlu N, Dursun N, Karamursel S. Neurofeedback in fibromyalgia syndrome. Agri. 2007;19(3):47-52.

[28] Hassan MA, Fraser M, Conway BA, Allan DB, Vuckovic A. The mechanism of neurofeedback training for treatment of central neuropathic pain in paraplegia: A pilot study. BMC Neurol. 2015;15(1).

[29] Caro XJ, Winter EF. EEG biofeedback treatment improves certain attention and somatic symptoms in fibromyalgia: A pilot study. Appl Psychophysiol Biofeedback [Internet]. 2011 Sep [cited 2019 Oct 22];36(3):193-200. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed12&NEWS=N&AN=51466220

[30] Collura TF, Siever D. Audio-Visual Entrainment in Relation to Mental Health and EEG. In: Introduction to Quantitative EEG and Neurofeedback. 2009.

[31] Timmers D. Treating Attention Deficits and Impulse Control. In: Clinical Neurotherapy: Application of Techniques for Treatment. 2013.

[32] Jensen MP, Hakimian S, Sherlin LH, Fregni F, M.P. J, S. H, et al. New Insights Into Neuromodulatory Approaches for the Treatment of Pain. J Pain [Internet].

2008 [cited 2019 Sep 29];9(3):193-9. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&NEWS=N&AN=50020976

[33] Jensen MP, Sherlin LH, Gertz KJ, Braden AL, Kupper AE, Gianas A, et al. Brain EEG activity correlates of chronic pain in persons with spinal cord injury: Clinical implications. Spinal Cord. 2013;51(1):55-8.

[34] Lim M, Kim JS, Kim DJ, Chung CK. Increased low-and high-frequency oscillatory activity in the prefrontal cortex of fibromyalgia patients. Front Hum Neurosci. 2016;10(MAR2016):1-11.

[35] Hawkinson JE, Ross AJ, Parthasarathy S, Scott DJ, Laramee EA, Posecion LJ, et al. Quantification of adverse events associated with functional MRI scanning and with real-time fMRI-based training. Int J Behav Med [Internet]. 2012;19(3):372-81. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=21633905

[36] Goldway N, Ablin J, Lubin O, Zamir Y, Keynan JN, Or-Borichev A, et al. Volitional limbic neuromodulation exerts a beneficial clinical effect on Fibromyalgia. Neuroimage [Internet]. 2019;186:758-70. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=30408596

[37] Guan M, Ma L, Li L, Yan B, Zhao L, Tong L, et al. Self-regulation of brain activity in patients with postherpetic neuralgia: a double-blind randomized study using real-time FMRI neurofeedback. PLoS One [Internet]. 2015 Apr;10(4):e0123675. Available from: http://www.plosone.org/article/fetchObject.action?uri=info:doi/10.1371/journal.pone.0123675&representation=PDF

[38] Goldway N, Ablin J, Lubin O, Zamir Y, Jacob Keynan N, Or-Borichev A, et al. Beyond pain in fibromyalgia: Limbic related eeg-neurofeedback training improves sleep and affect. Biol Psychiatry [Internet]. 2018 May;83(9 Supplement 1):S447. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emexa&NEWS=N&AN=621901919

[39] Elbogen EB, Alsobrooks A, Battles S, Molloy K, Dennis PA, Beckham JC, et al. Mobile Neurofeedback for Pain Management in Veterans with TBI and PTSD. Pain Med [Internet]. 2019;0(0):1-9. Available from: https://academic.oup.com/painmedicine/advance-article/doi/10.1093/pm/pnz269/5614403

[40] S. P, T. K, E. B, D. D, D. N. Neuromodulation as a treatment for chemotherapy-induced peripheral neuropathy (CIPN): Examining differences between placebo and neurofeedback. Psychosom Med [Internet]. 2019;81(4):A63. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emexb&NEWS=N&AN=627783404

[41] Kayıran S, Dursun E, Dursun N, Ermutlu N, Karamürsel S. Neurofeedback intervention in fibromyalgia syndrome; a randomized, controlled, rater blind clinical trial. Ahles Alanoglu, Anderberg, Babu, Basmajian, Bennett, Caruso, Carville, Chiarioni, Corapcoglu, Crider, Da Costa, Denk, Draizar, Dursun, Dursun, Dursun, Egner, Egner, Egner, Gentil, Grace, Gracely, Guedj, Hidalgo, Hisli, Ho, Howe, Intiso, Jensen, Jensen, r A, editor. Appl Psychophysiol Biofeedback [Internet]. 2010;35(4):293-302. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med7&NEWS=N&AN=20614235

[42] Vuckovic A, Hasan MA, Fraser M, Conway B, Allan DB. A Pilot Study on Clinical and Neurological Effects of Neurofeedback Training for Treatment of Central Neuropathic Pain. In: Jensen,

W and Andersen, OK and Akay M, editor. REPLACE, REPAIR, RESTORE, RELIEVE - BRIDGING CLINICAL AND ENGINEERING SOLUTIONS IN NEUROREHABILITATION [Internet]. GEWERBESTRASSE 11, CHAM, CH-6330, SWITZERLAND: SPRINGER INT PUBLISHING AG; 2014. p. 823-31. (Biosystems and Biorobotics; vol. 7). Available from: http://link.springer.com/10.1007/978-3-319-08072-7_113

[43] Al-Taleb MKH, Purcell M, Fraser M, Petric-Gray N, Vuckovic A. Home used, patient self-managed, brain-computer interface for the management of central neuropathic pain post spinal cord injury: Usability study. J Neuroeng Rehabil [Internet]. 2019 [cited 2019 Nov 18];16(1). Available from: https://doi.org/10.1186/s12984-019-0588-7

[44] Abul Hassan M, Fraser M, Conway BA, Allan DB, Vuckovic A. The mechanism of neurofeedback training for treatment of central neuropathic pain in paraplegia: a pilot study. BMC Neurol. 2015 Oct;15.

[45] Vuckovic A, Hasan MA, Fraser M, Conway B, Allan DB. A Pilot Study on Clinical and Neurological Effects of Neurofeedback Training for Treatment of Central Neuropathic Pain. In: Jensen, W and Andersen, OK and Akay, M, editor. REPLACE, REPAIR, RESTORE, RELIEVE - BRIDGING CLINICAL AND ENGINEERING SOLUTIONS IN NEUROREHABILITATION. 2014. p. 823-31. (Biosystems and Biorobotics; vol. 7).

[46] Farahani DM, Tavallaie SA, Ahmadi K, Ashtiani AF. Comparison of neurofeedback and transcutaneous electrical nerve stimulation efficacy on treatment of primary headaches: A randomized controlled clinical trial. Iran Red Crescent Med J. 2014 Aug 1;16(8).

[47] Jensen MP, Sherlin LH, Askew RL, Fregni F, Witkop G, Gianas A, et al. Effects of non-pharmacological pain treatments on brain states. Clin Neurophysiol [Internet]. 2013 Oct [cited 2019 Oct 22];124(10):2016-24. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med9&NEWS=N&AN=23706958

[48] Vučković A, Altaleb MKH, Fraser M, McGeady C, Purcell M. EEG Correlates of Self-Managed Neurofeedback Treatment of Central Neuropathic Pain in Chronic Spinal Cord Injury. Front Neurosci [Internet]. 2019 Jul 25;13. Available from: https://www.frontiersin.org/article/10.3389/fnins.2019.00762/full

[49] Jensen MP, Gertz KJ, Kupper AE, Braden AL, Howe JD, Hakimian S, et al. Steps toward developing an EEG biofeedback treatment for chronic pain. Amtmann Bazanova, Boord, Bromm, Bromm, Bromm, Cardenas, Caro, Chen, Chen, Cook, Egner, Egner, Ehde, Finnerup, Gannon, Gevensleben, Gevensleben, Hammond, Hays, Huber, Jasper, Jensen, Jensen, Jensen, Jensen, Jensen, Kayiran, Krupp, Llinas, Raymond, Ros, Sa B, editor. Appl Psychophysiol Biofeedback [Internet]. 2013 Jun [cited 2019 Oct 22];38(2):101-8. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med9&NEWS=N&AN=23532434

[50] Hershaw JN, Hill-Pearson CA, Arango JI, Souvignier CAR, Pazdan CRM. Semi-Automated Neurofeedback Therapy for Persistent Postconcussive Symptoms in a Military Clinical Setting: A Feasibility Study. Mil Med [Internet]. 2020 Oct 11 [cited 2019 Oct 22]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/31603218

[51] Prinsloo S, Novy D, Driver L, Lyle R, Ramondetta L, Eng C, et al. The Long-Term Impact of Neurofeedback on Symptom Burden and Interference in Patients With Chronic Chemotherapy-Induced Neuropathy: Analysis of a Randomized Controlled Trial. J Pain

Symptom Manage [Internet]. 2018 [cited 2019 Sep 29];55(5):1276-85. Available from: http://www.elsevier.com/locate/jpainsymman

[52] Farahani DM, Tavallaie SA, Ahmadi K, Fathi Ashtiani A, Sheikh M, Yahaghi E, et al. Comparison of Neurofeedback and Transcutaneous Electrical Nerve Stimulation Efficacy on Treatment of Primary Headaches: A Randomized Controlled Clinical Trial. Iran Red Crescent Med J [Internet]. 2014 Aug 5;16(7):e17799. Available from: http://ircmj.com/53808.pdf

[53] Jensen MP, Grierson C, Tracy-Smith V, Bacigalupi SC, Othmer S. Neurofeedback treatment for pain associated with complex regional pain syndrome type I. Turk BBBBCCCC deCharms EFHJMOOOPPQSS, editor. J Neurother [Internet]. 2007;11(1):45-53. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=psyc5&NEWS=N&AN=2007-13570-004

[54] Mayaud L, Wu H, Barthélemy Q, Favennec P, Delpierre Y, Congedo M, et al. Alpha-phase synchrony EEG training for multi-resistant chronic low back pain patients: an open-label pilot study. Eur Spine J [Internet]. 2019 [cited 2019 Nov 18];28(11):2487-501. Available from: https://doi.org/10.1007/s00586-019-06051-9

[55] Caro XJ, Winter EF. EEG biofeedback treatment improves certain attention and somatic symptoms in fibromyalgia: a pilot study. Appl Psychophysiol Biofeedback [Internet]. 2011;36(3):193-200. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med7&NEWS=N&AN=21656150

[56] Vuckovic A, Altaleb MKH, Fraser M, McGeady C, Purcell M. EEG Correlates of Self-Managed Neurofeedback Treatment of Central Neuropathic Pain in Chronic Spinal Cord Injury. Front Neurosci. 2019 Jul;13.

[57] Ibric VL, Dragomirescu LG. Neurofeedback in pain management. In: Budzynski, TH and Budzynski, HK and Evans, JR and Abarbanel A, editor. Introduction to Quantitative EEG and Neurofeedback [Internet]. SARA BURGERHARTSTRAAT 25, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS: Elsevier; 2009. p. 417-51. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780123745347000162

[58] Koberda JL. LORETA Z-Score Neurofeedback in Chronic Pain and Headaches. In: JF TR and L, editor. Z Score Neurofeedback [Internet]. 525 B STREET, SUITE 1900, SAN DIEGO, CA 92101-4495 USA: Elsevier; 2015. p. 115-39. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780128012918000066

[59] Koberda JL. Z-score LORETA neurofeedback as a potential therapy in depression/anxiety and cognitive dysfunction. Alonzo Choi, Kessler, Koberda, Koberda, Koberda, Koberda, Pittenger, Riva-Posse, Schlaepfer, Stevens, Thatcher, Williams A, editor. Z score neurofeedback Clin Appl [Internet]. 2015;93-113. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=psyc12&NEWS=N&AN=2014-45849-005

[60] Koberda JL, Koberda P, Bienkiewicz AA, Moses A, Koberda L. Pain management using 19-electrode Z-score LORETA neurofeedback. Caro Ibric, Jensen, Jensen, Kayiran, Kayiran, Kenchadze, Koberda, Koberda, Koberda, Moisset, Moont, Prinsloo, Sawamoto, Sime, Stern, Stokes, Thatcher, Thatcher, Thatcher, Thatcher, Walker H, editor. J Neurother [Internet]. 2013;17(3):179-90. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=psyc10&NEWS=N&AN=2013-30620-005

[61] Feingold D, Brill S, Goor-Aryeh I, Delayahu Y, Lev-Ran S. Depression and anxiety among chronic pain patients receiving prescription opioids and medical marijuana. J Affect Disord. 2017;

[62] Zis P, Daskalaki A, Bountouni I, Sykioti P, Varrassi G, Paladini A. Depression and chronic pain in the elderly: Links and management challenges. Clinical Interventions in Aging. 2017.

[63] Bonvanie IJ, Oldehinkel AJ, Rosmalen JGM, Janssens KAM. Sleep problems and pain: A longitudinal cohort study in emerging adults. Pain. 2016;

[64] N. G, J. A, O. L, Y. Z, J.N. K, A. O-B, et al. Volitional limbic neuromodulation exerts a beneficial clinical effect on Fibromyalgia. Neuroimage [Internet]. 2019;186:758-70. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=30408596

[65] M. G, L. M, L. L, B. Y, L. Z, L. T, et al. Self-regulation of brain activity in patients with postherpetic neuralgia: A double-blind randomized study using real-time fMRI neurofeedback. PLoS One [Internet]. 2015;10(4):e0123675. Available from: http://www.plosone.org/article/fetchObject.action?uri=info:doi/10.1371/journal.pone.0123675&representation=PDF

[66] S. K, E. D, N. E, N. D. Neurofeedback in fibromyalgia syndrome. Agri [Internet]. 2007;19(3):47-52. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&NEWS=N&AN=350246563

[67] J.N. H, C.A. H-P, J.I. A, C.A.R. S. Semi-Automated Neurofeedback Therapy for Persistent Postconcussive Symptoms in a Military Clinical Setting: A Feasibility Study. Mil Med [Internet]. 2019; Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emexc&NEWS=N&AN=629566784

[68] Luctkar-Flude M, Groll D. A Systematic Review of the Safety and Effect of Neurofeedback on Fatigue and Cognition. Integr Cancer Ther. 2015;14(4):318-40.