

Topic Exploration Report 1

TER590 Electroencephalogram neurofeedback systems for chronic pain

What is a Topic Exploration Report?

Topic Exploration Reports are not health technology assessments. These reports provide a high-level briefing on new topics submitted to Health Technology Wales and are not based on exhaustive or systematic literature searches. Instead, they rely on a focussed scan of key resources.

What evidence is used in a Topic Exploration Report?

Priority is given to summarising the most relevant or useful evidence, rather than covering all possible evidence. Information reported is typically based on abstracts and study authors' own conclusions, rather than detailed scrutiny of full texts.

What are the aims of a Topic Exploration Report?

Topic Exploration Reports offer an overview of the available evidence on a topic and aim to highlight any uncertainties or gaps in the evidence. These reports outline the quantity and type of evidence found, but no critical appraisal or formal evidence synthesis is conducted.

How should a Topic Exploration Report be used?

Topic Exploration Reports can be used to indicate what evidence may be available for a topic, and <u>do not</u> provide definitive guidance on how a technology should be used. The evidence presented within the reports should be interpreted with caution.

¹ <u>Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg</u>
<u>Translation of published technical HTW documents from English into Welsh</u>

Topic exploration report number	TER590
Topic	Electroencephalogram neurofeedback systems for chronic pain
Summary of findings	Electroencephalogram (EEG) neurofeedback is a non-invasive treatment that teaches people to consciously regulate their brain activity and reduce symptoms of pain.
	In 2021 NICE recommended that biofeedback, which includes EEG neurofeedback, should not be used in the management of chronic primary pain due to some evidence of harm. The guidance was based on limited evidence from small, low-quality studies.
	Since 2021, further studies, including randomised controlled trials (RCTs), have been published. Two systematic reviews, one in patients with chronic pain from any cause and one in patients with fibromyalgia, reported that EEG neurofeedback may have a clinically meaningful effect on pain in the short term. The included studies had different methods, and the reviews concluded that larger, higher quality, studies were needed.
	Five additional RCTs were identified, three of which were feasibility studies. The RCTs were conducted in participants with chronic pain from any cause, fibromyalgia, chemotherapy-induced peripheral neuropathy, chronic lower back pain and knee osteoarthritis. All the RCTs compared EEG neurofeedback with sham treatment. The largest RCT, with 116 participants, used a home-based system. The feasibility studies reported that the intervention was feasible and safe. All the studies reported that at least some pain outcomes improved in both active and sham arms but there was no clear difference between the arms for most outcomes in most studies.
	We did not identify any studies evaluating the cost-effectiveness of EEG neurofeedback.

Introduction and aims

Chronic pain is persistent or recurrent pain that lasts for more than three months. It is complex and multifactorial in that biological, psychological and social factors contribute to the experience. Chronic pain can lead to physical impairment, disordered sleep, anxiety, depression and low quality of life. There are multiple conditions that can cause chronic pain, including acute injury, degenerative and non-degenerative conditions and medical interventions. It has been estimated that chronic pain affects between a third and half of the UK population, although the prevalence in the literature varies depending on diagnostic criteria. Chronic primary pain is chronic pain that has a significant adverse effect on mental or physical health, independently from any underlying psychological or biological factors. The prevalence of chronic primary pain is estimated to be between 1% and 6% in England. Chronic secondary pain is pain in which an underlying condition accounts for the pain. Chronic primary and secondary pain can co-exist.

Treatment for chronic secondary pain is to identify and manage the underlying cause, using pharmacological and non-pharmacological treatments. For chronic primary pain, a range of treatments may be considered, including exercise programmes, acceptance and commitment therapy or cognitive behavioural therapy, acupuncture or off-label use of antidepressants. However, chronic pain can be difficult to treat, and fluctuates over time, even when the underlying cause is known.

Biofeedback therapy is a non-invasive treatment that teaches people to become aware of, and to control, involuntary physiological responses. Electroencephalogram (EEG) neurofeedback is a type of biofeedback that focusses on the brain and targets specific areas of the brain associated with a disease or cognitive state. EEG neurofeedback has been proposed as a treatment for chronic pain. EEG sensors, placed on the scalp, measure the brain activity associated with pain perception, regulation and emotional regulation. This can be visually represented on a screen. People are given stimuli, tasks or games that redirect activity away from brain frequencies associated with chronic pain and towards those associated with relaxation. Over time, through use of operant conditioning, people can learn to consciously regulate their brain activity and reduce symptoms of pain. The Axon System (Exsurgo Ltd) was identified by the topic proposer a specific example of this technology that can be used by an individual in their own home. It is a Class I medical device with a UKCA mark, awaiting certification for Digital Technology Assessment Criteria.

Health Technology Wales researchers searched for evidence on EEG neurofeedback for chronic pain.

Evidence overview

HTW identified one piece of guidance and two later systematic reviews. We also identified five primary studies comparing EEG neurofeedback with usual care or sham treatment, published after the reviews.

Guidance

NICE Guideline [NG193] (2021) 'Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain' recommends that biofeedback, including neurofeedback, should not be used in the management of chronic primary pain at this time. There was some evidence that pain increased with neurofeedback compared with sham biofeedback up to three months, although neurofeedback did show benefit after three months. The evidence for EEG neurofeedback was limited, being based on two studies and there was very serious uncertainty around the outcomes.

Evidence overview

Systematic reviews

Torres et al. (2024) conducted a systematic review of EEG neurofeedback in fibromyalgia of papers published between 2000 and 2022. Seventeen studies were included, of which eight included a comparison group, four of which were RCTs. It was reported that EEG neurofeedback improved pain as well as anxiety, depression, general health and symptom severity. The included studies showed a wide range of protocols and procedures making it difficult to synthesise findings.

Hesam-Shariati et al. (2022) conducted a systematic review and meta-analysis of EEG neurofeedback for people with chronic pain. Ten RCTs and 13 non-randomised studies were included. Meta-analysis of RCTs that did not have a high risk of bias indicated that EEG neurofeedback may have a clinically meaningful effect on pain intensity in the short-term. It was not possible to draw any conclusions from the non-randomised studies. Protocols varied between studies. The review concluded that evidence was promising, but higher quality studies with large sample sizes were needed to demonstrate if EEG neurofeedback is an effective treatment for chronic pain.

Primary studies

Rice et al. (2024) conducted an RCT investigating whether adding EEG neurofeedback to usual care was safe and more effective than adding sham control-EEG neurofeedback in 116 participants with chronic pain, around 60% with chronic primary pain. The primary outcome was pain, using the Brief Pain Inventory average pain score. The study was home-based, and participants were asked to complete a minimum of 4 sessions a week for eight weeks. 44% of intervention participants and 45% of control participants reported at least a moderate, clinically important improvement in pain with no difference between groups for pain (mean difference: -0.04 [95% confidence interval (CI): -0.39 to 0.31], p=0.90) or for any secondary outcomes. Post hoc analysis suggested that the intervention group received positive rewards during training 100% of the time and the control group received rewards around 25% of the time. The authors suggest that this means that the control group received a partially active sham intervention which obscured differences between groups. There were no side effects or safety issues reported. The RCT was conducted in New Zealand, although two, single arm, proof-of-concept studies with similar protocols have also been conducted in the UK (Birch et al. 2022, Sakel et al. 2024).

Anderson et al. (2025) conducted a feasibility RCT in 30 participants with fibromyalgia in New Zealand. Outcomes were feasibility outcomes and measures of pain using the Brief Pain Inventory. Participants received 12 sessions of EEG neurofeedback treatment or sham treatment and had mean adherence of 80% to the sessions although there was a drop-out rate of 20%. Improvements in pain and functional impact were comparable between groups. There were no adverse events reported.

Prinsloo et al. (2024) conducted a three arm RCT in 91 breast cancer survivors with chemotherapy-induced peripheral neuropathy in the USA. The main outcome was pain, using the unpleasantness rating on the Pain Quality Assessment Scale. The arms were EEG neurofeedback, waitlist control and sham treatment. Participants in the active/sham treatment groups received 20 sessions and reported significant symptom reduction with no difference between the groups, immediately after treatment or at one month follow-up. Authors report that the effect size between the active and waitlist control groups was larger than the effect size between sham treatment and waitlist control.

Evidence overview

Adhia et al. (2023) conducted a pilot RCT in 60 participants with chronic low back pain in New Zealand. Participants were randomised into one of four arms. Three arms were active EEG neurofeedback arms that targeted different areas of the brain (pregenual and dorsal anterior cingulate cortex (pgACC, dACC), and somatosensory cortex (SSC)) and one was a sham treatment arm. Outcomes were feasibility outcomes, pain, using the Brief Pain Inventory, and functional outcomes. The intervention was acceptable, and adherence was reported to be 80%, although there was a 25% dropout rate. No adverse events were reported. Participants in all groups experienced improvement in several of the domains on the Brief Pain Inventory. The authors suggest that the treatment arm that targeted the pgACC was superior to the others and that EEG neurofeedback training is a feasible, safe, and an acceptable treatment approach for chronic lower back pain.

Matthew et al. (2022) conducted a feasibility RCT in 22 participants with knee osteoarthritis in New Zealand. Participants received either nine 30-min EEG neurofeedback sessions or sham treatment. Outcomes were feasibility, pain measured using the Brief Pain Inventory, and functional outcomes measures. The intervention was acceptable, and retention rate was 91%. No serious adverse events were reported during the trial. A clinically significant mean difference was reported for pain unpleasantness for both groups (active group: 2.6 [95% CI: 0.17 to 5.1] and sham group: 2.8 [95% CI: 0.62–5.0]). The authors concluded that EEG neurofeedback training is a feasible and safe intervention.

Economic evaluations

We did not identify any economic evaluations. Evidence provided by the topic proposer indicated that the current UK retail price per patient is £699 for the EEG headset plus £46 per month for ongoing subscription charges. The topic proposer has indicated that this is an initial price and there are ongoing evaluations and discussions around different pricing models. It is estimated that more than half a million patients would be eligible to receive the treatment each year across the UK.

Additional evidence supplied by the topic proposer

The topic proposer submitted an unpublished study describing a secondary analysis of Rice et al. (2022) (Ozolins et al. under peer review). This study described pre- and post-intervention changes to the Brief Pain Inventory overall pain scores in 49 participants from the active arm only. It was reported that significant improvements were seen in all measures. 43% of participants experienced a clinically significant 30% improvement in overall pain score, with 22% experiencing a 50% improvement.

Ongoing research

The topic proposer has indicated that they are currently designing an RCT that will be conducted in the UK and will recruit 80 participants with neuropathic pain from early 2025 onwards. We also identified a protocol for an RCT being conducted in Australia in participants with neuropathic pain following spinal cord injury (Hesam-Shariati et al. 2024). 134 participants will be enrolled to receive either EEG neurofeedback, using a system specifically designed for the trial, or usual care. It is unclear when either trial will report.

Areas of uncertainty

- There is variation in the protocols used in terms of intervention duration, number of sessions and the areas of the brain that are targeted.
- It appears that the sham treatments may be partially active and produce clinically important reductions in pain scores, making it difficult to interpret study findings.

Areas of uncertainty

• It is not always clear whether studies have been conducted in patients with chronic primary or chronic secondary pain.

Health technology assessments and guidance

NICE. (2021). Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. Guideline 193. National Institute for Health and Care Excellence. Available at: www.nice.org.uk/guidance/ng193 [Accessed 6 February 2025].

Evidence reviews and economic evaluations

Hesam-Shariati N, Chang WJ, Wewege MA, et al. (2022). The analgesic effect of electroencephalographic neurofeedback for people with chronic pain: a systematic review and meta-analysis. Eur J Neurol. 29(3): 921-36. doi: https://dx.doi.org/10.1111/ene.15189

Torres CB, Barona EJG, Molina MG, et al. (2024). A systematic review of EEG neurofeedback in fibromyalgia to treat psychological variables, chronic pain and general health. Eur Arch Psychiatry Clin Neurosci. 274(4): 981-99. doi: https://dx.doi.org/10.1007/s00406-023-01612-y

Individual studies

Adhia DB, Mani R, Mathew J, et al. (2023). Exploring electroencephalographic infraslow neurofeedback treatment for chronic low back pain: a double-blinded safety and feasibility randomized placebocontrolled trial. Scientific reports. 13(1): 1177. doi: https://dx.doi.org/10.1038/s41598-023-28344-2

Anderson L, De Ridder D, Glue P, et al. (2025). A safety and feasibility randomized placebo controlled trial exploring electroencephalographic effective connectivity neurofeedback treatment for fibromyalgia. Scientific reports. 15(1): 209. doi: https://dx.doi.org/10.1038/s41598-024-83776-8

Mathew J, Adhia DB, Smith ML, et al. (2022). Source localized infraslow neurofeedback training in people with chronic painful knee osteoarthritis: A randomized, double-blind, sham-controlled feasibility clinical trial. Frontiers in Neuroscience. 16. doi: https://doi.org/10.3389/fnins.2022.899772

Prinsloo S, Kaptchuk TJ, De Ridder D, et al. (2024). Brain-computer interface relieves chronic chemotherapy-induced peripheral neuropathy: A randomized, double-blind, placebo-controlled trial. Cancer. 130(2): 300-11. doi: https://doi.org/10.1002/cncr.35027

Rice DA, Ozolins C, Biswas R, et al. (2024). Home-based EEG Neurofeedback for the Treatment of Chronic Pain: A Randomized Controlled Clinical Trial. The journal of pain. 25(11): 104651. doi: https://dx.doi.org/10.1016/j.jpain.2024.104651

Ongoing research

Hesam-Shariati N, Alexander L, Chen KY, et al. (2024). A home-based self-directed EEG neurofeedback intervention for people with chronic neuropathic pain following spinal cord injury (the StoPain Trial): description of the intervention. Spinal cord. 62(11): 658-66. doi: https://dx.doi.org/10.1038/s41393-024-01031-3

Evidence supplied by the topic proposer

Birch N, Graham J, Ozolins C, et al. (2022). Home-Based EEG Neurofeedback Intervention for the Management of Chronic Pain. Front Pain Res (Lausanne). 3: 855493. doi: https://doi.org/10.3389/fpain.2022.855493

Ozolins C, Biswas R, Almesfer F, et al (unpublished) Home-based EEG Neurofeedback for the Treatment of Chronic Pain: A secondary analysis of data from a randomized clinical trial

Sakel M, Saunders K, Ozolins C, et al. (2024). Feasibility and Safety of a Home-based Electroencephalogram Neurofeedback Intervention to Reduce Chronic Neuropathic Pain: A Cohort Clinical Trial. Arch Rehabil Res Clin Transl. 6(3): 100361. doi: 10.1016/j.arrct.2024.100361

Date of search	February 2025
Concepts used	Axon; Electroencephalogram neurofeedback; EEG; biofeedback; chronic pain

Proposed research question and evidence selection criteria (if selected)

Proposed Research	What is the clinical and cost-effectiveness of
question	electroencephalogram neurofeedback systems for chronic pain?

	Inclusion criteria	Exclusion criteria
Population	Adults diagnosed with chronic pain	Children Adults diagnosed with acute pain
Intervention	Electroencephalogram (EEG) neurofeedback	
Comparison/ Comparators	Standard care Sham EEG neurofeedback	Different EEG neurofeedback protocols
Outcome measures	Pain Functional outcomes Health related QoL Resource use Economic outcomes	

Proposed specialities	Nervous system; patient experience