Effectiveness of neurofeedback therapy for anxiety and stress in adults living with a chronic illness: a systematic review protocol

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Review question/objective: The objective of this review is to systematically examine the effectiveness of neurofeedback therapy for managing anxiety and stress in adults living with a chronic illness. The specific objectives are to identify which neurofeedback systems and/or protocols demonstrate effectiveness and determine the level of supporting evidence. The review question is as follows: What is the effectiveness of neurofeedback therapy for managing anxiety and stress in an adult population aged 18 years of age or older living with a chronic illness?

Keywords Anxiety; EEG biofeedback; mood disorder; neurofeedback; neurotherapy; stress


Background

Chronic illness is a substantial global burden, with the World Health Organization (WHO) reporting that 38 million of 56 million deaths worldwide in 2012 were due to non-communicable, or chronic, illness.1 Furthermore, chronic illness in the Canadian population is estimated to increase by 4.7% from 2010 to 2030.2 Chronic illness has numerous definitions, but commonalities include a lengthy time course, progressive severity and decreased overall functioning causing impaired quality of life.1,3 The WHO focuses on medically based chronic illnesses;4 however, mental illness, drug abuse and chronic pain can be included given their long persistence and drain on sufferers.2,5,6

Anxiety, stress and distress associated with chronic medical conditions have been well documented.7,8 Anxiety is the subjective psychological experience of environmental stressors which is marked by continued excessive worry, sleep abnormalities, difficulty concentrating, emotional lability, fatigue and restlessness.9,10 Stress/distress is the psychological and hormonal response to environmental pressures.10,11 Although separate definitions of anxiety and stress/distress are presented, these terms are often used interchangeably due to their inherent connection with each other.

Chronic anxiety and stress can increase catecholamine release, decrease growth hormones, and aberrantly activate immune and inflammatory cascades.12 As such, stress and anxiety can directly influence illness progression and can lead to irritable bowel syndrome exacerbations and increased cardiovascular risk.7 Increased frequency of general anxiety disorder has also been found in people with asthma, cancer and chronic pain.7 This comorbidity of anxiety with chronic illness can cause increased morbidity, mortality and decreased quality of life.13 Traditional treatment for anxiety includes psychological treatments such as cognitive therapy, cognitive behavioral therapy, exposure therapy and self-help groups, as well as pharmacological modalities such as benzodiazepines and antidepressants.14 Neurofeedback may reduce or eliminate the use of these medications.

Anxiety and stress also have direct neurobiological consequences. Stress hormones have been linked to neuronal remodeling, excitotoxic damage and neuroanatomical changes to the hippocampus and basolateral amygdala.15 Alpha electroencephalography (EEG) recordings have revealed right frontal lateralization in anxious aroused patients as...
compared to healthy control populations. Such brain-specific alternations hint at the usefulness of a therapy such as neurofeedback in regulating anxiety. Neurofeedback is a novel complementary and alternative medicine therapy that is being used mainly by psychologists to treat a number of psychological conditions, including anxiety, depression, post-traumatic stress disorder (PTSD) and attention deficit hyperactivity disorder (ADHD). As this is not a mainstream medical therapy, it is unclear whether individuals with anxiety and stress secondary to a chronic illness will also benefit from this therapy.

Alpha EEG biofeedback, neurotherapy or neurofeedback is a non-invasive drug-free technique. Brain activity is monitored by recording electrodes placed at designated locations on the scalp. Waveforms are then fed back to the patient through computer generated auditory or visual stimuli. When waveforms balance within a healthy threshold, the system provides positive reinforcement such as a pleasant tone. This treatment technique has been effectively used since the 1960s in many conditions, including ADHD, epilepsy, alcoholism, PTSD, stroke, depression, fibromyalgia and autism.

Neurofeedback has been used in phobic and psychiatric populations to decrease anxiety. In a randomized controlled trial (RCT), females with spider phobia underwent functional magnetic resonance imaging (fMRI) neurofeedback, which decreased self-rated anxiety levels as compared to cognitive reappraisal controls and decreased insular activity. In a pre- and post-test study, high frequency beta neurofeedback training in a PTSD population showed decreased self-rated anxiety. Finally, in a quasi-randomized study of psychiatric patients with prominent anxiety symptoms, alpha EEG biofeedback decreased Taylor’s Manifest Anxiety Scores in all anxiety groups.

The objective of the present systematic review is to determine the effect of neurofeedback therapy on anxiety in an adult chronic illness population. According to the Shifting Perspectives Model, coping with chronic illness can change throughout the course of the illness as influenced by external and internal variables. Neurofeedback targets the internal variables (operant brainwaves conditioning) in an attempt to decrease anxiety. Thus, in addition to its ability to decrease anxiety, neurofeedback is able to provide the appropriate level of intervention based on the patient’s own biofeedback. Furthermore, patients with chronic illnesses often cite their complex medication regimen as a barrier to care. Neurofeedback can benefit this population by thinning their pharmacopeia. This review will determine efficacy by compiling and analyzing the studies that have reported on neurofeedback therapy for anxiety in chronic illness populations. To guide this review, it is necessary to define key terms further:

**Chronic illness** is any condition lasting longer than one year, with progressive physical and/or mental deficits that lead to decreased quality of life. For the purposes of this review, chronic illnesses will include chronic pain in addition to medical diagnoses. In an effort not to overlap with past systematic reviews, ADHD, depression, PTSD, addiction, and other mood and psychiatric disorders will not be included in our definition of chronic illness.

**Anxiety** is a psychological condition that can manifest affectively, cognitively and somatically. Anxiety manifests affectively through pathological worry and emotional lability. Cognitively, anxiety can cause decreased concentration and frequent rumination. Somatic symptoms of anxiety include increased heart rate and autonomic activation, sleep difficulties, fatigue and restlessness, and altered immune function. Anxiety also causes neurobiological abnormalities that can be seen in brain scans and functional differences that manifest in EEG changes. For the purposes of this review, chronic illness and anxiety are viewed as synergistic.

**Neurofeedback, neurotherapy and EEG biofeedback** are used synonymously to indicate a technique where electrodes, numbering two to 19, are placed on the scalp to monitor EEG brain activity. When input falls into acceptable and healthy parameters, the system generates pleasant stimuli to reinforce the change. This operant conditioning is continued over numerous sessions to reinforce transient changes in brain function using the patient’s own input as a guide.

Alpha EEG wave patterns are categorized based on frequency in Hertz (Hz): delta (<4 Hz) usually seen during sleep, theta (4–8 Hz) associated with thoughtfulness, alpha (8–12 Hz) associated with relaxation, beta (13–30 Hz) associated with alertness and gamma (30–100 Hz) associated with...
The goal of neurofeedback is to alter the wave amplitudes of certain bandwidths. In individuals experiencing anxiety, the alpha range is targeted to optimize a state of relaxed wakefulness, often through alpha/theta training. Numerous neurofeedback set ups can be used. Targeted symptom-responsive approaches allow the selection of a brainwave target based on symptomatology. Quantitative EEG approaches work by selecting a structured frequency target to address EEG abnormalities. Nonlinear dynamical and low-energy neurofeedback system (LENS) approaches are often used to optimize non-clinical brain function. Finally, fMRI-based neurofeedback approaches provide feedback from deeper brain structures, such as the insula and amygdala in emotional regulation.

A search of the JBI Database of Systematic Reviews and Implementation Reports, Cochrane Database of Systematic Reviews, Medline and CINAHL found no existing or proposed systematic reviews of the treatment of anxiety with neurofeedback in a chronic illness population.

Inclusion criteria
Types of participants
The current quantitative review will consider studies that include any adult aged 18 years or older living with a chronic illness and reporting any level of anxiety. The focus of this systematic review will be on the treatment of anxiety in chronic medical conditions, including fibromyalgia, multiple sclerosis, cancer and stroke. Although psychological conditions may be chronic, their treatment with neurofeedback has been well documented in the literature. Past systematic reviews have explored neurofeedback, focusing on ADHD, PTSD and depression, therefore, these conditions will be excluded from the current review.

Types of intervention(s)
The review will examine studies that evaluate any type of neurofeedback, including but not limited to the NeurOptimal system (New York, NY, US), the LENS and mixed alpha/theta and alpha/beta protocols. There will be no exclusion based on the frequency, intensity or duration of the therapy. The experimental interventions will include any method/protocol of neurofeedback. The control group can consist of no treatment, any alternative treatment or another method/protocol of neurofeedback.

Outcomes
The current review will consider studies that include the primary outcome of anxiety and/or secondary outcomes of distress, stress and coping. Any validated tool measuring these outcomes will be considered.

Given our interest in the comorbidity between chronic illness and anxiety, some of the scales measure anxiety within illness-specific parameters. Examples of this include the Fibromyalgia Impact Questionnaire, PTSD Symptom Scale – Self-Report, the Symptom Checklist-90-Revised and the Millon Clinical Multiaxial Inventory III. Although not ideal, some papers have self-rated Likert type anxiety scales through which participants can rank their anxiety on a scale of one to 10.

Types of studies
The current review will consider both experimental and epidemiological study designs, including RCTs, non-RCTs, quasi-experimental, before and after studies, prospective and retrospective cohort studies, case control studies and analytical cross sectional studies. This review only considered studies that were published in English.

The review will also consider descriptive epidemiological study designs, including case series, individual case reports and descriptive cross sectional studies.

Search strategy
The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of MEDLINE, CINAHL and PsycINFO will be undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Third, the reference list of all identified reports and articles will be searched for additional studies. To be thorough, no date limit will be placed on the search strategy.

The databases and sources to be searched include the following: MEDLINE, CINAHL, PsycINFO,
Epistemonikos, Scopus, Embase, Web of Science, Trip Database and Cochrane Central Register of Controlled Trials.

The search for unpublished studies will include: Dissertation Abstracts, Google Scholar, Clinical-Trials.gov and grey literature databases/gateways (e.g. OpenGrey, Grey Literature Report, Grey Source).

Initial keywords to be used will be: “EEG biofeedback,” neurofeedback, neurotherapy, “chronic illness,” “mood disorders,” anxiety, stress, distress, “generalized anxiety disorder,” coping.

**Assessment of methodological quality**

Quantitative papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAS- tARI). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

**Data extraction**

Quantitative data will be extracted from papers included in the review independently by two reviewers, using the standardized data extraction tool from JBI-MAS tARI. The data extracted will include specific details about the interventions (e.g. duration, content and method of delivery), populations, study methods and outcomes of significance to the review question and specific objectives. For missing information or to clarify unclear data, the authors of primary studies will be contacted. Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

**Data synthesis**

Quantitative papers will, where possible, be pooled in statistical meta-analysis using JBI-MAS tARI. All results will be subject to double data entry. Effect sizes expressed as odds ratio (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard Chi-square and also explored using subgroup analyses based on the different quantitative study designs included in this review. Where statistical pooling is not possible, the findings will be presented in narrative form, including tables and figures to aid in data presentation where appropriate.

**References**