TITLE: Neurofeedback and Biofeedback for Mood and Anxiety Disorders: A Review of the Clinical Evidence and Guidelines – An Update

DATE: 26 August 2014

CONTEXT AND POLICY ISSUES

Post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), and depression are psychiatric disorders that interfere with daily-life activities and need psychological and pharmacological treatments.[1-3] These mental disorders result from brain dysregulation, such as neurological over-arousal (e.g. anxiety), neurological under-arousal (e.g. depression) or instable-arousal (e.g. PTSD), in that patients have problems in intentionally controlling neural functioning.[4] Approximately 5.7% of Canadians 18 years and older are affected by GAD, 6.8% by PTSD, and 4.8% by major depression.[1,5]

Patients with mental health disorders usually require pharmacological and/or psychological interventions such as cognitive-behavioral therapy.[5] However, patients may not have easy access to such treatments, especially for those living in rural areas, or may not respond well to them.[5-7] For example, approximately two-thirds of patients with major depressive disorder do not have adequate responses to pharmacological and/or psychological interventions.[6] Biofeedback therapies are non-pharmacological treatments that use non-invasive electrical devices with bio-monitoring system and sensors to measure, amplify and feed back information primarily from nervous system processes such as respiration, heart rate, muscle tension, skin temperature, blood flow and blood pressure, to the individual being monitored, thus promoting awareness of these processes in an individual to assist with gaining voluntary control over body and mind.[8,9] Neurofeedback is a specific form of biofeedback that monitors central nervous system activity via the measurement and regulation of brainwave activity from electrodes placed on the scalp.[10] Training with neurofeedback aims to enable the individual to modify patterns of cortical activity and normalize brain activity.[4,9,11,12] In general, biofeedback and neurofeedback are designed to increase patients' coping skills for their current situations, and usually multiple sessions of treatment are required.[13]

This report was undertaken to update a previous summary of the evidence on the clinical effectiveness and safety of neurofeedback and biofeedback which was completed in 2012.[14] In

that report, findings from preliminary analyses raised the possibility that biofeedback and neurofeedback may have a potential for the treatment of PTSD, GAD or depression.

RESEARCH QUESTIONS

1. What is the clinical evidence for the benefits and harms of neurofeedback provided by a health professional for mood and anxiety disorders?

2. What is the clinical evidence for the benefits and harms of biofeedback provided by a health professional for mood and anxiety disorders?

3. What is the clinical evidence regarding home use of biofeedback equipment for mood and anxiety disorders?

4. What are the evidence-based guidelines regarding the use of neurofeedback or biofeedback for the treatment of mood and anxiety disorders?

KEY FINDINGS

Limited evidence since the publication of a previous report suggested that biofeedback (such as heart rate variability biofeedback) may decrease the symptoms of post-traumatic stress disorder or depression. No studies were identified on neurofeedback therapy in the target population. No studies were found on generalized anxiety disorder. No relevant evidence-based guidelines were identified.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, Medline via OVID, PsycINFO via OVID, The Cochrane Library (2014, Issue 6), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was limited to English language documents published between Jan 1, 2012 and Jul 28, 2014.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD) or depression
Intervention	Neurofeedback or biofeedback provided by a health professional or patient self-treatment at home
Comparator	Other treatment for PTSD, GAD or depression (e.g. cognitive behavior therapy, exposure therapy, eye moment desensitization reprocessing)

	No treatment
Outcomes	Symptom reduction (e.g. reduced stress, anxiety) Safety
Study Designs	Health technology assessment, systematic review, meta-analyses, randomized controlled trials (RCTs), non-RCTs, evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if the effectiveness of one single session of biofeedback or neurofeedback therapy was assessed, if there was a lack of comparator group, if they were published prior to January 2012, if they were duplicate publications of the same study, or if they were referenced in at least one of the selected systematic reviews. Studies reporting only changes in physiological outcome variables were excluded.

Critical Appraisal of Individual Studies

The quality of the included systematic reviews was assessed using AMSTAR.[15] The quality of the included clinical trials was assessed using Downs and Black checklist.[16] Numerical scores were not calculated. Instead, the strengths and limitations of individual studies are summarized and presented.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 175 citations. No additional studies were identified by searching the grey literature. After screening of abstracts, 19 potentially relevant studies were selected for full-text review. Among these 19 studies, one was excluded because the full text article could not be retrieved,[17] and 15 did not meet the selection criteria.

Three studies[18-20] were included in the review: one on PTSD[18] and two on depression.[19,20] One was a systematic review,[18] one was a randomized controlled trial (RCT),[19] and one was a non-RCT (cohort study), in which patients from two long-term care facilities were assigned to either biofeedback therapy or usual care.[20] The RCT and non-RCT were published dissertations; however they were not peer-reviewed. No relevant evidence-based guidelines were identified. The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

Characteristics of the included systematic review and RCTs are summarized below and details are provided in Appendix 2.

<u>Systematic reviews</u>

Wahbeh and colleagues conducted a systematic review to evaluate the evidence of complementary and alternative medicine including biofeedback for PTSD (Appendix 2).[18] Multiple databases were searched from 1950 to March 2013. There was no restriction on

language. Controlled and uncontrolled studies enrolling at least five patients and reporting at least one measure assessing PTSD symptoms were eligible for this review. The quality of the included studies was assessed using the Cochrane Risk of Bias Tool (for RCTs only) and the Quality Assessment Tool (for RCTs and non-RCTs). The level of scientific evidence was graded for each treatment modality for PTSD to reflect the strength of available scientific data for or against the use of each therapy: A = strong scientific evidence; B = good scientific evidence; C = unclear or conflicting scientific evidence; D = fair negative scientific evidence; F = strong negative evidence; L = lack of evidence. These grades were determined based on the numbers, the design, the quality, as well as the results of the included studies. For instance, level A was assigned when there was statistically significant evidence of benefit from more than two properly conducted RCTs, or from one properly conducted RCT plus one properly conducted meta-analysis, or from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit in addition to supporting evidence in basic science, animal studies or theory. Level F was assigned when statistically significant negative evidence from more than one properly conducted RCT. A total of 33 studies (17 RCTs, 4 non-RCTs, 9 pre-post designs and 3 crossover interventions) were included in this review. Among them, four enrolled patients treated with biofeedback (heart rate variability [HRV] biofeedback, pain-focused cognitive behavioral biofeedback, and respiratory sinus arrhythmia biofeedback therapy). The number of patients involved in the four studies on biofeedback ranged from 13 to 50. The number of received treatment sessions ranged from six to 28 and the duration of each session ranged from 20 minutes to 90 minutes. The primary outcomes of included studies were changes in symptoms of PTSD, based on PTSD Checklist-Military Version (PCL-M), Clinician-Administered PTSD Scale (CAPS), Posttraumatic Diagnostic Scale (PDS), and Posttraumatic Stress-Total scale of the Detailed Assessment of Posttraumatic States (PTS-T).

Randomized and non-randomized controlled trials

The RCT by Breach was conducted in the US,[19] and the non-RCT by Bunthumporn was conducted in Thailand.[20] Patients in both studies received 10 sessions of HRV biofeedback therapy, for 20 minutes per session in the Breach study and 30 minutes per session in the Bunthumporn study. Detailed characteristics of the included studies are summarized in Appendix 2.

Population

Patients in these two studies were diagnosed with depression.[19,20] All patients were adults aged 18 years old and older. The Thai study recruited senior patients (mean age of 76 years old) living in assisted facilities.

Interventions and comparators

HRV biofeedback was investigated in both studies. It was compared to a sham control in the RCT, and compared to usual treatment such as morning exercise and social/recreational activities in the non-RCT.[19,20]

Outcomes

The primary outcomes of included studies were changes in symptoms of depression based on Hamilton Depression Inventory (HAM-D), Beck Depression Inventory (BDI), Thai Geriatric Depression Scale (TGDS), and Depressive Cognition Scale (DCS).

Summary of Critical Appraisal

A summary of the critical appraisal conducted for selected studies can be found in Appendix 3.

In the systematic review by Wahbeh et al., a comprehensive literature search was performed with no restrictions on language or study design. Two reviewers performed study selection independently. One single reviewer extracted data and a second reviewer verified the accuracy and completeness of data extraction. The methodological quality of the selected studies was examined by two reviewers independently. Level of evidence was graded to assist in drawing conclusions. A meta-analysis was not conducted due to the high degree of heterogeneity of the included studies. The quality of this systematic review was compromised by insufficient data reporting, limited number of included biofeedback studies, and small number of enrolled patients in the included individual studies. The minimal clinically important differences (MCIDs) were not reported; therefore the clinical relevance of the evidence was undetermined. The authors indicated that publication bias was present when studies with positive results were more frequently published compared to those with negative results, although the method used to detect publication bias was not described.

The RCT by Breach enrolled 11 patients. The author indicated that a restricted randomization procedure was adopted for treatment allocation without providing more details. The study investigators who entered and edited the data were not blinded to patient's condition; however, it is unclear whether the outcome assessors of this study were blinded to patient's condition and treatment assignment. Evidence from this study was inconclusive, potentially due to the small sample size, though a power calculation to determine the number of participants required to detect significant differences between treatment groups was not reported. Patients in this RCT may not reflect the broader population who would be typically seen in practice. The author stated that 45% of the participants in this study had severe or very severe depression, while 9% of the participants had mild depression.

The non-RCT was conducted in Thailand. In order to determine the sufficient number of patients needed in the study, three different statistical tests were performed and eventually the highest sample size calculated from one of the tests was used for the study. A convenient sample instead of consecutive sample was gathered in this study, therefore the study results may not be generalized to the entire patient population. The employed assessment scales had to be translated from English to Thai for the patients to complete. Therefore, the accuracy of the translation was uncertain. Generalizability of the study results to a Canadian population was unclear.

Summary of Findings

Main study findings and authors' conclusions can be found in Appendix 4.

1. What is the clinical evidence for the benefits and harms of neurofeedback provided by a health professional for post-traumatic stress disorder, generalized anxiety disorder, or depression?

No studies on the clinical evidence regarding the benefits and harms of neurofeedback for post-traumatic stress disorder, generalized anxiety disorder, or depression were identified.

2. What is the clinical evidence for the benefits and harms of biofeedback provided by a health professional for post-traumatic stress disorder, generalized anxiety disorder, or depression?

In the Wahbeh review, four studies examined the clinical effectiveness of biofeedback in patients with PTSD.[18] In three out of four studies, the results showed that the symptoms of PTSD were significantly reduced after biofeedback therapy (20 to 30 minutes per session, six to 28 sessions in total) or usual treatment (not specified in the review), but the difference between two treatment groups was not statistically significant. The fourth study had a pre-post study design and recruited 13 refugees with PTSD, chronic pain and experience of torture or war. Results from this study indicated no significant changes in PTSD symptoms were observed over time

A non-RCT examined the effect of HRV biofeedback on 100 senior Thai patients with depression.[20] Participants were treated with five weeks of HRV biofeedback therapy (twice a week and 30 minutes per session) or with usual treatment. Depressive symptoms were assessed using the Thai version of assessment scales specific for depression. At the end of the treatment, statistically significant reductions in depressive cognition and depressive symptoms scores were observed in the biofeedback therapy group, but not in the control group. Due to the absence of MCIDs, assessment of the clinical importance of the between-group differences could not be done. The authors indicated that the study suggested a beneficial effect of biofeedback on depressive symptoms in senior patients.

3. What is the clinical evidence regarding home use of biofeedback equipment for post-traumatic stress disorder, generalized anxiety disorder, or depression?

An RCT examined the effect of HRV biofeedback on 11 adults with depression.[19] Participants were treated with 10 weekly HRV biofeedback sessions or with sham biofeedback control. In the biofeedback group, patients firstly received 4 weeks training on HRV biofeedback, and the treatment continued at home thereafter. Reductions in depressive symptoms were observed in both treatment and control groups after 10-week HRV biofeedback therapy or sham therapy. The between-group differences for the outcome measures did not reach statistical significance evaluated by HAM-D and BDI-II.

4. What are the evidence-based guidelines regarding the use of neurofeedback or biofeedback for the treatment of post-traumatic stress disorder, generalized anxiety disorder, or depression?

The literature search did not identify any evidence-based guideline regarding the use of neurofeedback or biofeedback for the treatment of post-traumatic stress disorder, generalized anxiety disorder, or depression.

Limitations

In this update, the literature search did not identify clinical evidence regarding the effectiveness and safety of neurofeedback therapy. There were no studies identified for patients with generalized anxiety disorder. Due to the limited number of biofeedback studies identified (n = 3) and the poor quality of the clinical trials, it is difficult to draw definitive conclusions regarding the clinical effectiveness and safety of biofeedback on PTSD and depression. The two clinical trials were short-term studies with preliminary analyses on small number of participants, which limit

the generalizability of the findings to the target populations. Even though HRV biofeedback was evaluated in both studies, various HRV biofeedback techniques were employed (different equipment and treatment frequency/duration) and the study results were inconsistent in terms of statistical significance of the between-group difference.[19,20] In addition, the non-RCT used the Thai version clinical scales in outcome assessment. No relevant evidence-based guidelines were found.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Similar to the original CADTH review, evidence regarding the use of biofeedback for treatment of post-traumatic stress disorder or depression came mostly from pilot and exploratory studies with preliminary analyses ranging in size from 11 to 100 participants. HRV biofeedback was commonly evaluated in the newer clinical trials, and it was found to be associated with improvement in PTSD symptoms and depression symptoms: in one systematic review of patients with posttraumatic stress disorder, HRV biofeedback therapy was not shown to be better than unspecified usual treatment, but in an observational study of depressive patients, it had statistically significant benefit over usual care (such as morning exercise and social activities). One RCT implied the possible clinical benefits of HRV biofeedback therapy over a sham control in patients with depression; however a statistically significant between-group difference was not detected in this small patient group. Furthermore, the clinical relevance of an observed between-group difference was uncertain due to the lack of minimal clinically important difference for the employed clinical scales. No evidence on the use of biofeedback or neurofeedback in patients with generalized anxiety disorder was identified. Compelling evidence from larger scale randomized controlled trials with alternative therapies as the comparator is still needed to confirm the potential of biofeedback and neurofeedback, and to develop guidelines regarding the use of these non-pharmacological and non-invasive modalities for the treatment of mood and anxiety disorders.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

REFERENCES

1. The human face of mental health and mental illness in Canada [Internet]. Ottawa: Government of Canada; 2006. [cited 2014 Aug 18]. Available from: http://www.phac-aspc.gc.ca/publicat/human-humain06/pdf/human_face_e.pdf

2. Psychological treatments and pharmacological treatments for adults with post-traumatic stress disorder (PTSD) [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2011. (Evidence-based practice center systematic review protocol). [cited 2014 Aug 18]. Available from: http://effectivehealthcare.ahrq.gov/ehc/products/347/901/PTSD-Adults_Protocol_20111220.pdf

3. Meditation programs for stress and well-being [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2012. (Evidence-based practice center systematic review protocol). [cited 2014 Aug 18]. Available from: http://effectivehealthcare.ahrq.gov/ehc/products/375/981/MeditationProgramsForStressAndWellbeing_Protocol_20120222.pdf

4. Russell-Chapin LA, Chapin TJ. Neurofeedback: a third option when counseling and medication are not sufficient [Internet].Counseling Outfitters; 2011. [cited 2014 Aug 18]. Available from: http://counselingoutfitters.com/vistas/vistas11/Article_48.pdf

5. Clinical practice guidelines. Management of anxiety disorders. Can J Psychiatry [Internet]. 2006 Jul [cited 2014 Aug 18];51(8 Suppl 2):9S-91S. Available from: http://ww1.cpa-apc.org:8080/Publications/CJP/supplements/july2006/anxiety_guidelines_2006.pdf

6. Young KD, Zotev V, Phillips R, Misaki M, Yuan H, Drevets WC, et al. Real-time FMRI neurofeedback training of amygdala activity in patients with major depressive disorder. PLoS ONE [Internet]. 2014 [cited 2014 Jul 31];9(2):e88785. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3921228

7. Schoenberg PL, David AS. Biofeedback for psychiatric disorders: a systematic review. Appl Psychophysiol Biofeed. 2014 Jun;39(2):109-35.

8. Harvey R, Peper E. Future directions in applied psychophysiology: skills not pills. In: Edmonds WA, editor. Case studies in applied psychophysiology: Neurofeedback and biofeedback treatments for advances in human performance. 2012. p. 275-92.

9. Mann DTY, Janelle CM. Psychophysiology: Equipment in research and practice. In: Edmonds WA, editor. Case studies in applied psychophysiology: Neurofeedback and biofeedback treatments for advances in human performance. 2012. p. 257-74.

10. Weiskopf N. Real-time fMRI and its application to neurofeedback. Neuroimage. 2012 Aug 15;62(2):682-92.

11. Zucker T. The effects of respiratory sinus arrhythmia biofeedback on posttraumatic stress disorder symptoms . San Diego: Alliant International University; 2008.

12. Hammond DC, Bodenhammer-Davis G, Gluck G, Stokes D, Hunt Harper S, Trudeau D, et al. Standards of practice for neurofeedback and neurotherapy: a position paper of the International Society for Neurofeedback & Research. Journal of Neurotherapy:

Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience [Internet]. 2011 [cited 2014 Aug 18];15(1):54-64. Available from: http://www.tandfonline.com/doi/pdf/10.1080/10874208.2010.545760

13. Jones DE, Cusack K, Forneris CA, Wilkins TM, Sonis J, Middleton JC, et al. Psychological and pharmacological treatments for adults with posttraumatic stress disorder (PTSD) [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2013. (Comparative effectiveness review; no. 92). Report No.: 13-EHC011-EF. [cited 2014 Aug 18]. Available from: http://effectivehealthcare.ahrq.gov/ehc/products/347/1435/PTSD-adult-treatment-report-130403.pdf

14. Neurofeedback and biofeedback for post-traumatic stress disorder, generalized anxiety disorder, and depression: a review of the clinical evidence and guidelines [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2012. (Rapid response report: summary with critical appraisal). [cited 2014 Aug 18]. Available from: http://www.cadth.ca/media/pdf/htis/june-2012/RC0361%20Neurofeedback%20-%20final.pdf

15. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol [Internet]. 2007 [cited 2014 Aug 18];7:10. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1810543/pdf/1471-2288-7-10.pdf

16. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health [Internet]. 1998 Jun [cited 2014 Aug 18];52(6):377-84. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf

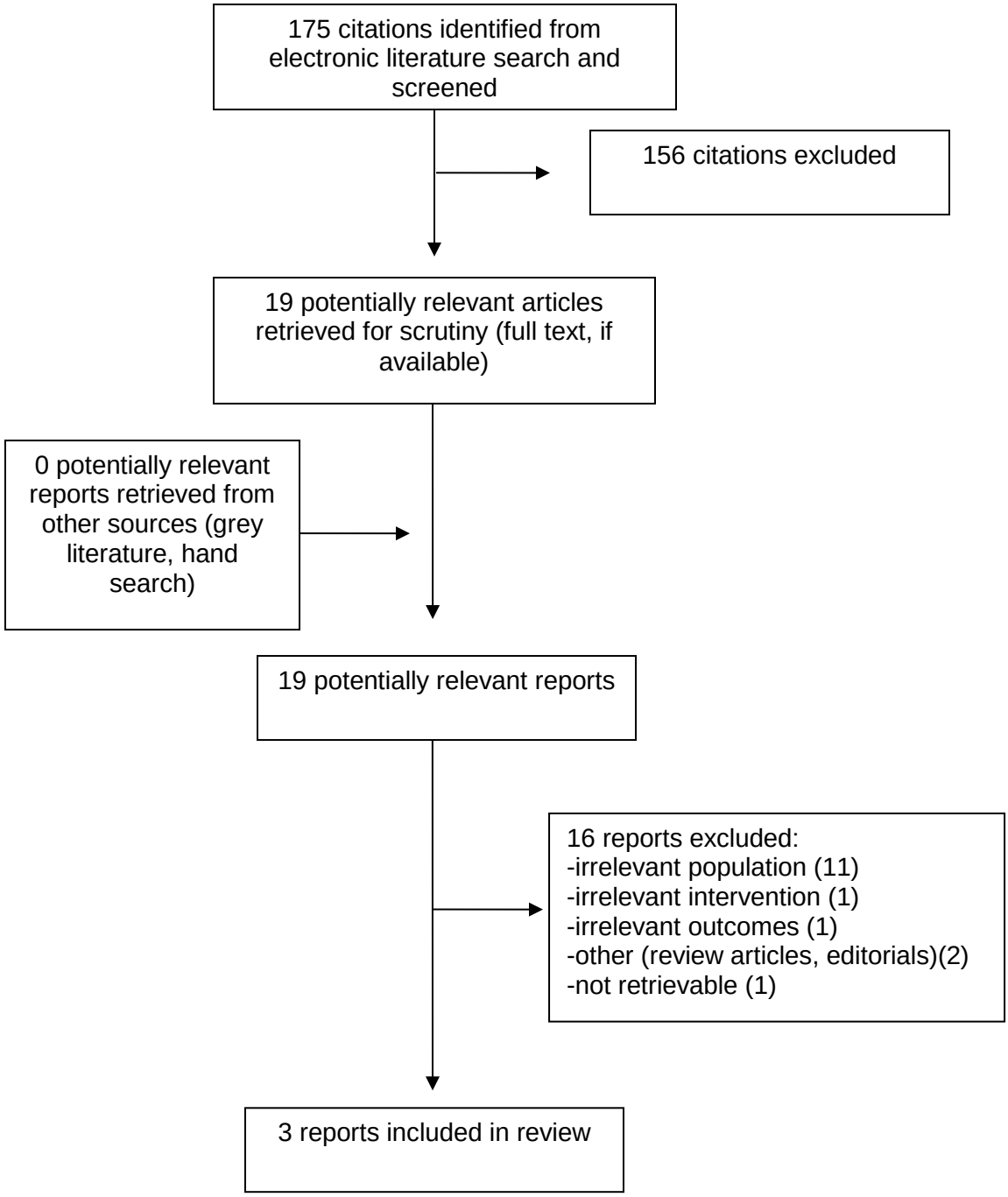
17. Sarraf S. Management of depression. Indian Journal of Community Psychology. 2012;8(2):354-61.

18. Wahbeh H, Senders A, Neuendorf R, Cayton J. Complementary and Alternative Medicine for Posttraumatic Stress Disorder Symptoms: A Systematic Review. J Evid Based Complementary Altern Med. 2014 Mar 27;19(3):161-75.

19. Breach NB. Heart rate variability biofeedback in the treatment of major depression [dissertation]. Piscataway (NJ): Graduate School of Applied and Professional Psychology, Rutgers, The State University of New Jersey; 2013.

20. Bunthumporn N. Effects of biofeedback training on negative affect, depressive cognitions, resourceful behaviors, and depressive symptoms in Thai elders [dissertation]. Cleveland (OH): Case Western Reserve University; 2013.

APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Studies

Characteristics of Included Trials					
First Author, Publication Year, Country	**Study Design and Trial characteristics**	**Patient Characteristics**	**Intervention**	**Comparator(s)**	**Main Outcomes Measured**
Wahbeh 2014, US[18]	SR, included any study design with sample size >= 5 patients. Literature search: 1950 to March 2013. 33 studies were included; 4 of them were BF studies.	Patients with PTSD, number of patients ranged from 13 to 50 in BF studies.	Complementary and alternative medicine (including BF therapy: HRV BF, pain-focused CBT, and RSA BF)	Usual treatment	Change in symptoms of PTSD
Breach 2013, US[19]	RCT; 10 weekly BF sessions Study duration: 10 weeks	11 adult patients with MDD, 6 in the BF group and 5 in the control group.	10 weekly 20-minute HRV BF (4 weekly training and home practice thereafter)	A sham respiratory control protocol (4 weekly training and home practice thereafter)	HAMD BDI-II
Bunthumporn 2013, Thailand[20]	Non-RCT; 10 bi-weekly BF sessions Study duration: 5 weeks	100 patients with depression in 2 senior assisted living facilities in Thailand were assigned to BF (n=50) or control group (n=50)	10 30-minute sessions HRV BF, twice a week	Usual care including morning exercise, playing games and social or recreation activities.	DCS TGDS

BDI = Beck Depression Inventory; BF = biofeedback; DCS = Depressive Cognition Scale; ESC = Emotional Symptom Checklist; HAM-D = Hamilton Rating Scale for Depression; HRV = heart rate variability; MDD = major depressive disorder; PTSD = Post-Traumatic Stress Disorder; RCT = randomized controlled trial; SR = systematic review; TGDS = Thai Geriatric Depression Scale

APPENDIX 3: Summary of Critical Appraisal of Included Studies

Summary of Critical Appraisal of Included Studies		
First Author, Publication Year	**Strengths**	**Limitations**
Systematic Review		
Wahbeh 2014[18]	• Objectives and inclusion/exclusion criteria were stated. • Multiple databases were searched without restriction in language and study design. • P values were provided for comparisons between biofeedback therapy and control. • % of dropout was reported for each included studies. • Publication bias was assessed. • Conflict of interest was declared.	• Results were insufficiently reported (actual change in symptom scores and MCIDs of the employed clinical scales were not reported, therefore clinical relevance of the study results couldn't be determined) • List of excluded studies was not provided.
Randomized Controlled Trial		
Breach 2013[19]	• Hypothesis explicit, objectives were stated. • The two groups did not differ significantly in age, gender, ethnicity, and psychological measures. • All patients completed the study.	• Small sample size; no power calculation • A restricted randomization procedure controlling for gender, current psychological treatment/medication and depression status was adopted. • Conflict of interest was not declared.
Non-Randomized Controlled Trial		
Bunthumporn 2013[20]	• Hypothesis explicit • Main outcomes, interventions, patient characteristics, and main findings explicit • The two groups did not differ significantly at baseline in demographic or medical characteristics • Sample size calculation was performed and possible missing data or attrition were considered. • No missing data • Source of funding was indicated.	• Non-randomized study design using a convenience sample • Several employed scales needed to be translated from English to Thai, therefore the accuracy of translation was unclear. • The minimal clinically important difference was not provided for the employed scales • The study was conducted in Thailand; therefore the generalizability of the study results was uncertain.

Appendix 4: Main Study Findings and Authors' Conclusions

Main Study Findings and Authors' Conclusions		
First Author	**Main Study Findings**	**Authors' Conclusions**
Systematic Review		
Wahbeh 2014[18]	**Four BF studies:** 3 out of 4 studies reported significant decrease in PTSD symptoms over time for both BF therapy (20-30 minutes/session, 6-28 treatment sessions) and the control group; however, no significant between-group differences were identified. 1 uncontrolled study reported no improvement in PTSD symptoms over time (90 minutes/session, 10 sessions) Level of evidence: Grade C (unclear or conflicting scientific evidence)	Evidence was unclear or conflicting for BF. (pg.161) The controlled trials had high Quality Assessment Tool scores, with either mixed results or no difference from the control group. The other studies had small sample sizes and methodological concerns. (pg.170)
Randomized Controlled Trial		
Breach 2013[19]	**Change in HAM-D** (mean, SD) HRV BF group Pre: 18.17 (4.79), Post at 10th week: 8.00 (3.58) Control group Pre: 19.60 (6.99), Post at 10th week: 9.00 (4.90) P = 0.27 **Change in BDI-II score** (mean, SD) HRV BF group Pre: 31.33 (10.11), Post at 10th week: 19.67 (8.55) Control group Pre: 31.00 (12.86), Post at 10th week: 10.20 (5.72) p = 0.10 No participants reported significant side effects	"No significant differences in depression symptom improvement between groups, although significant main effects for time were observed for both groups ($p < 0.05$). Results did however support the utility, feasibility, and tolerability of the credible sham respiratory control protocol." (pg.5)
Non-Randomized Controlled Trial		
Bunthumporn 2013[20]	**Change in depressive cognitions measured by DCS** (mean, SD) HRV BF group Pre: 14.32 (7.65), Post at 5th week: 10.42 (6.34) Control group Pre: 14.58 (8.77), Post at 5th week: 15.40 (9.42) p = 0.003 **Change in depressive symptoms measured by TGDS** (mean, SD) HRV BF group Pre: 18.28 (3.54), Post at 5th week: 9.38 (5.01) Control group Pre: 17.52 (3.93), Post at 5th week: 17.56 (5.15) p = 0.00	"the findings suggest beneficial effects of biofeedback training in reducing negative affect, depressive cognitions, and depressive symptoms and enhancing resourceful behaviors of Thai elders in assisted living facilities. This program may be a useful adjunct to existing programs in facilities." (pg.16)

BF = biofeedback; BDI-II = Beck Depression Inventory II; DCS = Depressive Cognition Scale; HRV = Heart rate variability biofeedback; HAM-D = Hamilton Depression Inventory; HRV = heart rate variability; PTSD = Posttraumatic stress disorder; SD = standard deviation; TGDS = Thai Geriatric Depression Scale