02.01.65 Neurofeedback

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Related Policies:

- 02.01.70 Biofeedback as a Treatment of Anorectal Disorders
- 02.01.71 Biofeedback as a Treatment of Chronic Pain
- 02.01.72 Biofeedback as a Treatment of Headache
- 02.01.73 Biofeedback as a Treatment of Urinary Incontinence
- 02.01.74 Biofeedback for Miscellaneous Indications

Summary

Description

Neurofeedback describes techniques for providing feedback about neuronal activity, as measured by electroencephalogram biofeedback, functional magnetic resonance imaging, or near-infrared spectroscopy, to teach patients to self-regulate brain activity. Neurofeedback may use several techniques in an attempt to normalize unusual patterns of brain function in patients with various psychiatric and central nervous system disorders.

Summary of Evidence

For individuals who have attention-deficit/hyperactivity disorder (ADHD) who receive neurofeedback, the evidence includes randomized controlled trials (RCTs) and meta-analyses. Relevant outcomes are symptoms, functional outcomes, and quality of life. Several meta-analyses and at least 5 additional moderately sized RCTs (n range, 144 to 202 patients) have compared neurofeedback with methylphenidate, biofeedback, cognitive behavioral therapy, cognitive training, physical activity, or sham neurofeedback. Collectively, these studies found either small or no benefit of neurofeedback. A meta-analysis also found no effect of neurofeedback on objective measures of attention and inhibition. Studies that used active controls have suggested that at least part of the effect of neurofeedback may be due to attention skills training, relaxation training, and/or other nonspecific effects. Also, the beneficial effects of neurofeedback are more likely to be reported by evaluators unblinded to treatment (parents) than by evaluators blinded to treatment (teachers), suggesting bias in the nonblinded evaluations. Additional research with blinded evaluation of outcomes is needed to demonstrate the effect of neurofeedback on ADHD. However, the completion dates for some registered trials of neurofeedback in ADHD have passed without publication of results, suggesting the potential for publication bias. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have disorders other than ADHD (e.g., chronic insomnia, epilepsy, substance abuse, pediatric brain tumors, and post-traumatic stress disorder) who receive neurofeedback, the evidence includes case reports, case series, comparative cohorts, small RCTs, and systematic reviews. Relevant outcomes are symptoms, functional outcomes, and quality of life. For these other disorders, including psychiatric, neurologic, and pain syndromes, the evidence is poor, and several questions concerning clinical efficacy remain unanswered. Larger RCTs that include either a sham or active control are needed to evaluate the effect of neurofeedback for these conditions. However, the completion dates for some registered trials of neurofeedback in disorders other than ADHD have passed without publication of results, suggesting the potential for publication bias. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information

Not applicable.

OBJECTIVE

The objective of this evidence review is to determine whether neurofeedback improves the net health outcome in individuals with attention-deficit/hyperactivity disorder or other psychiatric, central nervous system, or pain disorders.

PRIOR APPROVAL

Not applicable.

POLICY

Neurofeedback is considered **investigational**. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

POLICY GUIDELINES

Home neurofeedback devices include but are not limited to:

- Brain Master
- EEG biofeedback device: GSR/Tamp2xTM and RESPeRate
- EEG glasses
- EEG headwear
- NeurOptimal neurofeedback
- QEEG (Quantitative EEG)

Coding

See the Codes table for details.

BACKGROUND

Disorders of the Central Nervous System

Various disorders involve abnormal brain activity, including autism spectrum disorder, insomnia and sleep disorders, learning disabilities, Tourette syndrome, traumatic brain injury, seizure disorders, premenstrual dysphoric disorder, menopausal hot flashes, depression, stress management, panic and anxiety disorders, posttraumatic stress disorder, substance abuse disorders, eating disorders, migraine headaches, stroke, Parkinson disease, fibromyalgia, tinnitus, and attention-deficit/hyperactivity disorder (ADHD).

Treatment

Neurofeedback is being investigated for the treatment of a variety of disorders. Neurofeedback may be conceptualized as a type of biofeedback that has traditionally used the electroencephalogram (EEG) as a source of feedback data. Neurofeedback differs from established forms of biofeedback in that the information fed back to the patient (via EEG tracings, functional magnetic resonance imaging, near-infrared spectroscopy) is a direct measure of global neuronal activity, or brain state, compared with feedback of the centrally regulated physiologic processes, such as tension of specific muscle groups or skin temperature. The patient may be trained to increase or decrease the prevalence, amplitude, or frequency of specified EEG waveforms (e.g., alpha, beta, theta waves), depending on the changes in brain function associated with the particular disorder. It has been proposed that training of slow cortical potentials (SCPs) can regulate cortical excitability and that using the EEG as a measure of central nervous system functioning can help train patients to modify or control their abnormal brain activity. Upregulating or downregulating neural activity with real-time feedback of functional magnetic resonance imaging signals is also being explored.

Two EEG-training protocols (training of SCPs, theta/beta training) are typically used in children with ADHD. For training of SCPs, surface-negative and surface-positive SCPs are generated over the sensorimotor cortex. Negative SCPs reflect increased excitation and occur during states of behavioral or cognitive preparation, while positive SCPs are thought to indicate a reduction of cortical excitation of the underlying neural networks and appear during behavioral inhibition. In theta/beta training, the goal is to decrease activity in the EEG theta band (4 to 8 Hz) and increase activity in the EEG beta band (13 to 20 Hz), corresponding to an alert and focused but relaxed state. Alpha-theta neurofeedback is typically used in studies on substance abuse. Neurofeedback protocols for depression focus on alpha interhemispheric asymmetry and theta/beta ratio within the left prefrontal cortex. Neurofeedback for epilepsy has focused on sensorimotor rhythm up-training (increasing 12 to 15 Hz activity at motor strip) or altering SCPs. It has been proposed that learned alterations in EEG patterns in epilepsy are a result of operant conditioning and are not conscious or voluntary. A variety of protocols have been described for the treatment of migraine headaches.

Regulatory Status

A number of EEG feedback systems (EEG hardware and computer software programs) have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. For example, the BrainMaster™ 2E (BrainMaster Technologies) is "…indicated for relaxation training using alpha EEG biofeedback. In the protocol for relaxation, BrainMaster™ provides a visual and/or auditory signal that corresponds to the patient's increase in alpha activity as an indicator of achieving a state of relaxation." Although devices used during neurofeedback may be subject to FDA regulation, the process of neurofeedback itself is a procedure, and, therefore, not subject to FDA approval.

FDA product codes: HCC, GWQ.

RATIONALE

This evidence review was created in July 2001 with searches of the PubMed database. The most recent literature update was performed through December 4, 2024.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Attention Deficit-Hyperactivity Disorder

Clinical Context and Therapy Purpose

The purpose of neurofeedback is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as behavioral therapy and pharmacologic therapy, in individuals with attention-deficit/hyperactivity disorder (ADHD).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with ADHD.

Attention deficit hyperactivity disorder manifests in children as symptoms of hyperactivity, impulsivity, and/or inattention, and affects cognitive, academic, behavioral, emotional, and social function. It is one of the most common neurobehavioral disorders of childhood.

Interventions

The therapy being considered is neurofeedback.

Neurofeedback describes techniques for providing feedback about neuronal activity, as measured by electroencephalogram (EEG) biofeedback, functional magnetic resonance imaging, or near-infrared spectroscopy, to teach patients to self-regulate brain activity. Neurofeedback may use several techniques to normalize unusual patterns of brain function in patients with various psychiatric and central nervous system disorders.

Comparators

Guidelines for treatment of ADHD in children and adolescents generally recommend parent training in behavior management, US Food and Drug Administration (FDA)-approved medications (eg, stimulants), and educational interventions. ADHD also occurs in adults, with a prevalence of approximately 3.4% to 4.4% of US adults. Guidelines for the treatment of ADHD in adults include recommendations for psychoeducation, pharmacotherapy, and cognitive behavioral therapy.[2,]

Comparators of interest include behavioral therapy and pharmacologic therapy. Treatment includes support groups, cognitive behavioral therapy, anger management, counseling, psychology, psychoeducation, family therapy, and applied behavior analysis. Medications for treatment include stimulants, cognition-enhancing medication, and antihypertensive drugs.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life (Tables 1 and 2).

Table 1. Outcomes of Interest for Individuals with ADHD

Outcomes	Details

Symptoms	Outcomes as reported by assessors (parents most-often, or teachers, usually unblinded and with a high risk of bias); Attention Deficit Hyperactivity Disorder-Rating Scale (ADHS-RS, domains of inattention, hyperactivity/impulsiveness, and combined scores); Conners scale; Fremdbeurteilungsbogen für Hyperkinetische Störungen (FBB-HKS) [Timing: greater than 1 year]

ADHD: attention-deficit/hyperactivity disorder.

Table 2. Health Outcome Measures Relevant to ADHD in Children and Adolescents

Outcome	Measure (units)	Description	Clinically Meaningful Difference (If Known)
Attention-Deficit/Hyperactivity Disorder-Rating Scale (ADHD-RS)	Scale from 0 to 54 Higher scores indicate more symptoms 18 items are grouped into 2 subscales: hyperactivity/impulsivity and inattentiveness	Short scale that can be completed by parent, teacher, or investigator based on information provided by teacher or parent	Change between 5.2 and 7.7 points or 30% mean total score change between treatment groups[3,]
Conners Parent Rating Scale for ADHD	Scale from 0 to 144 Higher scores indicate more symptoms	Used by clinicians and researchers to assess parents' perception of children's behavior in the classroom Assesses conduct problems, learning problems, psychometric problems, impulsivity and hyperactivity, and anxiety	Not defined[3,]
Conners 3rd Edition-Parent (Conners 3-P)	Scale with 9 subscales Higher scores indicate more symptoms	Used by parents to assess symptoms of ADHD and common comorbid problems	Not defined
Fremdbeurteilungsbogen für Hyperkinetische Störungen (FBB-HKS)	Scale with 20 items Higher scores indicate more symptoms	Items can be rated by parents or teacher	Not defined

ADHD: attention-deficit/hyperactivity disorder.

In studies of neurofeedback, the duration of intervention was at least 1 month and ranged from 1 to 12 months. Follow-up studies of RCTs that reported longer-term outcomes have reported results at 6 months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought
- Within each category of study design, studies with larger sample sizes and longer duration were preferred;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews with Meta-Analysis

Numerous systematic reviews with meta-analyses have compared neurofeedback versus other treatments for ADHD in children, adolescents, and adults (Tables 3 to 5). Comparators included methylphenidate, biofeedback, cognitive behavioral therapy, cognitive training, or physical activity. The results of these analyses generally demonstrated either small to moderate or no benefit of neurofeedback versus other treatments for ADHD symptoms.

Table 3. Trials Included Systematic Reviews of Neurofeedback versus Other Treatments for ADHD

Trials	**Systematic Reviews**				
	Cortese et al (2016)	Van Doren (2019)	Yan et al (2019)	Lambez et al (2020)	Riesco-Matias (2021)
Linden et al (1996)	●				
Li et al (2001)		●			
Heinrich et al (2004)	●	●		●	
Klingberg et al (2005)				●	
Bauregard et al (2006)	●			●	●
Zhang et al (2006)			●		
Chen et al (2007)			●		
Drechsler et al (2007)				●	
Kong et al (2007)			●		
Chen et al (2009)			●		
Gevensleben et al (2009)	●				●
Holtmann et al (2009)	●				
Ji et al (2009)			●		
Zuo et al (2009)			●		
Gevensleben et al (2010)		●			

Virta et al (2010)				●	
Bakhshayesh et al (2011)	●			●	●
Chen et al (2011)			●		
Prins et al (2011)				●	
Steiner et al (2011)	●			●	
Chang et al (2012)				●	
Fan et al (2012)			●		
Zhou et al (2012)			●		
Arnold et al (2013)	●	●			
Li et al (2013)			●		●
Meisel et al (2013)		●	●		
Miranda et al (2013)				●	
Ogrim et al (2013)					●
VanDongen et al (2013)	●				●
Chang et al (2014)				●	
Christiansen et al (2014)	●	●			
Du et al (2014)			●		
Maurizio et al (2014)	●				●
Meisel et al (2014)					●
Steiner et al (2014)	●	●			●
Vollebregt et al (2014)	●				
Bink et al (2015)	●	●			●
Choi et al (2015)				●	
Gapin et al (2015)					
Menezes et al (2015)				●	
Miranda et al (2015)					
Moreno et al (2015)			●		
Salomone et al (2015)				●	
Pan et al (2016)					
Yang et al (2016)			●		
Duric et al (2017)		●	●		●
Gelade et al (2017)		●	●	●	

Strehl et al (2017)					●
Tang et al (2017)			●		
Gelade et al (2018)					●
Minder et al (2018)					●
Sudnawa et al (2018)			●		●
Moreno-Garcia et al (2019)					●

ADHD: attention-deficit/hyperactivity disorder.

Table 4. Characteristics of Systematic Reviews and Meta-Analyses of Neurofeedback for ADHD

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Cortese et al (2016)	To August 30, 2015	13	Children and adolescents with ADHD (any subtype) or hyperkinetic disorder	520 (14 to 94)	13 RCTs of neurofeedback vs. other care	Follow-up: 2 to 12 months
Van Doren et al (2019)[,]	To November 29, 2017	10	Children and adolescents with a primary diagnosis of ADHD	256 (11 to 41)	10 RCTs of neurofeedback vs. other care	Follow-up: 2 to 12 months
Yan et al (2019)[,]	To August 22, 2018	18	Children, adolescents, and adults with ADHD	1535 (13 to 90)	18 RCTs of neurofeedback vs. methylphenidate	Follow-up: 1 to 6 months
Lambez et al (2020)	To December 2017	18	Children, adolescents, and adults with ADHD	618 (20 to 76)	18 RCTs of neurofeedback vs. biofeedback, cognitive behavioral therapy, cognitive training, or physical activity	Follow-up: 25 days to 8 months
Riesco-Matias et al (2021)[,]	To July 18, 2018	17	Children and adolescents with a primary diagnosis of ADHD	NR	16 RCTs of neurofeedback vs. active and nonactive controls	Follow up: NR

ADHD: attention-deficit/hyperactivity disorder; NR: not reported; RCT: randomized controlled trial.

Table 5. Results of Systematic Reviews and Meta-Analyses of Neurofeedback for ADHD

Study	ADHD Total Symptoms	ADHD Inattention Symptoms	ADHD Hyperactivity/Impulsiveness Symptoms	Inhibition
Cortese et al (2016)				
Total N	13 trials (n=NR)	11 trials (n=NR)	10 trials (n=NR)	NR
Pooled Effect (95% CI)	Parent-reported: SMD, 0.35 (0.11 to 0.59) Teacher-reported:	Parent-reported: SMD, 0.36 (0.09 to 0.63) Teacher-reported:	Parent-reported: SMD, 0.26 (0.08 to 0.43) Teacher-reported: SMD, 0.17 (-0.05 to 0.39)	NR

	SMD, 0.15 (-0.08 to 0.38)	SMD, 0.06 (-0.24 to 0.36)		
I^2 (p)	41% (.06)	43% (.07)	0% (.8)	NR
Van Doren et al (2019)				
Total N	NR	11 trials (n=NR)	11 trials (n=NR)	NR
Pooled Effect (95% CI)	NR	SMD, 0.31 (-0.01 to 0.63)	0.32 (0.15 to 0.49)	NR
I^2 (p)	NR	70% (.06)	0% (.0003)	NR
Yan et al (2019)[6,]				
Total N	4 trials (n=228)	4 trials (n=228)	4 trials (n=228)	NR
Pooled Effect (95% CI)	SMD, −0.578 (−1.063 to –0.092)	SMD, -0.667 (-1.245 to -0.109)	SMD, -0.474 (-0.860 to 0.088)	NR
I^2 (p)	59% (.062)	70% (.019)	38% (.156)	NR
Lambez et al (2020)				
Total N	NR	NR	NR	6 trials (n=203)
Pooled Effect (95% CI)	NR	NR	NR	SMD, 0.61 (-3.77 to 4.82)
I^2 (p)	NR	NR	NR	0% (<.05)
Riesco-Matias et al (2021)				
Total N	NR	Unblinded evaluation: 11 trials (n=674) Blinded evaluation: 9 trials (n=573)	Unblinded evaluation:11 trials (n=674) Blinded evaluation: 9 trials (n=573)	NR
Pooled Effect (95% CI)	NR	Unblinded evaluation: SMD, -0.33 (-0.56 to -0.10) Blinded evaluation: SMD, -0.25 (-0.45 to -0.04)	Unblinded evaluation: SMD, -0.17 (-0.33 to -0.02) Blinded evaluation: SMD, -0.16 (-0.32 to 0.01)	NR
I^2 (p)	NR	Unblinded: 49% (.005) Blinded: 30% (.02)	Unblinded: 0% (.03) Blinded: 0% (.06)	NR

ADHD: attention-deficit/hyperactivity disorder; CI: confidence interval; NR: not reported; SMD: standardized mean difference.

Randomized Controlled Trials not Included in the Meta-Analyses

Several RCTs not included in the above systematic reviews are described below (Tables 6 to 9). Hasslinger et al (2022) published a multi-arm, pragmatic, RCT [NCT01841151] in 202 children and adolescents with ADHD (see Table 6 for trial characteristics) that evaluated the efficacy of 2 neurofeedback treatments (slow cortical potential [SCP] and Live Z-score) compared to working-memory training (active comparator) and treatment as usual (passive comparator).[12,] The prespecified primary

outcome measure[14,] was the self-, teacher- and parent-reported assessment of ADHD symptoms post-treatment and at 6 months using the Conners 3rd Edition scale. As only the inattention and hyperactivity/impulsivity Conners subscales were reported by Hasslinger et al, its results are not reported in Table 7. Neither neurofeedback treatment was superior to working-memory training for these outcome measures. Significant differences between SCP and treatment as usual were observed post-treatment for teacher- and parent-rated inattention, with no difference for other outcome measures at either timepoint. A statistically significant difference in Live Z-score over treatment as usual was only observed at the 6-month endpoint for teacher-rated inattention and hyperactivity/impulsivity. No other differences between Live Z-score and treatment as usual were observed. Secondary outcomes in this study included measures of teacher- and parent-rated executive function and self-assessed health-related quality of life using the Behavior Rating of Executive Functions (BRIEF) and KIDSCREEN-27 scales, respectively. There were no consistent differences between neurofeedback interventions and control interventions for these outcomes except for teacher-assessed executive function at 6 months follow-up, which found both neurofeedback interventions superior to working-memory training and treatment as usual. Limitations of this RCT are presented in Tables 8 and 9.

Table 6. Characteristics of RCTs of Neurofeedback in ADHD

Study	Countries	Sites	Dates	Participants	Interventions
Lim et al (2019)	Singapore	1	January 2012 to June 2016	Children age 6 to 12 years diagnosed with ADHD	BCI-based neurofeedback attention training vs. untreated waitlist control for 8 weeks followed by BCI-based neurofeedback attention training for 20 weeks
Aggensteiner et al (2019)	Germany	NR (multicenter)	September 2009 to January 2013	Children age 7 to 9 years diagnosed with ADHD	SCP-based neurofeedback vs. EMG-based biofeedback
Arnold et al (2020)	US	2	NR	Children age 7 to 10 years diagnosed with moderate/severe ADHD and theta/beta ratio ≥4.5	Treatment consisted of downtraining theta power and uptraining beta power for 38 active neurofeedback treatments vs. 38 control treatments
Hasslinger et al (2022)	Sweden	1	2013 to 2019	Children age 9 to 17 years diagnosed with ADHD	4 arms: SCP neurofeedback, Live Z-score neurofeedback; working-memory training, and treatment as usual
Purper-Ouakil et al (2022)	France, Spain, Germany, Belgium, Switzerland	9	August 2016 to September 2017	Children age 7 to 13 years diagnosed with ADHD	At-home personalized neurofeedback training vs. methylphenidate

ADHD: attention-deficit/hyperactivity disorder; BCI: brain-computer interface; EMG: electromyography; NR: not reported; RCT: randomized controlled trial; SCP: slow cortical potential; US: United States.

Table 7. Results of RCTs of Neurofeedback on ADHD

Study	ADHD-RS	FBB-HKS	Conners 3-P

Lim et al (2019)			
N	172		
BCI-based neurofeedback	8 weeks of intervention: 3.5 ± 3.87 20 weeks of intervention: 3.3 ± 5.55 4 weeks post-intervention: 4.7 ± 5.94		
Waitlist control	8 weeks of intervention: 1.9 ± 4.42 20 weeks of intervention: 1.4 ± 3.94 4 weeks post-intervention: 2.0 ± 4.26		
Difference [Neurofeedback - Control] (95% CI)	8 weeks of intervention: 1.6 points (0.3 to 0.29) 20 weeks of intervention: 2.4 points (1.6 to 3.2) 4 weeks post-intervention: 3.3 points (2.5 to 4.2)		
Aggensteiner et al (2019)			
N	144	144	
SCP-based neurofeedback	1.28	1.33	
EMG-based biofeedback	1.30	1.38	
Difference [Neurofeedback - Control] (95% CI)	NR	-0.04 (-0.27 to 0.14)	
Arnold et al (2020)			
N			144
Neurofeedback			Change from baseline to end of treatment: -0.561 Change from baseline to 13-month follow-up: -0.612
Control (sham neurofeedback)			Change from baseline to end of treatment: -0.557 Change from baseline to 13-month follow-up: -0.524
Between-group difference for change from baseline to end of treatment (95% CI)			0.004 (-0.19 to 0.20)
Between-group difference for change from baseline to 13-month follow-up (95% CI)			0.087 (-0.32 to 0.79)
Purper-Ouakil et al (2022)			
N	149 (per protocol)		
Neurofeedback (day 90 - day 0)	-9.21		

Methylphenidate (day 90 - day 0)	-17.3		
Mean between-group difference at day 90 (90% CI)	8.09 (5.62 to 10.56)		
Noninferiority	Noninferiority of neurofeedback to methylphenidate not demonstrated		

ADHD-RS: attention deficit-hyperactivity disorder-rating scale; BCI: brain-computer interface; CI: confidence interval; Conners 3-P: Conners 3rd Edition-Parent; EMG: electromyography**;** FBB-HKS: Fremdbeurteilungsbogen für Hyperkinetische Störungen; NR: not reported; RCT: randomized controlled trial; SCP: slow cortical potential.

Table 8. Study Relevance Limitations of RTCs of Neurofeedback in ADHD

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Lim et al (2019)	4. Included patients from a single site in Singapore				1. Follow-up occurred only 4 weeks after intervention
Aggensteiner et al (2019)	4. Included patients from Germany				
Arnold et al (2020)					
Hasslinger et al (2022)	4. Included patients from a single site in Sweden		1. Treatment as usual was not specifically defined	2. Focused on symptom measures as outcomes, which may not correlate with functioning	
Purper-Ouakil et al (2022)			2. Absence of sham neurofeedback or another nonactive group 1. Methylphenidate "optimally titrated" but doses not specifically defined		1. Absence of follow-up

ADHD: attention-deficit/hyperactivity disorder; RCT: randomized controlled trial.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b]Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c]Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d]Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e]Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 9. Study Design and Conduct Limitations of RCTs of Neurofeedback in ADHD

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]

Lim et al (2019)	3.	1. Patients, parents, and investigators were unblinded; outcome assessors and teachers were blinded				
Aggensteiner et al (2019)	3.	1. Patients were unblinded; blinding of parents and teachers not reported			1.	
Arnold et al (2020)						
Hasslinger et al (2022)		1. Parents were unblinded		1. Missing data, especially for teacher ratings		
Purper-Ouakil et al (2022)		1. Parents and clinicians were unblinded			1. Sample size calculation done but power not specifically stated	1. Secondary analyses were exploratory only

ADHD: attention-deficit/hyperactivity disorder; RCT: randomized controlled trial.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b]Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c]Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d]Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e]Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f]Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Attention Deficit – Hyperactivity Disorder

Several meta-analyses and 5 additional moderately sized RCTs (N range, 144 to 202 patients) have compared neurofeedback with methylphenidate, biofeedback, cognitive behavioral therapy, cognitive training, or physical activity These studies found either small to moderate or no benefit of neurofeedback, and sustained long-term benefit (e.g., at 6 to 13 months) has not been consistently demonstrated. Studies using active controls have suggested that at least part of the effect of neurofeedback might be due to attention skills training, biofeedback, relaxation training, and/or other nonspecific effects. Two of the RCTs indicated that any beneficial effects were more likely to be reported by evaluators unblinded to treatment (parents), than by evaluators blinded (teachers) to treatment, which would suggest bias in the nonblinded evaluations. Moreover, a meta-analysis found no effect of neurofeedback on objective measures of attention and inhibition. Additional research with blinded evaluation of outcomes is needed to demonstrate the effect of neurofeedback on ADHD.

Disorders other than Attention Deficit – Hyperactivity Disorder

Clinical Context and Therapy Purpose

The purpose of neurofeedback is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as behavioral therapy and pharmacologic therapy, in individuals with disorders other than attention deficit – hyperactively disorder (ADHD).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with disorders other than ADHD, including psychiatric, central nervous system, or pain disorders.

Interventions

The therapy being considered is neurofeedback.

Comparators

Comparators of interest include behavioral therapy and pharmacologic therapy.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life (Tables 10 and 11).

Table 10. Outcomes of Interest for Individuals with Disorders other than ADHD

Outcomes	Details
Reduction of symptoms as observed by parents and patients	Attention Switching Task; Impact of Pediatric Epilepsy Scale; PTSD symptoms [Timing: 6 weeks]

ADHD: attention-deficit/hyperactivity disorder; PTSD: post-traumatic stress disorder.

Table 11. Health Outcome Measures Relevant to Disorders other than ADHD

Outcome	Measure (units)	Description	Clinically Meaningful Difference (If Known)
Attention Switching Task	msec Longer duration indicates more symptoms	Computerized task measuring ability to adjust behavior in accordance with changing task goals	Not defined

Impact of Pediatric Epilepsy Scale	Scale from 0 to 33 Higher scores indicate more symptoms	Questionnaire administered to parent or guardian measuring domains of academic improvement, social adaptation, and self-esteem	Not defined
PTSD symptoms	Various questionnaires Higher scores indicate more symptoms	Various questionnaires administered to patients measuring the frequency and intensity of PTSD symptoms	Not defined
Sleep efficiency	Percentage Lower values indicate more symptoms	Measure of percentage of total time in bed spent asleep	Not defined
Sleep fragmentation	Occurrences Higher values indicate more symptoms	Measure of the number of awakening episodes by polysomnography or patient diary	Not defined
Total sleep time	Minutes Lower values indicate more symptoms	Measure of time spent asleep among total recording time	Not defined

ADHD: attention-deficit/hyperactivity disorder; PTSD: post-traumatic stress disorder.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Within each category of study design, studies with larger sample size and longer duration were preferred;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Chronic Insomnia

Systematic Review with Meta-Analysis

A systematic review by Melo et al (2019) included 7 RCTs of biofeedback techniques, including neurofeedback, in the treatment of chronic insomnia. The authors identified conflicting results in comparisons of neurofeedback with other cognitive behavioral therapy techniques, placebo, and no

treatment. A majority of outcomes demonstrated no significant differences between comparison groups. A majority of studies had a high risk of bias related to blinding of participants and personnel and incomplete outcome data. Characteristics and results from the meta-analysis are summarized in Tables 12 and 13, respectively.

Table 12. Characteristics of a Systematic Review and Meta-Analysis of Neurofeedback for Chronic Insomnia

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Melo et al (2019)	To 2019	7	Adults with chronic insomnia	224 (18 to 48)	7 RCTs of biofeedback techniques	10 days to 36 months

RCT: randomized controlled trial.

Table 13. Results of Systematic Review and Meta-Analysis of Neurofeedback for Chronic Insomnia

Study	Total Sleep Time	Sleep Fragmentation	Sleep Efficiency
Melo et al (2019)			
Total N	2 trials (n=NR)	2 trials (n=NR)	2 trials (n=NR)
Pooled Effect (95% CI)	No significant difference between biofeedback and placebo (effect estimate NR)	Mean difference in number of awakenings, -4.5 (-8.33 to -0.67)	No significant difference between biofeedback and placebo as measured by either polysomnography or sleep diaries (effect estimates NR)
I^2 (p)	NR	NR	NR

CI: confidence interval; NR: not reported.

Epilepsy

Randomized Controlled Trials

An RCT by Morales-Quezada et al (2019) randomized children with focal epilepsy to sensorimotor rhythm neurofeedback, SCP neurofeedback, or sham neurofeedback for 25 sessions over 5 weeks. At the end of the intervention period, only the sensorimotor rhythm neurofeedback group demonstrated significant improvement in the activity switching task and all groups demonstrated significant improvements in quality of life. Characteristics and results from the RCT are summarized in Tables 14 and 15, respectively. Tables 16 and 17 summarize relevant limitations.

Table 14. Characteristics of a Recent RCT of Neurofeedback in Epilepsy

Study	Countries	Sites	Dates	Participants	Interventions
Morales-Quezada et al (2019)	Mexico	1	NR	Children and adolescents with focal epilepsy responsive to antiepileptic pharmacotherapy and cognitive difficulties in school	SMR neurofeedback, SCP neurofeedback, or sham neurofeedback over 5 weeks

NR: not reported; RCT: randomized controlled trial; SCP: slow cortical potential, SMR: sensorimotor rhythm.

Table 15. Results of a RCT of Neurofeedback in Epilepsy

Study	Attention Switching Task	Impact of Pediatric Epilepsy Scale
Morales-Quezada et al (2019)		
N	44	44
SMR neurofeedback	Significant improvement from baseline to postintervention (-757 msec; p=.015) and follow-up (-644; p=.04)	1.5-point change from baseline (p=.002)
SCP neurofeedback	Not significant (effect estimate, NR)	1.9-point change from baseline (p=.001)
Sham neurofeedback	Not significant (effect estimate, NR)	1.3-point change from baseline (p=.006)
Difference [Neurofeedback - Control] (95% CI)	NR	NR

CI: confidence interval; NR: not reported; RCT: randomized controlled trial; SCP: slow cortical potential; SMR: sensorimotor rhythm.

Table 16. Study Relevance Limitations of a RCT of Neurofeedback in Epilepsy

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Morales-Quezada et al (2019)	4. Included patients from a single site in Mexico				

RCT: randomized controlled trial.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b]Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c]Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d]Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e]Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 17. Study Design and Conduct Limitations of a RCT of Neurofeedback

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Morales-Quezada et al (2019)	3.				1.	

RCT: randomized controlled trial.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b]Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c]Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d]Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e]Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f]Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Substance Abuse

Systematic Reviews with Meta-Analyses

A systematic review by Sokhadze et al (2018) of neurofeedback as a treatment for substance abuse disorders described difficulties in assessing the efficacy of neurofeedback and other substance abuse treatments. Study shortcomings included a lack of clearly established outcome measures, differing effects of the various drugs, the presence of comorbid conditions, the absence of a criterion standard treatment, and use as an add-on to other behavioral treatment regimens. Reviewers concluded that alpha-theta training, when combined with an inpatient rehabilitation program for alcohol dependency or stimulant abuse, would be classified as level 3 or "probably efficacious." This level is based on beneficial effects shown in multiple observational studies, clinical studies, wait-list control studies, or within-subject or between-subject replication studies. Reviewers also noted that few large-scale studies of neurofeedback in addictive disorders have been reported and that the evidence for alpha-theta training has not been shown to be superior to sham treatment.

Randomized Controlled Trials

An RCT by Gabrielsen et al (2022) randomized adults with substance abuse disorders enrolled in outpatient abuse programs to either 20 sessions (30 minutes each) of infralow (ILF) neurofeedback plus standard of car alone, over a mean of 5 months. At the end of the intervention period, both groups demonstrated a significant improvement in quality of life scores from baseline, but there was no difference between groups. Restlessness was reportedly significantly lower in the ILF-neurofeedback group compared to standard of care post treatment, but this was a secondary endpoint, meaning the study was not powered to find differences only in this endpoint. Individuals were not stratified based on drugs of abuse and there was a lack of sham, neurofeedback, limiting results. Characteristics and results from the RCT are summarized in tables 18 and 19, respectively. Tables 20 and 21 summarize relevant limitations.

Table 18. Characteristics of a Recent RCT of Neurofeedback in Substance Abuse Disorders

Study	Countries	Sites	Dates	Participants	Interventions
Gabrielsen et al (2022)	Norway	1	September 2017 to March 2020	Adults enrolled in outpatient substance abuse program within the past month and not on opioid maintenance (65% male).	20 sessions (30 mins each) of ILF-neurofeedback plus standard care or standard care alone.

ILF: infralow; RCT: randomized controlled trial.

Table 19. Results of a RCT of Neurofeedback in Substance Abuse Disorders

Study	QoL post-treatment[a]	Restlessness[b]
Gabrielsen et al (2022)[21,]		
N	93	93
ILF neurofeedback + standard care	0.54±0.17	4.1±2.5
Standard care alone	0.58±0.16	5.9±2.8
Mean difference (95% CI); p-value	-0.04 (-0.13 to 0.04); p=.28	-1.8 (-3.1 to -0.5); p=.006

[a]Measured using the QoL-5 scale, ranging from 0.1 to 0.9, where 0.9 is the highest (best) score
[b]Measured using 10 cm visual analog scales
CI: confidence interval; ILF: infralow; QoL: quality of life; RCT: randomized controlled trial.

Table 20. Study Relevance Limitations of a RCT of Neurofeedback in Substance Abuse Disorders

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Gabrielsen et al (2022)	4. Included patients from a single site in Norway; 5. broad inclusion criteria		2. No sham neurofeedback control		

RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 21. Study Design and Conduct Limitations of a RCT of Neurofeedback in Substance Abuse Disorders

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Gabrielsen et al (2022)		1. No sham control to allow for participant blinding.			4. Study likely underpowered based on power calculation	

RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Pediatric Brain Tumor Survivors

De Ruiter et al (2016) reported on a multicenter, triple-blind RCT of neurofeedback in 80 pediatric brain tumor survivors who had cognitive impairments. The specific neurofeedback module was based on individual EEG, and participants, parents, trainers, and researchers handling the data were blinded to assignment to the active or sham neurofeedback module. At the end of the training and 6-month follow-up, there were no significant differences between the neurofeedback and sham feedback groups on the primary outcome measures for cognitive performance, which included attention, processing speed, memory, executive functioning, visuomotor integration, and intelligence.

Post-Traumatic Stress Disorder

Systematic Reviews with Meta-Analyses

A meta-analysis by Steingrimsson et al (2020) evaluated 4 RCTs of adults with post-traumatic stress disorder (PTSD) treated with neurofeedback. Compared with sham neurofeedback, no treatment or other treatment, neurofeedback was associated with significant improvement in PTSD symptoms. Other primary outcomes were only reported in 1 trial each, and the authors concluded there was uncertainty regarding the ability of neurofeedback to improve PTSD symptoms, self-rated suicidality, executive cognitive functioning, and medication use. All studies were at moderate to high risk for bias and were assessed as having some indirectness and imprecision.

Hong and Park (2022) conducted a meta-analysis of 7 RCTs of adults with PTSD treated with neurofeedback. Three studies used functional magnetic resonance imaging (fMRI) based neurofeedback and 4 studies used EEG-based neurofeedback. The overall effect of all studies pooled together demonstrated a significant improvement in PTSD symptoms with neurofeedback compared to sham neurofeedback, no treatment, of other treatment. When analyzed by type of neurofeedback, the significant improvement in PTSD symptoms remained with EEG-based neurofeedback, but not with fMRI. Five studies overall assessed anxiety and depression with various validated scales. Overall, there was no significant impact on anxiety and depression with neurofeedback compared to control group. Two studies demonstrated a high risk of performance or detection bias, while all other studies demonstrated overall low risk of bias. Characteristics and results of the meta-analyses are summarized in Tables 22 through 24.

Voigt et al (2024) evaluated 17 RCTs of adults and children/adolescents with PTSD treated with neurofeedback. Neurofeedback demonstrated clinically significant effect sizes based on various PTSD symptom outcome measures. Characteristics and results of the meta-analyses was summarized in Tables 22 through 24.

Table 22. Comparison of Studies Included in Systematic Review and Meta-Analyses of Neurofeedback for PTSD

Study	Steingrimsson et al (2020)	Hong and Park (2022)	Voight et al (2024)
Peniston et al (1991)	●		●
Kelson et al (2013)	●		●
Yeganeh et al (2015)			●
van der Kolk et al (2016)	●	●	●
Onton et al (2016)			●
Noohi et al (2017)	●	●	●
Antele et al (2018)			●
Misaki et al (2018)		●	●
Zotev et al (2018)		●	●
Bell et al (2019)			●
Rogel et al (2020)			●
Nicholson et al (2020)			●
Du Bois et al (2021)		●	
Leem et al (2021)		●	●
Misaki et al (2021)		●	●
Schurrmans et al (2021)			●
Fruchtman-Steinbok et al (2021)			●
Winkeler et al (2022)			●
Shaw et al (2023)			●
Nicholson et al (2023)			●
Zhao et al (2023)			●
Fine et al (2023)			●

PTSD: post-traumatic stress disorder.

Table 23. Characteristics of Systematic Reviews and Meta-Analyses of Neurofeedback for PTSD

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Steingrimsson et al (2020)	To 2019	4	Adults with PTSD	123 (12 to 52)	4 RCTs of EEG-based neurofeedback for PTSD vs. sham neurofeedback, other treatment, or no treatment	Follow-up: 4 weeks to 30 months
Hong and Park (2022)	To 2021	7	Adults with PTSD	194 (19 to 52)	3 RCTs of fMRI-based neurofeedback and 4 RCTs of EEG-based neurofeedback for PTSD vs. sham neurofeedback, other treatment, or no treatment	Range, 3 to 25 sessions between 6 and 40 mins each
Voight et al (2024)	To 2023	17	Adults and children/adolescents with PTSD	628 (10 to 77)	3 RCTS compared NF with yoked feedback, 4 RCTs compared NF with waitlist (the waitlist group	Treatment duration

					received the same NF after the trial was completed), 5 RCTs compared NF with the standard of care/treatment, 2 RCTs compared NF with no treatment, 1 RCT compared NF with a form of biofeedback, 1 RCT compared NF with a form of relaxation, and 1 RCT compared NF with sham neurofeedback	range: 3 to 20 weeks

EEG: electroencephalography; fMRI: functional magnetic resonance imaging; PTSD: post-traumatic stress disorder; RCT: randomized controlled trial.

Table 24. Results of Systematic Reviews and Meta-Analyses of Neurofeedback for PTSD

Study	Self-Harm	PTSD Symptoms
Steingrimsson et al (2020)		
Total N	1 trial (n=NR)	4 trials (n=123)
Pooled Effect (95% CI)	1.4-point improvement with neurofeedback (p=.002)	SMD, 2.3 (-4.37 to -0.24)
I^2 (p)	89% (<.0001)	NR
Hong and Park (2022)		
Overall effect	**Anxiety and Depression**	
Total N	5 trials (n=123)	7 trials (n=194)
Pooled Effect (95% CI)	difference, -0.562 (-1.230 to 0.106)	difference, -0.789 (-1.004 to -0.395)
I^2 (p)	68.221% (.013)	67.188% (.006)
fMRI-based neurofeedback only	NR	
Total N		3 trials (n=74)
Pooled Effect (95% CI)		difference, -0.368 (-0.851 to 0.115)
I^2 (p)		0.0 (.925)
EEG-based neurofeedback trials only	NR	
Total N		4 trials (n=120)
Pooled Effect (95% CI)		difference, -1.132 (-2.061 to -0.203)
I^2 (p)		NR
Voigt et al (2024)		
BDI pretest-posttest		
Total N		3 trials (n=95)
Pooled Effect (95% CI; p value)		MD: 8.30 (95% CI, 3.09 to 13.52; p =.002)
I^2 (p)		0%
BDI pretest-follow-up		

Total N		2 trials (n=NR)
Pooled Effect (95% CI; p value)		MD: 8.75 (95% CI: 3.53 to 13.97; p <.00001)
I^2 *(p)*		0%
CAPS-5 pretest-posttest		
Total N		7 trials (n=221)
Pooled Effect (95% CI; p value)		MD: 7.01 (95% CI: 1.36 to 12.66; p =.02)
I^2 *(p)*		86%
CAPS-5 pretest-follow-up		
Total N		3 trials (n= 103)
Pooled Effect (95% CI; p value)		MD: 10 (95% CI: 1.29 to 21.29; p =.006)
I^2 *(p)*		77%
PCL-5 pretest-posttest		
Total N		7 trials (n=166)
Pooled Effect (95% CI; p value)		MD: 7.14 (95% CI: 3.08 to 11.2; p =.0006)
I^2 *(p)*		0%
PCL-5 pretest-follow-up		
Total N		4 trials (n=117)
Pooled Effect (95% CI; p value)		MD: 14.95 (95% CI: 7.95 to 21.96; p <.0001)
I^2 *(p)*		0%

Bdi: Beck Depression Inventory; CAPS-5: Clinician Administered PTSD scale; CI: confidence interval; EEG: electroencephalography; fMRI: functional magnetic resonance imaging; MD: mean difference; NR: not reported; PCL-5: PSTD Checklist for DSM-5; PTSD: post-traumatic stress disorder; SMD: standardized mean difference.

Other Disorders

Literature searches and a systematic review by Schoenberg et al (2014) assessing biofeedback for psychiatric and neurologic disorders have identified small studies (case reports, case series, comparative cohorts, small RCTs) of neurofeedback for the following conditions:

- Anxiety
- Asperger syndrome
- Autism spectrum disorder
- Cigarette cravings
- Chronic pain
- Cognitive impairment
- Depression
- Depression, pain, or fatigue in patients with multiple sclerosis
- Depression in alcohol addiction
- Dissociative identity disorder

- Fall risk
- Fibromyalgia
- Insomnia
- Headache
- Lower back pain
- Multiple sclerosis
- Overweight and obesity
- Obsessive-compulsive disorder
- Parkinson disease
- Schizophrenia
- Stroke
- Tinnitus
- Tourette syndrome

Section Summary: Disorders other than Attention Deficit-Hyperactivity Disorder

The evidence for neurofeedback in individuals with disorders other than ADHD includes case reports, case series, comparative cohorts, small RCTs, and systematic reviews of these studies. For these disorders, the evidence is poor, and a number of questions regarding clinical efficacy remain unanswered. Larger RCTs that include either a sham or active control are needed to evaluate the effect of neurofeedback for these conditions.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Pediatrics

In 2019, the American Academy of Pediatrics (AAP) published a guideline update to the 2011 guideline for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. The guideline states that electroencephalogram (EEG) biofeedback is one of several nonmedication treatments that have either too little evidence to support their recommendation for use or have little or no benefit.

The AAP Section on Integrative Medicine (2016), in a clinical report on mind-body therapies in children and youth, stated that research suggests benefits of peripheral forms of biofeedback, including EEG biofeedback (neurofeedback) in ADHD. The report noted no significant contraindications to the use of

biofeedback, with the only barriers potentially being financial in nature. Of note, this clinical report has expired and is under review by the authorship team.

National Institute for Health and Care Excellence

In 2013, NICE issued guidance on management and support of children on autism spectrum. The institute stated that a number of treatments were considered but are not recommended, including neurofeedback.

In 2018, NICE issued guidance on the diagnosis and management of ADHD in children, young people, and adults. Neurofeedback is not mentioned in the guidance document as a treatment option.

Society for Developmental and Behavioral Pediatrics

The Society for Development and Behavioral Pediatrics (SDBP) published a guideline in 2020 on the assessment and treatment of children and adolescents with complex ADHD. Regarding neurofeedback, the guidelines state: "Additional nonpharmacological ADHD interventions have been developed such as cognitive training (e.g., working memory training) and neurofeedback. Although these approaches have shown some improvement in laboratory-based, task-specific outcomes, none have demonstrated sufficient evidence of effectiveness in real-world domains of functioning (e.g., behavior at home and school, academic performance, peer relationships) to recommend them for use in practice with children and adolescents with ADHD."

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

REFERENCES

1. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry. Apr 2006; 163(4): 716-23. PMID 16585449
2. Kooij JJS, Bijlenga D, Salerno L, et al. Updated European Consensus Statement on diagnosis and treatment of adult ADHD. Eur Psychiatry. Feb 2019; 56: 14-34. PMID 30453134
3. Canadian Agency for Drugs and Technologies in Health. Guanfacine Hydrochloride Extended Release (Intuniv XR) Tablets: For the Treatment of Attention-Deficit/Hyperactivity Disorder. NCBI Bookshelf. Published July 2015. https://www.ncbi.nlm.nih.gov/books/NBK349436/ Accessed April 14, 2023.
4. Lambez B, Harwood-Gross A, Golumbic EZ, et al. Non-pharmacological interventions for cognitive difficulties in ADHD: A systematic review and meta-analysis. J Psychiatr Res. Jan 2020; 120: 40-55. PMID 31629998
5. Van Doren J, Arns M, Heinrich H, et al. Sustained effects of neurofeedback in ADHD: a systematic review and meta-analysis. Eur Child Adolesc Psychiatry. Mar 2019; 28(3): 293-305. PMID 29445867
6. Yan L, Wang S, Yuan Y, et al. Effects of neurofeedback versus methylphenidate for the treatment of ADHD: systematic review and meta-analysis of head-to-head trials. Evid Based Ment Health. Aug 2019; 22(3): 111-117. PMID 31221690

7. Aggensteiner PM, Brandeis D, Millenet S, et al. Slow cortical potentials neurofeedback in children with ADHD: comorbidity, self-regulation and clinical outcomes 6 months after treatment in a multicenter randomized controlled trial. Eur Child Adolesc Psychiatry. Aug 2019; 28(8): 1087-1095. PMID 30610380
8. Gevensleben H, Holl B, Albrecht B, et al. Neurofeedback training in children with ADHD: 6-month follow-up of a randomised controlled trial. Eur Child Adolesc Psychiatry. Sep 2010; 19(9): 715-24. PMID 20499120
9. Cortese S, Ferrin M, Brandeis D, et al. Neurofeedback for Attention-Deficit/Hyperactivity Disorder: Meta-Analysis of Clinical and Neuropsychological Outcomes From Randomized Controlled Trials. J Am Acad Child Adolesc Psychiatry. Jun 2016; 55(6): 444-55. PMID 27238063
10. Riesco-Matías P, Yela-Bernabé JR, Crego A, et al. What Do Meta-Analyses Have to Say About the Efficacy of Neurofeedback Applied to Children With ADHD? Review of Previous Meta-Analyses and a New Meta-Analysis. J Atten Disord. Feb 2021; 25(4): 473-485. PMID 30646779
11. Lim CG, Poh XWW, Fung SSD, et al. A randomized controlled trial of a brain-computer interface based attention training program for ADHD. PLoS One. 2019; 14(5): e0216225. PMID 31112554
12. Hasslinger J, Bölte S, Jonsson U. Slow Cortical Potential Versus Live Z-score Neurofeedback in Children and Adolescents with ADHD: A Multi-arm Pragmatic Randomized Controlled Trial with Active and Passive Comparators. Res Child Adolesc Psychopathol. Apr 2022; 50(4): 447-462. PMID 34478006
13. Purper-Ouakil D, Blasco-Fontecilla H, Ros T, et al. Personalized at-home neurofeedback compared to long-acting methylphenidate in children with ADHD: NEWROFEED, a European randomized noninferiority trial. J Child Psychol Psychiatry. Feb 2022; 63(2): 187-198. PMID 34165190
14. U.S. National Library of Medicine. Neurofeedback and working memory training for children and adolescents with ADHD (KITE). NCT01841151. Updated September 5, 2021. https://clinicaltrials.gov/ct2/show/NCT01841151?term=01841151&draw=2&rank=1 . Accessed April 14, 2023.
15. Arnold LE, Arns M, Barterian J, et al. Double-Blind Placebo-Controlled Randomized Clinical Trial of Neurofeedback for Attention-Deficit/Hyperactivity Disorder With 13-Month Follow-up. J Am Acad Child Adolesc Psychiatry. Jul 2021; 60(7): 841-855. PMID 32853703
16. Morales-Quezada L, Martinez D, El-Hagrassy MM, et al. Neurofeedback impacts cognition and quality of life in pediatric focal epilepsy: An exploratory randomized double-blinded sham-controlled trial. Epilepsy Behav. Dec 2019; 101(Pt A): 106570. PMID 31707107
17. Steingrimsson S, Bilonic G, Ekelund AC, et al. Electroencephalography-based neurofeedback as treatment for post-traumatic stress disorder: A systematic review and meta-analysis. Eur Psychiatry. Jan 31 2020; 63(1): e7. PMID 32093790
18. Shrivastava D, Jung S, Saadat M, et al. How to interpret the results of a sleep study. J Community Hosp Intern Med Perspect. 2014; 4(5): 24983. PMID 25432643
19. Melo DLM, Carvalho LBC, Prado LBF, et al. Biofeedback Therapies for Chronic Insomnia: A Systematic Review. Appl Psychophysiol Biofeedback. Dec 2019; 44(4): 259-269. PMID 31123938
20. Sokhadze TM, Cannon RL, Trudeau DL. EEG biofeedback as a treatment for substance use disorders: review, rating of efficacy, and recommendations for further research. Appl Psychophysiol Biofeedback. Mar 2008; 33(1): 1-28. PMID 18214670
21. Gabrielsen KB, Clausen T, Haugland SH, et al. Infralow neurofeedback in the treatment of substance use disorders: a randomized controlled trial. J Psychiatry Neurosci. 2022; 47(3): E222-E229. PMID 35705204
22. de Ruiter MA, Oosterlaan J, Schouten-van Meeteren AY, et al. Neurofeedback ineffective in paediatric brain tumour survivors: Results of a double-blind randomised placebo-controlled trial. Eur J Cancer. Sep 2016; 64: 62-73. PMID 27343714

23. Hong J, Park JH. Efficacy of Neuro-Feedback Training for PTSD Symptoms: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. Oct 12 2022; 19(20). PMID 36293673
24. Schoenberg PL, David AS. Biofeedback for psychiatric disorders: a systematic review. Appl Psychophysiol Biofeedback. Jun 2014; 39(2): 109-35. PMID 24806535
25. Jarusiewicz B. Efficacy of neurofeedback for children in the autism spectrum: a pilot study. J Neurother. Sep 8 2002;6(4):39-49. PMID
26. Sokhadze EM, El-Baz AS, Tasman A, et al. Neuromodulation integrating rTMS and neurofeedback for the treatment of autism spectrum disorder: an exploratory study. Appl Psychophysiol Biofeedback. Dec 2014; 39(3-4): 237-57. PMID 25267414
27. Kim DY, Yoo SS, Tegethoff M, et al. The inclusion of functional connectivity information into fMRI-based neurofeedback improves its efficacy in the reduction of cigarette cravings. J Cogn Neurosci. Aug 2015; 27(8): 1552-72. PMID 25761006
28. Pandria N, Athanasiou A, Styliadis C, et al. Does combined training of biofeedback and neurofeedback affect smoking status, behavior, and longitudinal brain plasticity?. Front Behav Neurosci. 2023; 17: 1096122. PMID 36778131
29. Hesam-Shariati N, Chang WJ, Wewege MA, et al. The analgesic effect of electroencephalographic neurofeedback for people with chronic pain: A systematic review and meta-analysis. Eur J Neurol. Mar 2022; 29(3): 921-936. PMID 34813662
30. Lavy Y, Dwolatzky T, Kaplan Z, et al. Neurofeedback Improves Memory and Peak Alpha Frequency in Individuals with Mild Cognitive Impairment. Appl Psychophysiol Biofeedback. Mar 2019; 44(1): 41-49. PMID 30284663
31. Lee YJ, Lee GW, Seo WS, et al. Neurofeedback Treatment on Depressive Symptoms and Functional Recovery in Treatment-Resistant Patients with Major Depressive Disorder: an Open-Label Pilot Study. J Korean Med Sci. Nov 04 2019; 34(42): e287. PMID 31674161
32. Linden DE, Habes I, Johnston SJ, et al. Real-time self-regulation of emotion networks in patients with depression. PLoS One. 2012; 7(6): e38115. PMID 22675513
33. Mehler DMA, Sokunbi MO, Habes I, et al. Targeting the affective brain-a randomized controlled trial of real-time fMRI neurofeedback in patients with depression. Neuropsychopharmacology. Dec 2018; 43(13): 2578-2585. PMID 29967368
34. Amatya B, Young J, Khan F. Non-pharmacological interventions for chronic pain in multiple sclerosis. Cochrane Database Syst Rev. Dec 19 2018; 12(12): CD012622. PMID 30567012
35. Shahrbanian S, Hashemi A, Hemayattalab R. The comparison of the effects of physical activity and neurofeedback training on postural stability and risk of fall in elderly women: A single-blind randomized controlled trial. Physiother Theory Pract. Feb 2021; 37(2): 271-278. PMID 31218913
36. Kayiran S, Dursun E, Dursun N, et al. Neurofeedback intervention in fibromyalgia syndrome; a randomized, controlled, rater blind clinical trial. Appl Psychophysiol Biofeedback. Dec 2010; 35(4): 293-302. PMID 20614235
37. Wu YL, Fang SC, Chen SC, et al. Effects of Neurofeedback on Fibromyalgia: A Randomized Controlled Trial. Pain Manag Nurs. Dec 2021; 22(6): 755-763. PMID 33579615
38. Cortoos A, De Valck E, Arns M, et al. An exploratory study on the effects of tele-neurofeedback and tele-biofeedback on objective and subjective sleep in patients with primary insomnia. Appl Psychophysiol Biofeedback. Jun 2010; 35(2): 125-34. PMID 19826944
39. Walker JE. QEEG-guided neurofeedback for recurrent migraine headaches. Clin EEG Neurosci. Jan 2011; 42(1): 59-61. PMID 21309444
40. Moshkani Farahani D, Tavallaie SA, Ahmadi K, 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. Aug 2014; 16(8): e17799. PMID 25389484

41. Mayaud L, Wu H, Barthélemy Q, et al. Alpha-phase synchrony EEG training for multi-resistant chronic low back pain patients: an open-label pilot study. Eur Spine J. Nov 2019; 28(11): 2487-2501. PMID 31254096
42. Kober SE, Pinter D, Enzinger C, et al. Self-regulation of brain activity and its effect on cognitive function in patients with multiple sclerosis - First insights from an interventional study using neurofeedback. Clin Neurophysiol. Nov 2019; 130(11): 2124-2131. PMID 31546180
43. Kohl SH, Veit R, Spetter MS, et al. Real-time fMRI neurofeedback training to improve eating behavior by self-regulation of the dorsolateral prefrontal cortex: A randomized controlled trial in overweight and obese subjects. Neuroimage. May 01 2019; 191: 596-609. PMID 30798010
44. Chirita-Emandi A, Puiu M. Outcomes of neurofeedback training in childhood obesity management: a pilot study. J Altern Complement Med. Nov 2014; 20(11): 831-7. PMID 25188371
45. Kopřivová J, Congedo M, Raszka M, et al. Prediction of treatment response and the effect of independent component neurofeedback in obsessive-compulsive disorder: a randomized, sham-controlled, double-blind study. Neuropsychobiology. 2013; 67(4): 210-23. PMID 23635906
46. Deng X, Wang G, Zhou L, et al. Randomized controlled trial of adjunctive EEG-biofeedback treatment of obsessive-compulsive disorder. Shanghai Arch Psychiatry. Oct 2014; 26(5): 272-9. PMID 25477720
47. Subramanian L, Hindle JV, Johnston S, et al. Real-time functional magnetic resonance imaging neurofeedback for treatment of Parkinson's disease. J Neurosci. Nov 09 2011; 31(45): 16309-17. PMID 22072682
48. Tinaz S, Kamel S, Aravala SS, et al. Neurofeedback-guided kinesthetic motor imagery training in Parkinson's disease: Randomized trial. Neuroimage Clin. 2022; 34: 102980. PMID 35247729
49. Anil K, Hall SD, Demain S, et al. A Systematic Review of Neurofeedback for the Management of Motor Symptoms in Parkinson's Disease. Brain Sci. Sep 29 2021; 11(10). PMID 34679358
50. Pazooki K, Leibetseder M, Renner W, et al. Neurofeedback Treatment of Negative Symptoms in Schizophrenia: Two Case Reports. Appl Psychophysiol Biofeedback. Mar 2019; 44(1): 31-39. PMID 30267339
51. Bauer CCC, Okano K, Ghosh SS, et al. Real-time fMRI neurofeedback reduces auditory hallucinations and modulates resting state connectivity of involved brain regions: Part 2: Default mode network -preliminary evidence. Psychiatry Res. Feb 2020; 284: 112770. PMID 32004893
52. Markiewicz R, Markiewicz-Gospodarek A, Dobrowolska B, et al. Improving Clinical, Cognitive, and Psychosocial Dysfunctions in Patients with Schizophrenia: A Neurofeedback Randomized Control Trial. Neural Plast. 2021; 2021: 4488664. PMID 34434228
53. Nan W, Dias APB, Rosa AC. Neurofeedback Training for Cognitive and Motor Function Rehabilitation in Chronic Stroke: Two Case Reports. Front Neurol. 2019; 10: 800. PMID 31396152
54. Cho HY, Kim K, Lee B, et al. The effect of neurofeedback on a brain wave and visual perception in stroke: a randomized control trial. J Phys Ther Sci. Mar 2015; 27(3): 673-6. PMID 25931705
55. Güntensperger D, Thüring C, Kleinjung T, et al. Investigating the Efficacy of an Individualized Alpha/Delta Neurofeedback Protocol in the Treatment of Chronic Tinnitus. Neural Plast. 2019; 2019: 3540898. PMID 31049052
56. Sukhodolsky DG, Walsh C, Koller WN, et al. Randomized, Sham-Controlled Trial of Real-Time Functional Magnetic Resonance Imaging Neurofeedback for Tics in Adolescents With Tourette Syndrome. Biol Psychiatry. Jun 15 2020; 87(12): 1063-1070. PMID 31668476
57. Zhuo C, Li L. The application and efficacy of combined neurofeedback therapy and imagery training in adolescents with Tourette syndrome. J Child Neurol. Jul 2014; 29(7): 965-8. PMID 23481449
58. Wolraich ML, Hagan JF, Allan C, et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. Oct 2019; 144(4). PMID 31570648

59. McClafferty H, Sibinga E, Bailey M, et al. Mind-Body Therapies in Children and Youth. Pediatrics. Sep 2016; 138(3). PMID 27550982
60. National Institute for Health and Care Excellence. Efficacy of neurofeedback for children in the autism spectrum: a pilot study: management and support [CG170]. 2013; https://www.nice.org.uk/guidance/cg170.
61. Barbaresi WJ, Campbell L, Diekroger EA, et al. Society for Developmental and Behavioral Pediatrics Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder. J Dev Behav Pediatr. 2020; 41 Suppl 2S: S35-S57. PMID 31996577
62. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Biofeedback Therapy (30.1). Centers for Medicare and Medicaid Services. https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=41&ncdver=1&bc=AAAAQAAAAAAA&
63. UpToDate Attention deficit hyperactivity disorder in adults: Psychotherapy. Mary V Solanto PhD. Topic last updated October 2023. Also available at https://www.uptodate.com
64. Voigt JD, Mosier M, Tendler A. Systematic review and meta-analysis of neurofeedback and its effect on posttraumatic stress disorder. Front Psychiatry. 2024; 15: 1323485. PMID 38577405
65. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder: diagnosis and management [NG87]. 2018; https://www.nice.org.uk/guidance/ng87/

CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	90875	Individual psychophysiological therapy incorporating biofeedback training by modality (face-to-face with the patient) with psychotherapy (e.g., insight oriented, behavior modifying or supportive psychotherapy); 30 minutes (When utilized for EEG neurofeedback)
	90876	Individuals psychophysiological therapy incorporating biofeedback training by any modality (face-to-face with the patient), with psychotherapy (e.g., insight oriented, behavior modifying or supportive psychotherapy); 45 minutes (When utilized for EEG neurofeedback)
	90901	Biofeedback training by any modality (When utilized for EEG neurofeedback)
HCPCS		

	E1399	Durable Medical Equipment, miscellaneous (May be utilized for home EEG neurofeedback devices: Brain Master, EEG biofeedback devise: GSR/Tamp2xTM and RESPeRate, EEG glasses, EEG headwear, NeurOptimal neurofeedback, NeurOptimal neurofeedback or QEEG [Quantitative EEG])
Type of Service	Medicine; Psychiatry	
Place of Service	Outpatient/Inpatient	

POLICY HISTORY

Date	Action	Action
December 2024	Annual Review	Policy Renewed
August 2024	Annual Review	Policy Renewed
August 2023	Annual Review	Policy Revised
July 2022	Annual Review	New policy created content moved from medical policy Biofeedback 02.01.04

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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