Title: Neurofeedback

Description/Background

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

DISORDERS OF THE CENTRAL NERVOUS SYSTEM

Various of 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.

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 CNS functioning can help train patients to modify or control their abnormal brain activity. Upregulating or downregulating neural activity with real-time feedback of fMRI signals is also being explored.

Two EEG training protocols, training of SCPs and theta/beta training, are typically used in children with attention deficit/hyperactivity disorder (ADHD). For training of SCPs, surface-negative SCPs 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 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 (4-8 Hz) and increase activity in the EEG beta band (13-20 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 12-15 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.

**Medical Policy Statement**

Neurofeedback training as an alternative therapy for individuals with attention deficit/hyperactivity disorder (ADHD) has been established. It may be a useful treatment option when indicated.

Neurofeedback training for other disorders, such as autism spectrum disorder, substance abuse, epilepsy, anxiety, depression and insomnia, is experimental/investigational. There is a lack of evidence in the peer reviewed published medical literature on the clinical utility and effectiveness of neurofeedback for these conditions.
Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Inclusions:
- The patient has a DSM-5 diagnosis of ADHD rendered within the last twelve months prior to initiation of neurofeedback therapy that is confirmed by a practitioner independent of the neurofeedback provider, using evidenced based tools/scales to support the diagnosis and assessment. Traditionally, a definitive diagnosis of ADHD is rendered by a mental health professional. However, an independent diagnosis may also be rendered by clinicians in other specialties, including primary care practitioners as long as their medical records fully support the diagnosis and that the diagnosis was made using a validated, standardized tool such as the Vanderbilt or the Connors or similar established tool in conjunction with a DSM-5 (or most currently published edition) based interview.
- Traditionally, patients receive between 20 – 40 sessions of neurofeedback training. The medical record should support the clinical need for additional sessions over 40; and should demonstrate ongoing benefit and progress to goals.

Exclusions:
- Neurofeedback training/therapy for all other diagnoses, including but not limited to other mental health disorders

CPT/HCPCS Level II Codes (Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)

Established codes:
90875 90876 90901

Other codes (investigational, not medically necessary, etc.):
N/A

Note: Code(s) may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

Rationale

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 patients with ADHD.

The question addressed in this evidence review is: Does neurofeedback reduce symptoms and improve functional outcomes in patients with ADHD or other psychiatric, central nervous system, or pain disorders?
The following PICOs were used to select literature to inform this review.

**Populations**
The relevant population of interest are 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**
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. Treatment is actively managed by psychologists, psychiatrists, and primary care providers in an outpatient clinical setting.

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. Treatment is actively managed by psychologists, psychiatrists, and primary care providers in an outpatient clinical setting.

**Outcomes**
The general outcomes of interest are symptoms, functional outcomes and quality of life.

**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.
- Studies with duplicative or overlapping populations were excluded.
Review of Evidence

Systematic Reviews with Meta-Analysis
Miccoulau-Franchi et al (2014) reported on a systematic review of neurofeedback in children with ADHD which included five studies with a total of 263 patients. The active treatment was theta/beta ratio training or slow cortical potential training. Control treatments included cognitive remediation, sham neurofeedback, or electromyography (EMG) biofeedback. Meta-analysis found a significant benefit from parent (probably not blinded) assessment on the overall ADHD score (standardized mean difference [SMD] = -0.49), the hyperactivity/impulsivity score (SMD = -0.34), and the inattention score (SMD = -0.46). This is considered to be a moderate effect size. For teacher assessment, which is more likely to be blinded, only the inattention score showed significant improvement with neurofeedback (SMD = -0.30).

Cortese et al (2016), on behalf of the European ADHD Guidelines Group, reported on a meta-analysis of 13 RCTs (total n=520 participants) evaluating neurofeedback for ADHD. When outcomes were reported by assessors who were the least likely to be blinded (parents), there were small-to-moderate effects for total symptoms, inattention, and hyperactivity/impulsivity. However, the effects were not significant when the likelihood of blinding was higher (teacher reported). There were no benefits on objective measures of attention and inhibition. The larger trials included in the meta-analysis are described in the next section.

Arns et al (2020) conducted a study exploring the effect of neurofeedback in children with attention-deficit/hyperactivity disorder. A stricter version of the APA guidelines for rating “well-established” treatments was utilized with a focus on efficacy for remission and long-term effects. No significant side effects, specific to neurofeedback, were reported in any of the studies. In comparison to multi-component-behavior therapy, neurofeedback was proven to be of comparable clinical efficacy, and only marginally below the multi-centre NIMH Multimodal Treatment Study of Children with ADHD medication arms. Authors conclude that standard neurofeedback protocols in the treatment of ADHD can be concluded to be a well-established treatment with medium to large effect sizes and 32–47% remission rates and sustained effects as assessed after 6–12 months.

Randomized Controlled Trials

RCTs Included in the Meta-Analysis
To control for nonspecific effects (attention training) and confounding variables (parental engagement), Gevensleben et al (2009) compared neurofeedback with a control intervention using computerized attention skills training. All children were drug-naïve or drug-free without concurring psychotherapy for at least 6 weeks before starting training. The two training conditions were designed to be as similar as possible, using computer games, positive reinforcement by a trainer, homework, and parental encouragement in using the skills and strategies learned during training in real-life situations. Both groups participated in two blocks of nine sessions (≈100 minutes/session plus a break), with two to three sessions per week, and parents were informed that both treatments were expected to be beneficial but were not informed as to which type of training their child had been assigned. A total of 102 children were randomized in a 3:2 ratio; eight children were excluded due to need for medical treatment or noncompliance with the study protocol by either the children or their parents, with 59 enrolled in the intervention group and 35 randomized to the control group; the majority completed follow-up (92%). Slow cortical potential and theta/beta training were compared by starting with
one type of training in the first block and then the other (counterbalanced order) in the second block. Evaluations were performed by the teachers, who were not blinded to the treatment.

At the end of training/testing, there were no significant differences in parents’ attitudes toward the two training conditions or in the perceived motivation of their children. Approximately 40% of the parents either did not know which training their child had participated in or guessed the wrong group. Both parents and teachers rated the neurofeedback group as more improved on the hyperactivity subcomponent of a Strength and Disabilities Questionnaire (SDQ; eg, 19% vs 3%, respectively, improved) and on a German ADHD scale (eg, 26% vs 9%, respectively, improved). Thirty children (52%) in the neurofeedback group and 10 children (29%) in the attention training group improved more than 25% on FBB-HKS scores (odds ratio, 2.68), which was the primary outcome measure. Scores on other components of the Strength and Disabilities Questionnaire including emotional symptoms, conduct problems, peer problems, and prosocial behavior did not differ between the two training conditions. No significant differences were noted between the two neurofeedback training protocols. Results of this RCT suggested that neurofeedback may have specific effects on attention and hyperactivity beyond those achieved by attention training and parental involvement. The authors noted that future studies should further address the specificity of effects and how to optimize the benefit of neurofeedback as a treatment module for ADHD.

The six-month follow-up to this RCT was reported by Gevensleben et al in 2010. Of the 94 children who completed treatment, 17 started medication during the follow-up interval, and parents of 16 children did not return the questionnaires. Follow-up was obtained in 61 children (65%) of the original per-protocol (n=102). Although the percentage of dropouts did not differ between the two groups, dropouts tended to have higher scores on the FBB-HKS, particularly in the control group. The difference in dropouts between the groups limits the interpretation of the comparative data because scores in the two groups included in follow-up were dissimilar at baseline (eg, baseline FBB-HKS score, 1.50 for the neurofeedback group and 1.37 for the control group). The improvement observed in the neurofeedback group after treatment appeared to be preserved at six-month follow-up. For example, the inattention subscore of the FBB-HKS improved from 2.02 to 1.51 after treatment and remained at 1.49 at 6-month follow-up (moderate effect size [ES], 0.73). The hyperactivity/impulsivity subscore improved from 1.10 to 0.79 after treatment and remained at 0.76 at six-month follow-up (small effect size of 0.35). The authors of this European study noted that the treatment effects appear to be limited but considered neurofeedback to be potentially effective as a component of a multimodal treatment approach.

Steiner et al (2014) randomized 104 children ages 7 to 11 years with ADHD to neurofeedback, cognitive training, or a no-intervention control condition in their elementary school. Both the neurofeedback and cognitive therapies were administered with commercially available computer programs (45-min sessions three times per week), monitored by a trained research assistant. The neurofeedback EEG sensor was embedded in a standard bicycle helmet with the grounding and reference sensors located on the chin straps on the mastoids. There were some small differences in baseline measures between the groups. The slope of the change in scores over time was compared. Children in the neurofeedback group showed a small improvement on the Conners 3-Parent Assessment Report (ES=0.34 for inattention, ES=0.25 for executive functioning, ES=0.23 for hyperactivity/impulsivity), and subscales of the Behavior Rating Inventory of Executive Function—Parent Form (global executive composite, ES=0.23) when compared with baseline. Interpretation of these findings is limited by the use of a no-
intervention control group and lack of parental blinding. Evaluator-blinded classroom observation (using Behavioral Observation of Students in Schools software) found no sustained change with a linear growth model but a significant improvement with a quadratic model. No between-group difference in change in medication was observed at the six-month follow-up.

**RCTs Not Included in the Meta-Analysis**

Several RCTs not included in the Cortese systematic review are described below.

**Duric et al (2012)** reported a comparative study of neurofeedback and methylphenidate in 91 children with ADHD. The children were randomized into 3 groups, consisting of 30 sessions of neurofeedback, methylphenidate, or a combination of neurofeedback and methylphenidate. The neurofeedback sessions focused on increasing cortical beta activity and decreasing theta activity. Parental evaluations found improvements in ADHD core symptoms for all 3 groups. Only the neurofeedback group showed a significant improvement in self-reported school performance.

**Gelade et al (2016)** reported on a randomized comparison of neurofeedback (n=39) with either stimulants (n=36) or physical activity (n=37). Neurofeedback and physical activity were balanced for the number and duration of sessions (3 sessions a week for 10-12 weeks). The trial was adequately powered to detect a medium ES. Intention-to-treat analysis with last observation carried forward showed an improvement in parent-reported behavior for all interventions, while teachers, who were not blinded to treatment, reported a decrease of ADHD symptoms only for the methylphenidate group compared with placebo.

**In a triple-blind RCT conducted in Germany, Schönenberg et al (2017)** identified 113 adults with ADHD and randomized them to neurofeedback (n=37) or sham neurofeedback (n=38) or meta-cognitive therapy (MCT; n=38). Patients in the neurofeedback group received 30 verum θ-to-β neurofeedback sessions over 15 weeks; sham neurofeedback patients received 15 sham followed by 15 verum θ-to-β neurofeedback sessions over 15 weeks, and the MCT patients received 12 sessions over 12 weeks. Patients in the neurofeedback and sham neurofeedback groups were masked to treatment assignment; however, patients in the MCT group knew their treatment assignment. The primary outcome was symptom score on the Conners’ Adult ADHD Rating Scale, which was measured before, during (week 8), and after treatment (at week 16 and at 6 months). At the six-month follow-up, patients in all treatment groups reported a reduction in ADHD symptoms (B = -2.58; 95% confidence interval, -3.48 to -1.68; p<0.001; neurofeedback vs sham neurofeedback, B = -0.89; 95% confidence interval, -2.14 to 0.37; p=0.168; neurofeedback vs MCT, -0.30; 95% confidence interval, -1.55 to 0.95; p=0.639). Reviewers concluded that neurofeedback training is not superior to sham or MCT but that all 3 treatments have merit in managing ADHD.

**In a blinded RCT, Zilverstand et al (2017)** investigated the utility of rtfMRI-NF when used to target the dorsal anterior cingulate cortex, which is a part of the brain that harnesses cognition and motor control, in adults with ADHD. Trialists sought to use rtfMRI-NF training to reduce clinical symptoms and improve cognitive functioning. Thirteen individuals (7 active, 6 control) underwent 4 weekly training of mental exercises designed to help them learn how to upregulate dorsal anterior cingulate cortex activation. The analysis of self-regulation performance during the training runs revealed learning effects in both groups. There was no significant difference between control and an active group (p=0.38), but both groups showed
significant improvements in activation level between the second and the third sessions; moreover, activation levels remained to stay high until training completion (p<0.05). Small sample size limited this trial, though results suggested neurofeedback training might improve cognitive function.

**Section Summary**
Several studies have evaluated neurofeedback for the treatment of children with ADHD, and systematic reviews of these studies have been performed. Overall, the available studies suggest that neurofeedback training improves core symptoms of ADHD and its associated cognitive and behavioral manifestations. Studies that used randomization and blinding methods demonstrate that neurofeedback has beneficial effects for children with ADHD. The study results also suggest that the effects of neurofeedback may be similar to those of ADHD medications; large randomized controlled studies are needed to validate these findings. Neurofeedback has not been extensively studied in adolescents and adults; however, for the children that participated, long-term studies suggest that the lasting effects of neurofeedback are maintained beyond treatment. Neurofeedback may serve as a useful alternative treatment for children with ADHD.

**DISORDERS OTHER THAN ADHD**

**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 patients with disorders other than ADHD.

The question addressed in this evidence review is: Does neurofeedback reduce symptoms and improve functional outcomes in patients with other psychiatric, central nervous system, or pain disorders other than ADHD?

The following PICOs were used to select literature to inform this review.

**Populations**
The relevant population of interest is individuals with disorders other than ADHD.

**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.

| Table 1. Outcomes of Interest for Individuals with disorders other than attention-deficit/ hyperactivity disorder |
|---------------------------------|-------------------------------------------------|----------------|
| Outcomes                        | Details                                         | Timing         |
| Reduction of Symptoms as observed by parents | Attention Switching Task; Impact of Pediatric Epilepsy Scale; PTSD symptoms | 6 weeks        |

PTSD: post-traumatic stress disorder
Table 2. Health Outcome Measures Relevant to Disorders other than ADHD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Measure (units)</th>
<th>Description</th>
<th>Clinically Meaningful Difference (If known)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention Switching Task</td>
<td>msec</td>
<td>Longer duration indicates more symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Computerized task measuring ability to adjust behavior in accordance with changing task goals</td>
<td></td>
</tr>
<tr>
<td>Impact of Pediatric Epilepsy Scale</td>
<td>Scale from 0 to 33</td>
<td>Higher scores indicate more symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Questionnaire administered to parent or guardian measuring domains of academic improvement, social adaptation, and self-esteem</td>
<td></td>
</tr>
<tr>
<td>PTSD symptoms</td>
<td>Various questionnaires</td>
<td>Higher scores indicate more symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Various questionnaires administered to patients measuring frequency and intensity of PTSD symptoms</td>
<td></td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>Percentage</td>
<td>Lower values indicate more symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measure of percentage of total time in bed spent asleep</td>
<td></td>
</tr>
<tr>
<td>Sleep fragmentation</td>
<td>Occurrences</td>
<td>Higher values indicate more symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measure of number of awakening episodes by polysomnography or patient diary</td>
<td></td>
</tr>
<tr>
<td>Total sleep time</td>
<td>Minutes</td>
<td>Lower values indicate more symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measure of time spent asleep among total recording time</td>
<td></td>
</tr>
</tbody>
</table>

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.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Chronic Insomnia
A systematic review by Melo (2019) reviewed seven 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 were at high risk of bias related to blinding of participants and personnel and incomplete outcome data.
Systematic Review with Meta-Analysis

Table 3. Characteristics of a Systematic Review and Meta-analysis of Neurofeedback for Chronic Insomnia

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melo et al (2019)</td>
<td>To 2019</td>
<td>7</td>
<td>Adults with chronic insomnia</td>
<td>224 (18-48)</td>
<td>7 RCTs of biofeedback techniques</td>
<td>10 days to 36 months</td>
</tr>
</tbody>
</table>

RCT: randomized controlled trial

Table 4. Results of Systematic Reviews and Meta-analyses of Neurofeedback for Chronic Insomnia

<table>
<thead>
<tr>
<th>Study</th>
<th>Total Sleep Time</th>
<th>Sleep Fragmentation</th>
<th>Sleep Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melo et al (2019)</td>
<td>2 Trials (n=NR)</td>
<td>2 Trials (n=NR)</td>
<td>2 Trials (n=NR)</td>
</tr>
<tr>
<td>Pooled Effect (95% CL)</td>
<td>No significant difference between biofeedback and placebo (effect estimate NR)</td>
<td>Mean difference in number of awakenings, -4.5 (-8.33 to -0.67)</td>
<td>No significant difference between biofeedback and placebo as measured by either polysomnography or sleep diaries (effect estimates NR)</td>
</tr>
</tbody>
</table>

I² (p) | NR | NR | NR

CI: confidence interval; NR: not reported

Epilepsy

An RCT by Morales-Quezada (2019) randomized children with focal epilepsy to sensorimotor rhythm neurofeedback, slow cortical potential (SCP) neurofeedback, or sham neurofeedback for 25 sessions over five 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.

Table 5. Characteristics of a Recent RCT of Neurofeedback in Epilepsy

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morales-Quezada et al (2019)</td>
<td>Mexico</td>
<td>1</td>
<td>NR</td>
<td>Children and adolescents with focal epilepsy responsive to antiepileptic pharmacotherapy and cognitive difficulties in school</td>
<td>Sensorimotor rhythm neurofeedback, SCP neurofeedback, or sham neurofeedback over 5 weeks</td>
</tr>
</tbody>
</table>

NR: not reported; SCP: slow cortical potential; RCT: randomized control trial; SMR: sensorimotor rhythm

Table 6. Results of a RCT of Neurofeedback in Epilepsy

<table>
<thead>
<tr>
<th>Study</th>
<th>Attention Switching Task</th>
<th>Impact of Pediatric Epilepsy Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morales-Quezada et al (2019)</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>SMR neurofeedback</td>
<td>Significant improvement from baseline to postintervention (-757 msec; p=0.015) and follow-up (-644; p=0.04)</td>
<td>1.5 – point change from baseline (p=0.002)</td>
</tr>
<tr>
<td>SCP neurofeedback</td>
<td>Not significant (effect estimate, NR)</td>
<td>1.9-point change from baseline (p=0.001)</td>
</tr>
<tr>
<td>Sham neurofeedback</td>
<td>Not significant (effect estimate, NR)</td>
<td>1.3-point change from baseline (p=0.006)</td>
</tr>
<tr>
<td>Difference [Neurofeedback - Control] (95% CI)</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

CI: confidence interval; NR: not reported; RCT: randomized control trial; SCP: slow cortical potential; SMR: sensorimotor rhythm
Table 7. Study Relevance Limitations of a RCT of Neurofeedback in Epilepsy

<table>
<thead>
<tr>
<th>Study</th>
<th>Populationa</th>
<th>Interventionb</th>
<th>Comparatorc</th>
<th>Outcomesd</th>
<th>Duration of Follow-upe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morales-Quezada et al (2019)</td>
<td>4. Included patients from a single site in Mexico</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RCT: randomized control trial
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

aPopulation key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
bIntervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
cComparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
dOutcomes 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.
eFollow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Substance Abuse
A systematic review by Sokhadze et al (2008) 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, presence of comorbid conditions, 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 III 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.

Pediatric Brain Tumor Survivors
De Ruiter et al (2016) reported a multicenter, triple-blinded 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 training and at six-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
A meta-analysis by Steingrimsson (2020) evaluated four 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.

### Table 8. Characteristics of Systematic Reviews and Meta-analyses of Neurofeedback for PTSD

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steingrimsson et al (2020)</td>
<td>To 2019</td>
<td>4</td>
<td>Adults with PTSD</td>
<td>123 (12-52)</td>
<td>4 RCTs of EEG-based neurofeedback for PTSD vs sham neurofeedback, other treatment or no treatment</td>
<td>Follow-up: 4 weeks to 30 months</td>
</tr>
</tbody>
</table>

EEG: electroencephalography; PTSD: post-traumatic stress disorder; RCT: randomized control trial

### Table 9. Results of a Systematic Review and Meta-analysis of Neurofeedback for PTSD

<table>
<thead>
<tr>
<th>Study</th>
<th>Self-Harm</th>
<th>PTSD Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steingrimsson et al (2020)</td>
<td>1 Trial (n=NR)</td>
<td>4 Trials (n=123)</td>
</tr>
<tr>
<td>Pooled Effect (95% CI)</td>
<td>1.4-point improvement with neurofeedback (p=0.002)</td>
<td>SMD, 2.3 (-4.37 to -0.24)</td>
</tr>
<tr>
<td>$I^2$ (p)</td>
<td>89% (&lt;0.0001)</td>
<td>NR</td>
</tr>
</tbody>
</table>

CI: confidence level; NR: not reported; 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 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
- Depression
- Depression and fatigue in patients with multiple sclerosis
- Depression in alcohol addiction
- Dissociative identity disorder
- Fibromyalgia
- Insomnia
- Headache
- Childhood obesity
- Obsessive-compulsive disorder
- Parkinson disease
- Post-traumatic stress disorder (PTSD)
- Schizophrenia
- Stroke
- Tourette syndrome

### Section Summary: Disorders Other Than ADHD

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.
SUMMARY OF EVIDENCE
For individuals who have ADHD who receive neurofeedback, the evidence includes RCTs, systemic reviews and a meta-analysis. The relevant outcomes are symptoms, functional outcomes, and QOL. For ADHD, assessors (i.e. parents and teachers) reported small-to-moderate effects for total symptoms, inattention and hyperactivity/impulsivity control issues. Overall, the available studies suggest that neurofeedback training improves core symptoms of ADHD and its associated cognitive and behavioral manifestations.

For individuals who have disorders other than ADHD (e.g., chronic insomnia, epilepsy, substance abuse, pediatric brain tumors and PTSD) 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.

Supplemental Information

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Academy of Pediatrics
The American Academy of Pediatrics (2012) published a report designating biofeedback, as a “Level 1 – Best Support” treatment for children with ADHD. The AAP (2014) further supported its position, stating that neurofeedback “can contribute to lasting improvements” for children with ADHD, citing the Steiner et al (2014) article. The AAP (2019) published a guideline update to the 2011 guideline for the treatment of ADHD in children and adolescents. The guideline states that EEG biofeedback is one of several nonmedication treatments that have either too little evidence to support their recommendation or have little or no benefit.

The AAP (2018), 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 use of biofeedback, with the only barriers potentially being financial in nature.

National Institute for Health and Care Excellence
The National Institute for Health and Care Excellence (2013) issued guideline on management and support of children on the autism spectrum. The Institute stated that the number of treatments were considered but are not recommended including neurofeedback.
International Society for Neurofeedback & Research

European Society for the Study of Tourette Syndrome
Clinical guidelines on behavioral and psychosocial interventions for Tourette syndrome and other tic disorders were published in 2011 by the European Society for the Study of Tourette Syndrome. The guidelines consider neurofeedback experimental.

American Psychological Association
The American Psychological Association (APA) provides general information on biofeedback (including neurofeedback) on its website, stating that “Biofeedback helps treat some illness, may boost performance, helps people relax, and is even used to help children with Attention Deficit-Hyperactivity Disorder.”

American Academy of Child and Adolescent Psychiatry and American Psychiatric Association
No information on neurofeedback was identified from the American Academy of Child and Adolescent Psychiatry or the American Psychiatric Association.

U.S. PREVENTATIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 10. The completion date for various registered trials of neurofeedback have passed without publication of results, suggesting the potential for publication bias.

Table 10. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT04097522</td>
<td>The Effectiveness of Neurofeedback for the Treatment of Chronic Pain</td>
<td>102</td>
<td>Oct 2020</td>
</tr>
<tr>
<td>NCT04220112</td>
<td>Comparing Real-time fMRI Neurofeedback Versus Sham for Altering Limbic and Eating Disturbances in Anorexia Nervosa</td>
<td>47</td>
<td>Sep 2022</td>
</tr>
<tr>
<td>NCT04408521</td>
<td>Effect of Long-lasting EEG-Neurofeedback on Attention Control and Impulsivity in Adult Attention-Deficit/Hyperactivity Disorder (ADHD)</td>
<td>48</td>
<td>Apr 2023</td>
</tr>
<tr>
<td>NCT04469335</td>
<td>Comparative Clinical Trial With Double-blind Randomized Sham Control and Additive Treatment Toward Efficacy of Mobile Neurofeedback for ADHD Youth : An Exploratory Study.</td>
<td>165</td>
<td>Dec 2021</td>
</tr>
<tr>
<td>NCT04654130</td>
<td>An Effectiveness Trial Examining Neurofeedback in Adults With PTSD</td>
<td>65</td>
<td>Apr 2023</td>
</tr>
<tr>
<td>Unpublished</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02991781</td>
<td>Multidisciplinary Tools for Improving the Efficacy of Public Prevention Measures Against Smoking</td>
<td>140</td>
<td>Jun 2019</td>
</tr>
<tr>
<td>NCT01841151</td>
<td>Does Neurofeedback and Working Memory Training Improve Core Symptoms of ADHD in Children and Adolescents? A Comparative, Randomized and Controlled Study</td>
<td>220</td>
<td>Dec 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.
Government Regulations
National/Local:
CMS does not have a national or local coverage determination specific to neurofeedback.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Biofeedback

References


randomized controlled clinical trial. Iran Red Crescent Med J. Aug 2014; 16(8): e17799. PMID 25389484


The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 7/23/21, the date the research was completed.
<table>
<thead>
<tr>
<th>Policy Effective Date</th>
<th>BCBSM Signature Date</th>
<th>BCN Signature Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/1/13</td>
<td>10/16/12</td>
<td>11/8/12</td>
<td>Joint policy established</td>
</tr>
<tr>
<td>7/1/13</td>
<td>4/16/13</td>
<td>4/29/13</td>
<td>Policy position changed to “established” for children with ADHD</td>
</tr>
<tr>
<td>1/1/15</td>
<td>10/24/14</td>
<td>11/3/14</td>
<td>Routine maintenance</td>
</tr>
<tr>
<td>1/1/16</td>
<td>10/13/15</td>
<td>10/27/15</td>
<td>Routine maintenance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Removed age and visit limits</td>
</tr>
<tr>
<td>1/1/17</td>
<td>10/11/16</td>
<td>10/11/16</td>
<td>- Routine maintenance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Continue to diverge from BCBSA policy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Clarification added to inclusions</td>
</tr>
<tr>
<td>1/1/18</td>
<td>11/10/17</td>
<td>10/31/17</td>
<td>Routine maintenance</td>
</tr>
<tr>
<td>1/1/19</td>
<td>10/16/18</td>
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<td>Routine maintenance</td>
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<tr>
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<td>10/15/19</td>
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<td>Routine maintenance</td>
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<tr>
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<td>10/20/20</td>
<td></td>
<td>Routine maintenance</td>
</tr>
<tr>
<td>1/1/22</td>
<td>10/19/21</td>
<td></td>
<td>Routine maintenance</td>
</tr>
</tbody>
</table>

Next Review Date: 4th Qtr, 2022
BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: NEUROFEEDBACK

I. Coverage Determination:

<table>
<thead>
<tr>
<th>Plan Description</th>
<th>Coverage Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial HMO (includes Self-Funded groups unless otherwise specified)</td>
<td>Covered</td>
</tr>
<tr>
<td>BCNA (Medicare Advantage)</td>
<td>Refer to the Medicare information under the Government Regulations section of this policy.</td>
</tr>
<tr>
<td>BCN65 (Medicare Complementary)</td>
<td>Coinsurance covered if primary Medicare covers the service.</td>
</tr>
</tbody>
</table>

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.