Quantitative EEG Neurofeedback for the Treatment of Pediatric Attention-Deficit/Hyperactivity Disorder, Autism Spectrum Disorders, Learning Disorders, and Epilepsy

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**KEYWORDS**
- Neurofeedback
- Neurotherapy
- EEG biofeedback
- Quantitative EEG
- ADHD
- Autism spectrum disorders
- Learning disorders
- Epilepsy

**KEY POINTS**
- Quantitative electroencephalogram neurofeedback (qEEG NF) aims to improve brain functioning by targeting brain-wave correlates of functional deficits, based on the quantitative evaluation of the individual's EEG rather than on traditional diagnostic categories or observable symptoms.
- qEEG NF for attention deficit/hyperactivity disorder, based on 12 randomized controlled trials (RCTs) with medium effect sizes (\(d = 0.57–0.72\)), is recommended with reservations, and only as an adjunctive intervention after families have tried or at least considered conventional treatments.
- For autism, in 4 small RCTs, NF showed improvements in sustained attention, sensory/cognitive awareness, communication, sociability, set shifting/flexibility skills, and some long-term maintenance of treatment gains. NF may be recommended, again with reservations.

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This article provides a definition of neurofeedback (NF), theories of its mechanisms of change, types of NF, a brief history of the research, and efforts to measure the specific effects of NF as distinguished from nonspecific treatment effects. The focus is on NF treatment of attention deficit/hyperactivity disorder (ADHD), autism spectrum disorders (from here on referred to as autism), learning disorders (LD), and epilepsy in children and adolescents, using signal from surface electrodes. For each disorder, it is initially noted how this treatment might be beneficial, the results of empirical studies, their strengths and limitations, and directions for future research. The article concludes with clinical recommendations for the use of NF treatment for these disorders.
WHAT IS NEUROFEEDBACK?

Neurofeedback (also called neurotherapy or electroencephalogram [EEG] biofeedback) is a type of biofeedback that uses operant conditioning to train people to improve regulation of their brain-wave patterns by providing them with real-time video/audio information about their brain’s electrical activity measured from scalp electrodes. In effect, the conditioning is based on feedback given to the patient that is contingent on the patient’s EEG pattern (see article by Simkin and colleagues in this issue for more technical details).

First described qualitatively as “brain waves” on the EEG by Hans Berger in 1924, the electrical activity of the brain was thought to reflect changes in the brain’s functional state while awake or asleep, or to denote brain diseases such as epilepsy. EEG activity, characterized in terms of rhythmic activity measured in hertz (Hz, the number of waves per second), is divided into specifically named frequency bands, corresponding to functional activity and arousal state: the δ band corresponds to slow-wave sleep state (up to 4 Hz), θ to a drowsy/inattentive state (4–8 Hz), α to a relaxed/wakeful/alert state (8–12 Hz), and β to an active/attentive state (12–30 Hz). Most of the brain electrical activity occurs in the 1- to 20-Hz range.

Within each band, there are recognizable functionally significant rhythms. For example, a specific type of low β activity (12–15 Hz) observed in the sensorimotor cortex is called the sensorimotor rhythm. The amplitude of the sensorimotor rhythm is higher when the sensory-motor areas are inactive (eg, during immobile states) and decreases when those areas are activated (eg, during motor tasks). Therefore, the amplitude of the sensorimotor rhythm is a measure of sensory-motor inhibition; that is, higher amplitude when the “brake is on” and lower when the “brake is off.” A mathematical approach to analyzing EEG data, called quantitative electroencephalography (qEEG), can be used to develop a visual map of the type and location of brain waves or rhythms. Other more specific wave patterns, such as event-related potentials, can also be seen in the EEG. Event-related potentials are electrical representations associated with sensory and cognitive processing occurring in response to a stimulus or event. Slow cortical potentials (SCPs) are one specific group of event-related potentials. They are slow event-related direct-current shifts of the EEG that correspond to the excitation threshold of large cortical cell assemblies. Shifts in the positive direction indicate an increase of the excitation threshold and a corresponding inhibition of activation, whereas shifts in the negative direction, called the contingent negative variation, reflect a reduction of the excitation threshold and represent cognitive preparation and increased cortical activation of a network.

The classical conditioning of human EEG was first shown in the mid-1930s, when researchers trained human subjects to block α waves. Operant conditioning, in which EEG-derived information is used as instant feedback to the patient in real-time, was first used to alter the human EEG in the 1960s (see also Ref. for a historical review). Since the 1960s, mainly using operant conditioning, there has been a significant increase in the clinical application of NF to several neuropsychiatric conditions, including ADHD, LD, developmental disabilities, cognitive/memory enhancement, epilepsy, traumatic brain injury, stroke, alcoholism, substance abuse, antisocial personality, autism, anxiety, depression, insomnia, and migraines. There has also been a significant increase, especially in the 21st century, in the number of published research and dissertation studies (eg, PsychINFO/Medline journal searches for title terms neurofeedback, electroencephalographic/EEG biofeedback, or neurotherapy: pre-1970 = 11 studies, 1970–1979 = 212 studies, 1980–1989 = 145 studies, 1990–1999 = 226 studies, 2000–2012 = 1279 studies). The International Society for
Neurofeedback and Research (ISNR; www.isnr.org) and Journal of Neurotherapy were established in 1995, with annual ISNR conferences since 1993. More recently, NF was introduced to the general public by Jim Robbins’ book, A Symphony in the Brain: The Evolution of the New Brain Wave Biofeedback.12

TYPES OF NEUROFEEDBACK

Hammond11 defines 7 types of NF and their use for various disorders:

1. The traditional and most frequently used is Frequency/Power NF, and it is the NF method usually meant by the general term “neurofeedback.” This technique typically entails the use of 2 to 4 surface electrodes and is sometimes called “surface neurofeedback.” Developed in the 1960s to change the amplitude or speed of specific brain waves in particular brain locations, it is used to treat ADHD, anxiety, insomnia, and LD.

2. Slow Cortical Potential Neurofeedback (SCP-NF) modifies the direction (positive or negative) of slow cortical potentials and has been used to treat epilepsy, migraines, and ADHD.

3. Low-Energy Neurofeedback System (LENS), developed in 1992, is a passive type of NF involving delivery of a very weak electromagnetic signal to change a patient’s brain waves while the patient is motionless and has their eyes closed; it has been used to treat traumatic brain injury, fibromyalgia, anger, restless legs syndrome, ADHD, anxiety, depression, and insomnia.

4. Hemoencephalographic (HEG) Neurofeedback, developed in 1994, provides feedback about cerebral blood flow to treat migraine.

5. Live Z-score Neurofeedback, developed in 1998, involves the continuous comparison of multiple variables of brain electrical activity (eg, power, asymmetries, phase-lag, coherence) to a normative database to give moment-to-moment feedback; it has been used to treat insomnia.

6. Low-Resolution Electromagnetic Tomography (LORETA) was developed in 1994 to treat depression, addictions, and obsessive-compulsive disorder. LORETA involves the use of 19 electrodes that are used to monitor phase, power, and coherence (see article by Simkin and colleagues in this issue).

7. The most recent type of NF, developed in 2003, is functional magnetic resonance imaging (fMRI) NF, which allows patients to regulate their brain activity based on feedback of activity from deep subcortical areas of the brain.

Although Hammond’s article can be found on the web site of the ISNR and is published in their journal, the Journal of Neurotherapy, not everyone agrees with these definitions. Martijn Arns, PhD, an NF expert at Research Institute Brainclinics in the Netherlands, noted that “…the simple lack of published controlled efficacy studies does not justify including all them as NF. Furthermore, HEG has not been demonstrated to penetrate the skull, so that should be considered biofeedback, not NF. Also, LENS does not provide any feedback, since LENS consists of measuring a single-channel EEG, having the computer apply a specific algorithm, with no physical or yet measurable form of feedback.” (Martijn Arns, PhD, personal communication, 2013). Only one randomized placebo controlled study has been conducted using LENS and found no difference between sham and active-LENS.13 Unfortunately, the lack of a standard definition of NF, standard protocols of applying different forms of NF to different disorders, and an agreed-on certification process of its professionals has limited the progress of the NF field from its inception.
CONTROLS FOR NEUROFEEDBACK RESEARCH

A methodological topic that is currently being debated in NF is the necessity for double-blind, placebo-controlled randomized trials. The disagreement involves whether NF should be evaluated as an unblindable psychological treatment (like cognitive-behavioral therapy), using American Psychological Association guidelines,14–16 or as a blindable treatment similar to new medications, using double-blind sham-controlled studies.17–20

Randomization is essential for any treatment study,17–20 conventional or otherwise. Although psychiatrists are well aware of the need for randomized double-blind, placebo-controlled studies, one can forget the full range of advantages that these procedures can provide. Without randomization, it would not be known whether reported results were caused by a specific treatment effect (eg, an actual treatment-induced change in EEG brain waves) or because of nonspecific treatment effects, such as self-selection of treatment, expectations of parents and participants (eg, from choosing their preferred treatment), family motivation and resources to manage the time and cost of NF, nonrandom participant experiences (ie, participant history), practice with assessment measures, maturation, and regression to the mean; or interactions among these factors. Other nonspecific treatment effects can threaten the internal validity of treatment outcome research, including the expectations regarding study outcome of the research staff and raters (ie, parents, teachers, and clinicians), provider qualities, staff attention to the patient, practice paying attention/sitting still/inhibiting responses, treatment structures and apparatus, participants’ motivation for improvement and/or therapeutic alliance.21

Most of the nonspecific treatment effects of a procedure like NF can be controlled by randomizing part of the sample to a “fake” (“sham”) NF condition, akin to a placebo, or to some other treatment comparable to NF except lacking the specific active treatment component, that is, the feedback to the patient that is contingent on the person’s EEG. The expectations of subjects, experimenters, trainers, and raters in NF research can all be controlled by blinding them to the treatment condition to which they have been randomly assigned. For effective blinding, the treatment and control groups need to be matched in duration, intensity, and apparatus.

The use of sham controls in NF research to obtain valid double-blinding has been questioned on both ethical and practical levels.20 On ethical grounds, based on the Declaration of Helsinki,22 some NF researchers23 have argued against using a placebo in the form of sham NF, claiming that it would “withhold or deny ‘the best proven diagnostic and therapeutic’ treatment to any participant” (p. 23); instead they recommend an active-control condition with known clinical efficacy. However, it seems presumptuous and even antiscientific to assert that NF is so obviously effective that there is no need for placebo-controlled studies. Others have disagreed with this recommendation to omit placebo-controlled studies for several reasons and have addressed it by suggesting ethical ways to use a sham-NF condition.17,20 The practicality of using a sham-NF in research involves 3 sequential questions:20 (1) Is it possible to develop a truly inert sham NF condition, in accordance with principles of learning theory and conditioning principles,24 that does not lead to learning via unintentional feedback? (2) If question 1 is answered, can this sham-NF condition then be effectively blinded to participants, informants, and experimenters? (3) Finally, if questions 1 and 2 are both answered, can a sample be recruited and retained throughout the lengthy pretreatment and posttreatment assessments and a full NF treatment schedule (eg, 40 sessions for ADHD) using a truly inert sham treatment that remains validly blind to
all? By fulfilling these conditions, the use of a sham-NF control in NF research would be presumably both practical and ethical.

Recently, a collaborative group of researchers from NF and traditional treatment outcome research has, for the first time, proposed, and is seeking funding for, a design that meets these ethical and practical concerns by (1) reinforcing the sham subject based on a pre-recorded EEG from another patient, (2) superimposing the sham subject’s real-time artifacts on the stored EEG to keep the technician/trainer/therapist blinded, and (3) time-stamping the reinforcement events on the sham subject’s real EEG, to determine post-hoc if there were any contingencies that were inadvertently providing unintended systematic feedback (eg, randomly reinforcing at the same time they were paying attention).

TREATMENT OUTCOMES IN NEUROFEEDBACK RESEARCH

The following sections describe the research on NF for ADHD, autism, LD, and epilepsy based on a PsycINFO/Medline search in September 2012 using the title words: neurofeedback, EEG biofeedback, or neurotherapy crossed with (1) ADHD or attention-deficit; (2) autism, Aspergers, or pervasive developmental disorder (PDD); (3) seizure, epilepsy, epileptic, grand mal, or petite mal; and (4) learning, reading, dyslexia, dyslexic, math, mathematics, dyscalculia, spelling, writing, written, dysgraphia, and dysgraphic.

NEUROFEEDBACK FOR ADHD

NF has been suggested for the treatment of ADHD because research indicates that many patients with ADHD have more slow-wave (especially $\theta$, 3.5–8 Hz) power and less $\beta$ (12–20 Hz) power, especially in the central and frontal regions, as well as reduced cortical negativity (ie, a deviance in contingent negative variation) during cognitive preparation. These brain-wave patterns probably reflect underarousal of the central nervous system associated with the core ADHD symptoms of inattention, hyperactivity, and impulsivity. The goal of this treatment is to reverse these functional characteristics of abnormal CNS physiology by countering the physiological underarousal associated with ADHD.

To quantify treatment effects in the clinical trials discussed in this article, the effect size (ES) is described using the Cohen’s $d$ statistic, based on posttreatment means and standard deviations, with the assumption that randomization controlled for any pretreatment differences between groups. Cohen’s $d$ values between 0.2 and 0.4 are considered small ESs; values between 0.5 and 0.8 are considered medium, and values greater than 0.8 are considered large. For comparison with other empirically validated treatments for ADHD, stimulant medications have ESs of 0.8 to 1.2, atomoxetine 0.4 to 1.0, and behavior modification 0.5 to 1.0.

Since the first report of an RCT on NF for ADHD in 1996, 12 RCTs and 2 meta-analyses on youth have been published, with 11 RCTs since 2006; most of these RCTs used either traditional NF targeting the $\theta$-$\beta$ ratio or slow-cortical-potential NF. Summing across the 9 RCTs that provided ESs or the means and standard deviations to calculate them, the mean ES for measures of inattention was 0.72; the mean ES for measures of hyperactivity/impulsivity was 0.70; the mean ES for measures of all ADHD symptoms was 0.62; and the mean ES for measures of all problems (ADHD or otherwise) was 0.57. Four of these studies also showed neurophysiologic changes that were specifically associated with NF treatment (EEG, fMRI, and N2-amplitude). One study reported continued improvements for NF at 6 months following the end of treatment, but that study had serious methodological limitations.
However, the reported benefits of NF have only been replicated in one of the 4 double-blinded RCTs conducted, but those studies had methodological flaws, including small samples.

Of the 12 RCTs, only 4 studies used a sham-NF design, and none of them examined the validity of the sham’s inertness. Therefore, it is not known whether any of these were truly comparing EEG-contingent feedback to noncontingent feedback rather than, in some manner, giving unintentional contingent feedback in the control condition. Similarly, only 2 of these 4 sham-controlled studies tested the accuracy of their blinded testing and found them to be valid, so it is not known whether the other 2 studies were correctly blinded. Another criticism of these 4 studies is that they used unconventional NF protocols that are not typically used in the field, such as the use of automatic (auto-thresholding) rather than manual modulation of training thresholds by the NF clinicians who continuously monitor the subject’s qEEG. Recalculating the aforementioned ESs, without these 4 sham-controlled studies, leads to slightly higher values (previous ESs in parentheses): Inattention 0.81 (vs 0.72), hyperactivity/impulsivity 0.73 (vs 0.70), all ADHD problems 0.71 (vs 0.62), and any problems (ADHD or otherwise) 0.68 (vs 0.57). However, these ES are now based on studies that do not include a full-validated blinded control comparator.

A recent open-label clinic-based study examined the effects of qEEG-guided NF for ADHD using a pretreatment qEEG to develop personalized NF protocols for 7 children and 14 adults with ADHD. The use of qEEG indicates that a patient’s EEG is compared with a normal database. If the brain-wave pattern of the patient is 2 or more standard deviations above or below the mean, and these abnormal brain-wave patterns are in a part of the brain corresponding with the symptoms, then these brain-wave patterns will be the target of the NF sessions. Pre-post treatment comparisons indicated significant improvements for the entire sample on self-reported ratings of attention (P = .000, within-subject ES = 1.78), hyperactivity/impulsivity (P = .001, within-subject ES = 1.22), and depression (P = .003). The study authors noted these ESs were much larger than those calculated in the meta-analysis of 16 studies (6 RCTs) of NF with pediatric ADHD (inattention = 0.81, impulsivity = 0.69, hyperactivity = .40) and similar to an open-label clinic study that preselected children with deviant θ/β ratio (attention ES = 1.8). Open-label studies, with no double-blind or sham-placebo controls, often show stronger effects than rigorously designed studies and are unable to separate the specific from the nonspecific effects of treatment. However, the personalized approach to NF based on pretreatment qEEG seems sensible and worth pursuing in controlled research. In this open-label study, although results were not reported separately for children and adults, no significant differences were found between children and adults on pre-post measures of attention and impulsivity, suggesting that, in this study, the effects of NF on ADHD in youth and adults were comparable.

The meta-analysis by Arns and colleagues of 15 studies (6 with randomization) on NF for children and adolescents reported ESs of d = 0.81 for inattention, d = 0.69 for impulsivity, and d = 0.40 for hyperactivity, and it concluded that “Neurofeedback treatment for ADHD can be considered ‘Efficacious and Specific’ Level 5 (p. 180).” However, because of the inclusion of nonrandomized studies and the lack of studies with blinding and sham-NF controls, the authors disagree and instead conclude that NF has not been shown superior to a credible placebo or to established treatment for ADHD in youth.

Readers may also be interested in a paper-commentary-reply series of articles based on the position paper by Sherlin and colleagues on NF for ADHD and the authors’ recent reviews of published or conference-presented RCTs on this topic. Fig. 1 compares the pre-post improvement in parent-rated inattentive
Pre-post ES (Cohen’s d) for parent-rated ADHD inattentive symptoms in various NF studies

Pre-post % change in parent-rated ADHD inattentive symptoms in various NF studies

A

Pre-post ES (Cohen’s d) for parent-rated ADHD inattentive symptoms in various NF studies

B

Pre-post % change in parent-rated ADHD inattentive symptoms in various NF studies

Fig. 1. Comparison of parent-rated pre-post inattention symptoms in controlled randomized studies of NF. Gray columns show improvement with active and sham placebo NF treatment in the Ohio State University (OSU) trial (Arnold and colleagues, 2013) at mid treatment (24 sessions) and end of treatment (40 sessions). Black columns show improvement with active NF treatment in other studies, with varied treatment durations. Striped columns show, for comparison, improvements with 2 standard treatments (carefully monitored medication and multicomponent behavioral treatment) after 14 months in the Multimodal Treatment Study of ADHD (MTA, MTA Cooperative Group, 1999). This figure illustrates the difficulty of assessing efficacy in the absence of a double-blind control group. Parent-rated inattention was the most common measure across studies, presenting the opportunity for comparison. A different outcome measure may have shown a different picture. (A) pre-post ESs; (B) percentage change in ratings.
symptoms across available controlled studies for active treatment and sham placebo treatment in the Ohio State University study. The pre-post improvement in 2 of the 14-month evidence-based treatments in the Multimodal Treatment Study of ADHD is also shown for comparison. Parent-rated inattention was selected for comparison because it was the most common of reported outcomes; other outcomes may show a different picture.

The American Academy of Pediatrics (AAP) recently declared “biofeedback” to be an evidence-based child and adolescent psychosocial intervention with “level 1, best support.” “Biofeedback” was used to refer to feedback interventions to train either the brain (ie, NF) or the body (traditionally referred to as biofeedback). This rating was based on recommendations derived from the PracticeWise Evidence-Based Services Database (www.practicewise.com), which attributes “Level 1, Best Support” for treatments with at least 2 RCTs, each involving at least 30 subjects, showing that the treatment approach was better than another active treatment or placebo. PracticeWise cited Gevensleben and colleagues and Bakhshayesh and colleagues for NF, and for biofeedback, Rivera and Omizo and Omizo and Michael. Although it is true that all of these studies were RCTs with more than 30 subjects and demonstrated that the treatment was more effective than another active treatment, neither PracticeWise nor AAP considered or explained the possible contribution to these results of nonspecific treatment factors and did not alert the public to these potential confounds.

In general, the quality of research on NF for ADHD is mixed but improving. On the positive side, many available studies incorporate randomization, standardized diagnostic assessments, Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnoses, control of concomitant medication, measurement of comorbidity, multidomain assessment, standard treatment outcome measures, some type of blind (typically single) in a few studies, and a sham or control treatment condition in 4 studies. Current limitations in most studies, and so areas to be addressed in future studies, include recruitment of participants with abnormal EEGs, standardization of NF protocols, triple-blinding (of subjects, NF trainers, and raters, such as parents, teachers, and clinicians), testing validity of blinding, testing inertness of sham, reporting of adverse effects, and controlling for concurrent treatments (such as medications, psychotherapy, special education), increased sample size, monitoring of long-term follow-up, and examining for potential age-related (youth vs adult) differences in response.

In summary, applying the US Preventive Services Task Force (USPSTF) Level of Certainty of Research Evidence and Recommendation Grade, which rates the quality of data-based evidence as poor, fair, or good, the authors rate the quality of evidence for the NF treatment of ADHD as fair to good. This rating fits the USPSTF criteria of “recommend,” defined as fair evidence of benefit and safety (Tables 1 and 2). However, despite the endorsement of this treatment by the AAP, and despite the “recommend” language of the USPSTF criteria, the authors would nonetheless hesitate to place NF for ADHD into a simple “recommend” category, because of the failure of current studies to sufficiently rule out nonspecific effects contributing to the apparent outcome. The authors are concerned that the current data might overestimate the clinical value of NF for ADHD. Nonetheless, for families who have tried or at least considered conventional treatments for ADHD, and who have the time and money to invest in NF, an empirical trial could be considered in conformity with the clinical recommendations at the end of this article. Based on the current standard NF protocols examined in the 12 available RCTs, a typical treatment course for ADHD would involve about 30 to 40 sessions, lasting 30 minutes, 2 to 3 times weekly.
The treatment would aim to reduce $\theta$ and increase $\beta$ power, with manual modulation of training thresholds by the NF clinician monitoring the in-session qEEG.

**NEUROFEEDBACK FOR AUTISM**

NF was initially proposed for the treatment of autism because qEEG studies of autism demonstrate (1) reduced connectivity between cortical areas, especially with increasing distance; (2) a lack of hemispheric differences; and (3) a wide variety of significant and sometimes contradictory EEG differences, including decreased and increased frontal $\delta$ power; increased generalized $\delta$ activity; increased and reduced $\theta$ activity in frontal, central, and temporal regions; decreased $\alpha$ activity, and increased $\beta$ and $\gamma$ activity. These diverse and variable physiologic differences in the brain probably reflect the “pervasive” functional variability that characterizes autism.

Four small RCTs and one review of qEEG NF treatment of autism have been published. The first 2 RCTs, appearing in the same article as 2 separate studies, focused on decreasing $\mu$ brain-wave frequency (8–25 Hz) over the sensorimotor cortex, which is an EEG correlate of mirror-neuron activity associated with imitation abilities that are thought to be limited in autism. The first study randomized 8 youths (ages 7–17) with an unverified diagnosis of high-functioning autism to either NF ($N = 5$, $\mu$ rhythm, right hemisphere C4, 30 half-hour sessions, 3 times weekly for 10 weeks) or a sham-NF control ($N = 3$). Participants and parents were blinded to the treatment assignment. Compared with sham controls, NF significantly increased sustained attention and sensory/cognitive awareness scores on subscales of the parent-rated Autism Treatment Evaluation Checklist (ATEC). The second study

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<th>Disorder</th>
<th>Quality of Evidence for Children or Adolescents/Clinical Recommendation</th>
<th>Basis of Recommendation</th>
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<td>ADHD</td>
<td>Fair to good/recommend (with reservation)</td>
<td>12 published RCTs (4 are sham-controlled with nonsignificant effects that did not use optimal protocols)</td>
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<tr>
<td>Autism</td>
<td>Fair/recommend (with reservation)</td>
<td>4 small RCTs (2 sham-controlled with significant effects, 1 wait-list control with several improvements, reportedly maintained over a period of 6 mo, and 1 compared with a biofeedback condition and a wait list)</td>
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<tr>
<td>Learning disorders</td>
<td>Poor to fair/insufficient evidence to make a recommendation</td>
<td>2 studies using operationalized definitions and assessments of LD, and 1 small RCT</td>
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<td>Epilepsy</td>
<td>Poor/insufficient evidence to make a recommendation</td>
<td>There are no clinical trials specific to pediatric epilepsy, although children and adolescents have been included in trials of NF for epilepsy; 2 meta-analyses of NF reported 82% of subjects experienced $\geq$50% seizure reductions and 79% statistically significant reduction in frequency of seizures</td>
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examined 19 youths (ages 7–17) with rigorously diagnosed autism diagnoses in a randomized (NF = 9, sham NF = 10) double-blind design involving NF training of a higher μ band (10–13 Hz). This study confirmed significant improvements in sustained attention but not in sensory-cognitive awareness and also reported significant parent-rated ATEC improvements in speech/language communication, sociability, health/physical behavior subscales, and overall score. In addition, this second study found decreases in amplitude but increases in phase coherence in μ rhythms and

<table>
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<tr>
<th>Diagnosis</th>
<th>Quality of Evidence for NF for Children or Adolescents/ Clinical Recommendation</th>
<th>Authors’ Recommendation, Clinical Tips, and Cautions</th>
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| ADHD               | Fair to good/recommend with reservations                                        | • Currently NF is not recommended for most families.  
• Due to lack of benefit in several sham-controlled trials, NF cannot be strongly recommended as a stand-alone treatment of pediatric ADHD at this time.  
• NF is an acceptable treatment for families with the time and money to invest in the treatment without diverting resources from other treatments or family needs. |
| Autism             | Fair/recommend with reservations                                                 | • NF should not replace evidence-based practice in the treatment of autism, including applied behavior analysis, medication management for comorbid behavior problems, allied health intervention (eg, speech therapy, occupational therapy), and educational intervention.  
• As there are currently no evidence-based treatments for the core symptoms of autism, and given the positive findings in most of the controlled trials, NF is an acceptable complementary adjunctive intervention for pediatric autism. |
| Learning disorders | Poor to fair/not recommended                                                     | • Given small sample sizes in current literature, NF should not replace evidence-based educational intervention for children with learning disabilities.  
• NF may be acceptable as a complementary adjunctive intervention, particularly for children with comorbid ADHD symptoms and whose families have the resources (time, money, energy) to invest in the treatment. |
| Epilepsy           | Poor/not recommended                                                             | • Given the lack of data, NF should not replace anticonvulsant medications for the treatment of pediatric epilepsy. In cases of uncontrolled seizures unresponsive to medication, it would be reasonable to try for those with the time and money to invest. |
normalization of μ rhythm. Although both studies demonstrated normalization of the NF-targeted μ rhythm as well as improvements in a variety of behaviors associated with autism, neither study showed the expected behavioral improvements in imitation. The authors were unable to compute ESs, because means and standard deviations were not reported for either study.

The 2 most recent RCTs were conducted by Kouijzer and colleagues as a follow-up to their nonrandomized pilot study of 8- to 12-year-olds with PDD–not otherwise specified, in which NF led to improved executive functioning, social communication, and atypical behavior, which was sustained for 6 months after the termination of treatment; qEEG changes included significantly reduced θ and increased β power in central and frontal brain regions. In their first RCT, Kouijzer and colleagues examined 20 youths (ages 8–12) with high-functioning autism, whose diagnoses were verified by a study psychiatrist. They were randomized to individualized qEEG-guided NF treatment (N = 10) or a wait-list control (N = 10). NF involved forty 21-minute sessions, twice weekly for 20 weeks, and focused on decreasing excessive θ power in central and frontal brain areas. Excessive θ power reflects altered activity in the anterior cingulate cortex, which is thought to be involved in the social and executive problems associated with autism. Various individualized treatment protocols were used (different θ frequency bands and electrode placements), depending on each participant’s baseline qEEG, which led to (1) successful reductions in excessive θ power; (2) significant improvements on a reciprocal social interactions (d = 1.61), communication (d = 1.19), initializing peer interactions (d = 1.13), nonverbal communication (d = 1.1), semantics (d = 0.93), and linguistic coherence (d = 0.71); and (3) significant improvements in neuropsychologic set-shifting and cognitive flexibility skills on the Trail Making Test (d = 0.99). The treatment gains were maintained at 6-month follow-up, and some additional treatment gains were demonstrated at 6 months for the NF group but not for the control group.

In their second small RCT, Kouijzer and colleagues attempted to control for some nonspecific treatment effects by comparing NF, skin-conductance biofeedback, and a wait-list control. In this study, 38 adolescents (ages 12–18) with rigorously diagnosed autism were randomly assigned to individualized qEEG-guided NF (n = 13; forty 21-minute sessions, twice weekly for 20 weeks), skin-conductance biofeedback (n = 12; identical treatment to NF except feedback was based on skin-conductance from the index and ring fingers of the nondominant hand); or a wait list (n = 13). Subjects and parents were blinded to treatment assignment for the NF or skin-conductance biofeedback, but not for the wait list. This blinding was reported to be successful, with 58% of subjects in both treatment groups believing that they had received a combination of NF and skin-conductance biofeedback, and 33% of the NF group and 42% of the skin-biofeedback group believing that they had received NF alone. In addition, the treatment expectations of subjects and their parents were found comparable among all 3 groups and were not a significant covariate of treatment outcome.

In the NF group 54% of the NF group were classified as “EEG regulators” because they were able to significantly reduce their δ and/or θ power during treatment sessions; none of the skin-conductance biofeedback group were classified as EEG regulators. Unexpectedly, this in-session EEG regulation did not generalize beyond the training sessions and lead to pre-post EEG changes. In the skin-conduction biofeedback group, 75% were “skin-conductance regulators” who were able to significantly reduce in-session skin conductance; 38% of the NF group was also classified as “skin-conductance regulators.” EEG regulators showed significant pre-post
treatment improvements on laboratory measures of cognitive flexibility ($d = 0.53$), with pre-post treatment gains maintained at 6 months after the end of treatment ($d = 1.4$). However, EEG regulators did not show changes in EEG regulation beyond the training sessions, significant changes in parent-rated autistic symptoms, or clinician-rated global clinical functioning outside of the laboratory. No significant pre-post treatment differences were found on any outcome measure for the EEG non-regulators, skin-conductance nonregulators, or wait-list controls, suggesting that the change in cognitive flexibility was due to specific effects of NF and that NF did not lead to any nonspecific treatment effects on other outcomes. That is, NF-facilitated reduction of $\delta$ and/or $\theta$ power led to a highly specific improvement in cognitive flexibility in adolescents with autism.

In the 2 RCTs that provided means and standard deviations allowing calculation of posttreatment ESs (2/4, 50%), the mean ESs for NF in autism on all measures was $d = 1.11$, which is a large ES. However, 9 of the 10 ESs were derived from one study, which was the first Kouijzer RCT.47

Several of the studies of NF for autism include the use of randomization, some form of blinding, formal assessments of autism diagnoses, multidomain assessment, and documentation of EEG changes. Future directions for research include larger double-blind sham-controlled RCTs with follow-up, tests of the validity of the blind, use of standardized outcome measures, assessment and control of comorbidity and concomitant treatments, and monitoring/reporting of adverse effects.

Regarding clinical recommendations, applying the USPSTF Level of Certainty of Research Evidence and Recommendation Grade,43 the quality of data-based evidence of NF for autism is rated as “fair,” and according to the USPSTF guidelines, the clinical recommendation is to “recommend” NF for treating autism (see Tables 1 and 2). However, given that the main positive results on NF for autism derive from one small study,47 this recommendation is again qualified with reservations and mainly relevant for families who have tried or considered conventional psychosocial treatments for autism, have the time and money to invest in NF, and follow the clinical recommendations outlined at the end of the article.

NEUROFEEDBACK FOR LD

The NF literature on LDs is confounded because many studies profess to examine participants with LD who instead have ADHD, general academic issues and/or developmental delays rather than the more specifically defined DSM-IV reading disorders, disorders of written expression, mathematics disorders, or LD—not otherwise specified. LDs, as defined by the DSM-IV,52 require that the “individual’s achievement on individually administered, standardized tests in reading, mathematics, or written expression is substantially below that expected for a particular age, schooling, and level of intelligence.”

NF treatment of LDs has been suggested because the presence of more $\theta$ and less $\alpha$ power, compared with same-aged controls, can be viewed as suggestive of maturation delay.53 Following early case studies of youths with poorly defined learning problems, an important but flawed series of studies was conducted by Fernández and colleagues.54 In a 2003 controlled study using the DSM-IV operational criteria for reading, math, or writing disorders54 in 10 youths (ages 7–11), selected for abnormally high EEG $\theta/\alpha$ ratios for their age and no comorbid neurologic or psychiatric disorders, participants were nonrandomly assigned to either NF ($n = 5$, location based on initial qEEG) or sham-NF ($n = 5$, random feedback noncontingent on EEG), with both groups receiving twenty 30-minute sessions on a twice-weekly basis for 10 to
12 weeks. Although this study had a sham-NF control group, no comparisons of NF and sham-NF were conducted; instead, only pre-post treatment analyses were made for each treatment group separately, defeating the purpose of a controlled study. Under these circumstances, NF seemed to lead to significant improvements in both global and performance Wechsler Intelligence Scale for Children (WISC) scores and in Test of Variables of Attention (TOVA) ADHD scores, changes that were not shown by the sham control group. Both NF and sham-NF groups showed EEG improvements compatible with maturation, but the NF group showed a greater number of regions with significant EEG changes, including larger magnitudes. Without randomization or a statistical comparison of the NF and sham-NF control groups, inferences about treatment efficacy cannot be drawn.

A 2-year follow-up study of this sample found significant improvements (relative to baseline and to treatment end) again in WISC performance scores and TOVA ADHD scores, for the NF group only, but again with no statistical comparison of active and control groups. Using DSM criteria at the 2-year follow-up, DSM-IV criteria for an LD were no longer fulfilled in 80% of the NF group compared with 0% of the sham-NF group. The NF group showed a further increase in EEG improvements, but the control group experienced an actual worsening on EEG, including an increase in frontal $\theta$ “reaching abnormally high values.”

This study was extended further with the nonrandom assignment of 6 additional children to the NF group. For this larger data set (NF increased to 11 subjects, sham-NF remaining at 5), the NF group now showed significant clinical improvements in verbal WISC-R scores but not performance WISC-R scores. A significant improvement in TOVA scores was also reported. EEG data indicated a decrease in $\theta/\alpha$ ratio. In this study, a more advanced method called frequency domain variable resolution electromagnetic tomography was used to estimate EEG changes in cortical subregions. No immediate posttreatment changes were observed at the end of treatment, but various EEG changes were observed 2 months later in several areas involved in executive functioning: $\theta$ power was decreased in the left frontal and cingulate regions; $\alpha$ power was enhanced in the right temporal lobe and right frontal regions, and there was increased $\beta$ power in the left temporal, right frontal, and cingulate cortex regions.

Taken together, this series of studies by Fernández and colleagues leaves numerous methodological questions. In their nonrandomized studies of NF or sham-NF in youth with DSM-IV LDs, the unorthodox statistical analyses suggested that functional improvements (WISC-R and TOVA) were accompanied by delayed EEG improvements (decrease in $\theta/\alpha$ ratio) in cortical regions subserving executive functions. However, these changes were not observed at the end of the treatment, but instead emerged several months later, perhaps consistent with a beneficial effect on general maturation rather than a specific therapeutic effect on the DSM-IV LD. Because many of the subjects seemed to have concurrent ADHD, it is possible that some or all of the improvement in LDs may have been due to a therapeutic effect of NF on ADHD, again rather than a direct effect on LD. It is unclear whether the blinding methods were effective in these nonrandomized studies. The strongest finding suggestive of a specific effect was the apparent resolution of LD diagnoses in the NF group and not in the sham-NF group, which renders this series of studies suggestive of some possibility of effectiveness.

The most recent study on NF for LD involved 19 youths (ages 8–15) with developmental reading disorder (dyslexia, diagnosed by their remedial teacher using a structured assessment of reading and spelling), who had no other personal or family history of mental illness. Participants were randomized to individualized qEEG-based NF
(n = 10, 20 sessions over a period of 10 weeks) and a wait-list control group (n = 9). All participants also received reading and spelling remedial counseling. NF led to a small but significant (ES; \( d = 0.26 \)) improvement in spelling; this was associated with a significant increase in \( \alpha \) coherence, suggesting that attentional processes may have mediated the improved spelling. In contrast, there was no significant improvement in reading or any related frontocentral changes.

The mean ESs for all measures across the 2 studies\(^{56,57} \) were modest (\( d = 0.39 \)). In addition to very small sample sizes, the overall limitations of these few studies include the lack of randomization, blinding, testing of validity of blinding, testing of sham inertness, standardized outcome measures, parent/teacher ratings, functional ratings, reporting of adverse effects, reporting of or controlling for concomitant treatments, and long-term follow-up.

Regarding clinical recommendations, applying the USPSTF Level of Certainty of Research Evidence and Recommendation Grade,\(^{43} \) the rating of the quality of data-based evidence for NF of LD is “poor” to “fair,” and the clinical recommendation is “insufficient evidence to make a recommendation” (see Tables 1 and 2). The authors are not recommending NF for LDs because findings were weak and only one study\(^{57} \) involved randomization. However, if NF is pursued by families of children with LD, a short trial is suggested using an individualized qEEG-based approach involving 20 sessions over a period of 10 weeks to assess whether continued treatment is worthwhile in that individual.

NEUROFEEDBACK FOR EPILEPSY

Because epileptic seizures are time-limited abnormalities in the electrical activity of the brain that disrupt normal brain functioning, NF would seem a natural treatment option for researchers to explore. In the initial work of Sterman\(^{59} \) on the operant conditioning of slow-wave rhythms in the sensorimotor cortex in cats, it was found that these sensorimotor rhythms were functionally related to thalamocortical inhibitory discharges that could suppress drug-induced seizures.\(^{60} \) Sterman and Friar\(^{61} \) then took a similar approach in one of the first clinical applications of NF in 1972, in successfully treating a case of epilepsy. Since then, most investigators have focused on the operant conditioning of the sensorimotor rhythm (12–15 Hz over sensorimotor cortex), but others have examined NF of slow cortical potentials\(^{62} \) or EEG-guided NF\(^{63} \) for the treatment of epilepsy.

No randomized controlled study of NF for pediatric epilepsy has been published to date. Most published studies on the NF treatment of epilepsy have been single or multiple case studies involving adults, or a mixed sample of adults and youth, but without reporting age-related effects. Two meta-analyses concluded that 82% of subjects with epilepsy experienced a greater than 30% reduction in seizures,\(^{64} \) and that 79% of subjects had statistically significant reduction in the frequency of medication-resistant seizures.\(^{65} \)

The only RCT of NF in adult epilepsy, conducted by Lantz and Sterman,\(^{66} \) involved 24 patients (ages 15–53) with chronic drug-refractory epilepsy who were randomized to 3 groups: (1) sensorimotor rhythm NF (30 minutes, 3 times weekly for 6 weeks), (2) noncontingent NF (specifically, a sham treatment condition in which NF was not contingent on participants’ EEG but instead was yoked to the EEGs of participants in the first NF group), and (3) a wait-list control. Anticonvulsant medication doses and serum levels remained constant throughout the study. Only the NF group experienced a significant pre-post treatment reduction in seizures, with a
median seizure reduction of 61% (individual responses ranged from 0% to 100%), accompanied by significant improvements in cognitive and motor functioning. Subjects with the most sizable seizure reductions had fewer pretreatment self-rated psychological problems, higher baseline problem-solving scores on a neuropsychologic test of problem-solving, more baseline motor performance deficits (presumably signifying more pretreatment sensorimotor rhythm problems), and a greater ability to learn to modulate their EEG. This study is one of the most rigorous in NF, involving randomization, control groups including both a sham-NF (that was shown to produce no change) and a wait list, objective treatment outcome measures, blinded assessment evaluators, and control of concomitant medication treatment. However, NF trainers were not blinded, and the validity of participant blinding was not examined (eg, by asking participants which treatment they think they received), so it is possible that participants’ and trainers’ expectations may have influenced the study outcome.

Another important study by Lubar and colleagues examined 8 subjects (a 13-year-old and 7 adults) with drug-refractory epilepsy (most of whom had brain damage and intellectual disability) using a within-subjects ABA reversal design. Subjects were “subdivided” (random assignment not noted) into 3 treatment groups. In the 4 months of phase A of the ABA design, the 3 groups either were (1) trained to suppress 3 to 8 Hz (n = 3), (2) trained to enhance 12 to 15 Hz (n = 2), or (3) trained to suppress 3 to 8 Hz simultaneously and enhance 11 to 19 Hz (n = 3). Phase B consisted of 2 months during which the contingent EEG feedback was reversed for each individual protocol: for example, those originally trained to suppress 3 to 8 Hz were trained to enhance 3 to 8 Hz. Finally, for the 4 months of the final phase A, participants received their initial EEG feedback schedules again. Medication doses and verified blood levels remained constant throughout the study. Subjects in group 1 were able to complete the NF protocol and showed a decrease in seizures in phase A, an increase in phase B, and a decrease in the return to phase A. Group 2 subjects were less able to complete the NF and showed an increase in seizures in phase A, a decrease in phase B, which continued through the return to phase A. Group 3 showed a seizure decrease in all 3 phases, but only 1 of the 3 participants was able to complete the NF. This study demonstrates the effect NF can have on the frequency of seizures, with suppression of 3 to 8 Hz apparently being therapeutic. The results in group 2 also raise a question of possible seizure risk from enhancing 12 to 15 Hz, commonly done in the treatment of ADHD. This result illustrates the importance of accurate diagnosis before initiating NF.

Although both of these studies are frequently cited as strong evidence in favor of NF for epilepsy, major limitations include small samples, lack of evaluation of the blind, contradictory individual results within the ABA phases and groups of Lubar’s study (although this may be associated with the ability of those participants to learn the protocol), and lack of statistical analysis to assess whether the observed changes were greater than chance alone.

Regarding clinical recommendations, applying the USPSTF Level of Certainty of Research Evidence and Recommendation Grade, the authors’ classification for the quality of data-based evidence for NF of childhood or adolescent epilepsy is “poor” and their clinical recommendation is “insufficient evidence” to make a recommendation (see Tables 1 and 2). However, in extreme cases, such as a youth with uncontrolled seizures that are unresponsive to medication, it would be reasonable to try NF as a desperation measure, following the clinical recommendations outlined in the next section. However, the lack of any controlled trials of NF in youth with epilepsy prevents any reasonable prediction of success.
SAFETY AND RISKS OF NEUROFEEDBACK

NF is usually considered a safe procedure by specialists in the field, but published research trials have not systematically monitored or reported adverse effects. Hammond noted mild adverse effects can occur during NF sessions, such as fatigue, spacey feelings, anxiety, headaches, insomnia, and irritability. Although he noted that these adverse effects either usually disappear shortly after the session or can be addressed by changing the training protocol, he does warn about more serious negative effects, such as worsening of the symptoms the NF is intending to treat if the wrong frequency is reinforced or suppressed. Such effects may result from NF procedures that are not conducted or at least supervised by a certified expert or that have not been effectively individualized to the particular patient.

Unfortunately, there are no published studies that focus specifically on the adverse effects of NF, either in adults or in youth. There are no systematically collected data on their frequency, severity, or duration. There are no accepted guidelines or protocols used for collecting data on the adverse effects. Questions about possible differences in adverse effects in adults and youth have not been addressed, and there has been no discussion of a possible adverse impact on child development. It is not known whether NF can, in some vulnerable individuals, aggravate or induce depression, mania, or psychosis. There are no real discussions or proposals regarding possible contraindications to NF. Drug interactions are not adequately evaluated, but there are some suggestions that psychostimulant doses might need to be reduced following NF treatment of ADHD.

The lack of such information is peculiar in a field of clinical medicine, especially one involving the treatment of minors. It is all the more troublesome that, despite the lack of this type of safety data, that some specialists have argued that placebo-controlled studies are not needed. The failure to provide routine systematic evaluation of possible adverse effects of NF may be associated with the general lack of standardization in this field, but it will need rectification before NF will be taken seriously as a viable treatment with demonstrable safety.

CLINICAL SUMMARY AND CLINICAL RECOMMENDATIONS

1. Current status of evidence of the effectiveness of NF: Applying the USPSTF levels of certainty of research evidence and recommendation grade. Based on these guidelines, it is currently concluded that the evidence for NF is “fair” to “good” for ADHD, “fair” for autism, “poor” to “fair” for LD, and “poor” for epilepsy. Using these criteria, the evidence technically allows a “recommend” (based on fair evidence of benefit and safety, but with reservations) for ADHD and autism, and “insufficient data” to make a recommendation for LD and epilepsy. However, a closely monitored trial could be defensible after conventional treatments have been tried or at least considered, and assuming that the families have the time and money to invest in multiple sessions.

2. The SECS (safe, easy, cheap, and sensible) criterion: A treatment that is SECS needs less evidence to justify an individual patient trial than one that is RUDE (risky, unrealistic, difficult, or expensive) based on basic research of EEG abnormalities and the effects of operant conditioning. NF seems to be a sensible treatment with a solid biologic rationale. Despite the lack of systematically collected data on the safety of NF, current clinical opinion supports the belief that NF is reasonably safe. However, NF usually requires 30 to 40 treatment sessions lasting 30 to 40 minutes (typically 2–3 weekly sessions for 3–5 months), so it is definitely not easy or inexpensive in time or money.
3. *Technical Procedures:*

   a. As a baseline evaluation, either an initial qEEG using 1 or 2 scalp electrodes or a comprehensive qEEG using 19 electrodes should identify specific brain-wave patterns to be targeted in the individual, to increase the likelihood of successful treatment and also to reduce the risks of adverse effects.\(^{11}\) This initial EEG or qEEG evaluation should be conducted by a specialized professional trained in NF methodology. Certified professionals may be found at the EEG and Clinical Neuroscience Society (www.ecnsweb.com/provider-directory.html) or the Quantitative Electroencephalography Certification Board (www.qeegboard.org).

   b. Periodic qEEGs should be done to monitor progress and adjust the treatment target. If there is not a learning curve, the diagnosis and treatment should be re-evaluated.

   c. Similarly, for the NF treatment itself to be successful and safe, it needs to be conducted or supervised by a trained professional with expertise regarding brain function, beyond the mere ability to operate EEG equipment.\(^{11}\) Certified NF professionals may be found at the Biofeedback Certification International Alliance (www.bcia.org) or the ISNR (www.isnr.org).

   d. As current evidence indicates NF works through the mechanisms of operant conditioning, clinical applications (as well as research) should follow the principles of learning theory.\(^{24}\)

   e. Medical or neurologic mimics should be ruled out before initiation of NF, because they may require a different specific treatment. As a corollary, it would be important to distinguish petit mal or absence seizures from ADHD because the type of NF indicated may differ.

4. *Potential for abuse or dependence:* Unlike stimulant treatment of ADHD, there seems to be no risk of abuse using NF treatment. There are no current data regarding risks of dependence on NF treatment.

5. *Interactions of treatment:* Although not formally reported, NF experts have informally observed an apparent interaction with stimulant medication in patients with ADHD: as NF improvement builds up, a child becomes more irritable and moody, which is relieved by reducing or discontinuing the stimulant dose,\(^{68}\) suggesting the possibility that NF might be used to lower the stimulant dose needed for optimal effect, or possibly even allowing discontinuation entirely. However, there has not yet been a well-controlled study specifically demonstrating this possibility.

6. *Duration of effects:* Several studies have reported persistence of benefit for up to 6 months after treatment end. If NF could be established as having a permanent effect beyond the treatment period, this would be an advantage over medication and might make it fiscally competitive by considering the initial high cost amortized over several years of saved medication.

7. *Physiologic mechanism of action of NF:* It should be noted that qEEG NF, the type of NF described in this article, is only one of several approaches, albeit the best established. Other types of NF are described by Simkin and colleagues in their article also in this issue. NF targets different aspects of brain functioning in the different conditions it can treat. In ADHD, physiologic underarousal is improved by suppressing frontal and central $\theta$ and enhancing $\beta$ activity. The diversity of functional abnormalities in different individuals with autism leads to a more differentiated approach in which NF targets selective EEG abnormalities that are identified on an individual basis. Similarly, both LDs and epilepsy are treated mainly based on the specific EEG abnormalities identified at baseline evaluation, rather than by a diagnosis-specific approach. Indeed, NF may target specific features that are
characteristic of certain diagnoses, but more generally, it tends to target the individualized aspects of brain functioning that are manifest in qEEG findings rather than being a diagnosis-based intervention.

REFERENCES


