ELSEVIER
SAUNDERS

Child Adolesc Psychiatric Clin N Am
14 (2005) 105–123

CHILD AND
ADOLESCENT
PSYCHIATRIC CLINICS
OF NORTH AMERICA

Neurofeedback with anxiety and affective disorders

D. Corydon Hammond, PhD, ABEN/ECNS

Physical Medicine and Rehabilitation, University of Utah School of Medicine, PM&R 30 No 1900 East, Salt Lake City, UT 84132-2119, USA

Compelling evidence exists for a neurophysiologic basis for obsessive-compulsive disorder (OCD). A large number of positron emission tomographic and single photon emission computed tomographic studies have found increased blood flow and metabolism in the mediofrontal, anterior cingulate, right frontal, or orbitofrontal areas [1–14], which implicates a cortico-striato-thalamocortical network. Functional abnormalities also have been documented in a large number of quantitative EEG (qEEG) studies [15–22] and evoked potential studies [23–27]. OCD seems to be somewhat heterogeneous, however, with at least two qEEG subtypes that have been found [17–21]. Prichep et al [20] and Kuskowski et al [15] found a group with excess alpha brain waves throughout most of the head, with frontal excess beta, whereas another subgroup has an excess of theta activity, particularly in frontal and posterior temporal areas. Clinical experience in conducting qEEG assessment with patients with OCD also has shown that excess beta activity is often found along the midline, in cortical areas approximately over the anterior cingulate.

Strong research evidence also indicates that there are functional brain abnormalities associated with anxiety and panic disorder [28–30] and post-traumatic stress disorder (PTSD) [31]. A particularly robust body of research, summarized by Davidson [32], has documented that depression is associated with an activation difference between the right and left prefrontal cortex. A large number of EEG studies, reviewed in earlier papers by Davidson [32–34], have established that the left frontal area is associated with more positive affect and memories, whereas the right hemisphere is more involved in negative emotion. A biologic predisposition to depression exists when there is a frontal asymmetry in

E-mail address: D.C.Hammond@m.cc.utah.edu

1056-4993/05/$ – see front matter
doi:10.1016/j.chc.2004.07.008 childpsych.theclinics.com

brain wave activity, with more left frontal alpha activity. This imbalance with more left frontal alpha means that the left frontal area is less activated. Such persons may be anticipated to be less aware of positive emotions while at the same time being more in touch with the negative emotions that are associated with the right hemisphere. This asymmetry in EEG activity is best seen when the EEG is examined with an average reference or a reference on the vertex at Cz [32,35,36].

Researchers have observed for decades that individuals who are depressed are also typically withdrawn. We know that there is a neurophysiologic basis for such withdrawal. Henriques and Davidson [37] found that the frontal area in the left hemisphere is associated with approach motivation and behavior, whereas the right frontal area is involved in avoidance motivation and withdrawal behavior. Researchers found that when the left hemisphere is basically "stuck" in an alpha idling rhythm, there is not only a deficit in positive affect but also more withdrawal behavior. This biologic predisposition to depression is also firmly documented in research findings that have shown that infants of depressed mothers display this same reduced left frontal EEG activation [38,39], even as young as 3 to 6 months [40] and 1 month of age [41].

The belief has been expressed (J.H. Askew, unpublished data) [35] that this frontal alpha asymmetry may represent a state marker of depression, as well as reflecting a biological or trait marker of a vulnerability [37,42] to depression. This has been supported in a study (J.H. Askew, unpublished data) that found a strong correlation between alpha asymmetry scores and the Beck depression Inventory ($P < 0.0001$) and the Minnesota Multiphasic Personality Inventory (MMPI-II) depression scale ($P < 0.0001$).

Davidson [43], who has contributed more research in this area than any other individual, has expressed his belief that this asymmetry is not necessary or sufficient for the production of a specific type of affective style or psychopathology but that differences in prefrontal asymmetry are perhaps most appropriately perceived as diatheses that bias a person's affective style and then modulate someone's vulnerability to developing depression. He does not subscribe to a purely biologic model of depression, but he believes that the frontal alpha asymmetry does predict a vulnerability to depression so that when negative life events occur over a prolonged period of time to such an individual, there is an increased probability that he or she will become depressed. Based on his research, Davidson [43] believes that not everyone with this asymmetry will be depressed, despite being more vulnerable to becoming so, and someone can experience negative life events and still become depressed in the absence of this asymmetry.

The need for new treatments for depression, anxiety, and obsessive-compulsive disorder

Responding to these well-established biologic predispositions, there has come to be a strong reliance in psychiatry on the use of medication for the treatment of

depression and anxiety, although some evidence currently suggests that medication may not be as effective in treating these conditions as has often been believed [44–48]. Similarly, Greist [49] estimated the degree of symptomatic improvement in OCD from treatment with serotonin drugs to only be 30%. Goodman et al [44] similarly found that symptom amelioration in OCD treatment with serotonin uptake inhibitors is approximately 35% on average and that only 50% of patients experience this partial symptomatic improvement.

The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is widely regarded as the finest research measure of OCD. The mean from four separate samples [45,46] of patients with OCD on the Y-BOCS is 24.7 ± 6. A recent meta-analysis of 25 drug studies found that with the most effective pharmacologic treatment for OCD (clomipramine), the average drug treatment effect on the Y-BOCS was 10.64 (uncorrected for placebo effects; corrected for placebo effects it was 8.7), which is a 1.33 standard deviation improvement [50]. In fluoxetine (Prozac) studies, the mean Y-BOCS improvement was only 5.4 points (4.1 points when corrected for placebo effects). In OCD cases that are resistant to medication and therapy, psychosurgery has been the next treatment of choice. Even using a liberal criteria of 35% or more improvement on the Y-BOCS, however, cingulotomies have only benefited from one fourth to one third of patients [47,50], even with the confounding factor that most of the patients continued receiving pharmacotherapy after cingulotomy. Rauch [51] concluded that "For neurosurgical treatment of OCD, the overall rate of efficacy is quite modest, the costs are high, and the risks are considerable."

In light of this brief review and the fact that an increasing number of patients and parents seem interested in less invasive treatments, a need exists for nonmedication treatment alternatives that still address the underlying biologic factors associated with depression, anxiety, and OCD. We know that psychotherapy for depression compares favorably with medication in short-term follow-ups [52] and seems to be superior in long-term follow-ups [53,54]. With OCD, results from behavior therapy [55] are clearly superior to those found with medication, although there is a significant drop-out rate and behavior therapy methods are not well liked by patients. It would be desirable to find a treatment that also would help address the biologic aspects of mental health disorders. Neurofeedback holds promise for offering such an alternative.

What is neurofeedback?

Neurofeedback is EEG biofeedback or brain wave training. Neurofeedback training begins with a qEEG assessment. A tremendous body of research exists on the abnormal EEG and qEEG patterns associated with various medical and psychiatric disorders [48]. The assessment for neurofeedback training may consist of anywhere from 2 to 19 electrodes being placed on the head at standardized electrode sites to gather EEG data. These data then may be compared statistically to a normative database, which provides scientifically objective

information on how a patient's brain activity differs from age-appropriate norms. These data then guide the neurofeedback training process. During neurofeedback training, there usually are two electrodes placed on the scalp at locations where the EEG activity diverges most from norms. Reference and ground electrodes are placed on the earlobes. Nothing intrusive is introduced into the brain. The electrodes simply measure the ongoing brain wave activity. Ordinarily we are unable to reliably influence our brain wave activity because we lack awareness of it. When we are able to see representations of our brain wave activity on a computer screen a few thousandths of a second after it occurs, however, it allows us to modify our brain wave patterns through operant conditioning.

The patient is placed in front of a computer screen. The computer display may be as complex as a computer/video game type of display. It also may be as simple as two bar graphs, one representing slow and inefficient brain wave activity and the other representing efficient, beta brain wave activity. The patient concentrates on the screen. When the inappropriate activity decreases slightly and the appropriate activity increases slightly, a pleasant tone is heard. At first, changes in brain wave activity are transient. As sessions are repeated, however, and the therapist gradually modifies the thresholds for inhibiting inappropriate activity and reinforcing healthier brain wave activity, enduring changes are gradually conditioned. Research with uncontrolled epilepsy [56], for example, in which researchers have used pre- and post-sleep laboratory evaluations, has documented that positive changes in EEG activity after neurofeedback training are not just a voluntary waking change associated with learning a certain mode of concentration on a computer screen. The positive changes in reduced epileptogenic activity were seen even during sleep.

As is seen in other articles in this issue, EEG biofeedback (neurofeedback) has been found to be effective in modifying brain function and producing significant improvements in clinical symptoms in children, adolescents, and adults who have several different biologic brain disorders. These conditions include such things as epilepsy, attention deficit disorder and attention deficit hyperactivity disorder (ADHD), and learning disabilities and have included up to 10-year follow-ups of patients [57].

Neurofeedback treatment of depression, anxiety, and obsessive-compulsive disorder

Neurofeedback for anxiety and obsessive-compulsive disorder

A review of the literature on the neurofeedback treatment of anxiety disorders was conducted by Moore [58]. He was able to identify eight studies of generalized anxiety disorder, three studies with phobic anxiety disorder, two studies of OCD, and one report of using neurofeedback with PTSD. He noted several problems with this literature. One problem was that most of the research studies only used brief neurofeedback training in comparison with what clinicians tend to

do. For example, in the generalized anxiety disorder studies, treatment only averaged 3.2 hours, whereas clinicians often anticipate needing 7 to 12 hours of neurofeedback training with anxiety problems. The eight studies of generalized anxiety disorder also only averaged 6.25 subjects per study, but seven of the eight studies that he reviewed produced positive changes in clinical outcome.

The best studies of neurofeedback with anxiety were three outcome studies [59] with phobic (test) anxiety. These studies included random assignment, four alternative treatment control groups, and a wait-list control group. In one study, the group that received alpha EEG enhancement training produced 33% more alpha after treatment, and all three feedback groups (who received alpha enhancement biofeedback, electromyography [EMG] [muscle] biofeedback, and alpha plus EMG biofeedback) demonstrated significant reductions in test anxiety. In comparison, the untreated control group and the relaxation training group experienced no significant reduction. In another study, subjects received phases of alpha enhancement training and EMG biofeedback training. The alpha training was found to increase alpha production from 64% to 78%, and anxiety scores dropped significantly ($P < 0.001$) for this combined treatment group compared with a nontreatment group. Moore [58] concluded in his review that a placebo effect was present in these neurofeedback studies but that alpha and theta enhancement training provided additional effects beyond placebo and are effective treatments for anxiety disorders. When these results are compared with the American Psychological Association Clinical Psychology Division criteria [60,61] and comparable biofeedback specialty criteria [62] for evaluating the status of efficacious treatments, neurofeedback for phobic anxiety qualifies for the status of a probably efficacious treatment.

Before proceeding further, an outline of these guidelines for evidence-based support is reviewed. According to the biofeedback efficacy guidelines [62], the status of ''possibly efficacious'' is accorded for treatments that have been investigated in at least one study and had sufficient statistical power and well-identified outcome measures but lacked randomized assignment to a control condition internal to the study. For the last two decades, randomized, controlled trials have been emphasized as the scientific gold standard by the pharmaceutical industry, in medicine, and in the recent clinical psychology guidelines for defining empirically supported therapies. Recently, however, this academic ''gold standard'' has been challenged by two research reports in the scientifically prestigious *New England Journal of Medicine* [63,64] and another study [65]. The three studies discovered that results from nonrandomized observational studies were similar to randomized, controlled trials. To attain the lower evidence-based status of ''possibly efficacious,'' a randomized, controlled trial was deemed unnecessary.

The biofeedback efficacy guidelines define a treatment as meriting the status of ''probably efficacious'' when multiple observational studies, clinical studies, wait-list controlled studies, and intrasubject or within-subject replication studies demonstrate efficacy. A biofeedback treatment is considered to have reached the higher ''efficacious'' status when research by at least two independent research

groups (which has included comparison with a no-treatment control group, alternative treatment group, or sham/placebo control group with randomized assignment) has found that the experimental treatment is significantly superior statistically to control conditions or equivalent to a treatment of established efficacy. Finally, a biofeedback treatment is considered as having reached the status of ''efficacious and specific'' if, in addition to the previous criteria, the treatment has been demonstrated to be statistically superior to a credible sham therapy, pill, or bona fide treatment in at least two independent studies. With regard to requiring placebo-controlled studies to establish efficacy for psychological treatments, however, in which a known effective treatment is already available, this has been deemed unethical by medical ethicists [66,67] and by the Declaration of Helsinki of the World Medical Association [68]. Supporting the Declaration of Helsinki, a university Institutional Review Board (IRB) committee deemed that a study proposal to include a placebo control condition compared with neurofeedback to treat attention deficit disorder and ADHD would be considered unethical because a medication treatment with known effectiveness existed already for this condition [69].

Returning to the literature review, two relevant studies of neurofeedback for the treatment of anxiety were not reviewed by Moore [58]. Passini et al [70] used 10 hours of alpha neurofeedback training, comparing 25 anxious patients (23 of whom were alcoholics) with a control group of 25 anxious patients (22 of whom were also alcoholics), most of whom were seeking treatment at a Veterans Administration hospital brief treatment unit. While most subjects were assigned to one group or the other randomly, deliberate placement of younger patients in the control sample occurred toward the end of data collection and was implemented to offset an age difference that had developed earlier between the groups. Thus, this would be considered to be a matched control group study. Although they did not evaluate drinking status, the alpha neurofeedback training produced significant ($P < 0.001$) changes in state and trait anxiety compared with controls. This was accompanied by an increase in eyes-closed alpha production from 38% to 55%, whereas controls dropped slightly. An 18-month follow-up of those patients was published, with virtually identical results of lower anxiety still found, which validated that the anxiety changes from alpha neurofeedback were enduring [71]. A recent randomized, blinded, controlled study was conducted at London's Royal College of Music to evaluate the ability of alpha-theta neurofeedback to enhance musical performance in high talent level musicians when they were performing under stressful conditions in which their performance was being evaluated [72]. When compared with five alternative treatment groups, only the neurofeedback group that received training to increase alpha and theta resulted in enhancement of real-life musical performance under stress. These results qualify under the guidelines reviewed earlier as meeting probably efficacious status for neurofeedback treatment of anxiety.

Two neurofeedback outcome studies have focused on chronic PTSD, only the first of which was reviewed by Moore [58]. In a randomized, controlled group study [73], 30 30-minute sessions of alpha-theta EEG biofeedback training were

added to the traditional Veterans Administration hospital treatment that was provided to a group of 15 Vietnam combat veterans with PTSD. The study compared them after treatment and at follow-up with a contrast group of 14 veterans who only received traditional treatment. One strength of this study is that in addition to the posttreatment testing, on a monthly basis, patients and informers were contacted for a full 30-month follow-up period to determine if there had been PTSD symptoms (eg, flashbacks, nightmares, anxiety attacks, depression). At follow-up, all 14 traditional treatment patients had experienced relapse, whereas only 3 of 15 neurofeedback training patients had experienced relapse. Another outcome measure involved psychotropic medication requirements. Medications were equivalent at the onset of treatment, with 14 of the neurofeedback group receiving medication and 13 of the 14 standard Veterans Administration hospital treatment group on medication. All 14 patients who were treated with neurofeedback had decreased their medication requirements at follow-up, whereas in contrast, only 1 traditional treatment patient had decreased medication needs, 2 reported no change, and 10 required more medications. Changes on the MMPI may be seen in Figs. 1 and 2. Neurofeedback training patients improved significantly on all ten MMPI clinical scales—in many in-

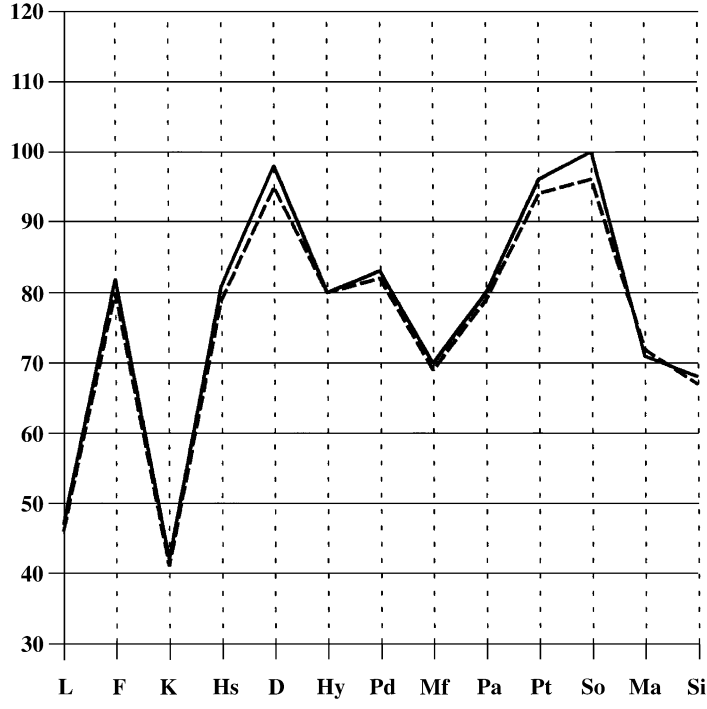

Fig. 1. Peniston-Kulkosky 1991 PTSD study. Pre- and post-MMPI changes from traditional treatment. Solid line indicates pretreatment. Dotted line indicates posttreatment.

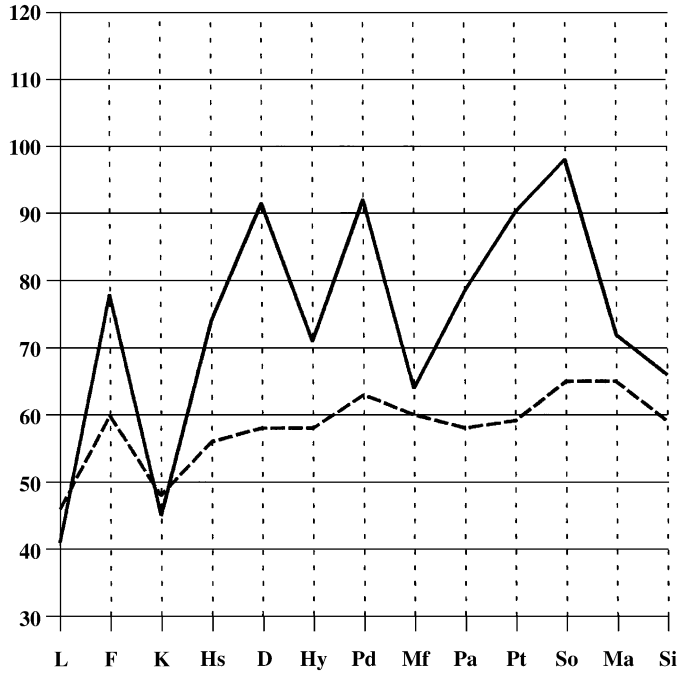

Fig. 2. Peniston-Kulkosky 1991 PTSD study. Pre- and post-MMPI changes after neurofeedback treatment. Solid line indicates pretreatment. Dotted line indicates posttreatment.

stances dramatically—but there were no significant improvements on any scales in the traditional treatment group.

In examining the figures, T-scores may be seen down the left hand side of each figure. A T-score of 50 represents the mean average of a ''normal'' population, and only 2.5% of normals score higher than the heavy line that goes across the figures at T-score 70. For readers unfamiliar with the MMPI, a brief overview of what the clinical scales measure is helpful. The first three scales (L, F, and K) are validity scales. When the F scale is elevated, as it is in these two samples, it is associated with an endorsement of more problematic symptoms. Scale 1 measures somatic symptoms. Scale 2 is the depression scale, and both treatment groups showed a severe level of depression before treatment. Scale 3 is associated with over-emotionality and repression. Scoring high on scale 4 indicates tendencies to be nonconforming, resentful of rules and authority, manipulative, and self-centered. Scale 5 measures traditionally masculine versus more feminine or more passive interest patterns. Elevations on scale 6 suggest that a patient is more paranoid, suspicious, hostile, and prone to project blame and responsibility. Scale 7 is associated with obsessive-compulsive symptoms, anxiety, and feelings of inferiority or inadequacy. Higher scores on scale 8 tend to be associated with being withdrawn, having odd or peculiar (thought disorder) thinking patterns, and feeling alienated from self and others. Scale 9, when it is elevated, can be

associated with impulsiveness, high energy level, or manic tendencies. Scale 0 is an introversion/extroversion scale, with elevations associated with being introverted and having a deficit in social skills.

In another Veterans Administration hospital uncontrolled study [74], 20 Vietnam veterans with chronic PTSD, all with comorbid alcohol abuse, were randomly selected. All patients showed frequent (eg, two to three times per week) episodes of PTSD symptomatology and had been hospitalized for PTSD an average of five times. They were treated with 30 30-minute sessions of alpha-theta neurofeedback training. Follow-up interviews occurred with the patients and their wives or family members on a monthly basis for 26 months. In that time, only 4 of the 20 patients reported a few (one to three) instances of recurrence of nightmares or flashbacks, and the other 16 patients had no recurrence of PTSD symptoms. The status of alcohol symptoms was not reported. According to the biofeedback efficacy criteria [62], neurofeedback treatment of PTSD qualifies for the status of probably efficacious.

Two published studies of OCD were reviewed by Moore [58]. Both studies used alpha enhancement training, without positive results. Viewed from a modern perspective, these studies, which were published in the mid-1970s, used a naïve and simplistic treatment approach of only doing alpha enhancement training. Literature since that time [17–21] has shown that there are at least two subtypes of EEG patterns that are found in OCD, neither of which would be anticipated to benefit from alpha enhancement training.

Recent reports are available on the successful treatment, with lengthy follow-ups, of three consecutive cases of OCD. In each of these cases, neurofeedback protocols were individualized to the unique neurophysiologic characteristics of each patient through using a qEEG assessment. In the first report [75], scores on the Y-BOCS and the Padua Inventory normalized after treatment, with the two patients improving on the Y-BOCS from scores of 26 and 25 to scores of 4 and 7 (showing 3.7 and 3 standard deviation improvements, respectively). This should be considered particularly significant because a meta-analysis of 25 drug studies found that even the most effective pharmacologic treatment for OCD only produced an average treatment effect on the Y-BOCS of a 1.33 standard deviations improvement (uncorrected for placebo effects) and approximately one half that much improvement across studies with fluoxetine (Prozac) [50]. Improvements also were documented with an MMPI, and follow-ups of the two cases at 15 and 13 months after treatment (which included interviews with relatives) found that changes were maintained.

A third case of neurofeedback treatment of OCD with a college student also has been reported [76]. The individual suffered with obsessional OCD, which is the type of OCD that has proven most resistant to cognitive-behavioral treatment [58]. He proved resistant to improvement with trials of eight previous medications. On his pretreatment MMPI he scored 115 T-scores on the Pt (7) scale. After treatment, his Pt scale decreased to 60 T-scores. Before treatment he scored 16 on the Y-BOCS, which is the cut-off score generally used for inclusion in OCD medication trials. On the obsessions subscale he scored 10; the mean for

patients with OCD is 10.7. At the completion of neurofeedback treatment, his Y-BOCS score had improved to 3 (a 2.2 standard deviation improvement) and his obsessions subscale score decreased to 0. Changes were maintained at 10 months, with external validation of improvements with his family.

All three of these cases had been treated unsuccessfully with various medications. In addition to these published cases, there are many clinical reports of comorbid OCD and ADHD improving with neurofeedback. Although these are uncontrolled case reports and do not yet even meet criteria for the status of a possibly efficacious treatment, the outcomes from treatment with neurofeedback in these preliminary reports are encouraging. The father of one of these patients, after having completed 21.5 hours of neurofeedback, said, "This week my daughter told me, 'Dad, for the first time in my life, I feel normal.'" The patient has been followed for more than 2 years and she has maintained her improvements.

Neurofeedback for depression

In relation to the research reviewed earlier on the presence of a frontal alpha asymmetry in depression, Rosenfeld [77] developed a neurofeedback protocol for modifying this asymmetry. This ALAY protocol (which stands for alpha asymmetry; F4 − F3/F3 + F4, with a reference electrode at Cz) has been used in case studies [35,36,78] with encouraging preliminary results, but no controlled research has been conducted. Baehr et al [78] did 1- to 5-year follow-ups on patients treated with the ALAY protocol and documented that the changes in depression were enduring and that the frontal alpha asymmetry not only had changed at the end of treatment but that this physiologic asymmetry continued to be reversed on long-term follow-ups. This is of particular relevance because several studies [42,79–81] have found that after pharmacologic treatment that produced a remission of depression, the frontal alpha asymmetry remained unchanged, which suggests that patients in drug treatment continue to have a biologic vulnerability to future depression.

A different protocol for modifying the frontal alpha asymmetry also was developed in association with a successful case report with an 8.5-month follow-up [82]. In this protocol electrodes are placed at Fp1 (on the left forehead) and F3 (approximately 2.5–3 inches straight above Fp1). During the training, slow brain wave activity is inhibited in the alpha and theta frequency bands during reinforcement of 15- to 18-Hz beta for the first 20 to 22 minutes of each training session, after which the reinforcement frequency band is decreased to 12 to 15 Hz for the final 8 to 10 minutes of each session. A 2-year follow-up of the initial case found that the depression remained in remission.

This second protocol has continued to be used clinically in the treatment of depression during the past 5 years, and there is a new report with a sample of nine consecutive patients who were treated with it [83]. All the patients in this series were relatively medication resistant and had been diagnosed with dysthymic disorder. They were all administered the MMPI and screened with the ALAY

protocol to verify the presence of the frontal alpha asymmetry associated with a biologic predisposition to depression. This screening takes approximately 15 minutes, and researchers have found that percentage scores of more than 60 indicate that there is no predisposition to depression, whereas scores of 58 or less indicate the presence of a predisposition [80]. The mean percentage score in the recent sample was 40.1, and their mean on the MMPI Depression scale (scale 2) was 93.8 T-scores. From the beginning, one patient seemed to have questionable motivation and dropped out after five sessions. The other eight patients received an average of 10.4 hours of training (20.8 30-minute sessions). No other psychotherapy was provided. After treatment, there was a mean decrease in the depression scale of 28.8 T-scores.

Improvement was categorized using the following criteria. Less than 60 T-scores on the depression scale was considered as representing normal, 60 to 70 T-scores represented mild depression, 71 to 80 T-scores represented moderate depression, 81 to 90 T-scores represented serious depression, and 91 T-scores and above represented severe depression. According to these criteria, overall this was a severely depressed patient sample. One patient was judged to have improved from being severely depressed to being normal, and two improved from being seriously depressed to normal. Three of the patients were judged to have improved from a severe to a mild level of depression, and one improved from moderately depressed to mildly depressed. In one case, a severely depressed individual only manifested mild improvement. He had lost his wife to cancer a year earlier, and this loss seemed to need further attention. He was referred for more traditional psychotherapy. All the patients had been treated with several antidepressant medications without substantive effect, and most of the patients were on medication at the beginning of neurofeedback training but not at the conclusion. The average length of individual follow-up of the eight patients was 1 year (range, 4 months to 2 years), at which time improvements had been maintained. Classifying the patient who only mildly improved as a failure, 87.5% of the cases improved, and if the drop-out is included as a failure, then 77.8% of the case series made significant improvements.

Patients in many of the published medication studies are moderately depressed, whereas in this case series, seven of the eight patients were classified as seriously to severely depressed, and only one patient was moderately depressed. The cases in the ALAY protocol studies [83] were only in the mild range of depression, with scores in the 62 to 64 T-score range on the MMPI, which also is reflected in their ALAY scores, which averaged 51.3, whereas the case series reported by Hammond [83] had a mean ALAY score of 40.1.

Although reports to date on the application of neurofeedback to depression only represent uncontrolled case reports that are not sufficiently rigorous to receive one of the levels of evidence-based support, they provide encouragement that neurofeedback may hold potential for treating mildly to severely depressed patients and that unlike medication, it may enduringly modify the functional brain abnormality associated with a biologic predisposition to depression. Controlled research seems warranted.

Clinical experience and further case examples

Depression

A case example illustrates the use of this second neurofeedback protocol with depression. Dan was an engineer in his 30s. He had originally entered treatment for a circumscribed complaint of fear of public speaking, which had been successfully treated in five sessions with self-hypnosis training. A year later he returned and indicated that he had experienced depression for many years but that it had been getting worse. His ALAY score of 36.1% indicated an extreme frontal alpha asymmetry, and his MMPI depression scale of 92 T-scores confirmed his severe depression. After informed consent, neurofeedback was started with the depression protocol. After three sessions he said that despite having had a difficult week at work, "I have been feeling a lot better. It's hard to believe that it's working this quickly." He explained that he had been skeptical about the possibility of neurofeedback being successful and was particularly surprised that he already could feel a difference. In clinical experience with this protocol, most patients can begin to perceive a difference in their depression level after three to six 30-minute training sessions. Usually by 10 to 12 30-minute sessions they feel significant improvement, and by 20 to 22 sessions treatment is completed.

Dan indicated after five sessions that he was still feeling depressed but that it was improving. After seven sessions he reported sleeping better, and after eight sessions he said that several people at work had commented on seeing a difference in him and had said, "We were worried about you there for a while." He explained that previously he had attributed his depression to his work situation but that his work had not changed and his depression was much improved. He continued to improve steadily. His total treatment consisted of 19 30-minute neurofeedback training sessions. Fig. 3 displays his before and after MMPI changes. His depression (scale 2) had decreased from a severe level (92 T-scores) to a mild, perhaps subclinical level (63 T-scores). The rest of his MMPI profile reflects changes that have been found in most cases after using this treatment protocol. His anxiety, obsessional rumination, and feelings of inferiority and inadequacy (as reflected in scales 7 and A) decreased, whereas ego strength (Es scale) increased. His withdrawal and feelings of alienation from people (scale 8) decreased and he changed from being moderately introverted and quiet (scale 0) to being on the mean between introversion and extroversion. The MMPI has proved to be a much better outcome measure than using a depression scale alone because it has illuminated the many other dimensions on which change has occurred. On the MMPI, a decrease in withdrawal and introversion (scales 8 and 0) commonly accompany the decline in depression, which would be anticipated because an area of the brain is being activated that is also associated with approach motivation. Dan's changes were maintained at 6.5-month follow-up, at which time he took a new job in another state.

Based on clinical experience with more than 25 patients with dysthymia, in which most of them have been followed for between 6 and 24 months,

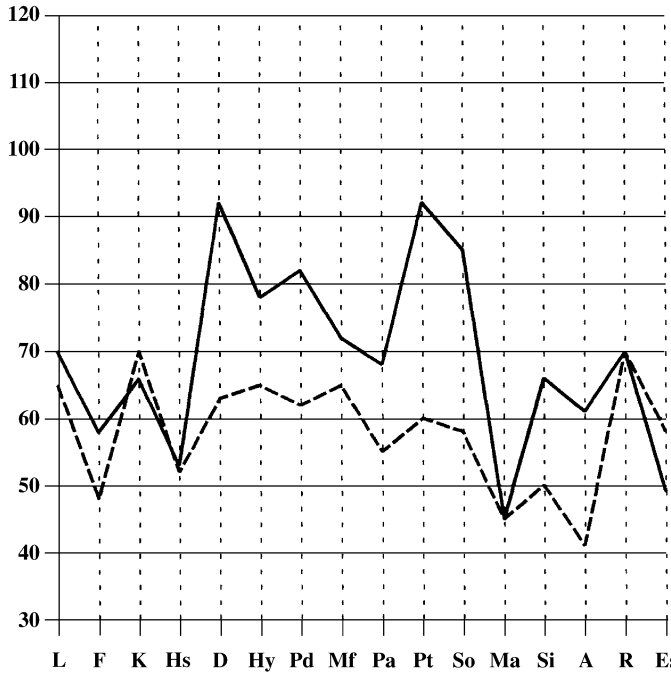

Fig. 3. Pre- and post-MMPI changes after neurofeedback for depression. Solid line indicates pre-treatment. Dotted line indicates posttreatment.

neurofeedback has seemed to be successful in producing significant and enduring change in approximately 80% of the patients. There have been no published research or clinical reports on the use of neurofeedback in a pediatric depression sample. Because the biologic marker of a frontal alpha asymmetry has been found in multiple studies with children and infants [38–41] of depressed mothers, and because there is abundant evidence that children respond to neurofeedback training for other conditions, it is reasonable to expect that this approach would be beneficial with depressed children. There are widespread clinical reports of improvements in mood among children treated with neurofeedback for ADHD, which further supports the expectation that neurofeedback may be effective with childhood depression. There also are anecdotal reports of improvements in bipolar disorder. Neurofeedback seems to involve minimal risk of side effects or adverse reactions [84], and it is less invasive than antidepressant medication or transcranial magnetic stimulation.

Anxiety and insomnia

In most cases, anxiety and insomnia are readily treated with neurofeedback [58,59,85–88]. Many children with ADHD are treated by inhibiting slow brain wave activity (eg, theta) while reinforcing the sensorimotor rhythm (12–15 Hz)

over the sensorimotor strip. In these cases, one of the first improvements that parents often notice is that the child falls asleep more easily and remains asleep. The reason may be that the sensorimotor rhythm overlaps in frequency with beta spindles, and when the sensorimotor rhythm is increased in a waking state, it also increases beta spindles that occur as one begins trying to go to sleep [87,88], which facilitates improvement in insomnia. Although anxiety often involves excess right frontal beta brain wave activity, clinical experience has shown that a qEEG assessment is often invaluable because the excess of fast beta activity may be in other locations. Someone who obsessively worries may have this beta excess along the midline or in the center of the top of the head at an electrode location known as Cz. In other cases, the excess beta may be in the parietal area. With anxiety patients, neurofeedback training often is done eyes closed while listening to auditory feedback, and in a sense it resembles high-technologic meditation training.

As a case example, a patient was referred by a physician who was a headache specialist, indicating that everything that could be done with medication seemed to have been done. The patient had a lengthy history of several migraines weekly, which had progressed to daily migraines. She had been given a self-hypnosis tape to use for anxiety management, but she complained that her mind was so busy that she was unable to obtain much relaxation from the tape. After 20 30-minute sessions of inhibiting fast beta and reinforcing alpha activity in the parietal area, she was off all her prescription medications. She sensed a migraine trying to begin approximately twice weekly but would take over-the-counter medication and could use the self-hypnosis tape successfully to abort the headache. She felt more relaxed in general and reported no longer feeling compelled to do two things at once.

Summary

As reviewed in other articles, the neuroscience technology known as EEG biofeedback (or neurofeedback) has considerable research support in areas such as uncontrolled epilepsy and attention deficit disorder and ADHD. In evaluating the studies in the overall broad area of the neurofeedback treatment of anxiety disorders, EEG biofeedback qualifies for the evidence-based designation of being an efficacious treatment [62]. When separate anxiety disorders are individually evaluated, the areas of phobic anxiety, generalized anxiety, and PTSD each qualify for designation as being a probably efficacious treatment. Currently there are only reports of cases and series of cases on the treatment of depression and OCD and no published reports thus far on treatment of bipolar disorder. Despite the lengthy follow-ups and use of objective measures, neurofeedback treatment for depression and OCD is not yet empirically supported.

EEG biofeedback is an exciting, cutting-edge technology that offers an additional treatment alternative for modifying dysfunctional, biologic brain patterns that are associated with various psychiatric conditions. It has the advantage of

not being as invasive as medication, transcranial magnetic stimulation, or electroconvulsive therapy, and it has been associated with few side effects or adverse reactions [84]. Frank H. Duffy, a professor and pediatric neurologist at Harvard Medical School, said that scholarly literature suggests that neurofeedback "should play a major therapeutic role in many difficult areas. In my opinion, if any medication had demonstrated such a wide spectrum of efficacy it would be universally accepted and widely used." "It is a field to be taken seriously by all" [89]. Duffy further pointed out that the field of neurofeedback also must produce more randomized, controlled studies. The efficacy of other biologic treatments (eg, medication and transcranial magnetic stimulation) for anxiety and affective disorders in children is not fully established, and many parents and patients increasingly seek less invasive treatment alternatives. It is desirable that more funded research be directed to providing further research evaluation of the potential of neurofeedback as a treatment with adults and children. Clinicians who are interested in learning more about neurofeedback training and qEEG may contact the International Society for Neuronal Regulation (www.isnr.org) or the Association for Applied Psychophysiology and Biofeedback (www.aapb.org).

References

[1] Baxter L, Phelps M, Mazziotta J. Local cerebral glucose metabolic rates in obsessive-compulsive disorder: a comparison with rates in unipolar depression and in normal controls. Arch Gen Psychiatry 1988;44:211–8.
[2] Baxter L, Phelps M, Mazziotta J, Guze BH, Schwartz JM, Selin C. Local cerebral glucose metabolic rates in obsessive-compulsive disorder. Arch Gen Psychiatry 1987;44:211–8.
[3] Benkelfat C, Phelps M, Mazziotta J, Guze BH, Schwartz JM, Selin RM. Local cerebral glucose metabolic rates in obsessive-compulsive disorder patients treated with clomipramine. Arch Gen Psychiatry 1990;147:846–8.
[4] Harris GJ, Pearlson GD, Hoehn-Saric R. Single photon emission computer tomography in obsessive-compulsive disorder. Arch Gen Psychiatry 1993;50(6):498–501.
[5] Machlin SR, Harris GJ, Pearlson GD. Elevated medial-frontal cerebral blood flow in obsessive-compulsive patients: a SPECT study. Am J Psychiatry 1991;148:1240–2.
[6] Nordahl TE, Benkelfat C, Semple WE, Gross M, King AC, Cohen RM. Cerebral glucose metabolic rates in obsessive-compulsive disorder. Neuropsychopharma 1989;2:23–8.
[7] Perani D, Colombo C, Bressi S, Bonfanti A, Grassi F, Scarone S, et al. 18[F]FDG PET study in obsessive-compulsive disorder: a clinical/metabolic correlation study after treatment. Br J Psychiatry 1995;156:244–50.
[8] Piacentini J, Bergman RL. Obsessive-compulsive disorder in children. Psychiatr Clin N Am 2000;23(3):519–33.
[9] Rauch SL, Whalen PJ, Dougherty D, Jenike MA. Neurobiologic models of obsessive-compulsive disorder. In: Jenike MA, Baer WE, Minichiello WE, editors. Obsessive-compulsive disorders: practical management. St. Louis: Mosby; 1998. p. 222–53.
[10] Rubin RT, Villaneuva-Meyer J, Anath J. Regional ^{133}Xe cerebral blood flow and cerebral 99m-HMPAO uptake in unmedicated obsessive-compulsive disorder patients and matched normal control subjects: determination by high-resolution single-photon emission computed tomography. Arch Gen Psychiatry 1992;49:695–702.
[11] Sawle GV, Hymas NF, Lees AJ. Obsessive slowness: functional studies with positron emission tomography. Brain 1991;114:2191–202.

[12] Saxena S, Brody AL, Schwartz JM, Baxter LR. Neuroimaging and frontal-subcortical circuitry in obsessive-compulsive disorder. Br J Psychiatry 1998;35:26–38.
[13] Swedo SE, Schapiro MG, Grady CL. Cerebral glucose metabolism in childhood onset obsessive-compulsive disorder. Arch Gen Psychiatry 1989;46:518–23.
[14] Szeszko PR, Robinson D, Alvir JM, Bilder RM, Lencz T, Ashtari M, et al. Orbital frontal and amygdala volume reductions in obsessive-compulsive disorder. Arch Gen Psychiatry 1999; 56(10):913–9.
[15] Kuskowski MA, Malone SM, Kim SW, Dysken MW, Okaya AJ, Christensen KJ. Quantitative EEG in obsessive-compulsive disorder. Biol Psychiatry 1993;33:423–30.
[16] Leocani L, Locatelli M, Bellodi L, Fornara C, Henin M, Magnani G, et al. Abnormal pattern of cortical activation associated with voluntary movement in obsessive-compulsive disorder: an EEG study. Am J Psychiatry 2001;158(1):140–2.
[17] Mas F, Prichep LS, John ER, et al. Neurometric quantitative electroencephalogram subtyping of obsessive compulsive disorders. In: Mauer K, editor. Imaging of the brain in psychiatry and related fields. Berlin: Springer-Verlag; 1993. p. 277–80.
[18] Perros R, Young E, Ritson J, Price G, Mann P. Power spectral EEG analysis and EEG variability in obsessive-compulsive disorder. Brain Topogr 1992;4(3):187–92.
[19] Prichep LS, Mas F, John ER, et al. Neurometric subtyping of obsessive compulsive disorders in psychiatry: a world perspective. In: Stefanis CN, Rabavilas AD, Soldatos CR, editors. Proceedings of the VIII World Congress of Psychiatry. Athens, October 12–19, 1989. New York: Elsevier Science; p. 557–62.
[20] Prichep LS, Mas F, Hollander E, Liebowitz M, John ER, Almas M, et al. Quantitative electroencephalography (QEEG) subtyping of obsessive compulsive disorder. Psychiatr Res 1993;50(1):25–32.
[21] Silverman JS, Loychik SG. Brain-mapping abnormalities in a family with three obsessive-compulsive children. J Neuropsychiatr Clin Neurosci 1990;2:319–22.
[22] Simpson HB, Tenke CE, Towey JB, Liebowitz MR, Bruder GE. Symptom provocation alters behavioral ratings and brain electrical activity in obsessive-compulsive disorder: a preliminary study. Psychiatr Res 2000;95(2):149–55.
[23] Gehring WJ, Himle J, Nisenson LG. Action-monitoring dysfunction in obsessive-compulsive disorder. Psychol Sci 2000;11:1–6.
[24] Hajcak G, Simons RF. Error-related brain activity in obsessive-compulsive undergraduates. Psychiatry Res 2002;110:63–72.
[25] Malloy P, Rasmussen S, Braden W, Haier RJ. Topographic evoked potential mapping in obsessive-compulsive disorders: evidence of frontal lobe dysfunction. Psychiatry Res 1989; 28(1):63–71.
[26] Posner MI, Rothbart MK. Attention, self-regulation and consciousness. Philos Trans R Soc Lond B Biol Sci 1998;353:1–13.
[27] Ursu S, van Veen V, Siegle G, MacDonald A, Stenger A, Carter C. Executive control and self-evaluation in obsessive-compulsive disorder: an event-related fMRI study. Presented at the Cognitive Neuroscience Society Meeting. New York, March 2001.
[28] Heller W, Etienne MA, Miller GA. Patterns of perceptual asymmetry in depression and anxiety: implications for neuropsychological models of emotion and psychopathology. J Abnorm Psychol 1995;104:327–33.
[29] Heller W, Nitschke JB, Etienne MA, Miller GA. Patterns of regional brain activity differentiate types of anxiety. J Abnorm Psychol 1997;106(3):376–85.
[30] Wiedemann G, Pauli P, Dengler W, Lutzenberger W, Birbaumer N, Buckkremer G. Frontal brain asymmetry as a biological substrate of emotions in patients with panic disorders. Arch Gen Psychiatry 1999;56:78–84.
[31] Brown D, Scheflin AW, Hammond DC. Memory, trauma treatment, and the law. New York: WW Norton; 1998.
[32] Davidson RJ. Affective style and affective disorders: perspectives from affective neuroscience. Cognition and Emotion 1998;12:307–30.

[33] Davidson RJ. Emotion and affective style: hemispheric substrates. Psychol Sci 1992;3:39–43.
[34] Davidson RJ. Cerebral asymmetry, emotion and affective style. In: Davidson RJ, Hugdahl K, editors. Brain asymmetry. Boston: MIT Press; 1995. p. 361–87.
[35] Baehr E, Rosenfeld JP, Baehr R. The clinical use of an alpha asymmetry protocol in the neurofeedback treatment of depression: two case studies. J Neurotherapy 1997;2(3):10–23.
[36] Rosenfeld JP, Cha G, Blair T, Gotlib I. Operant biofeedback control of left-right frontal alpha power differences. Biofeedback Self Regul 1995;20:241–58.
[37] Henriques JB, Davidson RJ. Left frontal hypoactivation in depression. J Abnorm Psychol 1991; 100:534–45.
[38] Dawson G, Grofer Klinger L, Panagiotides H, Hill D, Spieker S. Frontal lobe activity and affective behavior of infants of mothers with depressed symptoms. Child Dev 1992;63:725–37.
[39] Dawson G, Grofer Klinger L, Panagiotides H, Spieker S, Frey K. Infants of mothers with depressed symptoms: electroencephalographic and behavioral findings related to attachment status. Dev Psychopathol 1992;4:67–80.
[40] Field T, Fox N, Pickens J, Nawrocki R. Relative right frontal EEG activation in 3- to 6-month-old infants of "depressed" mothers. Dev Psychopathol 1995;26:7–14.
[41] Jones NA, Field T, Fox NA, Lundy B, Davalos M. EEG activation in 1-month-old infants of depressed mothers. Dev Psychopathol 1997;9:491–505.
[42] Henriques JB, Davidson RJ. Regional brain electrical asymmetries discriminate between previously depressed and health control subject. J Abnorm Psychol 1990;99:22–31.
[43] Davidson RJ. Anterior electrophysiological asymmetries, emotion, and depression: Conceptual and methodological conundrums. Psychophysiology 1998;35:607–14.
[44] Goodman WK, McDougle CJ, Price LH. Pharmacotherapy of obsessive compulsive disorder. J Clin Psychiatry 1992;53(Suppl):29–37.
[45] Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, et al. The Yale-Brown obsessive ompulsive scale. I. Development, use, and reliability. Arch Gen Psychiatry 1989;46:1006–11.
[46] Goodman WK, Pricee LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, et al. The Yale-Brown obsessive compulsive scale. II. Validity. Arch Gen Psychiatry 1989;46:1012–6.
[47] Jenike MA, Baer L, Ballantine T, Martuza RL, Tynes S, Giriunas I, et al. Cingulotomy for refractory obsessive-compulsive disorder: a long-term follow-up of 33 patients. Arch Gen Psychiatry 1991;48:548–55.
[48] Hughes JR, John ER. Conventional and quantitative electroencephalography in psychiatry. J Neuropsychiatr Clin Neurosci 1999;11(2):190–208.
[49] Greist JH. Treatment of obsessive compulsive disorder: psychotherapies, drugs, and other somatic treatment. J Clin Psychiatr 1990;51(8):44–50.
[50] Ackerman DL, Greenland S. Multivariate meta-analysis of controlled drug studies for obsessive-compulsive disorder. J Clin Psychopharmacol 2002;22(3):309–17.
[51] Rauch SL. Neuroimaging research and the neurobiology of obsessive-compulsive disorder: where do we go from here? Biol Psychiatry 2000;47:168–70.
[52] DeRubeis RJ, Gelfand LA, Tang TZ, Simons AD. Medications versus cognitive behavior therapy for severely depressed outpatients: mega-analysis of four randomized comparisons. Am J Psychiatry 1999;156:1007–13.
[53] Antonuccio DO, Danton WG, DeNelsky G. Psychotherapy vs. medication for depression: challenging the conventional wisdom with data. Professional Psychology: Research and Practice 1995;26:574–85.
[54] Hollon SD, Shelton RC, Loosen PT. Cognitive therapy and pharmacotherapy for depression. J Consult Clin Psychol 1991;59:88–99.
[55] Foa EB, Franklin ME. Obsessive-compulsive disorder. In: Barlow DH, editor. Clinical handbook of psychological disorders. 3rd edition. New York: Guilford Press; 2001. p. 209–63.
[56] Whitsett SF, Lubar JF, Holder GS, et al. A double-blind investigation of the relationship between seizure activity and the sleep EEG following EEG biofeedback training. Biofeedback Self Regul 1982;7:183–209.

[57] Lubar JF. Neurofeedback for the management of attention deficit/hyperactivity disorders. In: Schwartz MS, editor. Biofeedback: a practitioner's guide. New York: Guilford Press; 1995. p. 493–522.
[58] Moore NC. A review of EEG biofeedback treatment of anxiety disorders. Clin Electroencephalogr 2000;31(1):1–6.
[59] Garrett BL, Silver MP. The use of EMG and alpha biofeedback to relieve test anxiety in college students. In: Wickramasekera I, editor. Biofeedback, behavior therapy, and hypnosis. Chicago: Nelson-Hall; 1976.
[60] Chambless DL, Baker MJ, Baucaom DH, Beutler LE, Calhoun KS, Crits-Christoph P, et al. Update on empirically validated therapies. Clin Psychol 1998;51(1):3–16.
[61] Chambless D, Hollon SD. Defining empirically supported therapies. J Consult Clin Psychol 1998;66:7–18.
[62] La Vaque TJ, Hammond DC, Trudeau D, Monastra V, Perry J, Lehrer P. Template for developing guidelines for the evaluation of the clinical efficacy of psychophysiological interventions. J Neurotherapy 2002;6(4):11–23.
[63] Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. N Engl J Med 2000;342(25):1878–86.
[64] Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 2000;342(25):1887–92.
[65] Britton A, McPherson K, KcKee M, Sanderson C, Black N, Bain C. Choosing between randomized and non-randomized studies: a systematic review. Health Technol Assess 1998; 2(13):1–124.
[66] Lurie P, Wolfe S. Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. N Engl J Med 1997;337(12):853–6.
[67] Rothman DJ. Ethical and social issues in the development of new drugs and vaccines. Bull N Y Acad Med 1987;63(6):557–68.
[68] La Vaque TJ, Rossiter T. The ethical use of placebo controls in clinical research: the Declaration of Helsinki. Appl Psychophysiol Biofeedback 2001;26(1):23–37.
[69] Linden M, Habib T, Radojevic V. A controlled study of the effects of EEG biofeedback on cognition and behavior of children with attention deficit disorder and learning disabilities. Biofeedback Self Regul 1996;21(1):35–49.
[70] Passini FT, Watson CG, Dehnel L, Herder J, Watkins B. Alpha wave biofeedback training therapy in alcoholics. J Clin Psychol 1977;33(1):292–9.
[71] Watson CG, Herder J, Passini FT. Alpha biofeedback therapy in alcoholics: an 18-month follow-up. J Clin Psychol 1978;34(2):765–9.
[72] Egner T, Gruzelier JH. Ecological validity of neurofeedback: modulation of slow wave EEG enhances musical performance. Neuroreport 2003;14(9):1221–4.
[73] Peniston EG, Kulkosky PJ. Alpha-theta brainwave neuro-feedback therapy for Vietnam veterans with combat-related post-traumatic stress disorder. Medical Psychotherapy 1991;4:47–60.
[74] Peniston EG, Marrinan DA, Deming WA, Kulkosky PJ. EEG alpha-theta synchronization in Vietnam theater veterans with combat-related post-traumatic stress disorder and alcohol abuse. Advances in Medical Psychotherapy 1993;6:37–50.
[75] Hammond DC. QEEG-guided neurofeedback in the treatment of obsessive compulsive disorder. Journal of Neurotherapy 2003;7(2):25–52.
[76] Hammond DC. Treatment of obsessional OCD with neurofeedback. Biofeedback 2004;32:9–12.
[77] Rosenfeld JP. EEG biofeedback of frontal alpha asymmetry in affective disorders. Biofeedback 1997;25(1):8–25.
[78] Baehr E, Rosenfeld JP, Baehr R. Clinical use of an alpha asymmetry neurofeedback protocol in the treatment of mood disorders: follow-up study one to five years post therapy. Journal of Neurotherapy 2001;4(4):11–8.
[79] Allen JJ, Iacono WG, Depue RA, Arbisi P. Regional electroencephalographic asymmetries in bipolar seasonal affective disorder before and after exposure to bright light. Biol Psychiatry 1993;33:642–6.

[80] Gotlib IH, Ranganath C, Rosenfeld JP. Frontal EEG alpha asymmetry, depression, and cognitive functioning. Cognition and Emotion 1999;12:449–78.
[81] Kwon JS, Youn T, Jung HY. Right hemisphere abnormalities in major depression: quantitative electroencephalographic findings before and after treatment. J Affect Disord 1996;40:169–73.
[82] Hammond DC. Neurofeedback treatment of depression with the Roshi. Journal of Neurotherapy 2000;4(2):45–56.
[83] Hammond DC. Neurofeedback treatment of depression and anxiety. J Adult Dev, in press.
[84] Hammond DC, Stockdale S, Hoffman D, Ayers ME, Nash J. Adverse reactions and potential iatrogenic effects in neurofeedback training. Journal of Neurotherapy 2001;4(4):57–69.
[85] Hardt JV, Kamiya J. Anxiety change through electroencephalographic alpha feedback seen only in high anxiety subjects. Science 1978;201:79–81.
[86] Feinstein B, Sterman MB, MacDonald LR. Effects of sensorimotor rhythm training on sleep. Sleep Research 1974;3:134.
[87] Sterman MB. Effects of sensorimotor EEG feedback on sleep and clinical manifestations of epilepsy. In: Beatty J, Legewie H, editors. Biofeedback and behavior. New York: Plenum Press; 1977. p. 167–200.
[88] Sterman MB, Howe RD, Macdonald LR. Facilitation of spindle-burst sleep by conditioning of electroencephalographic activity while awake. Science 1970;167:1146–8.
[89] Duffy FH. The state of EEG biofeedback therapy (EEG operant conditioning) in 2000: an editor's opinion [editorial]. Clin Electroencephalogr 2000;31(1):v–viii.