

Foundation and Practice of Neurofeedback for the Treatment of Epilepsy

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This review provides an updated overview of the neurophysiological rationale, basic and clinical research literature, and current methods of practice pertaining to clinical neurofeedback. It is based on documented findings, rational theory, and the research and clinical experience of the authors. While considering general issues of physiology, learning principles, and methodology, it focuses on the treatment of epilepsy with sensorimotor rhythm (SMR) training, arguably the best established clinical application of EEG operant conditioning. The basic research literature provides ample data to support a very detailed model of the neural generation of SMR, as well as the most likely candidate mechanism underlying its efficacy in clinical treatment. Further, while more controlled clinical trials would be desirable, a respectable literature supports the clinical utility of this alternative treatment for epilepsy. However, the skilled practice of clinical neurofeedback requires a solid understanding of the neurophysiology underlying EEG oscillation, operant learning principles and mechanisms, as well as an in-depth appreciation of the ins and outs of the various hardware/software equipment options open to the practitioner. It is suggested that the best clinical practice includes the systematic mapping of quantitative multi-electrode EEG measures against a normative database before and after treatment to guide the choice of treatment strategy and document progress towards EEG normalization. We conclude that the research literature reviewed in this article justifies the assertion that neurofeedback treatment of epilepsy/seizure disorders constitutes a well-founded and viable alternative to anticonvulsant pharmacotherapy.

KEY WORDS: neurofeedback; neurotherapy; EEG; operant conditioning; epilepsy.

BACKGROUND

The origins of neurofeedback for the treatment of clinical disorders can be directly traced to the first systematic demonstration of EEG operant conditioning in general (for an in-depth review, see Sterman, 1996). In the context of sleep research, Sterman and associates conducted a series of studies investigating learned suppression of a previously rewarded cup-press response for food in cats (Roth, Sterman, & Clemente, 1967; Sterman

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& Wyrwicka, 1967; Sterman, Wyrwicka, & Roth, 1969; Wyrwicka & Sterman, 1968). During learned suppression of this response, the appearance of a particular EEG rhythm over sensorimotor cortex emerged above non-rhythmic low-voltage background activity. This rhythm was characterized by a frequency of 12–20 Hz, not unlike EEG sleep spindles, with a spectral peak around 12–14 Hz, and has been referred to as the “sensorimotor rhythm” (SMR) (Roth et al., 1967). The investigators decided to study this distinct rhythm directly, attempting to apply the operant conditioning method to see if cats could be trained to voluntarily produce SMR, by making a food reward contingent on SMR production. Cats easily accomplished this feat of EEG self-regulation, and the behavior associated with SMR production was one of corporal immobility, with SMR bursts regularly preceded by a drop in muscle tone (Sterman et al., 1969; Wyrwicka & Sterman, 1968).

In a serendipitous twist, Sterman’s laboratory was soon afterwards commissioned to establish dose–response functions of a highly epileptogenic fuel compound. When employing the cats that had previously taken part in SMR conditioning as experimental animals, these cats were found to display significantly elevated epileptic seizure thresholds compared to untrained animals, suggesting that SMR training had somehow inoculated the cats against experiencing seizures. Subsequently, this research was successfully extrapolated to humans, where it was repeatedly documented that seizure incidence could be lowered significantly (or on rare occasions abolished) by SMR feedback training (see Section Clinical Findings with Epilepsy).

Owing to its close link to intracranial recordings in animals, the neurogenesis of SMR is fairly well-understood. SMR appears to emanate from the ventrobasal nuclei (nVB) of the thalamus (Howe & Sterman, 1972), which are generally concerned with conducting afferent somatosensory information (Fig. 1). During conditioned SMR production, nVB firing patterns shift from fast and non-rhythmic (tonic) discharges to systematic, rhythmic bursts of discharges (Harper & Sterman, 1972), which in turn are associated with suppression of somatosensory information passage (Howe & Sterman, 1973) and reduction in muscle tone. Upon reduction of afferent somatosensory input, the nVB cells hyperpolarize. Instead of remaining at a stable level of inhibition, however, a gradual depolarization mediated by a slow calcium influx causes the nVB neurons to discharge a burst of spikes, which are relayed to sensorimotor cortex and thalamic reticular nucleus (nRT) neurons. Stimulation of the latter in turn leads to a GABAergic inhibition of VB relay cells, thus returning them to a hyperpolarized state and initiating a new cycle of slow depolarization. In this way, the interplay between neuronal populations in nVB, nRt, and sensorimotor cortex results in rhythmic thalamocortical volleys and consequent cortical EEG oscillations.

While attenuation of efferent motor and afferent somatosensory activity can initiate SMR, the oscillatory activity is also largely influenced by non-specific cholinergic and monoaminergic neuromodulation, which can affect excitability levels both in thalamic relay nuclei and in the cortical areas receiving the relayed signals. During waking activity, the neuromodulator influences as well as cortical projections normally keep VB cells depolarized and thus suppress rhythmic bursting patterns, while during behavioral stillness, oscillations at SMR frequency may be observed. As SMR constitutes the dominant “standby” frequency of the integrated thalamocortical somatosensory and somatomotor pathways, operant training of SMR is assumed to result in improved control over excitation in this system. Increased thresholds for excitation in turn are thought to underlie the clinical benefits of SMR training in epilepsy and other disorders characterized by cortical and/or thalamocortical hyper-excitability. For instance, SMR training has been shown to be an

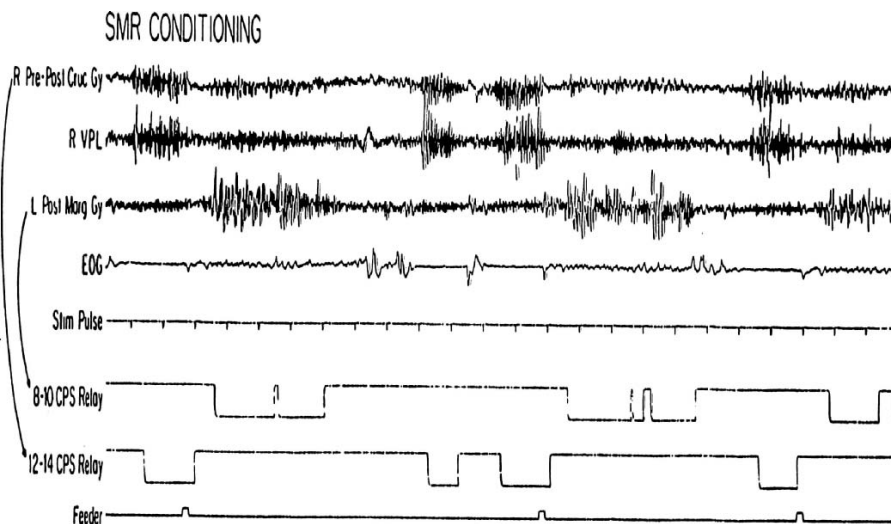


Fig. 1. Sample of recorded sensorimotor EEG (*top*), nVB activity (RVPL). Posterior cortical EEG (R Post. Marg Gy), electro-oculogram (EOG), and timing, relay and feeder indicators during SMR training in a cat. Note correspondence in SMR between cortical EEG and VPL activity, reflecting origin of the SMR EEG rhythm in thalamus. Note also that eye movement activity ceased during SMR. Additionally, it can be seen that each rewarded burst of SMR is followed by a slower rhythmic pattern in posterior cortex, labeled as “post-reinforcement synchronization”, or PRS (from Howe & Serman, 1972).

effective treatment of attention deficit hyperactivity disorder (ADHD) (Fuchs, Birbaumer, Lutzenberger, Gruzelier, & Kaiser, 2003; Monastra, Monastra, & George, 2002; Rossiter & LaVaque, 1995; for a recent review see Monastra et al., 2005) and has furthermore been documented to result in reduced impulsive response tendencies in healthy volunteers (Egner & Gruzelier, 2001, 2004).

More recently, fMRI studies in human subjects have shown that the SMR EEG pattern is clearly associated with an increase in metabolic activity in the striatum of the basal ganglia nuclear complex (Birbaumer, 2005). Further, examining fMRI changes in children with ADHD who improved significantly in cognitive tests after SMR neurofeedback training, Lavesque and Beauregard (2005) have observed a specific and significant increase in metabolic activity in the striatum. Collectively, these findings support the notion that the state changes underlying the SMR are associated with functional changes in the striatum.

The striatum, which is the anterior component of the basal ganglia, has been characterized anatomically as a system of fiber connections, which form a loop from cerebral cortex and back to cerebral cortex via thalamic relays (Brodal, 1992). The two major components of the striatum include the putamen/globus pallidus complex and the caudate nucleus. The striatum has been attributed a role in managing background motor tone and the planning phase of movements (Chevalier & Deniau, 1990; DeLong, 1990). The putamen provides an inhibitory input to the globus pallidus. When the putamen is *excited* by pre-motor and sensorimotor cortex the globus pallidus, which functions to inhibit various thalamic relay nuclei projecting back to motor and pre-motor cortex, is itself inhibited, thus releasing excitatory input to motor and sensorimotor cortex via the thalamic relays. When input to

the putamen from the sensorimotor cortex is *reduced*, as would be expected during SMR activity, the globus pallidus becomes more *active*, thereby imposing inhibition upon its thalamic relays to motor cortex. This inhibition would alter involuntary motor regulation, reducing muscle tone and the intention to move.

Consistent with an activation of striatal inhibitory mechanisms, the studies mentioned earlier have documented a reduction in background motor tone, reflex excitability, and activity in extrapyramidal motor pathways during SMR bursts (Babb & Chase, 1974; Chase & Harper, 1971; Harper & Serman, 1972; Serman & Wyrwicka, 1967; Serman et al., 1969). It is also evident that both animals and humans suppress the intention to move (Serman, 1996). This convergence of findings suggests that facilitation and/or regulation of the SMR substrate alters motor output, and sets the stage for reduced proprioceptive afferent input to thalamus. The important fact here may be that this reorganization of motor and thalamic status is accompanied by volleys of strong oscillatory discharge to cortex with each trained SMR response (for example, see Fig. 1), the relevance of which derives from a different and highly significant area of investigation.

Findings in the study of synaptic mechanisms mediating experience-based neuronal reorganization, and thus learning, provide an appealing theoretical basis for a potentially unique consequence of SMR training (Serman, 2005). Many studies have shown that strong, repetitive afferent input to cortical and other forebrain neurons can promote increased synaptic strength in relevant circuits (see reviews by Abel & Lattal, 2001; Malenka & Nicoll, 1999; Soderling & Derkach, 2000; Walker, 2005). These changes, produced over time by protein synthesis and the insertion of new excitatory transmitter channels at post-synaptic receptor sites, result in a synaptic state called “long-term potentiation”, or LTP. Under appropriate circumstances LTP increases synaptic sensitivity and the probability of future activation in affected neuronal circuits.

The thalamocortical oscillatory volleys underlying the SMR constitute recurrent bursts of strong afferent discharge to sensorimotor cortex. This recurrent discharge arrives on the apical dendrites of cortical pyramidal cells in layer 4 of this cortical area. The unique timing and location of these strong, recurrent afferent bursts appears to be particularly significant. Activation of distal portions of these same pyramidal neurons must accompany this input due to the requisite attention associated with SMR conditioning. This convergence of excitation provides a potentially ideal milieu for LTP and synaptic reorganization, consistent with recent concepts of “coincidence detection” and synaptic plasticity (Froemke, Poo, & Dan, 2005). That is, the coincidence of strong thalamic afferent input near the pyramidal cell body and back-depolarization from cognitively based distal excitation of the *same cell*, magnifies local depolarization and subsequent LTP. Thus, the functional changes in sensorimotor circuits mediating the discrete and recurrent onset of SMR activity in the EEG may be *specifically strengthened* during feedback training through a progressive potentiation process, resulting in a lasting decrease in sensorimotor excitability. Such changes presumably would not occur during spontaneous sensorimotor rhythmic activity due to the absence of coincident cognitive engagement.

There is abundant indirect evidence that such changes can indeed occur with SMR operant conditioning. For example, when cats were provided with several weeks of SMR training and then subjected to an extinction trial where the reward was withheld, there was a marked increase in the expression of SMR activity during the initial period of extinction

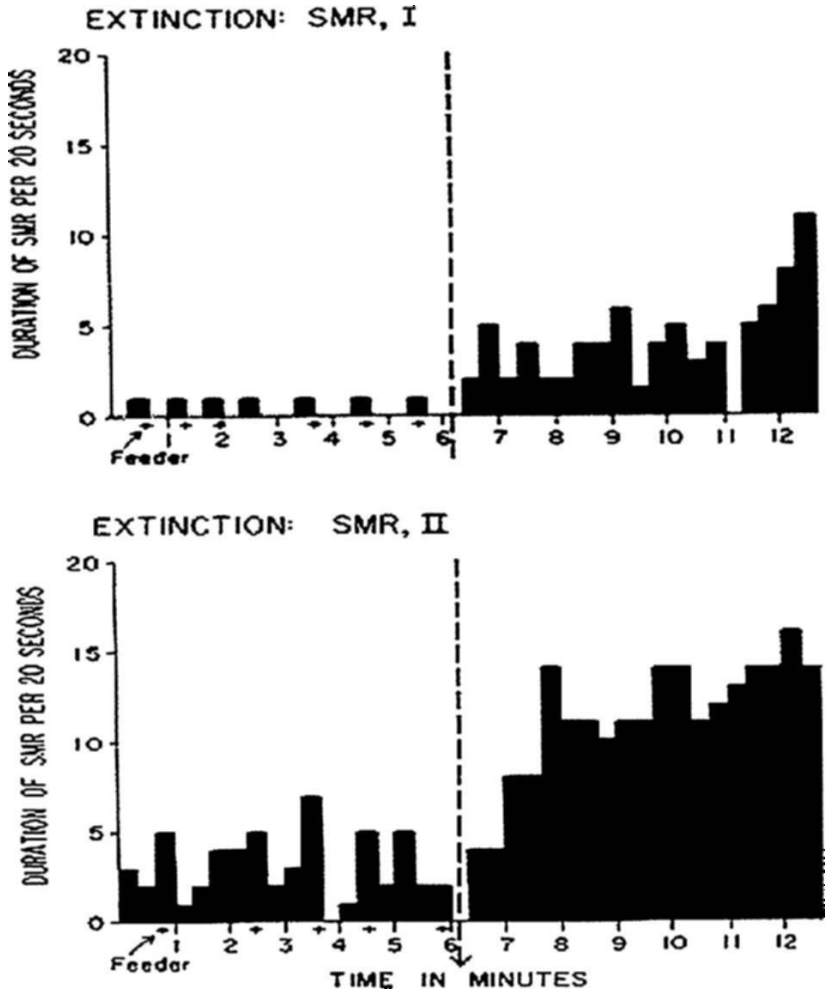


Fig. 2. Plots showing the output of SMR in the EEG of a cat per 20 s over 6 min periods of feedback training prior to and after an extinction test where the milk reward was withheld (dashed vertical line). Feeder operation on variable interval schedule is indicated by plus marks under abscissa. Plot at the top shows performance after approximately 1 month of 3/week training sessions. Plot at the bottom shows identical trial after 3 months of training. Note that despite stable SMR performance and marked increase with extinction early in training, output during both performance and extinction is significantly increased after extended training (from Wyrwicka & Serman, 1968).

(Fig. 2). Such an increase is expected with true operant conditioning. However, when an identical test was performed after several more months of training both the output of SMR during rewarded trials and the response to the extinction procedure were significantly, and in fact dramatically, increased. Additionally, studies in both animals and humans have found that sleep recordings obtained after several months of SMR training were characterized by a lasting increase in sleep spindle density when compared with pre-training recordings

(Hauri, 1981; Serman, Howe, & Macdonald, 1970; Serman & Macdonald, 1978). Control feedback conditions had no such effect.

A second EEG oscillation associated with SMR conditioning is seen after reward is delivered, in the form of “post-reinforcement synchronization” (PRS), as shown in Fig. 1. In animal studies, the incidence and magnitude of PRS has been found to be directly related to the desirability of the reward (Serman & Wyrwicka, 1967) and the rate of learning in an operant conditioning task (Marczynski, Harris, & Livezey, 1981). Similar patterns have been seen in humans as well (Serman, 2005; Serman, Kaiser, & Veigel, 1996). While beyond the scope of this review, other neurophysiological findings have linked the PRS to a transient suppression of arousal accompanying positive rewards in several learning contexts. We propose that it provides an operational definition for drive reduction (Serman, 2005). It is suggested further that, through additional LTP development, this EEG oscillation following a correct operant response supports stabilization and further consolidation of the emerging acquisition process.

To summarize, SMR activity reflects synchronized thalamocortical oscillations initiated by reduced proprioceptive input to ventrobasal thalamus, resulting from decreased background muscle and reflex tone and suppressed movement. In the context of directed attention, these oscillations project strong afferent volleys to cortical target neurons, which result in a cascade of LTP-enhanced motor alterations. These changes are stabilized and consolidated over time. This “unconscious” learning process is further stabilized through arousal reduction and related EEG oscillations following reward in the form of PRS. This enhancement appears to be progressive and sustained, effecting function beyond the neurofeedback context.

It should be noted that a different neurofeedback approach, based on the measurement of “slow cortical potential” (SCR) shifts (between positive and negative polarity) has also proved successful in the treatment of epilepsy (e.g., Kotchoubey et al., 1999, 2001; Rockstroh et al., 1993). Conceptually, SCP and SMR neurofeedback share the same goal of reducing cortical excitability. As negative slow potentials are reflective of lowered excitation thresholds (through depolarization) in the apical dendrites of cortical pyramidal neurons, while positive slow potentials represent raised excitation thresholds (for a review, see Birbaumer, 1997), SCP training in epileptics is aimed at enabling the patient to voluntarily produce cortical inhibition (i.e., positive SCPs), and thus interrupt seizure onset. Interestingly, Birbaumer (2005) also reports that both the SMR pattern in the EEG and learned increases in positive SCPs were associated with increased metabolic activity in the striatum of the basal ganglia, suggesting a convergent effect of SMR and SCP training (Birbaumer, 2005, also personal communication).

However, as SCP neurofeedback is only now gaining increased attention and is not very commonly employed by clinicians, the current review will focus exclusively on the more widely used SMR neurofeedback. Further, we shall focus on SMR neurofeedback in the treatment of epilepsy, primarily because this treatment has now been so well-documented that the American Academy of Child and Adolescent Psychiatry (AACAP) considers neurofeedback for seizure disorders to meet criteria for “Clinical Guidelines” of evidence-based treatments, a recommendation that states that a particular practice should always be considered by the clinician. As a comparison example, the same criterion is met by stimulant medication treatment for ADHD (see Hirshberg, Chiu, & Frazier, 2005), a treatment that is abundantly and perhaps excessively utilized today.

CLINICAL FINDINGS WITH EPILEPSY

Since the first single-case study, reported over 30 years ago (Sterman & Friar, 1972), a fair number of controlled clinical studies, stemming from many different laboratories, have produced consistent data on the efficacy of SMR training in epileptic patients. It is particularly noteworthy that these results have been achieved in an extremely difficult subgroup of epilepsy patients, those with poorly controlled seizures who had proven unresponsive to pharmacological treatment. We will here provide only a cursory overview of this clinical research literature. For a more detailed treatment the interested reader is referred to Sterman (2000), while other recent summaries have also been provided by Monderer, Harrison, and Haut (2002) and Walker and Kozlowski (2005).

In initial studies involving relatively small sample sizes and pre-treatment baseline measures as a control condition, on average 80% of patients trained at enhancing SMR amplitudes were shown to display significant clinical improvements (Kaplan, 1975; Seifert & Lubar, 1975; Sterman, MacDonald, & Stone, 1974). For instance, Cott, Pavloski, and Black (1979) reported that 3 months of SMR training was associated with significantly reduced seizure incident in five out of seven patients who had previously suffered from very poorly controlled seizures. These high success rates of SMR training were further confirmed in investigations that employed more elaborate control conditions, such as non-contingent, or random feedback (Finley, Smith, & Etherton, 1975; Kuhlman & Allison, 1978; Quy, Forrest, & Hutt, 1979; Wyler, Robbins, & Dodrill, 1976). In addition, a number of investigations employing ABA crossover designs have emphasized the causal and frequency-specific nature of SMR training, by documenting symptom reversal when reversing training contingencies (Lubar & Bahler, 1976; Lubar et al., 1981; Sterman & MacDonald, 1978). In a larger scale study ($n = 24$), Lantz and Sterman (1988) employed a double-blind design, with age- and seizure-matched patients assigned to either a contingent training schedule of enhancing 11–15 Hz SMR activity (while simultaneously inhibiting slower and higher frequencies), a non-contingent, “yoked control” training schedule, or a waiting list control group. Significant reduction of seizure incidence with a median of 61% (range 0–100%) was found in the contingent SMR feedback group only. In the largest study to date, Andrews and Schonfeld (1992) documented clinical improvements from pre-treatment baseline in 69 out of 83 patients participating in a mixed relaxation and SMR feedback protocol.

In reviewing the data accumulated in these studies, Sterman (2000) found that 82% of 174 participating patients who were otherwise not controlled had shown significantly improved seizure control (defined as a minimum of 50% reduction in seizure incidence), with around 5% of these cases reporting a complete lack of seizures for up to 1 year subsequent to training cessation. While existing studies have thus produced overwhelmingly positive results, it has to be pointed out that additional replications are still highly desirable. For a very promising treatment targeting such a serious condition as epilepsy, the number of large-scale clinical trials of neurofeedback training to date is disappointing. A likely reason for this state of affairs is that neurofeedback research is a very time- and work-intensive enterprise that has traditionally not received extensive research funding and has, for obvious reasons, not been pursued by the pharmaceutical industry. Nevertheless, the research literature as it stands today in our view provides very good grounds for considering neurofeedback training a valuable treatment option, particularly in drug non-responders.

NEUROFEEDBACK TODAY

Neurofeedback therapy has been greatly aided by advances in computer technology and software. However, the ease in the development of new software programs for feedback functionality and displays, together with the entry into the field of a diverse group of professionals and semi-professionals, has led to an unfortunate lack of consensus on methodology and standards of practice. In turn this has contributed to reluctance by the academic and medical communities to endorse the field.

Based on the history outlined above, the practice of neurofeedback requires a fundamental understanding of the principles of relevant neurophysiology, operant conditioning, neuropathology, and, ultimately, basic clinical skills. Concerning the latter, the unique opportunity for extended contact with the client provided by this modality favors skilled clinical insight and guidance. Further, since objective EEG, operant performance, and clinical outcome data are the realm of neurofeedback, documentation and accountability can and must be its coin. While some who practice neurofeedback pursue different models, this review and its recommendations will be restricted to a consideration of practice that respects and adheres to these principles.

Rational standards require that the neurofeedback treatment plan begins with a comprehensive quantitative EEG study (qEEG). This involves the collection of appropriate samples of EEG data from at least 19 standardized sites over the cerebral cortex (placement according to the International 10/20 System) during states of rest with eyes closed and open, and states of task engagement, such as reading, visuo-spatial tracking, memory recall, and problem-solving. These data are then digitized and subjected to frequency and amplitude analysis using various versions of spectral transform and database procedures (Etevenon, 1986; Johnston, Gunkelman, & Lunt, 2005; Lorensen & Dickson, 2004). Quantitative and descriptive data exhibiting the magnitude or its squared derivative, spectral power, as well as the distribution of relevant frequencies recorded during these conditions, are then displayed as tables and graphics and compared statistically with group data from an appropriate normative database. Deviant local patterns, as well as disturbed interactions among sites, can be identified through this analysis and used to direct neurofeedback training strategy. Recent improvements to this methodology have reduced distortions produced by non-EEG events (artifacts), biological cycles, and certain mathematical and statistical corruptions (Kaiser & Serman, 2001, 2005). The importance of accuracy in this analysis cannot be overemphasized, since these findings will guide the development of neurofeedback treatment strategies and, in turn, determine the quality of its application. Follow-up qEEGs after a course of neurofeedback training can then provide for an objective assessment of EEG changes related to treatment outcomes.

An example of a statistically significant deviant frequency pattern from a 37-year-old epileptic patient is shown in Fig. 3. This patient suffered from a documented seizure focus in the left temporal lobe and adjacent areas caused by a severe blow to the head. The brain map shown are from the qEEG analysis program of the Serman–Kaiser Imaging Laboratory (SKIL). Plotted is the distribution of mean spectral magnitudes in five frequency bands across 19 standard sites. Data were derived from three minute EEG recordings with the eyes open, and are compared statistically with an age-matched normative database. Prior to treatment (top) statistically significant and clearly abnormal magnitude increases can be seen in left temporal lobe at both 5–7 and 7–9 Hz frequencies. Adjacent central cortical and

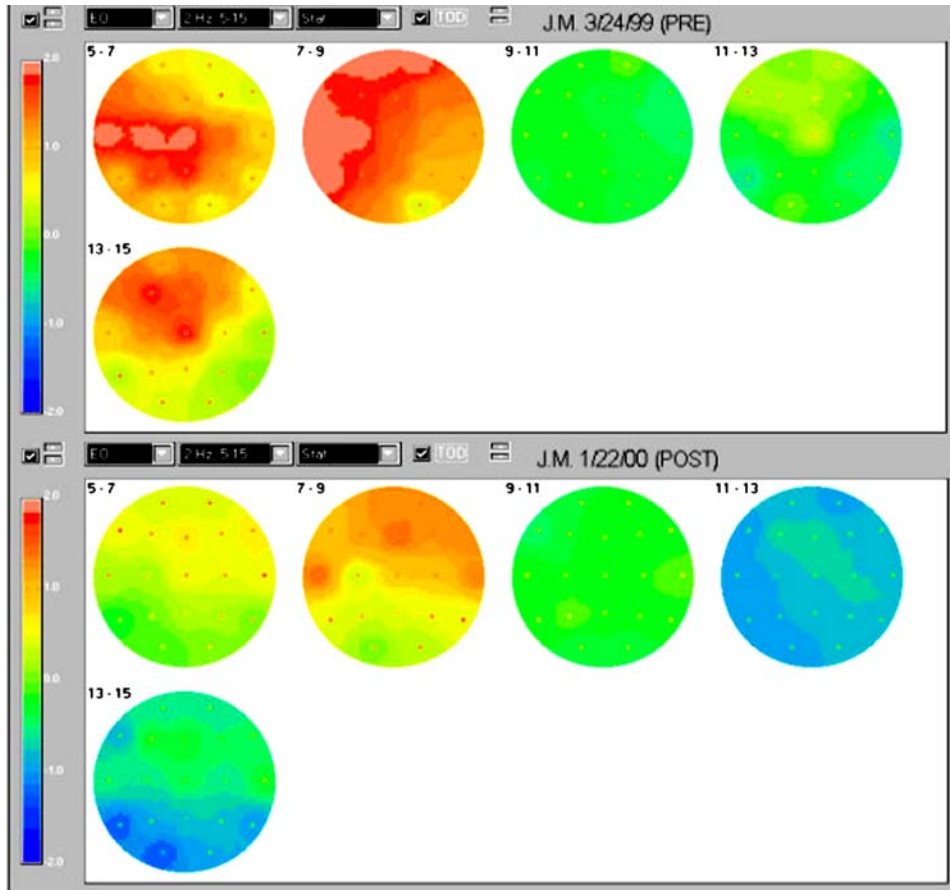


Fig. 3. Brain maps from eyes open data showing mean spectral magnitude distributions of five 3 Hz bands both before and after neurofeedback training in a patient with partial-complex seizures secondary to brain injury. Color scale at the left indicates database variance distribution as standard deviation. Pink areas show ≥ 2 standard deviations. Prior to the treatment, there was significantly elevated abnormal activity at left centro-temporal and pre-frontal cortex in 5–7 and 7–9 Hz bands. After treatment, approximately 1 year later, an identical study showed complete normalization. See text for details.

pre-frontal areas were corrupted as well. The neurofeedback treatment strategy employed and the clinical outcome of this case is discussed below. It is important to note that this strategy was based on the relevance of the SMR and the guidance of the qEEG findings, both of which were essential for a truly functional approach to treatment.

The hardware and software used in the application of neurofeedback training strategy should provide for the collection and evaluation of quality EEG signals needed both for qEEG data acquisition and valid operant conditioning. A variety of equipment options is available for qEEG recording, with a broad range of pricing, depending on component quality and software functionality. It is important to note, however, that the more expensive systems have been developed for research and medical applications, and were not designed to address the assessment issues relevant to neurofeedback. This is, of course, more a function of software than hardware.

Most systems provide for the collection of valid EEG data but the interested professional should do their homework in understanding and inquiring about such important issues as amplifier noise, dynamic range, sampling rate, and filter settings.

The objective of the qEEG for neurofeedback treatment is to provide for the detection and frequency/topography characterization of relevant EEG pathology. Analysis software should thus give an accurate indication of localized frequency and topographic deviations, and disturbances in the functional coordination of these variables among brain regions, as indicated by metrics such as coherence or comodulation (Serman & Kaiser, 2001; Thatcher, 1992). It is important, however, to point out that the power transform (squaring of magnitudes) is never used for neurofeedback treatment. Accordingly, some programs avoid using this transform in the qEEG analysis, expressing data only as magnitude. This correction also prevents the excessive skewing which results from squaring of EEG values, and thus increases statistical validity (Kaiser, 2000; Serman, Mann, Kaiser, & Suyenobu, 1994). Additionally, accurate specification of both normal and abnormal frequencies requires analysis based on single frequency bins, and avoid the traditional bands such as “theta” and “alpha”. These traditional “clinical bands” overlook significant individual differences, and often distort the accuracy of relevant frequency specification (Kaiser, 2001; Klimesch, Schimke, & Pfurtscheller, 1993).

Software used for neurofeedback training should be based on the need to apply meaningful operant conditioning procedures to training objectives. A well established scientific literature dictates the functional characteristics required for effective operant conditioning. For example, feedback training should be configured to provide for discrete trials, a fundamental element of both classical and operant conditioning (Brogden, 1951; Ferster & Skinner, 1957). That is, each rewarded response is an independent event, followed by at least a brief pause prior to the next effort. Additionally, empirical data have demonstrated that the response and reward must be truly contingent for optimal learning to occur, with reward immediately following response (Felsing, Gladstone, Yamaguchi, & Hull, 1947; Grice, 1948). Further, events associated with both response and reward must not contain content that can block or overshadow the desired EEG response (Pearce & Hall, 1978; Williams, 1999). For example, a visual or auditory stimulus just preceding reward but not related to the desired EEG response may acquire much of the reinforcement effect of the reward. These requirements may not be met by all developers of neurofeedback programs, and deserve close scrutiny by the potential customer. Finally, and perhaps of equal importance to the technical issues discussed above, software programs and training strategies should stress exercise rather than entertainment, at least most of the time.

By definition, neurofeedback treatment for seizure disorders is today directed by the pattern of EEG pathology detected through qEEG analysis, and by an appreciation for the anti-epileptic effects of SMR training. Concerning the former, there are many different ways in which seizure pathology may manifest in the EEG. Also, the EEG can be significantly affected by the anticonvulsant medications taken by the patient.

Atypical slow or fast EEG patterns may be observed. In some cases, these are accompanied by such transients as spike-and-wave discharge, sharp waves, or poorly organized, high-amplitude events termed paroxysms, all of which should be noted but deleted from the qEEG analysis in order to focus training on the more stable background EEG. Knowledge of these EEG characteristics and complexities is essential for the appropriate application of neurofeedback treatment. However, despite corruption produced by medications, the literature in this field indicates that feedback strategies directed to the suppression of either

background and/or transient abnormal patterns, together with the enhancement of central cortical SMR activity, results in the most effective therapeutic outcomes (for review see Sterman, 2000).

Often the EEG abnormality disclosed by the qEEG is rather specific. For example, in the case described above the most relevant pathology observed was essentially restricted to the left centro-temporal area (Fig. 3, top), where the cranial impact was delivered. This injury resulted in localized cortical hyper-excitability, with cognitive disturbances and the emergence of partial-complex seizures. This patient had been a high-level administrator at a financial institution, and was unable to resume work at the time he entered neurofeedback treatment. He experienced memory difficulties and emotional lability due to this injury, and felt slowed by the anticonvulsant medications prescribed. He wanted to get his life back together.

Data from the eyes open qEEG were selected for neurofeedback guidance, since this most approximated the training condition (Fig. 3). However, it should be pointed out that a similar pattern of abnormality was seen in task states as well. The most affected frequency range was between 6 and 8 Hz, which was significantly elevated. Thus, neurofeedback treatment involved the suppression of 6–8 Hz activity from the left anterior temporal site T3, while simultaneously increasing 12–15 Hz activity at the adjacent medial central site C3. Rewards were obtained only when both conditions were met for at least a quarter of a second.

One-hour treatment sessions were provided twice per week for the first 6 weeks and then once per week for the next 30 weeks. The equipment and procedures used conformed to all of the principles discussed above. The display presented to the patient included two adjacent vertical bars, one dark blue and the other light blue in color. He was required to suppress the light blue bar (6–8 Hz activity at T3) below an established threshold line set at 20% less than his baseline mean value, while raising the dark blue bar (12–15 Hz activity at C3) to a threshold line at least 20% above baseline. If both of these objectives were achieved simultaneously a counter in the top-center of the screen advanced one digit and the unit sounded a pleasant tone. The system paused for 2 s and the task was repeated. Prior to each in a series of sequential 3 min sets, the patient specified a numerical goal in the final count for that set. At appropriate intervals the thresholds were adjusted to increase the challenge and achieve “shaping” of the desired EEG response pattern.

Other display material can be used for neurofeedback as well. Puzzles, engaging picture sequences, stop/start video clips, and other action themes have been used. These materials can be used to focus initial attention on the task for some patients, or as occasional alternatives to more simple displays like that described here. However, the issue of exercise versus entertainment mentioned above is relevant in this regard. The patient should be motivated to view the task much like a workout at a gym, and the feedback objectives as a special exercise for the brain. Discrete trials with simple but relevant displays achieve this best.

The patient described above completed 42 training sessions. His seizure rate, which had previously averaged 2–4 per week, declined progressively after the first month or so of treatment to less than 2 per month. Some 4 months into the training he was involved in a court case with serious personal implications. During these proceedings his seizure rate again increased. This was to be expected due to the stress and related sleep loss caused by these circumstances, since seizure disorders are at best managed but only rarely cured. Subsequent to this disturbance his seizure rate again declined, and he experienced prolonged

seizure-free periods. His medications were reduced and he was able to return to work and resume a more or less normal life. A follow-up qEEG obtained approximately 1 year after the beginning of treatment showed no focal abnormalities, and a complete normalization of quantitative EEG characteristics (Fig. 3, bottom).

This case was rather straightforward, and was not complicated by co-morbidities, a long history of failed medications and their side effects, behavioral or economic adaptations, or other disruptive factors. In general, patients seeking this remedy often present such complications, a reality that necessitates cooperation with the neurologist and other professionals associated with the case, as well as a competent appreciation for, and attention to, family and personal dynamics. But perhaps the most important variable determining the success of neurofeedback is the clinician's ability to instill a motivation to succeed in the patient. Unlike operant conditioning of behavioral responses, where the organism has a conscious awareness of the responses leading to rewards, with neurofeedback the response is a subtle pattern of physiological changes of which the subject has little or no direct experience. The drive to obtain a symbolic reward results in the reinforcement that ultimately strengthens this response. This is where neurofeedback differs from traditional operant conditioning, and why refined methodology, clear and meaningful rewards, proper preparation of the patient, and appropriate clinical skills are essential.

It is important to point out that most of the epileptic patients who have participated in neurofeedback research studies and many who seek this treatment today represent unquestionable failures of anticonvulsant drug therapies, particularly with complex-partial seizure disorders. It is particularly noteworthy that positive outcomes have often been obtained in the context of treating this extremely difficult sub-population of epilepsy patients. We view it as unfortunate, therefore, that some professionals still criticize neurofeedback treatment for the lack of more consistent or successful outcomes. On the contrary, evidence has shown that most of these difficult patients benefit beyond any chance or placebo outcome, and some do so dramatically. Considering the common side effects and costs associated with life-long pharmacotherapy, we do not view neurofeedback treatment as a "last resort" option for drug treatment-resistant cases only, but rather as a generally viable alternative consideration for any patient suffering from seizures. Furthermore, in contrast to drug-dependent symptom management, the altered modulation of thalamocortical excitability through neurofeedback training may raise seizure thresholds sufficiently to greatly improve the prospects for the long-term, non-dependent management of epilepsy. It must be added, however, that the skilled application of neurofeedback requires a committed, well-trained, and motivationally adept professional.

REFERENCES

- Abel, T., & Lattal, K. M. (2001). Molecular mechanisms of memory acquisition, consolidation and retrieval. *Current Opinion in Neurobiology*, *11*, 180–187.
- Andrews, D. J., & Schonfeld, W. H. (1992). Predictive factors for controlling seizures using a behavioral approach. *Seizure*, *1*(2), 111–116.
- Babb, M. I., & Chase, M. H. (1974). Masseteric and digastric reflex during conditioned sensorimotor rhythm. *Electroencephalography and Clinical Neurophysiology*, *36*, 357–365.
- Birbaumer, N. (1997). Slow cortical potentials: Their origin, meaning, and clinical use. In G. J. M. Bostel & K. B. E. von Böcker (Eds.), *Brain and behaviour—past, present and future* (pp. 25–39). Tilborg: University Press.

- Birbaumer, N. (2005). Breaking the silence: Brain–computer interfaces in paralysis. *Proceedings of the Annual Conference, Int. Soc. for Neuronal Reg.*, 13, 2.
- Brodal, P. (1992). The basal ganglia. In *The central nervous system: Structure and function* (pp. 246–261). New York: Oxford University Press.
- Brogden, W. J. (1951). Animal studies of learning. In S. S. Stevens (Ed.), *Handbook of experimental psychology* (pp. 568–612). New York: Wiley.
- Chase, M. H., & Harper, R. M. (1971). Somatomotor and visceromotor correlates of operantly conditioned 12–14 c/s sensorimotor cortical activity. *Electroencephalography and Clinical Neurophysiology*, 31, 85–92.
- Chevalier, G., & Deniau, J. M. (1990). Disinhibition as a basic process in the expression of striatal functions. *Trends in Neuroscience*, 13, 277–280.
- Cott, A., Pavloski, R. P., & Black, A. H. (1979). Reducing epileptic seizures through operant conditioning of central nervous system activity: Procedural variables. *Science*, 203, 73–75.
- DeLong, M. R. (1990). Primate models of movement disorders of basal ganglia origin. *Trends in Neuroscience*, 13, 281–285.
- Egner, T., & Gruzelier, J. H. (2001). Learned self-regulation of EEG frequency components affects attention and event-related brain potentials in humans. *NeuroReport*, 12(18), 4155–4160.
- Egner, T., & Gruzelier, J. H. (2004). EEG biofeedback of low beta band components: Frequency-specific effects on variables of attention and event-related brain potentials. *Clinical Neurophysiology*, 115, 131–139.
- Evenon, P. (1986). Applications and perspectives of EEG cartography. In F. H. Duffy (Ed.), *Topographic mapping of brain electrical activity* (pp. 113–141). Boston: Butterworth.
- Felsing, J. M., Gladstone, A. L., Yamaguchi, H. G., & Hull, C. L. (1947). Reaction latency (StR) as a function of the number of reinforcements. *Journal of Experimental Psychology*, 37, 214–228.
- Ferster, C. B., & Skinner, B. F. (1957). *Schedules of reinforcement*. New York: Appleton-Century-Crofts.
- Finley, W. W., Smith, H. A., & Etherton, M. D. (1975). Reduction of seizures and normalization of the EEG in a severe epileptic following sensorimotor biofeedback training: Preliminary study. *Biological Psychiatry*, 2, 189–203.
- Froemke, R. C., Poo, M. M., & Dan, Y. (2005). Spike-timing-dependent synaptic plasticity depends on dendritic location. *Nature*, 434, 221–225.
- Fuchs, T., Birbaumer, N., Lutzenberger, W., Gruzelier, J. H., & Kaiser, J. (2003). Neurofeedback treatment for attention-deficit/hyperactivity disorder in children: A comparison with methylphenidate. *Applied Psychophysiology and Biofeedback*, 28, 1–12.
- Grice, G. R. (1948). The relation of secondary reinforcement to delayed reward in visual discrimination learning. *Journal of Experimental Psychology*, 38, 1–16.
- Harper, R. M., & Serman, M. B. (1972). Subcortical unit activity during a conditioned 12–14 Hz sensorimotor EEG rhythm in the cat. *Federation Proceedings*, 31, 404.
- Hauri, P. (1981) Treating psychophysiological insomnia with biofeedback. *Archives of General Psychiatry*, 38, 752–758.
- Hirshberg, L. M., Chiu, S., & Frazier, J. A. (2005). Emerging brain-based interventions for children and adolescents: Overview and clinical perspective. *Child and Adolescent Psychiatric Clinics of North America*, 14, 1–19.
- Howe, R. C., & Serman, M. B. (1972). Cortical-subcortical EEG correlates of suppressed motor behavior during sleep and waking in the cat. *Electroencephalography and Clinical Neurophysiology*, 32, 681–695.
- Howe, R. C., & Serman, M. B. (1973). Somatosensory system evoked potentials during waking behaviour and sleep in the cat. *Electroencephalography and Clinical Neurophysiology*, 34, 605–618.
- Johnstone, J., Gunkelman, J., & Lunt, J. (2005). Clinical database development: Characterization of EEG phenotypes. *Clinical EEG and Neuroscience*, 36, 99–107.
- Kaiser, D. A. (2000). QEEG: State of the art or state of confusion. *Journal of Neurotherapy*, 4, 57–75.
- Kaiser, D. A., & Serman, M. B. (2001). Automatic artifact detection, overlapping windows, and state transitions. *Journal of Neurotherapy*, 4(3), 85–92.
- Kaiser, D. A., & Serman, M. B. (2005). Correcting sampling bias of tapering windows. *International Journal of Psychophysiology* Manuscript submitted for publication.
- Kaplan, B. J. (1975). Biofeedback in epileptics: Equivocal relationship of reinforced EEG frequency to seizure reduction. *Epilepsia*, 16, 477–485.
- Klimesch, W., Schimke, H., & Pfurtscheller, G. (1993). Alpha frequency, cognitive load and memory performance. *Brain Topography*, 5, 241–251.
- Kotchoubey, B., Strehl, U., Holzapfel, S., Blankenhorn, V., Froscher, W., & Birbaumer, N. (1999). Negative potential shifts and the prediction of the outcome of neurofeedback therapy in epilepsy. *Clinical Neurophysiology*, 110(4), 683–686.
- Kotchoubey, B., Strehl, U., Uhlmann, C., et al. (2001). Modification of slow cortical potentials in patients with refractory epilepsy: A controlled outcome study. *Epilepsia*, 42, 406–416.
- Kuhlman, W. N., & Allison, T. (1978). EEG feedback training in the treatment of epilepsy: Some questions and some answers. *Pavlovian Journal of Biological Science*, 12(2), 112–122.

- Lantz, D., & Serman, M. B. (1988). Neuropsychological assessment of subjects with uncontrolled epilepsy: Effects of EEG biofeedback training. *Epilepsia*, *29*(2), 163–171.
- Levesque, J., & Beauregard, M. (2005). Effect of neurofeedback training on the neural substrates of selective attention in children with attention-deficit/hyperactivity disorder: A functional magnetic resonance imaging study. *Neuroscience Letters*.
- Lorenzen, T. D., & Dickson, P. (2004). Quantitative EEG Normative Databases: A comparative investigation. *Journal of Neurotherapy*, *8*, 53–68.
- Lubar, J. F., & Bahler, W. W. (1976). Behavioral management of epileptic seizures following EEG biofeedback training of the sensorimotor rhythm. *Biofeedback and Self Regulation*, *7*, 77–104.
- Lubar, J. F., Shabsin, H. S., Natelson, S. E., et al. (1981). EEG operant conditioning in intractible epileptics. *Archives of Neurology*, *38*, 700–704.
- Malenka, R. C., & Nicoll, R. A. (1999). Long-term potentiation—a decade of progress? *Science*, *285*, 1870–1874.
- Marczynski, T. J., Harris, C. M., & Livezey, G. T. (1981). The magnitude of post-reinforcement EEG synchronization (PRS) in cats reflects learning ability. *Brain Research*, *204*, 214–219.
- Monastra, V. J., Monastra, D. M., & George, S. (2002). The effects of stimulant therapy, EEG biofeedback, and parenting style on the primary symptoms of attention-deficit/hyperactivity disorder. *Applied Psychophysiology and Biofeedback*, *27*, 231–249.
- Monastra, V. J., Lynn, S., Linden, M., Lubar, J. F., Gruzelier, J., & LaVaque, T. J. (2005). Electroencephalographic biofeedback in the treatment of attention-deficit/hyperactivity disorder. *Applied Psychophysiology and Biofeedback*, *30*, 95–114.
- Monderer, R. S., Harrison, D. M., & Haut, S. R. (2002). Neurofeedback and epilepsy. *Epilepsy and Behavior*, *3*, 214–218.
- Pearce, J. M., & Hall, G. (1978). Overshadowing the instrumental conditioning of a lever-press response by a more valid predictor of reinforcement. *Journal of Experimental Psychology: Animal Behavior Processes*, *4*, 356–367.
- Quy, R. J., Hutt, S. J., & Forrest, S. (1979). Sensorimotor rhythm feedback training and epilepsy: Some methodological and conceptual issues. *Biological Psychology*, *9*, 129–149.
- Rossiter, T. R., & LaVaque, T. J. (1995). A comparison of EEG biofeedback and psychostimulants in treating attention deficit hyperactivity disorders. *Journal of Neurotherapy*, *1*, 48–59.
- Rockstroh, B., Elbert, T., Birbaume, N., et al. (1993). Cortical self-regulation in patients with epilepsies. *Epilepsy Research*, *14*, 63–72.
- Roth, S. R., Serman, M. B., & Clemente, C. C. (1967). Comparison of EEG correlates of reinforcement, internal inhibition, and sleep. *Electroencephalography and Clinical Neurophysiology*, *23*, 509–520.
- Seifert, A. R., & Lubar, J. F. (1975). Reduction of epileptic seizures through EEG biofeedback training. *Biological Psychology*, *3*, 157–184.
- Soderling, T. R., & Derkach, V. A. (2000). Postsynaptic protein phosphorylation and LTP. *Trends in Neuroscience*, *23*, 75–80.
- Serman, M. B. (1996). Physiological origins and functional correlates of EEG rhythmic activities: Implications for self-regulation. *Biofeedback and Self Regulation*, *21*, 3–33.
- Serman, M. B. (2000). Basic concepts and clinical findings in the treatment of seizure disorders with EEG operant conditioning. *Clinical Electroencephalography*, *31*(1), 45–55.
- Serman, M. B. (2005). Principles of neurotherapy. *Proceedings of the Annual Conference, Int. Soc. for Neuronal Reg.* 13, 23.
- Serman, M. B., & Friar, L. (1972). Suppression of seizures in an epileptic following sensorimotor EEG feedback training. *Electroencephalography and Clinical Neurophysiology*, *33*, 89–95.
- Serman, M. B., & Kaiser, D. A. (2001). Comodulation: A new QEEG analysis metric for assessment of structural and functional disorders of the CNS. *Journal of Neurotherapy*, *4*(3), 73–83.
- Serman, M. B., Kaiser, D. A., & Veigel, B. (1996). Spectral analysis of event-related EEG responses during short-term memory performance. *Brain Topography*, *9*(1), 21–30.
- Serman, M. B., & MacDonald, L. R. (1978). Effects of central cortical EEG feedback training on incidence of poorly controlled seizures. *Epilepsia* *19*, 207–222.
- Serman, M. B., MacDonald, L. R., & Stone, R. K. (1974). Biofeedback training of the sensorimotor EEG rhythm in man: Effects on epilepsy. *Epilepsia* *15*, 395–417.
- Serman, M. B., Mann, C. A., Kaiser, D. A., & Suyenobu, B. Y. (1994). Multiband topographic EEG analysis of a simulated visuomotor aviation task. *International Journal of Psychophysiology*, *16*, 49–56.
- Serman, M. B., Howe, R. D., & Macdonald, L. R. (1970). Facilitation of spindle-burst sleep by conditioning of electroencephalographic activity while awake. *Science*, *167*, 1146–1148.
- Serman, M. B., & Wyrwicka, W. (1967). EEG correlates of sleep: Evidence for separate forebrain substrates. *Brain Research*, *6*, 143–163.
- Serman, M. B., Wyrwicka, W., & Roth, S. R. (1969). Electrophysiological correlates and neural substrates of alimentary behavior in the cat. *Annals of the New York Academy of Sciences*, *157*, 723–739.

- Thatcher, R. W. (1992). Cyclic cortical reorganization during early childhood. *Brain and Cognition*, *20*, 24–50.
- Walker, M. P. (2005). A refined model of sleep and the time course of memory formation. *Behavioral and Brain Sciences*, *28*, 51–64.
- Walker, J. E., & Kozlowski, G. P. (2005). Neurofeedback treatment of epilepsy. *Child and Adolescent Psychiatric Clinics of North America*, *14*, 163–176.
- Williams, B. A. (1999). Associative competition in operant conditioning: Blocking the response–reinforcer association. *Psychonomic Bulletin and Review*, *6*, 618–623.
- Wyler, A. R., Robbins, C. A., & Dodrill, C. B. (1976). EEG operant conditioning for control of epilepsy. *Epilepsia*, *20*, 279–286.
- Wyrwicka, W., & Sterman, M. B. (1968). Instrumental conditioning of sensorimotor cortex EEG spindles in the waking cat. *Physiology and Behavior*, *3*, 703–707.