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### Databases or Specific Training Protocols for Neurotherapy? A Proposal for a “Clinical Approach to Neurotherapy”

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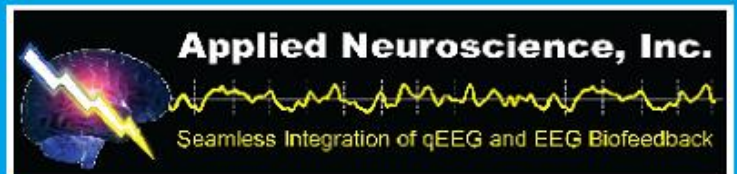
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# Databases or Specific Training Protocols for Neurotherapy? A Proposal for a “Clinical Approach to Neurotherapy”

Jaime Romano-Micha, MD

**SUMMARY.** This paper reviews and summarizes the use of quantitative electroencephalography (EEG) and normative databases in the design and application of EEG biofeedback (neurotherapy) for clinical purposes. It is argued that such a statistical approach to EEG analysis ignores important individual patient data observed in the raw EEG.

While databases provide important information for understanding brain function, they have important limitations for patient diagnosis and as guides to the training of brain waves. On the other hand, although the use of specific training protocols and the training of specific electroencephalographic frequencies have been shown to be useful in improv-

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ing symptoms in different neurological and psychological disorders, they are insufficient to structure a rational neurofeedback training protocol.

It is assumed that neurotherapy produces fundamental changes in brain function. Although there have been no published reports to date of iatrogenic problems arising from neurotherapy, the potential for such problems raises ethical concerns the individual practitioner should consider. In this paper the advantages and limitations of databases and the use of specific training protocols are discussed, and a “clinical approach” for neurotherapy is proposed.

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**KEYWORDS.** Brain mapping, neurofeedback, EEG databases, neurotherapy, qEEG, clinical approach to neurotherapy, neurofeedback training protocols

### ***INTRODUCTION***

Neurofeedback and brain mapping represent two related new fields in neuroscience (Romano-Micha, 2000). Their evolution in the last two decades has been possible due to technological developments and more specifically to the increased power of computers used in the fields of neurophysiology and psychophysiology. As in any new field of knowledge, neurofeedback and brain mapping are going through different stages of development. At present, neurofeedback is in a stage of growth and maturation. With time, cumulative experience, and verification via clinical and research data, the strengths and weaknesses of neurofeedback will be identified. Thereafter it will assume its proper place as both a research and clinical tool for various applications.

### ***NEUROFEEDBACK***

Neurofeedback began in the late 1960s, when Kamiya (1968) reported that it was possible to voluntarily control alpha waves. Other investigators (Beatty, Greenberg, Deibler, & O’Hanlon, 1974) implemented further experiments on theta waves, evoked cortical responses, and EEG phase synchrony in specialized learning processes. More experiments followed, with specific rhythms such as the sensorimotor rhythm (SMR) emerging as having therapeutic effects in epilepsy (Serman, 1972) and in patients with attention deficit disorders (Lubar, 1991).

Since then, there have been an increasing number of different training protocols for specific frequencies and frequency ratios and success reported in treating a wide variety of disorders such as addictive behaviors (Ochs, 1992; Rosenfeld, 1992; Peniston & Kulkosky, 1989), affective disorders (Rosenfeld, 1997) and stroke rehabilitation (Rozelle & Budzynski, 1995) among others.

### **NEUROPHYSIOLOGY**

Electroencephalography (EEG) as one of the neurophysiological techniques has its own history, starting in the early 1920s. Electroencephalography has evolved tremendously since the time in 1924 when Hans Berger was able to record an electric signal from his son's brain for the first time. Berger was obsessed with trying to find material events (electrical brain potentials) that were related to mental phenomena, in which he included telepathy. Although he did not accomplish his final goal, he was able to establish the fundamentals necessary for the development of a powerful instrument for analysis of the cerebral cortical function (Berger, 1969).

Since then and with the use of powerful computer techniques for signal analysis—such as Fourier analysis—the era of quantitative EEG began. Grass and Gibbs (1938), Walter (1963), and Bickford, Brimm, Berger, and Aung (1973) were among the investigators who pioneered the area of computerized EEG.

With sophisticated visual representation of this analyzed signal, starting with the Compressed Spectral Array designed by Bickford and later as brain maps with the use of mathematical algorithms such as linear, Laplacian or quadratic interpolations, it was possible to increase the capacity of the EEG to characterize more precisely some of the parameters of analysis of the EEG such as frequency, amplitude, locus and interhemispheric coherence (symmetry and synchrony). As computer technology developed and faster computers and color monitors were available, the processing and display of analyzed EEG progressed until brain mapping was created.

There are a number of investigators who have contributed to the development of quantitative EEG. Some of the pioneers in this area are: Brazier (1961), John, Pritchep, Fridman, and Easton (1988), Nuwer (1988a, 1988b), Gevins, Martin, Brickett, Desmond and Reuter (1994), Dumermuth and Molinari (1987), Duffy, Burchfiel, and Lombroso (1979), and Thatcher, Walker, and Guidice (1987), just to mention a few.

At present, no one questions the fact that the cerebral cortex is the site of mental functions (e.g., Penfield, 1954). The EEG is the method that records the function of this “enchanted loom.” To paraphrase Sir Charles Sherrington, “The human brain is an enchanted loom where millions of flashing shuttles weave a dissolving pattern, always a meaningful pattern, though never an abiding one. It is as if the Milky Way entered upon some cosmic dance.” EEG represents a window through which we can examine the functioning of this “machinery of the mind.”

With the passage of time, EEG has shown its utility in the diagnosis and characterization of different pathologies that affect brain functioning with a well-defined application in neurology and an increasingly important one in neuropsychiatry.

Clinical neurophysiology evolved as a branch of medicine, and has become a specialty in itself. At present clinical neurophysiologists are grouped in local societies, which are part of the International Federation of Clinical Neurophysiology. There are also local councils that certify and support rational and careful use and application of this technique.

### ***QUANTITATIVE EEG AND BRAIN MAPPING***

The earliest researcher to anticipate the use of numerical computation in EEG was, not surprisingly, Hans Berger. Berger collaborated with a physicist, G. Dietsch, at the Institute of Technology and Physics in Jena, Germany. Together they worked on the theoretical basis for calculating the frequency spectrum of the EEG using the Fourier Transform. Although the theoretical basis was established by Berger and others, quantitative analysis of EEG had to wait until computers were available.

Grass and Gibbs (1938) and Bickford et al. (1973) were among the investigators who pioneered the area of computerized EEG. Dr. John Knott built a frequency analyzer in 1949 at the University of Iowa in collaboration with Drs. Henry, Gibbs and Grass. This group was the first to coin the term “CSA” for “continuous or compressed spectral array.” Reginald Bickford at the University of California, San Diego (UCSD), developed and introduced the technique in 1972.

### ***SPECTRAL ANALYSIS***

One of the main features of EEG analysis corresponds to frequency. Traditionally, EEG frequency has been separated into frequency bands. These are:

Delta from 0.1 to 4 Hz

Theta from 4 to 8 Hz

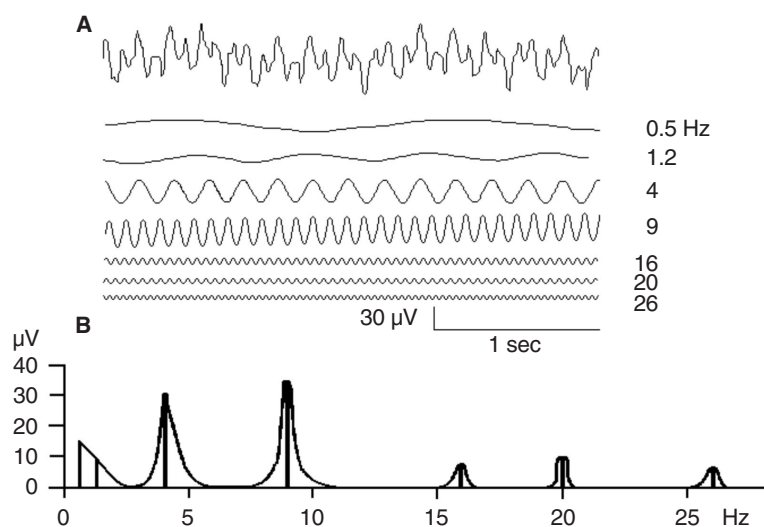
Alpha from 8 to 13 Hz

Beta from 13 Hz up

Arranging EEG frequencies into bands was useful at the beginning of EEG analysis because of the limitations in visual analysis. Quantifying frequency by visual analysis is an almost impossible task. What we see in an EEG tracing is the result of a combination of frequencies, and visually quantifying a frequency would involve counting each component of a rhythm in one-second intervals. It would be very time consuming if not impossible to count every rhythm in an 8- or 16-channel tracing for the entire EEG record.

Fortunately, with computer analysis we are now able to quantify frequency very efficiently. Spectral decomposition of the EEG can be performed by Fourier analysis (Figure 1) which allows separation of various rhythms and estimation of their frequencies independently of each

FIGURE 1. The frequency spectrum can be obtained by performing Fourier analysis on a sample of raw EEG.



other, a task difficult to perform visually if several rhythmic activities occur simultaneously. Spectral analysis can also quantify the amount of activity in a frequency band.

Spectral analysis is based on the Fourier theorem, developed by a French mathematician in the 19th century who was obsessed with the idea of analyzing the propagation of heat through solids. In his treatise, *Théorie analytique de la chaleur (The Analytical Theory of Heat)*, Fourier (1822) employed trigonometric series, usually called the Fourier series, by means of which discontinuous functions can be expressed as the sum of an infinite series of sines and cosines.

In order to understand what Fourier analysis does to EEG, we could compare it to what happens to light when it passes through a glass prism. The beam of light decomposes into its main components thus obtaining the spectrum. Since the EEG is composed of a mixture of frequencies, its spectrum can also be obtained when processed by Fourier analysis.

Spectral analysis is only one of a wide variety of EEG analysis techniques, which includes analysis in the time and frequency domain. Power spectrum, coefficient of variation, coherence, ratios, period amplitude, and zero-crossing analysis are other analytic tools available, just to mention a few. There are more than ten thousand pages in the literature that cannot be summarized here. The interested reader is encouraged to consult Bickford et al. (1973), Brazier (1961), Dietsch (1932), Duffy (1986), Frost (1987), Gevins (1984), Hjorth (1986), John (1977), Kellaway and Petersen (1973), Nuwer and Jordan (1987), and Lopez da Silva et al. (1977).

### **BRAIN MAPPING**

After digitizing and processing the EEG, there are also a number of display formats, which include colored bar displays, compressed spectral array, histograms, numerical tables, and topographic maps. Continuous or compressed spectral array (CSA) and brain mapping are the two most frequently used types of display for neurofeedback; therefore, we will focus on those.

CSA, developed by Reginald Bickford, consists of performing the spectral analysis of EEG, sorting the mixed frequencies into an orderly sequence from low to high (0.25 to 16 or more Hz) and plotting the graphs in a series, stacking one graph upon another in sequential temporal order (each epoch in chronological sequence).

Brain mapping involves the construction of a topographic map from the results of a multi-channel recording analysis. Interpolation is required to build these maps. It starts with the values measured at each electrode, then the values at intermediate locations are mathematically calculated by assuming smooth changes of the values between electrodes. Interpolated values can be displayed in different ways. Currently the most popular method assigns a color to a value, most commonly using a color spectrum scale, arranging the hues in an orderly fashion. Because phase is lost by performing frequency analysis through the use of Fourier analysis, the blue hues represent low values and the red hues high values (see Figure 2). When both positive and negative values are present as in voltage distribution maps, blue hues represent positive polarity and red hues negative polarity. (Note: In neurophysiology, negative is upward deflection of the trace, and positive is downward. See Figure 3.)

Brain maps can represent different types of analysis or information (i.e., voltage distribution at one instant of time, frequency data at one

FIGURE 2. Topographic maps in the frequency domain, arranged in frequency bands.

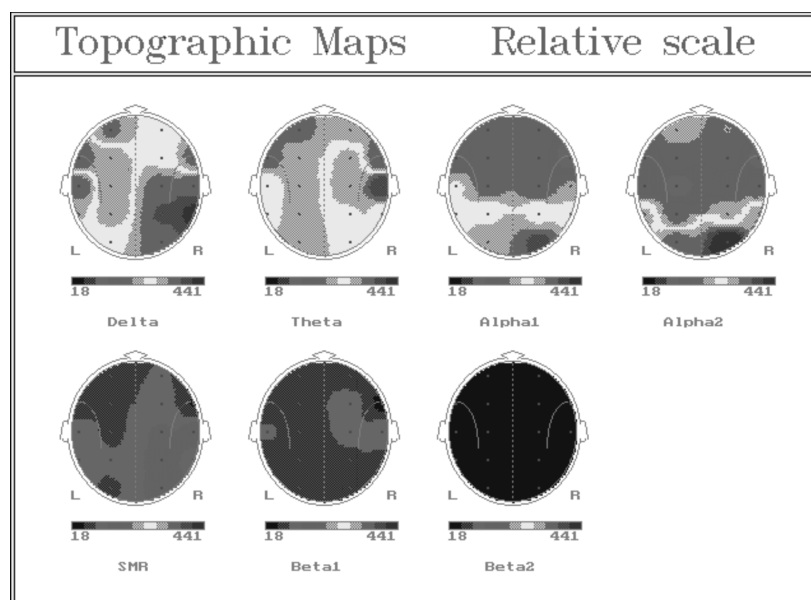
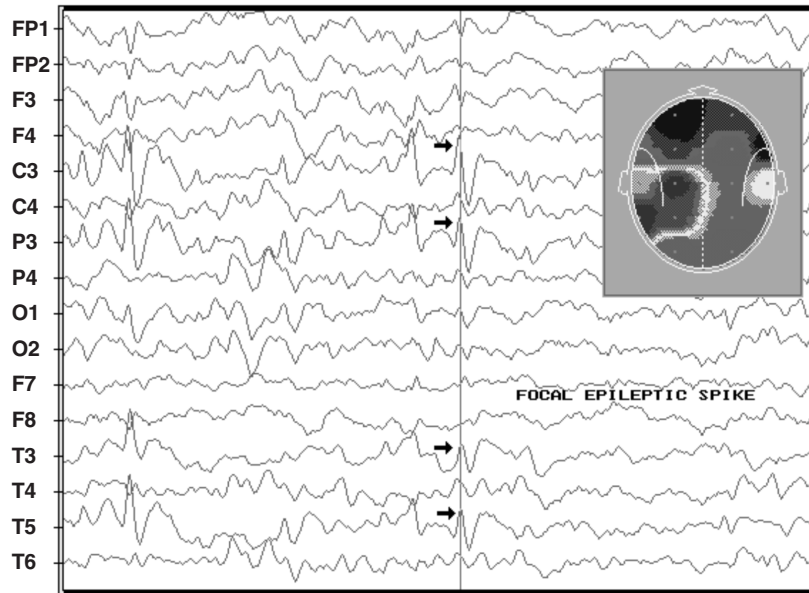




FIGURE 3. A transient event such as an epileptic spike can be precisely located by displaying a potential field distribution map in the time domain.



frequency or frequency bands, or a z-score of such time or frequency activity). Other more complex representations are also possible (Nuwer, 1988a, 1988b).

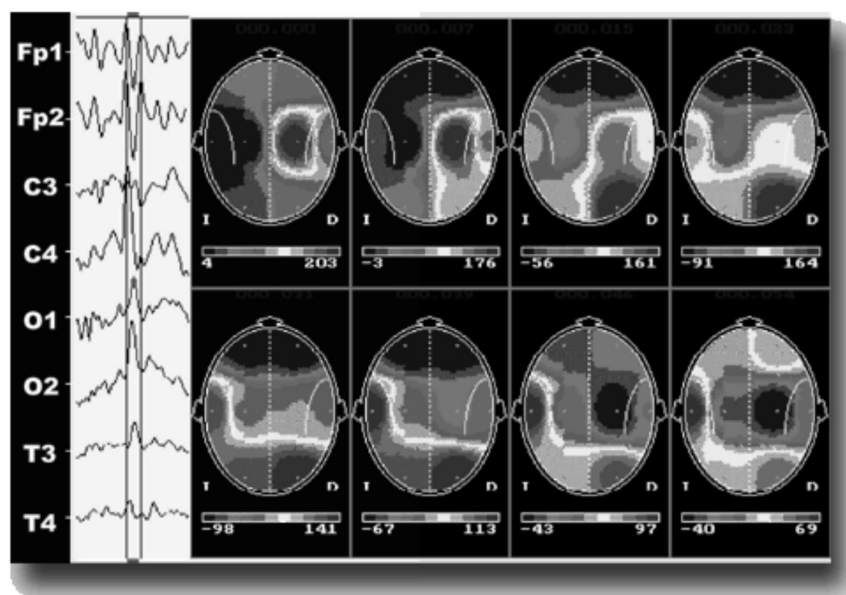
In the time domain, a map can be displayed at one instant of time, which is useful to analyze the potential field distribution of a phasic or transient event such as an epileptic spike. A series of maps can be displayed in progressive periods of time in order to assess how such events evolve over milliseconds of time (see Figure 4).

### ***NORMATIVE DATABASES***

The use of normative databases has become a common practice in the field of neurofeedback. Some of its advantages and limitations are discussed.

The use of normative databases is very important to the clinical neurophysiologist in terms of the information they provide in relation to quantification of different features of the EEG in normal populations,

FIGURE 4. By displaying a series of maps in progressive periods of time, propagation of a transient event along the cortex can be clearly assessed.



and also because they permit comparisons between populations of different pathologies. However, the assessment of the state of normality of an individual patient has a substantial array of difficulties.

The first difficulty relates to the technical quality of the data. It is of the utmost importance to have artifact-free samples of EEG. As Thatcher et al. (1987) pointed out, “The importance of this aspect of EEG data acquisition cannot be overstated.” Even the small amount of artifacts easily tolerated in traditional EEG readings can wreak havoc in computer EEG analysis. It is a matter of “garbage in-garbage out” (Nuwer, 1988b).

Patients cannot always be compared to a normal database, even if the technical quality of a record is perfect. The normal subjects included in the databases may vary from the patient’s own group in a number of ways that may affect results. Some databases have been collected on subjects rigorously excluding anyone who uses drugs or medicines, who has a history of any significant medical problem or head trauma, or who fails a physical examination. The population from which they are derived can influence databases.

It has been customary to use the normalcy criteria of Matousek and Petersen (1973) for membership in a normative QEEG database. This standard has been followed in the development of subsequent quantitative EEG databases by most authors. If one critically analyzes the required criteria for entry into the normative database (uneventful prenatal, perinatal and postnatal period, no disorders of consciousness, no head injury with cerebral symptoms, no history of central nervous diseases, no convulsions of emotion, febrile, or other nature, no abnormal deviation with regard to mental and physical development), then it is not difficult to see that this is an arbitrary standard for normalcy. To be strictly reliable and consistent, the “patients” compared to this reference normative database should also match the same criteria.

One may also question the clinical significance of a quantitative EEG feature lying outside normal limits. Even when data is collected in a technically adequate manner and a reasonably appropriate database is employed, an abnormality determined solely by statistics may not reflect a clinically meaningful abnormality. Electroencephalographers have long known about clinically meaningless normal variants in EEG records. These normal variants serve as reminders that EEG features may be statistically unusual in a group of normal subjects and may still be clinically meaningless. When quantitative EEG techniques rely on statistics and normal databases, they are predisposed to confusion between statistical and clinical abnormalities.

There are also further serious statistical issues that must be addressed. The types of statistics used in a simple z-score analysis are predisposed toward over-emphasizing some statistical abnormalities. The roots of this problem lie in part with statistical issues such as nongaussian distribution, the redundancy of testing similar data with separate tests, and a lack of independence of results from separate scalp sites. A simple z-score may show a result three standard deviations (SDs) above control values, and yet it does not necessarily imply that the patient’s value lies outside the range of values observed in normal control subjects. Statistics can overemphasize abnormalities or erroneously find abnormality where none exists.

There are other important issues in EEG analysis that relate to the characterization of other parameters that are as important as frequency analysis. Some of them (waveform, regulation, manner of occurrence and reactivity) are better analyzed visually by an experienced clinical neurophysiologist. Also, even small amounts of artifact that can wreak havoc in computer EEG analysis provide important information in visual analysis for the clinical neurophysiologist in relation to the cooper-

ation of the patient, the technical quality of the recording, the state of the patient, etc.

Relying only on databases to analyze an EEG, as has been previously discussed, has many disadvantages. Analysis and interpretation of the EEG is both a science and an art. On one hand, it is a rational and systematic process involving a series of orderly steps to characterize the electrical activity of the brain in terms of specific parameters such as frequency, amplitude, locus, interhemispheric coherence (symmetry and synchrony), waveform, regulation, manner of occurrence, and reactivity. On the other hand, the clinical neurophysiologist has to evaluate and correlate all these results in the light of a specific patient and conditions in order to derive a “clinical impression”; that is, an assessment of the probable significance of the EEG findings in relation to the patient’s history and the clinical findings.

EEG analysis is so complicated that it requires arduous and constant training. A clinical neurophysiologist has to know what a normal EEG looks like at different ages (databases are useful for this), at different states and conditions, how all the different pathologies are expressed in the EEG, the normal variants, and the artifacts. If the clinical neurophysiologist wants to include quantitative EEG techniques, the reader needs to be expert as well in computer analysis of EEG. The interpretation of EEG requires substantial clinical experience. The interpreter must understand also that the increased power of these techniques also increases their potential for misinterpretation.

### ***SPECIFIC TRAINING PROTOCOLS FOR NEUROTHErapy***

Specific training protocols for different disorders or symptoms have been widely used since the beginning of neurotherapy practice. Sterman (1982) found that training SMR in epileptic cats was useful in lowering seizure frequency. Lubar (1997) found that children with ADD benefited with SMR training. Since then, many practitioners have come up with different protocols, most of them arbitrary and discovered by chance, and without clear and scientific foundation. These types of findings, although they have provided important information and have proven to be useful in different pathologies, have caused conceptual errors in interpretation. There is a tendency to oversimplify brain function and to interpret it in a reductionist way by pretending to explain it in a direct cause-effect way. Practitioners tend to relate alpha with relax-

ation, SMR with attention, and specific frequencies with specific brain functions. In brain neurophysiology this is not the case. As one can see in electroencephalography, there is no relationship between a specific frequency and a specific disease or symptom. As we have learned from qEEG, a brain frequency such as alpha or beta is actually a mixture of frequencies; millions of cortical generators are contributing to a specific frequency. We now know with certainty that there is a correlation between cortical topography and brain functions and not one with specific brain frequencies. Neurophysiology has provided important information in this respect.

Some neurofeedback practitioners have even tried to further oversimplify neurotherapy by trying to obtain a description of symptoms and decide by the application of an initial interview and a series of clinical questions if the brain is in a specific brain state or in a specific state of performance so they train frequencies to acquire a “high performance” brain state. That is an even more inexact approach. One could easily reach wrong conclusions such as thinking that a patient with migraine is in a brain state dominated by fast brainwaves. Clinical neurophysiologists have shown that migraine patients actually have slow waves in their EEGs.

The brain is a very complex organ, with a complexity that we cannot even conceive with our imagination. Knowledge about the brain has increased tremendously in the last two decades. Technical development has provided more precise and powerful tools to the fields of neurophysiology, neuropharmacology, neuropsychology, and other neurodisciplines to understand the most complex organ known in nature. Recently, we have seen an ever increasing dialogue between disciplines. We see more neurologists interested in psychological processes and more psychologists looking for an “organic” basis for the patient’s complaints. At the end, there is no division. Brain and behavior are part of the same whole. This organ is so complex that there is no single individual who can cover all aspects of knowledge. We have to dedicate a whole human life just to understand the tip of the iceberg of only one point of view. That is why we specialize in a specific field of knowledge so we become psychophysiologicals, neuropharmacologists, neurophysiologists, etc.

Neurofeedback is a very special discipline because it stands right at the landmark of brain and behavior so it deals with all the complexities of brain function and brain functions.

**A PROPOSAL FOR A “CLINICAL APPROACH  
TO NEUROTHERAPY”**

We have discussed some important aspects in relation to a substantial array of difficulties that the use of databases has in order to assess the state of normality of an individual patient. We have also mentioned the weakness of the conceptual foundation and the arbitrary approach of the use of specific protocols in neurotherapy. Both approaches share the intention to simplify what is not simplifiable—that is understanding and manipulating brain function. On one hand, data bases by the use of statistics pretend to show anatomical locations that are most deviant from normal when compared to a group of “normal” individuals, in an effort to individualize neurotherapy treatment. One frequent question that arises between neurofeedback practitioners who use this approach is whether one should train an area that is statistically deviant from the norm although it does not correlate with the symptoms of the patient. In this case, who is right, the statistics or the patient?

If the investigator relies upon inferential statistics in an isolated way without verifying the clinical meaning, a fundamental error of clinical interpretation can occur. Often investigators do not question the clinical meaning of the inferential statistics because numbers are supposed to be exact and true in nature.

If neurofeedback is going to be used in patient care, the model of therapeutic neurofeedback that should be used is what I call a *clinical approach* to neurofeedback. This means collecting and analyzing an EEG in a conventional and quantitative way using a trained professional, then evaluating and correlating all the results of a specific patient and specific conditions to derive a “clinical impression” in concert with a good clinical history, physical exam, and psychological or neuropsychological tests. That is, a neurofeedback protocol should be based upon an assessment of the probable significance of the EEG findings in relation to the patient’s history and clinical findings. Building an individualized neurofeedback training protocol should take into account the relevant EEG findings, including the training of specific frequencies which have been clearly demonstrated to improve different states and symptoms, such as inattention or epilepsy (Lubar, 1997; Sterman, 1982).

This proposed approach is a very complex one, but not as complex as the brain. It requires a multidisciplinary team of professionals, not only to build a neurofeedback training protocol, but to make a correct medical and psychological diagnosis and to treat a patient in a multidisci-

plinary way, not forgetting that neurofeedback is just another piece of the therapeutic procedure, as is psychotherapy, pharmacotherapy, etc.

### ***AN ETHICAL ISSUE***

There is significant evidence for a neurological effect of neurofeedback. Abrams and Kandel (1988) found that there is activity-dependent enhancement of pre-synaptic facilitation in classical conditioning. They found that action potentials allow calcium ( $\text{Ca}^{++}$ ) to move into sensory neurons. This influx of  $\text{Ca}^{++}$  acting through calmodulin is thought to amplify the activation of adenylyl cyclase by serotonin and other modulatory transmitters thus producing greater amounts of transmitter release.

Another piece of evidence comes from the work of Merzenich et al. (1983) who demonstrated that the brain cortex architecture can be modified by the manipulation of external stimuli. Cortical maps are subject to constant modification on the basis of environmental influence.

Jenkins et al. (1990) demonstrated reorganization of the cortex through learning activities. They encouraged monkeys to use their middle three fingers at the expense of other fingers by having them obtain food by contacting a rotating disc with only the middle fingers. After several thousand disc rotations, the area in the cortex devoted to the middle three fingers was greatly expanded. Now, there is abundant evidence that learning produces structural changes in the cortex.

Previous evidence strongly suggests that neurofeedback can be an important tool for neuroplasticity. As has been clearly demonstrated, (e.g., Goldensohn, 1979) EEG activity is generated in the pyramidal cells of the cortex. As pointed out previously, there is evidence of synaptic facilitation and structural modification of the cerebral cortex by external stimulation and learning, so it is most probable that the changes obtained in EEG activity with neurofeedback reflect structural changes in the cell generators.

As pointed out at the beginning of this paper, neurofeedback provides an opportunity for the integration of neurological and psychological sciences. Neurofeedback lies right at the interface of mind and brain interaction. It seems to integrate the psychological aspect of healing, the positive attitude, and the neurological aspect that relates to neuroplasticity.

If neurofeedback can bring about structural modification of the brain—as growing evidence suggests—then an ethical issue has to be out-

lined. So far, there have been no reports of iatrogenesis (a harmful effect produced by the healer or the healing process) through the use of neurofeedback. However, this does not guarantee that there cannot be harmful effects through changing the physiology and probably the structure of a brain area where such changes are not needed.

Homeostasis is a fundamental natural system preserving health. If neurofeedback can change homeostatic processes, then it is of the utmost importance to maintain a very careful and responsible attitude in order to help nature and not to disrupt it.

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