

NINETEEN CHANNEL QUANTITATIVE EEG AND EEG BIOFEEDBACK

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Quantitative electroencephalography (QEEG) is distinguished from visual examination of EEG¹ traces, referred to as “non-quantitative EEG” by the fact that the latter is subjective and involves low sensitivity and low inter-rater reliability (Cooper et al, 1974; Woody, 1966; 1968) while the former involves the use of computers and power spectral analyses and is more objective with higher reliability and higher sensitivity (Hughes and John, 1999). The improved sensitivity and reliability of QEEG was first recognized by Hans Berger in 1934 when he performed a QEEG analysis involving the power spectrum of the EEG with a mechanical analog computer (Berger, 1934; Niedermeyer and da Silva, 1995). QEEG in the year 2009 clearly surpasses conventional visual examination of EEG traces because QEEG has high temporal and spatial resolution in the millisecond time domain and approximately one centimeter in the spatial domain which gives QEEG the ability to measure network dynamics that are simply “invisible” to the naked eye. Over the last 40 years the accuracy, sensitive and resolution of QEEG has steadily increased because of the efforts of hundreds of dedicated scientists and clinicians that have produced approximately 90,000 QEEG studies cited in the National Library of Medicine’s database . It is recommended that the reader search the National Library of Medicine database (<https://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed>) using the key word “EEG” and the few representative citations in this chapter.² Because of space limitations no reviews of this vast literature will be attempted, instead, the purpose of the present chapter is to briefly describe some of the most recent advances in QEEG as they relate to EEG biofeedback/Neurofeedback.³

Neurological evaluation of space occupying lesions has been correlated with the locations and frequency changes that have been observed in the EEG traces and in QEEG analyses, e.g., lesions of the visual cortex resulted in distortions of the EEG generated from the occipital scalp locations or lesions of the frontal lobe resulted in distortions of the EEG traces arising in frontal regions, etc. However, early neurological and neuropsychological studies have shown that function was not located in any one part of the brain (Luria, 1973). Instead the brain is made up of complex and interconnected groupings of neurons that constitute “functional systems”, like the “digestive system” or the “respiratory system” in which cooperative sequencing and interactions give rise to an overall function at each moment of time (Luria, 1973). This widely accepted view of brain function as a complicated functional system which became dominant in the 1950s and 1960s is still the accepted view today (July 2009). For example, since the 1980s new technologies such as functional MRI (fMRI), PET, SPECT and QEEG/MEG have provided ample evidence for distributed functional systems involved in perception, memory, drives, emotions, voluntary and involuntary movements, executive functions and various psychiatric and psychological dysfunctions. Modern PET, QEEG, MEG and fMRI studies are consistent with the historical view of “functional systems” presented by Luria in the 1950s (Luria 1973), i.e., there is no absolute functional localization because a functional systems of dynamically coupled

¹ EEG or the Electroencephalogram is measured from the scalp surface and is produced by the algebraic summation of cortical synaptic potentials.

² Since approximately 1975 it has been very difficult to even publish studies that only use visual examination of EEG traces. The estimate of 90,000 arises when one uses the search term “EEG” and examines the abstracts to confirm that quantification of EEG was used. It is necessary to use the search term “EEG” and not “QEEG” because the National Library of Medicine indexes articles based on words in the titles and most QEEG studies do not use the term “QEEG” in their titles.

³ While EEG Biofeedback is sometimes referred to as “Neurofeedback” the later term is not specific since many treatments other than EEG may involve neurofeedback. However, in the present chapter these terms are considered synonymous and will be used interchangeably.

sub-regions of the brain is operating. For example, several fMRI and MRI studies (e.g., diffusion tensor imaging or DTI) have shown that the brain is organized by a relatively small subset of “Modules” or “Hubs” which represent clusters of neurons with high within cluster connectivity and sparse long distance connectivity (Hagmann et al, 2009; Chen et al, 2008; He et al, 2009). Modular organization is a common property of complex systems and ‘Small-World’ models in which maximum efficiency is achieved when local clusters of neurons rely on a small set of long distance connections in order to minimize the “expense” of wiring and shorten time delays between modules (Buzsaki, 2006; He et al, 2009). Also, recent QEEG and MEG analyses have demonstrated that important visually invisible processes such as coherence, phase delays, phase locking and phase shifting of different frequencies is critical in cognitive functions and various clinical disorders (Buzsaki, 2006; Sauseng, and Klimesch, 2008; Thatcher et al, 2009a). Phase shift and phase synchrony has been shown to be one of the fundamental processes involved in the coordination of neural activity located in spatially distributed “modules” at each moment of time (Freeman and Rogers, 2002; Freeman et al, 2003; Thatcher et al, 2009a; 2009b).

QEEG for Assessment and Neurofeedback for Treatment: A Parent-Child Relationship

This use of the EEG changed dramatically in the 1960s when computers were used to modify the EEG thru biofeedback, referred to today as Neurofeedback (NF). Studies by Fox and Rudell (1968); Kamiya (1971) and Serman (1973) were a dramatic departure from the classical use of conventional visual EEG and QEEG in that for the first time clinicians could consider treating a disorder such as epilepsy or attention deficit disorders and other mental disorders by using operant conditioning methods to modify the EEG itself. Thus, QEEG and EEG Biofeedback have a “parent-child” relationship in that EEG Biofeedback necessarily uses computers and thus is a form of QEEG that is focused on treatment based on the science and knowledge of the physiological meaning and genesis of the EEG itself. Ideally, as knowledge about brain function and the accuracy and resolution of the EEG increases, then EEG Biofeedback should change in lock step to better link symptoms and complaints to the brain and in this manner treat the patient based on solid science. To the extent the EEG can be linked to functional systems in the brain and to specific mental disorders then EEG Biofeedback could “move” the brain toward a healthier state (i.e., “normalize” the brain) (Thatcher 1998; 1999). Clearly, the clinical efficacy of EEG Biofeedback is reliant on knowledge about the genesis of the electroencephalogram and specific functions of the human brain. The parent-child relationship and inter-dependencies between QEEG and EEG Biofeedback is active today and represents a bond that when broken results in reduced clinical efficacy and general criticism of the field of EEG biofeedback. The traditional and logical relationship between QEEG and NF is to use QEEG to assess and NF to treat based on a linkage between the patient’s symptoms and complaints and functional systems in the brain. This parent/child linkage requires clinical competence on the one hand and technical competence with computers and the EEG on the other hand. Competence in both is essential and societies such as ISNR, SAN, ABEN, ECNS, BCIA, AAPB and other organization are available to help educate and test the requisite qualifications and competence to use EEG biofeedback. The parent/child link is typically optimized by following three steps: 1- perform a careful and thorough clinical interview and assessment of the patient’s symptoms and complaints (neuropsychological assessments are the most desirable), 2- conduct a QEEG in order to link the patient’s symptoms and complaints to functional systems in the brain as evidenced in fMRI, PET and QEEG/MEG and, 3- devise a EEG biofeedback

protocol to address the de-regulations observed in the QEEG assessment that best match the patient's symptoms and complaints. This approach reinforces the close bond between parent (QEEG) and child (Neurofeedback) and allows for the objective evaluation of the efficacy of treatment in terms of both behavior and brain function.

Figure one illustrates a common modern quantitative EEG analysis where conventional EEG traces are viewed and examined at the same time that quantitative analyses are displayed so as to facilitate and extend the analytical power of the EEG. Seamless integration of QEEG and Neurofeedback involves two basic steps: 1- visual examination of the EEG traces and 2- Spectral analyses of the EEG traces⁴. Numerous studies have shown a relationship between the time domain and frequency domain of an EEG time series and LORETA 3-dimensional source analyses which provide 7 mm³ maximal spatial resolution in real-time (Pascual-Marqui et al, 1974; Gomez and Thatcher, 2001) (see footnote 6). There is a verifiable correspondence between the time series of the EEG and the power spectrum and LORETA 3-dimensional source localization, for example, visual cortex source localization of hemiretinal visual stimulation, temporal lobe source localization of auditory simulation, theta source localization in the hippocampus in memory tasks, localization of theta in the anterior cingulate gyrus in attention tasks, linkage between depression and rostral and dorsal cingulate gyrus, etc.⁴ The number of clinical QEEG studies cited in the National Library of Medicine attests to the linkage between patient symptoms and functional systems in the brain and protocols for treatment are commonly guided by this scientific literature .

⁴ Spectral analysis includes space and time sequences that are transformed such as Joint-Time-Frequency-Analysis, FFT and all other methods that decompose EEG energies at different frequencies in space and time.

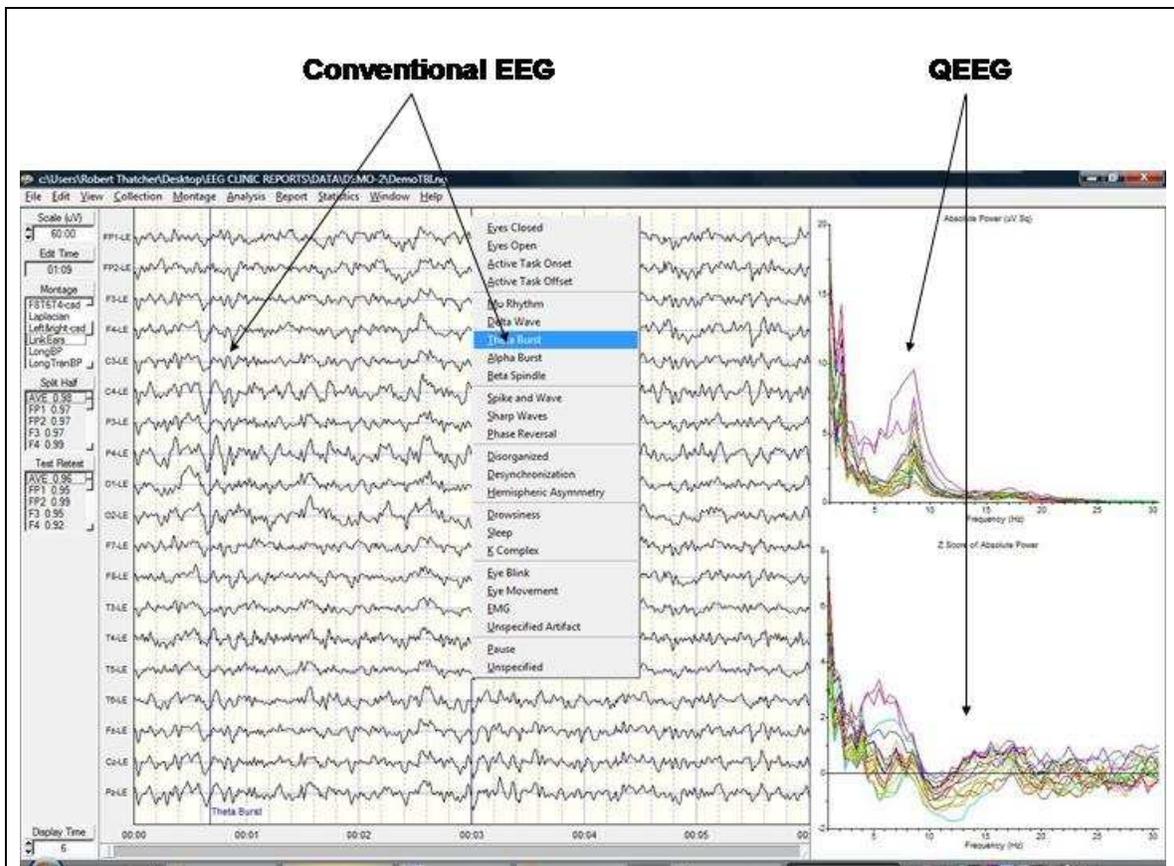


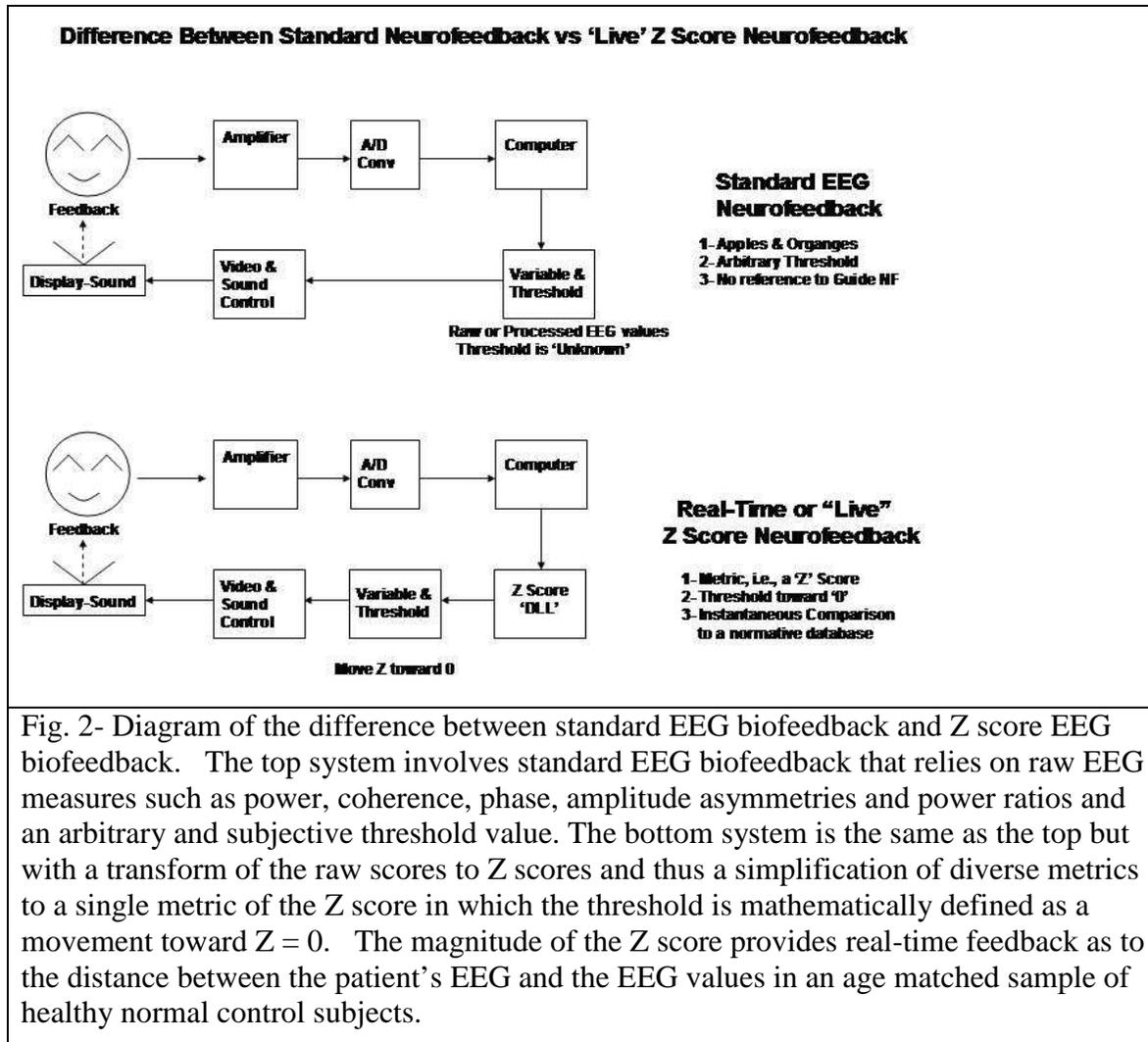
Fig. 1 – Example of conventional digital EEG (left) and QEEG (right) on the same screen at the same time. The conventional EEG includes examination and marking of EEG traces and events. The QEEG (right) includes the Fast Fourier Transform (Top right) and normative database Z scores (Bottom right).

The Use of 19 Channel Surface QEEG Z Scores and EEG Biofeedback

As described by Thatcher and Lubar (2008), scientists at UCLA in the 1950s (Adey et al, 1961) and later Matousek and Petersen (1973) were the first to compute means and standard deviations in different age groups and then Z scores to compare an individual to a reference normative database of means and standard deviations. The Z statistic is defined as the difference between the value from an individual and the mean of the normal reference population divided by the standard deviation of the population. John and colleagues (John, 1977; John et al, 1977; 1987) expanded on the use of the Z score and reference normal databases for clinical evaluation including the use of multivariate measures such as the Mahalanobis distance metric (John et al, 1987; John et al, 1988). For purposes of assessing deviation from normal, the values of Z above and below the mean, which include 95% to 99% of the area of the Z score distribution is often used as a level of confidence necessary to minimize Type I and Type II errors. The standard-score equation is also used to cross-validate a normative database which again emphasizes the importance of approximation to a Gaussian for any normative QEEG database (Thatcher et al, 2003).

The standard concepts underlying the Z score statistic and QEEG evaluations were recently combined to give rise to real-time EEG Z score biofeedback, also referred to as “Live Z Score Biofeedback” (Thatcher 1998a; 1998b; 2000a; 2000b; Thatcher and

Collura, 2006; Collura et al, 2009). The use of real-time Z score EEG biofeedback is another method to advance the integration of QEEG and Neurofeedback. Figure two illustrates the differences between raw score EEG biofeedback and real-time Z score EEG biofeedback.



There are several advantages of real-time Z score biofeedback including: 1- Simplification by reducing different metrics (power, coherence, phase, asymmetry, etc.) to a single common metric of the Z score; 2- Simplification by providing a threshold and direction of change i.e., $Z = 0$ to move the EEG toward a normal healthy reference population of subjects,⁵ and 3- improved linkage between patient's complaints and symptoms and localization of functional systems in the brain. Figures three, four and

⁵ Simultaneous suppression of excessive theta and reinforcement of deficient beta is achieved by using a absolute Z score threshold, which is a simplification compared to standard raw score EEG biofeedback. For example, if the threshold is set to an absolute value of $Z < 2$, then reduced theta amplitude and elevated beta amplitude will both be rewarded when the instantaneous EEG event exhibits a $Z < 2$ theta and beta power value.

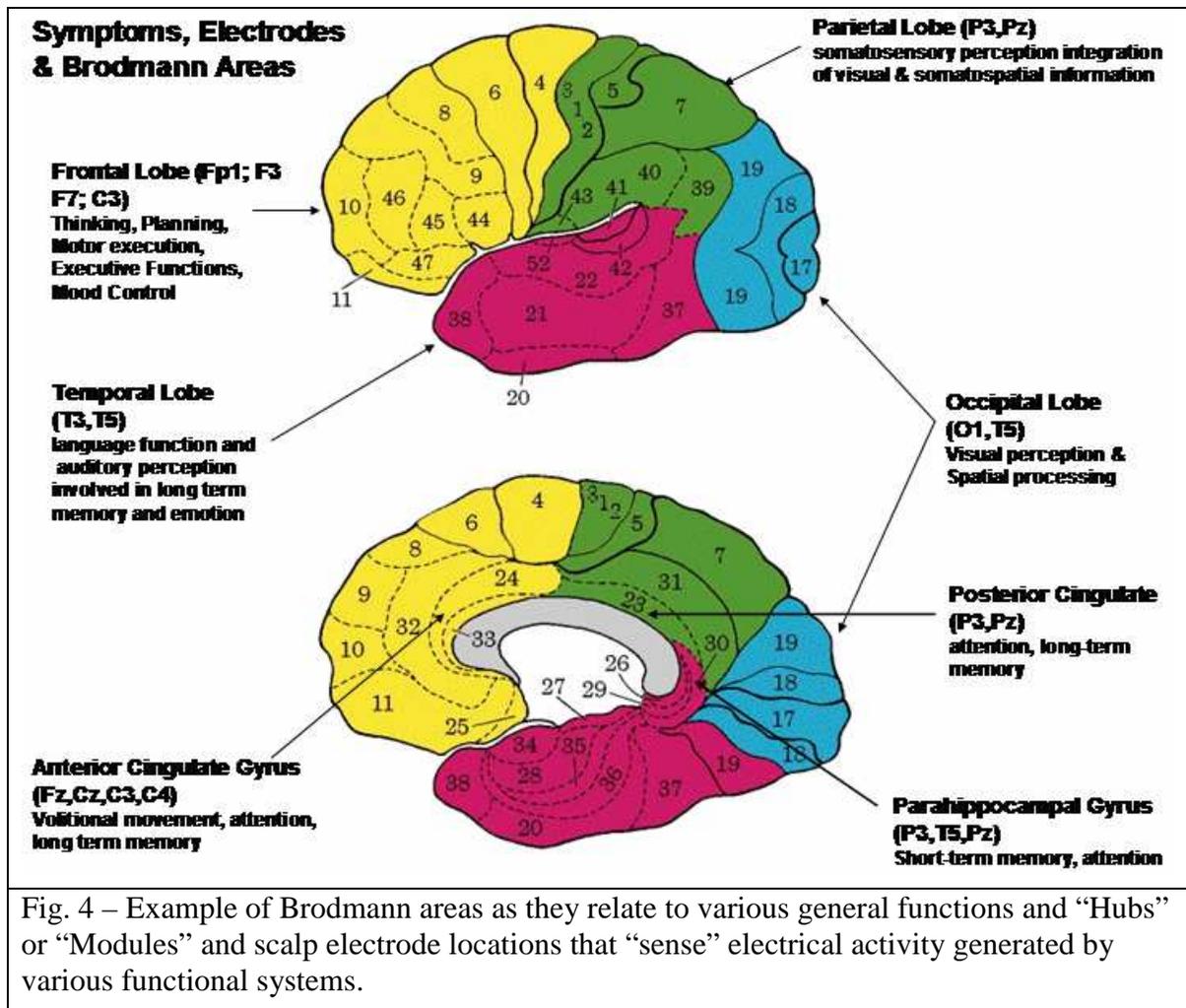
five show examples of how a symptom check list and QEEG evaluation are linked to give rise to a neurofeedback protocol.

Symptom Check List to Create Hypotheses for Neurofeedback

Symptoms Check List		Hypothesis	Hypothesis
Symptom / Complaint	Severity	Channel	Region of Interest
Perception of Letters Problems	0	FP1	Angular-Super Parietal-Supramarginal Gyrus
Slow Reader	0	FP2	Anterior Cingulate
Problems with Spatial Perception	0	F3	Cingulate Gyrus
Orientation in Space	0	F4	Cuneus
Auditory Sequencing	0	C3	Fusiform Gyrus
Short-Term Memory Problems	0	C4	Inferior Frontal-Extra Nuclear Gyrus
Depression	0	P3	Inferior Parietal Lobule
Word Finding Problems	0	P4	Inferior Temporal Gyrus
Problems Multi-Tasking	0	O1	Inferior-Middle-Superior Occipital Gyrus
Poor Judgement	0	O2	Insula
Attention Deficits	0	F7	Lingual Gyrus
Hyperactive	0	F8	Medial Frontal-Subcallosal Gyrus
Skilled Motor Movements	0	T3	Middle Frontal Gyrus
Obsessive Thoughts	0	T4	Middle Temporal-SubGyral Gyrus

Fig. 3 - Example of a computer generated Symptom Check list in which the clinician first evaluates the patient's symptoms and complaints using clinical and neuropsychological tools and then enters a score of 0 to 10 based on the severity of the symptoms. Hypotheses as to the most likely scalp locations and brain systems are then formed based on the scientific literature that links symptoms and complaints to the locations of functional specialization. (From NeuroGuide 2.5.7)

Modules or “Hubs” are linked to various basic functional systems that are involved in cognition and perception (Hagmann et al, 2009; Chen et al, 2008; He et al, 2009). Recent neuroimaging studies show that all of the various “modules” are dynamically linked and interactive and that sub-sets of neural groups in different modules “bind” together for brief periods of time to mediate a given function (Sauseng, and Klimesch, 2008, Thatcher et al, 2008a; 2008b). An illustration of Brodmann areas and electrodes as they relate to functional systems is shown in figure 4.



The linkage of a patient’s symptoms and complaints to the localization of functional systems in the brain is based on the accumulated scientific and clinical literature from QEEG, MEG, fMRI, PET and SPECT studies conducted over the last few decades as well as the basic neurological and neuropsychological lesion literature. The Russian neuropsychologist Alexandra Luria (1973) and the American neuropsychologist Hans-Lukas Teuber (1968) are among the leading scientists to make important linkages between symptoms and complaints and localization of functional systems in the brain. The integration of QEEG and EEG biofeedback relies upon such linkages as the initial stage in the formation of neurofeedback protocols as illustrated in figures 3, 4 & 5. The idea is to first produce hypotheses about likely linkages between a patient’s symptoms and complaints and the location of functional systems based on the scientific literature prior to conducting a QEEG. Step two is to confirm or disconfirm the linkage by evaluating brain locations of deviations from normal using QEEG and LORETA 3-dimensional imaging and step three is to produce a biofeedback protocol based on the match between hypothesized locations and the QEEG and/or LORETA evaluation. Luria (1973) emphasized that de-regulation of neural populations is reflected by reduced homeostatic balance in the brain in which symptoms are represented as “loss of function”

that are often accompanied by “compensatory” processes. One goal of the linkage of QEEG and neurofeedback is to identify and contrast the weak or “loss of function” components in the EEG from the compensatory processes where the weak systems are the initial target of the EEG biofeedback protocol.

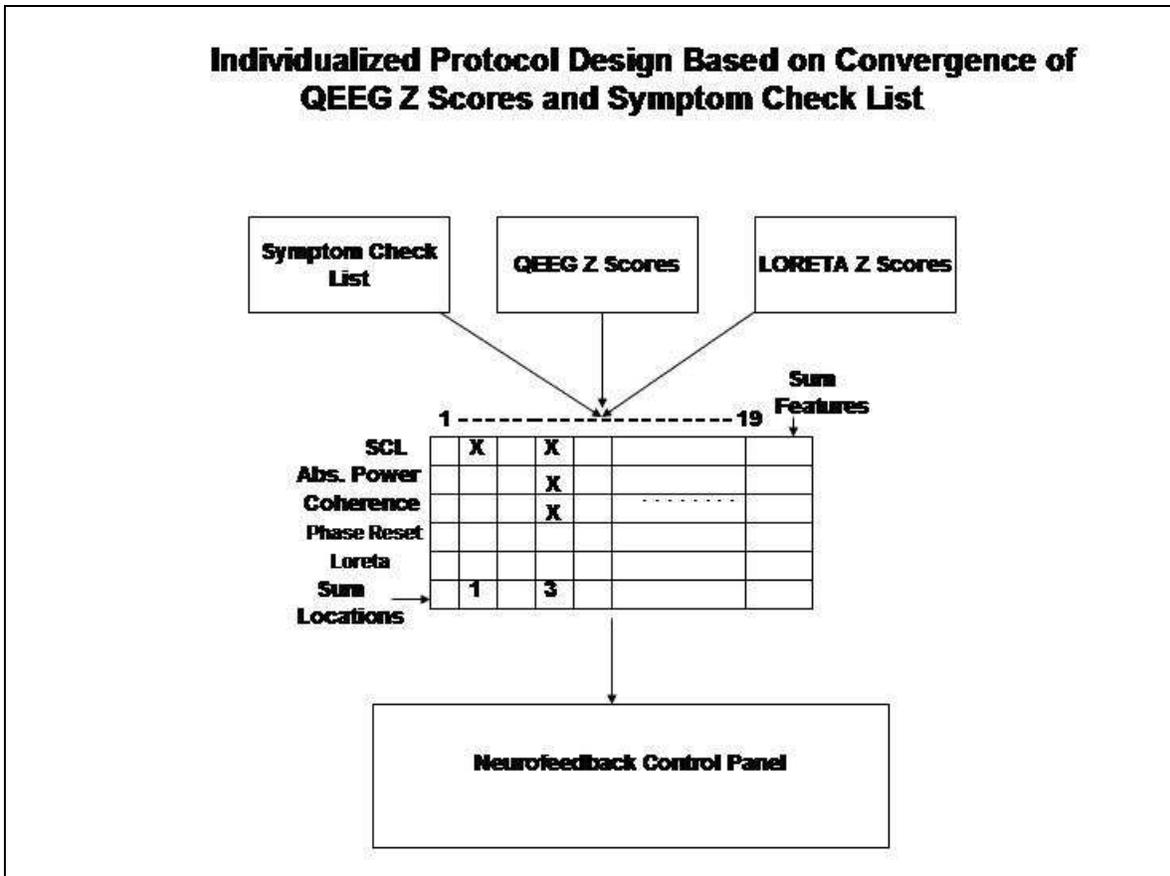


Fig. 5 - Flow diagram of individualized protocol design based on linkage of patient’s symptoms and complaints with surface QEEG Z scores and LORETA Z scores. The columns of the matrix are the 19 channels of the 10/20 International electrode sites and the rows are symptoms and QEEG EEG features. Hypotheses are formed as to the most likely electrode site locations associated with a given symptom and complaint based on the scientific literature. The hypotheses are then tested based on QEEG and LORETA Z scores. Weak systems representing “loss of function” are identified when there is a match of QEEG Z scores with the hypothesized scalp locations based on symptoms. Compensatory locations are identified by a mismatch between hypothesized symptoms and complaints and the locations of observed QEEG Z scores. A suggested neurofeedback protocol is then produced based on the locations of the “weak” systems.

Figure six is an example of a 19 channel surface EEG biofeedback setup screen in Neuroguide where users can select a wide variety of measures or metrics all reduced to the single metric of the Z score. This includes, power, coherence, phase differences, amplitude asymmetries, power ratios and the average reference and Laplacian montages. 19 channels is a minimum number of channels in order to compute accurate average

references and the Laplacian montage which is an estimate of the current density vectors that course at right angles thru the skull.

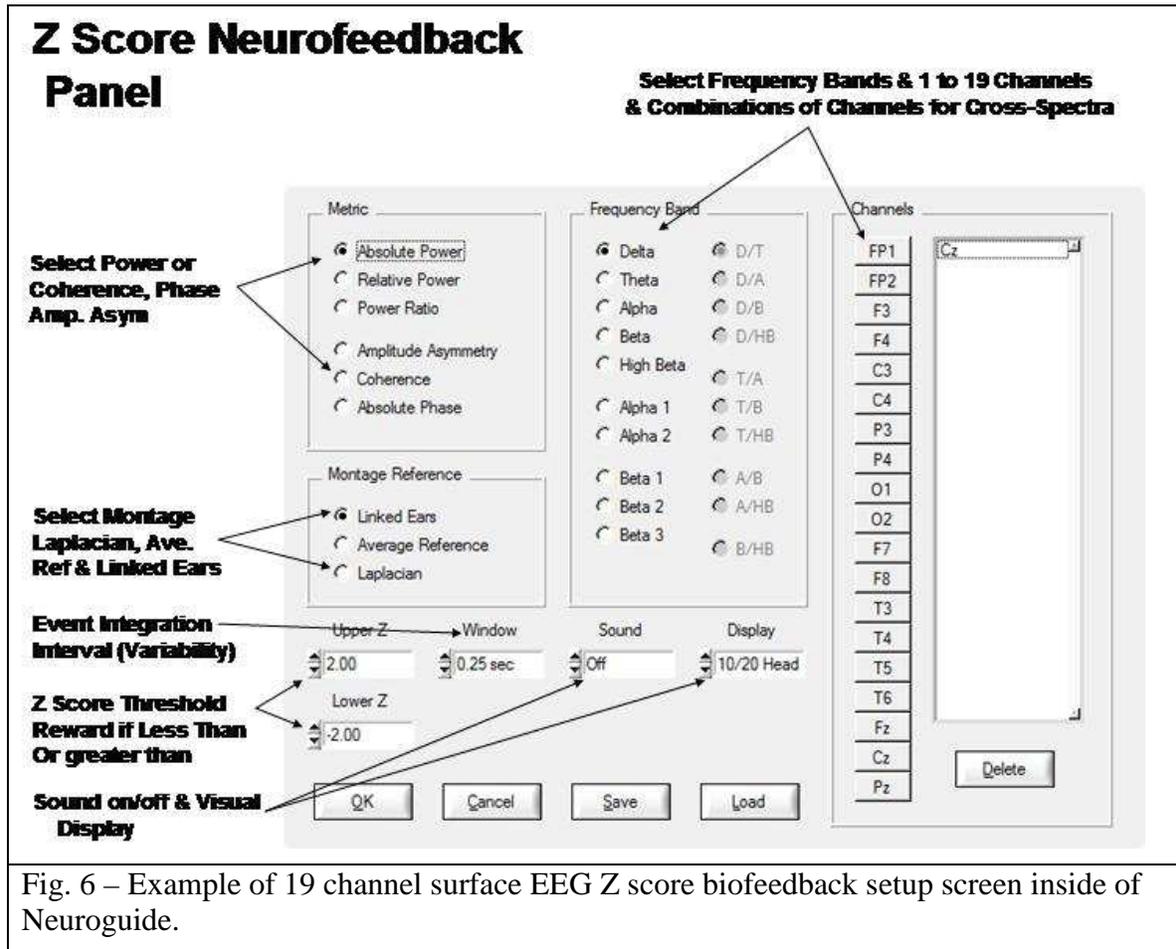


Fig. 6 – Example of 19 channel surface EEG Z score biofeedback setup screen inside of Neuroguide.

Multiple frequencies and multiple metrics may be selected in which a threshold must be reached before a visual and/or auditory reward is given (e.g., $Z < 2.0$). The 19 channel Z score approach provides for seamless integration of QEEG assessment and 19 channel Z score neurofeedback or treatment. Because there are approximately 8,000 possible instantaneous Z scores, it is important to limit and structure the biofeedback protocol in a manner that best links to the patient's symptoms and complaints. The linkage of patient's symptoms and complaints as hypotheses that are confirmed or disconfirmed by QEEG assessment are used to develop a neurofeedback protocol. Blind and random selection of Z score metrics runs the risk of altering "compensatory" systems and not focusing on the weak or "loss of function" systems that are linked to the patient's symptoms and complaints.

Figure seven shows an example of a simple 10/20 head display for feedback where the circles turn green when threshold is met (e.g., $Z < 2.0$) and provides feedback about the scalp locations that are meeting threshold.

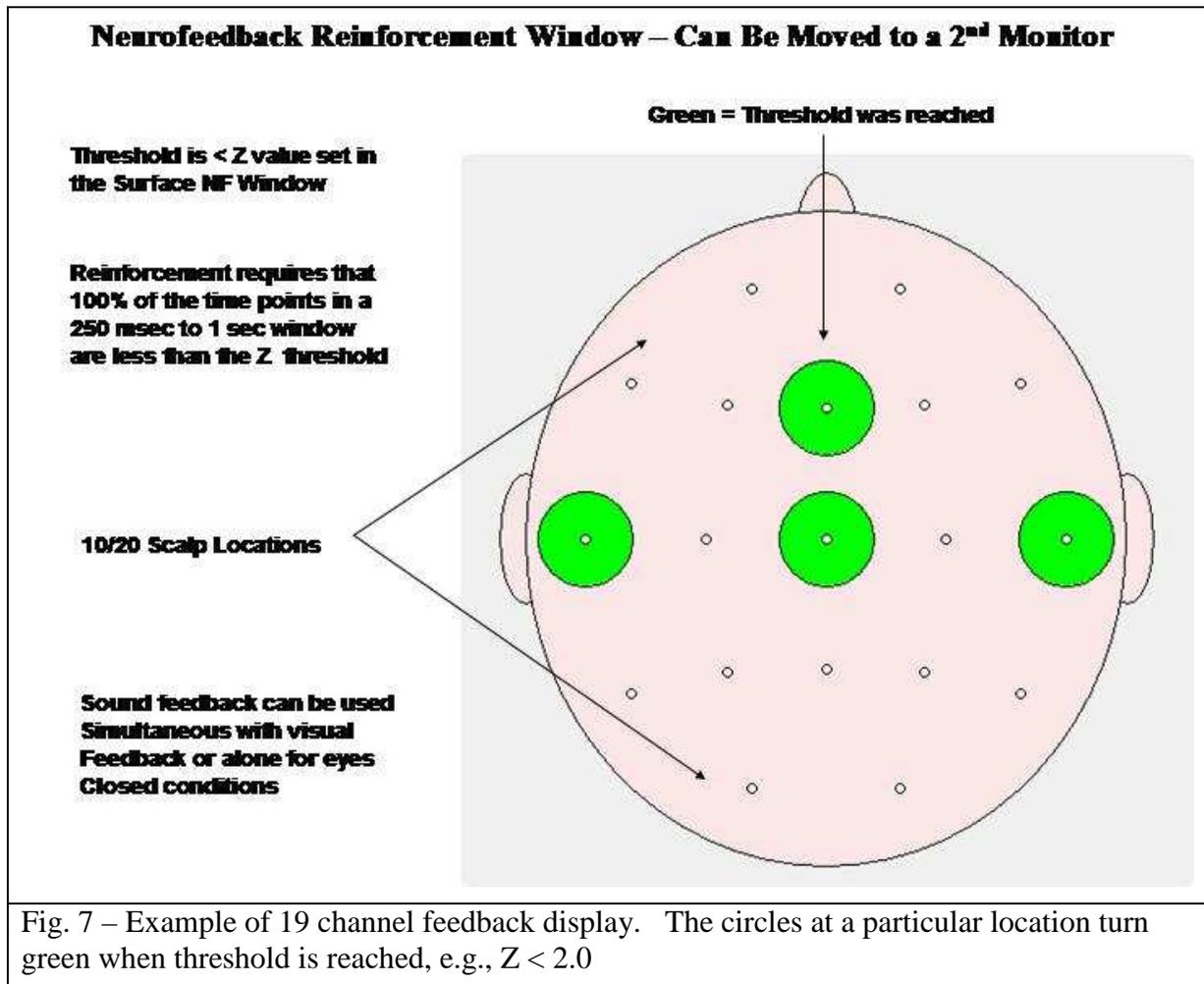
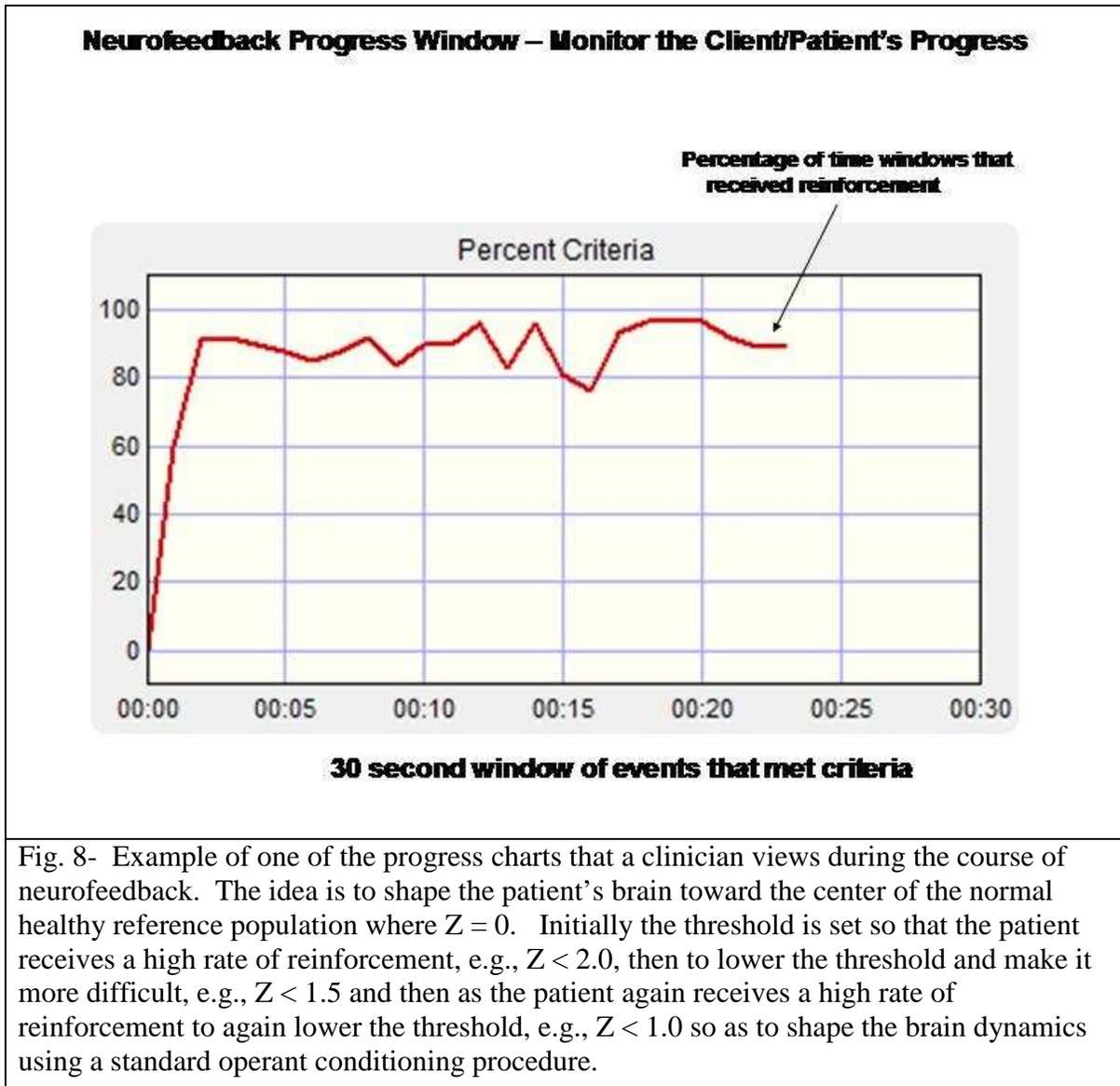


Figure eight is an example of a progress monitoring chart that is displayed for the clinician during the course of biofeedback. One strategy is to develop a protocol based on the linkage to the patient's symptoms and complaints as discussed previously and then to set the Z score threshold so that it is easy for the subject to meet threshold and thus produce a high rate of successful 'Hits' or rewards. Step two is to lower the threshold and make the feedback more difficult, e.g., $Z < 1.5$ and as the patient or client gains control and receives a high rate of reinforcement to again the lower the threshold, e.g., $Z < 1.0$ in a "shaping" process in which operant conditioning is used to move the patient's brain metrics toward the center of the normal reference population or $Z = 0$.



NeuroImaging Neurofeedback or Real-Time LORETA Z Score Biofeedback

Improved accuracy in the linkage between a patient's symptoms and complaints and the localization of functional systems can be achieved by the biofeedback of real-time 3-dimensional locations or voxels in the brain. This method has been successfully implemented with functional MRI (i.e., fMRI) for chronic pain, obsessive compulsive disorders and anxiety disorders (Apkarian, 1999; Yoo et al, 2006; Weiskopf et al, 2003; Cairia et al, 2006; Bray et al, 2007; de Charms et al, 2004; de Charms, 2008). Figure 9 shows an example of fMRI biofeedback displays

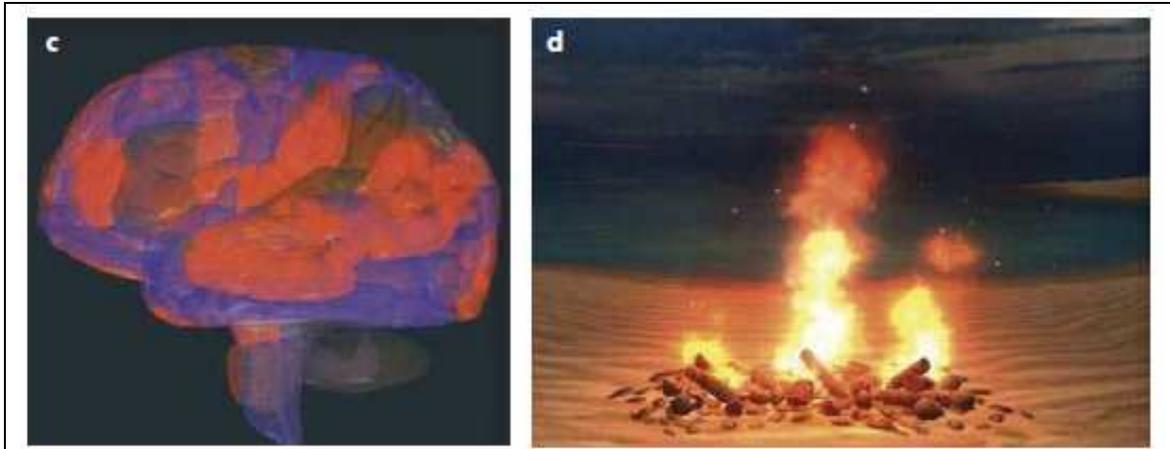


Fig. 9- Information from individual spatial points can be segregated into multiple anatomically defined three-dimensional regions of interest. Here the activation levels (represented as colours) of three brain regions are rendered on a translucent 'glass brain' view. (d) -Activation in these regions can either be plotted second-by-second in real time or can be presented to subjects in more abstract forms, such as this virtual-reality video display of a beach bonfire, in which each of the three elements of the flickering fire corresponds to activation in a particular brain region. Brain activation can control arbitrarily complex elements of computer-generated scenarios. (From de Charms, 2008).

However, fMRI biofeedback also referred to as Neuroimaging Therapy has several significant limitations in comparison to LORETA 3-dimensional EEG biofeedback⁶: 1- A long time delay between a change in localized brain activity and the feedback signal, e.g., 20 seconds to minutes for fMRI while LORETA EEG biofeedback signals involve millisecond delays; 2- fMRI only provides indirect measures of neural activity because blood flow changes are delayed and secondary to changes in neural activity whereas EEG biofeedback is a direct measure of neural electrical activity and, 3- Expense in which fMRI costs 3 million dollars for the MRI machine plus \$30,000 per month for liquid helium whereas EEG biofeedback equipment and maintenance costs are less than \$10,000. The spatial resolution of LORETA source localization is approximately 7 mm³ which is comparable to the spatial resolution of fMRI.⁷ fMRI, however, offers the advantage of imaging of non-cortical structures such as the striatum, thalamus, cerebellum and other brain regions where as QEEG is limited to imaging of cortical dipoles produced by pyramidal cells. Nonetheless, even with this limitation several studies have proven that biofeedback using LORETA real-time 3-dimensional sources is feasible and results in positive clinical outcomes (Lubar et al, 2003; Cannon et

⁶ LORETA means "Low Resolution Electromagnetic Tomography" (Pascual-Marqui et al, 1994). Since the inception of this method in 1994 there have been over 500 peer reviewed publications (see <http://www.uzh.ch/keyinst/NewLORETA/QuoteLORETA/PapersThatQuoteLORETA05.htm> for a partial listing of this literature).

⁷ The voxel resolution of LORETA is 7 mm³ which is adequate spatial resolution because the Brodmann areas are much greater in volume than 7 mm³. Also, the biological resolution of functional MRI may be worse than LORETA because it depends on the vascular architecture of the brain. For example, Ozcan et al (2005) showed that maximal fMRI spatial resolution is > 12 mm³.

al, 2005; 2006a; 2006b; 2007; 2008). Figures ten and eleven shows an example of LORETA EEG biofeedback of the anterior cingulate gyrus and corresponding increases in current density as a function of biofeedback sessions.

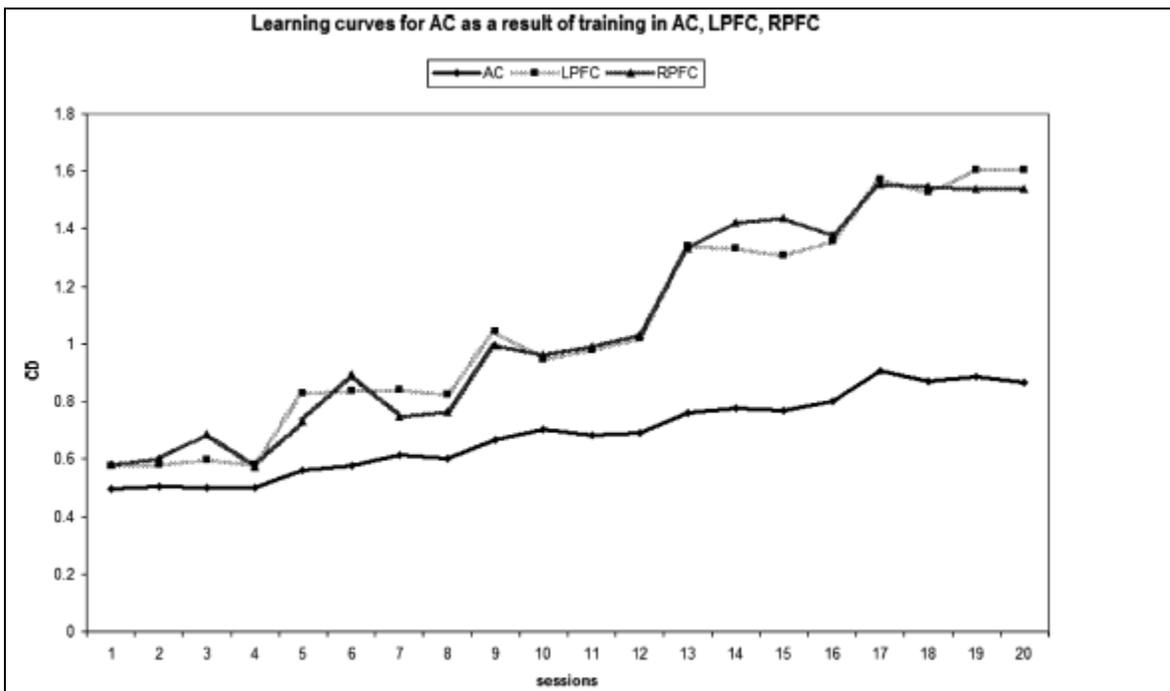
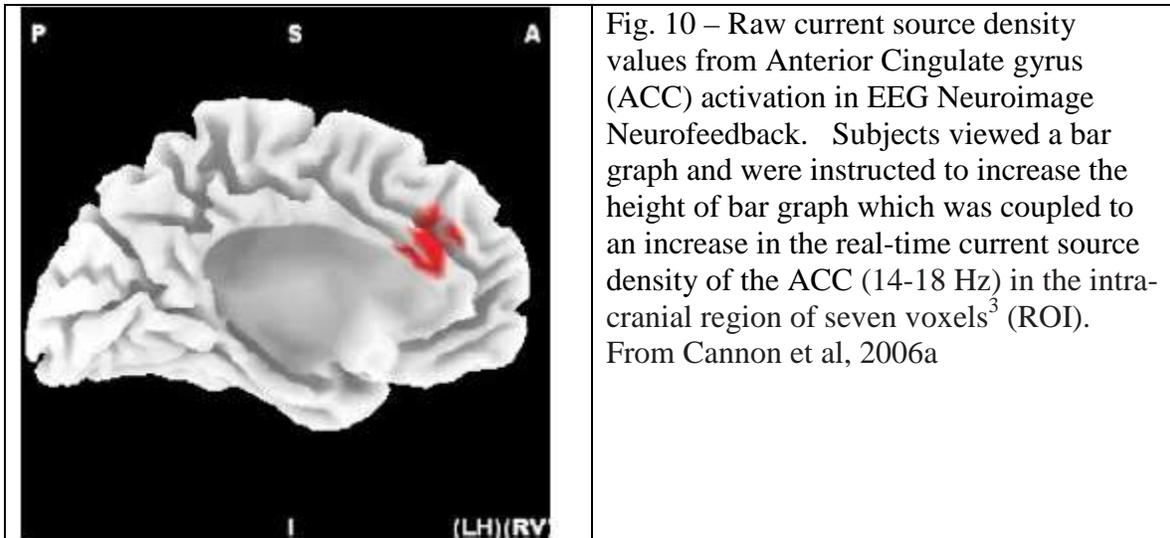


Fig. 11 - Increase in current density (14–18 Hz) from three different ROIs, resulting from training of the Anterior Cingulate gyrus (AC). LPFC = left pre-frontal cortex; RPFC = right pre-frontal cortex. The AC appears to influence increases in the LPFC & RPFC higher than the increase for itself although all three ROIs increased current density as a function of training. Corresponding improvements in working memory and attention were also measured. From Cannon et al, 2009.

Future Directions of QEEG and Neurofeedback

Dramatic improvements in sensitivity and spatial resolution of neural sources linked to patient's symptoms and complaints have occurred in the last 80 years since EEG was first discovered. The development of EEG biofeedback occurred almost in parallel with the sudden growth of QEEG in the 1960s and today there is ever more integration of QEEG for clinical evaluation and EEG biofeedback for treatment. QEEG assessment and EEG biofeedback treatment are inextricably bound in which advancements in sensitivity and spatial resolution of QEEG as a clinical evaluation tool are immediately translated to treatment using biofeedback. There has been a veritable explosion of new discoveries in neuroscience related to basic mechanisms of memory, attention, arousal and cognition and correlations to various, neurological, psychiatric and psychological disorders. In parallel with these advancements it is expected that EEG biofeedback will keep pace by advancing new methods of non-invasive treatment of a wide variety of clinical disorders. Today high speed computers are available in which 19 or more channels of EEG can be measured and biofeedback applied in almost the same amount of time as 1 or 4 channel biofeedback was applied in the past. Thus, there is little practical limitation in using high density electrode arrays for EEG biofeedback in the future. As knowledge about basic neurophysiological control measures emerge, for example, thalamic mediated phase shift and phase lock, coherence, cross-frequency phase synchrony and LORETA spatial coordination of brain modules underlying perception and cognition then the clinical efficacy of EEG biofeedback will improve. Given the expense of health care and the need for non-invasive treatment the marriage of QEEG and EEG biofeedback will continue to evolve.

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