Clinical Database Development: Characterization of EEG Phenotypes

J. Johnstone, J. Gunkelman and J. Lunt

Key Words
EEG
EEG Databases
EEG Phenotypes
Neurofeedback
Quantitative EEG

ABSTRACT

We propose development of evidence-based methods to guide clinical intervention in neurobehavioral syndromes based on categorization of individuals using both behavioral measures and quantification of the EEG (qEEG). Review of a large number of clinical EEG and qEEG studies suggests that it is plausible to identify a limited set of individual profiles that characterize the majority of the population. Statistical analysis has already been used to document "clusters" of qEEG features seen in populations of psychiatric patients.[1] These clusters are considered here as intermediate phenotypes, based on genetics, and are reliable indices of brain function, not isomorphic with DSM categories, and carry implications for therapeutic intervention. We call for statistical analysis methods to be applied to a broad clinical database of individuals diagnosed with neurobehavioral disorders in order to empirically define clusters of individuals who may be responsive to specific neurophysiologically based treatment interventions, namely administration of psychoactive medication and/or EEG neurofeedback. A tentative set of qEEG profiles is proposed based on clinical observation and experience. Implication for intervention with medication and neurofeedback for individuals with these neurophysiological profiles and specific qEEG patterns is presented.

INTRODUCTION

Development of protocols for Neurofeedback (NF) training and selection of medication often is based exclusively on behavioral aspects of a patient's history and clinical presentation. It is clear that this approach has been reasonably successful, particularly in the hands of experienced clinicians.[2,3] Recent studies of predicting response to psychotropic medication strongly suggest increased clinical benefit by considering the patient's neurophysiological profile, based on EEG analysis, when selecting medication.[4,5] By developing predictive algorithms based on standardized and comprehensive behavioral and neurophysiological patient assessment, more uniformly positive clinical outcomes can be expected.

This paper is an attempt to characterize a number of commonly seen neurophysiological profiles ("intermediate phenotypes") and directly relate specific qEEG patterns, as measures of neurophysiological substrate, to clinical interventions. This is based largely on our personal experience in reviewing a large number of clinical EEG and qEEG studies, using a variety of techniques and databases, as well as practicing neurofeedback, and reviewing the developing literature on these topics.

A number of EEG phenotypes have been described in some detail in the literature, for example, the low-voltage fast pattern has been linked to alcoholism and $GABA_A$ receptor genes,[6] and related work has demonstrated links between low voltage EEG, low voltage ERP (P300), and alcohol.[7] Other investigation links specific genes to EEG abnormalities in epilepsy.[8] A phonemic approach has also been emphasized in electrophysiological characterization of developmental language impairment[9] and schizophrenia.[10] Characterizations linking genomic information, intermediate phenotypes, and behavioral manifestation are likely to have important implications for therapeutics.

The identification of specific patient profiles using *both* behavioral and neurophysiological measures may aid NF providers in accurately determining the optimal frequency selection and how to best increase the activity and stability of particular qEEG features in specific brain regions. The same general method may be used medically to more objectively prescribe psychoactive medication. It should be made clear that these two forms of intervention are not mutually exclusive. Medication is generally fast acting and may be most appropriate for intervention in acute disorders. Neurofeedback may be used to augment or titrate medications to reduce side effects and extend positive outcome over time.

J. Johnstone, PhD, and J. Gunkelman, QEEG-D, are with Q-Metrx, Inc., Burbank, California, and J. Johnstone is in the Department of Psychology, University of California, Los Angeles. J. Lunt, RN, BCIA, is with Brain Potential, Inc., Burbank, California.

Address requests for reprints to Dr. Jack Johnstone, Q-Metrx, Inc., 1612 W. Olive Ave, Suite 301, Burbank, CA 91506, USA.

Email: Jack@q-metrx.com

Table 1

Summary of qEEG databases

	Neurometrics (John & Prichep)	NeuroGuide (Thatcher)	SKIL (Sterman & Kaiser)	NeuroRep (Hudspeth)	Eureka3 (NovaTech)	International Brain Database (Brain Resource Company)
No. of Cases						
Adults	N=426	N=155	N=135	N=55 + 30 replicates	N=84	N=1284
Children	N=356	N=470	None	None	None	N=607
Age Adjustment	Yes-Regression Equation	Yes-age subsets 16 < n < 45	No-(adults only)	No-(adults only)	No-(adults only)	Yes-Non-linear regression
Screening for Normalcy	Questionnaire screening for significant medical history	Questionnaire, WISC/WAIS IQ, WRAT, School gradepoint	Questionnaire screening for significant medical history, life events	Luria-Nebraska, medical history, life events	Questionnaire, interview for medical and clinical histories, negative for substance use	23 different questionnaires and scales, for medical and neurological history, cognitive screening
No. of EEG Channels	19	19	19	19	19	26
EEG Frequency Range	EEG spectra banded as Delta, Theta, Alpha, Beta (.5-25 Hz)	EEG spectra banded and in 1 Hz bins (0-30 Hz)	EEG spectra in 1 Hz bins (1-24 Hz)	EEG spectra banded as Delta, Theta, Alpha, Beta (.5-22 Hz)	EEG spectra in 1 Hz bins (2-32 Hz)	EEG spectra banded as Delta, Theta, Alpha, Beta, Gamma (0-40 Hz)
EEG Features Used	Absolute and Relative Power, Coherence, Frequency, Symmetry	Relative Power, Asymmetry, Coherence, Phase	Absolute Magnitude, Comodulation	Absolute Magnitude, Relative Power, Frequency Ratios, Coherence, Phase, Symmetry	Absolute and Relative Power, Power Ratios, LORETA	Absolute Power, Relative Power, Absolute Magnitude, Phase, Frequency, Symmetry, ERPs, Coherence, Frequency Ratios, LORETA
Recording Conditions	Eyes Closed	Eyes Closed, Eyes Open	Eyes Closed, Eyes Open, 2 tasks	Eyes Closed, Eyes Open	Eyes Closed	Eyes Closed, Eyes Open, Task battery
Reference Electrode	Linked Ears, Selected Sequential Pairs	Linked Ears, Average, Laplacian	Linked Ears	Linked Ears	Common Average	Linked Mastoid (also, average reference in analysis)

A notion central to the determination of EEG abnormalities is the comparison of an individual to a "normative" or "reference" database. Clinicians use statistical deviations of an individual from the mean values in the database, along with other clinical information, to identify abnormalities of brain function. A number of databases are currently available for evaluation of individuals compared to normal or "reference" values. These databases are listed in Table 1, with a brief description of the major features of each. Note that these databases have been reviewed in detail[11,12] and differ with respect to sample size, screening criteria, and EEG features normed. The International Brain Database includes numerous other measures in addition to EEG, and is unique in allowing for an integrative approach, combining neurophysiology, neuroanatomy, cognition, and genetics.

Table 2

qEEG patterns/phenotypes with implications for intervention

qEEG Profile	Description of Pattern	Medication	Neurofeedback
Diffuse slow activity, with or without low frequency alpha	Increased delta and theta (1-7 Hz) with or without slow posterior dominant rhythm	Stimulant	Inhibit midline frontocentral activity below 10 Hz, add reward anterior beta frequencies for increased effect
Focal abnormalities, not epileptiform	Focal slow activity or focal lack of activity	???	Inhibit slow activity (<10 Hz) and reward higher frequencies (> 12 Hz)
Mixed fast and slow	Increased activity below 8 Hz, lack of alpha, increased beta frequency activity	Combine across classes, e.g., stimulant + anticonvulsant?	Inhibit slow frequencies, reward middle frequencies. Reward SMR
Frontal lobe disturbances	Frontally dominant excess theta or alpha frequency activity	Antidepressant, stimulant	Inhibit midline frontocentral activity below 10 Hz, add reward anterior beta frequencies for increased effect
Frontal asymmetries	Variable asymmetry L>R or R>L, primarily at F3, F4	Antidepressant	Reward F3 beta, inhibit F3 theta and alpha frequencies
Excess temporal lobe alpha	Increased alpha activity generated in temporal lobe	Stimulant	Inhibit 9-12 Hz activity over affected temporal region(s), + inhibit frontal slow activity
Epileptiform	Transient spike/wave, sharp waves, paroxysmal EEG	Anticonvulsant	Inhibit low and high frequencies over affected regions, central strip training, reward SCP
Faster alpha variants, not low voltage	Alpha frequency greater than 12 Hz over posterior cortex	???	Reward 9-10Hz alpha at Pz, shift alpha frequency lower with alpha/theta protocol
Spindling excessive beta	High frequency beta with a spindle morphology, often with an anterior emphasis	Anticonvulsant	Inhibit beta frequencies, wide band inhibit
Generally low magnitudes (fast or slow)	Low voltage EEG overall	Metabolic support, nutraceuticals	Reward alpha activity posteriorly
Persistent alpha with eyes open	Lack of appreciable alpha blocking with eye opening	???	Reward beta frequencies, inhibit alpha. Reward higher frequency alpha

Note: The above information is not intended as a substitute for professional consultation. See text for more complete descriptions.

Note that individuals comprising the normative databases are medication-free. It is important to recognize the influence of psychoactive medications used by individual patients in interpreting results of individual qEEG studies. We recommend recording EEG with the patient off medication, but this is often not practical and is always the decision of the attending physician. Further, washout times for certain medications, such as the SSRI type antidepressants, can be quite lengthy (depending on the degree of washout, sometimes over a month), and recording with medications may be the only clinically acceptable course of action.

QEEG SUBTYPES AND PROFILES AS INTERMEDIATE PHENOTYPES

Numerous reports suggest the presence of neurophysiological "subtypes" within behaviorally homogeneous pop-

ulations. For example, work by Chabot et al.[13-16] indicates common subtypes seen in an ADD population, most prominently an excess of frontal theta frequency pattern. However, it is clear that this pattern is not specific to ADD and has been reported in a number of other clinical disorders, including major depression.[4] The notion of a subtype should be restricted to a particular disorder, otherwise it is more appropriately described as a qEEG profile or neurophysiological "phenotype," that has variable representation in one or more disorders defined behaviorally.

The presence of multiple qEEG profiles within a given behavioral category, and varied behavioral presentations within a given qEEG profile, suggests that a simple listing of each qEEG profile with associated behavior and associated interventions is not plausible. Physicians are already knowledgeable about treatment intervention based on behavior and standard clinical evaluation. We also emphasize the critical need for standard medical evaluation, typically by a neurologist or psychiatrist, using all available tools, including neuroimaging, psychological testing, and other methods to characterize disorders involving diffuse or focal slowing, epileptiform features, or patterns considered to be associated with various encephalopathies or other neurological disorders. Appropriate medical intervention clearly is indicated in such cases. It also is clear that neurofeedback has been clinically applied with varying degrees of success with frank neurological disorders, and is rarely, if ever, contraindicated when used in combination with other medical intervention.

An individual qEEG profile may contain predominately one of the patterns described in more detail below, but profiles may be complex and frequently contain elements of several of these patterns described below. Note that qEEG results also may be considered generally "within normal limits for age." This may indicate less need for aggressive therapeutic intervention. Critical to the use of qEEG profiles is the question of whether qEEG is a reliable measure and whether individual qEEG profiles are stable over time. Our research has shown that EEG spectra are quite stable and reliable and as such may be useful as indicators of an individual's characteristic profile.[17]

Classes of EEG abnormalities are well known in the clinical EEG literature. The genetic basis for a number of patterns has been described in detail.[18-20] Indeed, qEEG profiles may be regarded as intermediate phenotypes, that is, manifestations seen between the genome and behavior. These intermediate phenotypes are highly heritable, are reliable indices of brain function, are not isomorphic with DSM categories, and have implications for therapeutic intervention.

EEG abnormalities are often differentiated as to nonspecific patterns, such as focal slow activity, and abnormalities attributable to epileptic and paroxysmal features. Comprehensive reviews of these classes of abnormality are available.[18] The present review does not include certain severely abnormal patterns such as might be seen in coma, status epilepticus, or barbiturate anesthesia.

The following profiles and proposed intervention strategies are proposed based on clinical experience with neurofeedback and a developing literature on use of qEEG to predict medication responsivity. The emphasis in NF here is in modulating the amount of low and high frequency EEG activity. It is important to recognize that other features of the EEG, such as phase synchrony or variability, are the subjects of active clinical research and may offer additional valuable tools to reliably modulate brain activity. Candidate qEEG phenotypes are summarized in Table 2. The efficacy of these factors is testable, and if proven useful could then be used in evidence-based therapeutic intervention.

COMMONLY SEEN EEG PHENOTYPES AND ASSOCIATED PROPOSED INTERVENTION STRATEGIES

Diffuse Slow Activity, With or Without Low Frequency Alpha

The general arousal level of the brain is largely determined by the ascending reticular activating system (RAS), which stimulates the diffuse thalamic projection system. When there is a decrease in CNS activation level, there is a decrease in mean frequency of alpha and an increase in slow activity. This is often due to specific neuropathology which should be medically identified and treated, as discussed above. The pattern is often seen in pervasive developmental disorders, dementing illness, and other disorders of consciousness. The slow activity appears as a generalized dysrhythmia, a mixture of diffuse lower voltage delta and theta, usually with a weak vertex prominence in linked ear montages. A pattern of diffuse slow activity and a pattern of low alpha frequency may be seen either separately or coexistent.

Implications for intervention

When diffuse slow activity with low frequency alpha is identified, NF rewarding higher frequency activity, for example enhancing activity in the 12-18 Hz range, at the vertex or central sensorimotor strip can increase mean alpha frequency and decrease the lower frequency activity. When decreased amounts of frontal beta are seen in the qEEG, the subject may respond to a more anterior placement for training increased beta frequency activity.

When this combination of excess slow activity and low frequency alpha is seen, but with alpha spreading frontally (occasionally with less slow activity), the protocol should include frontal beta enhancement and alpha suppression, as well as parietal "high alpha." High alpha is defined as 11-16 Hz in the classical EEG literature, but usually in neurofeedback, this is from 10 or 11 Hz to 14 Hz. This parietal high alpha shifts the alpha mean frequency higher. Often it is the lower alpha frequencies that are spreading frontally, and they are reduced with this shift.

Early clinical trials suggest that slow patterns may also be particularly responsive to use of stimulant medication.

Focal Abnormalities, not Epileptiform

An electroencephalographer or neurologist should evaluate focal slow activity that is not an artifact (such as a pulse, electrode, electrodermal, eye movement or other artifactual source of slowing). The focal slowing may be from a tumor, ischemia, stroke, trauma, inflammation or other medical condition. The etiology should be identified prior to any intervention or consideration of NF or medication.

Another finding involves focal low amplitude across the frequencies for a specific region. The EEG can be seen with areas of decreased amplitude, not just a beta deficit, but an area of general amplitude minima. This phenomenon is seen well in topographic EEG mapping. These areas have been observed frontally in attentional and affective disorders.[21]

Implications for intervention

Should the etiology be known, generally the reduction of the slowing and enhancement of faster activity improves the brain function following NF. Excess slow activity is reported in specific learning disabilities and sensory processing problems.[13,14,15]

Neurofeedback training to increase amplitude for regions with little activity across the frequency spectrum, so-called "dead areas," appears to be effective when increased activity in the beta frequencies is rewarded and the slower frequencies are suppressed. Beta is correlated highly with PET measurements of metabolic activity.[22]

In similar fashion, stimulant medications are at times indicated to help activate these "dead areas" and suppress the slower frequency production.

Mixed Fast and Slow

The mixed fast and slow profile has decreased content in the traditional alpha band (8-13 Hz) as well as in the lower beta frequencies, and increased relative fast (higher beta) and slow (theta and delta) EEG components. The coexistent fast and slow activity often is distributed with an anterior emphasis but may also show a posterior or diffuse distribution. This pattern is commonly seen as an effect of medication, but may also be seen in the absence of medication(s) where this result is usually considered encephalopathic.

Implications for intervention

In our experience, using neurofeedback to inhibit the slower activity, and reward the middle alpha frequencies is useful. Reinforcing higher frequencies may produce undesirable activation effects, in contrast to diffusely slow profiles seen without the presence of higher frequency activity. SMR (sensorimotor rhythm, 12-15 Hz) enhancement training is also useful in this clinical subgroup as an appropriate attempt to activate these areas.

It has been our experience that the use of stimulants has been helpful with this pattern, particularly when this pattern shows the slower frequency distribution to be more anterior in location. Combining medications across classes (e.g., stimulant and anticonvulsant) may be useful in addressing this complex pattern.

Frontal Lobe Disturbances

The frontal lobe has general regulatory control over the brain. In attentional and affective disorders as well as motor dyscontrol, such as hyperkinetic disturbances, the locus of the dysfunction is commonly predominantly the frontal lobe. Recent work on ADD/ADHD and affective disorders shows a variety of frontal disturbances seen with the qEEG. These varieties include a theta or alpha excess, and even excess beta.[4] The frontal midline overlies the cingulate gyrus, seen as disturbed in perseverative disorders, including Obsessive Compulsive and Oppositional Defiant Disorders (OCD/ODD), Reactive Attachment Disorder (RAD) and Generalized Anxiety Disorders (GAD). Frontal EEG may be disturbed as a result of cingulate dysfunction.[23]

The midline frontal EEG may also be associated with structures other than the cingulate, such as the marginal gyrus or supra-marginal gyrus. Careful correlation is required to ascertain whether the frontal midline activity has cingulate related features associated with it. Alternatively, low-resolution electromagnetic tomography (LORETA), an advanced "inverse solution" algorithm, may be used to project the "source" of the midline EEG generators.

Implications for intervention

When excessive activity is seen in the frontal lobe neurofeedback can be used to inhibit any or all of these EEG frequencies. Activation of the frontal lobe may be facilitated by inhibition of slow frequencies, reward of higher frequencies or a combination of both. It is critical to monitor client responses to adjust these protocols.

Patterns of excessive frontal beta are also seen. The frontal beta type seems to respond to normal frequency alpha enhancement training posteriorly as well as frontal beta suppression. In general, we do not recommend enhancement (reward) training frontally when there is excessive beta present.

QEEG profiles including excess frontal alpha respond less well to frontal alpha suppression training than to posterior high frequency alpha enhancement training with concurrent frontal beta enhancement training. Reduced alpha frontally has been reported following training to increase the faster frequency alpha over parietal regions, generally at Pz.[24] Rewarding 11-14 Hz activity at Pz can be used to promote increased faster parietal alpha. Increased 11-14 Hz activity over parietal cortex has also been associated with increased cognitive performance, termed "brain brightening"[25] and with better memory.[26]

The presence of excessive frontal theta frequency activity has been noted as a marker for response to a number of types of stimulant medications. The presence of excessive frontal alpha activity has been proposed as a marker for

response to antidepressant medication.[4] When midline EEG showed a dominance of alpha activity, SSRI medications showed an 85% probability of success, though the theta pattern at the midline yielded only a 15% positive outcome.

A recent study using prospective evaluation of the predictive power of qEEG measures demonstrated that relative theta power measured after 1 week of medication predicts response to open-label, flexible dose treatment with SSRIs in MDD. Relative theta power at week 1 correlated with percent improvement in HAM-D (R=-0.498, p=0.002).[27]

Frontal Asymmetries

In addition to frontal disturbances generally, there is literature suggesting the special importance of asymmetries over frontal cortex. Frontal interhemispheric alpha and beta ratios seem to correspond well with the perceptual style of the subject. Right hemispheric dominant (more beta and less alpha than the left hemisphere) subjects have a "glass is half empty" perception and a lower mood state, or more depression.[28] Increased alpha activity is occasionally seen over the frontal lobes bilaterally, but when there is right frontal excess alpha, anxiety or agitated type of depression may be manifest.[29]

Implications for intervention

NF with the frontal lobes needs to keep the left dominance, or to establish such a dominance to avoid deteriorating mood states and perceptual styles in the client. This is accomplished by rewarding left frontal beta and inhibiting left frontal alpha and/or theta. If care is taken to measure and assure the desired symmetry, frontal lobe training on either side may be done without significant difficulty.

Excess Temporal Lobe Alpha

With respect to excessive temporal lobe alpha activity, it is useful to make a distinction between temporal lobe alpha that represents spread from high amplitude occipitally generated alpha and excess alpha generated by intrinsic temporal lobe mechanisms. The increased alpha generated by the temporal lobe suggests decreased function in these areas[22] (see also[40]). When excessive alpha is seen in the temporal lobe, it may also be an effect seen in response to decreased activity by the ipsilateral frontal lobe. The decrease in stimulation from the frontal lobe allows the temporal lobe to be idle. This usually will be seen with one of the frontal lobe patterns discussed previously.

Elevated alpha at P7 (older nomenclature: T5) or P8 (older nomenclature: T6) can contaminate the ear references, yielding apparent frontal alpha in the qEEG.[21] The ears with alpha contamination and the frontal lobes without alpha are compared in the differential amplifier, and show apparent alpha in the frontal channel. Use of a variety of montages helps to evaluate this pattern. In particular, use of the Laplacian transform and Current Source Density analysis can help constrain the problem of volume conduction, and better define or "sharpen" the localization of EEG power and amplitude measures.[30,31]

Implications for intervention

The temporal lobes may be overly responsive to beta enhancement training and, as such, lower frequency beta enhancement training is used more commonly than higher frequency intervention. The temporal idling may be cleared up with the direct frontal work discussed earlier, but may require lower band beta enhancement training directly on the temporal site.

Recommendations often include inhibiting (training down) alpha – excessive alpha is not normally generated in the temporal lobes. There is often some reward of lower beta recommended (13-16 Hz) to attempt to activate the temporal lobes without activating the limbic temporal lobe structures. The temporal sites are selected based on the qEEG distributions of the alpha and in our experience are more often P7 or P8 than T7 (older nomenclature: T3) and T8 (older nomenclature: T4), though this varies individually.

Careful client monitoring to identify "overactivation" or agitation, is required when training increased temporal lobe beta.

Epileptiform Sharp Wave and "Spike and Wave" Activity

Wherever epileptiform activity occurs – for example, at the left temporal lobe – it means that part of the brain is experiencing significant dysregulation, and may not be communicating well with other parts of the brain. Application to epileptiform abnormalities using NF is the most thoroughly validated of any application area, with well-designed randomized trials and double-blinded results.[32] In contrast to surgery for epilepsy, NF can produce good outcome without the significant risk of invasive procedures and the possibility of other medical complications.[33]

Implications for intervention

Sharp wave discharges, which occur in epileptiform waves, are quick transient events: occurring in less than 1/10th of a second. Most EEG biofeedback systems are not set to inhibit such fast bursts, though this may not be necessary. According to Sterman,[32] reducing overall slow wave activity and training increased Sensory Motor Rhythm (SMR) in the area lowers cortical hyper-excitability, which is a key trigger to generating the sharp waves. Therefore, by reducing overall slow wave activity using inhibit filters, and increasing system stability through enhancing SMR, sharp wave transients and epileptiform activity should be reduced.

The location selected for NF training has changed from standard placements in the initial studies by Sterman,[32] to now having locations and filter tuning selected by analysis of the EEG. In the selection of the site, careful attention to the location of onset is required, with visual auras often having a location in the occipital and parietal areas, and auditory or olfactory auras having localization in the temporal areas, etc.

Beta spindling in the location of the kindling is also reported, and direct suppression of these findings may cause a rapid cessation of the ability to initiate a convulsion of more fully expressed disturbance of brain function. The spindling has a fairly narrow beta band, often ranging from the upper teens to the upper 20 Hz frequencies, but with a specific peak and narrow frequency range, thus the spindling morphology. This requires individual tuning for optimal feedback matching to the client. Feedback of the DC part of the EEG signal (direct current, seen as a baseline shift) has been used in NF since the 1970s in Europe, showing that the shift to electropositivity can even stop an epileptiform discharge from occurring.[34]

Epileptiform activity has traditionally been managed medically using anticonvulsant medications. More generally, abnormalities of EEG coherence have been proposed as markers for responsivity to anticonvulsant medication.[4]

Faster Alpha Variants, Not Low Voltage

The alpha frequencies may be faster than usual, above 11Hz, sometimes corresponding with anxiousness or hypervigilance. These individuals often present with complaints about attentional problems. Hypervigilance may act as a source of distraction, different from the more usual ADD/ADHD presentations. The faster alpha often has increased EMG associated with it.

Alpha activity generated secondary to old head trauma is usually a faster alpha variant, adjusted for the individual's alpha "tuning." This is typically seen after the acute changes have dissipated and the initial healing stages are completed, which may be as much as 1-2 years post injury.

Implications for intervention

Rewarding lower alpha frequency activity (8-11Hz) at Pz can be helpful in these cases. In addition, Alpha/Theta neurofeedback can be helpful. Most often it is necessary to begin the Alpha/Theta work at the higher alpha frequencies (those found in the individual's qEEG information) with a goal of gradually rewarding lower alpha frequencies. Clients with these findings often do respond with paradoxical increases in anxiety if the lower alpha frequencies are introduced too soon in the Alpha/Theta work.

Spindling Excessive Beta

Large amounts of beta activity may be seen as a normal variant in very young children. Most commonly, excessive beta is a medication effect, particularly evident with the use of sedatives. If these factors are not applicable, spindling excessive beta is probably best considered as a nonspecific sign of dysfunction or encephalopathy.

Focal excessive spindling beta has been noted in areas associated with pre-epileptic auras. In our experience, it was seen in one case occipitally during visual auras and in another frontotemporally with auras affecting the client more subtly as a smell or even a remembrance. This type of spindling beta may be associated with "cortical irritability," viral or toxic encephalopathies and in epilepsy.[35] Beta amplitudes persistently greater than 20 μV are classically defined as abnormal.[36]

The focal excessive spindling beta pattern is seen in less than 10% of the ADD/ADHD and affective disordered population,[16] but when seen, it is an important finding. It is also reported in bipolar disorder frontotemporally, often more on the right.[37]

Implications for intervention

This pattern responds very poorly to any higher frequency beta enhancement training, exacerbating the symptom complex. Beta enhancement training is strongly contraindicated, though this may be limited to training beta over the areas seen with this excess beta pattern, and not elsewhere on the cortex.

Beta suppression directly in the area of concern has shown good clinical response. The band of frequencies to be suppressed should be selected based on individual profiles, not by standard bands. Broader bands like 14-22 Hz or bands as narrow as 16-18 Hz, and higher 20-30 Hz beta are occasionally involved as well, with many individual variations. The customizing of these interventions would be very difficult, if not impossible, without the qEEG to provide distribution and frequency range information to the NF practitioner.

The spindling beta excess pattern seems to have a positive response to anticonvulsants in other applications, including Depakote and Neurontin.[38]

Generally Low Magnitudes (Fast or Slow)

The occurrence of a low voltage EEG is considered a normal variant when it is a low voltage fast EEG. When the low voltages appear slow however, it is a diffuse and non-specific abnormality.[36] The difference between the two patterns is somewhat more qualitative than quantitative.[39] When power is excessively low, the poor signal/noise ratio may preclude qEEG analysis. Further, findings of deviant asymmetries or coherence may be due to poor signal level.

In these profiles, the magnitudes are generally low, though the low voltage fast pattern is a normal variant. When a low voltage slow pattern is seen, and is confirmed not to be related to drowsiness, it should be evaluated for possible diffuse encephalopathies such as metabolic, toxic, degenerative or post hypoxic etiologies. The low voltage slow type is also reported as an early EEG change in dementia.

Implications for intervention

The low voltage fast pattern responds well to alpha enhancement training with a normal alpha distribution of 8-12 or 9-11 Hz. In low voltage slow patterns, the various encephalopathies should be ruled out. If the patient has no pathology identified, training to increase the faster frequencies and increase alpha activity seems indicated, though there is not enough experience with this pattern to make specific recommendations at this time.

Pharmacologically, overall low voltage may require metabolic support. The use of amino acids or nutraceuticals may be helpful.

Persistent Alpha With Eyes Open

Alpha generally drops in amplitude or magnitude by 50% or more with eyes open compared to the alpha with eyes closed. The mechanism of this is via the specific projection system of the thalamus, as well as more diffusely via the non-specific (or diffuse) projection system. The stimulation desynchronizes the thalamic generators, dropping the amplitudes or magnitudes. The failure of this system suggests a reticulo-thalamic activation system problem, and may be seen in under-arousal. The exception to this is in cases where the alpha is attenuated with eyes closed, as can be seen in low voltage fast EEGs and anxious/nervous individuals.

Implications for intervention

The suppression of alpha over posterior cortex is done by a combination of increasing the arousal level with beta enhancement training to increase brainstem stimulation of the thalamus, as well as direct alpha suppression. The alpha may have slower content, in which case training to enhance the faster alpha frequencies and suppressing any slower content may be advised.

SUMMARY AND CONCLUSIONS

This review has identified some major groupings of EEG/qEEG findings, and discussed the underlying systems that produced the findings. Based on these data, the rationale for selecting the neurofeedback and/or medication intervention appropriate to the patterns has been described. These interventions are based on extensive experience with NF and clinical EEG/qEEG, and more limited experience with predicting response to medications.

These approaches to treatment have been shown to compare favorably to other NF methodologies.[24] The use of neurophysiological measures to predict medication responsivity helps to make the process of selecting psychoactive medications more objective, and may aid in reducing side effects. Further, qEEG may assist in identifying the need for polypharmacy, particularly using combinations of medications from different classes, without an extensive trial-and-error period.

The brain's adaptive and flexible nature and the ability of systems receiving feedback to self regulate can be coupled with modern brain imaging techniques to provide evidence-based methods of selecting specific medication, and what to train and how to train the brain using NF. The power of these techniques can be demonstrated by objective measurement of outcomes. Although selection of medication or the NF training sites and frequencies for tuning using behavioral indicators may be sufficient for clinical response to occur, it is clear that increased precision based on evidence from qEEG studies can be used to optimize outcome.

REFERENCES

1. John ER, Prichep LS, Almas M. Subtyping of psychiatric patients by cluster analysis of qEEG. Brain Topogr 1992; 4:321-326.
2. Nelson LA. Neurotherapy and the challenge of empirical support: a call for a neurotherapy practice research network. J Neurotherapy 2003;7(2): 53-67.
3. Yucha C, Gilbert C. Evidence-based practice in biofeedback and neurofeedback. Association of Applied Psychophysiology and Biofeedback; 2004. (www.aapb.org).
4. Suffin SC, Emory WH. Neurometric subgroups in attentional and affective disorders and their association with pharmacotherapeutic outcome. Clin Electroencephalogr 1995; 26:76-83.
5. Leuchter AF, Cook IA, Morgan ML, Witte EA, Abrams M. Changes in brain function of depressed subjects during treatment with placebo. Am J Psychiatry 2002; 159(1):122-129.
6. Porjesz B, Almasy L, Edenberg HJ, Wang K, Chorlian DB, Foroud T, et al. Linkage disequilibrium between the beta frequency of the human EEG and a $GABA_A$ receptor gene locus. Proc Natl Acad Sci USA 2002; 99(6): 3729-3733.
7. Enoch MA, White KV, Harris CR, Rohrbaugh JW, Goldman D. The relationship between two intermediate phenotypes for alcoholism: low voltage alpha EEG and low P300 ERP amplitude. J Study Alcohol 2002; 63(5):509-517.
8. Huag K, Warnstedt M, Alekov AK, Sander T, Ramirez A, Poser B, et al. Mutations in CLCN2 encoding a voltage-gated chloride channel are associated with idiopathic generalized epilepsies. Nature Genetics 2003; 33:527-532.
9. Phillips C. Electrophysiology in the study of developmental language impairments: prospects and challenges for a top-down approach. Appl Psycholinguistics. In press.
10. Light GA, Braff DL. Human and animal studies of schizophrenia-related gating deficits. Current Psychiat Rep 1999; 1:31-40.
11. Johnstone J, Gunkelman J. Use of databases in QEEG evaluation. J Neurotherapy 2003; 7(3/4):31-52.
12. Lorensen TD, Dickson P. Quantitative EEG databases: A comparative investigation. J Neurotherapy 2003; 7:53-68.
13. Chabot RJ, Merkin H, Wood LM, Davenport TL, Serfontein G. Sensitivity and specificity of QEEG in children with attention deficit or specific developmental learning disorders. Clin Electroencephalogr 1996; 27:26-34.

14. Chabot RJ, Merkin H, Wood L, Davenport T, Serfontein G. Quantitative EEG profiles of children with attention and learning disorders and the role of QEEG in predicting medication response and outcome. Aspen, CO: Society for Neuronal Regulation, 5th Annual Meeting; September 18-21, 1997.
15. Chabot RJ, di Michele F, Prichep L, John ER. The clinical role of computerized EEG in the evaluation and treatment of learning and attention disorders in children and adolescents. Neuropsychiat Clin Neurosci 2001; 13(2):171-186.
16. Chabot RJ, di Michele F, Prichep L. The role of quantitative electroencephalography in child and adolescent psychiatric disorders. Child Adoles Psychiat Clin N Am 2005; 14: 21-53.
17. Fein G, Galin D, Yingling CD, Johnstone J, Nelson MA. EEG spectra in 9-13-year-old boys are stable over 1-3 years. Electroencephalogr Clin Neurophysiol 1984; 58(6):517-518.
18. Niedermeyer E. EEG patterns and genetics. In: Niedermeyer E, Lopes da Silva F, (eds). Electroencephalography: Basic Principles, Clinical Applications and Related Fields. 3rd ed. Baltimore, MD: Lippincott, Williams and Wilkins;1993:192-195.
19. Vogel F. Genetics and the Electroencephalogram. New York: Springer-Verlag Telos; 2000.
20. Van Beijsterveldt CE, Van Baal GC. Twin and family studies of the human electroencephalogram: a review and a meta-analysis. Biol Psychology 2002; 61(1-2):111-138.
21. Gunkelman J. Evaluating the frontal lobes in affective and attentional disorders with QEEG and EP - the electrophysiology of frontal lobe disconnection syndrome: implications for neurotherapy. J Neurotherapy 1998.
22. Cook IA, O'Hara R, Uijtdehaage SH, Mandelkern M, Leuchter AF. Assessing the accuracy of topographic EEG mapping for determining local brain function. Electroencephalogr Clin Neurophysiol 1998; 107(6):408-414.
23. Prichep LS, Mas F, Hollander E, Liebowitz M, John ER, Almas M, et al. Quantitative electroencephalographic subtyping of obsessive-compulsive disorder. Psychiat Res 1993; 50(1):25-32.
24. Wright C, Gunkelman J. QEEG evaluation doubles the rate of clinical success. Series data and case studies. Austin, TX: 6th Annual Conference, Society for the Study of Neuronal Regulation; September 10-13, 1998. Abstracts.
25. Budzynski TH. Reversing age-related cognitive decline: use of neurofeedback and audio-visual stimulation. Biofeedback 2000; 28:19-21.
26. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res, Brain Res Rev 1999; 29(2-3), 169-195.
27. Iosifescu D, Greenwald S, Devlin P, Alpert J, Hamill S, Fava M. Frontal EEG predicts clinical response to SSRI treatment in MDD. Phoenix, AZ: 44th Annual NCDEU; June 2004.
28. Rosenfeld JP. EEG biofeedback of frontal alpha asymmetry in affective disorders. Biofeedback 1997; 5(1) 8-25.
29. Lawson R. Different measure of anterior EEG asymmetry and depression severity: continuous performance task, grade point average, and self-report scales. Society for Neuronal Regulation; 2000.
30. Perrin F, Bertrand O, Pernier J. Scalp current density mapping: value and estimation from potential data. IEEE Trans Biomed Eng 1987; 34(4):283-288.
31. Srinivasan R, Nunez PL, Tucker DM, Silberstein RB, Caducsh PJ. Spatial sampling and filtering of EEG with spline Laplacians to estimate cortical potentials. Brain Topogr 1996; 8(4):355-366.
32. Sterman MB. Basic concepts and clinical findings in the treatment of seizure disorders with EEG operant conditioning. Clin Electroencephalogr 2000; 31(1):45-55.
33. Lantz D, Sterman MB. Neuropsychological assessment of subjects with uncontrolled epilepsy: effects of EEG biofeedback training. Epilepsia 1998; 29(2):163-171.
34. Birbaumer N, Elbert T, Rockstroh B, et al. Biofeedback of event-related slow potentials of the brain. Intl J Psychology 1981; 16:389-415.
35. Gibbs FA, Gibbs EL. Atlas of Electroencephalography. Vol. 2. Redding, MA: Addison-Wesley; 1950.
36. Gibbs FA, Gibbs EL. Medical Electroencephalography. Reading, MA: Addison-Wesley; 1967.
37. Prichep LS, John ER. QEEG profiles of psychiatric disorders. Brain Topogr 1992; 4(4):249-257.
38. Donaldson S. Society for Neuronal Regulation. Scottsdale, AZ; 2002.
39. Gunkelman J. Low voltage or absolute power. J Neurotherapy 2001; 5:1-2.
40. Kolb B, Whishaw I. Fundamentals of Human Neuropsychology. 5th ed. New York, NY: W. H. Freeman Co; 2003.