Quantitative analysis of the human EEG (qEEG) was accomplished as early as the 1930s (Berger, 1931). With the availability of powerful desktop computers at relatively low cost, along with high speed Internet transmission of data, digital EEG with quantitative analysis is now available in clinical settings. However, results with qEEG techniques overall must be considered mixed at best. While it is clear that quantification of the EEG signal is useful in obtaining more objective and detailed information, there has been only limited success in using the procedure diagnostically. The position of the American Academy of Neurology is that the technique has “limited clinical utility”, because it is not “diagnostic”. The AAN panel endorsed the use of digital EEG and considered the qEEG technique promising and with additional clinical validation studies, likely to be used increasingly in clinical medicine, as with computer technology in general (Nuwer et al. 1997).

Quantitative EEG is a difficult technique in that scalp electrodes are used to measure microvolt level electrical signals in conscious, behaving humans. There are significant problems due to extracerebral artifact contaminating the EEG signal, including movement, muscle activity, eye blinks, electrodermal activity, and EKG. A well-trained technician is able to identify and minimize some of these contaminants at the time of recording. Further, there are fluctuations in level of patient arousal that are difficult to identify and quantify. In addition, most studies analyze the EEG while the patient is at rest. EEG correlates of cerebral activation accompanying cognition and affect are typically not considered. This is a particularly difficult issue, since studying EEG human performance is of great interest but often carries with it the problem of significantly increased artifact and makes factors such as drowsiness even more critical.

These are important factors, but other, more fundamental questions also must be considered. Why does the clinician use qEEG? The usual answer is to assist in diagnosis in difficult cases.
The neuropsychologist may use the test in developmental disorders to evaluate a child with difficult learning or attentional problems. The psychiatrist may use the test to evaluate patients with complex schizoaffective disorders. The behavioral neurologist may use the qEEG study to evaluate concentration and memory difficulties in head trauma. However, these are all conditions defined by behavioral disturbance. The qEEG technique measures neurophysiological activity, not behavior. Complex behaviors are the final common pathway of the integrated activity of the nervous system. There are many neurological events underlying such complex behaviors and psychological processes as reading, mood lability, and mental concentration, and alterations in many aspects of neurophysiological function can cause significant disturbance of these behaviors. It is well accepted that there is not a direct correspondence between mental activity and behavior. It also is obvious that there is not a direct correspondence between neurophysiology and behavior. Therefore, it is not surprising that qEEG is of limited utility in behavioral diagnosis. How then might the clinician best use qEEG?

The qEEG technique does not substitute for neuropsychological evaluation. If the intent is to clarify a behavioral diagnosis, behavior, not neurophysiology must be studied. However, if the intent is to determine how to intervene neurophysiologically, such as by administration of centrally acting pharmaceuticals, neurophysiological measurement logically is the technique of choice. New research demonstrates medication responsivity can be improved and side effects minimized through the use of qEEG techniques to guide prescription. EEG conditioning, or neurofeedback (NFB), is a neurophysiological intervention as well (for reviews see Sterman, 1996; Evans & Abarbanel, 1999). By inference, determination of an individual's neurophysiological profile may also be useful in development of EEG conditioning strategies.

A substantial literature exists on effects of medications on the EEG (Wauquier, 1993; Bauer, 1993), and a number of reviews of methodological aspects and clinical applications of pharmaco-EEG are available (Anderer et al., 1987; Saletu, et al., 1987). Progress has been made on classification of psychotropic drugs based on effects on the EEG (Itil, et al., 1979; Herrmann, et al., 1979). In contrast, relatively little attention has been directed toward prediction of medication response.

Among the non-invasive technologies for investigating brain responsivity to pharmacotherapy in psychiatric disorders, some researchers have analyzed EEG recorded as a part of polysomnographic studies (Buysse, et al., 1997; Perlis, et al. 1997). One group has reported increased relative delta power and decreased relative alpha power during sleep in depressed patients who were responsive to antidepressant treatment (Luthringer, et al., 1995). Others have studied the reactivity of the alpha rhythm in depression. Increased reactivity of EEG alpha to eye opening was reported in unmedicated depressed patients. Excess reactivity was normalized with medication (Shagass, et al., 1982).

Chabot, et al. (1996) studied qEEG profiles in children with attention deficit disorder and specific learning disability. They report that pre-treatment qEEG could be utilized to distinguish ADD children responsive to dextroamphetamine from those responsive to methylphenidate with a high level of accuracy. These results confirm and extend other reports in the literature (McIntyre, et al., 1981; Prichep & John, 1990; Steinhausen, et al. 1984).
An association with qEEG alpha frequency excess and therapeutic response to antidepressant agents was reported in obsessive compulsive disorder. In contrast, OCD patients with theta excess were not responsive to antidepressants (Prichep et al., 1993). Increased interhemispheric coherence has been noted in psychotic patients who failed to respond to haloperidal (Czobor & Volavka, 1991).

Psychotropic medications can be classified by effects on the EEG. Benzodiazepines can produce an increase in 20-40 cycle per second EEG/qEEG activity. Three types of antidepressant induced EEG/qEEG effects are observed: 1) initial alpha amplitude reduction with increased slow and fast activities, 2) initial alpha amplitude increase with attenuation of slow and fast activities and 3) changes similar to those found with stimulants. Neuroleptics can decrease fast and increase slow activity. Stimulants can decrease EEG slowing and increase fast activity.

In 1995, two physicians, Stephen C. Suffin and W. Hamlin Emory, reported a retrospective qEEG study of patients with DSM categorized attentional and mood disorders seen in their private practice (Suffin & Emory, 1995). Each DSM group was found to contain subgroups of patients with characteristic neurophysiological profiles. Figure 1 shows relative power profiles for two subgroups of patients with attentional disorders. Figure 2 shows relative power profiles for two subgroups of patients with affective disorders. Note the similarity of the profile for each subgroup within each DSM defined group. Patterns of each subgroup are nearly identical.

The presence of specific qEEG features predicted medication response. There was a robust correlation between a patient’s pretreatment qEEG feature(s) and medication outcome, without regard to DSM disorder. The subgroups with features including alpha frequency excess responded favorably to antidepressants, the subgroups with features including theta frequency excess responded favorably to stimulants and the subgroups with features including EEG coherence deviations responded favorably to lithium or anticonvulsants.

Suffin and Emory subsequently reported that similar qEEG markers are present across the range of DSM disorders, and that different qEEG markers are found within the same DSM disorder (Suffin & Emory, 1996). These findings suggest a new approach to pharmacotherapy: 1) identify pretreatment qEEG feature(s), 2) assess the similarity of the individual case to qEEG features from patients with known outcomes, and 3) prescribe based on a match of the individual to qEEGs with known responsivity to specific agents. This approach does not require explanation of the complex relationship between brain disturbance and symptomatic behavior.

Suffin and Emory have constructed and described a database that contains the pretreatment qEEGs of greater than 1,600 patients with a variety of DSM disorders. qEEG features predicted favorable clinical outcomes with antidepressant, stimulant and anticonvulsant medications in training and validation set analyses, demonstrating that qEEG data contain sufficient information to classify patient populations into medication response groups (Suffin, et al., 1997). In addition, predictions could be made that individual patients would require a combination of agents from more than one category, e.g. a stimulant and an anticonvulsant.
A follow-up study by Suffin et al. (submitted, 2000) used a random assignment of patients with chronic, refractory major depression into two treatment groups. These patients had major depression without improvement over an average of 16 years, despite multiple treatment attempts. One group received medications prescribed based on standard procedures and one group received medications prescribed based on results of qEEG analysis. Clinicians blind to the method of prescription evaluated patient outcome using a clinical global improvement scale (CGI). There was significant improvement in the group treated based on qEEG profiles and little or no improvement in the group receiving treatment according to current standards of practice.

Prescriptions based on qEEG results differed markedly from those based on standard clinical evaluation. QEEG data suggested use of more anticonvulsant/anticyclic agents and stimulants. With behavioral based medication selection, combination pharmacotherapy is recommended for in major depressive disorder only after failures of antidepressant class agents.

These findings are preliminary and require further replication and validation. However, the implication is clear: assessment of neurophysiological profiles using qEEG is useful in guiding medication selection across a wide range of DSM disorders. The development of a longitudinal database of psychiatric patients including patient outcome data provided the basis for development of predictive algorithms. Medication response prediction may now be extended to patients already taking medication and those with neurological disorders such as stroke, epilepsy, and head trauma.

The important role of behavioral evaluation must be understood in context. Behavioral disturbance is usually the precipitating factor that leads a patient to seek treatment. In addition, it is behavioral evaluation that provides the critical measure of clinical outcome. It would not be useful to normalize the EEG without behavioral improvement.

In contrast to medication response studies, no such database or predictive algorithms are currently available in neurofeedback. At this time, recommendations for use of specific NFB protocols are made based on the experience of expert clinicians. Frank H. Duffy, a physician well known for his use of quantitative EEG methods, notes that NFB is a promising treatment modality but, there is not general agreement on how to determine which EEG signal to use for feedback purposes (Duffy, 2000). Development of qEEG databases with outcome data and predictive algorithms similar to those used with medication response studies will likely help in selecting treatment protocols and increase the clinical efficacy of neurofeedback.
References


**Figures**

**Figure 1:** Profiles of EEG relative power deviations from normal database in two subgroups of patients with attentional disorders.

Figure 2: Profiles of EEG relative power deviations from normal database in two subgroups of patients with affective disorders.