

Online brainmapping

Version 5

A Monthly Publication presented by Professor Yasser Metwally

May 2008

EEG SHARP ACTIVITY...CLINICAL SIGNIFICANCE

Epilepsy is defined as "paroxysmal transient disturbances of brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system. A seizure, or ictus epilepticus, is an epileptic attack or recurrence. The classification of epilepsies used by International League Against Epilepsy (ILAE) includes two major categories: partial epilepsies and generalized epilepsies. A partial seizure disorder is considered to have a focal region of onset in the brain, and awareness may be either preserved (simple partial seizure) or lost (complex partial seizure). A generalized seizure disorder is considered to involve most, if not all, of the brain at onset. The generalized seizure types may involve cessation of activity with loss of awareness (absence seizure) or generalized tonic-clonic activity (generalized tonic-clonic seizure). Both partial and generalized seizure disorders are further subdivided into idiopathic and symptomatic types, previously called primary and secondary, respectively. Idiopathic epilepsies are thought to be genetically heritable, are associated with normal intelligence, and occur during specific age periods. The symptomatic epilepsies are likely the result of a CNS injury, which in a symptomatic partial epilepsy consists of a focal lesion and in a symptomatic generalized epilepsy consists of diffuse cerebral abnormality. Symptomatic epilepsies are typically lifelong conditions.

It cannot be overemphasized that the diagnosis of epilepsy is based primarily on the clinical history. As noted above, a clinical seizure rarely occurs during an EEG, and thus the EEG is rarely diagnostic of a seizure disorder or epilepsy. In a large, population-based EEG study by Zivin and Ajmone-Marsan [2] involving subjects without a history of seizures, approximately 2 percent of the subjects had EEGs with epileptiform discharges. Of the individuals in this subgroup, only 15 percent subsequently developed a seizure disorder. Therefore, epileptiform discharges seen on an EEG should not be referred to as interictal discharges unless it is known that the patient has a clinically defined seizure disorder. Focal or generalized epileptiform discharges should be noted as consistent with the interictal expression of either a partial or a generalized epilepsy, respectively. When applied in the appropriate clinical setting, the EEG is useful in classifying the seizure type, predicting the long-term outcome, and choosing the appropriate antiepileptic medication.

Overall, symptomatic partial seizure disorders are the most common type of epilepsy. The clinical semiology of the partial seizure generally depends on the site of onset. In children, focal epileptiform discharges arising from the temporal region have the greatest incidence of clinical seizures, ranging from 85 to 95 percent. The next highest incidence (70 to 75 percent) is associated with frontal discharges. The central, parietal and occipital regions have the lowest incidence of seizures related to epileptiform discharges, estimated at 40 to 70 percent. In addition to the characteristics of recorded epileptiform activity, the age of the patient and the presence or absence of neurological deficits on examination are important factors that are helpful in determining the clinical significance of epileptiform discharges and in classifying the partial seizure disorder as either symptomatic or idiopathic. The occurrence of a clinical seizure with a focal electrographic correlate is diagnostic of a partial epilepsy. Blume and colleagues [3] presented several types of scalp EEG correlates for partial seizures, most of which began with rhythmic sinusoidal activity or repetitive sharp wave activity that subsequently evolved in frequency. Most patients with complex partial seizures were noted to have a scalp correlate on the EEG. Patients with simple partial seizures were less likely to have a scalp correlate.

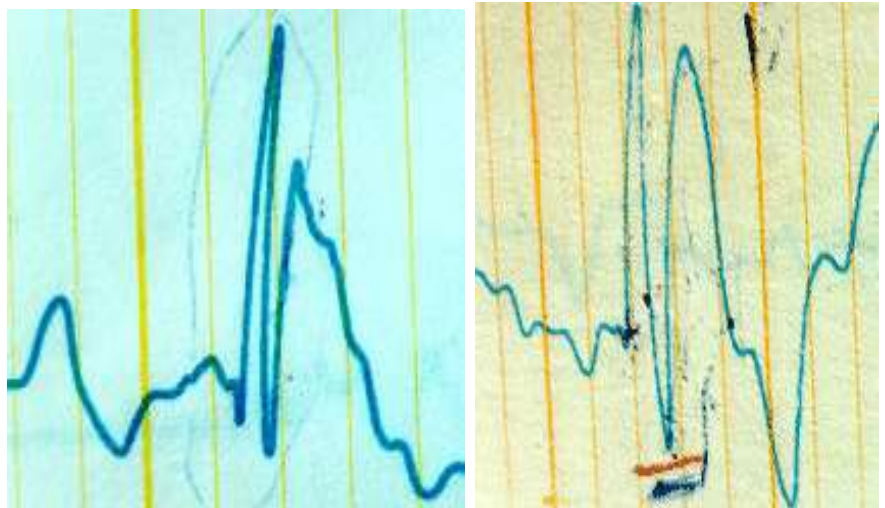


Figure 1. Examples of sharp waves [left] and spike [right]

The best-defined idiopathic partial epilepsy is benign rolandic epilepsy. The classic EEG finding in this childhood seizure disorder is a characteristic monomorphic centrottemporal sharp wave. The sharp waves are often seen independently in the centrottemporal and adjacent regions, and they are accentuated by light sleep. The waking background rhythm is generally normal.

Of the idiopathic generalized epilepsies, the absence seizure is the most common type. The interictal EEG feature of this type of seizure disorder consists of generalized, high-amplitude, anteriorly predominant 3-Hz spike and wave discharges, called typical 3-Hz spike and wave. When the

spike and wave discharges occur repetitively, they are called bursts. Although these discharges are called "3-Hz," the initial frequency of the burst is 3 to 4 Hz, and the frequency may slow to 2.5 Hz during more prolonged bursts. The discharges are reactive to alerting maneuvers and may become fragmented in deeper stages of sleep. Juvenile myoclonic epilepsy (JME) is another type of idiopathic generalized epilepsy. The spike and wave discharges of this seizure disorder are also generalized and anteriorly predominant, but they have an initial frequency of 4 to 6 Hz and may begin with a polyspike discharge. The EEG of a patient with an idiopathic generalized epilepsy who is maximally alerted is generally normal. During photic stimulation, there may be a photoparoxysmal response in both absence epilepsy and JME, which may be helpful in classifying recognized epileptiform discharges as consistent with an idiopathic generalized epilepsy rather than a symptomatic partial or generalized epilepsy.

Epileptiform patterns in symptomatic generalized epilepsies are of three types. A slow spike and wave pattern at approximately 2 Hz is seen in patients with mental retardation having multiple seizure types (atypical absence, tonic, atonic, or tonic-clonic seizures), which is known as the Lennox-Gastaut syndrome. A second type of interictal or ictal EEG pattern seen in patients with symptomatic generalized epilepsy is generalized paroxysmal fast activity (GPFA), which consists of bursts of rhythmic, generalized beta activity. When the bursts are seen during wakefulness, they are commonly accompanied by a tonic seizure. During sleep, bursts of GPFA not accompanied by clinical changes are considered an interictal pattern. The third pattern of epileptiform activity in secondary generalized epilepsy is an atypical generalized spike and wave pattern, consisting of generalized 3 to 6-Hz spike or polyspike and wave activity. The waking background in patients with secondary generalized epilepsies is abnormally slow, including slowing of the posterior background rhythm and generalized slowing.

In patients suspected of having a seizure disorder, a normal routine, awake EEG should be followed with either a natural or medication-induced sleep EEG or a sleep-deprived EEG. Before the advent of long-term video-EEG monitoring for the diagnosis of possible seizures, three or more EEGs were often obtained to confidently conclude normality and absence of epileptiform activity. Because antiepileptic medications have been shown not to affect the frequency of focal interictal epileptiform discharges, the decision to treat a patient for a suspected partial seizure disorder should not be based solely on the initial EEG findings. Conversely, the EEG has not proven to be a reliable tool in predicting whether a patient's antiepileptic medication can be discontinued. In patients with an idiopathic generalized epilepsy, treatment with appropriate antiepileptic medication may eliminate all interictal epileptiform activity on the EEG. Therefore, the decision to discontinue an antiepileptic medication in a patient with a seizure disorder should be based on the type, etiology and response to medications of the seizures and not on interictal EEG findings.

Interictal epileptic activity

The interictal marker of a seizure focus is the spike or sharp wave. The distinction between these two patterns has no etiologic significance, the only difference being one of EEG pattern morphology. A spike is defined as being less than 70 milliseconds in duration, and a sharp wave has a duration of 70-200 milliseconds. The terms spike or sharp wave, while having particular meaning to the electroencephalographer, are often used interchangeably. Spikes and sharp waves are almost always of negative polarity at the scalp surface. These epileptiform discharges may arise from any region of the cerebral hemispheres but most commonly are manifested in the anterior temporal, frontal, or centrotemporal regions. (Click for more details)

An anterior temporal spike or sharp wave is highly associated with the occurrence of clinical focal-onset seizures. When this pattern is seen on the EEG, the likelihood of the individual manifesting clinical seizures is over 90%. However, the converse is not necessarily true. While the EEG of most patients with temporal lobe seizures demonstrates anterior temporal spikes, an EEG negative for this finding does not exclude a diagnosis of epilepsy. Often, repeated EEG recordings or prolonged EEG monitoring is required to demonstrate the epileptiform pattern.

Frontal spikes and sharp waves also are highly associated with clinical seizures but not to the same degree as temporal discharges. Approximately 70-80% of individuals whose EEG demonstrates frontal spikes have clinical seizures. Frontal spikes or sharp waves are more likely to be associated with mass lesions such as neoplasms, traumatic lesions, or congenital cerebral malformations.

Centrotemporal or rolandic sharp waves are often a marker for a particular epilepsy syndrome of childhood known as benign rolandic epilepsy or benign focal epilepsy of childhood with centrotemporal spikes. This is a disorder in which a child, typically aged 4-12 years, develops focal seizures with sensory or motor seizures in the mouth or face region. These children also may have generalized seizures; typically, these seizures are nocturnal. The EEG pattern is unusual in that there is often a simultaneous negative waveform in the centrotemporal region and a positive one in the frontal region. This pattern of EEG polarity is virtually diagnostic of benign rolandic epilepsy.

Epileptiform EEG patterns are seen less commonly in the occipital, central, or parietal regions. Occipital spikes typically are seen in young children and may or may not be associated with clinical seizures. Discharges in any of these regions may indicate the presence of partial epilepsy.

EEG QUANTIFICATION

This issue will discuss the limitations of the conventional method of EEG interpretation and the steps necessary to substitute more objective quantitative techniques. The application of such quantitative techniques to several clinically important problems will also be considered. Two points must, however, be stressed at the outset. First, performance and economic considerations do not generally justify the substitution of automated analyses for human interpretation of the wide variety of EEGs obtained in routine clinical practice. Second, the potential utility of quantitative analyses is in narrowly defined clinical problems in which there is sufficient medical justification to incur the high costs of development.

In order to render comprehensible the ensuing review of current research, techniques of digital signal processing and pattern recognition as applied to the EEG will be briefly summarized, with emphasis on the most common forms of analysis, namely power spectral (frequency) analysis and transient (paroxysmal waveform) detection, and on the methods by which the findings so obtained have been validated. The ambiguities caused by extracerebral artifact and drowsiness will be discussed, and some initial solutions to the problem of automatic artifact rejection will be presented.

DIFFICULTY IN QUANTIFYING THE EEG

The desirability of standardized recording procedures and interpretation has inspired efforts towards quantified analysis almost since the inception of electroencephalography. There has traditionally been the hope that with a more powerful computer, or a more complicated form of analysis, Hans Berger's original dream that the EEG would be a "window on the mind" might be fulfilled. Every promising new technology, from analog band pass filtering to multivariate pattern recognition technology, has been applied to the EEG, with varying success. As long ago as 1938, Grass and Gibbs wrote: "After having made transforms of 300 electroencephalograms, we are convinced that the system not only expresses data in a manner more useful and concise than is possible by present methods, but that in many cases it indicates important changes in the electroencephalogram which would otherwise remain hidden." Although 40 years old, this summary of the first Fourier analysis of an EEG could very well have been used verbatim in any one of a number of recent studies.

The EEG is one of the last of the standard clinical tests to be quantified. Factors contributing to this delay include the relatively low volume of EEG examinations performed, the complexity of the EEG signal, the lack of knowledge concerning the anatomic and physiologic basis of the EEG, the fact that the EEG findings are corroborative rather than diagnostic per se, the subjective method of polygraph interpretation, and the application of quantitative methodologies without adequate consideration of the idiosyncracies of the EEG.

The considerable efforts made towards quantification have not substantially altered the daily practice of clinical electroencephalography. The reasons for this will be considered below, as well as possible solutions to this impasse.

● **Limitations of the Traditional Method of EEG Polygraph Interpretation**

◆ **Complexity of Visual Assessment.**

Electroencephalographers (EEGers) employ complex, subjective techniques to reduce the polygraph recording to a few interpretive statements. Electroencephalographic activity is characterized by its frequency, amplitude, and wave morphology, and by its spatial and temporal distribution. Patterns of activity are either considered to constitute a background continuum or are regarded as transients, such as are the paroxysmal sharp transient wave forms (sharp waves and spikes) associated with the epilepsies. Interchannel comparisons aimed at discovering major discrepancies in amplitude, frequency, and wave morphology (e.g. hemispheric asymmetries and focal patterns) are central to the interpretive process, since these abnormalities may be associated with various pathologic conditions, but an evaluation of the total gestalt of the multi-channel tracing is also essential. Since wave features vary with recording conditions, and no precise definitions of most wave properties exist, electroencephalographic decisions and recommendations are made largely on a contextual basis. In complex records, the analysis and identification of the individual components are often so difficult that specific analysis must be neglected in favor of a general interpretation of the overall pattern. Few of these methods are directly amenable to quantification, or to precise definition. Efforts made by the International Terminology Committee to standardize commonly used terms have resulted in official definitions which are too vague to directly embody in computer algorithms.

◆ **Intrarater Reliability and Interrater Validity.**

Surprisingly few studies have been concerned with the intrarater reliability (reproducibility) and interrater validity (agreement) of subjective assessments of EEG polygraphs.

Interrater validity studies have also been conducted in connection with the development of computer algorithms to detect specific EEG patterns, including sharp transient paroxysmal activity associated with the seizure disorders, extracerebral artifact (Gevins et al, 1977a), and EEG signs of drowsiness. In summary, while there is good overall agreement as to presence and type of abnormality, there are large interrater variations in the characterization of individual elements of the EEG. This presents an obstacle to the development of quantitative analyses.

METHODOLOGIC CONSIDERATIONS IN EEG QUANTIFICATION

◆ **Standardizing Assessment of the Polygraph**

There have been many methods for standardizing the assessment of the EEG. The Mayo system of classification, which was the prototype, classifies an EEG according to its pattern class (normal, asymmetry, dysrhythmia, delta, etc.), intensity (Grades, 1, 11, and 111), location of the abnormality, wave description (spike, spike and wave, etc.) and additional descriptors. Classification of an EEG according to this system is routinely included with the EEG report. The various categories and descriptors are defined in terms of voltage or percentages. The system provides a summary that is more meaningful than the conventional report for nonEEGers, allows for computer storage and retrieval, and helps to standardize interpretation.

Assessment systems of this sort call for the extraction of such basic features of the EEG as dominant frequency, amplitude, and interchannel relations. A checklist is often used for this purpose, and judgments are then drawn from it. These procedures are collectively referred to as structured methods of EEG interpretation. The use of such methods is essential to the evaluation and validation of quantitative methods of analysis.

One such structured method of polygraph assessment, which has the virtue of attempting to concisely classify the wide variety of routinely occurring clinical EEGs, will be briefly described, attention being confined to its application to the analysis of the EEG recorded while the patient is lying quietly with his eyes closed. The EEG is first classified into normal, borderline, or abnormal categories. Normal EEGs are then classified as dominant or minimal alpha activity types. Borderline EEGs are those which show only minimal changes from the normal. Abnormal EEGs are subdivided in turn into nonparoxysmal, paroxysmal, or mixed categories. Nonparoxysmal EEGs are further subclassified as slow, fast, or mixed types, while paroxysmal EEGs are divided into sharp transient, burst patterns, or mixed types. Decisions concerning localization and severity (the latter based on a three-point ordinal scale) are reached using semi-objective criteria.

◆ **Digital Signal Processing and Pattern Recognition**

Techniques for quantifying the EEG are collectively known to electrical engineers, computer scientists, and statisticians as methods of digital (and analog) signal processing and pattern recognition. Analog methods are mostly used for prefiltering or other signal processing functions prior to digitization.

Table 1. is a simplified table of a complete EEG analysis. Five major steps are shown in the Table, namely: (1) signal conditioning and digitization, (2) primary analysis, (3) feature extraction, (4) classification and/or decision, and (5) validation.

◆ **Signal Conditioning.**

During signal conditioning the signals from the EEG amplifiers are prepared for sampling by the computer. This typically consists of attenuating the high (above 50 Hz) and low (below 1 Hz) frequency components by passing the signals through filters with strong attenuation (24 dB per octave or more). In most circumstances this is necessary because the filters incorporated in commercial electroencephalographs do not attenuate strongly enough for efficient computer analysis. Signal conditioning is followed by digitization, in which the analog EEG signals are sampled by the computer, converted to a digital representation, and stored in the computer's memory.

◆ **Primary Analysis**

Following signal conditioning and digitization, one or both of two different classes of primary analysis are performed, namely frequency analysis and transient detection.

◆ **Frequency Analysis.**

During frequency analysis, which may be performed in a variety of different ways, the EEG is broken down into its constituent components. In electrical engineering, frequency analysis is referred to as spectral analysis, which makes clear the analogy to a prism breaking down white light into a spectrum. Frequency analysis generally results in the separation of activity into groups based on frequency, that is, delta (less than 4 Hz), theta (4 to 7 Hz), alpha (8 to 13 Hz), beta (14 to 22 Hz), and higher frequency activity (from 22 to 35 or 50 Hz).

The most popular current way of applying this analysis to EEGs is on a digital computer using the Fast Fourier Transform algorithm. Other methods are likely to become available in the near future, however, as a result of developments in integrated electronics (charge coupled devices) and computer science (number theoretic transforms).

Another common form of frequency analysis is period-amplitude analysis. In general, this method extracts frequency information by tabulating properties of the individual waves, such as the time between zero crosses. While in principle this method is more computationally efficient than spectral analysis, it may be subject to various practical problems, including distortions due to low amplitude, high frequency signal components. Because of space limitations, other forms of time domain analysis will not be discussed here.

The results of frequency analysis may be expressed as numerical tabulations of the amount of energy or activity in each frequency band, as a histogram or line graph, in an abstract form, or as a compressed spectral array (CSA). This latter form of display is currently very popular. It simply consists of displaying the successive results of frequency analysis, performed on short segments of data, as a series of vertically arranged graphs. Although it was originally thought that the interpretation of CSAS, in conjunction with transient detection, might routinely replace the interpretation of the polygraph, there is currently some doubt about this. Nevertheless, the CSA is a useful means of examining the results of primary analysis, prior to further feature extraction and multivariate analysis. The CSA in the form of somnograms is also being used to study EEG changes during sleep.

Table 1. Steps for a complete quantitative analysis of the EEG. Completion of all five steps is necessary in order to determine the validity and utility of any particular quantitative method. It is then no longer necessary to routinely perform the fifth step.

Step	Explanation	Example
1- Signal conditioning and digitization	1. Prepare EEG for analysis 2. Read into computer	Filter out low and high frequency components
2- Primary analysis	Compute important properties of the signal	1. Frequency Analysis 2. Transient Detection
3-Feature extraction	Summarize important properties	1. Heuristic: Location and shape of peak and amount of energy in delta, theta, alpha and beta bands 2. Statistical: Principal Components, Factor Analysis
4. Classification and/or decision	Decide how the EEG analysis relates to the dependent clinical variable.	Decide whether indicates remission or exacerbation in the patient's condition
5. Validation	Determine that the results apply in general .	If the same analysis were applied to a different group of the same category of patients, would the same results be obtained?

◆ **Transient Detection.**

As shown in table 1, the other major type of primary analysis is the detection of transient, infrequent but clinically important EEG events. The most familiar examples of such events are the paroxysmal waveforms (spikes, polyspikes, spike and wave discharges, etc.) associated with seizure disorders. Because a single isolated transient may have too little energy to stand out from the averaged background, or because transient events may have the same frequency distribution as other kinds of EEG activity, frequency analysis may not be sensitive to their occurrence. Moreover, in applying frequency analysis, information about individual wave morphology, crucial for the detection and characterization of transients, is lost. Since formal analytic solutions are not generally applicable to the detection of specific EEG transients, many different methods have been tried in the attempt to accurately detect transient waveforms.

◆ **Feature Extraction.**

The third step in a complete analysis of the EEG is feature extraction. The purpose of this step is to reduce the amount of data generated from the primary analysis by forming summary indices which characterize important properties of the EEG. There are both ad-hoc (heuristic) and formal (statistical) procedures for performing feature extraction,

◆ **Heuristic Methods**

A variety of indices may be formed based upon the traditional visual assessment of the polygraph. For example, by combining the individual 1 Hz frequency bins into bands, and by taking the ratio between homologous left-and right-sided placements, an index sensitive to the amount of asymmetry may be formed. One can derive such simple indices to characterize asynchronies, amount of abnormal slowing, recovery from hyperventilation, reaction to photic stimulation, etc. It must be noted, however, that such indices, while intuitively appealing, may not necessarily correspond with the visually assessed characteristics of the EEG polygraph. To determine the correlation of an index and a characteristic such as asymmetry, validation studies are necessary. Furthermore, before such indices can be submitted to statistical hypothesis-testing, study of their distribution must be undertaken; and, if needed, one of a variety of normalizing transforms must be applied.

◆ **Statistical Methods**

The other type of feature extraction is formally defined and does not make use of a priori knowledge of the EEG. The purpose of this type of feature extraction is the same as the heuristic type, namely to efficiently reduce the amount of data generated by the primary analysis. The most familiar example of such a procedure is principal components factor analysis, a technique well known to statisticians and experimental psychologists. This procedure simply forms a linear combination of a large set of variables (e.g. the results of frequency analysis) such that the resulting smaller set of variables both account for a large amount of the variance of the original data, and are maximally uncorrelated with each other. Although computationally time-consuming, this procedure has proven to be a valuable step in the analysis of the background EEG. Heuristic and statistical feature extraction may be used as sequential steps in the analysis.

◆ **Classification**

The fourth and most important step in the analysis of the EEG is the final classification or decision. This simply involves reaching a decision as to the relevance to the individual patient (or class of patients) of the results of the EEG analysis. This may be accomplished manually or with

further computation, depending on circumstances. Sometimes the results of feature extraction are obvious, and further computation is not required. For example, an index of the number and duration of 3 per second spike and wave discharges could be compared before and after alterations of an anticonvulsant drug regime, to determine whether a reduction of absence seizures had been achieved. (Of course, standards for such changes must previously have been compiled from a large group of patients in order to determine whether the observed change was significant.)

In many instances, the results of primary analysis and feature extraction are not obviously related to the clinical condition under investigation. For example, in attempting to predict the onset of a grand mal seizure 10 minutes or more prior to its occurrence, no simple relations between the results of feature extraction and the subsequent seizure onset are apparent. In this instance, it is necessary to employ one of a number of methods of multivariate statistical analyses. Since this subject is itself quite complex, mention will be made here of only one class of such analyses, namely multivariate pattern recognition. The most familiar and widely available type of multivariate pattern recognition is stepwise linear discriminant analysis. By examining many examples of EEGs from each of several different clinical categories, discriminant analysis can determine a mathematical rule (if one exists) to correctly classify the EEG with the associated clinical category. The value of such a mathematical decision rule is that it may then be used to classify an unknown EEG sample into the associated clinical condition. In the example given above, one may use this type of analysis to attempt to predict, from the EEG, if a grand mal seizure will occur in 10 or so minutes. The difficulty encountered in the practical application of multivariate pattern recognition is that it is generally quite difficult to gather an adequate sample of data for each of the clinical categories to be discriminated. The result of computing a decision rule on insufficient data is that when a previously unclassified EEG sample is presented, classification is likely to be incorrect because the actual invariant EEG patterns (if such exist) related to the clinical category may not have been extracted.

◆ **Validation.**

If the same analysis were applied to a different group of the same category of patients, would the same results be obtained?. The fifth step of a complete analysis of the EEG, validation (Table 1), is of paramount importance if practical application is to be made of the results of a study .

References

1. Metwally, MYM: Textbook of neurimaging, A CD-ROM publication, (Metwally, MYM editor) WEB-CD agency for electronic publishing, version 9.1a January 2008
2. Zivin, L., and Ajmone Marsan, C.: Incidence and prognostic significance of "epileptiform" activity in the EEG of non-epileptic subjects. Brain 91:751-778 1968.
3. Blume WT, McLachlan RS, Chovaz CJ, : Temporal lobectomy for intractable epilepsy in patients over age 45 years. Neurology 1992 Mar; 42(3 Pt 1): 662-5.

**The author,
Professor Yasser Metwally
Professor of clinical neurology, Ain Shams university, Cairo, Egypt.
www.yassermetwally.com**

- ◆ **A new version of this publication is uploaded in my web site every month**
- ◆ **Follow the following link to download the current version:
<http://brainmapping.yassermetwally.com/map.pdf>**

© Yasser Metwally, all rights reserved