Chapter

Clinical Applications of Brain Mapping in Epilepsy

Misciagna Sandro

Abstract

EEG brain mapping is a neurophysiological technique based on computer-assisted analysis of conventional EEG. This technique, generally consisting in quantitative analysis of EEG (QEEG), includes topographic displays of frequency or voltage, statistical comparison to normal values and discriminant analysis. QEEG assessment still remains controversy about its clinical role. QEEG topographic analysis could be useful in many neurological diseases: in cerebrovascular disease EEG analysis is useful since EEG parameters are highly correlates with regional blood and metabolism; in degenerative disease (as dementia or encephalopathies) quantitative EEG frequency analysis could suggest an organic base of the disorder even if it is not able to distinguish between the types of dementia. QEEG techniques are also potentially useful in identifying anomalies in patients with cerebral trauma or in children with cognitive disorders. In the field of epilepsy EEG brain mapping could help clinics to detect spikes, locate an epileptic focus and suggest the type of epilepsy. In this chapter author describes principles of EEG brain mapping and its potential applications in particular in the epileptic field.

Keywords: brain mapping, epilepsy, quantitative EEG, QEEG, brain maps, digital EEG, EEG spatial analysis, spike detection, spike analysis, seizure detection, epileptic focus, focus localization

1. Introduction

EEG was first described as a promise to provide a "window into the brain" in 1929 by Hans Berger [1]. In spite of recent advances, the analytic potential of EEG has not been fully employed. On the other hand, brain function studies and neuroimaging methods have been deeply improved, severely discrediting EEG use. However, it is important to insist that EEG can give relevant information about topography of cerebral activity, even if it is difficult to have topographic information with a conventional EEG recording.

EEG recording is based on two-dimensional representation of potential differences between two electrodes in function of time and topographic information is based on integration of information across different channels [2].

Introduction of digital EEG techniques not only displays the EEG tracing but can provide additional measurement with quantitative EEG (QEEG), also called "EEG brain mapping".

The use of EEG brain mapping is based on visualisation of coloured brain maps generated by digital analysis of cerebral electrical activity. These maps display many

features that can be instantaneous of an averaged period of time. The cerebral maps include topographic displays of voltage, frequencies, power and statistical analysis with comparison with a normal reference population.

Still nowadays the clinical utility of QEEG techniques remains a controversial matter so that it could be considered as a useful tool, but also as a dangerous toy.

2. Short history of EEG spatial analysis

EEG is traditionally analysed in terms of temporal waveforms at different channels, looking at power of rhythms in terms of frequency, latency of peaks or presence of particular grapho-elements. This type of traditional EEG analysis provides important insights about brain functioning in health subjects and diseases that interfere with electric brain activity, even if it cannot be considered as an imaging method.

Numerical analysis of cerebral activity was started as early as the 1930s by Dietsch [3], followed by Grass and Gibbs [4] and Drohocki [5] who applied Fourier analysis to disassemble EEG signal. Successively, in 1943, Walter [6] described an automatic analogue frequency analyser and later in 1951 Walter and Shipton [7] developed an automated topographic display called "toposcope".

With the development of microcomputers with colour graphic Duffy [8, 9] and many other researchers improved techniques for brain electrical activity mapping, EEG quantification and topographic analysis. Researchers as Lehmann directed their studies to the analysis of specific EEG spike–wave patterns, analysis of topography of a particular EEG feature at an instant time or the average of a recurring event [10].

3. General principles of EEG brain maps

EEG brain maps are produced using from 16 to 32 electrodes arranged in a grid pattern of human scalp, giving a spatial resolution of about 6 cm [11] (see **Figure 1**).

Brain maps are sensitive to the quality of data acquisition of the EEG in terms of montages, references, control settings or biological factors (such as medications, clinical problems or level of awareness), which must be considered in every cases before interpreting the data.

In fact, as Duffy himself has written "brain map without the EEG is blind" [12].

Cerebral maps are produced by a process of interpolation between the electrode sites. There are several methods of interpolation and still nowadays it is an object of controversy.

The use of EEG quantification, for example by spectral analysis, gives the possibility to reduce data and describe a long record by few numerical data. These data may be subjected to statistical analyses including visual EEG interpretation or clinical decision-making.

Recent development in the quantitative analysis of complex networks by using computer graphics has increased the availability of brain mapping, contributing to a renewed interest in quantitative investigations of EEG and it has been rapidly translated to studies of brain network organisation [13]. This is a welcome development, but the problem of mapping lies not so much in the method itself, particularly by uninformed users who can see cerebral maps as a neuroimaging technique.

But, instead, mapping systems must be operated by EEG certified neurologist expertise in the use of brain mapping [14].

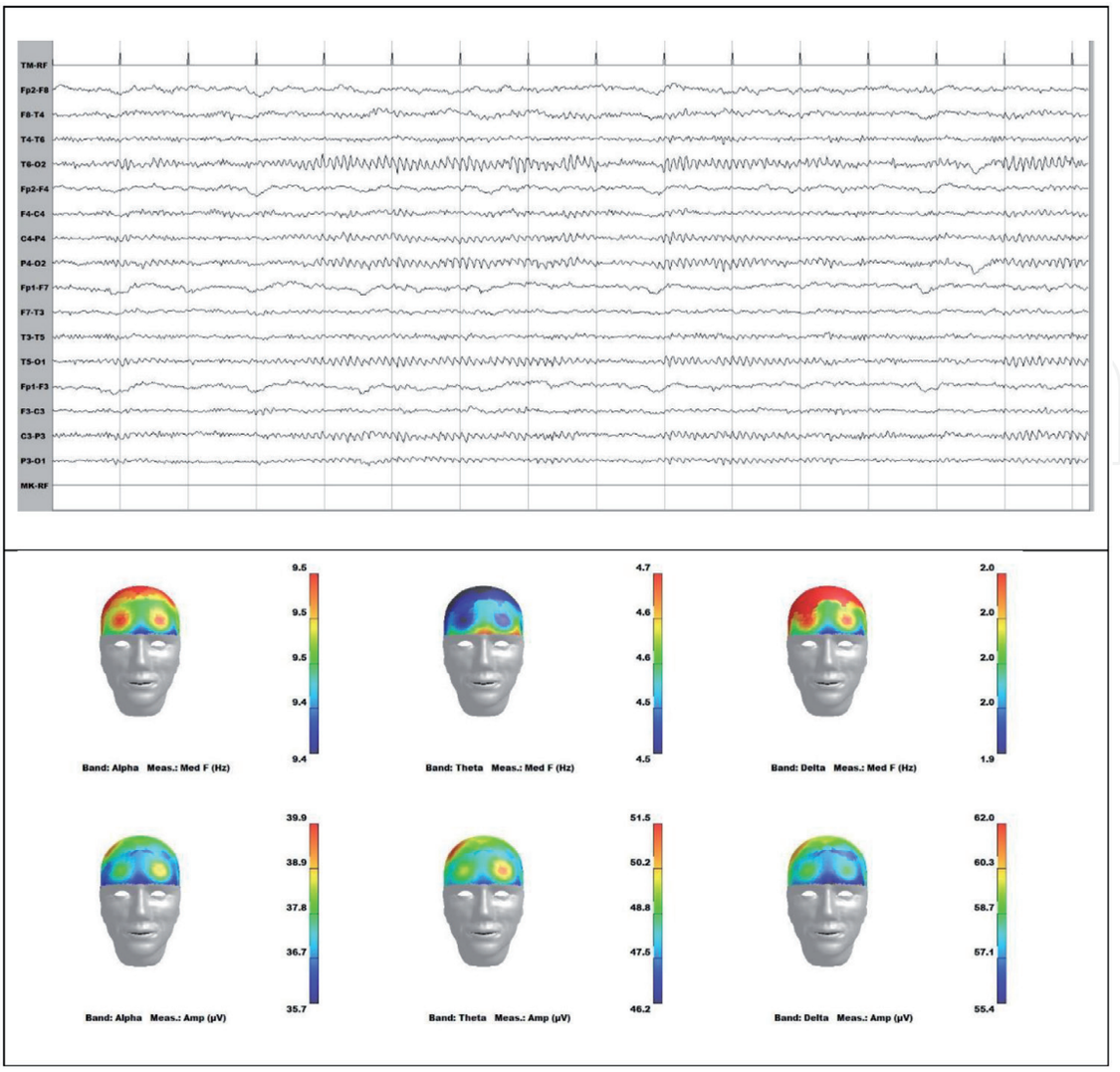

Figure 1.
Example of brain mapping in a traditional EEG showing absence of anomalies.

4. Problems related to use of EEG mapping

One of the major problems of the brain maps is that similarity of brain mapping to classical neuroimaging techniques (CT, MRI or PET scans) is illusory. In classical neuroimaging techniques there is a direct and close correspondence between the image and the affected structure. On the contrary, in the case of topographic changes in electrical activity, there is a more complex relationship to function and cerebral pathology.

Cerebral maps could be easily misinterpreted. In fact, the selection of what to map is at the discretion of the user, there aren't clear standards and interpretation is strongly subjective.

Maps do not distinguish between cerebral potentials and artefacts or between the feature of interest and a superimposed activity with different topography. Consequently, it is essential that users analyse with attention the trace recorded before plotting cerebral maps.

Another problem of quantitative EEG analysis is to determine the best method of deriving the signal to be analysed. Common reference derivation seems be the obvious choice. However asymmetrical activity involving ears reference is particularly open to misinterpretation so that asymmetries in alpha activity may be shown as reversed [15]. A paradox of EEG mapping is that when a focal activity occurs at

or near the reference, the deflections produced are greatest on channels recording from the most distant electrodes [16]. This effect is particularly liable to misinterpretation in spectral maps: thus focal temporal delta activity may be misallocated to the contralateral central region [17].

5. General applications of EEG mapping

EEG topographic analysis could be useful in many neurological diseases as cerebrovascular diseases, degenerative encephalopathies, demyelinating diseases, head injuries, headache and study of different cognitive disorders (such as learning and attention disorders) or psychiatric pathologies.

In cerebrovascular disease EEG quantitative parameters are highly correlated with regional blood flow and regional cerebral metabolism. When used by neurologist expertise in EEG interpretation, EEG mapping could be used for detection of focal ischemia related to a cerebral impairment [18]. However, EEG anatomical localization is inferior to that found with conventional neuroradiological techniques as CT or MRI that remain the examinations of choice. Moreover, EEG quantitative changes are unable to differentiate a cerebral infarction from an haemorrhage, a tumour or another focal cerebral lesion [19]. Conventional EEG remains indicated in patients with cerebrovascular problems as possible seizures or coma. Intraoperative EEG quantitative analysis, as frequency analysis, could be used in patients who undergo carotid endarterectomy, during surgical procedure to identify or better measure changes in electrical brain activity [20].

In neurological degenerative pathologies as dementia, EEG quantitative analysis is useful in detecting focal or generalised slowing that strongly suggest an organic basis rather than a depressive condition [21]. EEG frequency analysis cannot distinguish between the types of dementias, but EEG waves patterns are highly suggestive of certain dementing disorders. The degree of EEG frequency analysis abnormality corresponds to the degree of dementia and disease progression so that it has been experimentally used to separate normal controls from patients with mild–moderate Alzheimer disease [22]. EEG spatial analysis conducted on patients with Alzheimer disease has showed decreased duration and increased number of microstates [23]. Quantitative EEG in expert hands could also be useful in evaluation of certain patients with dementia whose neuroimaging and routine EEG studies are not conclusive.

In patients with demyelinating disease as multiple sclerosis, studies of topographic analysis of multichannel recording of evoked potentials have been directly compared in sensitivity and specificity of values obtained from canonical analysis of individual evoked potentials waveforms [24].

Some studies, reports and retrospective observations have addressed EEG brain mapping techniques in patients with head injury [25]. In a small group of patients with post-concussion syndrome it has been reported an increase in 8 to 10 hz of alpha rhythm [26]. Other reports have confirmed alpha reduction in a much larger group of patients after head injury so that it has been proposed as a prognostic element [27]. In coma patients due to severe head injury, EEG monitoring, with or without frequency analysis, has been shown to predict outcome and able to detect non-convulsive seizures or other complications [28]. Even if EEG brain mapping techniques have reported interesting changes in some studies the results are not sufficient to support its use in diagnosis of patients with minor-moderate head trauma or post-concussive syndrome.

In a study of patients with headache Pechadre et al. [29] have demonstrated that migraineurs have specific findings upon EEG mapping during photo-stimulation,

suggesting that neuronal excitability of visual cortex is altered in migraine patients [30].

EEG spatial analysis has been applied in the study of different cognitive disorders such as memory disorders, mechanism of memory formation and retrieval in human patients with amnesia [31] or language disorders such word production in stroke patients with aphasia [32]. EEG spatial analysis has also been applied to study the characteristics of brain function difficulties in children with Attention Deficits and Hyperactivity Disorders (ADHD) to evaluate time processing [33], to predict reading skills [34] or to evaluate treatment efficacy and predict changes in use of grammar in children with specific language disorders [35]. EEG specific patterns have been proposed in children with learning and attention disorders and researchers have proposed a relationship between EEG patterns and outcomes of therapy. EEG brain mapping have not been proven useful in establishing diagnosis or treatment for children with cognitive learning disabilities. Quantitative EEG is not recommended as an exam for diagnosing learning disabilities or attention disorders.

Finally, EEG spatial analysis, in the time as well as in the frequency domain, has been used to characterise different pathological states, particularly related to psychiatric pathologies. EEG analysis can identify slow wave or epileptiform abnormalities, which can occur in intoxication, delirium or other psychiatric disorders [36]. Frequency domain source localization has been used to identify brain regions with altered rhythms in patients with psychiatric disorders [37]. EEG microstate analysis has demonstrated that spatial characteristics of microstates are a sensitive measure of different mental states. For example, schizophrenic patients have a decreased duration and reduced number of some microstates [38] that could change and be normalised with medications [39]. Study of resting state in schizophrenic patients have showed that specific short microstates could be observed during auditory verbal hallucinations [40]. In depression microstates duration was also reduced or some microstates were repeated more frequently [41]. Anxiolytic or antipsychotic drugs as well as meditation or hypnosis can also alter the characteristics of cerebral microstates [42].

6. Applications of brain mapping in epilepsy

The most studied application of spatial EEG analysis is in the study of epilepsy in particular as a method to locate an epileptic focus (see **Figure 2**) and determine the type of epileptic syndrome [43].

Digital spike and seizure detection can help to identify electric cerebral events that might be epileptic spikes even if are frequent false-positive detections. In long-term EEG monitoring records, candidate spikes or seizure events are automatically selected and saved but there is need of a professional visual review and confirmation, especially in recording lasting several days [44].

Automated seizure detection can also identify non-convulsive seizure occurring in intensive care unit patients at risk for such complication [45] or to monitory convulsive status epilepticus in patients requiring neuromuscular blockade [46].

Quantitative analysis of spikes characteristic (as spike dipole analysis) can suggest location of cortical generators, existence of multiple separate spike generators and direction of propagation of spikes especially if this information is combined with visual review of voltage mapping.

These techniques might be useful in non-invasive evaluation of epileptic patient candidate for epilepsy surgery, even if the information obtained with dipole analysis is not mathematically and anatomically precise.

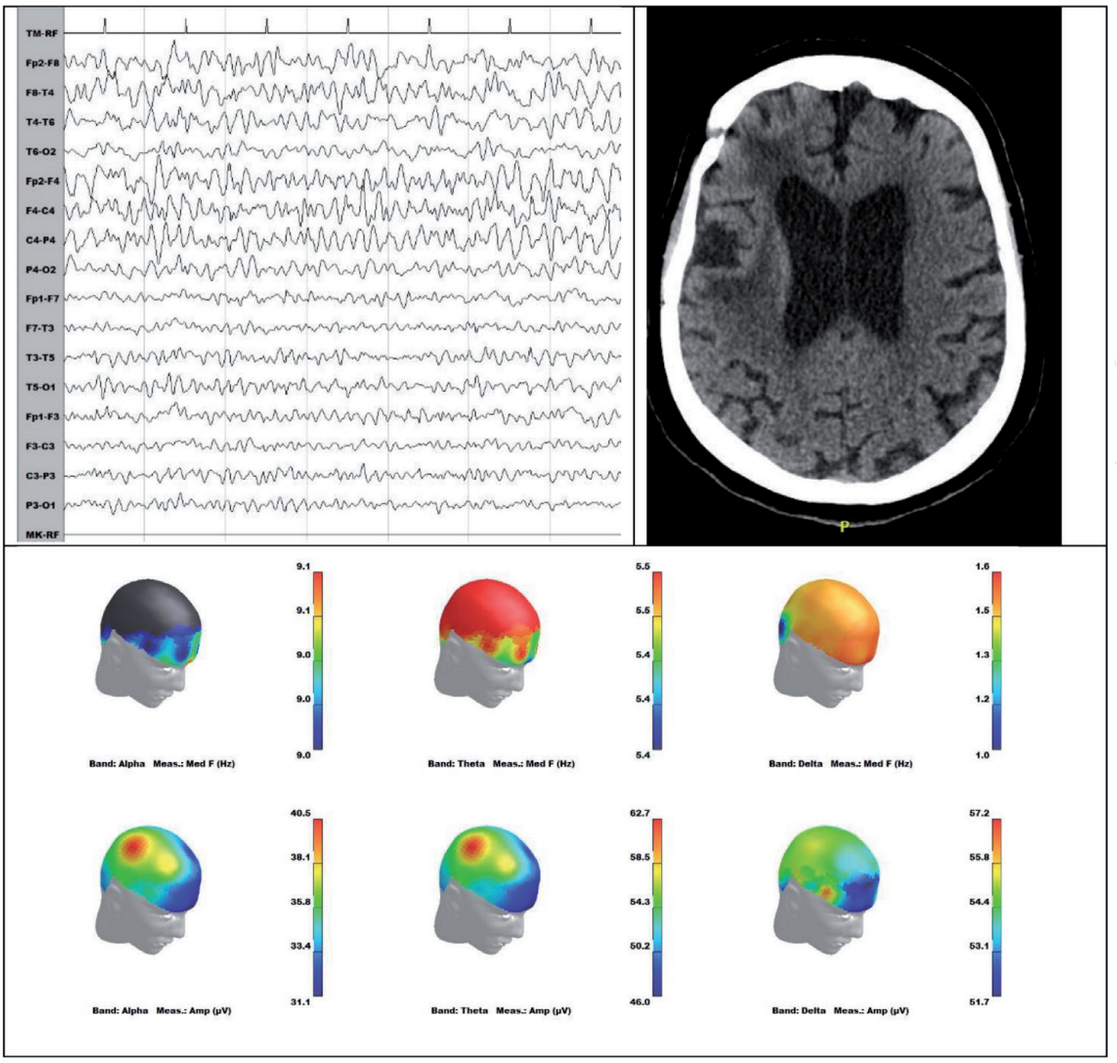

Figure 2.
Example of patient in which traditional electroencephalograms shows a right temporo-parietal epileptiform grapho-elements. TC brain scan shows ipodensity area in right hemisphere, where a cerebral glioma was surgically removed. EEG brain mapping confirms topography of discharges in right hemisphere with prevalence of rhythms in theta band.

A large number of studies have demonstrated that EEG mapping is a powerful tool to non-invasively localise an epileptic focus. The major advantage in the study of an epileptic focus localization compared to other neuro-functional conventional studies (such as fMRI or PET) is the high temporal resolution that allows for separating initiation from rapid propagation of epileptic activity.

The localization of epileptogenic foci with EEG mapping has been found in particular in mesial temporal lesions [47].

Sperli et al. [48], after EEG imaging analysis on 30 operated and seizure free children, reported correct localization of epileptic focus on a lobar level in 90% of cases. In another study, Michel et al. [49] showed 79% localization precision on a sublobar level. In a study conducted by Brodbeck et al. [50] were analysed 10 operated patients with normal MRI in which EEG spatial analysis showed in 8 of them correct localization within the resect margin. In a study conducted by Zumsteg et al. [51] in 2005, based on the analysis in 15 patients with mesial temporal lobe epilepsy the authors compared EEG imaging obtained by cortical electrodes with simultaneously recorded data from foramen ovale electrodes. They showed that 14 of the 19 patterns seen by foramen ovale electrodes could be correctly identified with source imaging, indicating that even mesial temporal sources can be recorded by scalp EEG as also previously demonstrated by Lantz et al. [52] in simultaneous cortical and

intracranial EEG recording. Brodbeck et al. [53] were also able to localise correctly spike activity within the resected zone in 12 of 14 patients with large cerebral lesions.

Regional or focal EEG slowing has long been valued to help to lateralize an epileptic focus that might be overlooked by a routine visual evaluation [54].

Brain mapping techniques may highlight to characteristics not obvious to the observer, drawing attention to particular features of a transient event. Clinical examples of applications in epilepsy include the mid-frontal positivity of typical Rolandic spike in benign childhood epilepsy [55]. In Benign Rolandic Epilepsy in Childhood (BREC) quantitative spike voltage analysis has been demonstrated to be useful in determining field complexity and dipole model stability and differentiating "typical" from "atypical" forms, a distinction with prognostic and therapeutic significance [56].

Some quantitative EEG techniques are useful to differentiate primary generalised discharges from secondary bilateral synchrony by looking for interhemispheric small time differences during spike–wave activity and the characteristic distribution of maximal activity [57]. This analysis could be useful to choose the best antiepileptic drug as well as pre-surgical localization of epileptic focus. This potential application has not been clearly demonstrated to be used in general clinical use.

Data manipulations used to enhance isopotential maps and mapping of averages have been used to show subtle features and pattern of propagations [55].

In a retrospective study conducted on 152 operated patients Brodbeck et al. [58] showed that EEG source imaging has a sensitivity of 84% and a specificity of 88% if the EEG is recorded with a large number of electrodes, 128–256 channels and the individual MRI is used as head model. The obtained values resulted comparable to those of structural MRI, PET and ictal-interictal PET. Specificity and sensitivity of EEG mapping and source imaging decreased significantly with use of a low number of electrodes (<32) and a template of head model. On the bases of this study authors concluded that EEG source imaging analysis should be used as standard tool in pre-surgical evaluation of epileptic patients, especially in consideration of its low costs and high flexibility if compared to other imaging methods. However, caution must be exercised since erroneous localizations could occur even for experienced users for the simplified spherical head model commonly used [59].

On the bases of the promising studies above illustrated, Plummer et al. [60] realised a comprehensive review proposing EEG source imaging as a routine work-up of patients with localization-related epilepsy, but concluded that a prospective validation study conducted on larger patients is still required.

EEG imaging has also been demonstrated to be useful in epileptic focus localization in combination with functional MRI. A series of studies conducted to evaluate spike-related analysis have revealed that the temporal resolution of EEG source imaging helps to identify spike-related BOLD responses that correspond to start of epileptic discharge [61–63].

Grouiller et al. [64] conducted a study in which they used EEG topographic analysis to help to analyse fMRI data of epileptic patients that had no spike in the scanner or no-related BOLD responses. In this study they used the average spike-map of EEG recorded during a long-term monitoring and demonstrated that 78% of the otherwise inconclusive fMRI studies could nonetheless be interpreted.

7. Conclusions

EEG analysis in recent times has moved from the traditional analysis of grapho-elements to a comprehensive study of brain's electric fields at the scalp.

Quantitative EEG provides more information than visual inspection of traditional EEG used for routine in neurology practice.

Quantitative EEG or other EEG brain mapping techniques cannot diagnose whether a patient has epilepsy but is useful to give additional information in epileptic patients for screening of spikes or possible epileptic spikes in long term EEG monitoring.

EEG spatial analysis is not only a synonymous of source localization but a new insight in brain functioning obtained just analysing the spatial changes of the scalp potential maps over time principally based on the quantitative analysis of EEG waveforms in terms of frequency and amplitude.

Given to the flexibility, non-invasively, easy use and cost-effectiveness EEG mapping is a powerful and interesting brain imaging device that can be easily combined with other traditional imaging techniques.

The potential use of this technique has limitations since quality of EEG mapping depends on the raw data inputs and lack of universally valid normative data due to inter-individual variability of EEG.

The problem of inter-individual variability is reduced with computer-assisted analysis of EEG even if more engineering and analysis tools are still needed to better develop this technique that can be actually used only by physicians highly skilled in clinical EEG and in conjunction with traditional EEG.

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