

# EEG in Epilepsy: Current Perspectives

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**ABSTRACT:** The electroencephalogram (EEG) plays an important diagnostic role in epilepsy and provides supporting evidence of a seizure disorder as well as assisting with classification of seizures and epilepsy syndromes. Emerging evidence suggests that the EEG may also provide useful prognostic information regarding seizure recurrence after a single unprovoked attack and following antiepileptic drug withdrawal. Continuous EEG video telemetry monitoring has an established role in the diagnosis of non-epileptic pseudo-seizures and in localizing the seizure focus for epilepsy surgery. Newer tools such as EEG mapping and magneto-encephalogram, although still investigational, appear potentially useful for defining the seizure focus in epilepsy. This review examines the traditional concepts of clinical EEG in the light of newly available data.

**RÉSUMÉ: L'ÉEG dans l'épilepsie: perspectives actuelles.** L'électroencéphalogramme (ÉEG) joue un rôle diagnostique important dans l'épilepsie et fournit des données étayant le diagnostic d'épilepsie et aidant à sa classification. Des données récentes suggèrent que l'ÉEG peut aussi fournir des informations utiles pour déterminer le pronostic quant à récurrence des crises après un épisode unique non provoqué et après le retrait de la médication antiépileptique. Le monitoring vidéo télémétrique continu de l'ÉEG a un rôle établi dans le diagnostic des pseudo-crisis non épileptiques et dans la localisation du foyer épileptogène en vue d'une chirurgie. Les nouveaux outils tels que la cartographie par ÉEG et le magnéto-encéphalogramme, bien qu'ils soient encore au stade expérimental, semblent potentiellement utiles pour identifier le foyer épileptogène dans l'épilepsie. Cet article de revue examine les concepts traditionnels de l'ÉEG en clinique à la lumière de données nouvelles.

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Although the diagnosis of seizures and epileptic syndromes is primarily made from careful history and examination, the EEG remains an important investigative tool. The EEG often provides supportive evidence of seizure disorder and assists with classification of seizures and epilepsy. Moreover, EEG findings are important for determination of seizure focus and may also help with prognosis under certain circumstances.

This review examines the traditional and emerging role of EEG in epilepsy.

## TECHNICAL CONSIDERATIONS

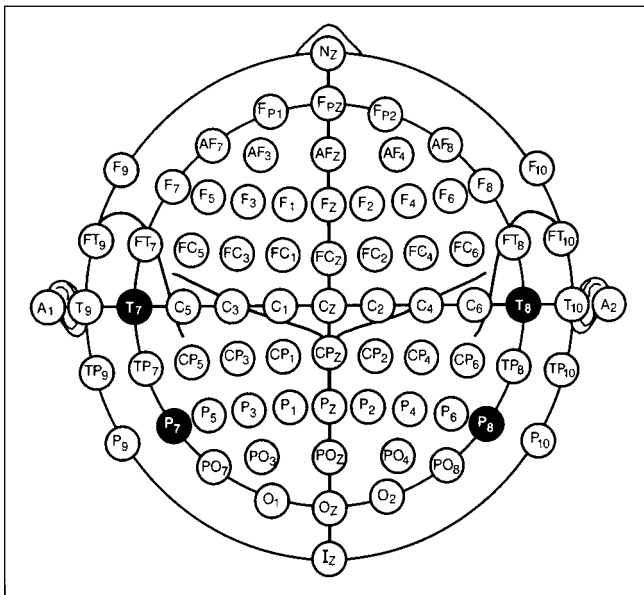
### Electrodes

The international ten-twenty system of electrode placement, originally proposed in 1958,<sup>1</sup> is now widely used and is the recommended standard method for recording scalp EEG. The American EEG Society has recently advocated slight modifications to the original alphanumeric nomenclature<sup>2</sup> and the recommended changes are shown in Figure 1. Note that the original T3, T4, T5 and T6 are now referred to as T7, T8, P7 and P8 respectively. This modification allows standardized extension

of electrode placement in the subtemporal region (e.g.: F9, T9, P9, F10, T10, P10) and designates named electrode positions in the intermediate coronal lines between the standard coronal lines (e.g.: AF7, AF3, FT9, FT7, FC5, FC3, FC1, TP9, TP7, CP5, CP3, CP1, PO7, PO3 and so on). Additional and more closely spaced scalp electrodes – placed midway between the standard electrodes of the 10-20 system – often provide further localization of epileptiform discharges in patients with partial seizures.<sup>3</sup> Several electrodes are available for demonstrating temporal lobe activity. Sphenoidal electrodes are particularly useful for detecting mediobasal temporal discharges and are inserted under the mandibular notch (app. 2.5 to 3 cm anterior to the tragus) and directed posterosuperiorly towards the foramen ovale.<sup>4</sup> Sphenoidal electrodes have now been shown to be superior to nasopharyngeal electrodes<sup>5, 6</sup> and their proximity to

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**Figure 1:** Electrode nomenclature proposed by The American Clinical Neurophysiology Society (reproduced with permission from the American Neurophysiology Society.)

the foramen ovale can be assured under fluoroscopic guidance.<sup>7</sup> Anterior “cheek” electrodes (placed on the maxilla approximately 2 cm anterior to the site of entry of the sphenoidal electrode) and anterior temporal electrodes (placed 1 cm above one third the distance from the external auditory meatus to the external canthus) are also useful for demonstrating epileptiform discharges (ED) from the temporal lobe and the yield appears comparable to that from sphenoidal electrodes.<sup>8,9</sup>

Routine scalp recordings may not show ED in approximately 10% of patients with frontal lobe seizures<sup>10</sup> and the yield in these patients may be increased by using closely spaced electrodes such as F1, C1, F2, C2 (placed halfway between Fz/F3, Cz/C3, Fz/F4 and Cz/C4 respectively) or supraorbital electrodes, placed 2.5 cm lateral to theinion on the supraorbital ridge.

### Digital EEG

Digital recording machines are rapidly replacing the traditional “paper” systems. Digital EEG is particularly useful for detecting and analyzing ED as the waveforms in question can be reformatted in various montages after the recording is completed. Other advantages of digital recordings include very little storage space requirement, elimination of paper costs, automatic event detection and the ability to network different recording stations. Filter and paper speed settings with digital recordings are accurate and automatic, thereby avoiding technician oversight. Problems due to pen alignment and curvilinear effect are not seen with digital systems. A major disadvantage of digital EEG is the incompatibility of systems made by different vendors, often forcing one to resort to paper printouts for transmission of EEG data between two centers. Authors also find comparing two separate epochs somewhat cumbersome, as only limited data can be observed simultaneously on the monitor. The reader is referred elsewhere for further details on digital technology.<sup>11</sup>

## ACTIVATION PROCEDURES

### Hyperventilation

Forster, in 1924, first demonstrated that hyperventilation (HV) may precipitate absence seizures in children<sup>12</sup> and this method of activation has since become routine during EEG recordings. Although HV is particularly useful for demonstrating generalized epileptiform discharges, it may also activate focal epileptiform discharges in up to 10% of patients with partial epilepsies.<sup>13,14</sup> The neuronal irritability during HV is considered to be due to brainstem mediated cerebral vasoconstriction induced by hypocapnia. This view, however, remains speculative and controversial.<sup>15</sup> Hyperventilation should be avoided in patients with potential for brain damage from further vasoconstriction, e.g. malignant hypertension, subarachnoid hemorrhage, sickle cell disease or trait.

### Photic Stimulation

Photic stimulation (PS) is useful for activation of generalized epileptiform discharges. Testing is generally done with stepwise increase of frequencies up to 30 Hz with a strobe light at a distance of 20 to 30 cm from the eyes. The authors recommend PS at low frequencies with eyes open and then closed. At medium and higher frequencies, stimulation should start with the eyes open, and the patient is asked to close the eyes during PS, thereby continuing with PS for a few more seconds with the eyes remaining closed. Eye closure during photic stimulation is particularly useful for augmenting ED and should routinely be used. Epileptiform discharges outlasting PS strongly suggest generalized seizure disorder, whereas those confined to the train of PS may be an incidental finding in nonepileptic subjects, especially in the setting of drug withdrawal or toxic metabolic encephalopathy, or simply represent a genetic trait.<sup>16,17,18,19</sup> Photic stimulation is particularly useful in primary generalized epilepsy and ED may occur during PS in up to 40% of these patients.<sup>20</sup> Recent evidence indicates that approximately a quarter to a third of EEGs with photic related ED also contain spontaneous focal or generalized ED elsewhere in the records.<sup>21</sup> Photoparoxysmal response is more prevalent among white epileptics than black or mixed race patients.<sup>22</sup>

### Sleep Deprivation (SD)

When the first EEG fails to show ED in patients with epilepsy, sleep deprived recording often helps. Several studies have convincingly documented that the chances of finding ED increase with sleep deprived recordings in both partial and generalized seizure patients of all ages.<sup>23-30</sup> Epileptiform discharges following sleep deprivation occur both in the awake and sleep portions of the EEG. Moreover, Rowan and co-workers have shown that EEGs following sleep deprivation are more likely to contain ED than the recordings of similar length done following sedation.<sup>31</sup> Mattson et al.<sup>25</sup> have shown that the increase in the quantity of ED after sleep deprivation is not simply a reflection of sample time but due to direct effect of loss of sleep itself. These observations suggest that sleep deprivation augments ED not just by inducing sleep but possibly by other as yet undefined mechanisms. Authors recommend sleep deprived EEG rather than recording under sedation if the first EEG is negative.

However, several issues still remain unresolved: is all night sleep deprivation superior to half night SD? What is the ideal,

practical duration of sleep deprived recordings? Future studies addressing these questions are awaited.

## CLINICAL SIGNIFICANCE OF INTERICTAL ED

### ED in nonepileptic subjects

Although the presence of interictal ED generally supports the diagnosis of seizure disorder, caution is necessary in interpreting the clinical significance as ED may occur in subjects without seizures. Among healthy adults without seizure history, the frequency of ED is approximately 0.5%.<sup>32,33</sup> Practically none of these healthy subjects subsequently develops seizures. "Incidental" ED occur slightly more often (app. 2%) in subjects with a history of previous neurological insults such as trauma, stroke, craniotomy, infections, cerebral palsy or during migraine.<sup>34</sup> Up to 14% of these patients subsequently develop seizures. In children without prior seizures, ED may occur in up to 5% and this may be as high as 8% if adequate sleep is recorded;<sup>35–38</sup> these tend to be benign rolandic or occipital spikes or generalized 3 Hz spike-wave discharges and likely represent incidental genetic trait. Risk of subsequent seizures in these children is around 6%.<sup>36</sup> Certain EEG patterns, however, almost always indicate associated clinical seizures and these include hypsarrhythmia and 1 or 2 Hz generalized slow spike-wave complexes.

### ED in the first and serial EEGs

First standard EEGs in patients with a reasonably certain diagnosis of seizure disorder contain ED in approximately 50%.<sup>39,40</sup> Yield from the first EEG in children with absence seizures, however, is higher, around 75%.<sup>41</sup> Apart from sleep, several other factors have been shown to increase the likelihood of ED and these include i) recording within 48 hours of a seizure and ii) ongoing seizure frequency of at least one attack per month.<sup>40</sup> The yield, however, is not significantly altered by neurological status, etiology of seizures, age of the patient and anti-epileptic drug therapy.<sup>40</sup>

Serial EEGs are often necessary for demonstrating ED. Most patients who eventually show ED do so by the fourth EEG.<sup>40,42</sup> Recordings are persistently negative in only 8% of epileptics although there is evidence that a higher proportion of patients with partial seizures may have persistently negative serial EEGs.<sup>39,40</sup>

The above observations suggest that i) the ideal time for obtaining an EEG is the first day or two after a seizure, ii) one should consider long-term monitoring if four routine recordings have remained negative in patients with ongoing "seizures".

### Cognitive Changes

Subtle and transient cognitive impairment has been demonstrated during brief "subclinical" generalized spike-wave discharges, especially during the first second.<sup>43–46</sup> Aarts and co-workers<sup>45</sup> have reported similar subtle cognitive impairment in some subjects during focal interictal ED. Such cognitive changes may occur in up to 50% of tested patients and may, if EDs are frequent, affect school performance and driving behavior under experimental conditions.<sup>47–49</sup> The clinical relevance and therapeutic implications of these observations currently remain unknown.

## ICTAL EEG

While interictal ED generally provides support for the diagnosis of seizure disorder, electrographic or clinical seizures during EEG confirm seizure(s). However, our experience indicates that the probability of capturing an ictal event during a routine 20 to 30 minute recording in a patient with an average of one random seizure per week is less than 1%. Moreover, the scalp EEG may not reflect all of the ictal activity as this depends on i) the frequency-filtering properties of the skull and scalp, ii) the distance and orientation of the focus from the recording electrode and, iii) the surface area of the focus with respect to the recording electrode. In spite of these limitations, scalp recorded seizures provide valuable information regarding the seizure type and focus.

### Partial Seizures

Partial seizures, in scalp EEGs, are metamorphic, i.e., they show two or more distinct phases.<sup>50–52</sup> The most common patterns consist of a series of rhythmic waves, sequential spikes/sharp waves, a mixture of spikes and rhythmic waves or regional voltage attenuation. Rhythmic waves and spikes typically change in amplitude, frequency and spatial distribution as the seizure spreads to adjacent or sometimes remote areas. Finally, the discharges contract in area as the seizure ends.<sup>50</sup> Most often the initial frequency of temporal lobe seizures is in the alpha or theta range with slower frequencies occurring in a lesser proportion.<sup>51</sup> Extra temporal seizures, however, often start in the beta frequencies rather than slower frequencies.<sup>52</sup> With scalp EEG, the frequency may diminish or augment, but as the seizure ends, rhythmic waves or sequential spikes change to a slow spike-wave pattern that gradually decreases in frequency. Focal electrodecremental events are of excellent localizing value, reflecting intense neuronal depolarization or high frequency firing.<sup>52</sup> However, generalized electrodecremental events preceding focal seizures are probably not truly ictal and may represent generalized cerebral changes that predispose to focal seizure development.<sup>53</sup> Following metamorphic seizures, there is often postictal delta slowing, suppression or activation of focal spikes. These postictal changes also have good localizing value for seizure origin and should be carefully sought.<sup>54</sup>

It is important to recognize that simple partial seizures – especially those with sensory rather than motor symptoms – may not be associated with discernable changes in routine scalp EEG in up to 80% of seizures.<sup>55</sup> However, the yield in these patients may be augmented by using additional closely spaced electrodes.<sup>56</sup>

### Generalized seizures

Typical absence seizures are characterized by isomorphic and stereotyped patterns that do not evolve as partial seizures. However, the spike-wave discharges may change from 3.5 or 4 Hz at the onset to 2 or 3 Hz as the seizure progresses. Also, the spike amplitude may decrease during the later part of the seizure. Atypical absence attacks frequently show gradual onset and offset with spike-wave discharges occurring at frequencies less than 3 Hz.

Generalized tonic-clonic seizures may be preceded by diffuse polyspike-wave complexes. Ictal recordings during the tonic

phase typically shows generalized attenuation with or without high frequency rhythmic waves that gradually increase in voltage (“epileptic recruiting rhythm”) and evolve into polyspikes. The clonic phase is characterized by paroxysmal spike activity mixed with slow waves and the post-ictal period shows generalized attenuation followed by gradual recovery of rhythms.<sup>57</sup>

Myoclonic seizures are associated with 10 to 15 Hz polyspikes with or without slow waves, whereas tonic seizures show generalized paroxysmal fast activity or diffuse voltage attenuation preceded or followed by sharp and slow wave complexes. Generalized atonic seizures may show 2-3 Hz spike-wave discharges or may not be associated with any scalp EEG change.

### PLEDs

Although PLEDs have traditionally been considered “interictal”,<sup>58</sup> there is some evidence that this pattern in some patients may be “ictal” in nature, especially when seen following traditional ictal patterns.<sup>59,60</sup> Moreover, Reiher and co-workers reported that the “PLEDs plus pattern”, consisting of periodic epileptiform activity closely followed by brief, low amplitude, stereotyped rhythmic discharges, is often associated with clinical seizures and may indeed be a foreteller of imminent seizures.<sup>61</sup> However, whether the PLEDs or PLEDs plus pattern requires aggressive treatment similar to status epilepticus remains unclear.<sup>62</sup>

### PROGNOSIS OF EPILEPSY

Routine EEG is useful for prognostic purposes in at least three situations: i) assisting in epilepsy syndrome classification, ii) predicting recurrence after the first seizure and iii) providing information on seizure relapse after anticonvulsant withdrawal.

### Classification of epilepsy

The EEG provides important information for classification of various epileptic syndromes and thereby assists in predicting the natural history of the syndrome. For example, a child with normal neurological examination and rolandic spikes in EEG has a high probability of “outgrowing” seizures and may not even need treatment following isolated, infrequent seizures. Similarly, generalized 4-6 Hz spike-wave and polyspike discharges in an adolescent with seizures suggest juvenile myoclonic epilepsy of Janz: a condition with a high response rate to valproic acid or medications such as primidone or acetazolamide when valproic acid fails.

### First seizure

Prediction of recurrence after a single seizure is clinically important and many studies have addressed this question. However, differences in methodology make comparison of these studies difficult and the results still remain somewhat controversial. A meta analysis of sixteen published reports suggests that EEG abnormalities may increase the risk of recurrence after first seizure.<sup>63</sup>

A recent large prospective study of children with single unprovoked seizure<sup>64</sup> showed that, in those without obvious etiology (“idiopathic”), the presence of epileptiform discharges in the EEG was associated with a recurrence rate of 54%

whereas the rate was only 25% when the first EEG was normal. In the above study, the EEG was not of any predictive value in children with remote symptomatic seizures.

Several recent prospective studies suggest that the EEG is useful in adults with first seizure – especially among those with idiopathic seizures.<sup>65-67</sup> The Dutch workers<sup>66</sup> showed that when two EEGs (one baseline and one sleep deprived recording) are normal, the recurrence rate was 12% at two years, whereas in those with one or both EEGs containing ED, recurrence rate increased to 83%. The Italian first seizure trial group also showed a 1.7 fold increase in seizure recurrence when the EEG contained ED. Some controversy still exists in this area as some authors maintain that the EEG findings are of no predictive value after first seizure.<sup>68</sup>

### Anti-epileptic drug withdrawal

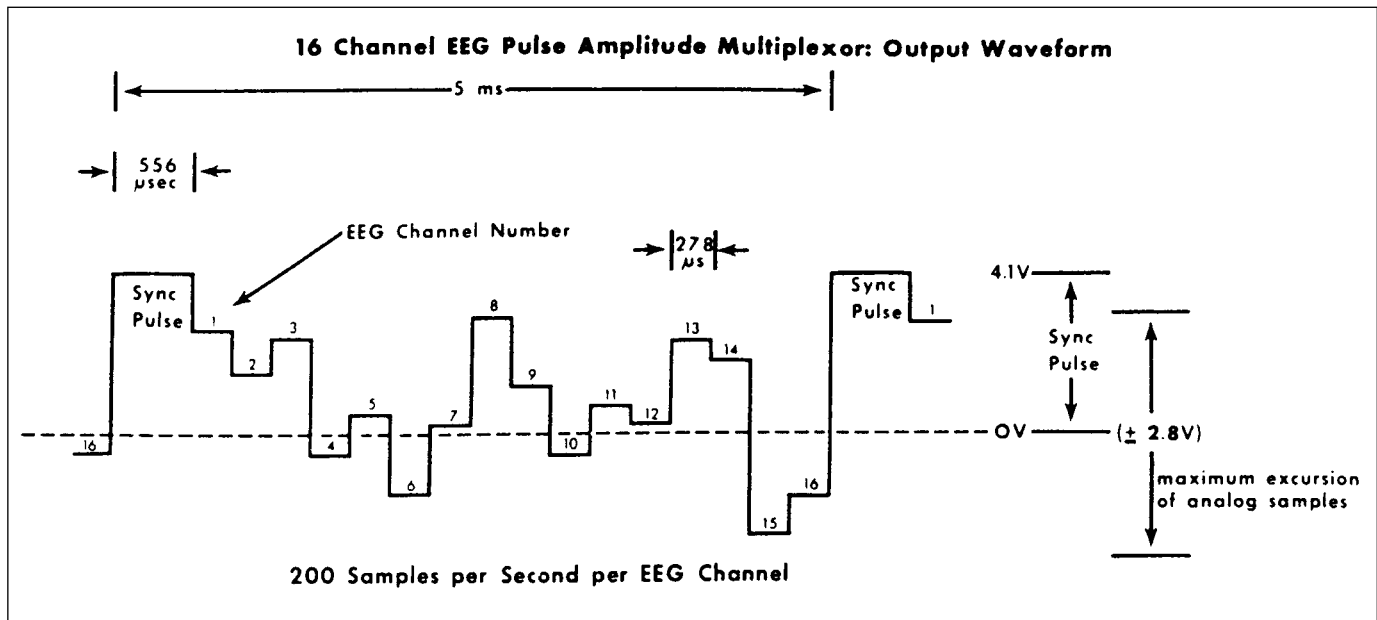
The role of EEG in predicting relapses after anti-epileptic drug withdrawal remains more controversial. Some studies show an increase in recurrence rate with abnormal EEG prior to or during the withdrawal,<sup>69</sup> whereas others suggest that the EEG findings are of no predictive value.<sup>70</sup> Yet others show that slowing – and not spikes – in EEG is associated with a higher recurrence in children with idiopathic seizures.<sup>71</sup> A recent meta analysis discussing in depth various factors in predicting relapses after anti-epileptic drug withdrawal indicates that any EEG abnormality (epileptiform activity or slowing) is associated with a relative relapse risk of 1.45.<sup>72</sup> Other factors found to increase the relapse rate in the above meta analysis were adolescent or adult epilepsy onset (rather than childhood onset) and known remote etiology.

### TELEMETRY MONITORING

Although the EEG remains the gold standard for confirming seizures, an actual attack or event is rare during a standard 20 to 30 minute recording. Even serial EEGs may fail to reveal ED in up to 10% of epileptics.<sup>39</sup> When the nature of attacks or the exact seizure focus cannot be ascertained with several routine EEGs, telemetry monitoring often provides necessary additional information. With current telemetry systems, EEG data may be collected continuously for several days or even weeks. This may be done as an inpatient procedure using cable telemetry or at home/work environment with radiotelemetry. Most cable telemetry equipment also has video capability and provides an opportunity to analyze physical changes during the ictus.

Telemetry monitoring is useful: i) for confirming the nature of epileptic attacks and nonepileptic events such as pseudoseizure,<sup>73</sup> paroxysmal movement disorders,<sup>74</sup> and sleep disorders,<sup>75</sup> ii) for exact classification of seizures prior to appropriate therapy,<sup>76</sup> iii) for determination of seizure focus in patients with atypical features (e.g. frontal lobe seizures, gelastic seizures),<sup>77,78</sup> or for presurgical evaluation,<sup>79</sup> iv) for assessing the response to anticonvulsant therapy,<sup>80,81</sup> and v) for research purposes, e.g. analysis of the relationship between the quantity of interictal spikes and clinical seizures.<sup>82,83</sup>

Video telemetry is generally indicated when visual analysis of physical changes during the event is necessary as in pseudo-seizure, frontal lobe seizures, and paroxysmal movement disorders. Ambulatory monitoring without video may be



**Figure 2:** Summary of multiplexing sixteen channels of EEG data using time-division method (reproduced from Ives JR, Thompson CJ, Gloor P. Seizure monitoring: a new tool in electroencephalograph. *Electroencephalogr Clin Neurophysiol* 1976; 41:422-427. with permission from Elsevier Science).

sufficient for confirming the nature of events such as syncope or absence attacks.

The following is a summary of the principles involved in telemetry technology: long term monitoring requires some amount of patient mobility and this often results in electrostatic artifacts from cable motion and friction between the insulating materials of the electrode leads. These artifacts, in telemetry, are minimized by attaching a miniature preamplifier close to the patient, thereby keeping the length of the leads from scalp electrodes to the preamplifier short. Several channels of signals thus amplified in the preamplifier are then encoded onto a single channel and this process is called "multiplexing" (Figure 2). Multiplexed signals then can either be carried along a flexible cable and stored in a nearby station ("cable telemetry"). Alternately, multiplexed signals could be relayed to a distant receiving station using a radiotransmitter ("radiotelemetry"). At the receiving station the transmitted signals are stored in the audio tract of a magnetic video tape or as a digital signal on an optical disc. In some ambulatory systems, EEG data are stored without multiplexing in a small cassette recorder carried by the patient. Recent advances in technology now enable us to record and store even video signals digitally with significant improvement in clarity.

Digital time signals can be encoded in the current systems for correlating events with EEG data. The patient (or relative) presses an event marker during the ictus, thereby registering the time, and this provides the technologist with a list of events. Automated seizure detection devices are also available and these ensure that the events are not missed even if the event marker is not manually pressed. Most current available telemetry systems can process up to 128 channels of EEG data.

In recent years, portable telemetry systems with simultaneous video capability have become available and provide good quality monitoring in home or work

environment.<sup>84</sup> This method would be cost saving as inpatient expenses are avoided. Video telemetry may also be done, especially for children, for three or four half or full days in an outpatient setting until the habitual event or suspected EEG abnormality has been recorded.

Additional information on telemetry technology may be found elsewhere.<sup>85,86</sup>

When carefully used, telemetry provides clinically useful additional information in approximately two thirds of monitored patients.<sup>87</sup>

## NEWER METHODS

### Brain mapping

Brain mapping refers to quantification and topographic display of various EEG frequencies or evoked potentials. This procedure requires special technical expertise for identification of artifacts and drowsiness as well as a thorough knowledge of statistical analysis and computer data processing. Interpretation thus requires a clear understanding of the pitfalls and limitations of this technique.<sup>88,89</sup> Currently, brain mapping is primarily a research tool with limited clinical applications.<sup>90</sup> Potential areas of clinical use include detection of subtle EEG frequency alterations in mild organic encephalopathies (e.g. Alzheimer's disease) or underlying ischemia and in determination of spike source in epilepsy.

In epilepsy, brain mapping appears to be a promising tool for determination of the source of focal interictal spikes in benign rolandic epilepsy of childhood<sup>91</sup> and temporal lobe epilepsy.<sup>92</sup> A recent paper by Ebersole describes the process involved in the analysis of spatial distribution of voltage fields and localization of spike generators in several patients with temporal lobe epilepsy.<sup>93</sup> Thus, brain mapping may provide another noninvasive localization technique prior to epilepsy surgery, but additional studies are necessary.

**Magneto-encephalogram (MEG)**

Traditional EEG records the extracellular electrical current, whereas MEG detects the corresponding magnetic fields. The neurons in the walls of the sulci produce current dipoles that are tangential to the skull and these are detected by MEG. However, neurons at the tip of the gyri are radial to the skull and do not contribute to MEG. Although the EEG records the electrical currents from both gyral and sulcal neurons, these currents are often distorted as they pass through various intervening tissues. Magnetic fields, however, pass through these tissues without any distortion and are easily recorded by MEG. Moreover, MEG measurements are absolute – rather than differential – thereby eliminating any active reference contamination. Thus, MEG offers a relatively simple, noninvasive, but still expensive method for monitoring the activity of the brain. Several studies show that the spatial and temporal resolution of spikes – especially those at the depths – is superior with MEG than conventional EEG.<sup>93,94</sup> Thus MEG appears to be another noninvasive tool in epilepsy for localization of spikes. With rapidly evolving technology, cheaper and more mobile MEG systems should be available for wider use within the next decade.

**SUMMARY**

After almost 70 years since Berger showed the usefulness of EEG in man, this procedure still remains the “gold standard” for the diagnosis of seizures and epilepsy. The role of EEG has expanded in recent years and the test now plays an important role in predicting seizure recurrence among patients with newly diagnosed epilepsy and during anti-epileptic drug withdrawal. Rapid advances in technology have made digital equipment and continuous monitoring more widely available and at the same time providing better quality recordings than ever before. Magnetoencephalography and brain mapping are rapidly evolving and appear to be promising for precise localization of spikes and detection of subtle non-epileptiform abnormalities in the brain.

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