1- Introduction & basic concept of brainmapping
2- Polymorphic delta activity and its brainmap counterpart
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4- EEG and brainmap spectral profiles in cortical lesions, subcortical white matter lesions and subcortical gray matter (diencephalic) lesions
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I have been working in the field of conventional EEG, and brainmapping for over 20 years. My master degree thesis was about brainmapping and quantitative EEG and its application in the field of neurological and psychiatric disorders. I have mapped till now over 4000 patients and over 1000 normal individual. Although many might not understand the basic concept of brain mapping and probably underestimate its significance in clinical practice and research work, however brainmapping is nothing but a quantification, objective analysis and description of what is qualitatively described by conventional EEG.

In fact conventional EEG has fallen short of expectation not because it contains too little informations but because it contains too much informations to be handled by the unaided visual analysis.

In brain mapping the following is done

1- **Spectral analysis:** where the various EEG frequencies (delta, theta, alpha, beta) are separated from each other.

2- **Quantification:** The percentage activity in each frequency band during a specific time rage is calculated

3- **Topographic display:** The percentage activity in each frequency band is drawn forming a surface image comparable to both CT scan and MRI

Thus the subjective, qualitative and impressionistic description of conventional EEG is transformed into an objective, and quantitative description of the same data (the brain electrical activity)

Alpha map in the eye closed awake state . Notice the following

1-The maximum percentage alpha activity is around 70 %

2-The middle line distribution of the alpha maximum. With maximum activity at O1,O2, F3,F4 electrodes

3-The topographic display of the alpha activity (alpha map) allows analysis of the alpha activity by just one look

In the same way we can analyze other frequency bands

http://brainmapping.yassermetwally.com is a section of my web site dealing with the issue of brainmapping.

The author, Professor Yasser Metwally
Although spikes and/or polyspikes constitute the most important epileptic interseizure EEG pattern, there has been no precise mathematical definition of an EEG spike. Various authors and committees have tried to define formally what constitute an EEG spike, these attempts were either qualitative, depending on the impressionistic visual inspection or even when quantitative were lacking in parameters which describe the phenomena exactly. In fact until now little progress has been made towards formulating a precise definition of an EEG spike. Although a trained person can detect spikes in the EEG through extensive definitions, but limitation of such impressionistic and idiosyncratic evaluation of the EEG data clearly exist. In this respect, Metwally, 1986 commented that the potentialities of the clinical and research EEG can not be realized until such impressions are replaced by numbers and until subjective descriptions are replaced with mathematically derived characteristics.

The clinical evaluation of the EEG, consists of visual inspection and has two parallel objectives, the first is to determine the presence or absence of discrete, often diagnostic, discontinuities such as the spike, and wave of epilepsy. In this endeavor, the visual inspection has proved successfully as transients often stands in clear contrast with the background of the EEG. In fact, visual inspection in this respect was found superior to C.EEG in detecting epileptic transients. The second objective is to screen the EEG for underlying background abnormalities, a complex process in which the EEG estimates the amount, spatial distribution, and temporal stability of the various EEG frequency bands, in this respect computer assisted power spectral analysis, where the amount of energy in all frequency bands is quantified, was found clearly superior to visual inspection.

Based on the idea that the EEGs of the epileptic patients more often than not contain very useful though subtle information, even when reported by visual inspection to be within normal some investigators have utilized the technique of power spectral analysis in order to detect these subtle abnormalities.

The introduction of power spectral analysis and subsequent brain electrical activity mapping (BEAM spectral studies) has further extended the clinical utility of the classical EEG as an investigatory tool in epileptology. BEAM spectral studies is now considered as an important contribution towards localization and characterization of epileptic foci, especially when the standard EEG is considered as within normal or showing non specific changes. In this respect, BEAM was capable of uncovering cases of covert epilepsy and of detecting subclinical epileptogenic foci. Using the technique of brain electrical activity mapping (BEAM spectral study) while investigating a group of epileptic patients. Metwally, 1986, 1998 found that focal increase of the spectral energy in all frequency bands signals epileptogenic cortex. The author reported that the increased spectral energy might involve the whole power spectrum, or it might be localized to the beta band. Occasionally, the focal increased energy in the beta band might be associated with decreased energy in the Delta, theta and alpha bands either at the site of the beta focus or in the nearby cortex.

Focal beta hyperactivity (Focal increase of the beta spectral energy) is a manifestation of a seizure focus. In less irritable foci, the power increase is limited to the beta band while more excitable epileptogenic foci show a BEAM spectral profile characterized by focal increase of the spectral energy in all frequency bands (Delta - theta, alpha as well as beta bands). In patients where the enhanced beta focus is associated with power reduction in the alpha theta and delta bands, a pattern of diminished and augmented activity in close proximity, might suggest a region of atrophy and gliosis surrounded by epileptogenic cortex. The diminished power in the delta band might, in this respect, indicates functionally destructive cortex.

The author,
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<table>
<thead>
<tr>
<th>The percentage % Theta activity</th>
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<tbody>
<tr>
<td>12.9/3.9</td>
</tr>
<tr>
<td>16.3/6.8</td>
</tr>
<tr>
<td>21.5/20.2</td>
</tr>
<tr>
<td>14.6/3.1</td>
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<tr>
<td>9.5/3.3</td>
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Two example of alpha and theta percentage activity maps, Notice the central & bitemporal topographic location of the theta maximum activity and the occipital & Bifrontal maximum alpha activity. In general the alpha percentage activity has a middle line maximum while delta percentage activity has an anterior bifrontal maximum. Absolute power in all frequency ranges has an occipital maximum. Numerical values for the theta percentage activity is shown in the table above. The theta maximum is localised at electrodes T5,T6,T3,T4, while the numerical values for the

To be cont on page 3
Alpha percentage activity is shown in the table below. Maximal alpha activity occurred at O2, O2 and F3, F4 and FZ electrodes.

<table>
<thead>
<tr>
<th>Alpha percentage activity, Notice the middle maximum</th>
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<tbody>
<tr>
<td>31.8/14.1 (FP1)</td>
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<tr>
<td>29.5/7.5 (F7)</td>
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<tr>
<td>26/7.9 (T3)</td>
</tr>
<tr>
<td>21.7/16.3 (T5)</td>
</tr>
<tr>
<td>67.7/7.1 (O1)</td>
</tr>
</tbody>
</table>

Maximal alpha activity occurred at O2, O2 and F3, F4 and FZ electrodes.

Percentage Delta activity map showing the frontal maximum

The author, Professor Yasser Metwally

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Some brainmapping terminologies

◆ Absolute power
This refers to the amount of activity within a specific frequency band of brain waves. It is the mean amplitude in a given frequency band. Activity in each frequency band is compared to a normative database to determine the presence of suspected abnormalities. The results for each frequency band are shown with the topographic activity maps. Green is the color representing average activity. Red means there is a large increase in activity when compared to the normative database, while blue means there is a large decrease. In all frequency bands, the absolute power is maximum posteriorly.

◆ Relative power..% Activity
This refers to the relative amount of activity within a specific frequency band compared to all the other frequency bands. Relative activity in each frequency band is compared to a normative database to determine the presence of suspected abnormalities. The results for each frequency band are shown with the topographic activity maps. Green is the color representing average activity. Red means there is a large increase in activity when compared to the normative database, while blue means there is a large decrease.

◆ Coherence
This refers to the similarity in EEG waves over different areas of the brain – i.e. the timing of activity in one area compared to another. Coherence in each frequency band is compared to a normative database to determine the presence of suspected abnormalities. The results for each frequency band are shown with the topographic connection maps. Thick lines represent larger deviations from ‘normal’ – red refers to increased coherence, while blue refers to decreased coherence.

◆ Symmetry
This refers to the relationship between the amount of activity in one area of the brain compared to another. Inter-hemispheric means differences between each side of the brain, while intrahemispheric means differences between areas on the same side of the brain.

Asymmetry in each frequency band is compared to a normative database to determine the presence of suspected abnormalities. The results for each frequency band are shown with the topographic connection maps. Thick lines represent larger deviations from ‘normal’ – red refers to increased asymmetry, while blue refers to decreased asymmetry.
Polymorphic delta activity (PDA) consists of arrhythmic slow waves that vary in frequency, amplitude, and morphology. PDA can occur in either a focal or generalized distribution. Continuous PDA is indicative of abnormalities involving subcortical white matter. One of the shortcomings of standard scalp EEG recordings is their limited spatial resolution. This holds true for the relationship of PDA to an underlying structural abnormality. Not only is the inherent localizing ability of the scalp EEG limited, but also the PDA of a structural lesion is referable not to the lesion itself but to the surrounding brain tissue. Because of this limitation, the area of a lesion is indicated not by the maximal amplitude of PDA but rather by a region of relatively low-amplitude slowing. Continuous, rather than intermittent, PDA is associated with large lesions, mass effect, and impairment of consciousness.

Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.

**Electroencephalographic criteria of polymorphic delta activity**

- Quite variable in wave shape morphology, frequency and amplitude.
- Commonly lateralized over a wide area of the scalp, persistent in eye closed, eye open state, during all sleep stages, with no visual reactivity. Polymorphic Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology.
- Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.
- Commonly due to a subcortical white matter lesion inducing deafferentation of the cerebral cortex.
- A purely cortical lesion does not induce polymorphic slow wave activity.

**Pathophysiology and clinical significance of polymorphic delta activity**

The diencephalon, as the pacemaker of EEG activity, sends arousal stimuli (through the thalamocortical pathways) to the cortical neurons which responds by generating the EEG waves. There are always a good degree of coherence and bilateral symmetry of the generated EEG waves because cortically neurons are paced by the subcortical pacemaker. Any subcortical destructive focal lesion (like infarction, abscess, tumors...etc.) interrupting the thalamocortical pathway will deprive the cortical neurons, in a particular cortical area, from the arousal stimuli resulting in cortical neuronal physiological dysfunctions. The neurons in that area, being deafferentated and deprived form the thalamocortical arousal stimuli, will fall out of synchrony and coherence and will start to generate waves in a chaotic pattern and at a much slower rate than normal, these waves are irregular in shape, amplitude and duration. and shows little variation with change in the physiological state of the patient. Cortical neurons, in the deafferentated cortical strip, are no longer paced (being cut from the pace maker by the subcortical destructive focal lesion) and each neuron will fire at its own rhythm resulting in polymorphic delta activity. Polymorphic delta activity is due to deafferentation of physically normal cortical neurons by a subcortical destructive focal lesion. Only subcortical white matter focal lesions can produce Polymorphic delta activity (PDA) and purely cortical lesions do not produce PDA.
• Please note

1- Cortical neurons that generate PDA are physically normal, however they are simply deafferentated, physiologically deranged and deprived from arousal stimuli.

2- PDA poorly localizes the destructive subcortical area and is generated from a much wider cortical area overlying the subcortical destructive focal lesion which is spatially much smaller than the affected cortical area that generates the PDA. The subcortical destructive focal lesions simply act by deafferentation of the cortical strip which contains the physiological deranged neurons that generate the PDA.

3- A cortical lesion that organically and physically affects cortical neurons (either a primary cortical lesion, a subcortical focal lesion extending to the cortical neurons or an extra-axial focal lesion compression or extending to the cortical neurons) does not produce PDA. Only normal, physiologically deafferentated, cortical neurons are capable of producing PDA.

The brainmap counterpart of polymorphic delta activity (PDA)

Two pattern are demonstrated by brainmapping

- Subcortical destructive lesion (infarction, brain tumors etc)

1. Theta percentage activity is focally increased, the theta focus exactly maps and matches the anatomical site of the lesion.

2. Delta percentage activity is Diffusely increased and is projected to the cortical area dysfunctioned by the subcortical destructive lesion. The delta percentage activity is seen surrounding the theta focus and mapping the deafferented cortical electrodes areas that showed PDA in conventional EEG. The delta wave projection, spatial extension, distribution, and percentage activity correlates nicely with the clinical picture and the degree of clinical disability.

3. The alpha and beta percentage activity are reduced in the affected hemisphere. Alpha is maximally reduced in the delta area while the beta percentage activity is maximally reduced in the theta focus area.

The pattern described above is aetiologically non-specific and occurs due to any destructive subcortical lesion of any aetiology.

The percentage delta activity maps the dysfunctioned cortical zone and exactly correlates with the clinical picture. The patient on the left side map presented clinically with left sided weakness and expressive aphasia due to a subcortical lacunar infarction. The delta activity is lateralized to the left frontal region in electrodes FP1, F7. The same electrodes area showed polymorphic delta activity on conventional EEG. That is to say delta activity, in this patient, is projected to the dysfunctioned cortical area and exactly correlates with the clinical picture. As is the case with polymorphic delta activity, delta activity was generated by deafferentated, physically normal cortical neurons.

In this patient theta maps showed focal increase in the percentage activity that was recorded from the cortical area that exactly overlies the deep destructive lesion. The theta focus, in this patient, showed a fairly good anatomical localization of the subcortical destructive lesion that exactly correlated with MRI study (theta band points to the site of the lesion). Probably this focal theta activity was generated by neurons in the cortical strip that directly overlies the deep lesion, these neurons are probably physically abnormal and is directly involved by the pathological process through the effect of edema or ischemia. These neurons are not deafferentated by the subcortical destructive lesions but rather they are directly affected by the pathological process. Because of their close proximity to the lesion, these neurons are probably directly implicated by the subcortical lesion by edema or ischemia.
Careful inspection of the conventional EEG data recorded at the same time from the electrodes that generated the focal theta activity by
brainmapping showed polymorphic theta activity, however this theta activity was not as disorganized as the polymorphic delta activity, although it showed variability in wave morphology, amplitude and duration. EEG wave recording from healthy, yet deafferentated cortical neurons is more likely to produce EEG activity that is much slower and more disorganized than EEG recording from diseased, yet pace-maker connected neurons.

Theta focus surrounded by diffuse delta activity from a patient presented clinically with global aphasia by a subcortical destructive lesion (infarction). The spatial extension of delta activity in this patient is more extensive compared with the above patient

Percentage alpha activity is almost invariably reduced in the affected hemisphere. The alpha activity is particularly markedly reduced at electrodes which show maximum delta activity. Alpha visual reactivity is impaired (diminished or reversed). Alpha percentage activity correlates inversely with the degree of clinical disability (The less alpha, the more of the clinical disability). Alpha percentage activity is an indicator of a more global hemispherical impairment than delta or theta activities which probably indicate a more focal or regional impairment restricted to regions of maximum theta or delta activity.

Beta percentage activity is commonly focally reduced at the electrodes which show focal theta activity. Beta activity might be increased in some patients, a pattern which probably indicates the existence of cortical irritability.

**Cortical destructive lesion**

As stated above, only subcortical destructive lesions deafferenting cortical healthy neurons are capable of producing Polymorphic delta activity. Cortical neurons that are not healthy (due to ischemia, compression, degeneration or any other pathological process) yet not deafferentated and well connected to the subcortical pace-making neurons do not produce Polymorphic delta activity.

EEG activity recorded from diseased, well afferentated cortical neurons (that are not cut from the pace-maker) are not as chaotic and as slow as EEG activity recorded from deafferentated healthy neurons. If the later is called polymorphic delta activity, the former is better called polymorphic theta activity.

Polymorphic theta activity is generated from neurons that are still paced by the subcortical pace making neurons, these cortical neurons will fire at a faster rate (theta range) and because they are still driven by the subcortical pace maker, their activity is faster, more regular and more synchronous (compared with deafferentated neurons) with less variability in shape, duration and amplitude of recorded EEG waves.

While neurons that are completely deafferentated and cut from the deep subcortical pace-making neurons will fire at their own slow rhythm (delta range) and because they are no longer driven by the subcortical pace maker, their activity are more chaotic and irregular and less synchronous with much more variability in shape, duration and amplitude of recorded EEG waves. (Polymorphic delta activity)
In general a purely cortical destructive lesion of any etiology produce increase of percentage theta activity that is not accompanied with any increase in the percentage delta activity. Alpha maps might be normal, however beta percentage activity maps might show focal increase, a pattern which probably indicates the existence of cortical irritability.

**Brainmapping & cortical and subcortical destructive lesions**

<table>
<thead>
<tr>
<th>Lesion location</th>
<th>Brainmapping characteristics</th>
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| Subcortical destructive lesion | • Theta focus pointing to the site of the lesion surrounded by diffuse increase of delta activity mapping the dysfunctioned cortical area  
• Alpha percentage activity is globally reduced at the affected cerebral hemisphere with maximum reduction at the region of maximum delta activity  
• Beta activity might be increased in some patients, a pattern which probably indicates the existence of cortical irritability. |
| Cortical destructive lesion    | • Theta focus pointing to the site of the lesion and not surrounded by diffuse delta activity. Percentage delta map are normal.  
• Alpha maps might be normal, however beta percentage activity maps might show focal increase, a pattern which probably indicates the existence of cortical irritability. |

**References**


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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
The occurrence of focal or generalized paroxysmal discharges in apparently healthy individuals is a puzzling and even annoying finding which requires some discussion. These findings may be quickly termed as false positives, but the EEG abnormalities are real and their irrelevance in view of the individual's good health is more apparent than real. Such spikes give testimony of certain cerebral dysfunctions which may or may not become manifest in the further course of events. These findings do not discredit the method of electroencephalography, which, after artifacts are ruled out, can only show facts. These disturbing facts are in need of a reasonable interpretation. Let us contemplate the indubitable fact that a complete medical evaluation will yield certain physical shortcomings and organic abnormalities in practically every healthy individual; even acne pimples are cutaneous lesions and hence abnormalities. What the electroencephalographer needs in such cases is a common sense philosophy as a basis for a wise interpretation. General medicine is full of examples of seemingly irrelevant and yet unmistakably present abnormalities which the prudent, seasoned physician will integrate into a holistic view of the individual. Seen from this angle, electroencephalography does not differ from the rest of medicine.

The EEG evaluation of comparatively large healthy populations usually shows a certain percentage of abnormalities such as spike, sharp wave or paroxysmal discharge. One should thoughtfully contemplated the clinical significance of spikes in healthy persons. Above all, the interpretation must take into consideration age. In childhood, the occurrence of central-midtemporal (also parietal) spikes is associated with overt seizures in only 50-70% of the cases; this pertains mainly to the age from 3-12 yr. In occipital spikes (mainly age 3-5 yr), the epileptogenicity is even lower. In general, "benign" focal spikes (such as seen in benign Rolandic epilepsy) is seen, in healthy individual, much more often than generalized synchronous bursts of spikes or spike waves. In most children, the abnormalities disappear on follow up EEG studies and the minority develop overt clinical symptomatology.

Both generalized synchronous (spike wave, polyspike wave) and Rolandic (centroparieto-midtemporal) spikes in nonepileptic children suggest a genetic predisposition if no neurological deficit and no history of insult to the CNS are present. In children with a history of cerebral palsy and with no seizures but prominent spiking, the spike activity may herald future epileptic seizures. Even in perfectly healthy children with spikes, the possibility of future seizures cannot be completely ruled out, although the chances are slim.

In healthy children and especially in healthy adults with spikes, stress must be laid on certain personality disorders which are not incompatible with normal functioning. Psychological and mild psychiatric deviations include poor impulse control, proneness to hysterical conversion reactions, and schizoid manifestations. In such individuals, the presence of a cerebral dysfunction with paroxysmal EEG changes may hamper the natural process of psychological maturation. In some of these cases, head injuries or infections of moderate severity might have prompted or facilitated the EEG changes as well as the psychological deviations.

The high incidence of anterior temporal-midtemporal sharp transients in older patients with no clinical epileptic fits has no significance. These patients may even have overt sharp waves; others show small sharp spikes. Unless there is evidence of epileptic seizures, these discharges only indicate some degree of temporal lobe dysfunction, often compatible with good health.

This section must be capped by a strong plea to refrain from rash and ill-advised statements that a seizure-free person has epilepsy and must be treated because of spikes in the EEG. These persons need further medical attention and repeat EEG should be done at reasonable intervals, such as every 2 yr in a child or adolescent and every 5 yr in an adult. Anticonvulsive treatment is not needed, but should not necessarily be denied to extremely apprehensive, introspective, and hypochondria-prone individuals.
Rhythmic delta activity consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized. In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies. FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy. In cases of encephalopathy with FIRDA, the pathophysiologic processes are believed to involve cortical and subcortical gray matter. OIRDA is associated with absence epilepsy in children aged 6-10 years.

Intermittent rhythmic delta activity (IRDA) usually occurs at frequencies of 2-2.5 Hz with relatively sinusoidal, stereotypic, bilaterally synchronous waveforms appearing in short bursts. The ascending phase is sloped more steeply than the descent, and waves are typically bilateral and widespread with peak amplitude frontally in older individuals (FIRDA) and occipitally in children (OIRDA). These patterns attenuate with alerting or eye opening. Eye closure, drowsiness, and hyperventilation accentuate IRDA. Although IRDA disappears in stage 2 and deeper non–rapid eye movement (REM) sleep, it may reappear in REM sleep.

Multiple etiologies can result in IRDA, including metabolic, toxic, hypoxic, or various diffuse or focal intracranial diseases. Even when IRDA occurs unilaterally in association with a focal cerebral lesion, the lateralization of IRDA may be ipsilateral or contralateral to the lesion. Thus IRDA is a nonspecific nonlocalizing EEG pattern, unless associated with other focal findings on the EEG. Although the mechanisms for production of IRDA are understood incompletely, studies correlating with pathologic specimens suggest that IRDA is associated primarily with diffuse gray matter disease.

The degree of encephalopathy manifested appears to correspond to the proportion of IRDA on the EEG. This pattern must be distinguished from the frequently encountered frontally maximal intermittent delta that can be seen in drowsy elderly patients.

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
- In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]).
- The intermittent rhythmic delta activity shows visual reactivity and is commonly suppressed in the eye open state unless the patient is comatose.
- Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies.
- FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy.
- OIRDA is associated with absence epilepsy in children aged 6-10 years.

Figure 2. The intermittent rhythmic delta activity [left image] and the polymorphic slow wave activity [right image]
In summary, OIRDA is found almost exclusively in children. This finding is probably epileptiform in nature. However, this pattern does not appear to be pathognomonic of epilepsy, and it may be occasionally encountered in encephalopathic patients. Previous studies have found that most children whose EEGs depicted OIRDA had primary generalized epilepsy. However, the author detected a higher proportion of cases with localization-related epilepsy. Furthermore, the frequency of the OIRDA discharge appears to be higher when it occurs in association with absence epilepsy, and these cases are more likely to depict epileptiform activity intermixed with the rhythmic delta pattern than are cases of focal epilepsy.

Frontal intermittent rhythmic delta activity is rare in children, is not associated with acute encephalopathy or with deep midline or infratentorial lesions, and tends to occur during wakefulness. The electrographic characteristics of frontal intermittent rhythmic delta activity appear to differ between cognitively normal and mentally retarded children.

Encephalopathy and coma result from conditions that affect both cerebral hemispheres or the reticular activating system in the midbrain. The differential diagnosis is broad, including metabolic, toxic, anoxic/ischemic, infectious, endocrinologic, degenerative, and inflammatory processes. These processes affect the brain diffusely, and, consequently, changes in the EEG often appear generalized. While most EEG findings in encephalopathy and coma are nonspecific with regard to etiology, information relevant to the clinical course and prognosis can be obtained using the EEG.

In cases of mild encephalopathy, theta and delta activity is intermixed with the background alpha rhythm. Occasional generalized delta transients are also seen. As the encephalopathy worsens, there is loss of background alpha-range frequencies and an increased amount of generalized theta and delta activity. Intermittent-rhythm delta activity (IRDA) may appear, which in adults generally is frontally predominant (FIRDA), and is consistent with moderate diffuse bihemispheric cerebral dysfunction. In severe encephalopathy, there is generalized delta activity. Loss of reactivity in anyone of these stages implies greater severity, and, in specific clinical settings, a worse prognosis. In the clinical setting of severe anoxia (e.g., after cardiac arrest) or severe closed head injury, invariant patterns of persistent, generalized alpha activity (alpha coma), generalized periodic epileptiform discharges, or the burst suppression pattern are associated with very poor outcome.

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**Figure 3.** Frontal intermittent rhythmic delta activity (FIRDA)

**The brainmap counterpart of intermittent rhythmic slow wave activity**

1. Intermittent rhythmic slow wave activity is seen in diffuse encephalopathic process (except hepatic encephalopathy which has a different brainmap spectral profile as will be explained in a different issue) and in middle line thalamic, or huge parasellar or infratentorial tumors. It was also seen by the author in vertebro-basilar insufficiency and migraine.

2. There is reduction of alpha percentage activity, and reduced or reversed alpha visual reactivity. The degree of reduction of alpha percentage activity correlates with prognosis. The alpha topography is normal and retains its middle line topography with posterior maximum and is more reduced anteriorly than posteriorly. There is a fairly good degree of symmetry, synchrony and coherence in alpha percentage activity maps. However it is not very infrequent to see some degree of asymmetry with more alpha percentage activity seen on one side than the other.

3. The alpha land (the middle line electrodes) is now occupied by theta and delta percentage activity, which is now maximum in the middle line electrodes at F3,F4,O2,O1. The maximum middle line percentage activity is now shifted down to the theta rage in most
patients and occasionally to the delta rage depending on the severity of the encephalopathic process and the state of the patient. Combined theta and delta percentage activity maps clearly demonstrates the midline maximum. The topography of theta percentage activity is identical to that of normal alpha percentage activity maps in the eye closed state. Slow wave activity commonly show visual reactivity exactly as alpha percentage activity behaves under normal physiological conditions.

4- There is a fairly good degree of symmetry, synchrony and coherence in theta percentage activity. However it is not very infrequent to see some degree of asymmetry with more theta percentage activity seen on one side than the other.

5- Beta percentage activity is reduced in the midline frontal, central/parietal and occipital electrodes.

Because the intermittent rhythmic slow wave activity occupies the same electrode regions that are normally occupied by the alpha activity, so it looks like that both (the intermittent rhythmic slow wave activity and alpha spindles) share a common generator. Similarities between both activities are:

- Both are sinusoidal activity that waxes and wanes (intermittent)
- Both show visual reactivity
- Both are maximum in the middle line electrodes

So it looks like that the generator that is responsible for the generation of the intermittent rhythmic slow wave activity is the same generator that is responsible for the generation of alpha spindles under normal conditions, however in the former condition the generator (the pace-maker) is diseased and firing at a lower rate.

A dysfunctioned pacemaker (subcortical gray matter, diencephalon) is probably necessary for the intermittent slow wave activity to be seen on EEG.

Arousal stimuli in the thalamo-cortical circuitry are responsible for the production of alpha spindles under normal physiological conditions. However when a diffuse encephalopathic process involves the diencephalic neurons bilaterally, the dysfunctioned diencephalic neurons fire at a slower rate and instead of producing alpha spindles they produce theta or delta spindles that retain the same characteristics of alpha spindles in spatial topography and visual reactivity.

In intermittent rhythmic slow wave activity cortical gray matter is not necessarily abnormal as this phenomenon is also observed in middle line tumors (thalamic) and some extra-axial tumors in the parasellar and infratentorial regions. A dysfunctioned subcortical gray matter affecting the diencephalic pace-making neurons is necessary for the generation of intermittent rhythmic slow wave activity. The diencephalic pace-making neurons are necessary for the genesis of alpha spindles under normal physiological conditions.

In intermittent rhythmic slow wave activity there is a down-shift of the predominant middle line activity (the alpha band) from the alpha range to lower frequencies in the theta and delta ranges. In the author experience the predominant middle line activity is down-shifted to the theta range more often than the delta range. The condition is better termed intermittent rhythmic theta activity rather than intermittent rhythmic delta activity, although the later is more commonly used. In intermittent rhythmic slow wave activity brainmapping has apparently shown that predominant middle line activity is more often down-shifted to the theta range rather than the delta range.

**Figure 4.** Two studies showing the brainmap counterpart of intermittent rhythmic slow wave activity. Notice the bilateral symmetrical theta activity occupying the same topography of the alpha activity with middle maximum. Some degree of visual reactivity is observed in the lower study. Some degree of asymmetry is observed in the lower maps.

**Figure 5.** The brainmap counterpart of intermittent rhythmic slow wave activity. Notice the Bifrontal middle line theta maximum with reduced alpha and beta activity. Maximum theta activity is seen at F3,F4,FZ electrodes.
Intermittent rhythmic slow wave activity is simply a condition where the predominant middle line activity is down-shifted from the alpha range to the theta range with maximum activity at F3, F4, FZ, O1,O2 electrode regions. During intermittent rhythmic slow wave activity the alpha spindle (as the dominant EEG activity in middle line electrodes) is replaced by slow wave spindles (mostly in the theta range rather than the delta range) which now dominate EEG activity in the middle line electrode regions.

- In frontal intermittent rhythmic delta activity (FIRDA) the maximum slow wave activity is recorded at F3, F4, FZ electrode regions by brainmapping. This pattern is more commonly seen in adult and it reflects a diffuse encephalopathic process, it is also seen in middle line tumors, parasellar and infratentorial tumors, vertebro-basilar insufficiency and migraine.

- In occipital intermittent rhythmic delta activity (ORDA) the maximum slow wave activity is recorded at O1,O2 electrode regions by brainmapping. OIRDA is found almost exclusively in children. This pattern is probably epileptiform in nature. However, this pattern does not appear to be pathognomonic of epilepsy. The 3 c/s spike/wave discharge of absence attacks is occasionally preceded by OIRDA.

- Whether OIRDA or FIRDA, the discharge is maximum in the middle line electrodes at F3, F4, FZ, C3, C4, CZ, P3, P4, PZ, O1,O2 and it replaces the alpha activity that normally reigns in these territories. The alpha activity is longer the prevalent activity at the middle line electrodes regions during intermittent rhythmic slow wave activity. Alpha activity is normally prevalent at O1,O2 and F3,F4,FZ electrode regions as well as the intermittent rhythmic slow wave activity which takes the upper hand in middle line electrodes and becomes the prevalent activity when they occur, they also retain the same characteristics of alpha spindles in spatial topography and visual reactivity.

- There is a fairly good degree of symmetry, synchrony and coherence in theta or delta percentage activity maps (during intermittent rhythmic slow wave activity). However it is not very infrequent to see some degree of asymmetry and lateralization with more theta or delta percentage activity seen on one side than the other.
Figure 7. The brainmap counterpart of intermittent rhythmic slow wave activity. Notice the Bifrontal middle line theta maximum with reduced alpha and beta activity. Maximum theta activity is seen at F3,F4,FZ electrodes.

References


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There is now considerable evidence from studies in experimental animals to suggest that the rhythmic activity normally recorded from the scalp has a cortical origin, being derived from the postsynaptic potentials of cortical neurons. In particular, it is the pyramidal neurons—cells that are vertically oriented with regard to the cortex and have a large apical dendrite extending toward the surface—that are important in this respect, while potentials arising from neuronal activity in subcortical structures or from horizontally oriented conical cells contribute little, if anything, to the normal, scalp-recorded EEG.

The cortical activity has a regular rhythmicity which seems to depend on the functional integrity of subcortical mechanisms. In the cat, for example, rhythmic cortical activity persists after the brainstem has been sectioned between, or just above, the colliculi, but is much reduced when the cortex is isolated by cutting its connections to other parts of the brain. The results of other lesion experiments suggest that it is the thalamus which serves as pacemaker of certain cortical rhythms that are recorded at electroencephalography. The midline nuclei of the thalamus were important in this respect, and this concept was subsequently modified and the activity from these nuclei relayed in various other intrathalamic nuclei before being projected to the cortex (Fig. 1).

This has led to the so-called facultative pacemaker theory in which thalamic rhythmicity is related to a recurrent inhibitory process, as shown in Fig. 2. Postsynaptic inhibitory potentials have a synchronizing effect on the activity of thalamic cells, thereby leading to the generation of a series of excitatory waves and governing the interval between successive waves. Rhythmic activity can arise in any or all of the thalamic nuclei, can spread from one nucleus to another, and is imposed on the cortex via the thalamocortical projections (Fig. 3).

Figure 1. The midline pacemaker theory. Rhythmic activity is imposed upon widespread cortical areas via a multineuronal system, including the intralaminar nuclei, the anterior thalamic nucleus (VA), and the thalamic reticular nucleus (Ret). (A) Association, (M) medial thalamic nuclei. The cortical projection from the relay nuclei (R) is separate from the rhythm-inducing system.

Figure 2. Schematic representation of the proposed inherent mechanism giving rhythmic discharges of thalamic neurons. (A) a discharge of the cell (hatched) causes recurrent inhibition via an interneuron (black) that hyperpolarizes many neighboring projection cells. During the postinhibitory rebound, many of these cells discharge action potentials and an increasing number of cells participate during the successive cycles (A, lower part). Alternatively, intrathalamic connections via distributor neurons (B) spread the rhythmic activity from one group to other parts of the thalamus (from-left-to-right group).
Alpha Rhythm

Alpha rhythm has a frequency of between 8 and 13 Hz, is found posterior portions of the head during wakefulness, and is best seen when the patient is resting with eyes closed. It is attenuated or abolished by visual attention, and transiently by other sensory stimuli. Alpha activity is well-formed and prominent in some normal subjects, while in others it is relatively inconspicuous. Its precise frequency is usually of little diagnostic significance, unless information is available about its frequency on earlier occasions.

Slowing occurs with advancing age, as a consequence of certain medication such as anticonvulsant drugs, and in patients with clouding of consciousness, metabolic disorders, or virtually any type of cerebral pathology. The alpha activity may increase in frequency in children as they mature, and in older subjects who are thyrotoxic. A slight asymmetry is often present between the two hemispheres with regard to the amplitude of alpha activity and the degree to which it extends anteriorly. In particular, alpha rhythm may normally be up to 50 percent greater in amplitude over the non-dominant hemisphere. A more marked asymmetry of its amplitude may have lateralizing significance but is difficult to interpret unless other EEG abnormalities are present, because either depression or enhancement may occur on the side of a hemisphere lesion. Similarly, a persistent difference in alpha frequency of more than 1 Hz between the two hemispheres is generally regarded as abnormal, but it is usually difficult to be certain which is the abnormal side unless other abnormalities are also found.

Beta Activity

EEG CHANGES DUE TO A PURELY CORTICAL LESION NOT INVOLVING SUBCORTICAL WHITE MATTER

A purely cortical lesion can be due to extraaxial tumors like meningiomas, cortical atrophy and others. In this situation cortical neurons are unhealthy, diseased (by edema, compression of ischemia...etc.) yet not deafferentated from the subcortical pace-maker.

EEG activity recorded from diseased, well afferentated cortical neurons (that are not cut from the pace-maker) are not as chaotic and as slow as EEG activity recorded from deafferentated healthy neurons. If the later is called polymorphic delta activity, the former is better called polymorphic theta activity.

Polymorphic theta activity is generated from neurons that are still paced by the subcortical pace making neurons, these cortical neurons will fire at a faster rate (theta range) compared with completely deafferentated neurons and because they are still driven by the subcortical pace maker, their activity is faster, more regular and more synchronous (compared with deafferentated neurons) with less variability in shape, duration and amplitude of recorded EEG waves. While neurons that are completely deafferentated and cut from the deep
subcortical pace-making neurons will fire at their own slow rhythm (delta range) and because they are no longer driven by the subcortical pace maker, their activities is more chaotic, irregular and less synchronous with much more variability in shape, duration and amplitude of recorded EEG waves. (Polymorphic delta activity).

Unhealthy, diseased cortical neurons, that are uncut from the incoming arousal stimuli but still viable, will not respond to the incoming arousal stimuli by degenerating alpha spindles (which is the normal situation), but rather their response will be down-shifted to the theta range (Polymorphic theta activity). The generated theta waves will not be as organized as the alpha spindles but, at the same time, will not be a chaotic, irregular and variable as the polymorphic delta activity that are generated by deafferentated neurons.

Polymorphic theta activity maps exactly the diseased neurons and points to the anatomical site of the lesion (picked up from electrodes that overly the lesion), this is in contrast to polymorphic delta activity which is projected to a much wider cortical area and has no localizing significance in so far as the anatomical site of the lesion is concerned. However it should be mentioned that the theta focus is totally non-specific and tells us noting about the nature of the cortical pathology.

In general a purely cortical destructive lesion of any etiology produces focal increase of percentage theta activity (that is lateralised to the anatomical site of the destructive lesion and exactly maps it). The theta focus is not accompanied with any increase in the percentage delta activity. Alpha maps might be normal or might show occipital reduction of the percentage Alpha activity ipsilateral to the cortical destructive lesion. Beta percentage activity maps might show a focal increase (that is lateralised to the anatomical site of the cortical lesion and might be present in the same electrodes that show the theta focus). The beta focus (when present) probably indicates the existence of cortical irritability.

Polymorphic delta activity (PDA) consists of arrhythmic slow waves that vary in frequency, amplitude, and morphology. PDA can occur in either a focal or generalized distribution. Continuous PDA is indicative of abnormalities involving subcortical white matter. One of the shortcomings of standard scalp EEG recordings is their limited spatial resolution. This holds true for the relationship of PDA to an underlying structural abnormality. Not only is the inherent localizing ability of the scalp EEG limited, but also the PDA of a structural lesion is referable not to the lesion itself but to the surrounding brain tissue. Because of this limitation, the area of a lesion is indicated not by the maximal amplitude of PDA but rather by a region of relatively low-amplitude slowing. Continuous, rather than intermittent, PDA is associated with large lesions, mass effect, and impairment of consciousness.

Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (white matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.

Pathophysiology and clinical significance of polymorphic delta activity

The diencephalon, as the pacemaker of EEG activity, sends arousal stimuli (through the thalamocortical pathways) to the cortical neurons which respond by generating the EEG waves. There are always a good degree of coherence and bilateral symmetry of the generated EEG waves because cortically neurons are paced by the subcortical pacemaker. Any subcortical destructive focal lesion (like infarction, abscess, tumors...etc.) interrupting the thalamocortical pathway will deprive the cortical neurons, in a particular cortical area, from the arousal stimuli resulting in cortical neuronal physiological dysfunctions. The neurons in that area, being deafferentated and deprived form the thalamocortical
arousal stimuli, will fall out of synchrony and coherence and will start to
generate waves in a chaotic pattern and at a much slower rate than
normal, these waves are irregular in shape, amplitude and duration, and
shows little variation with change in the physiological state of the
patient. Cortical neurons, in the deafferentated cortical strip, are no
longer paced (being cut from the pace maker by the subcortical
destructive focal lesion) and each neuron will fire at its own rhythm
resulting in polymorphic delta activity. Polymorphic delta activity is due
to deafferentation of physically normal cortical neurons by a subcortical
destructive white matter focal lesion. Only subcortical white matter focal
lesions can produce Polymorphic delta activity (PDA) and purely
cortical lesions do not produce PDA.

- **Please note**

1- Cortical neurons that generate PDA are physically normal, however
they are simply deafferentated, physiologically deranged and deprived
from arousal stimuli.

2- PDA poorly localizes the destructive subcortical area and is generated from a much wider cortical area overlying the subcortical destructive
focal lesion which is spatially much smaller than the affected cortical area that generates the PDA. The subcortical destructive focal lesions
simply act by deafferentation of the cortical strip which contains the physiological deranged neurons that generate the PDA.

3- A cortical lesion that organically and physically affects cortical neurons (either a primary cortical lesion, a subcortical focal lesion extending
to the cortical neurons or an extra-axial focal lesion compression or extending to the cortical neurons) does not produce PDA. Only normal,
physiological deafferentated, cortical neurons are capable of producing PDA.

**Brainmapping Correlates of PDA**

1. Theta percentage activity is focally increased, the
theta focus exactly maps and matches the
anatomical site of the lesion.

2. Delta percentage activity is Diffusely increased
and is projected to the cortical area dysfunctioned
by the subcortical destructive lesion. The delta
percentage activity is seen surrounding the theta
focus and mapping the deafferentated cortical electrodes areas that showed PDA in conventional EEG. The delta wave projection, spatial
extension, distribution, and percentage activity correlates nicely with the clinical picture and the degree of clinical disability.

3. The alpha and beta percentage activity are reduced in the affected hemisphere. Alpha is maximally reduced in the delta area while the beta
percentage activity is maximally reduced in the theta focus area.

The pattern described above is aetiology non-specific and occurs due to any destructive subcortical lesion of any aetiology.

The percentage delta activity maps the dysfunctioned cortical zone and exactly correlates with the clinical picture. The patient in figure 8 map
presented clinically with left sided weakness and expressive aphasia due to a subcortical lacunar infarction. The delta activity is lateralized to the
left frontal region in electrodes FP1, F7. The same electrodes area showed polymorphic delta activity on conventional EEG. That is to say delta
activity, in this patient, is projected to the dysfunctioned cortical area and exactly correlates with the clinical picture. As is the case with
polymorphic delta activity, delta activity was generated by deafferentated, physically normal cortical neurons.

In this patient theta maps showed focal increase in the percentage activity that was recorded from the cortical area that exactly overlies the deep
destructive lesion. The theta focus, in this patient, showed a fairly good anatomical localization of the subcortical destructive lesion that exactly
correlated with MRI study (**theta band points to the site of the lesion**). Probably this focal theta activity was generated by neurons in the cortical
条直接覆盖了深部病变，这些神经元可能是物理上异常的，并且直接参与病理过程，通过水肿或缺血。这些神经元没有因亚皮质破坏性病变脱失，而是直接受到病变的影响。由于他们与病变的近距离，这些神经元可能直接由亚皮质病变引起水肿或缺血。

仔细检查同一时间用脑电图数据记录生成的聚焦慢波活动的常规脑电图数据，显示了多形慢波活动，然而这种慢波活动不如多形δ波活动混乱，虽然它显示了波形变化、幅度和持续时间的变异性。从健康的、没有失去传出联系的皮质神经元记录的脑电图活动，更可能产生比病变，由起搏器连接的神经元记录的脑电图活动更慢、更混乱的脑电图活动。

受累半球的α波活动几乎总是减少的。α波活动的减少特别显著在显示出最大δ波活动的电极上。α视觉反应性受损（减小或反转）。α百分比活动与临床残疾的程度成反比关系（α越少，临床残疾越多）。α百分比活动是比δ波或θ波活动更广泛大脑半球损伤的指标，而δ波和θ波活动可能表示被θ波活动活动的区域的更集中的、区域的损伤。

β百分比活动在产生θ波活动的电极上通常显著降低。β活动在一些病人中可能增加，这可能表示皮质敏感度的增加。

Subcortical diencephalic lesion

Subcortical gray matter lesions: Intermittent rhythmic slow wave activity

亚皮质灰质病变：不规则的慢波活动

亚皮质灰质病变涉及的EEG起搏器产生不规则的δ波活动，该活动有以下特征：

- 由约2.5 Hz的正弦波形组成，它们在EEG记录中呈间歇性出现。它通常对称，但可以侧化。
- 在成人中，δ波活动有一个额部优势（额部不规则的慢波活动[FIRDA]）。在儿童中，它是最大后部（枕部不规则的慢波活动[OIRDA]）。
- 不规则的慢波活动表现出视觉反应性，并且在睁眼状态下通常被抑制，除非患者处于昏迷状态。
- 不规则的慢波活动与结构病变有关，最常见的是下丘脑、下部脑室或下部脑室病变，或与弥漫性脑病有关。
- FIRDA发生在正常EEG背景的患者中，该模式是由于结构病变引起的；当与EEG背景异常相关时，它更可能由脑病引起。
- OIRDA与6-10岁的儿童的失神癫痫有关。

图8. 用脑电图研究的患者与左侧深部前额叶-枕叶梗死并产生右侧偏瘫和表达性失语症。注意θ波焦点被由功能失调区域投射的差分δ波活动包围。

图9. 不规则的慢波活动

Subcortical diencephalic lesion

Subcortical gray matter lesions: Intermittent rhythmic slow wave activity
1- Intermittent rhythmic slow wave activity is seen in diffuse encephalopathic process (except hepatic encephalopathy which has a different brainmap spectral profile as will be explained in a different issue) and in middle line thalamic, or huge parasellar or infratentorial tumors. It was also seen by the author in vertebro-basilar insufficiency and migraine.

2- There is reduction of alpha percentage activity, and reduced or reversed alpha visual reactivity. The degree of reduction of alpha percentage activity correlates with prognosis. The alpha topography is normal and retains its middle line topography with posterior maximum and is more reduced anteriorly than posteriorly. There is a fairly good degree of symmetry, synchrony and coherence in alpha percentage activity maps. However it is not very infrequent to see some degree of asymmetry with more alpha percentage activity seen on one side than the other.

3- The alpha land (the middle line electrodes) is now occupied by theta and delta percentage activity, which is now maximum in the middle line electrodes at F3,F4,O2,O1. The maximum middle line percentage activity is now shifted down to the theta rage in most patients and occasionally to the delta rage depending on the severity of the encephalopathic process and the state of the patient. Combined theta and delta percentage activity maps clearly demonstrates the midline maximum. The topography of theta percentage activity is identical to that of normal alpha percentage activity maps in the eye closed state. Slow wave activity commonly show visual reactivity exactly as alpha percentage activity behaves under normal physiological conditions.

4- There is a fairly good degree of symmetry, synchrony and coherence in theta percentage activity. However it is not very infrequent to see some degree of asymmetry with more theta percentage activity seen on one side than the other.

5- Beta percentage activity is reduced in the midline frontal, central/parietal and occipital electrodes.

Because the intermittent rhythmic slow wave activity occupies the same electrode regions that are normally occupied by the alpha activity, so it looks like that both (the intermittent rhythmic slow wave activity and alpha spindles) share a common generator. Similarities between both activities are:

1. Both are sinusoidal activity that waxes and wanes (intermittent)
2. Both show visual reactivity
4. Both are maximum in the middle line electrodes

So it looks like that the generator that is responsible for the generation of the intermittent rhythmic slow wave activity is the same generator that is responsible for the generation of alpha spindles under normal conditions, however in the former condition the generator (the pace-maker) is diseased and firing at a lower rate.

A dysfunctioned pacemaker (subcortical gray matter, diencephalon) is probably necessary for the intermittent slow wave activity to be seen on EEG.

Arousal stimuli in the thalamo-cortical circuitry are responsible for the production of alpha spindles under normal physiological conditions. However when a diffuse encephalopathic process involves the diencephalic neurons bilaterally, the dysfunctioned diencephalic neurons fire at a slower rate and instead of producing alpha spindles they produce theta or delta spindles that retain the same characteristics of alpha spindles in spatial topography and visual reactivity.
Intermittent rhythmic slow wave activity cortical gray matter is not necessarily abnormal as this phenomenon is also observed in middle line tumors (thalamic) and some extra-axial tumors in the parasellar and infratentorial regions. A dysfunctioned subcortical gray matter affecting the diencephalic pace-making neurons is necessary for the generation of intermittent rhythmic slow wave activity. The diencephalic pace-making neurons are necessary for the genesis of alpha spindles under normal physiological conditions.

In intermittent rhythmic slow wave activity there is a down-shift of the predominant middle line activity (the alpha land) from the alpha range to lower frequencies in the theta and delta ranges. In the author experience the predominant middle line activity is down-shifted to the theta range more often than the delta range. The condition is better termed intermittent rhythmic theta activity rather than intermittent rhythmic delta activity, although the later is more commonly used. In intermittent rhythmic slow wave activity brainmapping has apparently shown that predominant middle line activity is more often down-shifted to the theta range rather than the delta range.

Because the intermittent rhythmic slow wave activity occupies the same electrode regions that are normally occupied by the alpha activity, so it looks like that both (the intermittent rhythmic slow wave activity and alpha spindles) share a common generator.

The generator (The pace maker) that is responsible for the generation of the intermittent rhythmic slow wave activity is the same generator which is responsible for the generation of alpha spindles under normal conditions, however in the former condition the generator (the pace-maker) is diseased and firing at a lower rate.

In summary, although the condition is frequently termed frontal intermittent rhythmic delta activity (FIRDA) or occipital intermittent rhythmic delta activity (ORDA) in conventional EEG, However by using the brainmap technology The following are shown:

- Intermittent rhythmic slow wave activity is simply a condition where the predominant middle line activity is down-shifted from the alpha range to the theta range with maximum activity at F3, F4, FZ, O1,O2 electrode regions. During intermittent rhythmic slow wave activity the alpha spindle (as the dominant EEG activity in middle line electrodes) is replaced by slow wave spindles (mostly in the theta range rather than the delta range) which now dominate EEG activity in the middle line electrode regions.

- In frontal intermittent rhythmic delta activity (FIRDA) the maximum slow wave activity is recorded at F3, F4, FZ electrode regions by brainmapping. This pattern is more commonly seen in adult and it reflects a diffuse encephalopathic process, it is also seen in middle line tumors, parasellar and infratentorial tumors, vertebro-basilar insufficiency and migraine.

- In occipital intermittent rhythmic delta activity (ORDA) the maximum slow wave activity is recorded at O1,O2 electrode regions by brainmapping. OIRDA is found almost exclusively in children. This pattern is probably epileptiform in nature. However, this pattern does not appear to be pathognomonic of epilepsy. The 3 c/s spike/wave discharge of absence attacks is occasionally proceeded by OIRDA.

- Whether OIRDA or FIRDA, the discharge is maximum in the middle line electrodes at F3, F4, FZ, C3, C4, CZ, P3, P4, PZ, O1,O2 and it replaces the alpha activity that normally reigns in these territories. The alpha activity is longer the prevalent activity at the middle line electrodes regions during intermittent rhythmic slow wave activity. Alpha activity is normally prevalent at O1,O2 and F3,F4,FZ electrode regions as well as the intermittent rhythmic slow wave activity which takes the upper hand in middle line electrodes and becomes the prevalent activity when they occur, they also retain the same characteristics of alpha spindles in spatial topography and visual reactivity.

- There is a fairly good degree of symmetry, synchrony and coherence in theta or delta percentage activity maps (during intermittent rhythmic slow wave activity). However it is not very infrequent to see some degree of asymmetry and lateralization with more theta or delta percentage activity seen on one side than the other.

References

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.

The best-defined idiopathic partial epilepsy is benign rolandic epilepsy. The classic EEG finding in this childhood seizure disorder is a characteristic monomorphic centrotemporal sharp wave. The sharp waves are often seen independently in the centrotemporal 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
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 are also 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. Electrocerbral 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.
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**


INTRODUCTION.....TALKING "NORMAL EEG"

Despite advances in neuroimaging techniques over the past three decades that have helped in identifying structural lesions of the central nervous system, electroencephalography (EEG) continues to provide valuable insight into brain function by demonstrating focal or diffuse background abnormalities and epileptiform abnormalities. It is an extremely valuable test in patients suspected of epilepsy and in patients with altered mental status and coma. Patterns in the EEG make it possible to clarify the seizure type; it is indispensable for the diagnosis of nonconvulsive status epilepticus and for separating epileptic from other paroxysmal (nonepileptic) episodes. There are EEG patterns predictive of the cause of the encephalopathy (i.e., triphasic waves in metabolic encephalopathy) or the location of the lesion (i.e., focal polymorphic delta activity in lesions of the subcortical white matter). The various EEG characteristics of infantile, childhood, and adult epilepsies are described as well as the EEG patterns that are morphologically similar to interictal/ictal epileptiform discharges but unrelated to epilepsy. An EEG is most helpful in determining the severity and, hence, the prognosis of cerebral dysfunction. Lastly, EEG is extremely helpful in assessing normal or abnormal brain functioning in a newborn because of the serious limitation in performing an adequate neurologic examination on the neonate who is intubated or paralyzed for ventilatory control. Under such circumstances, the EEG may be the only available tool to detect an encephalopathic process or the occurrence of epileptic seizures.

Electroencephalography (EEG) is the technique of recording from the scalp the spontaneous electrical activity of the brain and correlating it to the underlying brain function. Since the first recording of a human EEG in 1929 by Hans Berger, improvement in electronics and technology has made EEG one of the most widely used laboratory tests for clinical evaluation of neurologic disorders. However, in the past three decades with continuing advances in neuroimaging, particularly magnetic resonance imaging (MRI), the role of clinical EEG has become restricted and progressively more focused. Its major utility at present is in the evaluation of focal and diffuse encephalopathies, comatose conditions, epileptic disorders, and cerebral disorders affecting neonates and infants. The present article is not an attempt to describe EEG comprehensively in normal subjects and in different disease processes but to highlight its usefulness/limitation and emphasize precautions/care needed in its optimal utility. The subject will be discussed under seven sections: EEG in normal subjects, EEG in patients with altered mental status or diffuse abnormalities and epileptiform abnormalities. It is an extremely valuable test in patients suspected of epilepsy and in patients with altered mental status and coma. Patterns in the EEG make it possible to clarify the seizure type; it is indispensable for the diagnosis of nonconvulsive status epilepticus and for separating epileptic from other paroxysmal (nonepileptic) episodes. There are EEG patterns predictive of the cause of the encephalopathy (i.e., triphasic waves in metabolic encephalopathy) or the location of the lesion (i.e., focal polymorphic delta activity in lesions of the subcortical white matter). The various EEG characteristics of infantile, childhood, and adult epilepsies are described as well as the EEG patterns that are morphologically similar to interictal/ictal epileptiform discharges but unrelated to epilepsy. An EEG is most helpful in determining the severity and, hence, the prognosis of cerebral dysfunction. Lastly, EEG is extremely helpful in assessing normal or abnormal brain functioning in a newborn because of the serious limitation in performing an adequate neurologic examination on the neonate who is intubated or paralyzed for ventilatory control. Under such circumstances, the EEG may be the only available tool to detect an encephalopathic process or the occurrence of epileptic seizures.

EEG In Normal Subjects

- The EEG in the normal awake child and adult is well known and needs no detailed description. The following are points of emphasis:
  - Alpha rhythm in the two hemispheres is very similar in frequency. A consistent difference of even 0.5 to 1.0 cps on the two sides is significant; the side showing a slower frequency may have a hemispheric dysfunction. Amplitude asymmetry is of relatively less significance, unless the asymmetry is prominent. In general, the alpha rhythm is higher in amplitude over the right hemisphere. If the amplitude of the alpha rhythm on the right side is more than 1 1/2 times that on the left side, the asymmetry is usually regarded as significant. When the alpha rhythm is over 25% higher in amplitude on the left side than the right side, this constitutes a significant asymmetry.[1]
  - Significant theta activity (4 to 7 Hz) is present in the EEG of children and adolescents. Delta activity in the awake tracing is rarely seen after the age of 5 years. A common EEG pattern in adolescents is the presence of intermittent delta waves intermixed with alpha rhythm over the posterior head regions, the so-called "slow waves of youth."
  - The EEG during non-rapid eye movement (NREM) sleep in children shows very prominent spikelike vertex sharp transients, which are often mistaken for epileptiform activity by EEG interpreters inexperienced with children's EEGs. Similarly, positive occipital sharp transients (POSTs), when high in amplitude and sharp in configuration, can be easily misinterpreted as abnormal spikes, especially in linkages where occipital electrodes are connected to input terminal 2 (grid 2) of the amplifier (e.g., "double banana run").
  - In a small proportion of normal adult subjects, clearly identifiable and countable alpha rhythm may be entirely absent. The background may consist of irregular mixtures of low amplitude (<20 µV) activities, mostly from 5.0 to 30.0 cps without a dominant frequency. Such low-voltage EEGs have been studied in detail.[2] The EEG is reactive to various physiologic stimuli such as sleep, drugs, and pathologic processes. In over half of the patients with low-voltage EEGs, hyperventilation may bring out an alpha rhythm. During sleep, normal activities such as vertex sharp transients and sleep spindles may be generated. It is essential that low-voltage tracings be clearly distinguished from EEGs showing electrocerebral inactivity, which have a grave prognosis. These EEGs lack reactivity and lability, and with increased instrumental sensitivities show no electrical activity of cerebral origin. Low-voltage EEGs are generally considered to be a normal variant...
Another EEG pattern associated with a mild form of encephalopathy is the presence of bursts of intermittent rhythmic delta activity (IRDA) also producing lateralized EEG slowing related to unilateral emphasis of the associated pathologic process. Focal clinical (e.g., focal seizures) and focal EEG findings. Herpes simplex encephalitis and Creutzfeldt-Jakob disease (in the early stages) may occur in an old infarct or tumor. An exception is nonketotic hyperosmolar coma, a form of metabolic encephalopathy, which is very often associated with a diffuse encephalopathy, the EEG showing spontaneous variability during the recording period and evidence of EEG reactivity to painful stimulation.

It is unusual to see prominent focal or lateralized EEG findings with a diffuse encephalopathy unless there is an associated focal process, such as an old infarct or tumor. An exception is nonketotic hyperosmolar coma, a form of metabolic encephalopathy, which is very often associated with focal clinical (e.g., focal seizures) and focal EEG findings. Herpes simplex encephalitis and Creutzfeldt-Jakob disease (in the early stages) may also produce lateralized EEG slowing related to unilateral emphasis of the associated pathologic process.

Another EEG pattern associated with a mild form of encephalopathy is the presence of bursts of intermittent rhythmic delta activity (IRDA) occurring in 7 to 10% of normal subjects over the age of 20 years. The low-voltage EEG does not correlate with neurologic or psychiatric disease.

Changes in the EEG during normal senescence has been described in detail.[3-5] The most frequent change is the slowing of the alpha frequency. By the age of 70 years, the mean alpha frequency decreases to 9.0 to 9.5 cps and decreases further to 8.5 to 9.0 cps beyond the age of 80 years. In healthy elderly subjects, even at or over the age of 100 years, the frequency of the alpha rhythm remains well above 8.0 cps.[6,7] Therefore, an average alpha frequency of less than 8.0 cps measured with the patient fully alert must be considered abnormal in elderly patients at all ages.

Another EEG finding is the presence of isolated transients of irregular focal slowing in the theta-delta frequency range over the anterior temporal region, reported in 40% of healthy elderly subjects.[4,5,8] They are most frequent over the left temporal area particularly during drowsiness. Sometimes poorly defined sharp waves are interspersed with focal slow components. The left-sided accentuation of this activity remains unexplained. Such intermittent slow activity, with or without sharp components over the temporal region, has no correlation with intellectual or cognitive functioning or presence of a seizure disorder. More recent investigations suggest that the temporal slowing in the awake tracing may, in fact, not be the inevitable consequence of advancing age. In neurologically and psychologically normal septuagenarians, Katz and Horowitz[9] found that the focal slow activity was seen in only 17% of records and when present occupied less than 1% of the tracing. Hence, intermittent temporal theta-delta activity occupying only a small proportion of the wake tracing should be considered as a normal aging phenomena. When the temporal slow activity comprises more delta than theta slow waves, which either recur frequently or occur in long runs and are widespread in distribution, a dementing process or focal lesion has to be seriously considered. Diffuse theta-delta activity in elderly subjects are likely to occur in those with intellectual impairment.[5]

**EEG IN ALTERED STATE OF CONSCIOUSNESS**

The term encephalopathy is usually applied to patients displaying altered mental status as a result of a diffuse disturbance of brain function. Common encephalopathies are divided into metabolic, toxic, inflammatory (encephalitis), anoxic, and degenerative types. The EEG in most encephalopathies shows an alteration of background activities and emergence of varying degrees of theta-delta slowing. Remember that the EEG findings are generally nonspecific from a differential standpoint. The EEG is unable to distinguish between different etiologies. The main contribution of the EEG is in providing an objective measure of severity of encephalopathy, prognosis, and effectiveness of therapy.[10]

There is a good correlation between the severity of the EEG changes, the severity of the encephalopathy, and the clinical state of the patient. In mild encephalopathy associated with mild clouding of consciousness and confusion, there is at first slowing of the posterior dominant rhythm, which decreases from a higher to a lower alpha frequency and then into the theta frequency range. More severe encephalopathy is associated with deeper levels of coma, and the background consists mainly of high-amplitude irregular delta activity. With further deterioration in the encephalopathy, the amplitude of all activities drop below 20 µV and the EEG may consist of relatively low-amplitude, invariant delta activity. Some tracings reveal suppression-burst pattern where there is regular alternation of very-low-amplitude EEG with relatively higher-amplitude EEG segments. The most extreme type of abnormality is, of course, lack of any cerebral activity (i.e., electrocerebral inactivity). Presence of the later three types of EEG patterns (invariant low-amplitude delta, suppression-burst, and electrocerebral inactivity) carry a grave prognosis, if drug intoxication can be excluded as the cause of encephalopathy. If due to drug intoxication, these severely abnormal patterns are quite reversible with treatment, with a high potential for complete recovery of neurologic functioning.

Besides the degree of background slowing, there are two other features in the EEG that must be evaluated to determine the severity of encephalopathy. These are spontaneous variability of the EEG over several seconds to minutes, and reactivity to painful stimulation. In milder encephalopathies, the EEG shows spontaneous variability during the recording period and evidence of EEG reactivity to painful stimulation. When the EEG shows reactivity, painful stimulation commonly results in reduction of the amplitude, increase in frequency of the background activity, and reduction in the slow activity. There is often a "paradoxical activation," which is a period of more severe delta slowing following painful stimulation. The presence of any type of reactivity (reduction in slow activity or increase in the degree of slowing) on painful stimulation suggests a lower grade of encephalopathy, whereas the EEG showing spontaneous variability (invariant EEG) and total lack of any reactivity to intense and prolonged stimulation suggests a severe degree of encephalopathy.

A grading system of EEG abnormalities in adults was proposed, similar.[11,12] It is helpful in prognosis, evaluation of effectiveness of therapy, and comparing serial EEG studies. The slow activities associated with an encephalopathy are usually widespread and symmetrical over the two hemispheres. In children, the slowing may predominate over the posterior hemisphere, and in adults, usually over the frontal areas. These are simply maturation-related spatial EEG features, which do not signify that the encephalopathy is more severe posteriorly in children and anteriorly in adults.

It is unusual to see prominent focal or lateralized EEG findings with a diffuse encephalopathy unless there is an associated focal process, such as an old infarct or tumor. An exception is nonketotic hyperosmolar coma, a form of metabolic encephalopathy, which is very often associated with focal clinical (e.g., focal seizures) and focal EEG findings. Herpes simplex encephalitis and Creutzfeldt-Jakob disease (in the early stages) may also produce lateralized EEG slowing related to unilateral emphasis of the associated pathologic process.
superimposed on a more or less normal background activity. Depending on the area of predominance, the IRDA is further divided into frontal or occipital types. IRDA has been traditionally considered a "projected rhythm" and a hallmark of EEG findings in patients with deep midline lesions of diencephalic, upper brain stem, or posterior fossa locations.[13] Critical evaluations subsequently have cast serious doubts on this classic concept because this EEG pattern has been found in a large variety of pathological conditions and is often absent in deep midline lesions. As a matter of fact, the most common etiology of IRDA is a mild to moderate encephalopathy associated with some disturbance in consciousness.[14]

Are there any unique or specific EEG features that help narrow the differential diagnosis of diffuse encephalopathy and point toward a more specific etiology? There are a few EEG patterns (e.g., triphasic waves, positive spikes, and periodic complexes) that, although not commonly encountered in encephalopathic patients, when present suggest a specific etiology for the encephalopathy. Periodic patterns are specifically encountered in anoxic encephalopathy and certain encephalitides, whereas triphasic waves and positive spikes characteristically occur in metabolic encephalopathies.

ENCEPHALOPATHY PATTERNS

METABOLIC ENCEPHALOPATHY

An EEG showing diffuse slowing of the background and presence of triphasic waves is highly suggestive of a metabolic encephalopathy. Triphasic waves are high amplitude (200 to 300 µV), usually bilaterally synchronous, symmetrical, and maximum in amplitude over the frontocentral regions. The most prominent component is a positive sharp wave that is preceded by a short-duration negative sharp wave and followed by a long-duration negative slow wave.[15] However, variations are quite common and the waveform may be monophasic or biphasic.

Although earlier authors[15] emphasized that the triphasic waves were highly specific for hepatic encephalopathy, this EEG pattern has been found to correlate best with any metabolic type of encephalopathy; hepatic, renal, and anoxic etiologies account for over 75% of EEGs with triphasic waves.[16-18] A feature of triphasic waves often stressed is the progressive time lag (25 to 140 milliseconds) of the positive component of the triphasic wave from the anterior to the posterior region. This feature was considered to be most specific for hepatic etiology.[17,19] Recent studies[18] demonstrated that the time lag is neither a consistent feature of triphasic waves, nor has any specificity with regard to the type of metabolic encephalopathy. The "peril" is that no single feature or group of features regarding triphasic waves distinguish hepatic from nonhepatic cases.

There are a few other "pearls" regarding triphasic waves. Patients with metabolic encephalopathies showing prominent triphasic wave activity in their EEG have an overall poor prognosis; in one series, over two thirds died in a matter of a few months.[20] Furthermore, triphasic waves occur essentially in adults; this pattern has been rarely reported below the age of 20 years.[21] This is particularly true with Reyes disease, an acute childhood encephalopathy with hepatic fatty infiltration, where triphasic waves are absent.[22] The EEG pattern of 14 to 6 per second, positive spikes are a well-known maturational EEG pattern normally seen in children in adolescence during NREM sleep. The presence of positive spike bursts in comatose patients with continuous delta activity is a unique, albeit rare, EEG pattern associated with hepatic or anoxic encephalopathy in children.[23,24]

Toxic Encephalopathy

Overdose of hypnotic-sedative drugs is a common cause of coma encountered in the emergency room; excessive beta activity is a prominent feature in the EEG over the anterior head regions. What is less well recognized is that with more severe intoxication, the fast activity assumes a slower frequency (usually 10 to 13 Hz), which is widespread but with anterior predominance. The presence of generalized theta-delta activity with superimposed alpha frequency activity is a unique encephalographic pattern highly characteristic of sedative drug intoxication. In the absence of prominent slow activity, the anterior dominant generalized fast activity produces alpha or spindle coma pattern in the EEG indistinguishable from that seen with severe anoxic encephalopathy.[25,26]

Very severe drug intoxication results in suppression-burst pattern or electrocerebral inactivity. Even though these patterns signify advanced intoxication, they do not carry as ominous a prognosis as when they occur in the setting of cardiopulmonary arrest. It has been repeatedly demonstrated that patients with drug-induced coma may have electrocerebral inactivity lasting over a day and may still make a full neurologic recovery.

Phencyclidine hydrochloride ("angel dust," "PCP pills") is associated with a distinctive EEG pattern similar to that of subacute sclerosing panencephalitis (SSPE). The EEG shows generalized sinusoidal 6.0 cps theta activity that is interrupted approximately every 4 seconds by generalized slow wave discharges.[27] A similar periodic EEG pattern is described transiently during ketamine (a phencyclidine derivative)
anesthesia.

**Anoxic Encephalopathy**

EEG is commonly performed in patients with anoxic encephalopathy due to cardiopulmonary arrest for assessing the severity of cerebral insult and for prognosis. Patients with normal or almost normal EEG tracings following an episode of cerebral anoxia have an excellent prognosis for full neurologic recovery. On the other hand, patients with advanced EEG abnormalities have a uniformly fatal prognosis; most of these patients die without regaining consciousness. An EEG should be obtained at least 5 or 6 hours after successful resuscitation since it takes an hour or more for the EEG to stabilize after an anoxic episode.[12] Besides electrocerebral inactivity, there are three other unique EEG patterns, encountered in association with anoxic encephalopathy, that carry a poor prognosis for neurologic recovery.

Periodic discharges in anoxic encephalopathy may be either bilaterally synchronous periodic epileptiform discharges (BiPLEDs)[28] or independently occurring periodic lateralized epileptiform discharges (bilateral PLEDs).[29] Both periodic EEG patterns are often associated with myoclonic seizures (or even myoclonic status) and carry an extremely poor prognosis and uniform mortality. Vigorous antiepileptic medication treatment of myoclonic seizures related to the two EEG patterns do not affect the ultimate prognosis.

Suppression-burst EEG pattern due to anoxic encephalopathy is at times associated with interesting clinical phenomena; during periods of activity both eyes may open or there are other brief body movements.[30,31] Whether this is an epileptic event (a brief myoclonic seizure) or a brain stem release phenomena remains unknown. At times these movements may cause confusion in the minds of relatives and even treating physicians about the patient's state of consciousness, as they may mimic volitional motor activity.

A rare EEG pattern seen in severe anoxic encephalopathy is the alpha coma pattern, denoting the conjunction of clinical coma associated with alpha frequency activity.[32-34] Because in such tracings the dominant frequency is alpha frequency activity without significant slower frequencies, the EEG superficially resembles that of an "awake" person, but there are major differences. The alpha frequency activity in alpha pattern coma is widespread in distribution and is often prominent over the anterior head regions. Reactivity to any type of sensory stimulation is usually absent. The prognosis of alpha pattern coma is extremely poor; all patients have either died or survived in chronic vegetative state.

Remember that EEG findings of alpha pattern coma are also seen in the setting of sedative/hypnotic drug intoxication[25,35] and in association with intrinsic brain stem lesions[36] with a much more favorable prognosis.

**Cerebral Death**

The EEG is being employed with increasing frequency for the determination of cerebral death in patients with irreversible coma, particularly when organs have to be salvaged for transplantation. It cannot be overemphasized that the absence of cerebral activity on the EEG is only one of the criteria, and should always be considered along with the clinical findings and blood flow studies for brain death. To properly identify very-low-voltage cerebral activity, to distinguish physiological or instrumental artifacts, and to eliminate the possibility of errors through malfunctioning equipment or inadequate techniques, the American EEG Society[37] has a number of recommendations that must be followed during EEG recordings in all cases of suspected brain death. In such "flat" tracings, EEG activity may be obscured by very-low-amplitude fast activity due to sustained contraction of scalp muscles, which can be eliminated by giving a short-acting neuromuscular blocking agent (suxamethonium, 20 to 40 mg IV). This step, which is very easy to undertake, is often overlooked to obtain a satisfactory recording in such patients.

A single EEG and a 6- to 12-hour clinical observation after an unequivocal acute cerebral insult are minimum requirements for brain death evaluation in an adult. In young children, the guidelines are slightly different because of the more difficult task of confirming brain death in this age group. A special task force[38] recommended the following:

1. Brain death should not be determined until at least 7 days of age.
2. Seven days to 2 months: two examinations and two EEGs separated by at least 48 hours are required.
3. Two months to 1 year: two examinations and two EEGs separated by at least 24 hours are required.
4. Older than 1 year: similar criteria as an adult (i.e., one EEG and at least 12 hours of observation).

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Primary generalized epilepsies

A patient with primary generalized epilepsy (PGE) has no identifiable etiology, normal brain imaging, and normal neurocognitive functioning. The epilepsy has a strong genetic basis and is highly responsive to antiepileptic medication. The patient may suffer from absence (petit mal), myoclonic, and tonic-clonic seizures, among other generalized seizures. Many different syndromes of PGE have been recognized depending upon the predominant seizure type and the age of onset. Classically, the presence of rhythmic, anterior-dominant generalized bisynchronous 3 Hz spike wave discharges superimposed on a normal background are considered to be the EEG hallmark of PGE.

However, the most common EEG abnormality associated with PGE is the so-called "irregular" or "atypical" or "rapid spike" wave activity. This is characterized by generalized paroxysms of spikes or spike wave complexes occurring with an irregular frequency of about 3 to 5 Hz. Although some spike wave complexes will approximate 3 Hz, the overall impression is that the EEG abnormality is much less regular than the classic 3 Hz spike wave discharges. Transient asymmetry of the bisynchronous spike wave activity and isolated "focal" spikes are common. Atypical generalized spike waves are not only seen in PGE but also in secondary generalized epilepsies such as progressive myoclonus epilepsies of different etiologies.

Besides the presence of brief (1 to 3 seconds) generalized spike wave discharges, there are no interictal epileptiform abnormalities that are specific for individual syndromes included under PGE (childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, epilepsy with myoclonic absences, and generalized tonic-clonic seizures on awakening). There are a few EEG features that are more common with certain syndromes: (1) polyspike wave discharges are more common with myoclonic epilepsies; (2) paroxysms of occipital-dominant rhythmic delta activity in the EEG is a feature most commonly encountered with childhood absence epilepsy; (3) short paroxysms of spike wave...
discharges of higher frequency (4.0 to 4.5 Hz) are more common with PGE manifesting primarily with generalized tonic-clonic seizures; and (4) PPR is most common with juvenile myoclonic epilepsy.

In patients with PGE, a routine EEG may capture one or more absence seizures or epileptic myoclonic jerks. In children an absence seizure may be induced during the EEG study by hyperventilation with characteristic generalized 3 Hz spike wave discharge, which is sustained for more than 3 seconds in duration. Epileptic myoclonic jerks are associated in the EEG with high-amplitude generalized polyspike wave discharges in association with myoclonic jerks. Not well recognized is the fact that the EEG in patients with PGE may record focal or lateralized spikes in addition to the overwhelming generalized bisynchronous spike activity.[1,2] Similarly, spike or spike wave activity occurring bilaterally but restricted to the frontal areas (where the generalized paroxysms are usually maximum) is also common. Such discharges are often called "abortive" spike wave complexes. Roughly one quarter of patients with 3 Hz spike wave activity in their EEG may show such focal or lateralized discharges,[1] which should generally be viewed as isolated fragments or limited expression of what is fundamentally a generalized epileptic abnormality. Such focal epileptiform discharges often shift from one electrode to the other and from one side to the other.

Table 1. Electroclinical criteria of the 3 c/s spike/wave discharge

- It is bilateral fairly symmetrical and synchronous.
- It has a frontal midline maximum.
- It has a sudden onset and sudden offset.
- Readily activated by hyperventilation.
- It might be proceeded by intermittent, rhythmic, bisynchronous monomorphic slow waves in the occipital regions.
- The 3 c/s SWD is usually associated with an ictal absence episode when it lasts over 5 seconds.
- The 3 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 3.5 years and disappear at the age of 16 years.
- This discharge pattern is markedly enhanced during nonREM sleep, usually during stage II. However the morphological features of this discharge pattern are altered during sleep with the discharge occurring in a more fragmented and atypical fashion, occurring in bursts of spikes, polyspikes and atypical spike/wave complexes. This discharge pattern usually occurs in conjunction with sleep spindles and has an invariant frontal midline maximum.
- Background activity is within normal before and after termination of the paroxysmal discharge.

Secondary generalized epilepsies

Secondary generalized epilepsy (SGE) is a more serious disorder, secondary to known diffuse cerebral hemispheric insult. Patients are children who have frequent seizures of generalized type, usually medically refractory. Many have significant developmental delay and neurocognitive deficits. In contrast to PGE, the background activity of the EEG in SGE syndrome is disorganized and there are variable degrees of slowing. In addition, there are several paroxysmal EEG patterns associated with SGE syndrome: (1) irregular bisynchronous spike wave activity described above, which can occur both with PGE or SGE; (2) slow spike wave (2.5 Hz or slower in frequency) discharges; (3) hypsarrhythmia; (4) independent multifocal spike discharges (IMSD); and (4) generalized paroxysmal fast activity (GPFA). These EEG patterns are largely nonspecific for etiology but are expressions of severe neocortical insult. Many of these EEG patterns are also age-dependent.

West's syndrome (infantile epileptic encephalopathy) is characterized clinically by infantile spasms (jackknife seizures). The EEG usually shows a distinctive interictal pattern called hypsarrhythmia. It consists of very-high-amplitude, asynchronous slow activity superimposed on frequent multifocal spikes, polyspikes, or sharp waves or generalized spike wave complexes. The absence of epileptiform activity, the entire absence of any organization ("chaotic" appearance), and absence of normal activities (e.g., alpha rhythm or sleep spindles) are constant features of a typical hypsarrhythmic pattern. When some of the characteristic features are lacking or are less prominent, some would interpret the EEG as showing "modified hypsarrhythmia." Often the classical hypsarrhythmic pattern occurs only during NREM sleep, and the awake tracing showing diffuse slowing with minimal epileptiform activity. During an actual infantile spasm, there is an abrupt generalized attenuation of the background (i.e., an electrodecremental response). This may be preceded by a high-voltage, usually generalized biphasic slow wave complex. During the electrodecrement there may be low-amplitude beta activity with varying spatial distribution. These electrodecremental events occur often during sleep but without behavioral accompaniment.

Hypsarrhythmia, which is an EEG pattern, and infantile spasms do not have an absolutely constant relationship and are not interchangeable terms. Typical and modified hypsarrhythmia occurs in two thirds of the EEGs of infants with infantile spasms, whereas the remaining one third show generalized slow spike wave discharges (described below).[3] Besides various pathologic conditions associated with a severe cortical insult, hypsarrhythmic pattern is often encountered in infants suffering from tuberous sclerosis or genetically determined metabolic conditions such as non-ketotic hyperglycemia.[4] Children with Aicardi's syndrome (agenesis of corpus callosum, mental retardation, infantile spasms, choreoretinal lesions) show a markedly asymmetric hypsarrhythmic pattern with virtually complete interhemispheric asynchrony of a suppression-burst-like background.[5]

The hypsarrhythmic pattern is a maturational pattern most commonly expressed between the ages of 4 and 12 months. As the infant grows older, beyond the age of 2 years, it is rare to encounter typical hypsarrhythmia, although infantile spasms may still continue. Hypsarrhythmia is
replaced by different EEG patterns such as a diffusely slow tracing, slow spike wave discharges as seen with Lennox-Gastaut syndrome, IMSD, and, rarely, a normal tracing.

Adrenocorticotropic hormone therapy often has a dramatic effect on infantile spasms as well as the hypsarrhythmic EEG pattern, which may virtually disappear in a matter of a few days to a few weeks after initiation of therapy. However, despite these clinical and EEG improvements, the long-term neurocognitive development remains subnormal.

Lennox-Gastaut syndrome (childhood epileptic encephalopathy) is another common form of SGE manifesting in early childhood with developmental delay, neurocognitive deficits, and frequent generalized seizures including tonic seizures. The EEG shows generalized, slow spike wave discharges (1.5 to 2.5 Hz) superimposed on abnormally slow background activity.[6,7] It is important to distinguish these EEG findings from those seen with primary generalized epilepsy where the background activity is normal for age and the generalized spike wave discharges are usually of faster frequency (3 to 5 Hz). Although appearing widespread and bilaterally synchronous, the slow spike wave activity is usually higher in amplitude over the anterior head regions (in 90% of patients); less commonly the amplitude is highest over the occipital areas. The duration of the paroxysms varies widely from isolated complexes to almost continuous slow spike wave activity, commonly without an identified behavioral or awareness change. Hence, the slow spike wave activity in Lennox-Gastaut syndrome is considered an interictal pattern, although it must be understood that subtle changes of behavior in retarded and uncooperative children are hard to recognize.

When one encounters prolonged episodes of slow spike wave activity lasting several seconds to minutes, the interpretative challenge is to decide if these electrographic events represent an ictal pattern (atypical absences or nonconvulsive status) or they simply represent more pronounced interictal pattern. A history of similar long episodes of slow spike wave activity in one or more previous EEGs would support an interictal finding. Also, giving a small dose of lorazepam intravenously will have no affect on an interictal pattern but will usually abort an ictal pattern, at least temporarily.

If a tonic seizure is recorded during the EEG of a patient with Lennox-Gastaut syndrome, the characteristic finding is an electrodecrement or "flattening" lasting several seconds. In addition, high-frequency rhythmic activity in the alpha-beta frequency range commonly occurs during the electrodecrement.

Another distinctive EEG pattern of a symptomatic generalized epilepsy syndrome is IMSD (independent multifocal spike discharges) characterized by the presence of three or more independent and noncontiguous foci of spike or spike wave activity with at least one focus in one hemisphere.[8,9] As expected, the background activity is invariably disorganized and slow in frequency.

There is a close correlation between the three EEG patterns of hypsarrhythmia, slow spike wave, and IMSD associated with SGE. All of them are associated with diffuse or multifocal cerebral abnormalities and have similar clinical correlates of mental retardation, multiple and medically intractable seizure types, and a high incidence of neurologic deficits.[8] Furthermore, serial studies over time may show a change of one pattern to the other in the same patient. Also, in the same EEG study, more than one of these patterns may coexist (e.g., IMSD during wakefulness and slow spike wave activity during sleep). It is very well known that at least 20% of infants with hypsarrhythmia may show slow spike wave usually by the second to fourth year of life. Both of these patterns may further change to IMSD in early childhood. Thus, these three EEG patterns have a common physiopathologic basis and are probably dependent more on cerebral maturation than on a particular kind of cerebral pathologic process.[8,9] Hypsarrhythmia is usually seen in the later half of the first year of life in response to a cerebral insult prenatally, perinatally, or in the immediate postnatal period. It rarely results from cerebral insults after the second year of life. The slow spike wave pattern associated with Lennox-Gastaut syndrome is commonly observed between the ages of 2 and 5 years. The IMSD pattern is seen commonly throughout the first decade of life.

A unique EEG pattern of GPFA is seen predominantly during sleep consisting of high-frequency, 12 to 25 Hz repetitive spike discharges occurring synchronously over both hemispheres.[10] It is associated most commonly with SGE (usually Lennox-Gastaut syndrome) but it may rarely occur also with PGE or in patients with focal seizures, particularly with a frontal lobe focus. This EEG pattern is usually not associated with an obvious clinical change, although subtle tonic seizures (opening of eyes and jaw, eye deviation upward) may be missed. In rare patients with PGE and 3 Hz generalized spike wave, the awake EEG may appear rather benign but the presence of GPFA during sleep is a warning that more severe encephalopathy may be present. In such patients, motor seizures are common and the disorder is likely to persist in adulthood.[11]
The word Hypsarrhythmia is originally derived from the Greek word hypsolos which means high and it refers to high voltage arrhythmia with a disorganized EEG pattern that consists of chaotic admixture of continuous, multifocal, high amplitude spikes, polyspikes, sharp waves and arrhythmic slow waves. This EEG pattern is dynamic and highly variable from one patient to another and between one study and another study for a single patient. Background activity is often disorganized with frequent slow wave activity.

Marked change in the Hypsarrhythmia pattern also occurs during sleep. In REM sleep there is marked reduction to total disappearance of this EEG pattern. There is also normalization of this discharge pattern immediately following awakening from sleep.

This discharge pattern is seen in children between the age of 4 months to 4 years and after the age of 4 years this pattern of discharge usually merges into the slow spike/slow wave complexes.

Hypsarrhythmia pattern is frequently equated with infantile spasm (West syndrome), (characterized by massive flexion myoclonus of the head and neck called jack-knifing or Salaam attacks), however this pattern is not specific to any disease entity and is seen in response to any severe cerebral insult or severe multifocal disease process that occurs below the age of 1 year.

Five different types of Hypsarrhythmia are present:
- Hypsarrhythmia with increased interhemispheric synchronization.
- Asymmetrical Hypsarrhythmia.
- Hypsarrhythmia with a constant focus.
- Hypsarrhythmia with episodes of voltage attenuation.
- Hypsarrhythmia composed only of high voltage slow waves without spikes or sharp waves.

Table 2. Electroclinical criteria of Hypsarrhythmia discharge

- This EEG pattern is bilateral but asymmetrical and asynchronous with frequent lateralization and focalization.
- It has a frontal midline maximum.
- It is frequently continuous without any definite onset or offset and might extend through the whole record and is not associated with any clinical accompaniment.
- The discharge is not activated by hyperventilation
- The 1-2.5 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 6 months (earlier than the 3 c/s SWD) and disappear at the age of 16 years and is replaced by anterior temporal sharp activity and the clinical seizure manifestations merge into the main stream of temporal lobe epilepsies
- Background activity is often disorganized with frequent slow wave activity.
- The clinical correlate of this discharge is Lennox-Gastaut syndrome with multiseizure clinical presentation (grand mal fits, atonic fits, akinetic fits, atypical absence attacks, absence status). The occurrence of two or more than two types of seizures is almost the rule, mental retardation is very common.
- This discharge pattern could be idiopathic of genetic origin, cryptogenic with no overt cause, or symptomatic to a variety of brain diseases that include CNS infection, birth trauma, lipidosis, tuberous sclerosis, etc.

Table 3. Electroclinical criteria of the slow 1-2.5c/s spike/wave discharge

- The role of steroid in the management of secondary generalized epilepsy

Treatment of epileptic encephalopathies can be very challenging as most anticonvulsant drugs fail to achieve good seizure control. Steroids are disease modifying as well as anticonvulsant in these conditions. Though steroids are accepted as the first-line treatment for infantile spasms, there are many unanswered questions with regard to the preparation, dose and duration of treatment. In this review a re-exploration of the literature is
The epilepsy syndromes that respond uniquely to ACTH and steroid therapy have an age-related onset during a critical period of brain development, as well as a characteristic regression or plateau of acquired milestones at seizure onset and long-term cognitive impairment.[12] Epileptic encephalopathies (EE) are a group of conditions in which cognitive, sensorial and/or motor functions deteriorate as a consequence of epileptic activity, which consists of frequent seizures and/or major interictal paroxysmal activity. The clinical condition produced by EEs depends on the age of onset and may change over time, according to the successive age ranges.[12] Steroids therapy is an accepted mode of pharmacological intervention in infantile spasms (IS). Sorel and Dusaucy-Bauloye, in 1958 reported that ACTH was effective in children with IS.[13] Since then steroids have been used in other conditions like Lennox-Gastaut syndrome (LGS), Ohtahara syndrome and, Landau-Kleffner syndrome (LKS).[14]

This review aims to discuss the evidence for the use of steroids in IS, putative mechanisms of action and some practical issues with regard to the clinical use of steroids in infantile spasms. Discussion on the role of steroids in other epileptic conditions and, neuroactive steroids follows at the end.

**Steroids in Infantile Spasms**

Infantile spasm is a catastrophic form of epileptic encephalopathy in childhood.[14,16] There are numerous studies in the literature reporting the effectiveness of ACTH and oral corticosteroids in the treatment of infantile spasms.[15] It is challenging to draw uniform conclusions from these studies as the methodology, inclusion criteria, dose and preparation of steroids, duration of therapy and outcome measures varied significantly across most studies. This is further compounded by the fact that most studies have been uncontrolled, un-blinded and retrospective, complicating the establishment of research-based recommendations for optimal treatment.[15,17] In the following few paragraphs the author tries to answer some questions that might arise in the mind of a pediatric neurologist to decide on the optimal steroid treatment for a child with infantile spasms. What is the evidence to support the use of ACTH in infantile spasms?

Several studies reported the effectiveness of ACTH in infantile spasms. [18,19,20,21,22,23,24,25,26,27,28,29,30] In these studies, age at onset of spasms ranged from one week to twenty four months and age at entry into the study ranged from one to thirty four months. All trials used video-electroencephalography (EEG) monitoring to document a treatment response. Two studies used synthetic ACTH[22,23] and one used, ACTH fragments.[25] ACTH dosage varied from 0.2 IU/kg/day up to 150 IU/m 2 sub /day and duration of treatment at the highest dose ranged from one to six weeks, with the total treatment time varying from four to twelve-weeks. Forty-two to eighty seven per cent of the patients across studies had cessation of spasms. Time from initiation of treatment to cessation of spasms as stated in three studies was 8-12 days. Hrachovy et al and Yanagaki et al found no dose-related difference in the response rate of infantile spasms to ACTH therapy.[21,23] In the randomized controlled trial by Baram et al of the 15 infants randomized to ACTH, 13 responded (86.6%).[19] In a double blind, placebo-controlled, crossover study to compare the therapeutic effectiveness of ACTH (20 to 30 units/day), the response rate to ACTH was 42%.[20] In 1980 Hrachovy et al reported that all the five children responded to low-dose ACTH,[24] whereas Snead et al reported a 93% response rate in 15 children treated with high-dose therapy.[26] Relapse rates were 20 and 36% respectively. Lombroso et al reported that in the 69 symptomatic patients treated with ACTH, 39% had cessation of spasms and EEG normalized in 32%.[18] Response rates for cessation of spasms in these studies ranged from 59 to 100% and resolution of hypsarrhythmia from 57 to 97%, but relapse rates ranged from 9 to 62%. It is clear from these studies that ACTH is effective in controlling spasms in infantile spasms.

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EEG IN NEONATES

In recent years there has been much interest in using EEG to evaluate full-term or premature neonates [1,2] due to the serious limitations in performing an adequate neurologic examination. The neonate may be confined to an isolette, may be intubated, or may be paralyzed for ventilatory control. Under such circumstances, EEG is a very important tool to assess an encephalopathic process or occurrence of epileptic seizures. In addition, the background abnormalities have been classified in neonates and used to predict neurologic outcome.

The EEG of a neonate shows distinctive patterns related to the conceptional age (CA) and the behavioral state (awake, active sleep, quiet sleep). Space does not permit a description of EEG patterns associated with different conceptional ages, but this is summarized in Table 1. It is important to emphasize that the EEG maturation runs parallel in utero and in incubator; only minimal or no differences have been found between babies of the same CA born after different periods in utero.

In a full-term neonate four EEG patterns are observed related to the wakefulness/sleep cycle: (1) low-voltage irregular (LVI) is characterized by the presence of continuous low-amplitude (<50 µV), mainly widespread theta activity; (2) mixed pattern is characterized by continuous moderate amplitude (usually <100 µV) theta and delta activities; (3) high-voltage slow (HVS) consists of continuous high-amplitude semirhythmic, mostly delta activity (0.5 to 3.0 cps) in all regions with an amplitude of 50 to 150 µV; and (4) tracé alternant (TA) pattern is characterized by the occurrence of 3 to 5 second bursts of high amplitude (50 to 100 µV) slow activity (0.5 to 3.0 Hz), which occur at intervals of 3 to 10 seconds when the background is relatively low amplitude (10 to 25 µV) consisting of theta waves. In other words, there is an alteration of bursts of large-amplitude slow activity separated by quiescent or “flat” periods of low-voltage activity.

These four EEG patterns are recorded in different states. The LVI EEG is usually recorded in wakefulness and in active sleep. The mixed pattern can also be recorded in active sleep and relaxed wakefulness. The TA and HVS patterns are characteristic of quiet sleep. A unique characteristic of neonate sleep is that as the neonate falls asleep, he usually enters a period of active (REM) sleep. This differs from older

### Table 1 EEG Maturation in Preterm Neonates

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<tbody>
<tr>
<td>Continuity</td>
<td>Discontinuous, long flat periods or tracé discontinua</td>
<td>Discontinuous or tracé discontinua</td>
<td>Discontinuous 50% of time, more or less continuous 50%</td>
<td>Continuous during awake and AS; TA during QS</td>
</tr>
<tr>
<td>Differentiation of awake and sleep</td>
<td>No differentiation</td>
<td>No differentiation</td>
<td>Wake/sleep diff. seen; also AS/QS diff. later in this period</td>
<td>Good</td>
</tr>
<tr>
<td>Temporal theta</td>
<td>Present</td>
<td>Prominent</td>
<td>Decreasing</td>
<td>Absent</td>
</tr>
<tr>
<td>Occipital theta</td>
<td>Prominent</td>
<td>Decreasing</td>
<td>Decreasing</td>
<td>Absent</td>
</tr>
<tr>
<td>Delta brushes</td>
<td>None or minimal</td>
<td>Prominent, AS &gt; QS</td>
<td>Present, mainly in QS, less or none in AS</td>
<td>Rare in QS</td>
</tr>
<tr>
<td>Tracé alternant (TA)</td>
<td>None</td>
<td>None</td>
<td>Prominent during QS (tracé discontinua)</td>
<td>Present in QS</td>
</tr>
<tr>
<td>Interhemispheric</td>
<td>Short bursts of synchronous EEG activity</td>
<td>Prominent</td>
<td>Progressively more synchrony</td>
<td>Minor asynchrony may still persist</td>
</tr>
<tr>
<td>synchrony</td>
<td></td>
<td>asynchronous</td>
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<tr>
<td>Sharp wave transients</td>
<td>Some (temporal)</td>
<td>Some scattered</td>
<td>Often prominent multifocal sharp waves</td>
<td>Sharp waves less prominent, seen over frontal/ temporal during QS</td>
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<td></td>
<td>sharp activity during bursts</td>
<td>sharp activity</td>
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AS, active sleep; QS, quiet sleep; CA, conceptional age; diff., difference.
A couple of perils and pitfalls need emphasized in interpreting the neonatal EEG. The TA pattern of quiet sleep in a normal full-term neonate and tracé discontinua pattern in a normal premature neonate during quiet sleep have a superficial resemblance to the suppression-burst pattern that carries a poor prognosis. Differentiation between normal and abnormal discontinuous patterns becomes an important challenge in interpreting the neonatal EEG. The suppression-burst pattern is invariant and nonreactive to stimulation. It usually signifies a severe encephalopathy (usually ischemic/hypoxic), although it may occur transiently due to recent intravenous sedative/hypnotic medication. On the other hand, the TA and tracé discontinua pattern associated with quiet sleep in full-term and premature neonates, respectively, are state dependent and react to stimulation. In addition, long recordings would demonstrate activities characteristic of wakefulness and active sleep in normal full-term and premature (over 32 weeks CA) neonates. The TA pattern gradually disappears over 6 weeks postterm when the HVS pattern becomes the sole EEG accompaniment of quiet sleep.[3]

Another striking feature of the neonatal EEG is the frequent occurrence of multifocal sharp transients during indeterminate and quiet sleep. These start appearing at 35 weeks CA and constitute a normal finding in full-term neonates. The clinical significance of these sharp transients remains controversial. It is difficult to clearly separate abnormal (pathologic) sharp waves from normal sharp transients of the neonate. In general, the normal sharp transients are infrequent in occurrence, usually blunt in morphology (rather than assuming spiky configuration), arise from any scalp location but are common over frontal and temporal regions, are truly random in occurrence, without persistent focality, and largely confined to the burst phase of the TA pattern. However, no universal criteria have been established to separate normal sharp transients of the newborn from the abnormal sharp wave activity. Unless the sharp wave discharges are repetitive, periodic, or localized over one region, an epileptogenic significance must not be assigned to them. When the multifocal sharp transients are very frequent and occur even during active sleep and wakefulness, the EEG is considered to be abnormal but suggestive merely of a nonspecific encephalopathic process.

A unique EEG pattern of pathologic significance is the presence of positive Rolandic sharp waves (PRS).[4] PRS may be confined to one hemisphere; if they are bilateral they may be consistently more abundant over one hemisphere. They are usually maximum at CZ but may be lateralized to C3 or C4 electrodes. Their positive polarity is a distinctive feature in addition to their localization. Although initially described as the EEG correlates of the intraventricular hemorrhage, PRS waves may be seen in other conditions, including periventricular leukomalacia, parenchymal hemorrhage, hydrocephalus, hypoxic/ischemic insult, and other conditions.[2,5-7] Presently, the view is that PRS waves represent a marker of different white matter lesions rather than being specific for periventricular/intraventricular hemorrhage. Positive polarity sharp waves at other locations (especially in the temporal region) have no distinctive significance and may just be a part of multifocal sharp transients in the neonates.

Abnormalities of the background activity in full-term neonates are usually classified as either severe or mild [8-11] and are summarized in Table 2. The severe EEG abnormalities indicate severe impairment of brain function and carry a poor prognosis for survival and/or neurologic development. Severely abnormal EEG patterns consist of: (1) isoelectric EEG showing activity consistently below 5 µV; (2) persistent low-voltage tracing, EEG showing activity between 5 and 15 µV with very little variability or sleep/wake differentiation; (3) paroxysmal tracing or suppression-burst pattern (discontinuous, invariant, and nonreactive pattern characterized by 1 to 10 second paroxysms of polymorphic activities such as sharp waves, spikes, and theta-delta activities interspersed with long quiescent periods as long as > 20 seconds); (4) invariant high-amplitude delta activity (persistent and nonchanging high-amplitude 0.5 to 3.0 Hz generalized activity); and (5) the presence of gross asynchrony and asymmetry of the EEG activity over the two sides of the head. Studies have established that the presence of these EEG abnormalities in a full-term neonate, particularly if the abnormalities have been persistent in serial EEGs, carry a very poor prognosis for survival or future neurologic development; over 90% of neonates with such severe abnormalities have an unfavorable outcome.[8,9]

Mild abnormalities of the background activities include more than the usual asynchrony and/or asymmetry; EEG being immature for the conceptional age; lack of recognizable sleep states; excessive discontinuity (“flat” periods longer than 30 seconds); abnormal monorhythmic activities; and excessive multifocal sharp transients. The presence of more than one mild abnormality may suggest an underlying encephalopathic process of varying severity, particularly if the EEG shows persistent abnormality on serial studies. Several of the above mild abnormalities do occur in neonates who are heavily sedated; hence, iatrogenic causes need to be excluded before ascribing them to permanent neurologic insult.

### Table 2. Classification of EEG Abnormalities in Neonates

<table>
<thead>
<tr>
<th>Type of Abnormality</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Grossly abnormal background activities</td>
<td>a. Inactive (isoelectric) EEG&lt;br&gt;b. Low-voltage EEG&lt;br&gt;c. Tracé paroxystique (suppression-burst)&lt;br&gt;d. Invariant delta activity&lt;br&gt;e. Gross interhemispheric asynchrony/asymmetry</td>
</tr>
<tr>
<td>2. Mild abnormalities of background activities</td>
<td>a. Immature for CA&lt;br&gt;b. Excessive asynchrony/asymmetry&lt;br&gt;c. Lack of sleep states&lt;br&gt;d. Excessive discontinuity&lt;br&gt;e. Focal abnormalities&lt;br&gt;f. Miscellaneous, e.g., excessive frontal slowing, excessive frontal or multifocal sharp for CA, excessive rhythmic activities, etc.</td>
</tr>
<tr>
<td>3. Positive Rolandic sharp waves</td>
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<tr>
<td>4. Isolated EEG patterns associated with neonatal seizures</td>
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</table>
One of the major reasons an EEG is performed is if a neonate is suspected of having epileptic seizures. In neonates, epileptic seizures are often characterized clinically by subtle motor behavior such as elevation of a limb, eye deviation, eyelid flutter, tonic posturing, bicycling movements of the legs, apnea, and so on. The EEG is indispensable in establishing the epileptic nature of the motor activity by demonstrating an associated ictal pattern. There are many unique features of neonatal seizures that are different from the seizures encountered in older children and adults. The International Classification of Epileptic Seizures is obviously inappropriate for neonates. The immature brain at this age is unable to initiate and sustain generalized epileptic discharges as in older children; hence, typical tonic-clonic seizures do not occur. Many of the neonatal seizures are subtle seizures as described above. At least some of these do not show a close relationship to an EEG change. The significance of such stereotypic motor events with no concomitant EEG changes becomes a controversial issue regarding diagnosis and management. Whether these events represent "epileptic" dysfunction (not "picked up" by scalp electrodes) or whether these stereotypic behaviors signify episodes of brain stem release phenomena has yet to be resolved.

The opposite situation is also common. An electrographic ictal pattern may occur without an obvious clinical change. Such "subclinical" seizures are common with a pharmacologic neuromuscular blockade, stupor and coma following severe hypoxic/ischemic encephalopathy, multifocal status epilepticus, and following apparently successful treatment of status epilepticus using antiepileptic drugs.

The EEG ictal pattern is highly variable but consists of rhythmic activity of some sort, which is well localized to a relatively small area of the brain. With rare exception, the ictal pattern in neonates is focal, unifocal, or multifocal. When multifocal, the ictal pattern may occur over two different regions at the same time but the discharges have different waveforms and different repetition rates. Multifocal seizures simultaneously occurring on the two sides is a unique feature of neonatal epileptogenesis.

Interictal epileptiform abnormalities are rarely present to aid in the diagnosis of neonatal seizures. Multifocal sharp transients over the frontal and temporal regions are common even in healthy neonates and, as mentioned above, do not correlate with present or future occurrence of epileptic seizures. It appears that in neonates the epileptic process exhibits "all or none" features: either a seizure manifests overtly with appropriate electrographic features or has no interictal epileptiform markers.

**Ictal EEG patterns associated with neonatal seizures are of four basic types**

- **Focal spikes or spike wave discharges** superimposed on a more or less normal background is an ictal pattern most commonly located over the Rolandic region (C3 or C4), and the frequency of the ictal discharge is usually over two per second (Fig. 1). In neonates, focal EEG discharges and clinical seizures do not necessarily imply focal brain lesions. Common etiologies include metabolic disturbances, such as hypocalcemia or hypoglycemia, and subarachnoid hemorrhage. Such an ictal pattern, when associated with normal a EEG background, is prognostically favorable.

- **Another focal ictal pattern** consists of slow-frequency sharp waves or complex waveforms repeating approximately one per second, never recruiting at a faster rate (Fig. 2). This pattern is similar to PLEDs. The background activity is almost always low in amplitude. This pattern, called "depressed" brain discharges,[11] is associated with a severe cerebral insult (e.g., hypoxic/ischemic encephalopathy, encephalitis, cerebrovascular accident, etc.). The accompanying clinical seizures are usually subtle or the EEG discharges are entirely subclinical.

- **Focal monorhythmic pattern** in the beta, theta, and delta frequency is a unique ictal pattern in neonates. It may start with low-amplitude focal 8 to 14 Hz activity that slows down to 4 to 7 Hz and then to 0.5 to 3.0 Hz rhythmic pattern. All types of combinations of the frequency band are possible but some ictal discharges may remain essentially monorhythmic ("alpha band" seizures) during a given seizure. The background is always abnormal and usually low in amplitude. This type of pattern has been referred to as pseudo-beta-alpha-theta-delta ictal pattern[1] and is usually associated with subtle seizures, tonic or myoclonic seizures, or no behavioral clinical change. This ictal pattern is associated with severe CNS dysfunction and correlates with a poor outcome.

- **Multifocal ictal pattern** is characterized by an abnormal background activity and the development of an ictal pattern independently or, rarely, simultaneously over two or more areas of one or both hemispheres. Two or more focal seizures may appear concomitantly in the same or, more commonly, the opposite hemisphere and appear to progress independently. This ictal EEG pattern is usually associated with subtle seizures; the underlying pathology consists of severe encephalopathy due to infection, congenital anomalies, birth trauma, or anoxia. This pattern carries a poor prognosis for normal neurologic development.
Figure 1. EEG of a 5-day-old neonate, showing focal ictal pattern characterized by rhythmic sharp waves in the left Rolandic region.

Figure 2. EEG of a 5-day-old neonate on ventilator, showing "depressed brain seizure" characterized by less than one per second, low-amplitude sharp waves over the right hemisphere.
Several technical points are of crucial importance to optimize neonatal EEG recording. The study should be long enough to include active and quiet sleep; the total duration of the recording may exceed the usual 30 minutes recommended in adults. In most neonates it may be necessary to record the EEG for 45 to 60 minutes.

- The presence of sleep differentiation is an important maturational feature for EEG interpretation.
- Some abnormal patterns such as the degree of discontinuity, asynchrony and asymmetry, presence of multifocal sharp transients, or delta brushes can be evaluated only in quiet sleep.
- Additionally, polygraphic variables must be routinely recorded in addition to several channels of scalp EEG. These include respiration, extraocular movements, EKG, and chin activity. These non-EEG variables are critical in identifying different states (awake, active sleep, or quiet sleep) and recognition of various artifacts. A neonatal EEG lacking such polygraphic variables is difficult to interpret unless it is grossly abnormal.

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TEMPORAL LOBE EPILEPSY: A CLINICAL VIEW POINT

Background: Temporal lobe epilepsy (TLE) was defined in 1985 by the International League Against Epilepsy (ILAE) as a condition characterized by recurrent unprovoked seizures originating from the medial or lateral temporal lobe. The seizures associated with TLE consist of simple partial seizures without loss of awareness (with or without aura) and complex partial seizures (ie, with loss of awareness). The individual loses awareness during a complex partial seizure because the seizure spreads to involve both temporal lobes, which causes impairment of memory.

TLE was first recognized in 1881 by John Hughlings Jackson, who described "uncinate fits" and the "dreamy state." In the 1940s, Gibbs et al introduced the term "psychomotor epilepsy." The international classification of epileptic seizures (1981) replaced the term psychomotor seizures with complex partial seizures. The ILAE classification of the epilepsies uses the term temporal lobe epilepsy and divides the etiologies into cryptogenic (presumed unidentified etiology), idiopathic (genetic), and symptomatic (cause known, eg, tumor).

Pathophysiology: Hippocampal sclerosis is the most common pathologic finding in TLE. Hippocampal sclerosis involves hippocampal cell loss in the CA1 and CA3 regions and the dentate hilus. The CA2 region is relatively spared. For more information, see Pathophysiology in the article Seizures and Epilepsy: Classification and management.

Frequency:
In the US: Approximately 50% of patients with epilepsy have partial epilepsy. Partial epilepsy is often of temporal lobe origin. However, the true prevalence of TLE is not known, since not all cases of presumed TLE are confirmed by video-EEG and most cases are classified by clinical history and interictal EEG findings alone. The temporal lobe is the most epileptogenic region of the brain. In fact, 90% of patients with temporal interictal epileptiform abnormalities on their EEG have a history of seizures.

History:

Aura

- Auras occur in approximately 80% of temporal lobe seizures. They are a common feature of simple partial seizures and usually precede complex partial seizures of temporal lobe origin.
- Auras may be classified by symptom type; the types comprise somatosensory, special sensory, autonomic, or psychic symptoms.

Somatosensory and special sensory phenomena

- Olfactory and gustatory illusions and hallucinations may occur. Acharya et al found that olfactory auras are associated more commonly with temporal lobe tumors than with other causes of TLE.
- Auditory hallucinations consist of a buzzing sound, a voice or voices, or muffling of ambient sounds. This type of aura is more common with neocortical TLE than with other types of TLE.
- Patients may report distortions of shape, size, and distance of objects.
- These visual illusions are unlike the visual hallucinations associated with occipital lobe seizure in that no formed elementary visual image is noted, such as the visual image of a face that may be seen with seizures arising from the fusiform or the inferior temporal gyrus.
- Things may appear shrunken (micropsia) or larger (macropsia) than usual.
- Tilting of structures has been reported. Vertigo has been described with seizures in the posterior superior temporal gyrus.
Psychic phenomena

- Patients may have a feeling of déjà vu or jamais vu, a sense of familiarity or unfamiliarity, respectively.
- Patients may experience depersonalization (ie, feeling of detachment from oneself) or derealization (ie, surroundings appear unreal).
- Fear or anxiety usually is associated with seizures arising from the amygdala.
- Patients may describe a sense of dissociation or autoscopy, in which they report seeing their own body from outside.

Autonomic phenomena are characterized by changes in heart rate, piloerection, and sweating. Patients may experience an epigastric "rising" sensation or nausea.

Physical Signs:

- Following the aura, a temporal lobe complex partial seizure begins with a wide-eyed, motionless stare, dilated pupils, and behavioral arrest. Oral alimentary automatisms such as lip smacking, chewing, and swallowing may be noted. Manual automatisms or unilateral dystonic posturing of a limb also may be observed.
- Patients may continue their ongoing motor activity or react to their surroundings in a semipurposeful manner (ie, reactive automatisms). They can have repetitive stereotyped manual automatisms.
- A complex partial seizure may evolve to a secondarily generalized tonic-clonic seizure.
- Patients usually experience a postictal period of confusion, which distinguishes TLE from absence seizures, which are not associated with postictal confusion. In addition, absence seizures are not associated with complex automatisms. Postictal aphasia suggests onset in the language-dominant temporal lobe.
- Most auras and automatisms last a very short period—seconds or 1-2 minutes. The postictal phase may last for a longer period (several minutes). By definition, amnesia occurs during a complex partial seizure because of bilateral hemispheric involvement.

Causes:

Approximately two thirds of patients with TLE treated surgically have hippocampal sclerosis as the pathologic substrate.

- The etiologies of TLE include the following:
  - Past infections, eg, herpes encephalitis or bacterial meningitis
  - Trauma producing contusion or hemorrhage that results in encephalomalacia or cortical scarring
  - Hamartomas
  - Gliomas
  - Vascular malformations (ie, arteriovenous malformation, cavernous angioma)
  - Cryptogenic: A cause is presumed but has not been identified.
  - Idiopathic (genetic): This is rare. Familial TLE was described by Berkovic and colleagues, and partial epilepsy with auditory features was described by Scheffer and colleagues.

Hippocampal sclerosis produces a clinical syndrome called mesial temporal lobe epilepsy (MTLE). MTLE begins in late childhood, then remits, but reappears in adolescence or early adulthood in a refractory form.

Febrile seizures: The association of simple febrile seizure with TLE has been controversial. However, a subset of children with complex febrile convulsions appear to be at risk of developing TLE in later life. Complex febrile seizures are febrile seizures that last longer than 15 minutes, have focal features, or recur within 24 hours.
Diagnostic work-up

Imaging Studies:

- **MRI is the neuroimaging modality of choice for patients with TLE.**
  - Thin coronal oblique slices of 1.5-2 mm with no gap using spoiled gradient recall images (SPGR) are recommended.
  - All patients with newly diagnosed TLE should have a high-resolution MRI.
  - High-resolution MRI shows hippocampal atrophy in 87% of patients with TLE by visual analysis alone. Hippocampal atrophy is bilateral in 10-15% of cases. An increase in the T2-weighted signal intensity in the hippocampus may be seen on fluid-attenuated recovery (FLAIR) MRI; this finding is also consistent with hippocampal sclerosis.

- **Positron emission tomography with 18-fluorodeoxyglucose (PET-FDG) is a useful tool for interictal seizure localization in surgical candidates when the MRI result is normal.**
  - It usually is performed as an adjunctive measure to delineate the epileptogenic zone.
  - Interictal deficits include reduced glucose metabolism in the medial and lateral temporal lobe.
  - Ictal PET recordings are rare.

- **Single-photon emission computed tomography (SPECT) is also an adjunctive imaging modality useful only for surgical candidates; the accuracy of seizure localization is about 80-90%**.
  - Ictal SPECT done with hexamethylpropyleneamine oxime (HMPAO) shows hyperperfusion in the region of seizure onset. The characteristic pattern is hyperperfusion of the medial and lateral temporal lobe. This requires ictal injection within 30 seconds of seizure onset.
  - Interictal SPECT testing is less sensitive than FDG-PET and ictal SPECT and is not used routinely for localization of the epileptogenic zone.
  - Investigational techniques such as MR spectroscopy may become clinically useful in the future in selected surgical candidates with normal MRI.

Other Tests:

Interictal EEG should be performed in all patients with suspected TLE.

- Interictal abnormalities, consisting of spike/sharp and slow complexes, usually are located in the anterior temporal region (F7/F8 and T3/T4 electrodes) or basal temporal electrodes (T9/T10 and F9/F10).
One third of patients with TLE have bilaterally independent, temporal interictal epileptiform abnormalities.

Ictal recordings from patients with typical TLE usually exhibit 5-7 Hz, rhythmic, sharp theta activity, maximal in the sphenoidal and the basal temporal electrodes on the side of seizure origin.

In documented temporal lobe seizures, lateralized postictal slowing, when present, is a reliable lateralizing finding.

Video-EEG telemetry is used as part of the presurgical evaluation. It also is used if the diagnosis of TLE is suspected but still in question.

Intracranial EEG with placement of intracranial subdural electrodes is done only if the patient is a surgical candidate and MRI and other non-invasive EEG data are not sufficiently localizing (see article Identification of Potential Epilepsy Surgery Candidates).

### Table 1 Electroclinical characteristic of temporal lobe epilepsy.

- Anterior temporal spikes (or sharp waves) are the EEG cornerstone for the diagnosis of temporal lobe epilepsy (commonly recorded at F7, F8 electrodes). Anterior temporal or frontal midline theta activity is occasionally the EEG correlate of temporal lobe epilepsy. Marked unilateral temporal polymorphic delta activity is very suggestive of a rapidly growing temporal lobe tumor.

- The spike (sharp wave) discharge is bilateral in about 25 to 35% of the cases. Patients with bilateral anterior temporal spikes (sharp waves) are more likely to have both psychomotor and grand mal seizures. Sleep has an important role in the facilitation of temporal spikes.

- Brain tumor is rarely discovered in patients with bilateral independent temporal spikes. Patients with unilateral spikes often prove to have mesial temporal sclerosis.

- Above age 50-60 yr, the anterior temporal spike or sharp wave is, in most cases, a simple exaggeration of temporal minor sharp activity, which is extremely common in elderly patients with mild or moderate degrees of cerebrovascular disorder and no seizure disorder whatsoever.

- Children and young adolescents with temporal lobe epilepsy and unequivocal complex partial seizures often have inconclusive EEG findings. Spikes or sharp waves may be over midtemporal or central regions (thus falsely suggestive of benign Rolandic epilepsy) or diffuse. Even generalized spike wave discharges may occur and slow spike wave complexes may overshadow all other abnormalities when one deals with a case of Lennox-Gastaut syndrome giving rise to psychomotor seizures.

- Temporal lobe epilepsy (as an electroclinical syndrome) is usually found in older adolescents and in young and middle-aged adults; childhood and senium tend to dilute the clinical and EEG semiology. In particular the anterior temporal spikes or sharp wave focus is not well developed in young children as it takes a while to develop. In older age the anterior temporal spike or sharp wave is, in most cases, a simple exaggeration of temporal minor sharp activity, which is extremely common in elderly patients with mild or moderate degrees of cerebrovascular disorder and no seizure disorder whatsoever.

### Medical Care:

- About 47-60% of new-onset partial seizures are controlled effectively by the first drug. Studies in 1985 and 1992 by the Department of Veterans Affairs (VA) have shown that the 4 major antiepileptic drugs (AEDs), phenytoin, phenobarbital, carbamazepine, and valproate, are equally effective in controlling partial seizures; however, phenobarbital and valproate have more severe adverse effects.

- The newer AEDs, such topiramate, lamotrigine, levetiracetam, oxcarbazepine, and zonisamide have similar if not better efficacy than the older AEDs. In patients with newly diagnosed epilepsy, lamotrigine appears to be significantly better than carbamazepine in terms of tolerability and health-related quality of life issues.

- Four other drugs were approved in the year 2000 by the US Food and Drug Administration (FDA) for treatment of partial seizures. These include zonisamide, oxcarbazepine, and levetiracetam.

- About 40% of patients continue to have seizures in spite of trials with 3 AEDs. Semah and colleagues showed that seizures are more likely to be refractory to AEDs in patients with hippocampal sclerosis.
Mesial temporal sclerosis consists of cell loss and astrogliosis in the mesial temporal cortex, the hippocampal formation, amygdala, parahippocampal gyrus, and entorhinal cortex. These changes have been best described in the hippocampus, partly due to its severe involvement and the lamellar pattern of hippocampal organization that lends itself to histopathologic study. Two forms of hippocampal cell loss have been identified in mesial temporal sclerosis. Classic sclerosis, also known as Ammon’s horn sclerosis, is the more frequent form. This consists of marked loss of the pyramidal cells in CA1, CA3, and the dentate hilus, with sparing of pyramidal cells in the CA2 sector. The second form is denoted as end folium sclerosis, which consists primarily of cell loss and astroglial proliferation in the end folium with relative sparing of the other sectors. Autopsy studies have demonstrated that mesial temporal sclerosis is present bilaterally, in up to 80% of cases. However, it is usually asymmetric in that one side is more severely involved than the other; the more severely involved of the two hippocampi typically denotes the site of origin of a patient’s seizures.

The MR image counterparts to these two pathologic abnormalities are atrophy and signal change. Hippocampal atrophy is best identified on T1-weighted images obtained coronally or, ideally, perpendicular to the principal axis of the hippocampal formation, which is variably canted downward from posterior to anterior. The identification of atrophy by MR imaging corresponds to cell loss identified in histologic specimens.

The other principal finding is a signal intensity change consistent with increased tissue-free water resulting in decreased signal intensity on T1-weighted images and an increased signal intensity on T2-weighted images. It is logical to assume that the abnormality in signal intensity is a function of astrogliosis. Several other findings on MR images have been helpful in identifying the temporal lobe predominantly involved in mesial temporal sclerosis; these include (1) loss of normal internal architecture of the involved hippocampus; (2) unilateral atrophy of the mammillary body; (3) unilateral atrophy of the columns of the fornix; (4) unilateral atrophy of the amygdala; and (5) unilateral atrophy of white matter bundle in the parahippocampal gyrus.

**Surgical Care:**

**Vagus nerve stimulation**

- Vagus nerve stimulation (VNS) was approved by the FDA in 1997 for treatment of intractable partial epilepsy for patients aged 12 years and older. VNS with a high-frequency stimulation rate resulted in a mean reduction in seizure frequency of 25-28%. The exact mechanism by which it exerts its antiepileptic effect is not known. A battery-operated stimulator device is implanted in the left vagus nerve subcutaneously in the neck.

- Adverse effects include hoarseness of voice, cough, local pain, paresthesias, dysphagia, and dyspnea. VNS does not have the adverse effects associated with AEDs.

**Anterior temporal lobectomy**

- Temporal lobectomy is the definitive treatment for medically intractable TLE (see article Identification of Potential Epilepsy Surgery Candidates). When seizures are not controlled by 2 different AED trials, the patient should be considered for a presurgical evaluation. These patients are not likely to achieve seizure control with medications alone (5-10% chance of becoming seizure free).

- The presence of unilateral hippocampal sclerosis and concordant EEG findings predict seizure-free outcome in patients considered for surgery. Foldvary and colleagues showed that a higher monthly preoperative seizure frequency is associated with a less favorable surgical outcome (see article Outcome of Epilepsy Surgery).

- An extensive presurgical assessment for the feasibility of surgery is essential. This includes MRI, interictal and ictal EEG, neuropsychological testing, and the intracarotid amobarbital test.

- Seizure-free state at 2 years postoperatively is predictive of long-term seizure-free outcome. In well-selected cases, 70-80% of patients with refractory TLE become seizure free after surgery (see article Outcome of Epilepsy Surgery).
Although all of these findings may occur in cases of mesial temporal sclerosis, the author believes that the small, bright hippocampus is the most reliable. Both of these findings are usually present in an individual patient. In some patients with mesial temporal sclerosis, however, the hippocampus may appear to be normal-sized but of increased signal, or atrophic without an obvious signal abnormality. Studies of the accuracy of visual perception have demonstrated that predominantly unilateral mesial temporal sclerosis can be identified with an accuracy of about 90% by knowledgeable readers. Although the unilateral dilatation of the temporal horn has been suggested as a useful marker of mesial temporal sclerosis, the author regards this finding as unreliable. Whereas this exists in cases of severe hippocampal atrophy because of mesial temporal sclerosis, it is not a reliable indicator of mesial temporal sclerosis because it also occurs as a common normal variant.

As mentioned, mesial temporal sclerosis is found bilaterally in approximately 80% of autopsy cases. However, the goal of imaging and the assumption underlying treatment by temporal lobectomy would indicate that in most cases of mesial temporal sclerosis, only one of the temporal lobes actually produces seizures. This apparent discrepancy is best explained by regarding the entire spectrum of mesial temporal sclerosis in four categories: (1) category I, one hippocampus is entirely normal and the other is abnormal; (2) category II, one hippocampus is slightly abnormal and the other severely abnormal; (3) category III, both hippocampi are abnormal to an equal degree; and (4) category IV, both hippocampi are normal. Clinical experience to date indicates that in category II patients, the more severely involved hippocampus typically represents the site of seizure onset. It is the distinction between categories I/II and III/IV that appears to be the most critical, both in terms of surgical outcome and imaging identification of the substrate of epilepsy.

Patients in categories I and II both respond well following removal of the abnormal temporal lobe. Furthermore, visual identification of the more abnormal hippocampus is fairly straightforward when there is a significant side-to-side discrepancy in volume and signal intensity. On the basis of imaging criteria, however, it is impossible to identify the more involved hippocampus in categories III and IV because, by definition, the two hippocampi are either symmetrically abnormal or symmetrically normal. These two categories appear to have a similarly mediocre response to temporal lobectomy: fewer than 50% of patients are seizure free postoperatively.
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.

The best-defined idiopathic partial epilepsy is benign rolandic epilepsy. The classic EEG finding in this childhood seizure disorder is a characteristic monomorphic centrotemporal sharp wave. The sharp waves are often seen independently in the centrotemporal 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.

Table 2. Electroclinical criteria of spike/ sharp wave discharge

- A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable. Spikes represent the basic element of paroxysmal activity in the EEG

- A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.

- Both spikes and sharp waves have multiphasic characters, being composed of a sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. The long duration of a sharp wave permits better insight into the multiphasic character of this potential.

- The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.

- Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.

- The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves and subsequently can not be easily detected.

Figure 6. Examples of sharp waves [left] and spike [right]
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Spike/sharp waves, morphological features:

The spike/sharp wave activity are hypersynchronous discharge pattern of large amount of epileptic neuronal aggregates.

◆ Spike

A spike is a pointed peak transient clearly distinguished from the ongoing EEG activity. The distinction between the spike and the ongoing activity is based upon the voltage and wave morphology. The spike stands out in clear contrast with the ongoing activity because of their higher voltage compared with the ongoing activity.

From the morphological point of view, the spike has a multiphasic feature, being composed of a minor positive, major negative and another minor positive component. The multiphasic characteristic of the spike is related to the fluctuating membrane potentials during the genesis of the hypersynchronous epileptic neuronal discharge.

The duration of the spike potentials ranges between 70-100 msec. The spike is usually followed by a large surface negative slow wave.

◆ Sharp waves

The only difference between spikes and sharp waves lies in their duration. While the spike duration does not exceed 100 msec. The sharp wave duration ranges between 100-200 msec. Otherwise no other differences exist between the spikes and the sharp waves. Both of them are frequently termed sharp activity. From the physiological view point, the sharp activity represents large excitatory post-synaptic potentials (EPSPS) called paroxysmal depolarization shifts (PDS), while the slow waves following them interictally represent inhibitory post-synaptic potentials (IPSPS).

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

Spike/sharp wave, a neurophysiological perspective:

The neuronal epileptic discharge consists of bursts of high voltage sustained and repetitive axosomatic unite spikes called paroxysmal depolarization shifts (PDS).

A unite spike represents multiphasic membrane potential fluctuation, its chief component is a steep negative potential, this component is of
high voltage, sustained and repetitive quality. In general the main components of the membrane potential oscillation are.

- Steep depolarization, which when exceed the membrane potential will trigger a series of high voltage, repetitive action potentials (PDS).
- Steep repolarization phase.
- Hyperpolarization phase.

The initial steep depolarization is usually preceded by massive slow depolarization shifts of an amplitude reaching up to 30 MV and of duration that may exceed 100 msec.

The slow and fast depolarization shifts are usually ushered by prominent changes in the ultra-slow activity, those ultraslow shifts are strongly negative at the center and show positivity at the periphery.

The ultra slow shifts, fast and slow depolarization shifts, associated with repolarization and hyperpolarization will collectively give rise to the neurophysiological phenomenon of PDS, morphologically, by intracellular recording, it is represented as bursts of high voltage, high frequency unit spikes (bursts of high voltage, high frequency action potentials). Paroxysmal depolarization shifts constitute the spikes of the micro-EEG (the spikes of the micro-neurophysiologists).

In general paroxysmal depolarization shifts are a giant excitatory post-synaptic potentials (EPSPS). Paroxysmal depolarization shifts are the hallmark of an epileptic neuron, when aggregates of epileptic neurons fire simultaneously and in synchrony, the summated potentials of Paroxysmal depolarization shifts will give rise to the macro EEG spike/sharp wave potentials. In short, the summated Paroxysmal depolarization shifts of a large number of epileptic neuronal aggregates is the pathophysiological phenomenon which is represented graphically as spike/sharp wave in the EEG.

- Role of inhibition

The inhibitory system in the CNS are based upon three different neurophysiological mechanism

- The post-synaptic inhibitory activity via hyperpolarization of the post-synaptic membrane. This occurs selectively in the brain and is mediated by the GABA-BNZ receptor complex.
- Pre-synaptic inhibition, via depolarization of the pre-synaptic terminal, thus reducing the amount of neurotransmitter release.
- Recurrent collateral inhibition by which the cell regulate its own activity.

The brain is protected by powerful anticonvulsant inhibitory system. Paroxysmal depolarization shifts are invariably followed by post PDS after hyperpolarization representing inhibitory post-synaptic potentials (IPSPS). The persistence of this IPSPS is responsible for the overall duration of spiking (PDS) and contribute to its termination.

The post-depolarization shifts after hyper polarization (inhibitory post synaptic potentials, IPSPS) is mediated by the GABA-BNZ receptor complex in the post synaptic junction. This GABA mediated IPSPS is represented morphologically, in the EEG, as a large surface negative slow wave (the slow wave that commonly follows the spike/sharp wave). This slow wave represents, from the neurophysiological viewpoint, the GABA mediated inhibitory tone which prevents the spiking from becoming self sustained and generalized.

Transition from interictal spiking to ictal spiking with clinical tonic clonic fit is invariably associated with failure of the local inhibitory process that create the post-depolarization shift (PDS) after hyper polarization. The loss of this local protective mechanism signifies the imminent transition from interictal to ictal discharge.

From the EEG point of view transition from interictal to ictal spiking is characterized by loss of the inhibitory slow wave that follows the spiking interictally, and the discharge is replaced by fast rhythmic self sustained spiking with frontal predominance during the tonic phase. The clonic phase is characterized by reappearance of the rhythmic slow wave alternating with bursts of polyspikes. The polyspikes are synchronous with the clonic jerks and the slow waves are synchronous with the periods of relaxation in-between the jerks. Finally, the inhibitory activity overcome the excitatory activity resulting in termination of the grand-mal fit.

To sum up, failure of the GABA mediated inhibition signal the start of the tonic-clonic fits. The tonic phase is characterized by complete failure of the GABA mediated inhibition. The clonic phase is characterized by partial reappearance of the GABA mediated inhibition. Finally GABA mediated post-synaptic inhibitory mechanism is responsible for seizure termination. Failure of this inhibitory mechanism is responsible for the status epilepticus.

In general, in epileptic foci the excitatory activity (PDS) is strongly counterbalanced by the strong inhibitory anticonvulsant system of the brain. So that epileptic discharge remains constrained and subclinical (interictal). Temporary failure of the GABA mediated anticonvulsant system of the brain is responsible for the start of a grand mal fit.
To end up the following potentials are recorded at the epileptic foci interictally.

1. Ultra slow DC current.
2. Slow and fast depolarization shifts
3. Repolarization potentials.
4. Hyperpolarization potentials, this potentials is due to:
   - Electrogenic pumps.
   - Slow and fast GABA mediated IPSPS

Those potentials results in marked increase of power (voltage) in the whole EEG spectrum starting from 0.30 Hz (increase of power in the delta-theta-alpha and Beta frequency bands or increase of the full band power).

**Neurobiochemistry of Paroxysmal depolarization shifts (EEG sharp activity)**

- **State of activation in focal epileptogenesis:**

Paroxysmal depolarization shifts are associated with marked increase of calcium conductance through the cellular membrane resulting in increased cytosolic intracellular calcium concentration coupled with reduction of the extracellular calcium. Increased intracellular calcium is the hallmark of Paroxysmal depolarization shifts which are regarded as a calcium dependant pathophysiological process. Paroxysmal depolarization shifts of a single epileptic neuron and of epileptic neuronal aggregates is suppressed by calcium channel blockers.

The increased calcium conductance during the Paroxysmal depolarization shifts occurs mainly through the NMDA glutaminergic receptors. The NMDA operates on ionic calcium channels, when the NMDA receptor is stimulated the channel opens and closes rapidly resulting in massive influx of calcium intracellularly coupled with the discharge of bursts of high voltage repetitive action potentials (PDS).

Repititive high frequency stimulation of the NMDA receptors condition the ionic channels, making the response to subsequent low frequency stimulation much greater, thus potentiating the efficiency of the NMDA synapses. This potentiation can last for weeks or months.

As activation of the NMDA receptors is coupled with increased intracellular calcium, this will ultimately results in the induction of the proto-oncogenes (cellular growth factors). So prolonged stimulation of the NMDA receptors results in increased in the number (hyperplasia) and the size (hypertrophy) of the NMDA synapses associated with sprouting of recurrent axonal collaterals making new synaptic contacts with the glutaminergic cell bodies, this will ultimately results in the establishment of closed excitatory circuits (self reverberating circuits or kindling).

This usually results in amplification of the excitatory impulses, so that the response to subthreshoold stimuli will be amplified and much prolonged.

However progressive increase of the intracellular calcium beyond the buffering capacity of the calcium binding protein, will ultimately unleash a cascade of events that eventually results in neuronal death (excitotoxic neuronal damage). Those include activation of protease and lipase enzymes, liberation of cytotoxic free radicals, and uncoupling of the oxidative phosphorylation reaction.

- **State of inhibition in focal epileptogenesis:**

Increased intracellular content in GABergic interneurons, secondary to activation of the NMDA synapsis, is associated initially with reduction in GABergic neuronal sensitivity with subsequent reduction of the GABergic inhibitory tone. Progressive increase of the cytosolic calcium content of the GABergic interneurons ultimately results in excitotoxic GABergic neuronal damage so ultimately there is quantitative reduction in the number of the GABA-BNZ post synaptic receptors. This will lead to a state of disinhibition that can create the necessary condition for Paroxysmal depolarization shifts to become repetitive and self sustained.

To sum up, in focal epileptogenesis there are:

- Hypertrophy and hyperplasia of the excitatory NMDA glutaminergic synopsis with sprouting of recurrent axonal collateral establishing excitatory closed circuits (The kindling process).
- Reduction of GABergic interneurons with reduction of GABA and GAD activity and reduction of the BNZ receptors post synaptically.
- Reactive gliosis.
A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable. Spikes represent the basic element of paroxysmal activity in the EEG.

A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.

Both spikes and sharp waves have multiphasic characters, being composed of a sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. The long duration of a sharp wave permits better insight into the multiphasic character of this potential.

The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.

Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.

The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. Low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves and subsequently can not be easily detected.

Table 1. Electroclinical criteria of spike/sharp wave discharge

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THE BRAINMAP COUNTERPART OF EEG SHARP ACTIVITY

The introduction of power spectral analysis and subsequent brain electrical activity mapping (BEAM spectral studies) has further extended the clinical utility of the classical EEG as an investigatory tool in epileptology. BEAM spectral studies is now considered as an important contribution towards localization and characterization of epileptic foci, especially when the standard EEG is considered as within normal or showing non specific changes. In this respect, BEAM was capable of uncovering cases of covert epilepsy and of detecting subclinical epileptogenic foci. As atated above.
As atated above the following potentials are recorded at the epileptic foci interictally.

1. Ultra slow DC current.
2. Slow and fast depolarization shifts
3. Repolarization potentials.
4. Hyperpolarization potentials, this potentials is due to:
   - Electrogenic pumps.
   - Slow and fast GABA mediated IPSPS

Those potentials results in marked increase of power (voltage) in the whole EEG spectrum starting from 0.30 Hz (increase of power in the delta-theta-alpha and Beta frequency bands or increase of the full band power). Focal increase of power (spectral energy) in all frequency bands is the hallmark of focal epileptogenesis in brainmapping studies and quantitative EGG analysis. In the author experience increase of the full band power (between 0-30 c/s) precisely map the epileptic cerebral lesions.

Focal increase of the spectral energy in all frequency bands signals epileptogenic cortex. Increased spectral energy might involve the whole power spectrum, or it might be localized to the beta band. Occasionally, the focal increased energy in the beta band might be associated with decreased energy in the Delta, theta and alpha bands either at the site of the beta focus or in the nearby cortex. Focal beta hyperactivity (Focal increase of the beta spectral energy) is a manifestation of a seizure focus. In less irritable foci, the power increase is limited to the beta band while more excitable epileptogenic foci show a BEAM spectral profile characterized by focal increase of the spectral energy in all frequency bands (Delta - theta, alpha as well as beta bands). In patients where the enhanced beta focus is associated with power reduction in the alpha, theta and delta bands, a pattern of diminished and augmented activity in close proximity, might suggest a region of atrophy and gliosis surrounded by epileptogenic cortex. The diminished power in the delta band might, in this respect, indicates functionally destructive cortex.

Various provocative techniques were used in conjunction with the power spectral analysis and BEAM studies to enhance the visualization of epileptic foci. As focal beta abnormality is found to be the BEAM substrate of epileptic foci, beta enhancing medications are subsequently used to enhance the localization of epileptic foci. Fast EEG activity induced by barbiturate could be used to localize brain lesions, where lesioned area does not respond by increased beta activity.

The spatial distribution of the EEG beta activity induced by thiopental - a beta enhancer - can change in 3 different ways:

1. Diffuse symmetrical and frontally maximal which is the normal response.
2. Generalized lack of response seen in diffuse encephalopathic process.
3. Regional or focal paucity of augmented beta activity seen over focal, often atrophic lesions.

Area with poor response to diazepam or any beta enhancer (lesser increase of the beta activity) always coincides with the area of maximum spiking.

**Figure 3.** A patient presented clinically with temporal lobe epilepsy. A brainmap study showing Bitemporal increase of power in all frequency bands with maximum involvement of the left temporal area. The full band power increase also involves the posterior frontal and the centroparietal areas.

Thiopental activation and brain electrical activity mapping (BEAM) can be combined to accurately localize and characterize epileptic foci.

1. Lesions which showed augmented focal beta activity on the BEAM profile following thiopental administration contained an irritable often epileptogenic cortex.

2. Epileptic foci showing diminished response to thiopental in the delta range are found to be more...
spatially extensive or functionally destructive.

BEAM spectral studies always localized the epileptic foci in an objective, quantitative and easily interpretable fashion. In some epileptic patients BEAM might be the only convincing evidence of focal disorder. Subclinical epileptic foci as well as residual cortical irritable foci in patients properly controlled by medications are clearly visualized on the BEAM spectral profile. In this respect, even transphenoidal electrodes failed to demonstrate convincing evidence of focal disorders in some temporal lobe epileptic patients whereas BEAM clearly visualized the epileptic foci in those patients.

Figure 4. A patient presented clinically with temporal lobe epilepsy. A brainmap study showing Bitemporal increase of the full band power with maximum involvement of the left temporal area.

Figure 5. A patient presented clinically with temporal lobe epilepsy. A brainmap study showing Bitemporal increase of power in all frequency bands with maximum involvement of the left temporal area. The full band power increase also involves the posterior frontal and the centroparietal areas.
Figure 6. A child with cortical dysplasia (lissencephaly, schizencephaly and septo-optic dysplasia. The schizencephalic cleft involved the left frontal area and is seen extending between the subarachnoid spaces and the frontal horn of the lateral ventricle on the left side. Brainmap study in this patient showed a left frontal increase of the full band power that precisely mapped and localized the schizencephalic cleft and the area of maximum sharp activity recorded in the conventional EEG.

THE SPATIAL DISTRIBUTION OF FOCAL EPILEPTIC DISCHARGE

The preferential localization of local epileptic discharge is related to a number of factors that include:

- The patient’s age:
  - There is a tendency of some form of focal discharges to the localized to certain brain areas depending on the state of maturation and the age of the patient.

- The site of the pathological lesions producing the seizures.

- The degree of epileptogenicity of the various brain areas:
  - There is a difference in the epileptogenicity of the various brain areas. For example, the temporal lobe has the lowest threshold for the development of epileptic focal activity while the parietal lobe has the highest threshold.

**Spatial distribution of focal epileptic activity includes:**

1. Centromidtemporal (sylvian, rolandic) spike discharge of childhood.
2. Occipital sharp activity of childhood.
3. Centro-parietal sharp activity of childhood.
4. Anterior temporal sharp activity.
5. Frontal sharp activity.

- Centromidtemporal spike discharge of childhood

The site of the discharge appear to be the perisylvian area (the posterior frontal, the anterior temporal and the central electrodes). The discharge is maximum in the lower rolandic or the motor strip areas of the face, and upper limb. The discharge has an age specific character, being seen only in children and adolescents between the ages of 4-16 years.

The discharge consists of high voltage, repetitive, multiphasic spike and sharp wave activity, usually followed by an after coming high voltage slow wave with a duration of 200-300 msec. This discharge pattern is very prominent and frequently occurs in clusters, and in serial trains. It could be unilateral or bilateral, or may shift from one side to another. This discharge is marked enhanced during non REM sleep.

About 60% of children with this discharge pattern has seizures. The seizures have been termed the benign rolandic epilepsy of childhood.
However this discharge pattern can be seen as an incidental finding in the EEG of asymptomatic children who do not have seizures.

This discharge pattern is seen with increased frequency in a symptomatic first degree relatives of patients with benign rolandic epilepsy of childhood and it appears to be the expression of a dominant genetic trait (genetic EEG trait), which is not necessarily associated with any clinical seizure disorders. Its occurrence in non-epileptic children should suggest a genetic predisposition rather than an epileptic disease entity. The genes locus responsible for this genetic EEG trait has not yet been mapped to a particular chromosome.

- **The occipital sharp activity of childhood.**

  Occurs mainly between the ages of 2-5 years. This discharge pattern has the same characteristics of the centromidtemporal discharge pattern and is seen in patients with benign occipital epilepsy of childhood.

  This discharge pattern is also the expression of a genetic trait, and is not necessarily associated with any seizure disorder. In fact only 50% of children with this discharge pattern has seizure disorder.

- **The centroparietal sharp activity of childhood.**

  A part from being maximum in the centroparietal region, this discharge pattern has the same criteria of the centromidtemporal and occipital sharp activity of childhood. This discharge pattern pattern is seen between the ages of 4-10 years.

- **Anterior temporal sharp activity:**

  This discharge pattern is seen mainly in the adult age usually after the age of 16 years. It has a maximum activity in the anterior temporal region. As the sharp activity is derived mainly from the medial (mesial) temporal structures (The hippocampus and amygdala), so it usually has much lower voltage compared with the more superficial centro-mid temporal discharge pattern. Because of its lower voltage, the spike activity may be drowned in the ongoing EEG activity, so that visual inspection of the EEG may fail to detect it, and the EEG is occasionally read as within normal. This discharge pattern is markedly enhanced by non REM sleep.

  About 90% of patients with this discharge pattern has clinical seizure disorders consist in of he various manifestations of complex partial seizures of temporal lobe epilepsy.

- **Frontal lobe sharp activity.**

  About 90% of patients with this discharge pattern have clinical seizure disorders. This discharge pattern is often secondary to an overt underlying pathology such as trauma, tumour, vascular lesion, scarring, or residual encephalitic changes. This discharge pattern can occur in any age and is not characteristic of the childhood period.

To sum up, most of the focal epileptic discharge in the childhood period is relates to the functional benign focal epilepsies. Apart from the site of the discharge (centro-midtemporal, centro-parietal or occipital), the discharge pattern of benign focal epilepsies share common characteristics, being composed of high voltage, repetitive, spike, sharp waves often occurring in clusters, and commonly followed by slow waves. This discharge pattern is enhanced by non REM sleep. It represents a genetic trait and is not necessarily associated with clinical seizure disorders. Anterior temporal spiking characteristic of temporal lobe epilepsy occurs much less commonly in the childhood period.

- **Benign focal epilepsies.**

Benign focal epilepsies are an age specific epileptic disorders that are encountered almost exclusively in children who have neither history nor evidence of brain damage.

**Benign focal epilepsies resemble in many ways primary generalized epilepsies because of the following:**

| 1. The fits is the disease being not secondary to any structural brain lesions. |
| 2. Neurological examination is free. |
| 3. Intact mentality of the patients. |
| 4. Strong genetic background. |
| 5. Very good prognosis, and most patients outgrow their disease even without medical treatment. |

Benign focal epilepsies, being focal, in the tradition sense, is paradoxical. They are unequivocally focal, both clinically and in the EEG, however they are not secondary to any structural brain lesion and they also have a good prognosis. In general benign focal epilepsies of childhood is the most common cause of focal epilepsies in the childhood periods.

The best studied and the most frequent of benign focal epilepsies is the centro-mid temporal subtype, the benign occipital epilepsies is the second most frequent subtype.
Benign focal epilepsy with centro-mid temporal discharge.

The source of disturbance in the seizure type lies in the lower rolandic cortex representing the face and the oropharynx. The seizure frequency in this disorder is very low occurring mostly at night especially during the first 1/3 of the night in 80% of cases. Past history of febrile convulsions is present in some patients with this seizure type.

The seizure usually takes the form of hemifocal convulsion that may spread to involve the upper limb. The seizures, especially the nocturnal ones often become generalized. The partial onset is occasionally missed and the seizure is described as grand mal fits.

Other form of focal onset include:
1. Somatosensory onset with unilateral paraesthesia involving the tongue and the lips.
2. Speech arrest, anarthria.
3. Drooling of saliva.

EEG of Benign focal epilepsy with centro-mid temporal discharge. (NFE)

The EEG shows the characteristic discharge pattern of high voltage, repetitive spikes/sharp waves that occur in clusters and serial trains and often followed by high voltage slow waves. The discharge is prominent in the central and temporal electrodes and becomes prominent in non REM sleep specially during stage II. The intensity of the spiking is not related to the frequency or the duration of the clinical seizures. Generalized SWD is occasionally seen in patient with centro-mid temporal epilepsy, however it is usually not accompanied by clinical absence.

Genetics of BFE with centro-mid temporal discharge.

The discharge pattern of the BFE with centro-mid temporal epilepsy is the expression of a single dominant gene with an age dependent penetrance that has the following characteristic.

1. Low penetrance below the age of 4 years.
2. The penetrance rise to 50% between 4-16 years.
3. It becomes very low after the age of 16 years.

In fact the discharge pattern of BFE with centro mid temporal should be regarded as genetic EEG trait as the number who bear this EEG trait but otherwise clinically free exceeds those who have clinical seizure disorder. Those who are seizure free represent a group of a symptomatic gene carrier who have high propensity to seizure.

In general the genetic profile of BFE with centro-mid temporal discharge is very close to that of type I primary generalized epilepsies as both are inherited by a single dominant gene that has a low penetrance before the age of 3.5-4 years and a low penetrance after the age of 16 years, from the EEG point of view, both discharge pattern could be found in either of them. This raised the question as to whether BFE with centro-mid temporal discharge and absence seizures are genetically linked.

References

INTRODUCTION: EEG IN DEMENTIA AND HEREDITARY ENCEPHALOPATHIES

EEG has been employed clinically for some time as a measure of brain function in the hope of determining and differentiating certain functional conditions of the brain. It is used in patients who suffer from cognitive dysfunction, either a general decline of overall brain function or a localized or lateralized deficit. This article addresses primarily the clinical use of EEG in evaluation of dementias and encephalopathies. In addition, aspects of digital EEG and other newer developments are discussed briefly at the end of the article.

**Definition of dementia**

Criteria from Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) should be used in the diagnosis of dementia. Clinical dementia is a fairly broad-based decline of brain function; most definitions center on the patient’s intellectual decline and memory dysfunction. This is, however, a fairly simplistic approach; dementia is much more than these fundamental deficits. Some of the dementias have distinguishing features. The process that constitutes normal aging is still an ongoing debate. As our understanding and testing procedures develop, more people are being classified as suffering from some type of dementia.

In 1998, Widagdo et al performed a quantitative EEG (QEEG) study of age-related changes during cognitive tasks. This study revealed no conclusive differences between the young and the elderly. Cognitive decline, unlike normal aging, is associated with alterations in the temporospatial characteristics of EEG. The diagnosis of the initial stages of dementia is based mainly on neuropsychological testing and clinical suspicion. The EEG findings are nonspecific.

**EEG findings in dementia**

In early dementia, the resting alpha frequency declines. Most authors agree that the lower limit of normal alpha frequency is 8.5 cycles per second. Medications can slow the posterior dominant rhythm; therefore, medication effect should always be excluded. In assessing the frequency of the alpha rhythm, alerting maneuvers are essential in order to ensure that the patient is in the best awake state and not drowsy. Computerized methods, such as EEG spectral analysis, coherence, and complexity (ie, correlation dimension), have been demonstrated to correspond to cognitive function.

Stevens et al recorded EEGs during 2 resting conditions (eyes closed and eyes opened) and 2 tasks (mental arithmetic and a lexical decision). The goal of the study was to evaluate which temporal and spatial EEG descriptors change with cognitive decline and normal aging. The EEGs were analyzed by using EEG microstates. The primary findings were a significant increase in the number of ultrashort EEG microstates and a reduction in the average duration of EEG microstates in cognitively impaired and demented patients. Cognitive impairment was associated with a reduction or loss of EEG reactivity. In contrast, no alterations in temporal or spatial EEG descriptors were found in normal aging. Cognitive tasks did not add to the information already obtained during the resting states. The reduction in EEG microstate duration correlated with loss of cognitive function.

Therefore, temporospatial analysis of the EEG record is a useful indicator of cortical dysfunction in dementia and correlates with degree of cognitive impairment. Apparently, temporospatial analysis may be useful in distinguishing patients with dementia from those experiencing normal aging. These data are largely preliminary; whether they contribute additional information to the clinical data in evaluating dementia is unclear.

**Definition of encephalopathy**

Encephalopathy represents a brain state in which normal functioning of the brain is disturbed temporarily or permanently. Encephalopathy encompasses a number of conditions that lead to cognitive dysfunction. Some of these conditions are multifactorial and some have an established cause, such as hepatic or uremic encephalopathy. Because the EEG patterns in most dementias and encephalopathies demonstrate few specific features, they are discussed together. Some notable exceptions include Creutzfeldt-Jakob disease (CJD) and subacute sclerosing panencephalitis (SSPE); however, no specific patterns exist for most dementias and encephalopathies. Other conditions, such as hepatic and renal encephalopathies, carry distinguishing features; nevertheless, similar patterns may be seen in a fairly wide range of illnesses under certain conditions.


**EEG findings in encephalopathy**

In general, the most prominent feature of the EEG record in encephalopathies (if there is a change) is slowing of the normal background frequency. A gradual and progressive decline over the course of the disease may be noted if serial EEGs are performed. Disorganization of the record may develop gradually. Reactivity to photic or other type of external stimulation may be altered. If a QEEG is done, it may show a frequency shift or decreased interhemispheric coherence of background frequencies. Some conditions are associated with an increase in seizure frequency, and in such cases, epileptic activity may be recorded.

In a given context, the EEG can play a clinically useful role, especially since functional MRI, positron emission tomography (PET), and single-photon emission computed tomography (SPECT) are either still in an experimental stage or require special settings not widely available.

**Use of digital EEG data**

Although in the following sections digital EEG data are cited frequently, these data represent primarily digital analysis of clinical EEG recording. The referenced data are presumed to be based on an EEG recording that is read by a clinician; presently, it is recorded by using computerized technology for ease and also for availability for further analysis. A variety of mathematical transforms are available after the initial clinical interpretation—for example, coherence, Fourier transform, wavelets, and microstates (see Digital EEG). These allow for further comparisons with norms and control groups but should be interpreted in conjunction with the primary EEG reading.

### EEG FINDINGS IN DEMENTIA

- **Alzheimer disease**

EEG is the only clinical diagnostic instrument directly reflecting cortical neuronal functioning. Although the EEG may be normal or minimally disturbed in a number of patients in the initial stages of Alzheimer disease (AD), an abnormal EEG usually is recorded later in the course. A large percentage of patients with moderately severe to severe AD exhibit abnormal EEGs.

In 1981, Stigsby reported diffuse increases of delta and theta frequencies, as well as decreases in the alpha and beta frequency ranges in AD. Frontal slowing was more prominent. The slowing was more prominent anterior to the sylvian fissure, while the blood flow was more decreased posterior to the sylvian fissure. These findings may be explained by the fact that the EEG reflects the functional decline of the anterior structures, while the flow decrease correlates more with the structural damage of the parietal lobe. The frontal slowing probably reflects the loss of functioning of the frontal cholinergic system.

Wada et al showed that EEG coherence provides a measure of functional correlation between 2 EEG signals. They examined intrahemispheric EEG coherence at rest and during photic stimulation in 10 patients with dementia of the Alzheimer type. In the resting EEG, patients with AD had significantly lower coherence than gender- and age-matched healthy control subjects in the alpha-1, alpha-2, and beta-1 frequency bands. EEG analysis during photic stimulation demonstrated that the patients had significantly lower coherence, irrespective of the stimulus frequency. The changes in coherence from the resting state to the stimulus condition showed significant group differences in the region of the brain primarily involved in visual functioning. The patients had significantly lower coherence of their EEG reactivity to photic stimulation at 5 and 15 Hz over the posterior head regions.

These findings suggest that patients with AD may have an impairment of interhemispheric functional connectivity in both nonstimulus and stimulus conditions. This suggests a failure of normal stimulation-related brain activation in AD. Jelic et al found a positive correlation between levels of tau protein in the cerebrospinal fluid (CSF) and EEG alpha/delta ratio. In a subgroup with high CSF tau levels, a strong relationship between EEG alpha/theta and alpha/delta power was found. No such correlation was found in healthy controls and mildly cognitively impaired individuals with elevated CSF tau levels.

Locatelli et al used EEG coherence to evaluate the functionality of cortical connections and to get information about the synchronization of the regional cortical activity. They studied EEG coherence in patients with suspected AD. Alpha coherence was decreased significantly in 6 patients. Significant delta coherence increase was found in a few patients between frontal and posterior regions. The group with AD demonstrated a significant decrease of alpha-band coherence in the temporo-parieto-occipital areas. This was expressed to a greater extent in patients with more severe cognitive impairment. They theorized that these abnormalities could reflect 2 different pathophysiological changes: (1) the alpha coherence decrease could be related to alterations in corticocortical connections, whereas (2) the delta coherence increase suggests lack of influence of subcortical cholinergic structures on cortical electrical activity.

Strik et al studied EEG microstates in AD. The microstates of the resting EEG of patients presenting with mild or moderately severe dementia of the Alzheimer type demonstrated a significant anteriorization of the microstate fields, and the duration of sustained microstates was reduced. These differences were more important than the diffuse slowing. The measurements of microstates may be useful in the early diagnosis of AD. Muller et al conducted a study comparing SPECT and QEEG. They concluded that QEEG may be as useful as SPECT brain scanning in staging the disease; however, the correlation with clinical status was weak.
Siennicki-Lantz et al studied the relation of cerebral white matter lesions to AD. Cerebral blood flow (CBF) in white matter correlated with systolic blood pressure and multichannel EEG in senile dementia of the Alzheimer type. The presence and functional significance of white matter lesions in the aging brain or in dementia and their relation to blood pressure is an unsettled issue. White matter lesions occur in both cerebrovascular disease and AD. Probably, the white matter lesions in hypertensive patients are not related to but simply are coexistent with the AD. Their influence on overall expression of the degree of dementia is unclear; intuitively, however, the lesions should be causing additional cognitive dysfunction.

They observed significantly lower CBF in the white matter (WMCBF) in patients with AD than in controls. This was more obvious in the posterior cerebral region (ie, parieto-temporo-occipital area). QEEG from the posterior cerebral regions correlated with WMCBF. Systolic blood pressure was significantly lower in the AD group and was correlated positively with WMCBF in the posterior and anterior brain regions. Epileptiform activity may occur more frequently in patients with AD than in the general population; clinical tonic-clonic seizures can occur. Bilateral synchronous periodic epileptiform discharges (BiPEDs), such as triphasic waves (TWs), may be recorded in AD, usually in the late stages (for more information on TWs, see Triphasic Waveforms). These findings are not specific for AD because they most often are observed in metabolic disorders, particularly hepatic encephalopathy and other degenerative diseases, such as CJD. While good correlation exists between severity of EEG abnormalities and cognitive impairment, epileptiform discharges or TWs are not predictive factors for seizures. EEG often can be useful in evaluating dementia in order to exclude a superimposed reversible metabolic etiology, and to confirm CJD when the dementia is rapidly progressive.

To investigate the relationship between QEEG band powers and CBF, Rodriguez et al studied 42 patients with suspected AD and 18 healthy controls who were elderly. They tried to differentiate patients with AD from the controls by QEEG and CBF measurements. Regional CBF and QEEG were correlated with one another, especially in the right hemisphere. Significant correlations were found between Mini Mental State Examination (MMSE) scores and relative power of the 2- to 6-Hz and the 6.5- to 12-Hz bands on either side and between MMSE scores and left regional CBF, while the correlation between MMSE scores and right regional CBF was less strong.

Employed together, QEEG and regional CBF sensitivity was 88% and specificity 89%, with a total accuracy of 88.3%. QEEG alone showed an accuracy of 77% in the whole group and of 69% in those with mild AD, and regional CBF alone an accuracy of 75% in the whole group and of 71% in those with mild AD. This study suggests that QEEG and regional CBF measurements used together are reasonably accurate in differentiating AD from healthy aging.

Lehtovirta et al studied the relation of apolipoprotein E (ApoE) to EEG changes. ApoE sigma-4 allele is a risk factor for late-onset AD and is proposed to have an impact on cholinergic function in AD. Because the cholinergic system has an important role in modulating EEG, an impairment of the cholinergic system may have a relation to the EEG slowing that is characteristic of AD progression. The QEEG of 31 patients with AD was recorded at the early stage of the disease and after a 3-year follow-up. Patients with AD were divided into several subgroups according to the ApoE sigma-4 allele (ie, 2 sigma-4, 1 sigma-4, and 0 sigma-4). These subgroups did not differ in clinical severity or duration of dementia. The AD patients carrying the sigma-4 allele had more pronounced slow-wave activity than AD patients without the sigma-4 allele, although the disease progression rate did not change. These differences in EEG may suggest differences in the degree of the cholinergic deficit in these subgroups.

The typical electrophysiological correlates of myoclonus in AD are similar to those of cortical reflex myoclonus, with a focal, contralateral negativity in the EEG preceding the myoclonic jerk. The electrophysiological correlate of polymyoclonus that can be seen in AD and other pathological states is a bifrontal negativity in the EEG that precedes the myoclonic jerk. This new type of electrophysiological correlate of myoclonus may reflect activity of a subcortical generator.

◆ Pick disease

Pick disease, which is a frontotemporal dementia, is much less common than AD. The age of onset is earlier than that of AD. The EEG is less abnormal than in AD, especially in the early stages. Posterior alpha rhythm is more preserved. Theta and delta are increased. Frequency analysis may demonstrate a difference at a time when simple visual reading may not pick up a clear abnormality. The major feature of Pick disease is a decline in judgment and insight with relative early preservation of memory. Because EEG correlates poorly with the clinical symptoms, impressive EEG changes are not observed in this condition. Blood flow measurements correlate with thinking processes; Ingvar demonstrated these changes in 1977. Stigsby demonstrated a decrease in anterior blood flow in patients with Pick disease. Because the anterior cholinergic system is relatively preserved in Pick disease, the EEG changes are not prominent frontally.

◆ Huntington chorea

Huntington chorea is a combination of a movement disorder and a dementia, which is dominated by cognitive impairment, psychotic features, and memory impairment. The EEG changes show gradual and progressive slowing over time. The amplitude also attenuates as the disease progresses. About 30% of the patients have very-low-voltage EEGs with amplitudes below 10 microvolts. Hyperventilation as a rule does not increase the background voltage as it usually does in healthy subjects. About 3% of the patients show epileptiform activity; they tend to be juvenile cases. The EEG has not been proven to be of any predictive value in identifying future affected family members. Genetic testing is far more useful.
Progressive supranuclear palsy

In progressive supranuclear palsy (PSP), usually the degree of dementia is not severe. The EEG may be normal initially but eventually shows increasing delta and theta activity. The delta may be rhythmic with frontal accentuation. Gross et al showed a decrease in background frequency down to 6-7/s and delta activity over the temporal regions. Sleep may show poor spindle development. Rapid eye movement (REM) sleep may be reduced or absent. These changes probably reflect the involvement of the locus ceruleus and the pontine raphe nuclei.

Parkinson disease

The EEG is frequently normal. In advanced cases, however, marked slowing is noted. Sleep may be markedly abnormal with frequent awakenings, prolonged sleep latency, reduced REM sleep, periodic leg movements, etc. Wszolek et al studied patients with rapidly progressive familial parkinsonism and dementia with pallidopontonigral degeneration (PPND). The patients had PPND linked to chromosome 17q21-22; 11 EEGs of 9 patients were studied. EEGs revealed normal findings early in the disease and diffuse slowing that became more prominent with disease progression. Electromyograms (EMGs) and nerve conduction studies (NCSs) showed no abnormalities. Visual evoked potentials (VEPs) and sensory evoked potentials (SEPs) were normal. The clinical neurophysiologic study findings were consistent with a cortical and subcortical degenerative process.

With clinical deterioration, progressive decline is seen in the mean parietal frequency and background rhythms. Theta and theta-delta mixture may be recorded bilaterally in the posterior head regions. After stereotactic surgery, focal theta or delta slowing may be observed.

Binswanger disease

Binswanger disease usually demonstrates slowing of background and a nonspecific pattern; however, Kuroda et al reported some other patterns. They described a 72-year-old patient with von Recklinghausen disease exhibiting akinetic mutism within 6 months of the onset of dementia. The EEG demonstrated periodic synchronous discharges (PSDs) suggesting CJD. The CT brain scan findings represented diffuse cerebral atrophy. Autopsy findings revealed diffuse subcortical white matter disease and marked arteriosclerotic changes of the subcortical arterioles. The cortex was relatively spared, and the pathologic diagnosis confirmed Binswanger disease. Binswanger disease, therefore, can present with PSD and should be included in the differential diagnosis of dementia. On the other hand, Dziaiek et al described a group of 15 patients with Binswanger subcortical atherosclerotic encephalopathy who showed different EEG appearance. The EEG records were pathological in most cases, with varying degrees of slow activity that was distributed symmetrically.

Circulatory encephalopathy

Atherosclerosis

Plachinda et al studied the correlations of cognitive disorders and the EEGs of elderly patients with circulatory encephalopathy. They explored the possibilities of using EEG for evaluating intellectual-mnemonic disorders in elderly patients with cerebral atherosclerosis. Ninety-five patients (aged 60-74 years) with atherosclerotic encephalopathy but without stroke were included in the study. Statistical analysis of the data demonstrated a correlation between psychological test results and EEG readings and computerized EEG data. In cerebrovascular disease, focal slowing is far more frequent than in nonvascular dementia; therefore, EEG can be useful in distinguishing the 2 conditions.

Multi-infarct dementia

No specific EEG pattern is associated with multi-infarct dementia. Some background slowing may be observed, especially in advanced disease. These changes are less prominent and do not show the progressive course observed in AD. Research is very scanty. Edman et al found a significant relationship between the increase in EEG slow-wave activity and increases in severity of the parietal brain syndrome. A somewhat lower significance was found for the relation between the increase in slow-wave activity and increases in the degree of dementia. These results suggest that the EEG deterioration mainly reflects the progressive and gradual decline of parietal brain function.

Iznak et al used QEEG to reveal the specific features of and study amplitude-frequency parameters in patients with mild dementia of different origins compared to healthy elderly individuals. They found that alpha rhythm was suppressed in AD and vascular dementia and that alpha rhythm was slower and theta activity higher in AD. Patients with AD were characterized by desynchronized EEG.

Transient global amnesia

A variety of records have been reported from normal to even epileptiform potentials in transient global amnesia (TGA). Nonepileptiform activity, such as bitemporal delta or bioccipital theta, has been reported. Kushner described patients with normal activity, one with occasional epileptic activity, and one with asymmetric alpha depression, while 2 patients had intermittent rhythmic slowing. TGA caused by a seizure is uncommon, and is believed to be caused by a vascular etiology or spreading depression. Patients with Korsakoff syndrome often have abnormal EEGs with theta-delta slowing.
Action myoclonus

Action myoclonus consists of arrhythmic muscular jerking induced by voluntary movement. It can be made worse by attempts at precise or coordinated movement (ie, intention myoclonus) and may be elicited by sensory stimuli. The effective stimulus for action myoclonus is thought to be feedback from muscle afferents, although it may be related to activity in the motor cortex relayed to the reticular formation preceding or coinciding with voluntary movement. The condition usually is associated with diffuse neuronal diseases, such as posthypoxic encephalopathy, uremia, and the various forms of peripheral neuroepithelioma, although action myoclonus may be limited to one limb in some cases of focal cerebral damage. It is caused by hyperexcitability of the sensorimotor cortex (ie, cortical reflex myoclonus) or reticular formation (ie, reticular reflex myoclonus), or both.

Autopsied cases have failed to reveal a clear pathology. Theories include loss of inhibitory mechanisms involving serotonin and possibly GABA transmitters. Myoclonus may be seen in degenerative disorders of the nervous system. It may be associated with tonic-clonic seizures or dementia. Myoclonus has been described in cases with Lafora inclusion bodies and cerebral storage diseases, as well as system degenerations: cerebellodentatorubral, pyramidal, extrapyramidal, optic, auditory, posterior columns and gracile and cuneate nuclei, spinocerebellar pathways, motor neurons of cranial nerves and anterior horns, and muscle fibers.

Action myoclonus usually responds to sodium valproate or clonazepam, and some patients with posthypoxic action myoclonus may improve with serotonin precursors.

Ramsay-Hunt and Unverricht-Lundborg syndromes

The clinical distinction between Ramsay-Hunt syndrome and Unverricht-Lundborg syndrome (ie, Baltic myoclonus) is unclear because cerebellar signs are found in patients described under both syndromes. Some have proposed that the names could be joined and referred to as Unverricht-Lundborg-Hunt disease. Some authors have suggested that the condition be known as systems degeneration type of progressive myoclonus epilepsy. Presently, the cause of the condition (or spectrum of conditions) is not known.

Mitochondrial encephalopathy with lactic acidosis and stroke (MELAS) and myoclonus, epilepsy with ragged red fibers (MERRF)

Isozumi et al described a 50-year-old woman with subacute dementia and myoclonus whose CT scan revealed brain atrophy and EEG revealed PSDs. She initially was thought to be suffering from CJD but dramatically recovered over 5 months. Based on further investigations, the final diagnosis was mitochondrial encephalomyopathy. In general, the EEG changes were described as background slowing, multifocal epileptiform discharges, and photosensitivity.

Poststereotactic surgery

Patients developed EEG slowing of different degrees about 50% of the time.

Alpers disease

This clinicopathological entity, consisting of progressive neuronal degeneration (ie, Alpers disease) of childhood with liver disease, has been studied by Boyd et al. The onset is in early childhood and consists of intractable fits and progressive dementia. EEG studies have been carried out in 12 children with this condition. The EEGs were similar and demonstrated abnormal patterns with high-amplitude, slow activity, as well as smaller polyspikes. The flash VEP was usually abnormal and often asymmetrical. In the appropriate clinical setting, the neurophysiologic features may aid the clinician in diagnosis of this autosomal recessive inherited disorder.

Adrenoleukodystrophy

Multifocal paroxysmal discharges, hypsarrhythmic pattern, and prominent arrhythmic delta are present in temporo-occipital areas. Epileptic discharges usually do not occur in adrenoleukodystrophy.

Zellweger syndrome

This is characterized by diffuse slowing.

Infantile neuroaxonal dystrophy

This condition is characterized by a high-voltage, 14- to 22-Hz activity that is not reactive to environmental stimuli.

Hallevorden-Spatz disease

In this disease the EEG is normal to slow.
Neuronal ceroid lipofuscinosis
In the infantile form, the EEG is slow and early, and posterior spikes may be present. Photic response is excessive and evokes high-voltage spikes that are polyphasic. The EEG abnormalities in the juvenile form are not as marked.

Gaucher disease
In patients with type III disease, posterior spikes and sharp waves, diffuse spike and waves, and photomyoclonic and photoparoxysmal responses may be present.

Metachromatic leukodystrophy
Diffuse slowing progresses to high-voltage generalized delta activity. Epileptic activity is rare; however, hypsarrhythmia may be observed.

Tay-Sachs disease
EEG is generally slow. Generalized or multifocal spikes accompany the seizures.

Rett syndrome
This is a progressive encephalopathy observed in girls. Al-Mateen et al reported 15 cases of Rett syndrome. The course is slowly progressive; it occurs only in girls and is characterized by early deterioration of higher brain function with dementia, autistic behavior, loss of purposeful use of the hands, and deceleration of head growth. When affected girls are aged 2-4 years, epilepsy may develop with minor motor seizures. Additional features may include an extrapyramidal disorder with dystonia and choreoathetosis, and lactic acidemia. A precise biochemical marker of this disorder has not been identified.

According to McIntosh et al, Rett syndrome consists of a progressive encephalopathy and psychomotor deterioration in young girls who have appeared clinically normal until age 6-18 months. The incidence is similar to phenylketonuria and autism in females. When the child is at least 6 months old, head growth decelerates in association with severe dementia, autism, apraxia, stereotypic "hand washing" movements, and loss of previously acquired skills. Other signs include breathing dysfunction, seizures, EEG abnormalities, and growth retardation. It appears to be sporadic in occurrence.

The EEG may demonstrate slowing, a variety of nonspecific patterns, and epileptiform discharges. The epileptic activity may include multifocal spikes, slow-wave spikes, and paroxysmal delta slowing with spikes that may appear in sleep; in certain cases, however, sleep may attenuate the EEG abnormalities. Background flattening occurs to some degree, corresponding with the stage of dementia and cognitive decline. Rolandic spikes may be elicited by noise.

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EEG EVALUATION OF FOCAL CEREBRAL LESIONS

Role of Electroencephalography in the Era of Computed Tomography

The role of electroencephalography (EEG) in detecting focal cerebral disturbances has undergone a significant change in the last decade owing to the development and availability of computerized imaging techniques. EEG is generally complementary to these as, with the exception of positron emission tomography (PET) and single photon emission tomography (SPECT), only EEG evaluates changes in brain physiology. Furthermore, EEG provides the only continuous measure of cerebral function over time. Computerized transaxial tomography (CT) and magnetic resonance imaging (MRI) scanning are clearly the procedures of choice for delineating structural lesions. However, they do not currently reveal abnormalities unless anatomic alterations in brain tissue have occurred.

In this edition, we will review the major electroencephalographic changes that occur with focal cerebral lesions, describe how they relate to CT findings, and indicate the relevance of focal physiologic dysfunction in the absence of structural pathology. Although this article deals with conventional electroencephalographic techniques, newer developments such as topographic EEG mapping and magnetoencephalography suggest that the monitoring of spontaneous and evoked electrical brain activity will continue to play an important role in neurologic diagnosis.

ELECTROENCEPHALOGRAPHIC ABNORMALITIES INDICATING FOCAL DYSFUNCTION

Focal Delta Activity

Focal delta activity is the classic electroencephalographic sign of a local disturbance in cerebral function. A structural lesion is most strongly suggested if the delta activity is continuously present, shows variability in waveform amplitude, duration, and morphology (so-called "polymorphic" or "arrhythmic" activity), and persists during changes in physiologic state. Delta waves that attenuate with eye opening (or other alerting maneuvers), or fail to persist into sleep, are less indicative of structural pathology.

Figure 1. A, Continuous left parietal-occipital polymorphic delta activity. Note associated loss of alpha rhythm and attenuation of faster frequencies over the occipital region. The responsible lesion was a malignant glioma of the left parietal lobe (B).

The localizing value of focal delta is increased when it is topographically discrete or associated with depression of superimposed faster background frequencies. 3,19,34 Superficial lesions tend to produce more restricted EEG changes, whereas deep cerebral lesions may result in hemispheric, or even bilateral, delta. Lesions involving the central and parietal areas are less likely to present with a circumscribed delta focus, and are also correspondingly more apt to produce delta activity falsely localized to the temporal areas.

Focal delta is often, but by no means always, maximal over the actual lesion. If sufficient destruction of cortex has occurred, the voltage of delta activity may actually be reduced over the area of maximal cortical involvement and thus be higher in the areas bordering the lesion. 19 If two or more delta foci are present, the one that is most persistent and least rhythmic indicates the site of the major lesion, regardless of voltage. Few studies have correlated focal delta with CT abnormalities. Gilmore and Brenner, 17 examined 100 consecutive EEGs containing focal polymorphic delta activity and reviewed the CT findings in these patients. Sixty-eight patients had focal CT lesions, 10 had nonfocal abnormalities, and 22 had normal scans. Although peak delta voltage was not always directly over the lesion, laterality was invariably correct.
Normal CT scans occurred in patients with seizure disorders (12), concussion or contusion (5), ischemic strokes (3), viral encephalitis (1), and a progressive undiagnosed neurologic syndrome (1). Twelve patients with focal neurologic examinations had normal CT scans.

Weisberg and associates studied 50 consecutive patients with a unilateral temporal delta pattern and neurologic signs. CT in these patients showed tumor (40 per cent), vascular lesions (20 per cent), diffuse atrophy (16 per cent), or hydrocephalus (4 per cent). Twenty per cent had normal CT scans, a figure similar to that of Gilmore and Brenner. Half of the patients with normal CT had probable epilepsy; the remainder had no further evolution of their neurologic findings over a 4-year follow-up.

In another study, Weisberg and colleagues reviewed CT findings in 20 patients who had a “unilateral delta pattern” but normal neurologic examination, cerebrospinal fluid (CSF), and isotope brain scan. Six had abnormal CT scans: three showing diffuse atrophy and three with infarcts. The three patients with atrophy developed Alzheimer’s disease within 1 year. The authors did not indicate why the remaining 14 patients with normal CT had been referred to the EEG laboratory.

Reports such as these demonstrate that although focal polymorphic delta is strongly correlated with localized anatomic pathology, EEG findings may occur in the absence of a demonstrable CT lesion. When focal delta is found without a corresponding CT abnormality, it is usually in the setting of seizures, nonhemorrhagic infarction, or trauma. Clinical, and experimental, observations indicate that polymorphic delta results primarily from lesions affecting cerebral white matter. Involvement of superficial cortex is not essential, and, indeed, lesions restricted to the cortical mantle do not generally produce significant focal delta. It is likely that functional deafferentation of cortex, rather than a change in cortical metabolic rate, is critical. Cerebral edema does not appear to make a substantial contribution to the production of delta waves.

Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.

Because the likelihood of a demonstrable structural change is strongly correlated with the degree of slowing, the clinical associations of focal theta activity are less striking, especially for acute or subacute lesions. Focal theta may be seen in the early stages of a slowly growing neoplasm or in the resolution of acute lesions caused by stroke or trauma.

Figure 2. Polymorphic slow wave activity in a patient with subcortical glioma, notice the marked variability in wave shape morphology, frequency and amplitude.

- **Beta Activity**

Abnormalities in beta activity are usually limited to voltage asymmetries. To be considered unequivocally abnormal, there should be a persistent amplitude difference of 35 per cent or greater (expressed as a percentage of the higher voltage).

Diminished beta activity results either from cortical dysfunction or from an increase in resistance of the medium separating cortex from scalp recording electrodes. Thus, local attenuation of beta may occur with a cortical infarction, for example, or in the presence of a subdural or epidural fluid collection. A beta asymmetry may also result from localized scalp edema caused by head injury or infiltration from an intravenous line. Similar considerations apply as well to the localized absence or attenuation of background rhythms other than beta.

Focally increased beta activity is usually associated with a skull defect. Occasionally, localized enhancement of beta may occur over a tumor or as the manifestation of an epileptogenic focus.

- **Epileptiform Activity**

Focal epileptiform activity (spikes or sharp waves) may antedate the appearance of focal EEG-slowing or other clues to a tumor by months or years. In a multicenter study of 1396 patients with epilepsy, 10 per cent had tumors detected by CT. However, the incidence of tumor rose to 22 per cent when only patients with partial seizures were considered. Brain tumor did not occur in patients with primary generalized epilepsy and was found in only 5 per cent of those with secondary generalized seizures.
Periodic lateralized epileptiform discharges (PLEDS) usually occur in the setting of an acute or subacute destructive process. Impaired consciousness is virtually always present, and seizures are evident nearly 80 per cent of the time. The complexes are most often composed of di- or triphasic spikes or sharp waves recurring at approximately regular 1 to 2-second intervals. However, the distribution, morphology, voltage, and rate of repetition vary substantially among patients. Schwartz and coworkers, 53 studied 52 patients and found a typical electrographic evolution for PLEDS. Gradual simplification in morphology and progressive prolongation of the interval between discharges usually occurred within 4 weeks. In a few patients, however, clinical relapses were accompanied by reappearance of PLEDS.

Figure 3. A, Left-sided PLEDS, maximally involving the left parietal-occipital region. Background rhythms are slowed bilaterally, and there is a slight reduction in faster frequencies on the left. The patient had an intracerebral tuberculoma on that side.

PLEDs may also occur independently over both hemispheres, a situation referred to as BIPLEDs. 11 In patients exhibiting BIPLEDs, diffuse diseases, rather than focal lesions, are the rule. Thus, BIPLEDs are most often seen with infections (particularly herpes simplex encephalitis), anoxic encephalopathy, epilepsy, and sickle cell anemia. 01,11

LATERALIZED AND GENERALIZED ELECTROENCEPHALOGRAPHIC FINDINGS

- Lateralized EEG changes

The character and distribution of the electroencephalographic changes produced by a focal lesion depend on size of lesion, its distance from the cortical surface, and the specific structures involved. A small lesion critically located in the thalamus, for example, may produce widespread hemispheric slowing and alteration in sleep spindles and alpha rhythm regulation. The same discrete lesion, however, located at the cortical surface, may produce few, if any, electroencephalographic findings. Indeed, cortical lesions must involve relatively large areas to produce attenuation of background rhythms in the relative absence of slowing. Examples include subdural hematomas and meningiomas. Large infarcts (due to middle cerebral or carotid artery occlusions, for instance) involve extensive areas of cortex as well as adjacent white matter, thus producing both hemispheric polymorphic delta and loss of overriding faster frequencies. Lesions that produce hemispheric depression of background rhythms affect both normal and abnormal patterns, as illustrated by the case of a subdural hematoma causing an interhemispheric asymmetry of triphasic waves in an alcoholic with hepatic failure.

Figure 4. A, Failure of alpha rhythm to attenuate normally with eye-opening on the left. The patient had a giant aneurysm of the left internal carotid-middle cerebral artery bifurcation with compression of the frontal and temporal lobes from below (B).

Focal lesions may slow or attenuate the alpha rhythm unilaterally. A particularly striking abnormality of the alpha rhythm is unilateral failure to attenuate normally with eye opening (Bancaud's phenomenon) or other alerting maneuvers. These changes are reliable indicators of an ipsilateral, usually posterior, cerebral lesion, but they do not provide more specific localizing information.

The photic driving response to repetitive flash stimulation may be consistently lateralized in normal individuals. 9 When it is the only finding in an otherwise normal record, an asymmetry of photic driving may usually be ignored. It is clear that a cortical lesion may depress the photic response unilaterally, but under these circumstances, the asymmetric photic response occurs in conjunction with other indications of focal dysfunction. Occasionally, focal lesions (especially subcortical or epileptogenic ones) may enhance the photic response on one side. 9 Hyperventilation will often enhance localized, low-amplitude polymorphic delta or convert intermittent slowing into a continuous focal abnormality. Focal spikes, or even seizures, sometimes appear only during hyperventilation. 42 A consistently asymmetric response to hyperventilation is always abnormal.
Generalized electroencephalographic abnormalities do not contribute to localization of a focal lesion or by themselves even suggest the presence of localized structural pathology. They do, however, provide information about the extent of dysfunction resulting from a focal lesion or about a coexisting abnormality (metabolic encephalopathy, for example).

Subfrontal, diencephalic, or infratentorial lesions may produce generalized electroencephalographic changes, usually a combination of intermittent bursts of rhythmic delta waves and continuous, widespread polymorphic theta and delta slowing. In the absence of obstructive hydrocephalus, electroencephalographic abnormalities are more frequent with rostral than caudal brain-stem lesions. Schaul and coworkers, 51 reviewed the EEGs of 154 patients with diencephalic or posterior fossa lesions. Only 12 per cent of patients with diencephalic lesions had normal EEGs, whereas 60 per cent and 73 per cent of patients with lower brain-stem or cerebellar pathology respectively had normal EEGs. If the EEG abnormality was clearly lateralized, an infratentorial lesion was unlikely.

Paroxysmal bursts of rhythmic delta waves with fronto or occipital predominance (the latter especially common in children) have been associated with subfrontal, deep midline, or posterior fossa lesions. In fact, however, intermittent rhythmic delta activity (IRDA) is nonspecific and is seen much more often in the setting of metabolic disorders or other encephalopathies affecting the brain diffusely than with focal lesions, regardless of location.

IRDA may appear against an otherwise normal background. In contrast to polymorphic delta, IRDA is usually reactive to alerting maneuvers, disappears in sleep, and is augmented by hyperventilation or drowsiness. Correlative studies using CT and PET 16,29,41,46 have failed to demonstrate a particular anatomic structure responsible for generating IRDA. Physiologic investigations, 18,46 implicate dysfunction of thalamocortical interactions.

Rhythmic delta activity consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized. In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]). Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies. FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy. In cases of encephalopathy with FIRDA, the pathophysiologic processes are believed to involve cortical and subcortical gray matter. OIRDA is associated with absence epilepsy in children aged 6-10 years.

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DEFINITION OF HEPATIC ENCEPHALOPATHY

Hepatic encephalopathy is a syndrome observed in patients with cirrhosis of the liver. It is characterized by personality changes, intellectual impairment, and a depressed level of consciousness. An important prerequisite for the syndrome is diversion of portal blood into the systemic circulation through portosystemic collateral vessels. Indeed, hepatic encephalopathy may develop in patients without cirrhosis who have undergone portocaval shunt surgery. The development of hepatic encephalopathy is explained, to some extent, by the effect of neurotoxic substances, which occurs in the setting of cirrhosis and portal hypertension.

Subtle signs of hepatic encephalopathy are observed in nearly 70% of patients with cirrhosis. Symptoms may be debilitating in a significant number of patients and are observed in 24-53% of patients who undergo portosystemic shunt surgery. Approximately 30% of patients dying of end-stage liver disease experience significant encephalopathy, approaching coma.

Hepatic encephalopathy accompanied by severe dysfunction of hepatic synthetic activity also is the hallmark of fulminant hepatic failure (FHF). Symptoms of encephalopathy in FHF are graded using the same scale employed to assess encephalopathy symptoms in cirrhosis. However, the pathogenesis of the encephalopathy in FHF differs from that of cirrhosis. In FHF, altered mental function is attributed to increased permeability of the blood-brain barrier and to impaired osmoregulation within the brain. The resulting brain cell swelling and brain edema are potentially fatal. In contrast, brain edema rarely is reported in patients with cirrhosis.

A number of theories have been proposed to explain the development of hepatic encephalopathy in patients with cirrhosis. One theory is that patients develop an alteration of the brain energy metabolism accompanied with increased permeability of the blood-brain barrier. The latter may facilitate the passage of neurotoxins into the brain. Putative neurotoxins include short-chain fatty acids; mercaptans; false neurotransmitters such as tyramine, octopamine, and beta-phenylethanolamines; ammonia; and gamma-aminobutyric acid (GABA).

Ammonia hypothesis

Ammonia is produced in the gastrointestinal tract by bacterial degradation of amines, amino acids, purines, and urea. Normally, ammonia is detoxified in the liver by conversion to urea and glutamine by the Krebs-Henseleit cycle. In liver disease or in the presence of portosystemic shunting, portal blood ammonia is not converted efficiently to urea. Increased levels of ammonia may enter the systemic circulation because of portosystemic shunting.

Normal skeletal muscle aids in the metabolism of ammonia in the conversion of glutamate to glutamine. The muscle wasting that is observed in patients with advanced cirrhosis may potentiate hyperammonemia.

Ammonia has multiple neurotoxic effects, including altering the transit of amino acids, water, and electrolytes across the neuronal membrane. Ammonia also can inhibit the generation of both excitatory and inhibitory postsynaptic potentials. Additional support for the ammonia hypothesis comes with the clinical observation that strategies designed to reduce serum ammonia levels tend to improve hepatic encephalopathy.

An argument against the ammonia hypothesis includes the observation that approximately 10% of patients with significant encephalopathy have normal serum ammonia levels. Furthermore, many patients with cirrhosis have elevated ammonia levels without evidence for encephalopathy. Also, ammonia does not induce the classic electroencephalogram (EEG) changes associated with hepatic encephalopathy when it is administrated to patients with cirrhosis.

GABA hypothesis

GABA is a neuroinhibitory substance produced in the gastrointestinal tract. Of all brain nerve endings, 24-45% may be GABAergic. Increased GABAergic tone is observed in patients with cirrhosis, perhaps due to decreased hepatic metabolism of GABA.

When GABA crosses the extrapermeable blood-brain barrier of patients with cirrhosis, it interacts with supersensitive postsynaptic GABA receptors. The GABA receptor, in conjunction with receptors for benzodiazepines and barbiturates, regulates a chloride ionophore. Binding of
GABA to its receptor permits an influx of chloride ions into the postsynaptic neuron, leading to the generation of an inhibitory postsynaptic potential. Administration of benzodiazepines and barbiturates to patients with cirrhosis increases GABAergic tone and predisposes to depressed consciousness.

The GABA hypothesis is supported by the clinical observation that flumazenil, a benzodiazepine antagonist, can transiently reverse hepatic encephalopathy.

An elevated blood ammonia level is the classic laboratory abnormality reported in patients with hepatic encephalopathy. This finding may aid in correctly diagnosing patients with cirrhosis who present with altered mental status. However, serial ammonia measurements are inferior to clinical assessment in gauging improvement or deterioration in a patient under therapy for hepatic encephalopathy. Checking the ammonia level in a patient with cirrhosis who does not have hepatic encephalopathy has no utility. Only arterial or “free venous” blood specimens must be assayed when checking the ammonia level. Blood drawn from an extremity to which a tourniquet has been applied may provide a falsely elevated ammonia level when analyzed.

Classic EEG changes associated with hepatic encephalopathy are high-amplitude low-frequency waves and triphasic waves. However, these findings are not specific for hepatic encephalopathy. When seizure activity must be ruled out, an EEG may be helpful in the initial workup of a patient with cirrhosis and altered mental status. Visual evoked responses also demonstrate classic patterns associated with hepatic encephalopathy. However, such testing is not performed in common clinical use.

Figure 1. Triphasic waves

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Hepatic encephalopathy is a syndrome observed in patients with cirrhosis of the liver. It is characterized by personality changes, intellectual impairment, and a depressed level of consciousness. An important prerequisite for the syndrome is diversion of portal blood into the systemic circulation through portosystemic collateral vessels. Indeed, hepatic encephalopathy may develop in patients without cirrhosis who have undergone portocaval shunt surgery. The development of hepatic encephalopathy is explained, to some extent, by the effect of neurotoxic substances, which occurs in the setting of cirrhosis and portal hypertension.

Subtle signs of hepatic encephalopathy are observed in nearly 70% of patients with cirrhosis. Symptoms may be debilitating in a significant number of patients and are observed in 24-53% of patients who undergo portosystemic shunt surgery. Approximately 30% of patients dying of end-stage liver disease experience significant encephalopathy, approaching coma.

Hepatic encephalopathy accompanied by severe dysfunction of hepatic synthetic activity also is the hallmark of fulminant hepatic failure (FHF). Symptoms of encephalopathy in FHF are graded using the same scale employed to assess encephalopathy symptoms in cirrhosis. However, the pathogenesis of the encephalopathy in FHF differs from that of cirrhosis. In FHF, altered mental function is attributed to increased permeability of the blood-brain barrier and to impaired osmoregulation within the brain. The resulting brain cell swelling and brain edema are potentially fatal. In contrast, brain edema rarely is reported in patients with cirrhosis.

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Figure 1. Triphasic waves

Triphasic waves (TWs) are a distinctive but nonspecific electroencephalographic (EEG) pattern originally described in a stuporous patient in 1950 by Foley as “blunted spike and wave.” In 1955, Bickford and Butt coined the term “triphasic wave.” Since their findings were limited to patients with hepatic failure, triphasic wave encephalopathy (TWE) became synonymous with hepatic encephalopathy. More recently, TWE has been associated with a wide range of toxic, metabolic, and structural abnormalities.

TWs are large-amplitude, generalized waves of 1.5-3.0 Hz. They are bilaterally synchronous and bifrontally predominant periodic waves with a characteristic morphology. Classic TWs have an initial small-amplitude, sharp-negative component followed by a large-amplitude, sharp-positive wave; they end with a slow negative wave.
The 3 most common causes of TWE are hepatic encephalopathy, renal failure, and anoxic injury. Other causes of TWs include the following:

1. Hepatic failure
2. Metabolic abnormalities such as hypernatremia, hyponatremia, hypercalcemia, and hypoglycemia
3. Thyroid disease - Hyperthyroidism or hypothyroidism
4. Encephalitis
5. Stroke
6. Creutzfeldt-Jakob disease (CJD)
7. Alzheimer disease
8. Postictal state
9. Serotonin syndrome
10. Cerebral abscess
11. Metrizamide poisoning
12. Naproxen overdose
13. Lithium toxicity
14. Head trauma
15. Cerebral lipidoses
16. Subdural hematoma
17. Carcinomatous meningitis
18. Tumors
19. Maple syrup urine disease

Regardless of the underlying etiology, TWs invariably are associated with an impaired consciousness that may range from mild confusion to deep coma. The background may be slower in hepatic failure than in other conditions. Patients with metabolic abnormalities as a cause for TWE are more likely to be in coma than those with another etiology of TWE.

Early theories suggested that moving cortical positivity due to cortical irritation produced TWE. The cause now is believed to be a dysfunction of the thalamocortical relay neurons due to structural or metabolic disruption. Abnormalities in glutamate metabolism may be one of the mechanisms of TWE. Metabolic or structural abnormalities at the thalamocortical level, particularly dysfunction in the thalamocortical relay neurons, are hypothesized to be responsible for the EEG and clinical findings associated with TWE.

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INTRODUCTION

Until the past 3 decades, localization of brain tumors and other focal lesions was difficult. Neuroimaging techniques consisted of skull x-rays, which were usually negative, and pneumoencephalograms, which were invasive, painful, and often uninformative. In 1936, Walter, who introduced the term “delta waves,” first identified the association between localized slow waves on EEG and tumors of the cerebral hemispheres. This established EEG as an important tool for localizing brain tumors. For the next 4 decades electroencephalographers mounted an enormous effort to improve accuracy of localization and to seek clues to underlying pathologic processes.

Experience has shown EEG to be somewhat reliable in localizing lesions involving superficial accessible portions of the cerebral hemispheres, though it is of limited value in deep-seated lesions, especially posterior fossa tumors. The role of EEG in detecting focal cerebral disturbances has undergone a significant change since the development of CT scan and MRI. Today EEG is primarily complementary to these studies and is used mainly for evaluating functional changes in the patient’s condition. It demonstrates aspects of brain physiology that are not reflected in structural neuroimaging. Functional neuroimaging techniques, such as positron emission tomography (PET), single-photon emission computed tomography (SPECT), and functional MRI (fMRI), can exhibit physiologic changes but not with the temporal resolution of EEG. Furthermore, EEG provides the only continuous measure of cerebral function over time.

This article reviews the major EEG changes that occur with different brain tumors, as determined by location, histologic type, associated complications, and surgical and nonsurgical treatments.

TYPES OF EEG ABNORMALITIES ASSOCIATED WITH BRAIN TUMORS

EEG abnormalities in brain tumors depend on the stage at which the patient presents for evaluation. EEG changes observed with tumors result mainly from disturbances in bordering brain parenchyma, since tumor tissue is electrically silent (with the possible exception of tumors containing neuronal elements, such as gangliogliomas). For this reason, EEG localization often is misleading, although lateralization is generally reliable.

The following are common findings:

- Polymorphic delta activity (PDA)
- Intermittent rhythmic delta activity (IRDA)
- Diffuse or localized theta activity
- Localized loss of activity over the area of the tumor
- Asymmetric beta activity
- Disturbance of the alpha rhythm
- Spikes, sharp waves, or spike-wave discharges

Activation procedures are usually of limited value in patients with tumors, although hyperventilation occasionally can accentuate focal slowing. Asymmetries of photic driving can be useful at times, although they also can be misleading.

- Slow Wave Activity

Focal delta activity is the classic electrographic sign of a local disturbance in cerebral function. A structural lesion is strongly suggested if the delta activity is continuously present; shows variability in waveform amplitude, duration, and morphology (polymorphic); and persists during changes in physiologic states, such as sleep or alerting procedures. When focal delta is found without a corresponding imaging abnormality, it is usually in the setting of acute seizures (especially postictally), nonhemorrhagic infarction, or trauma.

Clinical and experimental observations indicate that PDA results primarily from lesions affecting cerebral white matter; involvement of superficial cortex is not essential, and lesions restricted to the cortical mantle generally do not produce significant delta activity. Functional deafferentation of cortex likely is critical.

Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology, as is rhythmic or sinusoidal delta. The latter usually occurs intermittently and is termed IRDA. It is usually bilateral and of high amplitude and is
typically maximal occipitally (OIRDA) in children and frontally (FIRDA) in adults. Unlike PDA, IRDA increases in drowsiness and attenuates with arousal. IRDA often is observed without structural pathology, as in metabolic encephalopathies, but it also can occur with diencephalic or other deep lesions; in this situation, an amplitude asymmetry can be present, with higher amplitude ipsilateral to the lesion. As in other clinical settings, theta activity is indicative of less severe localized or diffuse dysfunction than delta activity and is observed more commonly with functional disturbances than with structural disturbances. When unaccompanied by delta activity, theta is less likely to indicate a lesion that produces a focal neurologic deficit or seizures.

- Localized Loss and Asymmetries of Background Activity

Since tumor tissue probably does not generate electrical activity detectable with conventional recording techniques, electrical silence is the best localizing sign of a cerebral tumor. However, it is a rare finding, occurring only when the tumor involves significant cortical areas with minimal subcortical disruption. Incomplete loss of activity, especially faster normal rhythms, is observed more commonly and is diagnostically helpful.

- Alpha rhythm

By the time the patient presents with focal or diffuse neurologic symptoms and signs, disturbance of the alpha rhythm may be present. Slowing of the alpha rhythm ipsilateral to a tumor is more common and significant than asymmetry of amplitude. However, disturbance of alpha rhythm depends on the site of the tumor. The more posterior the location, the more the alpha tends to be slowed, impersistent, or disturbed by admixed theta waves. The alpha rhythm also may fail to block to eye opening on the side of the neoplasm (ie, Bancaud phenomenon).

- Beta activity

Abnormalities of beta activity usually are limited to voltage asymmetries. To be considered unequivocally abnormal, a persistent amplitude difference of one third or greater (expressed as a fraction of the higher voltage) should be present. Diminished beta activity results either from cortical dysfunction, as in parenchymal tumors, or from an increase in resistance of the medium-separating cortex from scalp-recording electrodes, as in meningiomas or subdural collections. Focally increased beta activity usually is associated with a skull defect.

- Interictal Epileptiform Discharges
  - Isolated discharges

Spikes, sharp waves, or spike-wave complexes occurring with consistent localization are observed uncommonly early in the course of brain tumors. In one study predating the CT scan era, such discharges appeared with only 3% of gliomas and metastatic tumors at the time of craniotomy. However, they were more common either as early findings of slowly growing neoplasms associated with seizures or later after focal slowing had developed.

  - Periodic lateralized epileptiform discharges

Patients with tumors may exhibit periodic lateralized epileptiform discharges (PLEDs) at times, particularly after a series of seizures. In a study of 282 patients with typical PLEDs, tumor was present in 18%. Most patients with this EEG finding have had or will have seizures, if they are observed sufficiently closely and persistently; the pattern likely represents a transitional state between ictal and interictal epileptiform discharges. Aggressiveness of treatment depends in part on whether the discharges are resolving (becoming less sharp, more localized, and further apart) or the opposite.

  - Seizure patterns

When electrographic seizures are recorded during a routine EEG, suspect status epilepticus. Clinical accompaniments may be subtle, as in aphasic or other forms of nonconvulsive status, particularly when the patient’s baseline condition has been compromised by the tumor, its treatment, or complications.

**EEG CHANGES IN TUMORS BY LOCATION**

Since EEG reflects activity of cortical neurons, hemispheric tumors affect EEG most consistently and prominently. In older studies, a normal EEG occurred in approximately 5% of hemispheric, 25% of deep or basal, and 25% of infratentorial tumors. The overall figure now may be 50% or higher, given the earlier diagnosis allowed by modern neuroimaging. Location is an important determinant of the likelihood and nature of EEG abnormalities.

- Frontal Lobe Tumors

Frontal lobe tumors characteristically cause focal PDA, which accurately localizes the lesion. In approximately one third of patients, slow waves are bilateral and may be IRDA rather than PDA. This occurs most often when deep structures such as the corpus callosum are involved (butterfly glioma).
IRDA is more frequent with frontal tumors than with tumors in other hemispheric locations, even in children in whom the IRDA is often maximal occipitally (OIRDA).

The slow wave abnormality may be only in the theta range, particularly in small, slowly growing tumors.

The alpha rhythm usually is preserved, although it may be disrupted with large lesions.

Parasagittal tumors, particularly meningiomas, may cause decreased beta activity on the side of the tumor or runs of ipsilateral alpha and theta activity.

Sharp waves and spikes are most likely in slow-growing neoplasms and may be bilateral; occasionally, frontally predominant spike-wave complexes mimicking those of idiopathic epilepsies may be produced.

**Temporal Lobe Tumors**

Temporal gliomas are generally the easiest to localize on EEG, since PDA occurs over the tumor site in more than 80% of patients. Tumors in other locations, such as the thalamus, also may produce temporal delta; however, focal delta is more reliably localizing when background rhythms also are attenuated.

- **Anterior temporal**
  - When tumors are in this location, a well-preserved alpha rhythm occurs.
  - PDA is well localized.
  - EEG from the contralateral hemisphere is often virtually normal.
  - Since these tumors often are associated with seizures, they may demonstrate interictal epileptiform discharges. These may be identical to those associated with nonneoplastic lesions such as mesial temporal sclerosis, especially when the tumor is located medially, as is often the case with very slow-growing tumors, such as gangliogliomas and dysembryoplastic neuroepithelial tumors.

- **Posterior temporal**
  - Tumors in this location are characterized by PDA and usually disturbance of the ipsilateral alpha rhythm.
  - Slowing or disorganization of the alpha rhythm with intermixed theta is present.
  - Occasionally, alpha amplitude is decreased markedly rather than slowed.

**Parietal Lobe Tumors**

Tumors in this region less often produce localized slowing; PDA usually is lateralized but often not clearly localized. When phase reversals are present, they may be temporal or frontal rather than parietal.

- PDA is often slow (<2 Hz), but it is usually of lower amplitude than with frontal or temporal tumors.
- The alpha background generally is disturbed either ipsilaterally or bilaterally.
- Theta rather than delta activity may occur in meningiomas, low-grade gliomas, and small metastases.
- In centroparietal tumors, mu rhythms may be attenuated ipsilaterally but occasionally may be more persistent and of higher amplitude.
- Since seizures are common in patients with tumors in perirolandic areas, ipsilateral epileptiform discharges may be present; at times they may be difficult to distinguish from mu, especially after craniotomy.

**Occipital Lobe Tumors**

Most occipital gliomas produce focal changes, especially PDA, which spreads variably to more anterior and contralateral locations. Occipital meningiomas, mainly of the tentorium, can cause more focal EEG changes.

- The background alpha rhythm is rarely normal and may be impaired either ipsilaterally or bilaterally.
- Interictal epileptiform discharges are rare.

**Deep Hemispheric Tumors**

Deep hemispheric tumors include tumors impinging on the lateral and third ventricle and surrounding structures, including the diencephalon, basal ganglia, and corpus callosum. Neuroimaging has led to earlier diagnosis of smaller tumors that may be associated with normal EEGs. When abnormalities are observed, the following apply:

- The typical EEG finding is IRDA. This finding classically has been associated with hydrocephalus or increased intracranial pressure, but this assumption may be incorrect, since IRDA is uncommon in hydrocephalus of nonneoplastic origin and is not present in benign intracranial hypertension.
- PDA typically does not occur, although asymmetric IRDA is relatively common.
- Especially in older patients, rhythmic delta may be more continuous than intermittent.
- Alpha rhythm and sleep spindles may be disrupted ipsilateral to the lesion.
- Epileptiform discharges are very rare
Intraventricular and Sellar Tumors

- Lateral ventricle (ependymoma, meningioma)
  - EEG may exhibit PDA over the ipsilateral temporal lobe.
  - Theta and sharp waves may be present temporally.
- Third ventricle (colloid cyst, epidermoid, craniopharyngioma)
  - EEG is usually normal unless the lesion is large.
  - Slowing may be bifrontal or diffuse.
  - Runs of theta may be observed.
- Sellar region
  - EEG is usually normal
  - If present, slowing is usually bitemporal.

Infratentorial tumors

- Brain stem and cerebellum
  - EEG is more often abnormal in children.
  - If present, slowing is most often posterior and bilateral.
  - IRDA may be observed, especially if hydrocephalus is present.
- Cerebellopontine angle (acoustic neuroma)
  - EEG is usually normal, especially with small tumors.
  - When present, slowing is usually temporal or temporal occipital.
  - Slowing is often intermittent and usually but not always ipsilateral; it may be bilateral or even predominantly contralateral.

**TUMOR TYPE AND EEG**

EEG patterns are not specific for tumor pathology, but some general correlations exist.

- Slowly growing extra-axial tumors, such as meningiomas, produce the mildest EEG disturbances, whereas rapidly growing intraaxial tumors, such as glioblastomas, cause the most marked abnormalities.
- Benign intraaxial tumors, such as astrocytomas or oligodendrogliomas, are intermediate in their effects on the EEG.
- Interictal discharges most commonly are observed initially in slowly growing tumors and often are observed later in the course of higher grade lesions.

**Meningiomas**

Being extraaxial, meningiomas compress the brain but cause little destruction of brain tissue. Therefore, meningiomas of the anterior or middle cranial fossa, unless large, infrequently alter EEGs. Convexity meningiomas are more likely to cause EEG changes. With rolandic or parasagittal meningiomas, common EEG changes include the following:

- Focal theta activity
- FIRDA
- Diminished, or less often, augmented beta activity
- Focal PDA that is usually low in amplitude (50-60 mV), intermittent, and misleadingly prominent in temporal derivations
- Epileptiform discharges observed in as many as 45% of patients

**Gliomas**

Slowly growing gliomas such as oligodendrogliomas and fibrillary astrocytomas (excluding tumors of deep structures) often can be distinguished from the more rapidly growing anaplastic astrocytoma and glioblastoma multiforme.

- With the more benign tumors, which comparatively are circumscribed, the abnormalities tend to be localized and within the theta range.
In the rapidly growing tumors, relatively more overall abnormality is present, and the background (particularly the alpha rhythm) is more impaired and disorganized.

Glioblastomas produce the most widespread, slowest (often 1 Hz or less), and largest (100-200 mV) delta waves. These tumors cause prominent PDA, with marked alteration of background rhythms. Also, the high incidence of necrosis makes "flat PDA" (low-amplitude slow delta with diminished fast activity) more likely.

Indolent gliomas commonly cause seizures, and epileptiform activity may appear before significant slowing occurs. Later, delta appears, often intermittently and at 2-3 Hz. Still later, focal PDA becomes persistent.

Metastases

Metastatic tumors to the brain occur commonly with carcinomas of lung, kidney, and breast and with melanomas and chorionic carcinomas. When metastases are present bilaterally, slowing often appears diffuse, although it is often asymmetric; slowing from multiple bilateral lesions is often difficult to distinguish from a toxic-metabolic disturbance. Meningeal carcinomatosis usually causes changes that correlate with the clinical situation; when deposits are widespread and cause an encephalopathy, slowing is usually diffuse.

Isolated metastases usually cause less prominent abnormalities than gliomas of similar size and location. Slow waves show higher frequency, lower amplitude, and less persistence than with high-grade gliomas, and normal background rhythms are more likely to be preserved.

References

The EEG in meningitis shows various degrees of slow-wave abnormalities, depending on the type of meningitis and the degree of involvement of the central nervous system.

Moderate to severe diffuse slow-wave abnormalities are often present in acute purulent meningitis, and paroxysmal epileptiform activity may be present in those patients who have seizures.

The electroencephalographic findings in tuberculous meningitis vary according to the location of the inflammatory process. In basal meningitis, the EEG may be normal and show only mild nonspecific slowing. When the inflammatory process involves the cortical meninges, moderate to severe slowing occurs, depending on the degree of cortical involvement, the rate of progression of the disease process, the level of consciousness, the presence of metabolic or systemic factors, the pulmonary state of the patient, and the effects of medication. As with purulent meningitis, more severe slow-wave abnormalities are present in children, with the slowing often being maximal over the posterior head regions.

In aseptic meningitis, the EEG may be normal or show only mild slowing; the electroencephalographic findings may not necessarily correlate with the clinical severity of the inflammatory process or the development or degree of post-infectious sequelae.

Patients in whom meningoencephalitis develops in association with infectious mononucleosis may have mild to moderate diffuse or focal slow-wave abnormalities that may or may not coincide with the area of maximal neurologic dysfunction. On occasion, focal epileptiform abnormalities have been observed in patients who experience seizures.

The rate and degree of the improvement in the electroencephalographic abnormalities after treatment have some diagnostic and prognostic value. One of the characteristic features of meningococcal meningitis is the rapid improvement in the electroencephalographic findings, with the findings often returning to normal within 1 or 2 wk after treatment. In other types of purulent meningitis and tuberculous meningitis, the electroencephalographic abnormalities often require several weeks to resolve.

The EEG usually returns to normal in patients with uncomplicated meningitis; however, persistent electroencephalographic abnormalities or evidence of deterioration in the EEG suggests an unfavorable course, the development of a complication such as an abscess or hydrocephalus, or the presence of residual brain damage.

Although the electroencephalographic findings are not essential for making the specific diagnosis of meningitis, the EEG and particularly serial recordings are helpful in following the course of the disease, detecting the development of complications or relapse, and indicating the presence of sequelae or residual brain damage.

The electroencephalographic findings in encephalitis are similar to those in meningitis, although the abnormalities are often more severe; this may be a helpful point in the differential diagnosis.

The EEG is almost always abnormal during the acute phase of encephalitis, with the most frequent finding being the presence of diffuse high-voltage, arrhythmic and/or rhythmic delta slowing. Diffuse polymorphic arrhythmic delta activity is more likely to occur when the white matter is involved, whereas paroxysmal, bisynchronous slow-wave activity is more likely to be present when the disease process involves the subcortical gray matter. The degree of slowing depends on the severity of the infection, the amount of cerebral involvement, the level of consciousness, and other associated systemic or metabolic factors. In general, the leukoencephalitides, which primarily involve the white matter and which are caused by the group B non-neurotropic viruses (measles, rubella, variola) and the post-vaccinal states, are associated with more severe electroencephalographic abnormalities than are those caused by the group A neurotropic viruses (mumps, St. Louis and equine encephalitis). Children often show more severe electroencephalographic abnormalities than do adults. Epileptiform abnormalities also may be present, particularly if the patient is having seizures.

Slow-wave abnormalities have also been observed during the acute stages of uncomplicated childhood infections, such as measles, mumps, rubella, chickenpox, and scarlet fever, in which there is no overt evidence of nervous system involvement. The electroencephalographic
Brain abscesses may occur as a result of meningitis, septicemia, or septic emboli or as an extension of an infectious process involving the ears, mastoids, and sinuses.

In the early stages of an acute supratentorial abscess, the EEG may show diffuse slowing with a poorly defined focus. This pattern is more likely to occur with meningo-encephalitis, if the patient is obtunded, and when the more focal abnormalities are obscured by more generalized slow-wave abnormalities. Focal slowing becomes more apparent as the suppurative process becomes localized; marked focal polymorphic delta slowing can develop overlying the site of the abscess, particularly if the lesion is located close to the surface of the brain. If there are multiple abscesses, multiple electroencephalographic foci may be present. More generalized, intermittent, or shifting bursts of rhythmic slow waves (that is, a projected rhythm) also may be present; these bursts may be seen with a disturbance of the frontal lobe or as a secondary effect of the mass lesion on midline structures. On infrequent occasions, focal or lateralized periodic sharp- or slow-wave complexes (periodic lateralized epileptiform discharges) may be present over the involved area of the brain.

In general, the degree of the electroencephalographic abnormalities reflects the severity of the inflammatory process. The electroencephalographic

The entero-encephalitides caused by Coxsackie and ECHO viruses, which predominantly affect infants and young children, are accompanied by varying degrees of diffuse slow-wave abnormalities in the EEG. Western equine, Eastern equine, St. Louis, and Japanese encephalitis are also associated with variable slow-wave abnormalities in the EEG, which may or may not show a correlation with the clinical picture.

In tick-borne viral encephalitis (spring-summer encephalitis), slow-wave abnormalities may be present prior to the onset of symptoms. The abnormalities do not necessarily correspond with the clinical symptoms and severity of the infection; slow-wave abnormalities, however, may continue to be present in those patients with post-encephalitic symptoms. EEG recordings have only rarely been done in rabies. They have been described as showing a depression or “extreme desynchronization” in one case, and nonspecific findings in two other cases (Gastaut and Miletto, 1955; Radermecker, 1977). Diffuse slow-wave abnormalities similar to those seen in other post-vaccinal states may be present following rabies vaccination.

The EEG recordings in the rickettsial infections (Eurasian typhus or spotted fever, Rocky Mountain spotted fever, tsutsugamushi fever) range from normal to those showing diffuse or focal slow-wave abnormalities, with epileptiform activity being present in those patients who develop seizures. The degree of EEG abnormality usually reflects the degree of encephalitic involvement.

Encephalitis or meningitis caused by fungal diseases (histoplasmosis, blastomycosis, and coccidioidomycosis) are associated with diffuse slow-wave abnormalities in the EEG. These changes are similar to those produced by bacterial and viral agents. More focal EEG abnormalities may be present if there is focal cerebral involvement by mycotic abscesses. As fungal infections tend to recur, the EEG may be helpful in following the clinical course of the patient and alerting one to a recurrence of the infection or the development of complications. As a rule, most of the different types of encephalitis do not give rise to specific types of EEG patterns. Instead, the EEG abnormalities are most often expressed as diffuse or focal slow-wave abnormalities, with the degree and extent of the slowing reflecting the intensity of parenchymal involvement.

**EEG IN BRAIN ABSCESS**

Brain abscesses may occur as a result of meningitis, septicemia, or septic emboli or as an extension of an infectious process involving the ears, mastoids, and sinuses.

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The EEG often shows a characteristic pattern and temporal evolution which can be of great value in making the diagnosis of herpes simplex encephalitis, especially when serial recordings are obtained. During the earlier stages of the disease process, the background activity is disorganized and polymorphic delta activity develops in a focal or lateralized fashion, with a predominance over the involved temporal region. Soon after this, focal or lateralized sharp or slow-wave complexes appear, usually having a maximal expression over the involved temporal region. These complexes rapidly evolve into a periodic pattern, with the sharp waves having a stereotyped appearance and recurring every 1 to 3 seconds. The periodic pattern is usually seen between 2 and 5 days after the onset of the illness but, on occasion, has been observed up to 24 and 30 days after the onset of the illness. If there is bilateral involvement of the brain, bilateral periodic complexes may be present, occurring synchronously or independently over the two hemispheres but often having a time locked relationship with one another. Focal or lateralized electrographic seizure discharges, consisting of repetitive sharp or slow waves or spike or polyspike bursts, may be present over the involved area or hemisphere.

Figure 2. EEG showing focal delta slowing over the right frontal region in a 9-yr-old boy with a right frontal abscess.

Chronic abscesses develop more slowly and insidiously and often without overt clinical signs of the infectious process. These are usually well-encapsulated abscesses that develop after the initial infection has been cured. A chronic abscess behaves like a progressive mass lesion and shows the same type of electroencephalographic findings as a tumor (that is, focal slow-wave abnormalities, asymmetry, or attenuation of the background activity) and, if there is increased intraventricular pressure, a projected rhythm. If the abscess develops very slowly, only minor or subtle electroencephalographic changes may be present.

After treatment, the slow-wave abnormalities improve; however, the EEG rarely returns to normal. If surgical intervention is employed, the postoperative electroencephalograms show a rapid decrease in the degree of slow-wave abnormalities within the first few days after surgery; however, some slowing and asymmetry of activity often continue to be present over the surgical area. Epileptiform abnormalities are not very common in the acute stages of the abscess, however, about 75% of patients with cerebral abscesses subsequently suffer seizures, and those patients in whom the amount of epileptiform activity increases within the first 1 to 5 years have a greater tendency of developing subsequent seizures.

**EEG IN HERPES SIMPLEX ENCEPHALITIS**

The EEG often shows a characteristic pattern and temporal evolution which can be of great value in making the diagnosis of herpes simplex encephalitis, especially when serial recordings are obtained. During the earlier stages of the disease process, the background activity is disorganized and polymorphic delta activity develops in a focal or lateralized fashion, with a predominance over the involved temporal region. Soon after this, focal or lateralized sharp or slow-wave complexes appear, usually having a maximal expression over the involved temporal region. These complexes rapidly evolve into a periodic pattern, with the sharp waves having a stereotyped appearance and recurring every 1 to 3 seconds. The periodic pattern is usually seen between 2 and 5 days after the onset of the illness but, on occasion, has been observed up to 24 and 30 days after the onset of the illness. If there is bilateral involvement of the brain, bilateral periodic complexes may be present, occurring synchronously or independently over the two hemispheres but often having a time locked relationship with one another. Focal or lateralized electrographic seizure discharges, consisting of repetitive sharp or slow waves or spike or polyspike bursts, may be present over the involved area or hemisphere.

Figure 3. EEG of 68-yr-old man with herpes simplex encephalitis. Periodic sharp waves over the left hemisphere.

During this time, there is a transient obliteration of the periodic discharges on the side of the seizure discharges. In the later stages of a fatal herpes simplex infection, the electrographic seizure discharges may occur in association with the periodic discharges without altering them. Additionally, during the later stages of the disease process, the periodic complexes often have a more broad slow-wave appearance and a longer interburst interval. During the final stages of a fatal infection, the EEG assumes an almost isoelectric appearance.

In nonfatal herpes simplex encephalitis, the periodic complexes disappear as the disease process resolves and are replaced by focal or lateralized slow-wave abnormalities or attenuation of activity over the involved area. The resolution of the electroencephalographic abnormalities often lags
complexes in association with a febrile illness and a rapid evolution of neurologic signs is strongly suggestive of herpes simplex encephalitis.

As in adults, the presence of periodic complexes is a prominent feature in the EEG of infants with herpes simplex encephalitis, although the periodic discharges may show more of a shifting emphasis from area to area. After the resolution of the infection, the EEG frequently continues to show focal epileptiform discharges, as well as localized areas of attenuation of activity overlying residual cystic areas of the brain.

Although the findings in herpes simplex encephalitis are not pathognomonic for the disease, the presence of unilateral or bilateral periodic complexes in association with a febrile illness and a rapid evolution of neurologic signs is strongly suggestive of herpes simplex encephalitis.

**EEG IN SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE)**

SSPE is an inflammatory disease occurring in children and adolescents, believed to be caused by the measles virus and which is characterized by abnormal movements, a progressive intellectual deterioration, and a diagnostic electroencephalographic pattern. The characteristic electroencephalographic pattern consists of high-voltage (300 to 1500 mv) repetitive polyphasic and sharp- and slow-wave complexes ranging from 0.5 to 2 see in duration, usually recurring every 4 to 15 see. On rare occasions, these complexes may occur at intervals ranging up to 1 to 5 min. The periodic complexes may be present at any stage of the disease, but they usually are seen during the intermediate stages. Although the form and appearance of the periodic complexes is fairly constant and stereotyped in a single recording, the shape of the complexes varies in different patients and can change from time to time in the same patient at different stages of the disease process. The complexes are usually generalized and asynchronous, but at times they may be asymmetric, have a time lag from side to side or front to back, or occur in a more lateralized or focal fashion, particularly in the earlier stages of the disease.

Initially, the complexes may occur at irregular intervals, but, once established, the complexes recur at regular intervals, although the repetition rate may vary during the course of the disease. Afferent stimuli do not usually affect the periodic complexes; however, on rare occasions, the complexes can be evoked by external stimuli. This occurs when the complexes are present in an inconstant manner, either when they first make their appearance or toward the end of the period of remission. Once the regular pattern of the complexes has been established, however, the complexes are no longer influenced by external stimuli. Drugs usually have little effect on the periodic complexes, although one report described the occurrence of periodic pattern after an intravenous injection of diazepam.

A prominent feature of SSPE is the stereotyped motor jerks or spasms occurring with the periodic complexes. The movements are often described as myoclonic jerks; however, they do not have the momentary lightning-quick nature of true myoclonus; instead, the movements consist of an initial "shock-like abruptness," followed by a momentary arrest of the movement, and then a gradually melting away to the position of rest. On less frequent occasions, the periodic complexes may be associated with an inhibitory phenomenon such as an arrest of movement, loss of tone, or drop attacks. The abnormal movements usually become evident about the same time that the periodic complexes appear on the EEG, however, on occasion, and particularly in the early stages of the disease, the periodic complexes may be present without the associated motor movements. On the other hand, the presence of the MOTOR jerks in the absence of the periodic complexes is uncommon. The motor movements often disappear during sleep, despite a persistence of the periodic complexes. Certain drugs, such as diazepam, may reduce or abolish the motor movements without altering the electroencephalographic complexes.

The resting EEG may be relatively normal when the complexes first appear. As the disease evolves, however, the EEG shows various changes, consisting of slowing and disorganization of the background, an asymmetry of the background activity, or both. These changes are followed by an increase in the slow-wave abnormalities, usually occurring in a diffuse manner but at times having a focal or lateralized emphasis and coinciding with the area of maximal neurologic involvement. In the later stages of the disease, polymorphic delta activity or intermittent frontal dominant monorhythmic slow-wave activity may be present. On occasion, there may be a transient flattening or attenuation of activity after the periodic complexes. Various types of epileptiform discharges, spikes, sharp waves, or spike-and-wave complexes occurring in a focal or generalized fashion also may be present. Patients who have a remission or an improvement in the clinical state show a corresponding improvement on the EEG.

The typical stages of sleep become less recognizable as the disease progresses, and identifiable sleep stages become limited to two main types. These are a low-voltage fast pattern with or without spindle activity and a high-voltage slow-wave pattern. In the later stages of the disease, sleep spindles, V waves, and K complexes disappear and the electroencephalographic differentiation of the various stages of sleep is no longer possible. The periodic complexes often persist during sleep, although their shape and frequency may be modified. On rare occasions, periodic complexes may be activated or occur predominantly during the sleep recording.

In the final stages of the disease, there is often a reduction in amplitude and abundance of the electroencephalographic activity and the recording may become almost isoelectric. In some instances, however, alpha activity may still be present shortly before death.

Although other entities may be associated with a periodic pattern, the stereotyped electroencephalographic complexes occurring in a regular and periodic fashion and having a constant relationship to motor movements make this pattern one of the most characteristic and specific of all electroencephalographic patterns. Close attention to the EEG and clinical features aid in the diagnosis of SSPE and distinguish it from other types of encephalopathies or disease entities.
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NONSPECIFIC ABNORMAL EEG PATTERNS

Electroencephalogram (EEG) abnormalities can be divided into three descriptive categories:

a) Distortion and disappearance of normal patterns,
b) Appearance and increase of abnormal patterns, and
c) Disappearance of all patterns.

The description of the above EEG abnormalities can be further expanded by identifying their spatial extent (local or widespread, unilateral or bilateral) and their temporal persistence (brief and intermittent or prolonged and persistent). The intermittent abnormalities characterized by the sudden appearance and disappearance of a pattern are called "paroxysmal."

The above classification of EEG abnormalities is purely descriptive. In addition to descriptive categorization, EEG abnormalities can be subdivided on the basis of their usual clinical correlations. Most abnormal patterns, whether persistent or intermittent, are nonspecific because they are not associated with a specific pathological condition or etiology. However, some patterns usually occurring paroxysmally with distinctive wave forms (such as spike, spike and wave, sharp wave, seizure pattern, or periodic complexes) are specific in that they are frequently associated with specific pathophysiological reactions (such as epilepsy) or a specific disease process (such as SSPE or Jakob- Creutzfeldt). This chapter will deal with the nonspecific abnormalities.

In spite of the fact that nonspecific abnormalities are not related to a specific pathophysiological reaction or a specific disease process, they nonetheless can be divided into three basic categories based on their usual association with different types of cerebral disturbances. These three basic categories are:

1. Widespread intermittent slow abnormalities, often associated with an active (improving, worsening, or fluctuating) cerebral disturbance;
2. Bilateral persistent EEG findings, usually associated with impaired conscious purposeful responsiveness; and
3. Focal persistent EEG findings, usually associated with focal cerebral disturbance.

The above divisions are based on the usual clinical correlates, but it is important to realize that these correlations are statistical and not absolute. The best intuitive grasp of the somewhat variable relationship between EEG abnormalities and clinical or other laboratory evidence of central nervous system (CNS) disturbance is obtained when the EEG is viewed as an extension of the neurologic examination. When viewed from this perspective, the EEG studies electrical signs of neurologic function, whereas the neurologic examination studies physical signs. In any one patient, depending on the nature and location of the pathology, abnormalities may be found in both EEG and clinical examination, in only one examination, or in neither, just as abnormalities may be found in one, both, or neither of two subsets on the clinical examination (such as reflex and sensory examination). Furthermore, the results of both EEG and clinical evaluation may be normal although the patient has anatomic abnormalities detectable by contrast studies or computerized tomography. The opposite also holds, in that both the EEG and clinical examination may show distinct abnormalities when radiographic studies are normal. An intelligent integration of the results of functional tests (such as the EEG and clinical examination) with radiographic tests which study anatomy (such as contrast studies or computerized tomography) requires an understanding of the value and limitation of each test, as well as the overall clinical field of neurology. With this conceptual background, nonspecific EEG abnormalities will be discussed based on the three general categories of clinical correlation.

WIDESPREAD INTERMITTENT SLOW ACTIVITY ASSOCIATED WITH AN ACTIVE CEREBRAL DISTURBANCE

- **Description**

  Morphologically, this type of abnormality is characterized by intermittent rhythmic slow activity often in the delta frequency range, thus accounting for its descriptive acronym, IRDA (intermittent rhythmic delta activity). When in the delta frequency range, it is often composed of runs of sinusoidal or sawtoothed waves with more rapid ascending than descending phases with mean frequencies close to 2.5 Hz. The waves are relatively stereotyped in form and frequency and occur in short bursts. This pattern usually demonstrates reactivity; it is attenuated by alerting and eye opening and accentuated with eye closure, hyperventilation, or drowsiness (stage 1, nonREM sleep). With the onset of stage 2 and deeper levels of nonREM sleep, the abnormal IRDA disappears. However, in REM sleep the abnormal IRDA may again become apparent.
Intermittent rhythmic delta activity is usually bilateral and widespread in distribution, with peak localization strongly influenced by age. In adults, the peak amplitude of the pattern is usually localized over the frontal area, thus giving rise to the acronym, FIRDA (frontal IRDA), whereas in children the peak amplitude frequently develops over the occipital or posterior head regions, giving the acronym, OIRDA (occipital IRDA). This difference in location from adults to children is not related to difference in pathological processes, but simply reflects an age-determined variation in what is an otherwise similar, nonspecific reaction to a wide variety of changing pathological processes.

**Etiologic Nonspecificity of IRDA**

IRDA is not specific for a single etiology and can occur in response to systemic toxic or metabolic disturbances as well as diffuse or focal intracranial diseases. This may be due to diverse etiologies, such as infectious, inflammatory, degenerative, traumatic, vascular, or neoplastic disorders.

IRDA is also the nonspecific type of slowing that occurs in normal individuals in response to hyperventilation. In such cases, it should not be interpreted as an abnormality, but rather as the response of a normal CNS to the stress of an acutely changing pCO.

**Nonlocalizing Nature of IRDA**

Since IRDA may occur in response to systemic toxic or metabolic disturbances, diffuse intracranial pathology, or focal intracranial pathology, its localizing value obviously is limited. Even when it is due to a focal expanding lesion, the peak localization of the IRDA tends to be age-dependent (maximal frontal in adults and maximal posterior in children). It is independent of the localization of the lesion, which may be at some distance, either in the supratentorial or infratentorial space, from the maximum expression of the IRDA. The recognition that IRDA is a nonlocalizing rhythm, even when associated with an intracranial lesion, led to its earlier designation as a "projected" or "distant" rhythm. Such a designation, however, can be misleading because it encourages the misconception that the IRDA, associated with a "distant" lesion, is morphologically distinct from IRDA due to diffuse intracranial disease or a systemic toxic or metabolic disturbance.

Although frequently bilateral, IRDA may occur predominantly unilaterally. Even when it occurs unilaterally in association with a lateralized supratentorial lesion, the lateralization of the IRDA, although usually ipsilateral, may even be contralateral to the focal lesion. Therefore, when IRDA is present, determining whether it is due to a focal lesion (and if so, the location of the focal lesion) is best based on persistent localizing signs discussed later and not on the morphology or even the laterality of IRDA.

**Mechanisms Responsible for IRDA**

The mechanisms responsible for the genesis of IRDA are only partially understood. Earlier studies investigated the mechanisms of IRDA-associated lesions producing increased intracranial pressure. It was recognized early that with benign intracranial hypertension (pseudotumor cerebri), IRDA was not present. However, in increased intracranial pressure with tumor or aqueductal stenosis, IRDA is frequently present. Based on this, earlier workers related the appearance of IRDA to increased intraventricular pressure within the third ventricle tending to produce an acute or subacute dilatation of the third ventricle. Later studies investigated the appearance of IRDA in diffuse encephalopathies with documented post mortem histopathological changes. Based on these studies, it was concluded that the main correlate of IRDA was diffuse gray matter disease, both in cortical and subcortical locations. Finally, any comprehensive theory about the origin of IRDA must not only take into account that IRDA is found in diverse systemic and intracranial processes, but must also take into consideration that IRDA is more likely to appear during the course of an active (fluctuating, progressing, or resolving) cerebral disturbance and less likely to be associated with a chronic, stable, cerebral...
disturbance. Clinically, the earliest correlate of the appearance of IRDA, especially in an otherwise normal EEG, is a subtle, fluctuating impairment of attention and arousal. As the condition progresses, often leading to more persistent, bilateral abnormalities, frank alteration in consciousness appropriate to the degree of persistent, bilateral abnormalities usually appear.

In summary, IRDA is nonspecific in that it can be seen in association with a wide variety of pathological processes varying from systemic toxic or metabolic disturbances to focal intracranial lesions. Even when associated with a focal lesion, IRDA by itself is nonlocalizing. The common denominator in the wide variety of pathological processes producing IRDA is that, when such an abnormality appears, it is likely to be associated with the development of widespread CNS dysfunction; the earliest clinical correlates are fluctuating levels of alertness and attention. With focal lesions, one mechanism may be an increased transventricular pressure with secondary disturbances at both the subcortical and cortical levels. With primary intracranial encephalopathies, it appears to be due to widespread involvement of the gray matter at subcortical and cortical levels.

**FOCAL PERSISTENT EEG FINDINGS ASSOCIATED WITH FOCAL CEREBRAL LESIONS**

As was done in the preceding section on bilateral persistent EEG findings, focal persistent EEG abnormalities can be divided into the following general descriptive types. These are a) distortion and disappearance of normal patterns, b) appearance and increase of abnormal patterns, and c) disappearance of all patterns.

There is some overlap in the first two types of abnormalities, since abnormal rhythms may be related to the distortion of previously recognized normal rhythms. Disappearance of all rhythms in a focal area can seldom be seen at the cerebral cortex, although they may be detected with electrocorticography.

The focal distortion of normal rhythms may produce an asymmetry of amplitude, frequency, or reactivity of the rhythm. Amplitude asymmetries alone, unless extreme, are the least reliable finding. Amplitude may be increased or decreased on the side of focal abnormality. However, if there is focal slowing of physiologic rhythms (for example, the alpha rhythm) by 1 Hz or more, this usually identifies reliably the side of focal abnormality, whether or not the amplitude of the rhythm is increased or decreased. The unilateral loss of reactivity of a physiologic rhythm, such as the loss of reactivity of the alpha rhythm to eye opening or to mental alerting, also reliably identifies the focal side of abnormality. Because of shifting asynchronies and asymmetries of the mu rhythm, the exact limits of normal asymmetry become more difficult to define; however, the asymmetrical slowing of the central mu rhythm by 1 Hz or more, usually associated with an increase in amplitude, is a reliable sign of focal abnormality often of a chronic nature.

In addition to the waking rhythms discussed above, the normal activity of sleep inducing spindles and vertex waves may be distorted or lost by a focal lesion in the appropriate distribution.

As normal rhythms are distorted, focal abnormalities may produce focal persistent polymorphic delta activity (PPDA), one of the most reliable findings of a focal cerebral disturbance. The more persistent, the less reactive, and the more polymorphic such focal slowing, the more reliable an indicator it becomes for the presence of a focal cerebral disturbance. Intermittent rhythmic delta activity (IRDA) may be seen with a focal cerebral disturbance but, as mentioned earlier, it is both nonspecific as far as etiology and nonlocalizing. When present in association with a focal cerebral lesion, it usually implies that the pathological process is beginning to produce an active cerebral disturbance of the type that is likely to become associated with changing (fluctuating or progressive) impairment of attention and alertness.

Focal epileptiform abnormality may occur in association with focal cerebral abnormalities, but since they have a relatively specific association with additional symptomatology such as epilepsy.

- **Etiologic Nonspecificity**

The above abnormalities do not reflect the underlying etiology but simply reflect that a pathological process is present. Similar abnormalities may occur, whether they result from focal inflammation, trauma, vascular disease, brain tumor, or almost any other cause of focal cortical disturbance, including an asymmetrical onset of CNS degenerative diseases.
In general, no matter what the etiology, there is a rough correlation between the EEG evidence of focal cerebral disturbance and clinical as well as radiographic evidence of focal cerebral disturbance. However, in spite of this rough relationship, there are striking examples of lack of correlation in both directions. Some of this lack of correlation is understandable. For instance, a small infarct in the internal capsule is likely to be missed both by radiographic studies and EEG studies, in spite of the fact that its presence may be readily detected by significant abnormalities on clinical examination. On the other hand, both the clinical examination and the EEG may be strikingly normal in spite of the fact that the computed tomography (CT, MRI) scan shows evidence of a well-described cystic or calcified lesion in the silent area of the brain, which may have been present in a relatively nonprogressive form for a long period of time. Finally, the EEG may show major abnormalities in spite of a normal clinical examination with positive CT findings, provided the lesion is in a clinically silent area, such as one temporal or frontal lobe. With a transient ischemic attack, it is common for the clinical examination, the radiographic studies, and the EEG to be normal within attacks. Nonetheless, in our experience, there are a small percentage of patients who have transient ischemic attacks likely on a hemodynamic basis, rather than on the more common embolic basis, who retain a major EEG abnormality in spite of the fact that their CT scan/MRI are normal and their neurologic examination has returned to normal after the transient attack. The exact mechanism responsible for this is uncertain, but it is interesting to note that another apparent hemodynamic cause of transient neurologic deficit in complicated migraine also may be associated with a marked residual EEG abnormality even when the neurologic examination has returned to normal and even when the CT scan is normal. Finally, it is not uncommon for the EEG to show clear-cut abnormalities and focal lesions without neurologic deficit without CT abnormalities when there is an associated epileptogenic process.

Chronic widespread hemispheric disease, such as Sturge-Weber syndrome or infantile hemiplegia, characteristically produces widespread voltage attenuation over the abnormal hemisphere. In one study, this electrographic accompaniment was seen in every patient with Sturge-Weber disease even when there was no associated focal neurologic deficit. These asymmetries were noted even in young children prior to the development of the characteristic intracranial calcifications. Finally, local contusion or inflammatory disease may produce a dramatic and marked EEG change without CT accompaniment and with or without accompanying focal clinical deficit, depending on the location and intensity of the abnormality. However, even when the EEG picks up subclinical abnormalities not associated with roentgenographic changes, the abnormalities in general are quite nonspecific and require close correlation with the clinical history and other information before arriving at a specific diagnosis.

Mechanisms Responsible for EEG Findings Associated With Focal Cerebral Disturbance

In the absence of a clear-cut understanding of the mechanisms responsible for the generation of normal EEG activity, an accurate explanation of how focal cerebral disturbances result in distortion in the amplitude, frequency, and reactivity of normal scalp-recorded rhythms is not possible. However, in general, these distortions occur because focal abnormalities may alter the interconnections, number, frequency, synchrony, voltage output, and axis orientation of individual neuronal generators, as well as the size and location and integrity of the cortical area containing the individual generators giving rise to the total signal ultimately detected on the scalp.

There is general agreement among various workers that focal pathology in the underlying white matter is commonly associated with PPDA. In these cases, it is postulated that the white matter lesions produce PPDA by deafferenting the overlying cortex from its underlying white matter input. If so, this theory could also be extended to explain focal PPDA occurring post-ictally. Although it would not be reasonable to explain post-ictal focal PPDA on the basis of a primary white matter disturbance, it is reasonable to assume that the postictal state, either by exhaustion or inhibition, may functionally deafferent the cortex from its underlying white matter input. Finally, even if deafferentation of the cerebral cortex from its underlying white matter is the primary mechanism responsible for PPDA, whether focal or generalized, additional factors such as the acuteness or changing nature of the deafferentation would have to be postulated as an additional important factor, inasmuch as PPDA is more commonly associated with acute, active disturbances and less commonly seen in chronic, stable disturbances.
References

ROLE OF EEG IN NEONATAL SEIZURES

Generalized seizures are rare in neonates. Many of the so-called subtle, generalized tonic, and multifocal myoclonic seizures do not have an EEG correlate. These movements in the severely affected infant may represent brain stem release phenomena. Focal seizures, particularly clonic seizures, are highly associated with EEG changes. Thus EEG plays a crucial role in the evaluation of neonatal seizures. The EEG changes significantly with gestational age; therefore, calculation of gestational age and familiarity with age-specific norms is crucial in the interpretation of the EEG in infants.

There are 2 well-defined EEG seizure patterns seen in neonates. They include the following:

- Seizures with focal low frequency electrographic correlates - These may occur at 1-1.5 Hz frequency and are generally seen in severe cerebral insults, such as severe hypoxic-ischemic encephalopathy.
- Seizures with focal high frequency electrographic correlates - Typically evolve over 10-20 seconds and are usually seen with focal cerebral insults, such as strokes. Strokes in the neonate, unlike in the older individual, are typically associated with porencephalic cysts. Porencephalic cysts result from strokes that involve large portions of the cerebral parenchyma (i.e. loss of both gray and white matter leading to a communication between the subarachnoid space and the cerebral ventricles).

INFANTILE SPASMS & WEST SYNDROME

West syndrome is a triad of infantile spasms, developmental retardation or regression, and hypsarrhythmia on EEG. The syndrome presents between 6-18 months of age. Presence of a hypsarrhythmic EEG is diagnostic of infantile spasms. EEG patterns may evolve over a period; they initially appear in the sleep EEG record and subsequently present during the awake state. Hypsarrhythmia is seen in 75% of patients with West
Hypsarrhythmia consists of diffuse giant waves (high voltage >400 microvolts) with a chaotic background of irregular, multifocal spikes and sharp waves. There is very little synchrony between the cerebral hemispheres. During sleep the EEG may display bursts of synchronous polyspikes and waves. There may be a pseudoperiodic pattern. Persistent slowing or epileptiform discharges in the hypsarrhythmic background may be present and may represent an area of focal dysfunction. There may be several variations to the hypsarrhythmic pattern, which are referred to as hypsarrhythmic variants.

Clinical spasms are associated with a marked suppression of the background that lasts for the duration of the spasm. This characteristic response is called the "electrodecremental response."

EEG is useful in judging successful treatment of West syndrome. Typically, shortly after treatment with ACTH or vigabatrin is initiated, the spasms stop and hypsarrhythmia disappears.

Hypsarrhythmia rarely persists beyond the age of 24 months. It may evolve into the slow spike and wave discharges seen in Lennox-Gastaut syndrome.

**Definition of Hypsarrhythmia**

- The word Hypsarrhythmia is originally derived from the Greek word hypsolos which means high and it refers to high voltage arrhythmia with a disorganized EEG pattern that consists of chaotic admixture of continuous, multifocal, high amplitude spikes, polyspikes, sharp waves and arrhythmic slow waves. This EEG pattern is dynamic and highly variable from one patient to another and between one study and another study for a single patient. Background activity is often disorganized with frequent slow wave activity.

- Marked change in the Hypsarrhythmia pattern also occurs during sleep. In REM sleep there is marked reduction to total disappearance of this EEG pattern. There is also normalization of this discharge pattern immediately following awakening from sleep.

- This discharge pattern is seen in children between the age of 4 months to 4 years and after the age of 4 years this pattern of discharge usually merges into the slow spike/slow wave complexes.

- Hypsarrhythmia pattern is frequently equated with infantile spasm (West syndrome), (characterized by massive flexion myoclonus of the head and neck called jack-knifing or Salaam attacks), however this pattern is not specific to any disease entity and is seen in response to any severe cerebral insult or severe multifocal disease process that occurs below the age of 1 year.

- Five different types of Hypsarrhythmia are present

  1. Hypsarrhythmia with increased interhemispheric synchronization.
  2. Asymmetrical Hypsarrhythmia.
  3. Hypsarrhythmia with a constant focus.
  4. Hypsarrhythmia with episodes of voltage attenuation.

**LENNOX-GASTAUT SYNDROME (LGS)**

Lennox-Gastaut syndrome is a childhood (onset 3-5 years) epileptic encephalopathy that manifests with atonic seizures, tonic seizures, and atypical absence seizures associated with mental retardation and a characteristic EEG pattern. Infantile spasms and West syndrome frequently transform into LGS. Unlike West syndrome, LGS tends to be a lifelong epileptic encephalopathy.
EEG shows an abnormally slow background and diffuse slow spike and slow wave (<2.5 Hz) activity. The slow spike and wave activity serves to differentiate (poor-prognostic) LGS from absence epilepsy, in which diffuse 3Hz spike and wave of benign absence is seen and the fast spike and wave (>2.5 Hz) activity often seen with some of the more benign myoclonic types of epilepsy. Prognosis of fast and slow spike and wave activity is dramatically different; it is poor for slow spike and wave activity seen in LGS. Many epilepsy syndromes overlap with LGS, including myoclonic astatic epilepsy of Doose and other severe myoclonic epilepsies.

EEG features of LGS may be divided into interictal and ictal.

- **Interictal EEG features** - Background slowing and diffuse slow spike and wave lasting from several minutes to a near continuous state are characteristic. Duration of epileptiform discharges tends to correlate with epilepsy control, with shorter durations occurring in patients with better control of seizures. Spikes, or more commonly sharp waves, are typically 200 milliseconds in duration and are followed by slow waves. Polyspike discharges are seen in those epilepsy variants with prominent myoclonic seizures or during non-REM sleep. (click here to know more about EEG in Lennox-Gastaut syndrome)

- **Ictal EEG features** - Electrographic accompaniment varies with the seizure type.

**Electroclinical criteria of the slow 1-2.5c/s spike/wave discharge**

- This EEG pattern is bilateral but asymmetrical and asynchronous with frequent lateralization and focalization.
- It has a frontal midline maximum.
- It is frequently continuous without any definite onset or offset and might extend through the whole record and is not associated with any clinical accompaniment.
- The discharge is not activated by hyperventilation
- The 1-2.5 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 6 months (earlier than the 3 c/s SWD) and disappear at the age of 16 years and is replaced by anterior temporal sharp activity and the clinical seizure manifestations merge into the main stream of temporal lobe epilepsies
- Background activity is often disorganized with frequent slow wave activity.
- The clinical correlate of this discharge is Lennox-Gastaut syndrome with multiseizure clinical presentation (grand mal fits, atonic fits, akinetic fits, atypical absence attacks, absence status). The occurrence of two or more than two types of seizures is almost the rule, mental retardation is very common.
- This discharge pattern could be idiopathic of genetic origin, cryptogenic with no overt cause, or symptomatic to a variety of brain diseases that include CNS infection, birth trauma, lipidosis, tuberous sclerosis, etc.

**JUVENILE MYOCLONIC EPILEPSY (JME)**

JME is the most common epilepsy syndrome presenting with generalized tonic-clonic seizures between 12-30 years in a patient who is otherwise neurologically normal. It may account for up to 10% of all patients with epilepsy. Imaging studies are normal. In susceptible persons, sleep deprivation often precipitates seizures.

Typically, the patient may experience myoclonic jerks in the morning, although many patients do not mention that they are having myoclonic
Approximately 15% of patients have associated juvenile absence epilepsy or generalized tonic-clonic seizures upon awakening. Often the diagnosis is not made in a definitive fashion, which is unfortunate, since a correct diagnosis helps guide management, which, in turn, affects prognosis as the drugs used in this entity differ from those used in most other seizure types.

**EEG**

Interictal EEG shows a normal background with frequent generalized polyspike and wave discharges that may be anteriorly dominant or diffuse. Polyspike and wave discharges by definition have at least 3 spike-like components in them. Photosensitivity is present in at least 30% of patients. Photic stimulation, commonly at a frequency of 10-20 Hz, will elicit a photoparoxysmal response in at least 30% of patients.

**Electroclinical criteria of the fast 4-6 c/s spike/wave discharge**

- This discharge occurs in patients older than 16 years.
- It is bilateral but less symmetrical and synchronous compared with the 3 c/s SWD and usually takes the morphological feature of polyspike wave discharge.
- It has a frontal midline maximum.
- It has a sudden onset and sudden offset and lasts for a very short periods (usually less than 3 seconds).
- This discharge pattern is not activated hyperventilation, however phobic stimulation is a potent activator of this discharge pattern.
- The clinical correlate of this discharge pattern is myoclonus and grand mal fits (juvenile myoclonic epilepsy).
- Studies using video monitoring combined with EEG recording revealed that the spike components of this discharge coincide with the myoclonic jerks and the slow waves coincide with periods of relaxation between the myoclonic fits, accordingly the number of spikes in this polyspike/wave complexes were found to be proportional to the severity of the myoclonic fits.
- The fast spike/wave complexes of juvenile myoclonic epilepsy has a strong genetic background. The gene locus was mapped on the short arm of chromosome 6.
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AGE DEPENDENT EPILEPTIC SYNDROMES [PART I]

The age of the patients has great influence on the ictal, clinical and EEG characteristics of the epileptic seizures disorders and it also determines the course and prognosis of epilepsy in general. This is particularly true in the first two decades of life, especially for infancy and early childhood. There are certain age- determined epileptological entities or epileptic conditions which appear to be monolithic, in spite of a wide variety of etiologies and probably also despite variations in the localization of cerebral involvement. The role of age in epileptic seizure disorder has been substantiated by experimental work and clinical electroencephalographic investigations. We find in age-determined epileptic conditions a) certain condition-related types of seizures, b) certain condition-related EEG patterns, and c) certain condition-related characteristics of course and prognosis.

In the past, this aspect of epileptic seizure disorder had been neglected; too much emphasis was universally placed on locus and cause of the seizure. From the historical viewpoint, the description of infantile spasm and the discovery of a specific EEG pattern called hypsarrhythmia mark the first individualization of an age-determined polyetiological epileptic condition with certain clinical-electroencephalographic criteria. There is a long historical evolution of the very common condition known as febrile convulsions. The clinical picture of benign Rolandic epilepsy became clear due to the efforts of numerous authors. Neonatal convulsions, which are a particularly heterogeneous group, must also be listed in this context and the thought-provoking notion of primary generalized epilepsy also belongs in this category.

**Figure 1. The course of various age-dependent epileptic seizure disorders in a longitudinal view.**

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<th>0-3 months</th>
<th>4-24 months</th>
<th>2-5 years</th>
<th>6-10 years</th>
<th>11-15 years</th>
<th>16-20 years</th>
<th>21-30 years</th>
<th>above 30 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNCB</td>
<td>0-3 months</td>
<td>Often seizure free</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NNCS</td>
<td>0-24 months</td>
<td>Conversion to (IS) and/or (LGS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>IS</td>
<td>4 months-5 years</td>
<td>Conversion to (LGS)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>FC</td>
<td>4 months-5 years</td>
<td>Often seizure free</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LGS</td>
<td>4 months-30 years</td>
<td>TLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PGE 1</td>
<td>Often febrile convolution</td>
<td></td>
<td>2 years-20 years</td>
<td>11 years-30 years</td>
<td>Often seizure free</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PGE 2</td>
<td></td>
<td>2 years-10 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRE</td>
<td></td>
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</tr>
</tbody>
</table>

**Table 1. Comparison between the classical age-dependent generalized epileptic EEG discharge.**

<table>
<thead>
<tr>
<th>EEG TYPE</th>
<th>AGE</th>
<th>CLINICAL CORRELATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical 3 c/s SWD</td>
<td>3.5 years -16 years</td>
<td><strong>Petit mal epilepsy</strong></td>
</tr>
<tr>
<td>Slow SWD (1-2.5 c/s)</td>
<td>6 months -16 years</td>
<td><strong>Lennox-Gastaut syndrome</strong></td>
</tr>
<tr>
<td>Fast SWD (4-6 c/s)</td>
<td>Over 16 years</td>
<td><strong>Juvenile myoclonic epilepsy</strong></td>
</tr>
<tr>
<td>Hypsarrhythmia</td>
<td>4 months -4 years</td>
<td><strong>West syndrome</strong></td>
</tr>
</tbody>
</table>
NEONATAL CONVULSIONS

- Introductory Remarks

In the neonatal period of life, epileptic seizures are fairly common and may be caused by a wide variety of etiologies. There is some reason to presume that neonatal convulsions play a greater role in the lives of full-term infants than in premature infants, notwithstanding the high risk of brain damage caused by prematurity. The neonatal period may be extended to the first 3 mos of life by some, while holders of a stricter view limit this period to the first 3 wk. Neonatal convulsions are common; their prevalence may range from 0.2% to 1.2% of all live births. Tonic seizures are also quite common; they consist of opisthotonus, extension or elevation of limbs, and, often, rotation of head and eyes. "odd movements" of the limbs (swimming or rowing movements), chewing, eye blinking, opening of eyes, nystagmus, and an abnormal cry are also among the clinical manifestation of neonatal seizures. Episodes of apnea may be ictal or nonictal. Neonatal seizures are divided into a) tonic, b) clonic, c) atonic, d) autonomic, and e) automatism-like seizures.

- Clinical Ictal Manifestations of Neonatal Seizures

At this early age, convulsive movements are not easily distinguished from physiological motor activity, this is particularly true for seizures in premature infants with barely recognizable convulsive movements. Combined video recording and tele-encephalographic documentation has been helpful in the distinction of physiological and convulsive motions.

Organized tonic-clonic sequences of the grand mal type do not occur in the first 4 to 6 mos of patient's life and are precluded by the lack of cerebral maturation in terms of myelination. Poorly organized tonic-clonic attacks may occasionally occur in neonates. Clonic seizures may begin in any part of the body and progress from one region to another in an irregular fashion. Spread often remains ipsilateral although full-blown hemiconvulsions are not encountered. Clonic movements may remain localized throughout the seizure.

Seizures Versus Status Epilepticus in the Neonate

Neonatal seizures are often unusually prolonged or consist of a seemingly endless succession of seizures with brief inter-ictal interval. For this reason, the term "neonatal status epilepticus" has been used frequently. It simply appears to be the nature of severe neonatal convulsions to show status-like character. The convulsions themselves do not reach the degree of severity found in status epilepticus of a more mature age, especially grand mal status. The severity of the clinical condition lies in the disorder which causes the seizures rather than in the seizure as such.

- EEG Findings

In milder forms of neonatal convulsions (benign forms), chances are that the recording is obtained in the interictal state and the record shows no significant abnormalities.

In severe forms, ictal EEG abnormalities are the rule. Two types of ictal EEG changes ought to be distinguished. These are 1) repetitive long stretches of rhythmical spiking, often in the disguise of rhythmical slow activity with a disguised spike component often varying the frequency of ictal firing, ranging from alpha frequency down to the low delta range, and 2) a very irregular pattern with widespread nearly flat stretches and irregularly mixed bursts, of high voltage slow activity, with waves in the medium and fast range, and massive spikes or sharp waves.

The first pattern described is more often noted. Its character is essentially multifocal. The onset of an attack is practically always focal. The occipital and central areas are the most common sites of focal ictal spiking, whereas the frontal and temporal areas are less often involved. The temporal region is the most frequent site, followed by the occipital region. The ictal discharge in the newborn generally remains localized to one hemisphere, it may spread slowly to involve the entire hemisphere or the entire contralateral hemisphere rather than spreading to the opposite side as it is often observed in adult seizures.

There are no firm electro-clinical correlations, although it has been thought that clonic movements more often occur with spikes and tonic phenomena, with delta discharges. Swimming or rowing movements or tonic spasms are sometimes associated with artifact-disturbed stretches of low voltage.

For the novice in neonatal EEG recording, the rhythmical slow or spike activity in an ictal episode appears to be "unreal" and hence artifactual, since the type of discharge is hardly ever seen at other periods of life.

As to the second pattern described above, no rhythmical spiking is noted; irregular bursts, often asynchronous, and interspersed nearly flat stretches dominate the picture. Generalized synchronous bursts are essentially alien to neonatal convulsions and only faint suggestions of such bursts may materialize. The accompanying ictal clinical manifestations are usually short tonic spasms or short myoclonic jerks. The entire pattern represents a foretaste of hypsarrhythmia; it is present with little or no interruption for weeks and tends to convert into full-blown hypsarrhythmia. This occurs usually between the ages of 4 and 6 (or 3 and 5) mos when the voltage output reaches the typical high amplitudes of hypsarrhythmia.

In very severe forms of neonatal seizure disorder, the newborn shows an almost flat record in spite of numerous convulsive activities. This may be observed in neonatal herpes simplex encephalitis; the nearly flat character is prognostically ominous, although the infant will gradually show increasing voltage output and a more customary EEG type of neonatal convolution.
The interictal EEG depends heavily on the general state of the body, especially on the level of consciousness. Preserved consciousness with an "alert look" was found in 30% of the infants despite repetitive convulsions. The EEG may show ictal-subclinical patterns. Otherwise, the record usually lacks the typical interictal finding of random spikes or shows such spikes in an attenuated form only. There is no evidence that a particular state of sleep facilitates or depresses seizures; a low percentage of active REM sleep, 22-30% compared with 40-60% in normal newborns, has been reported.

Aetiological Considerations

The prognosis of neonatal convulsions depends heavily on its cause and the type of underlying pathology. This sets neonatal convulsions apart from other age-determined epileptic conditions, in which the etiology is usually less important than the epileptic condition as such. Causes range between extracranial infection (mainly gastroenteritis with dehydration and pneumonia), structural noninfectious brain damage (asphyxia for example) and metabolic disorder. It has to be kept in mind that structural brain damage from cerebral malformations, asphyxia, or birth injury manifests itself in the first few days of life, as opposed to seizures due to infections, which are more apt to occur after the first week. Hypocalcemia in the first week of life is usually a more serious cause of convulsions than hypocalcemia of the second week, which is due to dietary problems. Idiopathic infantile hypoglycemia has a very poor prognosis. In this EEG-oriented presentation, the multitude of causes can not be presented in detail.

Therapy and Prognosis

Anticonvulsant treatment is essentially based on phenobarbital (im or orally, 2 mg/kg within 24 hr); the use of adjuvants cannot be discussed in this context.

The immediate or short-range mortality of neonatal convulsions is considerable and may reach 54%. The long-range prognosis is good only for the benign forms of neonatal convulsions, usually caused by extracranial infections and milder forms of metabolic disturbances. Mild to moderate infections with meningeal more than encephalitic involvement also suggest a good prognosis. Next come the more serious CNS infections, while very severe and very early CNS infection, and some very damaging metabolic disturbances are most likely to result in "malignant" forms of neonatal convulsions, followed by either fatal outcome or severe CNS residues with mental retardation.

The EEG in the acute convulsive state has proved to be very helpful. 86% of the infants with normal neonatal EEG were normal at a mean age of 4 yr, whereas 69% of those with unifocal EEG abnormalities and 11.8% of those with multifocal EEG abnormalities were normal at a mean age of 4 yr.

INFANTILE SPASM (HYPSARRHYTHMIA)

Historical Remarks

Infantile spasms consist of sudden tonic and myoclonic phenomena. The term "infantile spasms" is quite satisfactory from the clinical viewpoint and should be preserved. "Hypsarrhythmia" is an EEG term which denotes the EEG correlate of the condition and has found surprisingly wide acceptance with clinicians; a clinical term such as infantile spasms is certainly preferable as far as the clinical condition as such is concerned.

Age

Infantile spasms are found in the age range from 4 to 30 mos; earlier and later occurrences of the condition are exceptional. This age range is particularly valid when one looks upon this condition from the combined clinical-electroencephalographic viewpoint. Then it becomes clear that a truly hypsarrhythmic EEG pattern does not develop before age 4 mos, although at 3 mos a very similar EEG picture may be present already. From a purely clinical viewpoint, one could define infantile spasms as beginning right after birth. The hypsarrhythmic pattern tends to develop out of the irregular pattern with bursts and flat stretches in neonatal convulsions as mentioned in the preceding section.

The end of the period of infantile spasms essentially parallels the disappearance of the hypsarrhythmic pattern; this usually occurs in the second half of the third year of life. In exceptional cases, the pattern may linger on for a year or even longer (up to 8 yr).

Clinical ictal Manifestations

Both clonic and tonic phenomena may occur in infantile spasms. The most common type is a massive flexion myoclonus of head, trunk, and extremities, known as "jackknifing." The lightning-like character of this sequence of movements permits an exact analysis only with the use of videotape documentation. The tonic phenomena are slower and may last 2 to 5 see with accompanying autonomic changes such as flushing or lacrimation.

The clonic spasm may show some variation. Instead of abduction of the extremities, adduction may occur to such a degree that the infant appears to be embracing himself, whereas the abduction pattern seems to simulate the Moro reflex. Extensor spasms are also observed; there is sudden extension of neck and trunk with symmetrical forward extension and extension of lower extremities at the hips and knees ("cheerleader spasm"). Head nodding may also occur.

The ictal manifestations of infantile spasms are short but tend to repeat themselves in rapid succession. Unilateral spasms have been described. Up to several hundred or even several thousand spasms per day may occur.
Clinical Signs of Nonictal Character

The general clinical picture of the baby depends on the degree of accompanying brain damage. A sizable number of infants with infantile spasms and hypsarrhythmia (about one-third) are brain damaged from birth; many of them have passed through a period of severe neonatal convulsions. Severe cerebral malformations or CNS infections are common causes in such cases. Signs of cerebral palsy in its various forms may be demonstrable.

In many other cases, infantile spasms suddenly start in a previously healthy baby and, at that time, the hypsarrhythmic EEG pattern is already present. When untreated, the psychomotor development of the infant shows signs of retardation starting with the onset of attacks.

EEG Findings

The EEG findings are quite unique and essentially unmistakable, although there is a certain gray zone of questionable or borderline cases. The term hypsarrhythmia is derived from the Greek word "hypselos," which means "high," thus indicating the high voltage which generally predominates. No hypsarrhythmic recording can be appropriately obtained with the standard sensitivity of the EEG apparatus; lowering the sensitivity is required. Bursts of very high voltage slow waves occur in irregular fashion with a varying degree of bilateral synchrony which usually increases in sleep. The stages of early nonREM sleep are particularly conducive to a typical hypsarrhythmic recording. Long stretches of high voltage slow and intermixed spike activity may suddenly be interrupted by a brief stretch of near flatness in all leads, or less commonly near flatness in a few leads or over one hemisphere; these flat stretches are practically limited to sleep tracings.

The spike activity shows single spikes and sharp waves, as well as very brief sequences of polyspikes which are usually of smaller amplitude. The spike activity is almost always of posterior accentuation. The posterior maximum of spike activity is quite helpful in differentiation from the Lennox-Gastaut syndrome, which sometimes starts exceptionally early (i.e., between the ages of 6 and 12 mos), when one usually sees the onset and evolution of infantile spasms with hypsarrhythmia. Large slow spike waves of frontal accentuation are found in babies with the Lennox-Gastaut syndrome. This unfortunately barely known distinction helps clarify the differentiation of these two conditions.

The ictal EEG, the concomitant of infantile spasms, is quite variable. Fast activity and high voltage spikes may accompany the attacks, polyspikes and slow waves may be present, no change of the hypsarrhythmic interval EEG may occur, but, most commonly, a sudden suppression of the EEG activity may be seen for several seconds. A sleep recording is a necessity since, in some cases, the waking record may be unreadable while hypsarrhythmia is confined to the sleep portion.

Hypsarrhythmia is almost but not always a reliable EEG correlate of infantile spasms. There are clinically convincing cases with no hypsarrhythmia, but in these rare exceptions the voltage output is unusually high. Unless there is a rapid response to treatment, the hypsarrhythmic pattern is likely to appear in the further course of such infants.

On the other hand, the clinician could be the one to be blamed when the expected hypsarrhythmia is not found; his presumptive diagnosis may be wrong. The clinical differential diagnosis of infantile spasms or hypsarrhythmia includes a variety of conditions:

- Spasmus nutans: EEG normal
- Jactatio capitis nocturna: EEG normal
- Salaam tic or "salutatory" spasms (Moro): Nonspecific EEG abnormalities sometimes with spikes in combination with epileptic seizures, but no hypsarrhythmia
- Myoclonic encephalopathy: EEG normal

Aetiological and Neuropathological Considerations

The etiologies are divided into the idiopathic group and the symptomatic group. There is general consensus among investigators that the symptomatic group with known neurological disease or evidence of any kind of brain damage is the larger one. The ratio is approximately one-third of cases with idiopathic forms to two-thirds with symptomatic forms. Computerized tomography can detect structural anomalies in cases which might have been diagnosed as idiopathic in earlier years.

The number of etiological factors is enormous. Traumatic or asphyxic perinatal brain damage may lead to cerebral palsy associated with hypsarrhythmia; many developmental and congenital CNS anomalies may lead to this condition, with tuberous sclerosis as a more common cause. Inborn errors of metabolism and post-infectious states must also be mentioned. The idiopathic form with no evidence of structural brain damage remains an enigma. This form was conceived as a nosological entity ("infantile myoclonic encephalopathy"), but this concept has not found general approval. Familial occurrence is not common, but certainly not negligible; it ranges from 3 to 6%.

The Aicardi Syndrome as a Special Form of Infantile Spasm

This syndrome consists of infantile spasms (flexor spasms), agenesis of the corpus callosum, and chorioretinal anomalies. The cause has remained obscure and the nature of this syndrome is poorly understood. The EEG shows hypsarrhythmia in some of these patients. Some of the hypsarrhythmic records showed remarkable asymmetries. Even the flexor spasms were often asymmetrical or limited to one-half of the body.
Pathogenetic Concepts

Infantile spasms with hypsarrhythmia (West syndrome) are now listed as "secondary generalized epilepsy," in company with the Lennox-Gastaut syndrome and specific epileptogenic encephalopathies, such as essential, hereditary myoclonus epilepsy or Tay-Sachs disease. This implies that there must be a primary focus which is eventually superseded by generalization of the EEG phenomena as well as the clinical manifestations, which are void of any specific focal character.

This basic concept of secondary generalization is not proven, although many of these cases show focal structural lesions. One could speculate, however, that a special genetic component predisposes certain infants to this type of epileptic reaction. Thus, a case of cerebral palsy may be accompanied by any type of epileptic seizure or infantile spasms-hypsarrhythmia if a special genetic predisposition is present.

Therapy and Prognosis

The goals of pharmacotherapy are to reduce morbidity and prevent complications. Infantile spasms used to be regarded as therapeutically hopeless in view of the poor response to the classical anticonvulsants, such as phenobarbital and diphenylhydantoin. The observation of an excellent response to ACTH represents one of the most important steps forward in the history of modern anticonvulsive therapy.

The EEG shows almost immediate improvement under effective therapy. This does not necessarily reflect clinical improvement. Complete normalization may occur, but such responses are mostly temporary; return of spike activity, mostly over posterior regions, is a common event.

In many cases with poor therapeutic response and especially in those with preexisting brain damage and history of neonatal convulsions, transition into the Lennox-Gastaut syndrome is common.

References


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AGE DEPENDENT EPILEPTIC SYNDROMES [PART 2]

The age of the patients has great influence on the ictal, clinical and EEG characteristics of the epileptic seizures disorders and it also determines the course and prognosis of epilepsy in general. This is particularly true in the first two decades of life, especially for infancy and early childhood. There are certain age- determined epileptological entities or epileptic conditions which appear to be monolithic, in spite of a wide variety of etiologies and probably also despite variations in the localization of cerebral involvement. The role of age in epileptic seizure disorder has been substantiated by experimental work and clinical electroencephalographic investigations. We find in age-determined epileptic conditions a) certain condition-related types of seizures, b) certain condition-related EEG patterns, and c) certain condition-related characteristics of course and prognosis.

In the past, this aspect of epileptic seizure disorder had been neglected; too much emphasis was universally placed on locus and cause of the seizure. From the historical viewpoint, the description of infantile spasm and the discovery of a specific EEG pattern called hypersynchrony mark the first individualization of an age-determined polyetiological epileptic condition with certain clinical-electroencephalographic criteria. There is a long historical evolution of the very common condition known as febrile convulsions, the clinical picture of benign Rolandic epilepsy became clear due to the efforts of numerous authors. Neonatal convulsions, which are a particularly heterogeneous group, must also be listed in this context and the thought-provoking notion of primary generalized epilepsy also belongs in this category.

Figure 1. The course of various age-dependant epileptic seizure disorders in a longitudinal view.

| NNCB | 0-3 months | Often seizure free |
| NNCS | 0-24 months | Conversion to (IS) and/or (LGS) |
| IS | 4 months-5 years | Conversion to (LGS) |
| FC | 4 months-5 years | Often seizure free |
| LGS | 4 months-30 years | TLE |
| PGE 1 | Often febrile convulsion | 2 years-20 years |
| PGE 2 | | 11 years-30 years |
| BRE | 2 years-10 years | Often seizure free |

NNCB=neonatal convulsion, benign; NNCS= neonatal convulsion severe; IS= infantile spasm; FC =febrile convulsion; LGS= Lennox-Gastaut syndrome; PGE 1= primary generalized epilepsy with absence attacks; PGE2= primary generalized epilepsy with myoclonic attacks; BRE= benign Rolandic epilepsy, TLE = temporal lobe epilepsy.

Table 1. Comparison between the classical age-dependant generalized epileptic EEG discharge.

<table>
<thead>
<tr>
<th>EEG TYPE</th>
<th>AGE</th>
<th>CLINICAL CORRELATE</th>
</tr>
</thead>
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<td>Classical 3 c/s SWD</td>
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<td>Petit mal epilepsy</td>
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<tr>
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<td>6 months-16 years</td>
<td>Lennox-Gastaut syndrome</td>
</tr>
<tr>
<td>Fast SWD (4-6 c/s)</td>
<td>Over 16 years</td>
<td>Juvenile myoclonic epilepsy</td>
</tr>
<tr>
<td>Hypsarrhythmia</td>
<td>4 months -4 years</td>
<td>West syndrome</td>
</tr>
</tbody>
</table>
FEBRILE CONVULSIONS

- **Introductory Remarks, Age and Definition**

This condition is probably the most common epileptic seizure disorder; about 3–4% of all children have at least one febrile seizure in infancy or early childhood. The attacks tend to occur between the ages of 6 mos and 5 yr, especially between 6 mos and 3 yr. The onset falls into the range of 6 to 24 mos. It is unwise to call fever-induced convulsions after the age of 4 yr “simple febrile convulsions.”

Febrile convulsions must be strictly separated from epileptic seizures in infants or children with an acute severe febrile disease giving rise to structural lesions. The differences are indicated in Table 2. Lumping together both groups would tarnish the predominantly excellent diagnosis of simple febrile convulsions.

- **Clinical Manifestations**

Simple febrile convulsions represent a tonic-clonic seizure, essentially an infantile version of a grand mal attack. Some degree of lateralization may be present, but a strict hemiconvulsion or focal-motor type of seizure would militate against the assumption of a febrile convulsion. Most of these infants and children have two attacks; many have one or more seizures in the course of a few years.

- **EEG Findings**

Ictal EEG tracings are hard to obtain in a truly simple febrile convulsion; grand mal-like EEG changes are most likely to occur. Tracings obtained in the hospital in the acute febrile state with convulsions show severe lateralized EEG changes, but these cases are most likely to fall into the category of epileptic seizures in infants with acute structural lesions.

In the interictal stage, the records are usually normalized and one seldom encounters abnormal tracings. When sedation is used, one is very often surprised to see the very large amount of sedation-induced fast activity, even using chloral hydrate, short spike wave-like bursts in drowsiness and sleep may occur (“pseudo petit mal discharge”). The most common site was the occipital lobe and, in 88%, the spike focus disappeared within 3 yr. This was often followed by the appearance of a spike wave focus.

Abnormal interictal tracings are likely to indicate underlying cerebral impairment with paroxysmal properties; these infants might be candidates for a febrile epileptic manifestation (i.e., for a chronic epileptic seizure disorder) in the future. The prognosis for these children is mostly favorable.

- **Etiological and Pathophysiological Considerations**

A genetic predisposition to febrile convulsions is indubitable. The seizure-precipitating action of hyperthermia is not yet fully understood. The limitation of this action to infancy and early childhood is particularly enigmatic. Brisk changes of the water and electrolyte balance may play an important part.

Table 2. Differences between Febrile convolution and Seizures during febrile brain disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Febrile convolution</th>
<th>Seizures during febrile brain disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical age</strong></td>
<td>6 months–3 years</td>
<td>0–3 years</td>
</tr>
<tr>
<td><strong>Genetic</strong></td>
<td>strong</td>
<td>None</td>
</tr>
<tr>
<td><strong>Type of seizure</strong></td>
<td>tonic-clonic</td>
<td>Tonic-clonic or hemiconvulsion</td>
</tr>
<tr>
<td><strong>Duration of seizure</strong></td>
<td>1–3 minutes</td>
<td>Prolonged, 10 minutes to hours or status epilepticus</td>
</tr>
<tr>
<td><strong>Clinical setting</strong></td>
<td>At the onset of fever, mostly due to upper respiratory tract infection, often coinciding with the first sharp rise of temperature</td>
<td>Mostly due to CNS infection or cerebrovascular accident of infancy</td>
</tr>
<tr>
<td><strong>Cerebral pathology</strong></td>
<td>None</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Post-ictal deficit</strong></td>
<td>None</td>
<td>Common</td>
</tr>
<tr>
<td><strong>EEG</strong></td>
<td>Rapidly normalize after convulsion, with normal interictal pattern in over 90% of cases</td>
<td>Abnormal during convulsion and interictally</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td>Not necessary (neither during the acute convulsion nor for prevention of future convulsion)</td>
<td>Often needed</td>
</tr>
<tr>
<td><strong>Prognosis</strong></td>
<td>Good, occasionally progress to primary generalized epilepsies</td>
<td>Guarded, non febrile seizures are common, occasionally progress to temporal lobe epilepsy</td>
</tr>
</tbody>
</table>

In addition to trivial upper respiratory tract infections, there are some diseases of infancy of potentially epileptogenic character. The mild and short-lasting roseola infantum (exanthema subitum) is quite often associated with convulsions of infancy and early childhood. The question
remains as to whether this represents a true febrile convulsion or a mild or larval encephalitic component. A seizure at the beginning of the first steep rise of fever would support the diagnosis of a simple febrile convulsion, while a seizure at the height of the hyperthermia would militate against it.

- **Therapy and Prognosis**

On the basis of risk/benefit analysis, neither long-term nor intermittent anticonvulsant therapy is indicated for children who have experienced 1 or more simple febrile seizures. In unusual circumstances, oral diazepam can be given with each fever.

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**THE LENNOX-GASTAUT SYNDROME**

- **Introductory Remarks**

This epileptological entity has been recognized as such over the past five decades, following earlier EEG observations and presumptive electro-clinical correlations. The severity and poor prognosis of the seizure disorder in patients with slow spike wave complexes was quite evident, by contrast to the classical 3-4/sec spike wave complexes in patients with petit mal absences and the prognostically more favorable "primary generalized epilepsy."

The diagnosis of this syndrome is based on the occurrence of certain types of seizures, some of them practically syndrome-specific, and typical EEG changes; furthermore, the poor treatment response (with few exceptions) accompanying mental retardation, and frequently demonstrable neurological deficits, lend strong support to the diagnosis. A multitude of etiologies may cause this condition and, in any case, the cause remains unknown.

- **Age**

This condition usually starts between the ages of 1 and 10 yr; onset in the second decade of life is much less common. Onset at age 6 to 12 mos has been observed and requires solid EEG documentation for differentiation from hypsarrhythmia-infantile spasms. About 10 to 20% of the cases have passed through a period of infantile spasms-hypsarrhythmia before the Lennox-Gastaut syndrome becomes evident.

- **Ictal Manifestations**

The types of seizure occurring in the Lennox-Gastaut syndrome are best divided into the following two groups.

- **Seizures also occurring in other epileptic conditions.**

In this group, we find grand mal, playing a major role only at the onset of the seizure disorder, often completely absent, psychomotor automatisms, in some cases dominating the picture, quite commonly myoclonus, focal (partial elementary) seizures such as adverive, and Rolandic focal motor attacks.

- **Seizures which are virtually specific for the Lennox-Gastaut syndrome.**

This group is composed of atonic seizures (drop attacks of particular diagnostic significance), akinetic seizures, purely tonic seizures, purely clonic seizures, a modified form of petit mal absence, and, as far as prolonged states are concerned, a variant of petit mal absence status.

The occurrence of more than one type of seizure is almost the rule in the Lennox-Gastaut syndrome; many children have more than two different types of seizures. Seizures also occurring in other epileptic conditions are described in the section on types of epileptic seizures. The more specific seizures, however, need a detailed presentation.

Atonic seizures are divided into a brief and more prolonged type. The attacks usually occur without provocation. In the brief atonic seizure, there is sudden more or less intense muscular hypotonia which may be preceded by a brief myoclonic jerk. Generalized severe hypotonia leads to an abrupt, almost lightning-like, fall: the knees buckle, the torso and head slump forward, and the head may hit the floor or an object in a traumatizing manner. There may be, instead, a fall on the buttocks or a rudimentary seizure with sudden head drop on the chest.

Preceding myoclonus is usually associated with generalized spikes or polyspikes; the atonia (best recorded in a supine patient) is accompanied by spikes, a few spike-waves, and a succession of slow waves. The attack usually lasts only 1 to 2 sec; the patient probably does not lose consciousness.

More prolonged atonic seizures are also called atonic absence or atonic epileptic seizures. Sudden atonia results in a fall, but the patient may remain lying on the floor, flaccid and immobile.

Generalized spikes, sharp waves, slow waves, and activity in the 10/sec range are found in these prolonged atonic seizures, which may last from 30 sec to a few minutes. The EEG changes and the traumatizing abruptness of fall distinguish this attack from the cataplectic attack, which is strictly nonepileptic. These children need to wear protective headgear.
Akinetic seizures are characterized by complete lack of mobility in spite of preserved muscle tone; there is impairment or loss of consciousness. There is no fall. In the supine child, the evaluation of muscle tone will tell the difference between this type and the atonic seizure. The attacks last from 30 sec to more than 1 min.

These attacks are not uncommon in children with Lennox-Gastaut syndrome, although they are not as frequently observed as atonic seizures. The ictal EEG findings are not absolutely conclusive. A very rhythmical slow spike wave discharge (1-2/sec) may be present in generalized synchrony for the duration of the attack. The occurrence of polyspike wave complexes are occasionally present in these attacks.

Tonic seizures show a variety of manifestations and their subdivision into axial, axorhizomelic, and global tonic seizures. Such purely tonic attacks of bilateral character are limited to children with the Lennox-Gastaut syndrome when properly differentiated from lateralized tonic attacks due to mesiofrontal epileptogenic foci and a variety of nonepileptic attacks (tetanic, decerebration, etc.).

The attacks are short and last from about 5 to 20 sec. There is extension of the axial musculature with some opisthotonus; moderate flexion of the arms is noted and this may be followed by extension. Tracheobronchial hypersecretion occurs with repeated attacks and a fairly dangerous status may evolve. These attacks or very short rudiments are quite common in nonREM sleep and often are observed in a routine sleep tracing. Bilateral synchronous fast or moderately fast spike activity of about 10 to 25/sec of medium to high voltage and frontal accentuation is the EEG concomitant of these attacks ("runs of rapid spikes;"). Simple flattening or desynchronization may also occur. A diffuse slow ictal pattern has been mentioned. Generalized synchronous 3/sec spike waves are also seen in frequent axial tonic seizures.

Clonic seizures consist of prolonged myoclonic activity bilaterally; these jerks occur in very rapid succession; asymmetries are not uncommon. The clonic motions are of small amplitude and may involve the entire body or certain (sometimes even distant) parts. There is loss of consciousness. The attacks occur mainly in nonREM sleep and are seen chiefly in childhood. The ictal EEG shows much generalized activity in the 10/i sec range, mixed with spike wave-like discharges, slower and faster frequencies. The duration lies around 1 min.

Seizures resembling petit mal absences are uncommon and usually show tonic and clonic elements. Episodes of petit mal absence status in the Lennox-Gastaut syndrome are quite common.

### Clinical Signs of Nonictal Character

About half of the infants, children, or adolescents with Lennox-Gastaut syndrome show no neurological deficit and no evidence of structural brain disease. This is supported by normal findings in computerized tomography in approximately 50% of the cases. The rest shows a wide variety of residual infantile brain lesions, which are often associated with neurological deficits such as forms of cerebral palsy.

Mental retardation ranges from the most profound to the slightest degree, essentially depending on the age at onset; the earlier the seizures start, the more serious the intellectual deficit appears to be. In patients with onset after age 10, no mental deficit may be present.

### EEG

EEG findings have been crucial in the individualization of the Lennox-Gastaut syndrome as a clinical entity. The outstanding feature is the slow spike wave complex ranging from 1 to 2.5/sec, which is more extensively described in the chapter on abnormal paroxysmal EEG patterns. It is more often an interictal rather than an ictal discharge and is most often of generalized synchronous character, although lateralization is also fairly common; local slow spike wave activity is quite rare. A maximum over the frontal midline is the rule.

This discharge is enhanced in nonREM sleep and may become almost continuous. The spike component shows considerable variation; it may be slow ("blunted") or quite fast with true spike character. The slow spike wave discharge may be present in early infancy between the ages of 6 to 12 mos. Classical 3/sec or 3-4/sec spike wave complexes may also be discernible.

Another important pattern is "runs of rapid spikes," which are seen in nonREM sleep only. This pattern is more common in older children, adolescents, or adults. More information can be found in the chapter on abnormal paroxysmal discharges.

The EEG as such ("background EEG") is often disorganized and excessively slow, but a sizeable number of patients show a normal frequency spectrum with unremarkable posterior alpha rhythm, the basic rhythm. The degree of general slowing and disorganization usually underscores the severity or advanced stage of the case. These children are often seen in a state of overtreatment with anticonvulsants, resulting in toxic anticonvulsant levels. Interestingly, high and toxic levels of phenobarbital may be completely unassociated with fast EEG activity; this absence of barbiturate-induced fast frequencies is quite characteristic in advanced cases with considerable cerebral impairment.

### Etiological and Neuropathological Considerations

The aforementioned normal computed tomography (CT) scan findings in 50% of the cases further support the view that about half of the cases are idiopathic and hence without structural cerebral changes. The nature of idiopathic forms is completely unclear. Genetic predisposition is certainly more than just a hypothesis.
Acquired pathology of residual character is present in a considerable number of cases; with CNS infection and birth trauma/asphyxia as the leading problems. One could argue that such pathology alone can hardly account for this severe form of epileptic seizure disorder and that a genetic predisposition is a prerequisite. Even progressive pathology such as intracranial tumors may be associated occasionally with Lennox-Gastaut syndrome. Phenylketonuria, forms of lipidosis, tuberous sclerosis, lead encephalopathy, and toxoplasmosis have been specifically mentioned as etiological factors. In essence, we are dealing with the same dichotomy of idiopathic and symptomatic forms as in infantile spasms-hypsarrhythmia.

Pathogenetic Concepts

The debatable concept of secondary generalized epilepsy was discussed earlier in the previous version of the publication (Version 19...Click to download) on infantile spasms. All that was said there also applies to the Lennox-Gastaut syndrome.

Management of Lennox Gastaut syndrome

Medical Care

The goals of treatment for patients with LGS are the same as for all epilepsy patients: the best quality of life with the fewest seizures (hopefully none), the fewest treatment side effects, and the least number of medications.

Antiepileptic medications (AEDs) are the mainstay of therapy for patients with LGS. Unfortunately, no one medical treatment gives satisfactory relief for all or even most patients with LGS. A combination of medical treatment modalities frequently is required.

The various medical treatment options for patients with LGS can be divided into the following 3 major groups:

- First-line treatments based on clinical experience or conventional wisdom (eg, valproic acid, benzodiazepines [specifically clonazepam, nitrazepam, clobazam])
- Suspected effective treatments based on open-label uncontrolled studies (eg, vigabatrin, zonisamide)
- Proven effective treatments based on double-blind placebo-controlled studies (eg, lamotrigine, topiramate, felbamate)

Surgical Care:

- Corpus callosotomy: Corpus callosotomy is effective in reducing drop attacks but typically is not helpful for other seizure types and is considered palliative rather than curative. Seizure freedom following corpus callosotomy is rare but can occur.
- Vagus nerve stimulation: In 3 published small studies, approximately three fourths of LGS patients experienced greater than 50% reduction in seizure frequency with a follow-up period as long as 5 years.
- Focal cortical resection: In rare cases, resection of a localized lesion (eg, vascular lesion, tumor) can improve seizure control.

Most cases of Lennox-Gastaut syndrome are not responsive to therapy. This is a gloomy picture; the course quite often leads to institutionalization, especially in patients with very early onset. The course of the disease, however, should not be conceived as a linear progression of deterioration. Observation of adult patients shows certain interesting trends.

In adulthood, the EEG may gradually lose the characteristics of the Lennox-Gastaut syndrome. The slow spike wave complex may disappear after age 20 or 15. and, instead, runs of rapid spikes in sleep only may become more prominent. This pattern, too, may gradually vanish and spikes or sharp waves of temporal and especially anterior temporal localization may then become predominant. Interestingly, this change may be associated with the appearance of psychomotor (complex partial) seizures as a new phenomenon or enhancement of pre-existing seizures of this type. Thus, the patient seems to merge into the mainstream of temporal lobe epilepsy but will remain a deteriorated case with mental deficit or behavioral changes, often fostered by years of institutionalization. This process has been described as "secondary temporalization". It is doubtful whether all patients take this course.

References

2. Issues in brainmapping...Generalized epilepsies [Click to download in PDF format]
3. Issues in brain mapping...Role of EEG in epileptic syndromes associated with myoclonus. [Click to download in PDF format]
AGE DEPENDENT EPILEPTIC SYNDROMES [PART 3]

The age of the patients has great influence on the ictal, clinical and EEG characteristics of the epileptic seizures disorders and it also determines the course and prognosis of epilepsy in general. This is particularly true in the first two decades of life, especially for infancy and early childhood. There are certain age-determined epileptological entities or epileptic conditions which appear to be monolithic, in spite of a wide variety of etiologies and probably also despite variations in the localization of cerebral involvement. The role of age in epileptic seizure disorder has been substantiated by experimental work and clinical electroencephalographic investigations. We find in age-determined epileptic conditions a) certain condition-related types of seizures, b) certain condition-related EEG patterns, and c) certain condition-related characteristics of course and prognosis.

In the past, this aspect of epileptic seizure disorder had been neglected; too much emphasis was universally placed on locus and cause of the seizure. From the historical viewpoint, the description of infantile spasm and the discovery of a specific EEG pattern called hypsarrhythmia mark the first individualization of an age-determined polyetiological epileptic condition with certain clinical-electroencephalographic criteria. There is a long historical evolution of the very common condition known as febrile convulsions. The clinical picture of benign Rolandic epilepsy became clear due to the efforts of numerous authors. Neonatal convulsions, which are a particularly heterogeneous group, must also be listed in this context and the thought-provoking notion of primary generalized epilepsy also belongs in this category.

**Table 1. Comparison between the classical age-depandant generalized epileptic EEG discharge.**

<table>
<thead>
<tr>
<th>EEG TYPE</th>
<th>AGE</th>
<th>CLINICAL CORRELATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical 3 c/s SWD</td>
<td>3.5 years - 16 years</td>
<td>Petit mal epilepsy</td>
</tr>
<tr>
<td>Slow SWD (1-2.5 c/s)</td>
<td>6 months - 16 years</td>
<td>Lennox-Gastaut syndrome</td>
</tr>
<tr>
<td>Fast SWD (4-6 c/s)</td>
<td>Over 16 years</td>
<td>Juvenile myoclonic epilepsy</td>
</tr>
<tr>
<td>Hypsarrhythmia</td>
<td>4 months - 4 years</td>
<td>West syndrome</td>
</tr>
</tbody>
</table>

**PRIMARY GENERALIZED EPILEPSY**

- **Introduction**

The entire concept of a primary generalized epilepsy has its foundation in the EEG. Who would have thought that a simple petit mal absence with its rather subtle clinical symptomatology could be the result of massive generalized synchronous epileptic discharges? The first observation of the ictal EEG pattern of petit mal has been the starting point for numerous attempts to explain the phenomenon of primary generalized seizure discharges.
Terminology

The term "primary generalized epilepsy" has been introduced by the International League against Epilepsy. This term deserves general acceptance. It implies that the clinical and electroencephalographic phenomena of the seizures occurring in this epileptic condition are generalized from the start. This term has superseded older terms such as "centrencephalic epilepsy", "cortico-reticular epilepsy", and "common generalized epilepsy". Its weakness lies in the fact that it seems to burn all bridges for a retreat if a truly focal cortical onset with extremely rapid generalization should ever be convincingly demonstrated in the future.

Age and Prevalence

The age depends on the type of seizure. Classical petit mal absences mostly start at age 4 to 6 yr; a special group starts at age 9 to 15 yr. Myoclonus and grand mal attacks usually start at age 11 to 14 yr. Improvement or full seizure control after age 20-25 yr is very common. A special manifestation is the petit mal absence status, which may occur in older children, adolescents, adults, and even the elderly.

Primary generalized epilepsy is sometimes preceded by a period of febrile convulsions in infancy and early childhood. It is never preceded by severe conditions such as infantile spasms or the Lennox-Gastaut syndrome.

Ictal Manifestations

The petit mal absence was discussed in detail in the section dealing with types of seizures. The two different forms are 1) simple petit mal absences, starting at age 4 or shortly thereafter, with a large number of absences/day (sometimes exceeding 100/day); and 2) "juvenile" petit mal absences with an onset at age 9 up to 15 yr, more prolonged or mixed with more motor activity.

Petit mal absences show a wide variety of mild to moderate motor accompaniment; rhythmical eye blinking in synchrony with the spike waves is the most common motor component. Retropulsion of the head is quite common ("retropulsive petit mal"); advesive movements and some rhythmically repetitive oral motions may also occur.

Children with petit mal absences often start having grand mal seizures in early adolescence. Figures range from 31% to 54%.

In most of these cases, the grand mal seizures do not pose a major problem and are readily brought under control.

Grand mal attacks in patients with primary generalized epilepsy are very often preceded by sudden bilateral myoclonus. These myoclonic jerks may also occur as isolated events, especially in the morning hours after a night of insufficient sleep. Many patients with this combination of grand mal and myoclonus may never have experienced any petit mal absences earlier in childhood. This petit mal-free form is a special variant of primary generalized epilepsy which also shows slightly different inter-ictal bursts in the EEG. These bursts are relatively short and dominated by 4/sec or 4-5/sec spike wave complexes which are, contrary to the classical 3/sec or 3-4/sec spike waves, not readily activated by hyperventilation. Many of these patients are flicker-sensitive (photoconvulsive response) and positive family histories are more often obtained in this group. Myoclonus may also be associated with brief petit mal absences.

Very prolonged absence-like stages, attacks of petit mal- like stupor, or petit mal automatisms have been termed "Petit mal status", whereas the modern terminology recommends the term "absence status." These states will be discussed in the section on status epilepticus. While all of the ictal manifestations of primary generalized epilepsy tend to occur in children and adolescents, the absence status not only occurs in elderlies but may even have its onset in old age.

Figure 1. The 3 c/s spike/wave discharge with frontal dominance

EEG

Most of the relevant EEG findings have been described in detail in the chapter on abnormal paroxysmal EEG patterns. May it suffice to reiterate that the 3/sec or 3-4 c/s spike wave pattern is the EEG correlate of the classical petit mal absence and also occurs, often abundantly, in the interval, sometimes in drowsiness and sleep. These generalized bursts, with or without clinical absence, are readily triggered by hyperventilation and may materialize after a few deep breaths in untreated patients. Intermittent photic stimulation may occasionally trigger petit mal absences with 3/sec spike waves; more often, it is associated with generalized polyspikes of frontal accentuation, with or without clinical myoclonic jerking, most often at frequencies of 14-18 flashes/sec. As was pointed out above, photosensitivity is more often noted in patients with 4/sec or 4-5/sec spike wave bursts and a history of grand mal and/or myoclonus.
The phenomenon of myoclonus is almost invariably linked with polyspike discharges as far as patients with primary generalized epilepsy are concerned. Polyspikes also contaminate the spike wave sequences in children with massive myoclonus as a variant of petit mal. In the majority of patients with primary generalized epilepsy, the EEG frequency spectrum appears to be normal aside from the generalized paroxysmal bursts, the so-called background activity. A remarkable exception is the occurrence of prolonged stretches of rhythmical high voltage 3/sec waves in occipital leads with moderate spread into the vicinity; these bursts occur in a significant number of children with petit mal absences. This rhythm is found in 55% of the patients with petit mal absences and persists in 60% of the cases following seizure control. Hyperventilation almost invariably activates this rhythm. In some cases, a very small spike component is discernible between the large rhythmical delta waves. The rhythmical posterior activity may be enhanced under treatment with ethosuximide (Zarontin), while the 3/sec spike wave complex disappears. Children with petit mal absences and rhythmical occipital delta trains fall into a special epileptological category. The occipital rhythmical slow activity is a very favorable prognostic sign.

The sleep records of patients with primary generalized epilepsy show frequent bursts of spikes, polyspikes, and spike waves; with common association between the K complex and the frontal midline maximum of the spike discharges. This maximum over the frontal midline is almost invariably present, not only in sleep but also in the waking state. This indicates that arousal plays an important role in the generation of these discharges. REM sleep is associated with an attenuation or total suppression of bilateral synchronous paroxysmal bursts. In exceptional cases, the maximum of the 3/sec spike wave bursts lies in the vertex region rather than in frontal midline; these children also show Rolandic spikes.

It goes without saying that genetic factors are particularly important in the field of primary generalized epilepsy. Generalized synchronous seizure discharges follow an autosomal-dominant pattern of genetic transmission, with variable penetrance regardless of presence or absence of seizures with an unusual characteristic of a very low penetrance at birth which rises to nearly complete penetrance (close to 50%) for age 4.5 to 16.5 years with a gradual decline to almost no penetrance at age 40 yr. These figures are in excellent agreement with the incidence of generalized synchronous seizure discharges of the 3-4/sec spike-wave type as well as the clinical seizure manifestations of primary generalized epilepsy. The Presence of Focal Spikes in Patients with Primary Generalized Epilepsy

A certain type of focal spikes in childhood ("benign Rolandic spikes") may be occasionally present in children who, suffer from petit mal absences, especially after suppression of the absences and the spike waves with medication. This view would shed more light on the demonstration of genetic factors in children with midtemporal spikes.

**Concluding Remarks**

The challenging problem of primary generalized epilepsy remains unsolved. Genetic predisposition and age (chiefly 4-20 yr) are significant factors. It is a specifically human disorder; for this reason, animal models can provide only partial insight into pathogenetic mechanisms. In the human, the generalized synchronous seizure discharge originates from the interhemispheric frontal portion bilaterally. Arousal stimuli play a crucial role in the detonation of these discharges. In some patients, however, the mechanism of photosensitivity is paramount.

**BENIGN ROLANDIC EPILEPSY**

**Introduction**

In children with spikes over the central region and/or adjacent midtemporal and parietal areas, a benign and readily controllable type of epileptic seizure disorder with focal motor seizures and/or grand mal is the rule. An increasing number of reports over the past 40 yr gives testimony to growing awareness of this special form of childhood epilepsy.

This form of childhood epilepsy is occasionally listed among the primary generalized epilepsies despite its prominent focal features in the ictal and electroencephalographic semiology. Such a classification certainly appears to be provocative. There are indeed certain relationships between benign Rolandic epilepsy and primary generalized epilepsies and conversion from one form to the other may occur. There is certainly good reason to separate benign Rolandic epilepsies from the bulk of focal (partial) epileptic seizure disorders which will be presented somewhat later.

**Age and Prevalence**

Benign Rolandic epilepsy occurs at age 3 to 12 yr. The majority of these children are in the range from 6 to 10 yr. Disappearance of the seizures during adolescence (or even prior to puberty) is the rule. The seizures may occasionally recur much later in life, probably due to seizure-facilitating factors such as severe illness or toxic-metabolic factors.

The sex distribution shows that boys are more often affected. The prevalence is not quite clear and might be somewhere between 5 and 10% in a population of epileptics below age 15 yr.

**Ictal Manifestations**

The seizures, regardless of focal or grand mal character, tend to occur during nocturnal sleep, mostly during the last hour of sleep or in the first 2 hr. About 80% of the attacks occur in sleep and, of the remaining 20%, about 10% take place shortly after awakening. (Note the similarities with primary generalized epilepsy.) Nocturnal seizures may awaken the child afterward. Preservation of consciousness and hence the ability to
describe the experienced seizure was found in 58%; this indicates the predominance of focal seizures. Grand mal (tonic-clonic) seizures were noted in 26%.

The seizures are hardly ever seen by the physician, even by the epileptologist who sees sizeable numbers of these children. One therefore depends heavily on descriptions by the patient or his family; nocturnal videotape or biotelemetry recordings are quite helpful. Focal seizures often involve the face. The midtemporal spike localization has been thought to be related to paroxysmal activity in the very closely located lower portion of the motor strip (facio-laryngo-pharyngeal muscles). Hemifacial twitching is definitely more common than clonic motions in the contralateral arm; least common is clonic activity in the leg. In some cases, the entire half of the body participates, but a typical Jacksonian march does not seem to occur. Speech arrest is quite common (39% of the seizures). This is apparently an ictal anarthria with preserved internal speech.

Oropharyngeal involvement is very often reported, with sounds described as "guttural," "gargling," "throaty," "wheezing," or "as if going to vomit." Feelings of suffocation are reported as coming from the mouth but not from the chest. These patients also have focal seizures which are not Rolandic, with blindness, vertigo, and torsion of the body as ictal signs. This underscores the complexity of the underlying neurophysiological mechanisms.

- **EEG**

Spiking over central-midtemporal area in children is of limited epileptogenicity. It is reasonable to presume that 50-70% of these children have seizures and the remaining 50-30% are seizure-free. These latter patients are referred to the EEG laboratory because of a variety of symptoms such as behavior disorder, headaches, and other complaints or derivations.

The spatial distribution of the spike activity requires an appropriate number of electrodes; the International Electrode System is particularly suitable. Otherwise, the Rolandic cortex may lie between a frontal and a parietal electrode and strictly local spiking may escape detection, especially when the midtemporal region is not explored ideally. In my personal experience, a central maximum of spike discharge is slightly more often noted than a midtemporal maximum.

The spikes themselves are large and may be either spikes in the strict sense or sharp waves (see chapter on abnormal paroxysmal patterns). Spiking is usually enhanced in light nonREM sleep, during which the discharges may become extremely abundant. Their random character may give way to quasirhythmic or periodical spiking at intervals of less than 1 second; previously unilateral spikes become bilateral synchronous or asynchronous. In many children, Rolandic spikes are found in the sleep portion only. REM sleep restores the unilateral character of the spiking. Bilateral parieto-occipital 4/sec spike wave-like discharges of moderate voltage is occasionally seen in the waking patient.

The rest of the tracing is usually normal in these patients and the frequency spectrum corresponds to age. Central mu rhythm is sometimes present and there is reason to presume that central spikes of childhood may be gradually replaced by mu rhythm, at least in some of the patients. There is indubitable evidence that, in a limited number of patients, the central spike activity can be blocked by contralateral fist clenching or, even better, by alternate clenching and opening of the fist. This provides further evidence for the functional character of the spikes.

In a small number of cases, the spike activity shows a consistent maximum over the vertex or over the centroparietal midline region, which may be the sole region of spiking, so that omission of midline leads would result in missing the abnormality. Some of these patients show focal motor or sensory ictal activity of leg predominance but, more often, the ictal symptoms do not correspond with the spike localization.

**Clinical Signs of Nonictal Character**

Neurological deficits are not compatible with benign Rolandic epilepsy. This condition is based on dysfunction rather than structural pathology. It is worthwhile, however, to search carefully for a true intracranial lesion. Arteriovenous malformation occasionally may be the cause of the discharges and associated seizure.

Central, midtemporal, or parietal spikes or spikes over the midline may also occur in children with evidence of cerebral palsy, in mostly diplegic, quadriplegic, or choreoathetoid forms. In these children, Rolandic spikes have a different connotation and do not herald a good prognosis for the seizure disorder. The reader will find more extensive discussion in the section on cerebral palsy.

Behavior disorders are very common in children with true Rolandic spikes; they may range from hyperkinetic behavior and signs of minimal cerebral dysfunction to severe anxiety neurosis. Various types of headaches may occur. The intelligence is normal in true benign Rolandic epilepsy.
Course

The seizures are easily controlled with routine anticonvulsive treatment. Treatment may even be withheld unless seizures repeat themselves. Freedom from seizures in adolescence is the rule. The return of a single major convulsion may occasionally occur under the influence of infections, stress, or toxic substances. These cases show no resurgence of the central spike focus, which renders the EEG diagnosis very difficult. The presence of central mu rhythm may serve as a hint that the patient has had central spikes in the past, but such conclusions can be made only with reservations.

Etiological Considerations

This form of epilepsy is due to dysfunction rather than pathology. A genetic basis is the most logical thought.

Problem of Differential Diagnosis

Benign Rolandic epilepsy must be differentiated from:

1. Children with Rolandic spikes and no seizures whatsoever (these children are certainly not epileptics; about 30 to 50% of the children with Rolandic spikes have no overt clinical seizures).
2. Children with Rolandic spikes and a history of antecedent brain damage or cerebral palsy.
3. Children who have typical psychomotor seizures and evidence of temporal lobe epilepsy which may gradually progress in severity; these children may have atypical spike localization (central, midtemporal), while the classical anterior temporal sharp wave focus does not materialize before adolescence.
4. Children with midtemporal spikes, marked tendency to generalization and spike wave formation, clinically with aphasia, probably a temporary inflammatory condition which gradually subsides.
5. Children with frequent focal motor seizures which become progressively worse: "malignant" Rolandic epilepsy of childhood.
6. Children with centroparietal spikes elicited by tactile stimulation of corresponding cutaneous areas of the body (see under benign parietal epilepsy). The differentiation of these conditions rests on a careful combined clinical-electroencephalographic assessment of each case. The EEG shows considerable slowing. There is evidence of constant muscle activity, but no authentic cerebral spikes are demonstrable.

Spike Foci Outside the Rolandic Region in Children.

- Occipital spike foci are usually found between the ages of 2 to 5 yr. These children show no neurological or ophthalmological deficit; about 40% of them have clinical seizures, mostly grand mal, with good prognosis.
- Frontal spike foci in children are associated with epileptogenicity, with about 80% having overt seizures, and a guarded prognosis. Multiple spike foci (two or more areas of independent spiking) are also highly epileptogenic; the prognosis is guarded and probably fairly good if Rolandic spikes predominate.

Considerations of Basic Mechanisms

True benign Rolandic epilepsy is likely to be based on temporary paroxysmal hyperirritability of the motor cortex, which naturally has a lower threshold of epileptic excitability. This is merely a working hypothesis in need of further substantiating evidence.

"Malignant" Rolandic Epilepsy

Cases of progressively worsening focal motor seizures and prolonged episodes of epilepsy partialis continua are quite rare but probably constitute a special epileptological entity. Motor deficits and mental decline are associated with the seizure disorder. Their etiology is poorly defined; chronic localized encephalitis may be one of the causes (Rasmussen syndrome). Hemispherectomy seems to be the only effective treatment; limited cortical excisions or lobectomies are ineffective.

The EEG shows endless sequences of ictal spike discharges during focal motor attacks but becomes uninformative in states of epilepsy partialis continua, which probably originate from deep structures or possibly from lamina V of the motor cortex without participation of the superficial layers.

Benign Parietal Epilepsy

The vast majority of these patients were children between the ages of 4 and 8 yr. The occurrence of spikes over the parietal region (parasagittal zone) following contralateral tactile stimuli characteristic of this condition. The paroxysmal response to tactile stimuli was found to be enhanced in nonREM sleep. Only 20% of children had clinical seizures; the remaining children were referred because of behavior problems.

Children with Midtemporal Spikes, Progressive Aphasia and Seizures

This syndrome of childhood epilepsy with progressive aphasia has stimulated much interest over the past 40 yr and may be regarded as an
epileptological entity unless the discovery of a consistently present pathogenic agent such as a virus turns this condition into a specific disease entity.

This condition is found in children around ages 4 to 6 yr. Speech becomes less intelligible and eventually is limited to a few words. Myoclonic jerking and other forms of brief seizures (akinetogenic) are reported. The EEG shows marked spiking, mainly over the left midtemporal region, but there are numerous generalized spike wave-like bursts, first 3-4/sec and later in the 1.5-3/sec range, suggestive of a Lennox-Gastaut syndrome. Cortical biopsy may show inflammatory changes and gliosis with mildly appearance of the meninges over left temporal region. In the course of years, the speech function starts to improve, the seizure frequency diminishes, and the EEG abnormalities gradually vanish.

- Considerations of "Functional" Versus "Autochthonous" Seizure Discharges

The presentation of age-determined epileptic conditions clearly shows benign and vicious forms. It was mentioned before that generalized synchronous spikes and spike waves in primary generalized epilepsy and focal spikes in benign Rolandic epilepsy can be easily suppressed for a limited period with small doses of iv diazepam, whereas many cases of chronic epileptogenic foci are not touched by such small amounts.

This dichotomy of responses of human epileptogenic EEG discharges reminds us of a similar dichotomy which has been widely discussed among neurophysiologists and basic science workers in the field of epileptology. Are we dealing with basically normal neurons which fire excessively due to hypersynchronous synaptic input? Such an epileptogenic focus would consist of a hyperexcitable "neuronal aggregate". On the other hand, one could view the epileptogenic focus as composed of intrinsically abnormal neurons.

There is accumulating evidence that epileptic seizure disorders based upon neuronal hyperexcitability do exist. The key areas of predisposition to epileptic neuronal hyperexcitability may be summarized as follows.

1. **Frontal lobe-supplementary motor area in interhemispheric fissure**: Presumed trigger: arousing stimuli in a state of reduced vigilance. Generalization: very common and very pronounced, exemplified by 3/sec spike waves, with or without petit mal absence (perhaps via cingulate and thalamocortical connections).

2. **Occipital lobe Trigger**: flickering light and other visual stimuli. Generalization: common, exemplified by polyspikes with or without myoclonus, occasionally by spike waves with or without petit mal absence, via occipito-frontocentral connections and/or geniculate-thalamocortical fiber systems.

3. **Rolandic region Trigger**: unclear; possibly sensorimotor idling. Generalization: is not quite as common; seizures, if occurring, are most often of focal motor character.

Hyperexcitability of all three key areas may occasionally exist in certain patients with primary generalized epilepsy. Such cases epitomize the significance of predisposition (i.e., genetic factors). The hyperexcitability of the sensory-parietal cortex with local spike responses to contralateral tactile stimuli seems to be a related phenomenon.

**References**

2. Issues in brainmapping...Generalized epilepsies [Click to download in PDF format]
DEFINITION OF COMPUTERIZED (DIGITAL) EEG

Digital EEG techniques have grown rapidly in popularity for recording, reviewing, and storing EEG. Digital EEG recordings are flexible in the way they display the EEG tracings, unlike analog paper EEG. Montage, filter, and gain settings can be changed retrospectively during record review. Quantitative EEG (QEEG) analysis techniques can provide additional measurements or displays of EEG in ways not available with analog paper EEG recordings. Several QEEG techniques, commonly called "EEG brain mapping," include topographic displays of voltage or frequency, statistical comparisons to normative values, and discriminant analysis. Although much scientific literature has been produced after decades of research in this field, there remains controversy about the clinical role of QEEG analysis techniques. This assessment is meant to help the clinician by providing an expert review of the current clinical usefulness of these techniques.

Evaluation process

Previous assessments on this subject were published by the American Electroencephalographic Society (American EEG Society, AEEGS) in 1987 and by the American Academy of Neurology (AAN) in 1989. Members of both societies were notified by newsletter to solicit their opinions with supporting information for this assessment. Commercial digital EEG vendors were identified by their participation in society meeting exhibits or by their known interests in this field, and they were asked to submit relevant scientific publications supporting clinical use. Many experts in the field were also contacted to request their opinions and to cite relevant scientific publications. A literature search was conducted using the Medline database, covering the years 1984-1995. Searched topics included EEG and evoked potentials, among others, and the identified citations were manually screened for relevance to this assessment. Review articles and published literature reference sections were also screened for relevant information. When outside reviewers and other experts presented viewpoints differing from circulated drafts of this assessment, their opinions and relevant cited literature were reviewed and any appropriate changes were made in the assessment.

In assessing the literature, clinical assessment criteria should include several ideal elements and concepts: The disease studied should be clearly defined. Criteria for test abnormality should be defined explicitly, clearly, and prospectively. Control groups should be used, including normal controls as well as patients with other diseases in the common differential diagnosis of the disease tested. The control groups should be different from those originally used to derive the test's normal limits. The severity of disease should simulate the severity in patients for which the use of the test is proposed. Test-retest reliability should be high. Various assessments of validity should be measured, e.g., sensitivity, specificity, positive predictive value, and negative predictive value. Validity measures for the evaluated test should be compared to such results obtained with other tests already clinically used in that differential diagnosis, including diagnosis based on signs and symptoms, routine EEG, or neuroimaging tests. Blinded observations were considered a more objective, preferred measure of a test's validity. Medical efficacy was evaluated in several ways. An effective test may reduce morbidity or mortality by clarifying which medical intervention is best. It may substitute a less risky test for one with greater medical complications. It may substantially clarify a diagnosis, leading to more accurate prognosis, or improved expectations and behavior. Incremental changes to already accepted tests and applications require less proof through new studies, whereas novel techniques and applications require a greater degree of demonstration of validity and utility.

Digital EEG

Digital EEG is the paperless acquisition and recording of the EEG via computer-based instrumentation, with waveform storage in a digital format on electronic media, and waveform display on an electronic monitor or other computer output device. The recording parameters and conduct of the test are governed by the applicable standards of the ACNS guidelines and are identical to or directly analogous to those for paper EEG recordings. [33]

Ideally, digital EEG creates a recording on a digital medium without loss of anything except the paper itself. In practice, there may be some loss of detail especially at the lower sensitivity settings. Digital EEG also allows for simple but extremely useful digital utilities such as post hoc changes in filters, horizontal and vertical display scale, and montage reformatting that allow greater flexibility in reading the EEG. These tools allow for better visual reading of the record than can be achieved with an analog paper record. Network storage allows access from remote sites. New improved derived references can be calculated and used, and very large numbers of recording channels can be processed and managed. Digital EEG is an excellent technical advance and should be considered an established guideline for clinical EEG.

Quantitative EEG (QEEG)

Quantitative EEG (QEEG) is the mathematical processing of digitally recorded EEG in order to highlight specific waveform components,
transform the EEG into a format or domain that elucidates relevant information, or associate numerical results with the EEG data for subsequent review or comparison.

- **Signal analysis**

Signal analysis is the quantitative measurement of specific EEG properties or a transformation of the raw, digitally recorded EEG signal into numerical parameters other than the traditional amplitude versus time. Several types of measurements or analyses can be made.

**Automated event detection**

Automated event detection is the use of mathematical algorithms to detect or identify events or abnormalities that the computer has been instructed to bring to the attention of medical personnel. No alteration is made in the raw EEG data, except optional data compression. This is used typically in long-term EEG recordings for spike and seizure detection.

- **Monitoring and trending EEG**

Monitoring and trending EEG. This technique uses mathematical algorithms to extract parameters from the raw data that summarize the important aspects of the EEG. The medical personnel can then be presented with simplified graphical displays of these trended parameters. Alterations of the trends may prompt the users to review in detail specific portions of EEG data. This is used typically in neurophysiologic monitoring applications in the OR or ICU.

- **Source analysis**

Source analysis is a form of mathematical analysis in which the recorded EEG values (typically scalp voltage values from an epileptiform abnormality) are compared with predetermined models of possible EEG generators. The analysis may specify the location, orientation, strength, and number of the possible sources of the analyzed spike or other EEG feature.

- **Frequency analysis**

Frequency analysis converts the original EEG data into a representation of its frequency content. The magnitude corresponds to the amount of energy that the original EEG possesses at each frequency. An example of the use of frequency analysis is to look for evidence of excess slow activity. Coherence analysis uses calculations similar to frequency analysis to obtain information about the temporal relationships of frequency components at different recording sites, typically for evaluation of seizure origin. The results of signal processing, such as frequency analysis, may be displayed as a table of numbers, a multidimensional graph, or a topographic display (see below).

- **Topographic EEG displays**

Topographic EEG displays can present visually a spatial representation of raw EEG data (i.e., voltage amplitude) or a derived parameter (e.g., power in a given frequency band, or peak latency). Typically, the parameter under study is mapped onto a stylized picture of the head or the brain, but may be mapped onto an anatomically accurate rendering of the brain, such as a three-dimensional volume-reconstructed MRI. Amplitude at a given anatomic site is ordinarily represented as a color or intensity, and amplitudes at unmeasured sites are interpolated to present a smooth display. These displays can highlight some spatial features of the EEG. These representations are often collectively referred to as EEG brain maps. This term, in this context, should not be confused with functional cortical brain mapping by direct electrical cortical stimulation or with brain mapping by neuroimaging techniques, which have no direct relationship to EEG brain mapping.

- **Statistical analysis**

Statistical analysis compares variables derived from the digitally recorded EEG between groups of people or between a patient and a group. These comparisons may be carried out on individual variables (e.g., the alpha frequency) or on many variables using appropriate multifactorial statistical methods. Spatial aspects may be included, e.g., by statistical comparison of topographic EEG maps.

1. Comparison to normative values uses group statistics to determine whether a parameter (or parameters) measured on an individual patient lies inside or outside the range of normal values. Statistical techniques employed may be simple thresholds based on the mean and standard deviation of a "normal" distribution. More advanced techniques may encompass age-adjusted norms, bayesian statistics, etc.

2. Diagnostic discriminant analysis gathers selected parameters for several different patient diagnostic subgroups, as well as for controls. A discriminant function can be mathematically determined that ascribes certain patterns of these parameters to each patient group. The technique then compares the pattern of the EEG parameters derived from one patient to all of the relevant patient groups to determine with
PROBLEMS ASSOCIATED WITH EEG COMPUTERIZATION

The potential advantages of QEEG's and its clinical usefulness is now undeniable, and it has substantial potential for future applications. At this time, most scientific reports more convincingly have demonstrated research applications rather than clinical applications. Among the reports suggesting clinical utility, few have been prospectively verified or reproduced, and some conflict with others. Techniques used in QEEG vary substantially between laboratories, and any clinical usefulness found with one specific technique may not apply when using a different technique. Many technical and clinical problems interfere with simple clinical application. Traditional EEG artifacts can appear in unusual and surprising ways, and new artifacts can be caused by the data-processing algorithms. Some artifacts, such as eye movements, are common in the EEG, and even subtle ones will produce highly significant QEEG abnormalities if they go unrecognized. Abnormal activity such as epileptiform spikes may be overlooked, considered artifactual, or misinterpreted. Transient slowing can be missed. The computer may score as "abnormal" some EEG activity known to have no clinical importance, such as mu, or slow alpha variant.

Automated assessment of normality must take into account the subject's age, state of alertness, and other facts. But, ways to accomplish this are not yet well defined in any way that has been widely accepted or consistently applied. These problems are compounded when the patient is receiving medication that alters the EEG. Substantial unresolved statistical issues are critical in automated assessment of normality. Because of these problems, EEG brain mapping and other QEEG techniques are very predisposed to false-positive errors, i.e., erroneously identifying normal or normal variant patterns as "abnormalities." Experienced users are aware of these problems, which represent challenges especially for less-experienced interpreters. These difficulties have been reviewed elsewhere, along with the controversy about their impact on potential clinical utility. [35-57]

Prospective evaluation of EEG discriminant analysis has not yet demonstrated its practical use in clinical differential diagnosis. Some studies have shown very interesting positive results, but these still await prospective assessment of clinical utility. Substantial variability in EEG features occurs among normal subjects as well as among patients with specific disorders, so that the discriminant matching of EEG features may be very difficult in practice. Mistaken diagnoses can readily occur in such QEEG discriminant analyses.58 When drowsiness occurs, or if the patient is taking certain medications, the tests are invalid. Drowsiness can mimic disease in EEG or QEEG. Even well-established routine EEG abnormalities such as focal slowing are generally nonspecific as to cause or disease.

A common mistake occurs when running a large battery of QEEG tests, sometimes encompassing hundreds or even thousands of individual statistical assessments on one patient. In this setting, many statistically positive "abnormalities" will occur by chance alone in normal subjects. These false-positive "abnormalities" average about 5% of the number of statistical tests run in some applications, but can reach 15 to 20% in some individual normal control subjects. [59] Many changes seen statistically are generally now regarded as clinically meaningless, e.g., diffusely decreased delta or increased beta. Others are controversial and still have no well-established clinical role, e.g., changes in coherence. Some retrospective and statistical analyses of coherence have shown interesting, positive results that await prospective validation in clinical practice. Given the complexity of studies or tests with very large volumes of statistical testing, some of these problems may be avoided by using QEEG techniques to ask a few specific measurement questions that are likely to be clinically meaningful, e.g., to localize or identify increases in slow-wave activity.

Many common QEEG mistakes have been reviewed by Duffy et al., [46] along with recommendations for controlling some of the difficulties. That review expresses some overly optimistic opinions about the clinical utility of QEEG. In general, the review's many specific technical suggestions and precautions are quite appropriate.

Visual and auditory long-latitude evoked potentials have also been used along with EEG brain mapping techniques. [60-81] At present, insufficient information is available about evoked potential topographic mapping and statistical normative scoring to assess its normal variants, normal limits, effects of medication, and other relevant technical and patient-related factors. No well-designed, prospectively verified clinical studies have demonstrated the clinical utility of topographic mapping of long-latency evoked potentials for diagnosis in clinical settings. When statistical methods (e.g., z-scores) do detect changes in topographic maps of long-latency EP amplitudes, the reader may not be able to differentiate between chance events, normal variants, and true pathology.

Overall, the problems of QEEG were weighed against its positive values. In some circumstances, QEEG has some positive values, but they are outweighed by the substantial problems encountered in trying to use the tests clinically. In other circumstances, QEEG's positive values outweighed its disadvantages, leading to positive recommendations for use. In the latter case, these positive values outweigh the technique's problems only when used in expert hands and with good clinical judgment.

HISTORICAL DIFFICULTIES IN EEG QUANTIFICATION

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 basic 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 yet substantially altered the daily practice of clinical electrencephalography.

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