

## ELECTROENCEPHALOGRAPHY IN NEUROLOGY

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**Abstract :** Electroencephalography (EEG) is the technique of recording from the scalp spontaneous electrical activity of the brain and correlating it to the underlying brain function. However with recent advances in neuroimaging, its role has become restricted and more focused. It remains an extremely valuable test in patients with suspected epilepsy and in patients with altered mental status and coma. EEG pattern helps to clarify the seizure type and are indispensable for the diagnosis of non-convulsive status epilepticus and for separating epileptic from non-epileptic episodes. There are EEG patterns predictive of the cause of encephalopathy or the location of the lesion. An EEG is most helpful in diagnosing severity and hence the prognosis of cerebral dysfunction. Lastly EEG is very helpful in assessing normal or abnormal functioning in a newborn because of the serious limitation in performing an adequate neurological examination on the newborn. 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 a normal awake child and adult shows an *alpha rhythm*<sup>1</sup>. However there may be normal variants which are often mistaken as abnormal patterns. In general the alpha rhythm is higher in amplitude in the right hemisphere. If the amplitude on the right side is more than 1½ times that on the left or is over 25% higher on the left than on the right side, it is considered significant<sup>2</sup>. The EEG during non-rapid eye movement (NREM) sleep in children shows very prominent spike-like vertex sharp waves which are often mistaken for epileptiform activity. Similarly 'positive occipital sharp transients (POSTs)' in children may also be mistaken as abnormal spikes. In a small proportion of normal adults, alpha rhythm may be entirely absent and the background may consist of a low amplitude rhythm of 5-30 cps frequency. This EEG is reactive to stimuli like sleep and drugs and hyperventilation may bring out an alpha rhythm. Moreover, during sleep normal activities like vertex sharp transients and sleep spindles are generated<sup>3</sup>. The alpha frequency decreases with normal aging to a minimum of 8cps.

### EEG IN EPILEPSY

The value of an EEG lies in the fact that it not only shows specific ictal discharges during a clinical seizure but also characteristic epileptiform abnormalities in many epileptic patients even in the interictal period. Specific patterns may help to classify the seizure type and guide the choice of antiepileptic medication. An EEG may be the only test demonstrating focal abnormalities responsible for the patient's epilepsy. It is indispensable for the diagnosis of nonconvulsive status epilepticus presenting as a 'twilight' state or a prolonged episode of abnormal behaviour. It may be the only way to establish whether the abnormal behavior is due to an epileptic seizure or a nonepileptic event. It is also required to localize the epileptogenic focus when resective surgery is undertaken in a patient with medically refractory focal epilepsy.

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Morphologically, interictal epileptiform abnormalities consist of spikes, polyspikes, sharp waves and spike slow wave complexes. Generalized discharges that are bilaterally synchronous and symmetrical are associated with generalized epilepsies, whereas focal discharges are seen in partial epilepsies. The topographic distribution of these interictal discharges is more important in the classification of epilepsies since most patients do not have a clinical seizure during an EEG. However, although the interictal epileptiform abnormalities have a high correlation with the occurrence of clinical seizures they do not necessarily mean that the patient has epilepsy. Different studies have found an incidence of less than 2% of epileptiform abnormalities in the EEG of nonepileptic subjects<sup>4</sup>. The irrefutable evidence of an epileptic seizure is a clinical seizure associated simultaneously with ictal discharges in the EEG, although this evidence may only be obtained on prolonged video EEG monitoring. Ictal seizure pattern is characterised by repetitive EEG discharges with relatively abrupt onset and termination, and characteristic pattern of evolution lasting several seconds. It is generally rhythmic and displays increasing amplitude, frequency and spatial spread during the seizure.

There are many EEG transients that resemble epileptiform discharges but need to be distinguished from epileptiform abnormalities to avoid over diagnosis. These include artifacts (e.g. electrode problem, muscle potentials, eye movements, ECG etc.), normal background activity (e.g. vertex sharp transients of sleep, POSTs etc) and other epileptiform variants of dubious clinical significance. Useful criteria have been formulated to properly identify epileptiform discharges<sup>5</sup>-

1. Epileptiform discharges should be discrete and clearly separable from ongoing background activity by higher amplitude and with their morphology and duration.
2. Most epileptiform discharges have a bi- or triphasic waveform.
3. The epileptiform events show asymmetric rising and falling phases.
4. Most spikes and sharp waves are followed by a slow wave
5. Epileptiform discharges should involve more than one electrode which helps to distinguish them from electrode related artifacts or muscle potentials.

6. Epilepsy manifested by loss of consciousness is accompanied by demonstrable changes in the scalp EEG. The absence of such changes during an episode of 'unconsciousness' or seizure like motor activity can be particularly important in diagnosing pseudo seizures.

The yield of epileptiform abnormalities in an interictal EEG study can be increased by various methods. Serial EEG studies increase the yield from 50% in the first record to 84% by the third EEG and 92% by the fourth EEG. Thus four or five EEGs spread over a few years provide diagnostic abnormalities in over 90% patients with epilepsy<sup>6</sup>. Serial negative EEGs in a patient with continuing paroxysmal events raise a suspicion of nonepileptic episodes. Obtaining an EEG immediately after a clinical seizure will also increase the chances of capturing interictal epileptiform discharges. Hyperventilation<sup>9</sup> for at least 5 minutes at the beginning and the end of the study and photic stimulation are potent activators of generalized discharges associated with primary generalized epilepsies. Photoparoxysmal response (PPR) has a high correlation with clinical epilepsy and is characterized by generalized bilaterally synchronous spike wave discharges occurring with photic stimulation. The incidence of epilepsy<sup>7</sup> is particularly high if the PPR is prolonged (93%) rather than self-limited (52%). About 10% of patients with primary generalized epilepsy show PPR with the highest incidence in juvenile myoclonic epilepsy<sup>8</sup>. PPR in nonepileptic subjects has a prevalence of 1-4% and is usually brief<sup>1</sup>. Other EEG responses induced by photic stimulation, like the photomyoclonic response have no significant correlation with epilepsy. Sleep tends to bring out focal epileptiform abnormalities in patients with focal epileptic seizures. All patients with suspected epilepsy should have a sleep recording unless there is an unequivocal abnormality seen during wakefulness. To ensure a sleep EEG one can instruct the patient to come for the EEG after remaining awake for the entire or at least a major part of the previous night. Sleep deprivation has a further activating effect that is additive to natural sleep, particularly in patients with complex partial seizures and juvenile myoclonic epilepsy. The use of special electrodes improves the chances of recording epileptiform abnormalities. They are particularly helpful in detecting abnormalities arising from the mesial temporal lobes which have high epileptogenicity but are not fully explored by conventional placement. Nasopharyngeal electrodes were used in the past but anterior temporal electrodes have now been found to be better in patients with temporal lobe epilepsy<sup>9</sup>. Sphenoidal electrodes have the best yield but are invasive and are used only as a part of the presurgical evaluation of patients with medically intractable temporal lobe seizures. However, seizures that remain very localized, including *epilepsia partialis continua*, may not have changes in the EEG because the diagnostic discharge may be deep-seated or involve only a small pool of neuronal tissue. In rare patients with reflex epilepsy, the specific trigger may be carried out during the EEG recording to promote a clinical seizure. Examples of these are playing specific music in music epilepsy, asking a patient to read from a book in reading epilepsy, bathing the patient in bathing epilepsy, asking a patient to eat his meals in eating epilepsy etc.

*Generalized epilepsies* may be primary (idiopathic) or secondary (due to diffuse cerebral hemispheric insult). The EEG hallmark of *primary generalized epilepsy* (PGE) is

rhythmic, anterior-dominant generalized bisynchronous 3 Hz spike wave discharges superimposed on a normal background. More common however are generalized paroxysms of spike wave complexes occurring at 3-5 Hz. Transient asymmetry and isolated focal spikes may also be seen. Although there are no interictal abnormalities which are specific for individual syndromes included under PGE, polyspike waves are more common with myoclonic epilepsies, paroxysmal occipital-dominant rhythmic delta activity is seen in absence epilepsy and PPR is most common with juvenile myoclonic epilepsy. In *secondary generalized epilepsy*, the background activity is disorganized, there are variable degrees of slowing and other patterns may be seen like hypsarrhythmia (high amplitude, asynchronous, slow waves associated clinically with infantile spasms) and generalized paroxysmal fast activity (bisynchronous 12-25 Hz discharges seen mainly during sleep and usually not associated with any clinical change).

*Focal epilepsies* may be primary (idiopathic) or secondary (due to acquired focal cortical processes). The interictal EEG hallmark of focal epilepsy is a focus of epileptiform activity. The frequency of epileptiform discharges do not correlate with the frequency of clinical seizures. However the interictal epileptiform discharges do become more frequent immediately after a clinical focal seizure<sup>10</sup>. Postictally, there may be a period of generalized followed by transient (from seconds to days) focal delta activity which is a reliable sign of a focal origin of the previous epileptic seizure. When the focal epileptiform activity occurs along with a focal abnormality of the background activity the possibility of a structural lesion is more likely and the epilepsy is more likely to be symptomatic. The most common primary focal epilepsy is *benign Rolandic epilepsy* in which epileptiform discharges are seen over the centrotemporal regions especially during sleep.

## EEG IN STATUS EPILEPTICUS

A common reason for ordering an emergency EEG is for the diagnosis and management of status epilepticus (SE). SE may be generalized convulsive status, *epilepsia partialis continua* or nonconvulsive status (including absence status and complex partial status). Patients with nonconvulsive status present with confusion and rarely coma. Some patients may continue to be obtunded and show epileptiform discharges in their EEG even after treatment of generalized convulsive status and are also grouped under subtle or nonconvulsive status.

Nonconvulsive status associated with focal epilepsy is easy to diagnose when there are frequent electrographic focal seizures. However, the ictal EEG pattern in complex partial status may be generalized as in absence epilepsy. Some helpful *criteria are proposed by Young et al<sup>11</sup>*. In patients who show continuous generalized epileptiform discharges in their EEGs, a rate faster than 3 per second likely represent an ictal pattern. Such discharges at a frequency less than 3 per second are likely to be ictal if significant clinical and/or EEG improvement is seen following small doses of IV lorazepam or diazepam. This type of improvement is most commonly seen in typical absence status. Rhythmic sinusoidal waves of any frequency may represent an ictal pattern if there is an evolving pattern at the onset (increasing amplitude and/or frequency) or a decremental pattern at the termination (decremental amplitude or frequency) or if there is post discharge slowing or attentation. Reviewing the previous EEG and obtaining follow up EEGs also help to

distinguish between ictal and interictal discharges. A period of repetitive generalized spike wave discharges associated with worsening of sensorium is more likely an absence status, particularly if the previous EEGs or follow-up EEGs display fewer epileptiform abnormalities.

The EEG of patients with subtle SE often shows repetitive discharges including unilateral or bilateral periodic discharges (PLEDs or BiPLEDs) or generalized periodic discharges (PEDs). Some epileptologists feel that this is an intermediary pattern before disappearance of all paroxysmal EEG activity and needs further aggressive treatment<sup>12</sup>. *Refractory SE* is usually treated by pentobarbital, propofol or midazolam infusions and requires continuous bedside EEG monitoring. The dose is regulated to control all clinical and electrographic seizures and to maintain a burst suppression pattern on the EEG.

### EEG IN FOCAL CEREBRAL LESIONS

The use of EEG in localizing focal cerebral lesions has become limited since the advent of computerized tomography and magnetic resonance imaging. However, it is still used to evaluate the epileptogenic potential of a focal lesion. There is slowing and decreased amplitude of the alpha rhythm on the side of the lesion, finally with replacement by slower frequency theta/delta activity<sup>13</sup>. Irregularity in the waveform, slower frequency of waves and persistence indicate a more severe and acute focal process. The process is best localized to the area showing the lowest amplitude. Such focal delta activity can appear transiently after a complex migraine attack or focal epileptic seizure. In such cases, a repeat recording in a few days is indicated to assess persistence of this focal abnormality. The amplitude of the background activity may be paradoxically higher on the side of the focal cerebral lesion<sup>14</sup> as in healed cerebral infarcts, in slowly progressive tumors and after craniotomy. Often this enhanced background activity is slower in frequency and less reactive to eye opening which alert the interpreter to the abnormality. Epileptiform activity such as focal spikes or sharp waves may occur in localized indolent hemispheric lesions. With acute hemispheric lesions, periodic lateralized epileptiform discharges (PLEDs) are seen which occur at one per second over a large area of the hemisphere during most of the EEG study.

### EEG IN PATIENTS WITH DIFFUSE ENCEPHALOPATHIES

The EEG in most encephalopathies shows a diffuse alteration of background activity and varying degrees of slowing. *Focal EEG findings* in a diffuse encephalopathy are seen in some conditions like hyperosmolar nonketotic coma, herpes simplex encephalitis (HSE) and early Creutzfeldt-jakob disease (CJD). *Periodic patterns* are specifically seen in anoxic encephalopathy and some encephalitis. *Triphasic waves* and *positive spikes* characteristically occur in metabolic encephalopathies. The EEG findings in most encephalopathies are nonspecific and the main contribution of the EEG<sup>15</sup> in providing an objective measure of severity of encephalopathy, the prognosis and effectiveness of therapy<sup>15</sup>.

With increasing severity of encephalopathy there is progressive slowing of the posterior dominant rhythm to theta and then delta activity with decreasing amplitude of the waveform. Some tracings reveal burst suppression pattern with regular alternation of very low amplitude EEG with higher amplitude EEG segments. The most extreme abnormality is

electrocerebral inactivity. The latter two patterns carry a grave prognosis unless they are due to drug intoxication in which case they are reversible. To determine the severity of encephalopathy, one must also look for spontaneous variability of the EEG over several seconds to minutes and the reaction to stimulation. An EEG lacking spontaneous variability (invariant EEG) and total lack of reactivity to intense and prolonged stimulation indicates a severe degree of encephalopathy.

Triphasic waves are highly suggestive of a metabolic encephalopathy and are high amplitude, bilaterally synchronous and symmetrical. They consist of a short negative sharp wave, followed by a positive sharp wave and then a long negative slow wave. They are not specific for any particular metabolic encephalopathy<sup>16</sup> and are rarely seen in patients below the age of 20 years. Patients with metabolic encephalopathies showing prominent triphasic waves in their EEG have an overall poor prognosis.

*Excessive beta* activity over the anterior head regions in the EEG is seen with overdose of hypnotic sedative drugs. With more severe intoxication, the fast activity assumes a slower frequency. An alpha coma pattern, burst suppression pattern or electrocerebral inactivity may also be seen but these do not carry as ominous a prognosis as in anoxic encephalopathy<sup>1</sup>.

EEG is commonly used to assess the degree of cerebral insult and to judge the prognosis in patients with anoxic encephalopathy. An EEG should be obtained at least 5-6 hours after successful resuscitation since it takes an hour or more for the EEG to stabilize after the episode<sup>17</sup>. Normal or near normal EEGs after an anoxic episode indicate an excellent prognosis. Poor prognosis is indicated by bilateral PLEDs, alpha coma pattern (severe coma with alpha frequency activity and lack of reactivity to sensory stimulation)<sup>18</sup>, burst suppression pattern and electrocerebral inactivity.

The EEG is being increasingly employed for *determination of brain death* particularly when organs have to be salvaged for transplantation. It has to be emphasized however, that electrocerebral inactivity is only one of the criteria and should always be considered along with other findings of brain death. The American EEG Society has laid down recommendations for EEG recordings in all cases of suspected brain death<sup>19</sup>. The 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 muscle relaxant. A single EEG and at least 12 hours of clinical observation after an unequivocal acute cerebral insult are minimum requirements for diagnosing brain death in any individual older than 1 year. Brain death should not be determined until at least 7 days of age. From 7 days to 2 months, 2 examinations and 2 EEGs separated by at least 48 hours are required; from 2 months to 1 year, 2 examinations and 2 EEGs separated by at least 24 hours are required.

In *viral encephalitis*, the severity of the EEG abnormalities generally parallels the clinical picture<sup>20</sup>. The EEG changes are usually nonspecific with a few exceptions. In HSE, the EEG may show a focus of polymorphic delta activity over a temporal region. The most characteristic feature is the occurrence of PLEDs usually over the more recently involved lobe and between 2-15 days after the onset of the illness. These are pseudo-periodic, focal or unilateral, large amplitude, sharp wave complexes that repeat at regular intervals of 1-3 seconds.

They are not unique for HSE (occurring also with infarcts, abscesses or tumors) but are highly suggestive in the appropriate clinical setting. The EEG in subacute sclerosing panencephalitis (SSPE) is highly specific and shows high amplitude, bilateral synchronous, symmetrical period complexes. They repeat every 4 to 10 seconds and each complex is associated with a clinical myoclonic jerk. In the early stages of the disease, they may occur after long intervals and sleep may activate them. A sleep recording is therefore recommended when the awake tracing is normal in a suspected case of SSPE. The characteristic EEG pattern in CJD consists of periodic, bilaterally synchronous bi- or triphasic sharp waves which repeat at a frequency of around one per second. In the early stages, focal periodic sharp waves (PLEDs) may be seen. As in SSPE, each periodic complex is associated with a clinical myoclonic jerk and this EEG pattern in the right clinical setting strongly supports the diagnosis.

### EEG IN NEONATES

In recent years, EEG has been used to evaluate full term or premature neonates due to limitations in performing an adequate neurological examination in newborns<sup>21</sup>. It is an important tool to assess an encephalopathic process or the occurrence of epileptic seizures and to predict neurological outcome. The EEG of a neonate shows distinctive patterns related to the conceptional age and the behavioral state (awake, active sleep and quiet sleep). Some of these neonatal EEG patterns resemble the burst suppression pattern that carries a poor prognosis. However the burst suppression pattern is invariant and not reactive to stimulation unlike the neonatal EEG. Severely abnormal neonatal EEG patterns consist of persistent low voltage tracing, invariant nonreactive burst suppression pattern and the presence of gross asymmetry over the two sides of the head. In neonates, seizures are often characterized clinically by subtle motor behavior and the EEG is indispensable in establishing epileptic activity by demonstrating an associated ictal pattern. This pattern often differs from that in older children and adults and is usually unifocal or multifocal. Interictal epileptiform abnormalities are rarely present to aid in the diagnosis.

Some technical points are important to optimize neonatal EEG recordings. The study should be long enough to include both

active and quiet sleep. It may be necessary to record the EEG for 45-60 minutes instead of the usual 30 minutes. Non-EEG variables like respiration, extraocular movements, ECG and chin activity should be routinely recorded as they are critical in identifying different states (awake, active or quiet sleep) and in recognizing various artifacts.

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### LONG-TERM FOLLOW-UP ABO-INCOMPATIBLE ADULT LIVING DONOR LIVER TRANSPLANTATION IN CIRRHOTIC PATIENTS Matsuno N. et.al. *Clin. Transp.* 2007,1:229-233

ABO-incompatible liver transplantation is usually contraindicated. The presence in the recipient of preformed anti-A/B antibodies located on endothelial cells raises the risk of antibody-mediated humoral rejection of the graft. We describe four successful cases of steroid withdrawal in adult patients who had living-donor liver transplantation from ABO-incompatible donors. Antirejection therapy included multiple perioperative plasmapheresis, splenectomy, and a triple immunosuppressive regimen with tacrolimus, methylprednisolone (MPSL), and cyclophosphamide or mycophenolate mofetil (MMF). The maintenance dose of immunosuppression did not differ from that of ABO-identical cases. After transplantation, intrahepatic arterial infusion therapy with prostaglandin E1 (PGE1) was used. As a result, all four patients were able to achieve long-term graft survival without steroid use. They all have good liver function and are leading normal lifestyles. Our experience with these four patients suggests the feasibility of controlling humoral rejection and other complications in adult ABO-incompatible living donor liver transplantations with intrahepatic arterial infusion of PGE1, splenectomy, and plasmapheresis with a regular base of immunosuppression protocol to prevent antibody-mediated humoral rejection.