Identification of interictal epileptiform activity (IEA), seizures and the specific EEG patterns that accompany epilepsy syndromes remains an electroencephalographer’s most critical task. Fortunately, IEA and seizures are also often easily distinguished and stand out in sharp contrast from background EEG frequencies. This chapter will focus on providing practical guidance in recognizing these patterns and understanding their significance in clinical application.

The definition of epileptiform activity is given in Chatrian’s glossary of terms as “distinctive waves or complexes, distinguished from background activity and resembling those recorded in a proportion of human subjects suffering from epileptic disorders.” (Chatrian 1974) These waves or complexes can appear as isolated focal spikes or sharp waves, generalized polyspike, spike and wave or paroxysmal fast activity, and sometimes as abrupt rhythmic evolution of the background that heralds seizures.

To recognize a wave as epileptiform, the pattern must include a wave that stands out from the background in frequency, amplitude and/or field. Most often, epileptiform activity is distinguishable by all of these characteristics. Often the sharpness of the wave at its maximum amplitude provides the first clue to its differentiation from the background. If there is an isolated wave with a peak that is sharper than the baseline background, the next helpful criteria are whether the amplitude is also distinctive, and whether there is a field of distribution that suggests a focal or more diffuse surrounding area of positivity or negativity (Lesser 85). An aftergoing slow wave with the same field of distribution is also very helpful in identifying epileptiform activity. To classify the epileptiform activity as a spike, the duration the waveform is, by convention, between 20 and 70 msec. Epileptiform activity that lasts from 70-200 msec is referred to as a sharp wave (or sharp and slow wave complex if followed by a delta frequency wave.) (Maulsby 68) The terms generalized polyspike and wave, or spike and wave activity refer to discharges with a diffuse field of distribution and aftergoing delta wave that are often repetitive. These are usually also described by identifying the rate of the frequency of repetition, e.g., 3.5 Hz generalized spike and wave, or fast (4 or more Hz spike and wave) or slow (2.5 or less Hz spike and wave).

Figure 1 a and b single spike and single sharp wave
Many of these patterns of epileptiform activity are associated with a specific epilepsy syndrome. However, not all activity that meets the criteria to be considered epileptiform relates to a diagnosis of epilepsy, or indeed any clinical abnormality.

**Epileptiform Activity in Normal EEGs**

*Vertex sharp waves in children*

The onset of sleep is generally heralded by the appearance of vertex sharp waves (see chapter 11). Vertex waves are generally diphasic sharply contoured activity with a maximum amplitude at C3 and C4, lasting up to 200 msec. The highest amplitude (150-250 uv) initial deflection is surface negative, and is followed by a generally slower and lower voltage surface positive wave with the same distribution. In young children, vertex waves appear by 8 weeks of age, and often have a slightly larger field through early childhood, involving both fronto-central areas. Particularly in children aged 2-5, these waves can become quite sharp, occur repetitively, and can appear in more than a single morphology. *(Figure 2 – sharp vertex waves)* Careful evaluation of the field, which will always be symmetric and synchronous, can be helpful in identifying the transients as vertex activity.

*Sharp transients in neonates*

During gestational and neonatal developmental maturation, scattered sharp transients occur in the normal EEG tracing during quiet sleep (see also Chapter 5). These transients begin to appear at about 34 weeks of gestation, are often most common in both frontal regions independently. They are usually negative in surface polarity and have a duration of 150-200 uv and a low amplitude (50-100 uv); they occur most often in frontal distributions, but are seen occasionally over other areas. These sharp transients reach a maximum between 35 and 36 weeks of gestation, and should be dissipating by term, with occasional sharp transients persisting up to the fourth week of life during quiet sleep *(Hrachovy 2000).*

*Lambda waves*

While a normal subject is visually scanning a pattern, a train of occipital biposterior sharp waves an occur called Lambda waves. These waves are usually biphasic, with an early positive component, followed by an occipital negativity. *(Figure 3 – lambda waves)* Lambda waves are usually repetitive, but can be attenuated by changes in illumination changes in fixation, or eye closure. They are more common in older children and adolescents than in adults and are occasionally seen unilaterally, depending on the level of asymmetry in stimulation. They can be most easily distinguished from epileptiform activity by demonstrating their dependence on visual scanning.

*POSTs and BETs in sleep*
During light NonREM sleep, positive, occipital sharp transients (POSTs) are often seen and can appear quite sharp in children and adolescents. (Figure 4 - POSTs) These waves are triangular with maximum positivity at the occipital electrode, and usually repeat with a frequency of between 0.5 and 5 Hz intermittently. They can occur synchronously or independently over the two hemispheres, and are usually moderate to high amplitude (70-150 uV).

Another epileptiform pattern commonly seen in drowsiness and light sleep, most commonly in adults, are the 50uV spikes referred to as benign epileptiform transients of sleep (BETS) or small sharp spikes (SSS). (Figure 5 - BETS) They are usually quite short in duration, rarely longer than 50 msec, and usually consist of an abrupt diphasic spike with a broad sloping potential field that can involve both hemispheres. They usually recur during sleep in several morphologies and distributions, and are best seen in montages with large inter-electrode distances. They can be distinguished from epileptiform activity because of the absence of aftergoing slow waves, absence of background disruption, and tendency to disappear in deeper stages of sleep. BETS may occur in up to 20% of the normal population (White 77). A recent low resolution electromagnetic topography study localized BETS to a transhemispheric scalp distribution in the insula and the posterior quadrant, which helps to explain the diffuse hemispheric field usually seen at the scalp. (Zumsteg 06)

**Wicket spikes**

In the mid temporal regions, the most common normal pattern that must be differentiated from focal sharp waves generated by an epileptogenic zone are wicket spikes. These sharp waves are usually midtemporal, archiform or wicket-shaped, and often occur in short trains or clusters. They repeat at frequencies of 6-11 Hz, are monophasic, 50-200 uV, and may actually be a fragment of temporal alpha activity in adults. Wicket spikes occur most frequently in drowsiness or sleep, and can be seen in each temporal region independently. When they occur singly, the most reliable way to distinguish wicket spikes from the epileptiform activity associated with temporal lobe epilepsy is that wicket spikes are not associated with an aftergoing slow wave, and do not disrupt the normal background activity present in this region. (Westmoreland 2003) (Figure 6 A and B – wicket spikes)

**14 and 6 Hz Positive Bursts and 6 Hz (phantom) spike and wave**

During stage 2 sleep in adolescents, trains of 14 or 6 Hz activity can occasionally be seen over the posterior temporal regions lasting from 0.5 to one second. These bursts are arch-shaped with alternating positive spiky waveforms that can occur synchronously or independently. Recognition of the characteristic combination of frequencies establishes this as the previously defined benign variant.

6 Hz low amplitude spike and wave activity (also referred to as Phantom spike and wave) also occurs most commonly in light sleep in adolescents, but is also seen in adults. The spike is very low amplitude and is followed by a more prominent diffuse slow-wave component. Bursts can be asymmetric or anteriorly or posteriorly dominant. Similar morphologies occurring in males in wakefulness, sometimes at slightly lower
frequencies, have been associated in some cases with epilepsy, but the low amplitude discharges occurring in sleep have no clear clinical significance.

Questions

1. Posteriorly-dominant positive triangular sharp waves that occur during visual scanning in normal patients are called:
   a. POSTs
   b. BETS
   c. Lambda waves
   d. Wicket spikes

2. Sharp transients during sleep in neonates should disappear by:
   a. One year
   b. Six months
   c. Term
   d. One month

General clinical significance of identification of IEA

Defining epilepsy syndrome after initial EEG

Between 12-50% of EEGs show epileptiform activity after a single seizure. (Pedley 03) This yield is substantially increased (51%) if the first EEG can be done within 24 hours of the event compared with later studies (34%) (King 98). Serial EEGs in patients might also increase the yield: in patients with defined epilepsy syndromes the incidence of IEA can increase from 50% after one EEG to as much as 84% overall after 3 EEGs (Salinski 87). The duration of the recording may also be important: in 46 patients with established epilepsy, 37% had IEA within the first 20 minutes, but 89% had positive findings after 24 hours of recording Narayanan 08). The occurrence of epileptiform activity also seems to be age dependant – older patients seem to have less focal and generalized epileptiform activity than children. (Drury 98, Aurlien 07, Franzon 07) In nearly all studies, IEA on EEG after a first seizure predicts a significantly higher risk of seizure recurrence (Berg 91). Some authors also feel that the frequency of focal interictal epileptiform activity in early EEGs may be somewhat helpful in determining which patients will ultimately have more refractory epilepsy (Hughes 2003).

In a few syndromes, the EEG is almost always positive – absence epilepsy, Benign Epilepsy with Centro-temporal Spikes (BECTS, formerly known as Rolandic Epilepsy), and Juvenile Myoclonic Epilepsy (JME), the likelihood of a normal EEG is less than 10%. West Syndrome and Landau-Kleffner syndrome (see later discussion) are typically defined by their EEG pattern at presentation. Activation procedures are particularly helpful to elicit IEA in the primary generalized epilepsies. Hyperventilation activates generalized spike and wave in absence in 50-80% of cases, and photic
stimulation increases its incidence by 18%. Photic stimulation is most likely to activate the polyspike and wave patterns of JME, with a photosensitivity rate of about 30%.

During sleep, the frequency of slow spike and wave in Lennox Gastaut syndrome increases, as does the number of polyspike discharges and fragments, while absence epilepsy discharges lessen in frequency and become slow and irregular in most cases. BECTS discharges occur much more frequently in drowsiness, indeed up to 30% of patients have their IEA only in light sleep. Childhood occipital epilepsy is also activated by both eye closure and NonREM sleep.

In general, the most effective strategy for capturing IEA after a first seizure is to record as soon as possible after the event, use activation procedures, encourage sleep, and perform a longer or repeated recording in cases where the information about IEA would be most likely to be clinically useful (e.g., those without structural lesions, without precipitating factors, or with possible prior seizures).

Specificity of IEA in subsequent diagnosis of epilepsy

Another way to examine the clinical relevance of IEA during an EEG is to look at the predictive value of finding IEA for the subsequent diagnosis of epilepsy. Patterns of IEA most likely to be associated with seizures regardless of the chief complaint are 3 Hz spike and wave, Focal anterior and mid temporal spikes, localized frontal spikes, and pseudoperiodic epileptiform discharges. (Fisch 2003) The likelihood seizures will occur in patients with anterior temporal spikes is over 90% in several series, and temporal intermittent rhythmic theta activity is associated with seizures in nearly 80%. Midline spikes in children have an 83% correlation with epileptic seizures. (Kutluay 01) A frontal lobe spike carries a likelihood of epilepsy of about 75%.

Between 0.5-2 % of the population may have IEA without ever developing seizures, with the higher end of the range often representing those hospitalized for psychiatric or neurologic illnesses (Zivin 68). In one series of patients with IEA without previous seizures or diagnosis of epilepsy, 73% had acute or progressive cerebral disorders at the time of the abnormal EEG (Sam 2001). The types of IEA patterns least associated with epilepsy include a photoparoxysmal response, occipital generalized spike and wave, BECTS, and occipital spikes. If centro-temporal spike complexes are seen, the incidence of the full-blown disorder with clinical seizures is 40% (Kellaway 81). The frequency of epilepsy in those with occipital spikes is less than 50% in most series.

Predicting prognosis of epilepsy based on EEG

In patients with known epilepsy syndromes, EEG has only limited value in predicting long-term seizure remission. In temporal lobe epilepsy, unilateral IEA is clearly correlated with better outcome after surgery than bilateral IEA, and to some extent, the frequency of IEA may also correlate with likelihood of remission after surgery (Hufnagel 94). However, the persistence of epileptiform activity after epilepsy surgery did not predict the prognosis for remaining seizure-free in this group (Mintzer 05).
In generalized epilepsies, Depakote reduces generalized IEA in 76% of patients, and reduces the photoparoxysmal response in 25%. In absence epilepsy, differences in EEG findings can correlate with likelihood of initial seizure remission, likelihood of status epilepticus, and the rate of long-term need for medications, with more atypical findings having a significantly worse prognosis (Sinclair 07).

Questions

3. After a single unprovoked seizure, EEG will be most helpful in defining a possible epilepsy syndrome if:
   a. EEGs are recorded more than 2 weeks after the initial seizure
   b. Patients age is older than 60
   c. Recorded in children with probable absence seizures
   d. The recording does not include any sleep

4. Which IEA finding is most likely to be associated with clinical epilepsy?
   a. Anterior temporal spikes
   b. Generalized fragments of 3 Hz spike and wave
   c. Centro-temporal transients in adolescents
   d. Photoparoxysmal discharge

Epileptiform Activity and Seizures in Specific Epilepsy Syndromes

Absence Epilepsy (Childhood and Juvenile)

The clinical syndrome defined by the International League Against Epilepsy (ILAE) as childhood absence epilepsy (also called pyknolepsy in the past) refers to a seizure disorder with only brief, frequent absence seizures (4s to 1 min, 10-100 per day) with an age of onset between 4-8 years (Nordli 05, Valentin 07). This syndrome generally remits in late adolescence and by definition does not include other seizure types, such as GTC or myoclonus. The incidence is clearly genetic, and in some families, calcium channel genes seem to play an important role (Vitko 05). The incidence of this type of epilepsy is relatively low, comprising 2-10% of epilepsy in children (Loiseau 90).

Juvenile absence epilepsy, on the other hand, begins between 9-13 years, often includes morning GTC and sometimes myoclonus, and has a much lower remission rate, with 44-55% persisting into adulthood (Tovia 06). EEG findings also differ somewhat between the two types.

Interictal EEG – The interictal EEG of a patient with typical childhood absence epilepsy generally has a normal background rhythm, although some authors report mild diffuse slowing in a small fraction of cases. The classic finding in absence epilepsy is the interictal and ictal 3 Hz spike and wave discharge. (Figure 7 A, B, C – 3 Hz spike and wave). This diffuse, symmetric discharge begins abruptly, with a single or diphasic sharp
wave, most often at a 3.5-4 Hz frequency, and slows to 2.5-3 Hz prior to its abrupt cessation (Drury 2002). Typically these discharges have a frontal maximum, but they may also appear centrally or bi-occipitally. These discharges have been descriptively referred to as “egg and dart,” and can be seen as a sharp column and high arch. There is no suppression of the background after the discharges. The most important feature to distinguish the typical spike and wave of absence from other generalized patterns is the very reliable frequency, the single or diphasic spike and the completely synchronous onset of the paroxysm.

In a 15-30% of young patients, the interictal EEG may also contain occipital intermittent rhythmic delta activity (OIRDA) at 3-4 Hz (Holmes 1987, Watemberg 2007), which is a high- amplitude 3 Hz paroxysmal synchronous bilateral discharge without sharp waves. OIRDA is correlated with increased sensitivity to hyperventilation. Some have even reported rare focal centro-temporal spikes, like those seen in BECTS in some patients (Hrachovy 2006). The typical 3 Hz discharges become fragmented and brief during sleep, and are often suppressed during REM. Hyperventilation may increase the rate of discharges in up to 30% of patients and about 18% may be photosensitive (Sato 82). One third to one half of patients treated with anti epileptic drugs (AEDs) completely attenuate these discharges (Sato 82, Bruni 80, Harding 78).

In juvenile absence epilepsy, discharges are generally associated with an initial polyphasic sharp wave and a somewhat more rapid repetition of sharp and slow waves at 4-6 Hz. (Figure 8 A and B – atypical absence) The frequency and distribution of the generalized discharges are more irregular, and there is a lower incidence of OIRDA and photosensitivity in this population (Paniayotopoulos 89). Prognosis of the syndrome can be monitored to some extent by the response of the generalized discharges to medications (Koutroumanidis 05).

Ictal findings – Defining an ictal event may be more difficult than in other syndromes, as it has been demonstrated that reaction time is delayed both in short and longer paroxysms of 3 Hz spike and wave (Browne 74). Clinically recognized typical absence events usually last longer than 3 seconds, with an average of 10 seconds, and as many as 92% demonstrate some type of retained slowed behavior, clonic movement or automatisms (Penry 75). Normal behavior resumes quite abruptly after the ictal events ends. During generalized tonic clonic seizures in those with juvenile absence, the seizure begins with a diffuse low- amplitude beta-frequency activity and progresses to slower repetitive complexes of spike and wave activity during the clonic portion of the event. After the generalized seizure, all frequencies are symmetrically suppressed for minutes to hours.

Benign Epilepsy with CentroTemporal Spikes (BECTS)

BECTs is one of the most common childhood epilepsy syndromes, and has the best prognosis, with seizures disappearing before age 16-18 in virtually all patients (Beaussart 78, Loiseau 83). Clinically, the syndrome most often presents between ages 4 and 10, with infrequent nocturnal seizures, often characterized by clonic facial twitching, pharyngeal spasms and interruption of speech with occasional generalization. Few patients have more than three seizures. In some patients, during the phase where the
EEG is significantly active, there may be subtle language difficulties (Riva 2007). The predisposition to the syndrome and to the interictal EEG findings is significantly genetically determined: up to 30% have relatives with similar EEG findings. (Bray 64)

Interictal EEG - The background in patients with BECTS is normal for age. Particularly during drowsiness, the record is punctuated by frequent, repetitive, diphasic to triphasic sharp waves with the middle negative component having the largest amplitude. The sharp wave complex is almost always followed by a lower amplitude negative delta frequency slow wave. These sharp waves are distributed roughly equally between central (C3-5 and C4-6) and mid-temporal (T3 or T4) derivations (Legarda 94), and may be unilateral, bilateral or sometimes synchronous. (Figure 9 A and B – BECTS) These discharges are usually very stereotyped, and often have a frontal positive dipole when seen on a referential montage. In 30% of patients, these discharges are seen only during sleep recordings (Blom 75) Photic stimulation and hyperventilation have no effect. In up to 15% of cases, occipital spikes or generalized spike and wave discharges can also be seen in recording of patients with this syndrome (Beaussart 72, Beydoun 92)

Ictal findings – Very few seizures have been captured on EEG. Reports of events recorded describe a low voltage centrotemporal fast activity with slowed and spreads before generalizing. There was no post-ictal slowing or attenuation after the seizure, but spikes were suppressed. (Bernardina 75)

Benign Occipital Epilepsy (BOE)

Benign Occipital Epilepsy has been defined by the ILAE as an idiopathic localization-related syndrome. Clinically, BOE most often presents as a young onset variant, in ages 3-5, often (@30%) with a genetic predisposition, sometimes also known as Panayiotopoulos syndrome (Panayiotopoulos 99). Infrequent partial seizures occur, often at night, and the most common semiology is tonic eye deviation accompanied by emesis, evolving at times to focal or generalized motor patterns. Imaging studies and development are normal, and the prognosis for response to medication and remission is excellent by age 12. There is a later variant, with a peak age of onset of 7-9 years, seizures more often present with visual hallucinations, without loss of consciousness, lasting only a few seconds, but commonly with associated post-ictal headache (Gastaut 82). The outcome is generally favorable, but worse than in the early onset form.

Interictal EEG – Electrographically, the background rhythm is normal. With closed eyes, there are unilateral or bilateral, very frequent (up to 1-3Hz), diphasic (surface negative then positive), high amplitude spikes in the occipital lobe (Ferrie 97). There is often, but not always, an aftergoing slow wave. The epileptiform activity can be suppressed by eye closure, and is often suppressed by visual fixation. (Lugaresi 84) Hyperventilation and photic stimulation usually have no effect on the discharges, although some patients have inhibition of spikes at high flash rates. In many patients, the interictal activity can persist long past the time the patient is clinically asymptomatic. A significant proportion of those of those with BOE also have generalized spike and wave or discharges or centro-temporal spikes in their interictal EEG studies (Ferrie 97).
Ictal findings – Seizures begin with an ictal spike pattern of increasing frequency, evolving to theta and delta rhythms that spread anteriorly, but these seizures have been infrequently recorded (Beaumanoir 83). In one case series, two seizures were recorded, one from the left and one from the right occipital lobe, both beginning with very focal repetitive activity and rapidly generalizing to involve both hemispheres (Andermann 98).

**Juvenile Myoclonic Epilepsy (JME)**

JME is the most common idiopathic generalized epilepsy syndrome, beginning between the ages of 12-15 years with significant genetic linkages to chromosomes 2, 3, 5, 6 and 15 (Gardiner 05, Beghi 06). The hallmark clinical characteristic is arrhythmic uni- or bilateral myoclonic jerks with retained consciousness. These jerks can affect any extremity, although the arms may be the most frequent site. Myoclonus is reliably most common in the hours after awakening. Most patients also suffer generalized tonic clonic seizures, and roughly one third have absence seizures. Sleep deprivation or disruption, or alcohol use also tend to bring on the jerks and seizures. Myoclonus and seizures can be triggered by photic stimuli or even eye closure. JME responds very well to medications, particularly valproic acid, but the medications usually need to be continued lifelong to avoid recurrence of the seizures.

Interictal EEG – The background is normal. Discharges in JME are marked by polyspike and wave discharges, often at faster frequencies between 3-5 Hz. (Figure 10 – JME) In general, the fronto-centrally dominant discharges are more brief and irregular than in absence, and may be more fragmentated with greater asymmetric emphasis. Polyspike discharges may occur without an aftercoming slow wave. Some JME patients demonstrate a more typical 3 Hz single spike and wave pattern, and absence seizures are more common in these patients (Panayiotopoulos 89).

The polyspike and wave activity diminishes in deeper slow wave sleep, and is absent during REM sleep. Arousal from sleep is often a potent activator of discharges. Hyperventilation also activates the bursts. There is a 30-40% rate of sensitivity to photic stimulation, the highest of any epilepsy syndrome (Janz 90, Alberti 94). Roughly half of patients have normalization of the EEG on medication (Panayiotopoulos 94).

Ictal EEG – The EEG associated with myoclonus or atypical absence seizures usually consists of a fast spike and wave, most often between 3.5 and 5 Hz. Myoclonic jerks occur concomitant with the polyspike discharges at a rate of 10-16 Hz (Hrachovy 2006), which are followed by a burst of 2.5-5 Hz spike and wave activity that can outlast the jerks. It is not uncommon for the jerks to recur with increasing frequency and lead up to a generalized seizure after minutes to hours (Delgado-Escueta 84).

**Questions:**

5. The syndrome with the best prognosis for remission by age 18 is:
   a. Juvenile myoclonic epilepsy
b. Juvenile absence epilepsy
c. Late onset benign occipital epilepsy
d. Benign epilepsy with centro-temporal spikes

6. Important electrographic features that define typical absence discharges include:
   a. Activation during hyperventilation in over 2/3 of patients
   b. Bilateral synchronous, frontally-dominant 3 Hz spike and wave
   c. Posteriorly-dominant over 250 microVolt spike and wave discharges
   d. Discharges that begin at 5 Hz and slow gradually to 3 Hz over 5 seconds

7. The ictal EEG pattern in JME usually include
   a. Progressively evolving occipital polyspikes
   b. 10-16 Hz polyspikes followed by 2-5 Hz spike and slow waves
   c. Unilateral posterior 3 Hz spike and wave that gradually generalizes
   d. Generalized spike and wave that lasts 3-10 seconds and ends at 3 Hz

**Infantile Epileptic Encephalopathy with Hypsarrhythmia/ West Syndrome**

West syndrome was first recognized in 1841 by William West, who carefully observed the syndrome in his own 4 month old son. (West 1841) In the 1950s, Gibbs described the pathognomonic EEG findings seen in this syndrome and called hypsarrhythmia. (Gibbs 1954). The clinical syndrome usually begins in the first year of life, and occurs most frequently in infants who have already exhibited some signs of developmental delay. (Hrachovy 2003). Seizures typically begin with a sudden phasic trunkal flexion or extension, followed by gradual tonic posturing lasting 10 seconds, usually coming in clusters. The classical spasm is a massive jack-knifing flexion at the waist, but the spasms can be asymmetric, or consist of subtle facial movements in some patients (Kellaway 79).

Both ACTH treatments and vigabatrin have been documented to be effective treatments for the spasms (Lux 06). In most cases, the spasms disappear by age 4, but over many are left with substantial cognitive deficits, and more than 50% go on to develop other forms of epilepsy (Hrachovy 2003). Patients with normal MRI and normal early development (cryptogenic) have a better prognosis and a 30-50% chance of normal development. Overall, up to 16% of patients with West syndrome may have a good prognosis (Frost 2003).

**Interictal EEG** – The hallmark of a typical hypsarrhythmia pattern is a high-voltage (usually over 250microV), asynchronous slow wave rhythm punctuated by multifocal independent spikes, originating independently in each hemisphere (Figure 11 A - Hypsarrhythmia).

The typical EEG frequencies vary independently in each hemisphere, and the distribution of sharp waves and amplitudes vary unpredictably from moment to moment. There are several variants of this background pattern, which are usually termed forms of “modified hypsarrhythmia.” One common modified pattern has a higher degree of interhemispheric synchrony. These patients still have multifocal spikes, and spontaneous
variability, but have more symmetric and synchronous background activity. This pattern may be more common in late stages of the illness. Other modifications of the classical pattern include 1) hypsarrythmia with a consistent single focus of epileptiform activity, 2) asymmetric hypsarrythmia (hemihypsarrythmia) with consistent amplitude asymmetry, 3) hypsarrythmia with episodic voltage attenuation or suppression burst variant, (this pattern is also seen in NREM sleep in many patients with the classical EEG patterns), or 4) hypsarrythmia with very little epileptiform activity. (Hrachovy 84)

During sleep, most records showing hypsarrhythmia demonstrate higher amplitude activity with electrodecremental periods in NREM sleep. In REM sleep, the hypsarrhythmia pattern is often completely attenuated. During arousal periods, both the amplitude and the scattered sharp waves are often attenuated for a period of time. Over months to years, the hypsarrhythmia pattern fades in all patients, generally by ages 5-7 (Livingston 1958). The subsequent EEG may gradually transition to diffuse slowing, with or without multifocal spikes, focal slowing or slow spike and wave activity. In the small fraction of patients who recover clinically, the EEG is normal.

Ictal findings - The most consistent ictal EEG feature in hypsarrhythmia is an abrupt voltage decrement (also referred to as an electrodecremental seizure) (Figure 11 B – Electrodecremental ictal pattern in hypsarrhythmia). The single most common pattern associated with a clinical seizure in this syndrome in one large series reported by Kellaway in 1979 was an initial high voltage, bifrontal slow wave transient followed by electrodecrement. The authors also described 10 other types of ictal patterns consist of various combinations of abrupt decremental voltage attenuation, a single bifrontal sharp and slow wave, generalized fast activity, poorly formed sharp and slow wave complexes, and/or diffuse rhythmic slow activity. Generalized spike and slow wave activity and superimposed fast activity were particularly common features as well. A single patient may have various patterns at different times. Asymmetric ictal patterns can be seen in those with hemihypsarrhythmia. There has been no specific correlation between semiology and EEG pattern, except that longer seizures were more often seen in those with cessation of behavior (Wong 2001). There is no clear correlate between ictal pattern and prognosis (Haga 1995).

Landau-Kleffner Syndrome

Landau-Kleffner syndrome has been recognized as a rare, invariably progressive, idiopathic acquired aphasia related to a focal epileptic disturbance in the area of the brain responsible for verbal processing (Hirsh 2006). The syndrome has a pathognomonic EEG pattern which was well-described when Landau and Kleffner reported the constellation of findings in 1957 (Landau 1957). The syndrome begins between ages 3 and 10 in a child with normally-acquired language abilities. The child develops a verbal auditory agnosia and infrequent nocturnal partial or secondarily generalized seizures. Treatment is usually with valproic acid and benzodiazepines (Mikati 05). Sometimes corticosteroids and IVIg or even surgery with subpial transection (Morrell 95) are used in refractory cases. The outcome for overall language and cognitive function depends in part on how early the syndrome is recognized and treated, but over 2/3 of children are left
with significant language or behavioral deficits (Beaumanoir 1992). (Figure 12 – Landau Kleffner)

Interictal EEG – High-voltage multifocal spikes, predominating in the temporal lobes, are a requirement for the diagnosis of Landau-Kleffner syndrome. These discharges can contain spikes, or sharp and slow waves, and can occur bisynchronously or independently in each hemisphere. Some patients have epileptiform activity in only one hemisphere. During NREM sleep there are high frequency, sometimes continuous, bilateral posterior temporal spikes. These tend to abate during REM sleep. When AEDs are started, the seizures and spikes tend to abate. Over time the interictal epileptiform activity lessens, and disappears in almost all patients by adolescence. As seizures are infrequent and often well-controlled, ictal patterns have not been described.

Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome was first described in the work of Lennox on different types of absence seizures in 1945 (Lennox 45), and more fully elaborated by Gastaut in 1966 (Gastaut 66). Classically, the syndrome begins between 2 and 5 years, and falls into the category of generalized symptomatic epilepsies. The defining characteristics of the syndrome are as follows. 1) multiple seizure types with a high seizure frequency, often including myoclonic, atypical absence, tonic and atonic seizures, although partial seizures and typical generalized tonic clonic seizures may also occur; status epilepticus is seen in the majority of patients at some time in the illness.(Beaumantor 82), 2) Mental retardation and/or behavioral disorders are always present. 3) EEG findings of diffuse slowing with slow spike and wave discharges (less than 3 Hz) that increase during sleep; multifocal independent spikes and generalized paroxysmal fast activity are also often recorded. In two thirds of cases, the cause is structurally or etiologically apparent, but in roughly 30% of cases the syndrome is cryptogenic. The prognosis for complete seizure control is poor, and cognitive deterioration can occur (Camfield 2002).

Interictal EEG – The EEG invariably shows significant background slowing. Slow spike and wave discharges are frequent throughout the tracing but distribution, amplitude and frequency (between 1-4 Hz) can vary. In up to 30% of the EEGs there is associated multifocal independent epileptiform activity. (Figure 13 A, B, and C – slow spike and wave with multifocal independent spikes) Multifocal epileptiform activity has been defined as at least 3 separate foci of spike or sharp wave activity, with at least one in each hemisphere, involving at least three non-contiguous recording electrodes. Hyperventilation and photic stimulation are not usually activating. Bursts of slow spike and wave are usually most common in drowsiness and sleep. The amount of Rapid Eye Movement (REM) sleep is relatively reduced, and epileptiform activity is not seen during REM. A suppression burst pattern with high amplitude slow spike and wave alternating with substantial suppression is not uncommon during slow wave sleep. In most patients, slow wave sleep also activates generalized paroxysmal fast activity (GPFA) ranging in frequency from 10-25 Hz and lasting several seconds. These bursts are usually frontally predominant and vary significantly in amplitude. GPFA during sleep is not usually associated with a clinical ictal event.
Ictal findings – GPFA is usually associated with a clinical tonic seizure when the discharge lasts longer than 6 seconds. (Brenner 82) This discharge is often preceded by generalized attenuation or slow spike and wave activity. (Figure 14 – generalized paroxysmal fast activity in tonic seizure) Atypical absence seizures are also common, and are usually associated with longer, more regular and more diffuse slow spike and wave discharges. Clinically, atypical absences usually involve more incomplete impairment of consciousness and preservation of some motor activity during the events. At times, atypical absences can be associated with faster 7-20 Hz activity similar to GPFA. With atonic seizures, the EEG most often shows polyspike and slow wave discharges although GPFA or slow spike and wave have also been described.

Questions

8. In Landau Kleffner syndrome the EEG characteristically shows:
   a. Nearly continuous posterior temporal spikes in sleep
   b. Centro-temporal triphasic spikes in drowsiness
   c. Generalized slow spike and wave
   d. Very high amplitude background with irregular spike and wave

9. Ictal EEG patterns in West syndrome are
   a. Very stereotyped across all patients
   b. Usually asymmetric
   c. Often associated with a sudden decrement in amplitude
   d. Most often associated with generalized paroxysmal fast activity

Frontal Lobe Epilepsy

Patients with frontal lobe epilepsy demonstrate frontal epileptiform activity on only 65-70% of EEGs (Verma 06). Semiology and imaging are very important to accurate identification of frontal epilepsy syndromes. Head trauma is a frequent predisposing factor, and autosomal dominant genetic determinants have been identified (Diaz-Otero 08). Frontal epilepsy can be cryptogenic, with normal structural imaging studies, or symptomatic, with orbitofrontal, interhemispheric, dorsolateral frontal or opercular neocortex, motor or supplementary motor cortex lesions. Ictal semiology in frontal lobe epilepsy most commonly consists of brief seizures, with somatosensory auras, frequent head and eye version, complex postures and hypermotor behavior, loud vocalizations and little postictal confusion (So 06). Frontal seizures often occur out of sleep or during an arousal. The prognosis for epilepsy surgery in frontal sites overall is recently estimated at 56% (Jeha 07), with negative predictors including negative MRI, and non-localizing ictal EEG patterns.

Interictal EEG: Various patterns of interictal epileptiform activity can be seen in patients with frontal lobe epilepsy. In addition to focal spikes or sharp waves over the frontal regions (Figure 15 A and B – focal frontal spike), several other types of
epileptiform activity can occur. Secondary bilateral synchrony due to a frontal focus consists of an apparently generalized bifrontally dominant spike and wave discharge, usually 3-4 Hz, with significant lead of between 300-500 microseconds in one frontal lobe. When this pattern is consistent in each discharge, and associated with focal slowing in the frontal lobe that seems to lead the discharge, it is likely to represent a frontal site of ictal onset. On some occasions, secondary bilateral synchrony discharges are seen in those with multiple spike foci, and for these patients localization is less clear (Blume 85). Focal paroxysmal fast activity or high voltage rhythmic sharply contoured slow waves are also seen in frontal lobe epilepsy. At times, focal or generalized spike and wave discharges can be associated with frontal epilepsy (Westmoreland 98).

Ictal findings: The ictal EEG in frontal lobe seizures is non-localizing in over 50% of patients. One of the most common patterns in frontal seizures is a diffuse attenuation in background activity followed by a generalized theta delta activity. Other difficulties in identification of frontal seizures include 1) prominent hypermotor activity with muscle artifact that can obscure the tracing quite early in the seizure and 2) rapid spread to the temporal lobes because of limbic connections, particularly in cingulate or orbitofrontal cortex seizures. Interhemispheric foci can produce prominent generalized spike and wave discharges during the ictal event. Supplementary motor cortex seizures can be associated with rhythmic discharge adjacent to the vertex. Dorsolateral frontal cortex seizures may have the highest incidence of localized focal fast activity, with one study indicating up to 80% focal patterns with this localization (Bautista 98). (Figure 16 Focal frontal ictal onset)

**Temporal Lobe Epilepsy**

The most common type of refractory epilepsy in adults is localization-related medial temporal lobe epilepsy. Over 80% of patients have had at least one early life seizure (usually a febrile seizure) and onset is usually in the second or third decade (French 93). The most common aura is a visceral sensation of midepigastic rising, although many other psychic phenomena occur, including, in decreasing order of frequency, fear, olfactory hallucinations, and déjà vu sensations. Ictal semiology usually begins with a bland stare, progresses through ipsilateral automatisms or contralateral dystonic posturing. Speech arrest is common with seizures that begin in the dominant temporal lobe, and post-ictal confusion is often prolonged. Secondary generalization can occur, but in most patients generalization is controlled with medications, while the complex partial seizures remain refractory to multiple drugs in many patients. MRI most commonly shows mesial temporal sclerosis, often severe on one side with some degree of volume loss on the opposite side. Epilepsy surgery has a likelihood of over 80% of producing a seizure-free outcome in patients with a well-localized temporal epileptogenic zone, MRI abnormalities and unilateral sharp waves and ictal onsets (Hufnagel 94).

Neocortical temporal lobe epilepsy can be difficult to distinguish from mesial temporal lobe epilepsy on the basis of historical and semiological characteristics, although it is often later in onset, with less association with febrile seizures. Manual and oral automatisms and dystonic posturing are rarely seen in neocortical temporal lobe epilepsy.
Interictal EEG: Mesial temporal lobe epilepsy is associated with focal temporal spikes in 96% of patients, and is generally localized to the anterior temporal region (sphenoidal or T1/2 electrodes) and associated with focal slow waves (Williamson 93). Bilateral independent epileptiform activity in each temporal lobe is seen in nearly half the cases, and is associated with a lesser likelihood of lateralization of the epileptogenic zone and success of epilepsy surgery. Interictal discharges often disappear after successful epilepsy surgery, but their presence does not necessarily imply a poor prognosis (Kipervasser 2007). Some authors do feel that absolute spike frequency may be a marker of worse surgical outcome (Krendl 2008). In some a minority of mesial temporal lobe patients, temporal intermittent rhythmic delta activity (TIRDA) is also seen. When this pattern occurs it is associated with temporal epilepsy up to 80% of patients, and can last 3-20 seconds (Geyer 1999). Interictal discharges in lateral neocortical temporal lobe epilepsy are similar, but may be more widely distributed, with a more prominent ipsilateral parasaggital field.

Ictal findings: Mesial temporal lobe epilepsy
Rhythmic localized anterior temporal theta activity is the hallmark of medial temporal lobe epilepsy, although the focal unilateral temporal theta discharge may develop 5-30 seconds after the onset (delayed focal onset) of the clinical seizure (Risinger 89). Focal postictal slowing is also seen after up to 70% of seizures and is useful in localizing the site of ictal origin (Ebersole 1996).

Ictal Findings: Lateral neocortical temporal seizures may have a wider hemispheric distribution at onset, and several studies of clearly localized surgical patients indicate that the lateralized rhythmic slowing in seizures of neocortical temporal onset is slower in frequency, and may be shorter in duration than mesial-onset seizures (Foldvary 97).

Questions:

10. Which feature is more characteristic of frontal lobe epilepsy than temporal lobe epilepsy?
   a. ictal speech arrest
   b. hypermotor behavior
   c. ipsilateral hand automatisms
   d. prolonged post-ictal state

11. Interictal epileptiform activity in frontal epilepsy can include:
   a. generalized spike and wave with a unilateral anterior onset
   b. focal paroxysmal fast activity in one frontal lobe
   c. multifocal independent spikes
   d. a and b
   e. all of the above
12. Temporal lobe epilepsy is associated with
   a. Interictal epileptiform activity in 70% of cases
   b. Focal onset ictal beta activity over the posterior quadrant
   c. Temporal intermittent rhythmic alpha activity
   d. Ictal theta activity that can be delayed by 30 seconds

_Parietal Lobe Epilepsy_

Seizures of parietal onset are among the most difficult to localize electrographically. Semiologies vary widely and may include dyesthesias or sensory illusions in some cases, along with rapid spread to adjacent temporal, occipital or motor cortical areas. Simple partial seizures can produce auras involving dyesthesias of the contralateral extremities or face, sometimes experienced bilaterally (Foldvary 2000). In complex partial seizures, manifestations often include symptoms arising from the areas of propagation (Geier 1977).

Interictal EEG: Interictal epileptiform activity is infrequent in parietal lobe epilepsy – one study described only 5-15% of those with surgically-documented parietal seizures had centroparietal epileptiform discharges (Salanova 95). (Figure 19 – Focal Parietal spike) The discharges may include bilateral secondary synchrony, false lateralization or false localization, most often to the temporal lobe (Cascino 93). Centro-parietal, or CP spikes, may occur in early childhood, and commonly occur in those with cerebral palsy or motor deficits. (Figure 20 CP spike) These discharges are often seen in patients without epilepsy or in those with a benign epilepsy syndrome (Kellaway 1980).

Ictal findings: Scalp EEG correlates of parietal lobe epilepsy are usually diffuse, sometimes falsely localizing or even lateralizing; one study indicated that in only 10% of patients was there a focal ictal parietal pattern. (Williamson 92) In general, without a focal lesion on structural imaging, localization of parietal epileptogenic foci is extremely challenging.

_Occipital Lobe Epilepsy_

Visual auras occur in 47% of those with interictal occipital spikes and presumed focal acquired occipital epilepsy (Ludwig 75). Most often simple colors, shapes or movement are seen, but more complex hallucinations, palinopsia or illusions are also frequent. Ictal amaurosis, often with white-out of a visual field, and epileptic eye movements are also suggestive of an occipital onset.

Interictal EEG: In those with documented focal occipital onset epilepsy, interictal discharges are localized to one occipital lobe in less than 20% of patients. (Figure 21 Occipital spike) IEA in these patients often shows bilateral occipital spikes, or false localization to the temporal region. In addition, epileptiform activity in the occipital region does not have a high correlation with refractory epilepsy; for instance, occipital
spikes are common in children under 4 with visual deficits without seizures (Gibbs 1968). In one study of children without any visual problems, only 59% of those with occipital spikes developed epilepsy (Smith 1964). Occipital spikes in children are also seen in benign occipital epilepsy (see above), or as one expression of Sturge-Weber syndrome or other symptomatic epilepsies.

Ictal findings: A minority of focal occipital seizures begin with focal rhythmic activity over one occipital lobe; one study estimates that only 15-20% of occipital seizures begin this way (Verma 2006, Ludwig 1975). (Figure 22 - Occipital seizure) Other ictal EEG characteristics include frequent spread to the ipsilateral temporal region or biposterior diffuse activity at onset. In intracranial recordings, occipital to frontal spread has also been recorded (Williamson 1992).

Questions

13. The ictal pattern in parietal lobe epilepsy is most likely to be:
   a. restricted to one or two electrodes over the parietal region
   b. longer than temporal lobe seizures
   c. diffuse at onset, with spread to adjacent lobes
   d. Falsely lateralizing to the opposite hemisphere

14. Occipital spikes:
   a. Are uncommon in children with visual deficits
   b. Often have a bilateral occipital field
   c. Are nearly always correlated with clinical epilepsy
   d. High amplitude, focal and periodic

Periodic Epileptiform Activity

Periodic Lateralized Epileptiform Discharges (PLEDs)

Periodic lateralized epileptiform discharges are high-amplitude repetitive stereotyped spike or spike/polyspike and slow wave complexes occurring over one hemisphere at a frequency of 0.5-2 Hz. (Figure 23 A and B – PLEDs) PLEDs generally occur in the setting of acute injuries, most commonly ischemic or hemorrhagic stroke, but also with focal herpes encephalitis, tumor or anoxia (Fitzpatrick 2007). Recently, it has been reported even in posterior reversible encephalopathy syndrome, alcohol withdrawal and neurosyphilis. PLEDs may also occur acutely after unilateral seizures. They generally disappear gradually over days to weeks. Background activity is usually abnormal, ranging from slowed to nearly completely suppressed. PLEDs are frequently associated with seizures – between 58 and 100% of patients with this pattern have clinical seizures, and a significant minority subsequently develop epilepsy (Walsh 1987, Pohlmann-Eden 1996). The discharges generally abate within a few weeks. When seen in association with acute stroke, the mortality rate associated with PLEDs is approximately 30%.
Bilaterally independent periodic epileptiform discharges (BIPLEDs) are similar to PLEDs in etiology and significance, except that they occur more commonly in infectious encephalidities (especially herpes) and after anoxic injuries (de la Paz 1981). By definition, BIPLEDs are independent asynchronous discharges with different frequency and amplitude in each hemisphere (Brenner 1990). The mortality rate in BIPLEDs is quite high in comatose patients with BIPEDs, and is generally significantly higher than in those with PLEDs (Fitzpatrick 2007).

Generalized Periodic Epileptiform Discharges (GPEDs)

Generalized periodic epileptiform discharges are bisynchronous, usually high amplitude discharges that recur periodically or pseudoperiodically for at least 50% of the EEG tracing. Figure 24 A – GPEDs, Figure 24 B – GPEDs with evolution in status epilepticus The most common setting for this pattern is anoxic cortical injury (Husain 1999), but many other etiologies are possible, including dementia, intracerebral hemorrhage, toxic metabolic encephalopathies or head injury with seizures. The most critical determination is a decision about when there is enough evolution in GPEDs to justify treatment for status epilepticus. The criteria of separating GPEDs from status are not straightforward (Treiman 1993, Nei 1999). Clear evolution in topography, frequency or amplitude over 5-10 seconds is the most usual criterion, but complete abolition of GPEDs after administration of benzodiazepines or other antiepileptic agents has also been convincing for some authors. The outcome of GPEDs with status epilepticus depends on etiology – those with anoxic insults fared worst. Another factor correlated with outcome is the amplitude of the inter-GPED cerebral activity; those with substantial suppression tended to have a poor outcome.

Creutzfeldt-Jakob Disease CJD

Creutzfeldt-Jakob Disease is the most common human prion disease, and EEG continues to serve a very important role in diagnosis of sporadic cases. Typical electrographic findings include a bianteriorly-dominant periodic triphasic sharp wave complexes, lasting 600-1000 milliseconds, recurring at a rate of roughly 1 Hz. These complexes can be purely unilateral in early stages of the disease; in late stages, the inter-complex interval progressively attenuates. Myoclonus is common in CJD, but is not time-locked with the discharges. (Figure 25 – CJD EEG). Specificity of EEG findings is quite high, with only a few other dementias producing EEGs that can resemble this pattern, but sensitivity is lower, with 58-64% of those ultimately diagnosed with CJD having this characteristic EEG pattern (Collins 2007, Steinhoff 2004).

The findings are generally present after the first two months of clinical symptoms of progressive dementia, and are most typical early in the illness, and in patients with later age of onset. Some genetically transmitted subtypes of CJD do not have associated EEG abnormalities (Zerr 2000). Dipole localization studies and perfusion tests have indicated that the spike wave complexes produced in CJD are generated both in frontal cortical areas and in the basal ganglia and thalamus (Jung 2007).

Herpes
Herpes simplex encephalitis is the most common sporadic acute viral encephalidities in the US. MRI and PCR tests are now vital to making the diagnosis accurately. Before the PCR test was readily available, EEG provided the earliest and most reliable clue to the diagnosis. Typical EEG findings in herpes encephalitis include periodic sharpwaves, usually in one or both temporal lobes (Figure 26 – Herpes encephalitis with PLEDs). The periodic EEG pattern or substantial focal slowing is present in 90% at the time of symptom onset in patients who eventually have a positive PCR (Al-Shekhlee 2006). The sensitivity of EEG declines after the first 48 hours.

**Subacute sclerosing panencephalitis (SSPE)**

SSPE is a chronic slow-virus encephalitis with measles virus that produces Cowdry body inclusions (Markand 1975). The illness usually begins 7-10 years after an early initial infection and results in progressive intellectual deterioration and intermittent pseudo-myoclonic spasms; it is generally fatal after a few years. The most specific diagnostic test is elevated CSF IgG to measles virus (Cole 2007), and MRI abnormalities are not unusual (Praveen-Kumar 2007). However, the EEG pattern is one of the diagnostic hallmarks of the infection, which often suggests the possibility of the diagnosis. The specific and unusual EEG pattern is characterized by very stereotyped delta wave and fast activity complexes that lasts 0.5 to 2 seconds and recur periodically every 4-14 seconds. (Figure 27 SSPE) These discharges occur during wakefulness and sleep. In wakefulness, the complexes are often associated with time-locked stereotyped myoclonus or other motor activity (Cobb 1966, Westmoreland 1979). The interictal backgound gradually slows and attenuates as the disease progresses, while the stereotyped complexes continue.

**Questions**

16. Clinical myoclonus is time-locked to the periodic discharges in:
   a. PLEDs
   b. GPEDs
   c. CJD
   d. SSPE

**IEA and other modalities**

The gold standard of IEA detection is intracranial recording. In one study of temporal lobe epilepsy, only 10% of spikes with a source area of less than 10 cm² resulted in discharges at the scalp, and no spikes affecting less than 6 cm² were able to produce scalp potentials (Tao 2005). (Figure 28 - spikes at surface and depth, Figure 29 - seizure at surface and depth) Several other non-invasive techniques have been developed to try to improve the yield of non-invasive recordings in cases with difficult localizations.
Magnetoencephalography (MEG) is an imaging technique used to measure magnetic fields produced by electrical discharges in the brain. In focal epilepsies, it can provide information that is complementary to scalp EEG. In some studies, MEG was able to show a higher sensitivity in detecting discharges over the lateral convexities, whereas EEG was best in detecting discharges in the mesial temporal regions (Oishi 2002). Many current authors feel the two modalities may function synergistically to improve localization of partial epilepsies when localization is difficult (Iwasaki 2005, Kirsch 2007). Other modalities under investigation to increase the yield of routine EEG in detection and localization of IEA include equivalent dipole modeling and EEG correlated fMRI techniques (Ebersole 2007, Zijlmans 2007). (see also Chapter 13)

Conclusion

The identification of interictal epileptiform activity on EEG continues to provide vital diagnostic information in many clinical situations. Examples include the young child with regression or episodes of staring or stereotyped motor behavior, where the EEG could show the 3 Hz spike and wave typical of absence epilepsy, slow spike and wave and background abnormalities, or focal temporal spikes. In a younger child, hypsarrhythmia might indicate the appropriate treatment course. In an adolescent with nocturnal episodes of unusual behavior, centrotemporal spikes would be treated very differently from polyspike and wave discharges. An adult with a single seizure and a negative EEG and MRI would likely not be initially offered anticonvulsants, whereas IEA on the EEG would make seizure recurrence much more likely. In an older adult with abrupt mental status changes or hemiparesis with negative imaging, CJD or nonconvulsive status might become evident only on EEG.

As Gibbs wrote in 1958, “ideally the clinical and EEG data should be interrelated and fused in the mind of the informed physician; this permits the full utilization of information from all sources and leads to the most accurate diagnosis and the selection of the most appropriate treatment.”
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