Summary

Paroxysmal and periodic patterns on continuously recorded EEG are commonly seen in the neurocritical care setting. As these patterns span the non-epileptic, interictal, and ictal continuum, accurate identification and appropriate management of these patterns present challenges. This review will survey the most commonly seen patterns, including sharp waveforms, lateralized and generalized periodic discharges, and subclinical seizures. Evidence based guidelines for management of these patterns are lacking; reasonable approaches to their management will be presented.

Where continuous monitoring is available, a measured approach with close follow-up of these uncertain patterns may be reasonable in a large number of these cases.

Epileptologie 2012; 29: 210 – 217

Key words: EEG, seizure, intensive care unit, periodic epileptiform discharges

EEG in der Intensivpflegestation: Was sollte man behandeln, was nicht?


Schlüsselwörter: EEG, Anfall, Intensivpflegestation, periodische epileptiforme Entladungen

Introduction

The proliferation of the use of continuous EEG monitoring in the intensive care unit has led to the discovery that paroxysmal and periodic patterns are very common. These EEG patterns encompass a spectrum between non-epileptic, interictal, and ictal. Management of such patterns is particularly challenging; delayed treatment of an ictal pattern may result in difficulty in ultimately controlling a seizure or may result in further brain damage. Overly aggressive treatment with antiepileptic drugs (AEDs) may result in iatrogenic complications, such as drug reaction, drug interaction, and increased sedation resulting in further morbidity in an already compromised patient.

In this review the most common patterns encountered in the neurocritical care setting will be discussed. Two important caveats should be noted. Treatment decisions should be tailored to take account of the patient’s comorbidities and severity of illness; with a similar brain injury and EEG pattern, one patient may be a candidate for aggressive intravenously infused anesthetic treatment whereas another patient should not be treated with such. In addition, similar paroxysmal discharges in one particular underlying condition may not confer the same risk for seizures as compared to another condition; PLEDS seen in metabolic dysfunction likely confer smaller risk for impending seizures as compared to PLEDS seen in brain tumors or other conditions with structural brain injury [1]. These caveats inherently limit the ability to give all-encompassing...
guidelines for management for EEG patterns. Nonetheless, reasonable generalizable approaches to their treatment can be made.

**Sharp waveforms**

In patients undergoing evaluation for epilepsy, isolated focal spikes or sharp waves have high specificity for impending clinical seizures. The existence of such discharges in a population with a reasonably high pretest probability for seizures translates into very high positive predictive value for seizures, and is an indication for starting an AED. Although it may seem reasonable to presume focal spikes or sharp waves have similar specificity in the neurocritically ill population as well, there are few formal studies that have examined this systematically. The mere existence of a sharp waveform that morphologically qualifies as a spike or sharp wave may not necessarily indicate similarly high risk for seizures. For example, in patients with acute ischemic strokes, focal spikes or sharp waves occur in 14% of patients, whereas seizures occur only in 2% [2].

The determination of a truly epileptiform focal spike/sharp wave is also challenging. Patients who have undergone a neurosurgical procedure may exhibit a “breach” rhythm. These waves consist of a wide variety of EEG changes, including predominantly a high voltage 6 to 11 Hz mu-like rhythm in the centrotemporal areas, as well as other sharp waveforms [3]. Discharges that markedly disrupt the background and are associated with a field spanning more than 2 electrodes are particularly concerning for cortical irritability; positive sharp waves should also be considered potentially epileptiform [4]. However, breach patterns mimic features of, and may indeed be virtually impossible to distinguish from epileptic sharp waves. Overly aggressive treatment of sharp waveforms is therefore not indicated, though patients are generally already on a conventional AED after neurological procedures.

In rare instances, one may encounter incontrovertible sharp waves from the hemisphere contralateral to a given lesion. The etiology of such patterns is unclear, but may be due to subtle mass effect or possibly a result of previous, possibly silent, compromise of the contralateral hemisphere, for example, due to a scarring nidus from a previous silent ischemic process. In the absence of other clinical or electrographic indications, such patterns do not warrant treatment with an AED.

**Periodic discharges**

Periodic discharges are seen commonly in the neurocritically ill population. The gamut of periodic activity runs from manifestations of encephalopathy without any proclivity towards epileptic activity, to instances where distinguishing from frank status epilepticus is difficult. As such, the American Clinical Neurophysiology Society position paper on nomenclature subdivides these into lateralized periodic discharges (LPDs), bilateral independent periodic discharges (BIPDs), multifocal periodic discharges, and generalized periodic discharges (GPD), replacing the frequently utilized terms periodic lateralized epileptiform discharges (PLEDs), bicleptiform discharges (GPEDs). However, the latter terms are still widely employed in both the clinical and research arenas.

PLEDs/LPDs (Figure 1) have been long recognized as abnormal findings on EEGs although their clinical significance has not been clear. They are associated with nearly any type of structural abnormalities, including infectious, neoplastic, ischemic, hemorrhagic, and anoxic etiologies. They are generally associated with poor prognosis, particularly in patients with neoplasms [5, 6]. Clinical seizures are seen up to 70% of patients [1]. It is unclear whether PLEDs present an ictal phenomenon, an interictal pattern, or an epiphenomenon of brain injury. PLEDs are associated with increase in glucose metabolism [7] and blood flow [8, 9], suggesting that at least some of them are definitely ictal phenomenon requiring aggressive treatment with AEDs [10]. PLEDs have been reported as a definite electrographic correlate to clinically apparent seizures [11]. On the other hand, patients with chronic PLEDs have been reported; in patients who experienced seizures, ictal discharges in the EEGs were distinct from the PLEDs, and during this time the PLEDs disappeared [12], suggesting PLEDs to be an interictal phenomenon. As such, other authors have advised against routinely treating patients with these patterns unless it can be established that they represent a true ictal phenomenon rather than merely an interictal pattern [13]. As depressed mental status is extremely prevalent in patients with PLEDs, determining whether PLEDs are ictal or not is challenging. It seems reasonable starting or maintaining a conventional AED in all patients with PLEDs without escalating treatment unless clear ictal electrographic or clinical semiology is observed. To distinguish electrographic characterization of PLEDs more likely associated with seizures, distinction of PLEDs into PLEDs proper versus PLEDs plus has been made [14] (Figure 2). PLEDs plus are associated with brief focal rhythmic discharges, and are more frequently associated with seizures than PLEDs proper. Care must be taken not to overtreat patients in whom pseudo-PLEDs appear because severe pathology in one hemisphere suppresses what otherwise would have been generalized periodic discharges, resulting in PLED-like patterns over an intact hemisphere.
BiPLEDs defined as periodic discharges are independently and simultaneously present in both hemispheres. They are far less common than PLEDs and are associated with higher risk for seizures, depressed consciousness, and mortality than PLEDs [15]. As such, greater vigilance regarding epileptic activity is required than in PLEDs, though the approach to AED management is the same.

GPDs are perhaps the most challenging pattern to analyze, as they commonly span the gamut from the nonepileptic to the interictal to status epilepticus, potentially within a short period of time. The most common etiology are anoxic/metabolic or infectious [16, 17], although GPDs are nonspecific and may be seen in nearly any cause of depressed mental status. There is decreased risk for seizures in patients whose GPDs exhibit a triphasic morphology [18] (Figure 3), defined as surface negative triphasic complexes discharging every 1-2 Hz, and often with an antero-posterior or postero-anterior phase lag. GPDs discharging greater
than 3Hz are generally considered to be ictal in nature [19, 20] (Figure 4). AED management of these patterns must truly be done in conjuction with careful clinical and pathophysiological assessment. For example, GPDs with a triphasic morphology due to purely metabolic etiology without clinical correlation should not be treated with AEDs whereas other GPDs are clearly manifestations of status epilepticus [17].

The differentiation between ictal GPDs and nonictal metabolic triphasic waves often cannot be made reliably. It has been suggested that a challenge dose of intravenous benzodiazepine be given, and determine whether there is clinical or incontrovertible electrographic improvement [21], which would suggest an ictal phenomenon. In reality, this procedure is rarely useful; benzodiazepines will electrographically resolve both ictal and nonictal GPDs. Observing clinical improvement is nearly impossible as benzodiazepines will depress mental status in both scenarios.

**SIRPIDs**

Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) are found in approximately 20% of patients undergoing continuous EEG monitoring. They are considered to fall somewhere along the ictal-interictal continuum. Clinical or subclinical/electrographic seizures are found in about half of these patients; status epilepticus is found more frequently in focal or ictal appearing SIRPIDs [22]. As such, treatment with a conventional antiepileptic drug is advisable. Other studies have shown no increase in regional cerebral blood flow, and as a result have advocated against aggressive treatment [23]. Experience in our own center indicates that SIRPIDs are a transitional, unstable pattern that either will devolve into more definitively ictal pattern, or more commonly, dissipate in time, in either case, losing the stimulus induced character. The recommendation of the author is to start a conventional antiepileptic drug; if already on an AED, escalation of treatment is not recommended. Although evidence for such is lacking, it seems reasonable to minimize stimulating the patient any more than medically necessary. After cardiac arrest, SIRPIDs are associated with poor outcome [24], especially during hypothermia, but in other instances, outcome is yet to be defined.

**Nonconvulsive seizures**

Nonconvulsive seizures (NCS) are commonly found in the neurocritical care setting, present between 18 and 35% of patients [25, 26]. Of these, up to 75% of patients are in nonconvulsive status epilepticus (NCSE) [27]. The determination of NCS can be challenging due to the fact that many of the observed waveforms lie in the interictal-ictal continuum. The Young criteria [19] (Table 1) provides a reasonable guideline in determining whether a pattern is consistent with NCS. This has been modified by other groups which emphasized the importance of frequency/locational evolution and de-emphasized amplitude changes [28] (Figure 5).

It has yet to be definitely determined whether
NCS or NCSE independently cause neuronal injury or are mere epiphenomena of the underlying insult. The mortality of NCSE is high, and most of the morbidity from NCS is likely due to the underlying condition rather than seizures themselves [29, 30]. Some studies have not shown neurocognitive deterioration after status epilepticus after eliminating progressive illness [31]. Aggressive treatment is likely to incur iatrogenic morbidities. However, other studies have shown deleterious effects associated with NCS. For instance, in patients with intracerebral hemorrhage, expansion of hemorrhage size has been demonstrated in patients with NCS [32]. In patients with traumatic brain injury, increase in intracranial pressure and lactate-pyruvate ratio [33] as well as hippocampal atrophy [34] has been observed in patients with NCS. However, the nature of the causality still remains unclear, e.g. whether seizures were the causes or effects of these changes.

It is reasonable to treat all patients with NCS with at least one conventional antiepileptic drug. Escalation of treatment must be decided on a case-by-case basis. In general, there are few, if any, scenarios where de novo intubation and administration of an intravenous anesthetic is indicated solely for the purpose of the treatment of an EEG pattern.

**General guidelines**

Sharp, rhythmic, or periodic appearing discharges are all extremely common in the neurocritical care setting, and in many instances, the delineation between nonepileptic, interictal, and ictal patterns is difficult. Although rapid treatment of status epilepticus has universally been advocated as it increases chance of seizure control, in patients with uncertain patterns, it is advisable to temper treatment. Firstly, the potential drawbacks of anticonvulsants in critically ill patients have been demonstrated [35]. Secondly, it is uncertain whether aggressive treatment of NCS or even NCSE will result in improved outcome, as it has been postulated that nonconvulsive epileptic activity may be an epiphenomenon of an injured brain [36]. Given the availability of medications that are easily administered with relatively low toxicity, a conventional AED at a relatively low dose can be administered in patients with uncertain rhythms. Thereafter, careful monitoring without escalation of therapy until an uncertain pattern declares itself to be a malignant rhythm may be a superior strategy rather than early escalation of treatment of such patterns; a large portion of the uncertain patterns will revert to clearly nonepileptic patterns. Further research is needed to determine the characteristics of patterns that will devolve into ictal patterns requiring escalation of treatment.

**References**


Figure 5: A 63-year-old man after meningioma resection. The evolution of morphology and frequency that defines this nonconvulsive seizure.
Figure 5: A 63-year-old man after meningioma resection. The evolution of morphology and frequency that defines this nonconvulsive seizure.
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