Periodic Lateralized Epileptiform Discharges

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Learning Objectives

- Understand the principal EEG features of PLEDs
- Describe the different types of PLEDs
- Understand the evolution of PLEDs
- List the main etiologies of PLEDs
- Know the clinical associations of PLEDs
Disclosure Statement

☑️ I have nothing to disclose
PLEDs

PLEDs = Periodic Lateralized Epileptiform Discharges

• First described by Echlin (1952)

• First defined by Chatrian (1964)

• Uncommon (0.4-0.1% of all EEG recordings)
Figure 1: Right-sided PLEDs in a 77-year-old man with an acute right parieto-temporal hemorrhagic contusion and overlying subdural hematoma.

PLEDs - Features

- Lateralized or focal
- Period (or near periodic)
- Usually electronegative bi-, tri- and polyphasic spikes and sharp waves
- Amplitude 50-300 µV, duration 20-1000 msec (mean 200 msec)
- Present for most of recording
- Usually maximal on the side of a structural lesion
- Ipsilateral background slowing on side of PLEDs
- Ipsilateral reduction of background reactivity
PLEDs plus

- First reported by Reiher (1991)
- PLEDs with admixed rhythmic high frequency, low voltage polyspikes
**Figure 2:** Right hemisphere PLEDs Plus in an 87-year-old woman with an acute stroke in the right middle cerebral artery territory, and persistent left arm epilepsia partialis continua.

BIPLLEDs

- Complexes are present over both hemispheres, but are asynchronous

- Discharges usually differ in morphology, amplitude, rate of repetition, and site of maximal involvement between hemispheres

- First recognized by Chartain (1964)

- Formally characterized by de la Paz & Brenner (1981)
Figure 3: Bilateral independent PLEDs (BiPLEDs) in a 69-year-old woman with Hashimoto’s encephalopathy. From Fitzpatrick & Lowry, CJNS 34:443-450, 2007.
Multifocal PLEDs

- First reported by Reeves & Thompson (1993)

- PLEDs occurring independently in 3 cerebral regions
Fig. 1. Typical example of multifocal PLEDs (arrows) using the Laplacian montage, recorded from a 69-year-old woman with liver failure, sepsis, and hypoxia. Focus 1 (C3) occurring every 1.5 s; focus 2 (O1) occurring every 0.5–1 s; focus 3 (O2) occurring every 0.5 s.

Chronic PLEDs

• First described by Westmoreland et al. (1986)

• Very rare

• PLEDs lasting at least 3 months (up to 20 years)

• Seen in patients with chronic brain lesions and focal seizures
Table 1: Definitions of PLED subtypes †

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>PLEDs</td>
<td>Repetitive, rhythmic lateralized or focal spike, spike-wave, or sharp wave complexes recurring at regular or nearly regular intervals throughout most or all of the EEG recording with return to background activity between discharges, and without clear evolution in frequency or location</td>
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<tr>
<td>PLEDs Plus</td>
<td>PLEDs admixed with rhythmic high frequency, low voltage, polyspike rhythms</td>
</tr>
<tr>
<td>BiPLEDs</td>
<td>Bilateral, independently occurring asynchronous PLEDs</td>
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<tr>
<td>BiPLEDs Plus</td>
<td>BiPLEDs with unilateral or bilateral PLEDs Plus</td>
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<tr>
<td>Chronic PLEDs</td>
<td>PLEDs persisting on multiple EEG recordings for a period exceeding three months*</td>
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PLEDs – Etiology

- Ischemic stroke (34%)
- Infection (16%)
- Tumor (13%)
- Hemorrhage* (9%)
- Metabolic (6%)
- Anoxia (5%)
- CJD (1%)
- Unknown (3%)
- Other (13%)

* Includes all intracranial hemorrhages: intracerebral, subdural, and epidural hematomas

62 year old female with HSV encephalitis

BIPLEDs – Etiology

- Infection (28%)
- Anoxia (28%)
- Chronic seizure disorder (22%)
- Other (22%)

* Includes all intracranial hemorrhages: intracerebral, subdural, and epidural hematomas

PLEDs – Evolution

• Typically a transient phenomenon
  – Usually seen in the acute state (usually < 24 hrs after onset of illness)
  – 50% of PLEDs disappear after several days
  – 90% of PLEDs disappear within 4 weeks
  – Exception: chronic PLEDs

• Morphological changes
  – Interval between discharges increase
  – Change into either monomorphic, high-voltage slow waves or sporadic spikes and sharp waves
  – Then evolves into focal, paroxysmal theta and delta waves (in the region of the PLEDs) and then totally disappearing
PLEDs – Clinical Correlates

• Focal seizures
  – Approximately 75% of patients have clinical seizures
    • Focal motor most common
    • Tend to arise from the site of maximal involvement
    • Generalized seizures without focal clinical signs or EEG onset more likely in BIPLEDs

• Focal neurologic signs

• Obtundation
  – More likely in patients with BIPLEDs
PLEDs: Interictal or Ictal Phenomenon?

• Generally considered an interictal phenomenon
  – EEG features do not meet strict criteria of an ictal rhythm

• Can be ictal in some cases
  – Epilepsia partialis continua
  – Case reports of recurrent, prolonged episodes of confusional states associated with PLEDs (Terazano 1986)

• PLEDs can be viewed as an EEG signature of a dynamic pathophysiological state with underlying neuronal injury that is influenced a variety of factors (e.g., toxic, metabolic, infectious, pre-existing illness).
FIG. 2. A: Right-sided PLEDs in a 56-year-old man. B: At the onset of a seizure, the PLEDs are replaced by rhythmic faster activity.

PLEDs – Imaging Correlates

• No unique anatomical site or distribution of sites associated with PLEDs

• No association of cortical vs subcortical vs combined cortical/subcortical involvement, although purely subcortical lesions less likely to be associated with PLEDs

• PET/SPECT may show increased activity in region where PLEDs are seen
PLEDs – Treatment

• Adequate data not available

• Seizures should be managed no differently than if PLEDs were absent

• Some authors recommend aggressive AED treatment whether or not seizures occur (e.g. Handforth et al. 1994)

• Consider continuous EEG monitoring in obtunded or comatose patients, to detect nonconvulsive seizures (seen in > 50% of pediatric patients)
PLEDs – Prognosis

- Largely determined by underlying process

- Acute stroke has worst prognosis (28.8-53%)
  - However, influence of PLEDs on prognosis unclear

- Potentially reversible conditions have (e.g., metabolic encephalopathies, EtOH withdrawal) have a better prognosis
PLEDs – Mechanisms

- Wide EEG distribution, suggests a large generator

- Cobb and Hill (1950) – cortical isolation hypothesis
  - Periodicity occurs when the cortex is disconnected

- Gloor (1968) refined explanation
  - Brain is in a functional state that permitted rapid synchronization/generalization of neuronal discharges
    - e.g., ephatic interactions, virus-induced fusion of neuronal processes, intrinsic Ca+ and K+ conductances
  - Periodicity is a result of the refractory state and recovery cycle of both cortical and subcortical neurons

- Glutamate-mediated excitotoxicity likely important
Future Directions

- What is true incidence of PLEDs?
- When do PLEDs occur and how do they evolve?
- What is relationship of PLEDs to seizures?
- Should PLEDs be treated prophylactically?
Thank you