Epilepsy

Basic concepts

Epilepsy is a chronic brain disease characterized by (unprovoked) repetitive epileptic seizures.

An epileptic seizure (paroxysm) is a sudden, transient disorder of perception, thinking, autonomous function or behavior, which is caused by the abnormal electrical activity of a brain neuronal population of diverse size referred to as an epileptic focus.

However, it is necessary to distinguish between epileptic seizure and epilepsy!

An epileptic seizure is only a symptom with a typical electroencephalographic correlate. A single epileptic seizure may also be provoked in a person without neurological disease, for example as a result of abstinence symptoms in the first few days after withdrawal of barbiturates or when chronic alcohol abuse is discontinued. It is not epilepsy as a disease. In epilepsy, a person has a long-term increased tendency to develop seizures, and therefore, they recur with a greater or lesser frequency (depending, among other factors, on treatment).

Although the manifestation of epileptic seizures can be different among affected individuals, there are common features of all epileptic paroxysms:

- sudden onset of symptoms
- transient duration of symptoms (usually seconds to minutes)
- the usual stereotype of seizure manifestation in the same individual
- existence of an epileptic focus

Epileptic focus

Epileptic focus (zone) can occur in different areas of the brain gray matter. The most vulnerable to its formation is usually the neocortex, hippocampus and thalamus. The focus can be morphologically defined (tumor, scar, malformation) or undefined. The epileptic focus contains abnormally functioning neurons (without neurons there would be no pathological activity), and the reasons and mechanisms for changing behavior of these neurons can be very diverse. Therefore, a number of causes can also lead to epilepsy (see below).

The neurons in an epileptic focus are characterized by **hyperexcitability and hypersynchrony**. Hyperexcitability is an abnormal, extreme electrical response of neurons to a normal stimulus. Hypersynchrony is a property of neuron population of epileptic focus to produce electrical discharges simultaneously.

Hyperexcitability

During intracellular recording of electrical voltage changes from the dendrite or soma of an individual neuron of the epileptic focus by a glass electrode, we can register an excessive high and prolonged excitatory postsynaptic potential (EPSP), the so-called **paroxysmal depolarizing shift**

(PDS). It is a sudden large depolarization of the resting membrane potential (the magnitude of voltage change is in the range of 20 - 40 mV and lasts 50 - 200 ms), which at its peak triggers a salvo of action potentials with a frequency of several hundred Hz. Paroxysmal depolarizing shift is followed by prolonged hyperpolarization (see Fig. 1). The cause of this abnormal epileptiform behavior of neurons is poorly understood.

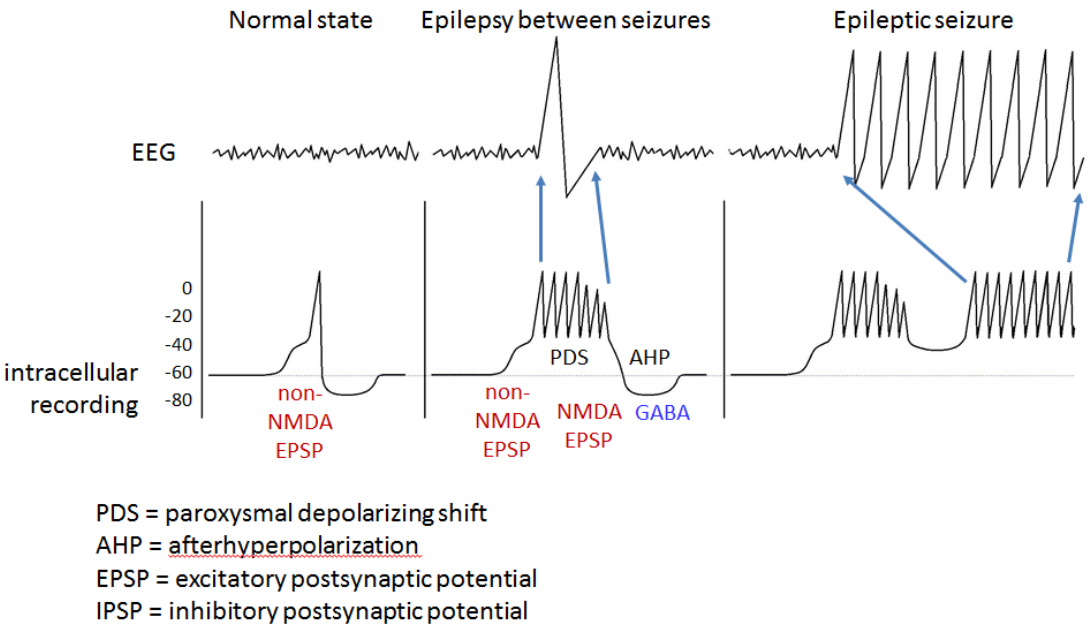

Fig.1. Abnormal epileptiform behavior of neurons.

Other factors determining epileptic seizure:

- threshold: given by properties of epileptic focus and recent situation (lack of sleep, glycemia, drugs, alcohol...)

- stimulus: the intensity and character of the stimulus (dangerous e.g. flashing light)

Etiology of epilepsy

We distinguish **primary epilepsy**, where the cause is usually unknown, the onset of seizures is in childhood or adolescence and there is some genetic predisposition. **Secondary (symptomatic)** epilepsy is characterized by a lack of genetic predisposition and there are so-called epileptogenic factors: e.g. conditions after stroke, scarring after trauma, tumors, inflammation and developmental brain disorders. In 5-9% of stroke patients can develop so-called vascular epilepsy. In general, damage of neurons can lead to epilepsy. However, epilepsy does not come from the center of the scar or post-malatic pseudocyst, but rather from its margin, where injured neurons survive.

Epileptic seizures according to topographic point of view

Epileptic seizures are divided into two major categories, partial and generalized.

Partial seizures

In partial seizures initial clinical manifestation or electroencephalographic recording performed during the period of paroxysm indicate abnormal electrical behavior of neurons in the restricted cortical area of one brain hemisphere. Partial seizures are further classified according to consciousness alteration (quantitative or qualitative disorders).

Simplex partial seizures

This type of seizure does not cause a disorder of consciousness. According to specific symptoms, seizures can be divided into paroxysms with motor, somatosensory, special sensory, autonomic and psychical symptoms. The specific manifestations of seizures depend on the functional specialization of cerebral cortex where the epileptic focus is located (e.g. gyrus praecentralis → muscle contractions on contralateral side of the body, gyrus postcentralis → paresthesia on contralateral side of the body, so-called motor or sensitive Jackson‘s epilepsy).

Complex partial seizures

There is a deterioration of consciousness. This may be an initial sign of seizure or the paroxysm begins as simplex and only later progresses to a disorder of consciousness. These seizures are also classified into paroxysms accompanied by or lacking automatisms. Automatisms are subconscious, ineffective, stereotypical movements (e.g. licking, smacking, chewing or touching). An example is so-called psychomotor seizure (running around, senseless activity, changes of affects, instincts). The epileptic focus is localized in the temporal lobe in this case.

Generalized seizures

Primarily generalized seizures are seizures where initial clinical and electroencephalographic manifestations indicate that abnormal electrical activity affects from the beginning neurons of whole brain cortex (both brain hemispheres). Consciousness is impaired in these paroxysms, although the consciousness disorder may not be noticeable in short-term seizures. Generalized seizures are classified into convulsive and non-convulsive paroxysms. The convulsive group includes tonic-clonic, tonic and clonic seizures. Non-convulsive seizures include absences, myoclonic and atonic seizures.

An **absence (petit mal)** seizure is typical for children under 10 years of age. It usually takes 5-15 seconds and can occur many times a day. The child looks stiffly in front of himself and does not react. The EEG record shows bilateral and symmetric spike oscillations with a frequency of about 3Hz.

Tonic-clonic seizure (grand mal) usually takes 1-5 minutes; typical are generalized tonic and clonic cramps, loss of consciousness, biting of the tongue, incontinence, later confusion, aggression, and amnesia to a seizure. The EEG record shows sharp waves with high amplitude and frequency up to 100 Hz. A serious complication is so-called status epilepticus: several seizures follow continuously without regaining consciousness. In high activation of glutamate receptors, this condition can lead to death of many neurons (so-called glutamate excitotoxicity).

Partial seizure with simplex or complex symptomatology can finally result in a generalized convulsive seizure. In this case, it is a partial seizure **secondarily generalized**.

EEG manifestation of epileptic focus

In practical medicine, cases that resemble an epileptic seizure (e.g. syncopes, hysterically conditioned disorders of consciousness) need to be diagnosed. To verify the seizure as epileptic, a description of paroxysm and electroencephalography (to detect the presence of the epileptic zone) can help us. Due to unpredictable beginning and short duration of epileptic seizure, the EEG examination is in most cases performed between seizures, in so-called **interictal period**. Abnormal electrical behavior of neurons may persist in subclinical form (without manifestation) even between the seizures. It can also be provoked during EEG examination by prompting the subject to hyperventilation, by making EEG record after sleep deprivation or by rhythmically flashing light (photostimulation). To detect an epileptic focus in a scalp EEG, its size must reach at least 6 cm^2 of the cortex area. In an evidence of epileptic focus, we speak about increased paroxysmal readiness. The presence of epileptic focus in the brain cortex signals during EEG examination the registration of so-called epileptiform patterns (abnormalities). There are transients such as spike, sharp wave and complexes of both; they have varying duration and exceed in their voltage over basal EEG activity. Epileptiform patterns may occur sporadically or in a more or less rhythmic paroxysm, may be focal (only in certain leads of the EEG record) or generalized (in all EEG leads).