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Epilepsy - epileptogenesis, epidemiology, genetics, seizure types and seizure phenomenology

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Epilepsy is a disease characterized by recurrent seizures (two or more) originating from the brain. Seizure activity arises as a sequel to abnormal hypersynchronous electrical activity which stems from a group of local cerebral neurons or from the whole cortex in collaboration with subcortical structures. Epilepsy is, above all, a consequence of an imbalance between excitatory and inhibitory mechanisms in the brain. Factors involved in epileptogenesis involve, among other things: neuroplasticity/synaptic plasticity, decreased GABA (gamma amino butyric acid) activity, increased glutamate activity, new formation of excitatory circuits, receptor alterations, ion channelopathies, dysfunction of glia cells, cortical dysgenesis, and intracranial pathology. The clinical picture of an epileptic seizure is that of sudden loss of control, paroxystic (episodic) manifestation (seizures which suddenly occur and suddenly cease), short duration (seldom longer than two minutes). The clinical seizure symptoms in the individual patient follow a repetitive pattern where symptoms and sequence are identical from episode to episode. Symptoms include an altered level of consciousness, motor, sensory, and autonomic symptoms, and behavioural disturbances. In individuals with epilepsy, seizures can be provoked by external factors such as excitement/agitation, flashes of light, and sleep deprivation.

Epilepsy is the most frequent occurring neurological disease in the dog and cat. In the literature, prevalence is estimated to vary between 0.5-5.7% in the dog and to be 0.5% in the cat. Genetic factors are increasingly being identified as the underlying mechanisms of specific types of epilepsy in both humans and canines (Prasad and Prasad, 1999; Bercovic and Scheffer, 2001; Chandler, 2006). In dogs, certain breeds express an accumulation of epileptic individuals in the population. Among others, the Belgian shepherd, Beagle, Keeshound, Labrador retriever, Golden retriever, Bernese mountain dog, Viszla, Shetland sheep dog, Irish wolfhound and English springer spaniel, are believed to have an increased risk of epilepsy with a suspected genetic influence.

Classification of epilepsy
The classification of epilepsy is based upon the underlying etiology. This classification includes three categories: idiopathic epilepsy, symptomatic epilepsy, and probable symptomatic epilepsy (previously known as cryptogenic, which means hidden). The term idiopathic epilepsy refers to epilepsy of unknown cause (there is no structural cerebral pathology). Idiopathic epilepsy in humans is associated with a possible or known genetic component. Animals suffering from idiopathic epilepsy will interictally appear clinically and neurologically normal.

Symptomatic epilepsy is defined as epilepsy caused by a known/identified disorder of the CNS, i.e. focal cerebral pathology can be identified. A very common cause of symptomatic epilepsy in people is micro-structural changes of the cortex cerebri (for example neuronal migration disorders). In these patients, seizures are often the only clinical indication of the subtle CNS pathology. Hippocampal changes are described in cats with epilepsy, and changes in the motor cortex are described in the dog and cat (18-20). In a group of dogs with medicine-refractory epilepsy, changes in the temporal region - a region in people that is often the site of an epileptic focus - has also been identified. Symptomatic epilepsy is characterized by partial seizures with or without secondary generalization. A patient with symptomatic epilepsy can have concurrent neurological symptoms, but the patient can also be symptom-free in the interictal period. Probable symptomatic epilepsy is used as a designation for epilepsy with a suspected symptomatic cause, which, however, remains obscure. This type of epilepsy is just like symptomatic epilepsy, characterized by partial seizures with or without secondary generalization.

Classification of Epileptic Seizures
The clinical manifestation of epileptic seizures is directly related to the amount and distribution of abnormal electrical activity in the brain. Epileptic seizures can be classified as primary generalized seizures, focal seizures (formerly known as partial seizures), or focal seizures with secondary generalization. With primary generalized seizures, there is a sudden outburst of abnormal electrical activity throughout both cerebral hemispheres. Without warning, the patient collapses with tonic, clonic, or tonic-clonic seizures.

With focal seizures, an abnormal electrical activity arises in a group of neurons localized to a specific area of the brain (an epileptic focus), and the clinical signs reflect the functions of the area involved. Focal motor, sensory, autonomic, or psychic signs can be seen. Focal seizure signs seen in animals with localized motor phenomena, could be for example, rhythmic twitching of an extremity, abnormal rhythmic blinking and in cats twitching of the whiskers. Focal seizure activity representing psychic and/or sensory seizure phenomena in the brain will in dogs result in behavioural changes such as...
e.g. uneasiness, anxiousness, restless wandering, pacing or abnormal clinging to its owner. Finally, focal seizures with parasympathetic/epigastric components may present as for example, hyper salivation, vomiting, or dilated pupils [10].

Focal seizures in the human are traditionally divided up in two categories: simple focal seizures (where the state of consciousness is maintained), and complex focal seizures (where the state of consciousness is impaired). It is difficult to appraise the state of consciousness in seizing animals, as this is limited to subjective interpretations by the one observing the seizures, whereas in people, a personal account can in many cases be given when the seizure is finished.

If the electrical activity in the epileptic focus becomes sufficiently massive, focal seizures can spread through subcortical structures to involve the entire brain (called a focal seizure with secondary generalization). The initial seizure symptoms will be localized then followed by tonic, clonic, or tonic/clonic convulsions. This is the most common seizure type observed in the dog [10]. The onset of the focal seizure is often very brief (from a few seconds to minutes) and the secondary generalisation (convulsions) follows rapidly. The focal seizure onset may therefore be difficult to detect.

The term “aura” has, in human terminology, historically been synonymous with the simple focal seizure signs that precede a complex focal seizure alone or one followed by secondary generalisation (convulsions). In humans the simple focal seizure signs are recognized as a warning sign of a forthcoming seizure development. In some epileptic animals, owners do indeed also report that they can foresee a convulsion when the (well known) initial focal seizure signs appear. In humans, aura has been used to only denote symptomatology that encompasses subjective sensory phenomena as well as vegetative signs (for example, the epigastric sensations accompanying mesial temporal epilepsy). Thus, in humans motor phenomena are not included in the symptomatology of aura.

An epileptic seizure can be divided into two phases: ictus (seizure activity) and postictal phase (reestablishment of normal brain function). Ictus can consist of a primary generalized seizure, a focal seizure, or a focal seizure with secondary generalization. In some cases, ictus can be preceded by a prodrome - a long-lasting (hours or days) change of disposition, in humans e.g. in the form of anxiety, irritability, withdrawal and other emotional aberrations. In dogs the most common prodromal signs described are restlessness a state lasting from hours to days [11]. Prodromes are traditionally considered to be a pre-ictal phenomena because abnormal electroencephalographic (EEG) brain activity cannot be registered. It is probable, however, that prodromes represent long-lasting, weak (subtle) focal seizure activity [11].

In the postictal phase, the brain returns to its normal function. Typically, the animal is tired, disoriented, ataxic, hungry, thirsty and/or, in some cases, aggressive. The postictal phase can last for few minutes or up to several hours.

References


