

Epilepsy in Cats: Theory and Practice

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The veterinary literature on epilepsy in cats is less extensive than that for dogs. The present review summarizes the most important human definitions related to epilepsy and discusses the difficulties in applying them in daily veterinary practice. Epileptic seizures can have a wide range of clinical signs and are not necessarily typical in all cases. Whether a seizure event is epileptic can only be suspected based on clinical, laboratory, and neuroimaging findings as electroencephalography diagnostic techniques have not yet been developed to a sufficiently accurate level in veterinary medicine. In addition, the present review aims to describe other diagnoses and nonepileptic conditions that might be mistaken for epileptic seizures. Seizures associated with hippocampal lesions are described and discussed extensively, as they seem to be a special entity only recognized in the past few years. Furthermore, we focus on clinical work-up and on treatment that can be recommended based on the literature and summarize the limited data available relating to the outcome. Critical commentary is provided as most studies are based on very weak evidence.

Key words: Diagnosis; Etiology; Review; Seizure; Terminology; Therapy.

Epilepsy Terminology

There is currently no universally accepted terminology does for veterinary epileptology, so we shall apply the concept for human epilepsy issued by the International League Against Epilepsy (ILAE), although with some differences. The terminology is changing and will be regularly updated (Table 1). The ILAE defines epileptic seizure as “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.”¹ This definition does not guide clinicians in distinguishing epileptic seizures from nonepileptic seizures, so it is necessary to adapt the pathophysiologic definition for clinical use. The most difficult aspect relates to the confirmation of abnormal activity in the brain. Electrical discharge can be detected by electroencephalography (EEG). However, this is the most challenging feature of epileptic seizures to apply in practice, as the electrical discharge is only recordable under certain circumstances. If electrical discharge is not considered, other episodic clinical events would meet the definition, although they are not epileptic seizures. Human patients with recurrent seizures can have normal scalp EEG interictally or even during seizures. The sensitivity of EEG in detecting epileptiform discharges (ED) can be increased by means of various invasive deep electrode techniques that can

Abbreviations:

BEL	basic epileptogenicity level
CFS	complex focal seizures
CSF	cerebrospinal fluid
ED	epileptiform discharges
EEG	electroencephalography
FeLV	feline leukemia virus
FIP	feline infectious peritonitis
FIV	feline immunodeficiency virus
FLAIR	fluid attenuated inversion recovery
FOPS	feline orofacial pain syndrome
GFAP	glial fibrillary acidic protein
HN	hippocampal necrosis
IE	primary (idiopathic) epilepsy
ILAE	International League Against Epilepsy
MRI	magnetic resonance imaging
REM	rapid eye movement
SE	secondary (symptomatic) epilepsy
TLE	temporal lobe epilepsy

be applied to human patients, especially in presurgical diagnostic evaluation when it is mandatory to confirm the precise location and features of “abnormal neuronal activity.”

The word *seizure* originates from the Greek, meaning “to take hold.” The term can be used for any sudden and severe event, regardless of the origin. All seizures can resemble epileptic seizures and in clinical practice, it is frequently not possible to establish the origin of a seizure. An epileptic seizure is “transient” with a clear beginning and ending, although termination is usually less evident than onset as the postictal period can cause delay in apparent termination. Epileptic seizures have a wide range of clinical manifestations. The ictal signs and clinical signs (ictal semiology) depend on the location of the electrical discharge in the brain. Seizures can affect sensory, motor, and autonomic functions as well as consciousness, cognition, behavior, and memory. For human patients, evaluation of the autoanamnesis is helpful to detect sensory, cognitive, and memory signs. However, in animals, only motor and autonomic functions can be evaluated suffi-

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Table 1. Most important terms and concepts related to epileptic disorders.^{1,3}

Human Terminology and Concept	Human Older Terms and Concepts No Longer Recommended	Common Corresponding Veterinary Terms
<i>Epileptic seizures</i> An epileptic seizure is a transient occurrence of signs, clinical signs, or both because of abnormal excessive or synchronous neuronal activity in the brain		Seizure, epileptic seizure, fit
<i>Epilepsy</i> Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychologic, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure		Epilepsy, epileptic disorders
<i>Genetic epilepsy</i> Genetic defect directly contributes to the epilepsy and seizures are the core symptom of the disorders	Idiopathic epilepsy	Idiopathic epilepsy, primary epilepsy
<i>Structural-metabolic epilepsy</i> Caused by a structural or metabolic disorder of the brain	Symptomatic epilepsy	Symptomatic epilepsy, secondary epilepsy
<i>Epilepsy of unknown cause</i> Unknown is meant to be viewed neutrally and to designate that the nature of the underlying cause is as yet unknown; it may have a fundamental genetic defect at its core or it may be the consequence of a separate as yet unrecognized disorder	Cryptogenic epilepsy	Cryptogenic epilepsy, probable symptomatic epilepsy
<i>Focal epileptic seizure</i> Focal epileptic seizures are conceptualized as originating within networks limited to one hemisphere	Complex partial seizure, simple partial seizure	Focal seizure, partial seizure
<i>Generalized epileptic seizure</i> Generalized epileptic seizures are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed networks		Generalized epileptic seizure
<i>Evolving to a bilateral convulsive seizure</i>	Secondary generalized seizure	Secondary generalized seizure

ciently. A further difficulty is that firing of neurons can cause inhibition as well as excitation, so epileptic seizures are not invariably associated with excessive excitation.

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures... The definition of epilepsy requires the occurrence of at least one epileptic seizure.¹

It is not clear how this definition can be applied in practice. The first question is which clinical circumstances predict the recurrence of seizure with certainty. This problem was discussed in detail.² The authors proposed further subdivision into “definite, probable and possible epilepsy” to reflect the level of diagnostic certainty. “Definite epilepsy” is defined when 2 unprovoked epileptic seizures occur at least 24 hours apart. “Probable epilepsy” is suggested after a single unprovoked seizure with a high likelihood of recurrence, whereas a diagnosis of “possible epilepsy” would be appropriate after a single unprovoked seizure in the absence of evidence for a high probability of recurrence. However, a diagnosis of epilepsy after a single unprovoked seizure can have serious negative consequences for the human patient: it can increase the risk

of overtreatment and worsen the patient’s psychosocial status.^{2,3}

Etiologic Classification for Cats

The main etiologic categories of epilepsy in cats are *idiopathic epilepsy*, *symptomatic epilepsy*, *probable symptomatic epilepsy*, and *reactive epileptic seizures*.^{4,5} *Idiopathic (primary) epilepsy (IE)* occurs when no underlying brain lesion is present. It is reported that all cats with seizures have structural brain disease and as a result of this statement, it was believed for a long time that IE occurs only very rarely in cats.⁶ However, a considerable proportion of cats with recurrent seizures show no underlying disease.^{3,7–11} In 3 larger retrospective studies, a total of 233 epileptic cats were evaluated and 77 (33%) classified as IE.^{7,11,12} At present, there is no test to confirm IE, so the diagnosis can only be suspected based on the elimination of possible etiologic factors. The inherent weakness in the diagnosis of IE will remain until other, eg, genetic, tests become available. *Symptomatic (secondary) epilepsy (SE)* implies the presence of an underlying brain lesion. The disease processes can be classified according to the mnemonic “VITAMIN D” (Table 2). In accordance with

the current ILAE classification, toxic and metabolic causes are not true epilepsies as they do not represent disorders of the brain, although they can cause *reactive epileptic seizures*. *Probable SE*, also called *cryptogenic epilepsy*, is the result of brain lesions that cannot be identified. A cat with central blindness and seizures after general anesthesia with normal brain magnetic resonance imaging (MRI) would represent a patient in this category, with suspected hypoxic etiology.

The ILAE has recently revised its terminology for use in human epilepsy, suggesting that genetic epilepsy should be used instead of idiopathic, structural-metabolic instead of symptomatic, and unknown etiology instead of cryptogenic (Table 1).^{3,13}

Table 2. Etiologic differential diagnoses for recurrent seizures in cats.

Main Etiologic Categories	Subcategory	Possible Causes	
Idiopathic epilepsy	Idiopathic		
Symptomatic epilepsy	Vascular	Hypertensive encephalopathy	
		Feline ischemic encephalopathy	
	Inflammatory	Thromboembolic diseases	
		Polycythemia	
		Coagulopathy	
		VGKC-associated limbic encephalitis	
		Meningoencephalitis of unknown origin	
		Cuterebriasis, dirofilariasis	
		Rabies, pseudorabies	
		Feline immunodeficiency virus-infection	
Feline leukemia virus-infection			
Feline infectious peritonitis			
Traumatic	Anomalous	Cryptococcosis, blastomycosis	
		Toxoplasmosis	
		Traumatic brain injury	
Neoplastic	Degenerative	Hydrocephalus	
		Lissencephaly	
		Meningioma, lymphoma, glioma	
		Pituitary neoplasm	
Reactive epileptic seizures	Metabolic	Metastatic neoplasm	
		Hippocampal necrosis*	
		Storage diseases	
		Hyperthyroidism	
		Renal encephalopathy	
	Toxic	Toxic	Thiamin deficiency
			Hepatic encephalopathy
			Hypoglycemia
			Hypocalcemia
			Electrolyte imbalance
Probable symptomatic epilepsy	Posttraumatic	Organophosphate, pyrethroids, lead	
		Ethylene glycol	
		Posthypoxic encephalopathy	
		Postencephalitic seizures	

*Heterogenous etiology (see Table 4).

Diagnostic Evaluation of a Cat with Suspected Epileptic Seizure

Clinical Signs of Epileptic Seizures

It is important to be aware of 4 characteristic stages of epileptic seizure as it is helpful to differentiate them from nonepileptic seizures. The 4 stages are the *prodrome*, *aura*, *ictus*, and *postictal stages*. The *prodrome* is the least consistent. It precedes seizure onset, lasts hours to days, and usually includes restless activity and attention-seeking or anxious behavior.⁴ *Aura* is a subjective initial feeling of the ictal event and without EEG, it is impossible to differentiate it from the prodrome in animals. It should be emphasized that aura is an ictal phenomenon and can precede an observable seizure. It might contain information about the initial localization of the ED. The *ictus* is the seizure event itself and is followed by the *postictal stage*. *Postictal* changes are more consistent in their presentation than *prodrome* or *auras* and can frequently give indications of whether the seizure event was epileptic. Different features have been frequently reported in cats such as aggression, polyphagia, polydipsia, blindness/deafness, and ataxia.^{4,7} Clinical signs in the *aura*, *ictus*, and *postictal* stages can have diagnostic value in localizing the origin of the seizure in the brain, although this point needs to be further analyzed in cats.

Seizures in cats are frequently complex focal seizures with or without secondary generalization.^{10,11,14,15} The ictal signs frequently include drooling, facial twitching, tremor, rapid running, mydriasis, hypersalivation, urination, and defecation. During focal seizure, a cat can remain in sternal recumbency or can show running or climbing activity. Seizures might be particularly violent. Generalized seizures might involve the whole body. Both focal and generalized seizure types can occur in an individual patient. However, focal epileptic seizures can become generalized so rapidly that their true nature is missed and the seizure might then be classified as primary generalized. The ictus usually lasts for not longer than 3 minutes.^{6-8,10}

Paroxysmal Clinical Signs Can Be Caused by Epileptic or Nonepileptic Disorders

Cats might exhibit a large number of paroxysms that can resemble epileptic seizures. The differential diagnosis includes a wide range of clinical conditions: behavioral changes, obsessive-compulsive disorder, movement disorders, narcolepsy/cataplexy, sleep disorders, increased intracranial pressure, pain-associated behavior, tremor syndromes, syncope, feline orofacial pain syndrome, vestibular or neuromuscular disorder, and other encephalopathies (Table 3).^{4,5,16,17}

Clinical Differentiation between Epilepsies

Idiopathic (primary) epilepsy in dogs is believed to be usually genetic in origin, but there is little information to support such an assumption in cats. One study

Table 3. Epileptic and nonepileptic paroxysms in cats.

Paroxysmal Events	Important Features for Differentiation
Generalized epileptic seizure	Most often tonic-clonic seizure with impaired consciousness
Focal epileptic seizure	Very variable, may include drooling, facial movement, vocalization, abnormal head and limb movement (secondary generalization possible)
Temporal lobe seizure (special type of focal seizure)	Orofacial automatism: salivation, facial twitching, lip smacking, chewing, licking, swallowing (secondary generalization possible)
Neuromuscular collapse	Exercised-induced
Cardiac syncope	Arrhythmia, evidence of heart disease
Neck pain	Pain on neck manipulation
Compulsive disorders	No loss of consciousness
Feline estrus behavior	Howling, rolling, lordosis
Vestibular disease	Nystagmus, head tilt, falling
Increased intracranial pressure	No sudden start and termination
Feline orofacial pain syndrome	Acute oral discomfort and automutilation
Feline hyperesthesia syndrome	Rolling skin on the lumbar region (unclear etiology, may be epileptic)

indicates that some cat breeds might have a predisposition to IE.⁷ The European shorthair breed was slightly overrepresented in cats with IE, but this finding cannot be considered as proof of a genetic origin for IE. Recently, a possible spontaneous model of human genetic epilepsy was detected in laboratory cats.¹⁸

The age of onset is important in epileptic dogs for differentiating between IE and SE. On average, cats with IE are younger than cats with SE, with the mean age of onset in the IE/SE groups of 4.6/8.4 and 3.5/8.2 years in the 2 studies.^{7,11} The information is of limited diagnostic value as there is an overlap between the groups. Nevertheless, a young adult cat is more likely to have IE and an older cat more likely to have SE.

Historically, focal seizures have been associated with structural brain disease, but there is increasing evidence that focal and generalized seizures occur with nearly equal frequency in IE and SE.^{6,7,11} In practice, this means that focal seizure does not rule out IE, nor does generalized seizure suggest IE.⁸ The situation is actually even less clear, as 40–50% of cats in the IE and SE groups showed both focal and generalized seizures.⁷ This observation is easier to understand when we are aware of the modern concept of epileptic networks. In modern epileptology, focal and generalized epilepsies are not thought of as different pathophysiologic phenomena but as representing a continuum. Generalized epilepsy also originates from a specific brain region, although it does so bilaterally. In addition, some individuals fall in a gray zone in the transition from focal to generalized epilepsy (Table 1).¹⁹

Seizures in cats with IE have been reported to be more frequent during resting conditions.⁷ Non-REM sleep in particular can activate ED and certain seizure events. There is an increase in cortical neuronal synchronization during sleep, decreasing the seizure threshold.^{20,21} Seizures frequently occur in cats with experimentally provoked epilepsy during drowsiness and slow-wave sleep, which is the feline equivalent of non-REM sleep in humans. Seizure activity is much less prominent during alert wakefulness and REM sleep.^{22,23} This effect is probably less important in the presence of an underlying disorder (SE), which presumably has a stronger effect on seizure threshold than do daytime changes and the sleep/wake cycle.

Despite the problem confirming IE, there are examples of IE where the diagnosis has a high degree of certainty. A classic case might be a cat with very similar convulsive seizure events for 1–2 minutes during resting, postictal disorientation for 5–20 minutes, and no interictal impairment. The age of onset is between 1 and 4 years, the episodes recur monthly, the complete work-up is negative, remission occurs after antiepileptic treatment, and there is recurrence after cessation of treatment. More problematic are cases where the episodes are nonconvulsive and the patient only shows unusual behavior, the work-up is not complete, the changes are only borderline (eg, inconsistent neurologic findings, very slightly enlarged lateral ventricles, mild azotemia), or antiepileptic treatment is unsuccessful.

There is less literature dealing with confirmation of SE than of IE, although it is generally difficult to confirm that a certain brain disorder is responsible for the clinical signs. SE can be a particularly problematic issue when more potentially epileptogenic conditions are present in an individual person. In such a case, it is difficult or even impossible to tell what is the cause and it is likely that different causes can lead to epileptic seizures together.²⁴ The diagnosis of SE can be made with a high degree of certainty, for example, in a 14-year-old cat with acute onset of cluster seizures and permanent neurologic deficits where MRI shows evidence of a meningioma. Cases without permanent neurologic deficits and negative work-up are more problematic.

Diagnostic Work-up

Careful history taking is the first step. Video recording of the episodic event could be helpful for differentiation.¹⁴ The important points to note are those described above: age of onset, focal or generalized, when the event occurred, recognition of 4 (usually only 2) possible stages of epileptic seizure, and the presence of autonomic signs such as urination and hypersalivation. Clinical and neurologic examination should be undertaken. Interictal clinical signs other than postictal signs are more likely to be indicative of structural brain disease. However, a normal neurologic examination does not eliminate the possibility of a brain lesion. Evaluation of behavior and movement

can best be carried out by permitting the cat to walk freely in the examination room, although some cats might refuse to walk in such a stressful situation.

Further diagnostic work-up ideally includes blood pressure monitoring, urinalysis, hematology, biochemistry, CSF analysis, and MRI of the brain. Routine laboratory tests are usually of little diagnostic value, but should be performed to rule out metabolic encephalopathy and could also be helpful for guiding anesthesia (for diagnostic procedure) and for the later evaluation of treatment-induced changes, for example, by phenobarbital.^{8,25} Bile acid testing can be diagnostic, as hepatic encephalopathy is known to occur in cats.^{7,8,11} Serology testing for feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), and toxoplasmosis is frequently requested, but there is little evidence for its usefulness. In North America, FeLV, FIV, FIP, and toxoplasmosis testing was nondiagnostic in all cats tested with seizure and concluded that those disorders are unlikely to be the primary cause of brain disorder, especially in the absence of any other systemic involvement.¹⁴ In a European study, infectious disease was rarely diagnosed in seizing cats (2 of 125 cases) in an urban environment, although the study suggested that there can be geographic differences.⁷ For older cats, thyroid hormone concentration should be tested to rule out hyperthyroidism, which is a possible etiology for epileptic seizures. Similarly, hypertensive encephalopathy is regularly suspected in older cats with seizures.^{7,11} Computed tomography and particularly MRI can be used to rule out the presence of structural brain disorders.

As previously noted, EEG diagnostic in small animals is of limited value. Consistently, most articles about seizure in cats do not recommend EEG for the routine work-up.^{8,10,14,15,26,27}

Electroencephalography

Epileptic discharge can be detected by EEG, which is a standard diagnostic procedure in the epilepsy work-up for a human patient. A problem in veterinary epilepsy is that EEG data are not consistent and there is no agreement about the appropriate technique and sedation protocol, or about the graphoelements that are associated with epileptic seizures. There are only limited data relating to clinical EEG in healthy cats and cats with recurrent seizures.^{9,12,28} Recently encouraging EEG results were reported in cats.²⁹ Under propofol restraint, 6 of 13 epileptic cats showed paroxysmal discharges (focal or generalized spikes), while such activity was not detected in any of 6 healthy control cats. In this study, interictal EEG records with ED were also presented. There have been no previous clinical studies to suggest convincingly that epileptic activity in cats can be recorded under clinical conditions. The practical consequence of this limitation is that it is usually not possible to confirm the "abnormal excessive or synchronous neuronal activity in the brain," so whether a seizure event is epileptic can only

be suspected based on clinical, laboratory, and neuroimaging findings. In accordance with the uncertainty that the episode is really epileptic, a diagnosis of "probable/possible epileptic seizure" would be more appropriate in small animals as the diagnosis of definite epileptic seizure requires confirmation by EEG. Such a diagnosis would be consistent with human terminology, not with regard to the likelihood of recurrence, but to the likelihood of an epileptic origin.

In contrast to the limited clinical EEG data, there has been a large amount of experimental research on EEG recording in cats. Either electrically or chemically induced epileptic seizures have been recorded. The most frequently used technique has been intracranial ictal recording with implanted electrodes for freely moving cats. However, ictal surface EEG patterns after electrically induced seizures were also reported.³⁰ Very characteristic hippocampal 14–39 Hz discharges were detected and found to be constant in an individual cat in different seizure episodes. In contrast, ED of the isocortex were usually at 8–16 Hz. The ictal termination was always abrupt and preceded by spike-wave activity.³⁰ Others found that 4–6 Hz is a typical ictal pattern for amygdala. The authors also indicated that during the spread of seizures, the pattern in the newly affected areas can be identical or slightly or completely different from that in the primary focus.³¹ Discharges after amygdala kindling were analyzed and interictal spikes were observed in amygdala, substantia nigra, putamen, globus pallidus, and midbrain reticular formation; the frequency was about 6 per minute during the experience, but thereafter diminished to 0.04 per minute.³²

There are significant problems in translating experimental results to the clinic. Ictal recording could be very time-consuming, the influence of anesthetic drugs reduces the recordable epileptiform activity, and surface electrodes only deliver limited information about what is happening in deeper structures. Healthy control cats have been included in some studies, although intracranial recording was usually performed and this is impossible in daily practice and provides very limited conclusions. For these reasons, EEG is currently not widely used clinically, although strictly speaking, it is necessary for the objective differentiation of the paroxysmal event and for confirming epilepsy. Based on the experimental studies, it is clear that EDs are detectable ictally and interictally in epileptic cats, but appropriate technique is needed. Systematic studies by multiple centers on various aspects of EEG might result in a protocol that can be recommended for practical use in the small animal clinic. Advances in EEG diagnostic procedures are urgently necessary for veterinary medicine.

Hippocampal Lesion in Cats with Epileptic Seizures

Necrosis of the hippocampus and piriform lobe in cats was first described in Switzerland and has subsequently been reported in Italy, Germany, Austria,

England, and the United States.^{7,11,33–36} The cats studied usually showed acute cluster seizures, and other signs such as salivation and aggression were additionally reported. There are limited numbers of MRI results of HN, although the available data suggest bilateral hippocampal T1 hypointensity and T2 and FLAIR hyperintensity.^{37,38} It is important to be aware of different potential etiologic factors for hippocampal necrosis in cats. The literature in cats shows inflammatory, neoplastic, vascular, and toxic causes of HN; in addition, seizures itself can cause HN as well (Table 4).

A similar but not identical pathologic condition was first described almost 200 years ago by human neuropathologists based on postmortem examinations.³⁹ Since the initial histologic description of the condition, it has been debated whether so-called “hippocampal sclerosis” (HS) is a cause or a consequence of seizures. Even the ILAE could not determine whether HS is a nonspecific result of primary epileptogenic lesion or coexists with them.⁴⁰ The issue is controversial and both possibilities are likely to be partially true.

The latest ILAE Commission report proposed the following histologic criteria for HS: neuronal cell loss and gliosis at the CA1 segment with relative sparing of other hippocampal regions, synaptic reorganization that is not limited to mossy fiber sprouting and dispersion of the granule cells; extrahippocampal pathology can be present and special staining is recommended, eg, with Timm’s stain or glial fibrillary acidic protein.⁴⁰ We found³⁷ that the neuronal loss in the hippocampus of epileptic cats displaying characteristic signs of HS is most severe in the CA1 segment, which is also known as the “vulnerable” or Sommer’s sector.⁴¹

The *basic epileptogenicity level (BEL)*, which is determined by the inherited tendency to generate seizures, is different for different regions of the brain. Statistically, the temporal lobe has the highest BEL in humans, although there are large individual differences.¹⁹ Based on clinical observations, it can be proposed that the temporal lobe of cats, similar to the human brain, is prone to generating epileptic seizures

with a high BEL. Support for this proposal comes from experimental studies on the feline brain, which showed a relatively low threshold against electrical stimulation along the fornix, amygdaloid nucleus, and near the alveus of the temporal lobe.⁴²

Many experimental studies support the notion that facial twitching and oroalimentary automatisms can be elicited with an induced lesion to the hippocampus in cats.^{43,44} There is an established staging system for feline temporal lobe epilepsy based on the observation on a kindling model.⁴⁵ Kindling is an experimental model of epilepsy that induces increased excitability in some areas of the central nervous system by the repeated brief, low-intensity electric stimulation of different brain regions that does not initially produce manifestations of seizure. In Wada’s staging system, cats in stage 1 showed unilateral facial twitching, in stage 2 bilateral facial twitching, in stage 3 head nodding, in stage 4 tonic extension of a forelimb contralateral to the stimulus and contralateral head turning, sometimes rapid circling, in stage 5 clonic jumping while standing, and in stage 6 falling down with generalized convulsion. The temporal lobe seems to be frequently affected in epileptic cats, although this conclusion remains preliminary.

Antiepileptic Treatment

There is no consensus among veterinary neurologists about when antiepileptic treatment should be started. It was suggested not to start antiepileptic treatment after a single epileptic seizure, but the occurrence of frequent seizures over a short period of time would warrant beginning treatment.²⁶ Others recommended aggressive treatment for cats after a few seizure episodes.⁴⁶ Recent study indicates that an “early start of phenobarbital treatment can be associated with a better outcome.”²⁵ The strategy that is frequently recommended to initiate treatment when an identifiable structural etiology is present, status epilepticus has occurred, 2 or more isolated seizures have occurred within a 6-week period, 2 or more cluster seizures have occurred within an 8-week period, or the first seizure was within 1 week of trauma.^{14,47}

An aggressive, early start of treatment can be beneficial, as the cat could avoid cluster seizures and refractory epilepsy. The decision to start treatment should be taken on a case-by-case basis after considering the severity of seizure, ictal signs, risk of treatment, owner compliance, serum monitoring possibilities, and the difficulties with long-term oral application.

Antiepileptic treatment might be required for life. Reduction in treatment can be considered based on a seizure-free status for a longer period of time (after 6–24 months). Treatment should be reduced gradually and abrupt discontinuation is contraindicated.

There are several oral antiepileptic therapeutic options for cats (Table 5). Phenobarbital is usually recommended as a first-line drug,^{5,48} although there has not yet been any study to compare the efficacy of phenobarbital with that of other drugs in cats. The

Table 4. Etiologies of hippocampal necrosis in cats

Category	Disease/Etiology	References
Inflammatory (Immune mediated)	Antibody-associated encephalitis VGKC-complex encephalitis	54
Neoplastic	Secondary epilepsy	55
Seizure-induced	Idiopathic epilepsy (probably any frequent convulsive seizures*)	b,56
Vascular	Stroke, Hypoxia, Ischemia	57,58
	Anesthetic procedures	59
Toxic	Jodochinolin derivatives	11
	Kainic acid	44
Unknown	Many cases of feline hippocampal necrosis	33–38

*Author’s comment.

Table 5. Oral antiepileptic treatment for cats.

Medicine	Dosage	Possible Adverse Effects	Notes	References
Phenobarbital	1–5 mg/kg q12h	Sedation, ataxia, PU/PD/PP, leukopenia, thrombocytopenia, lymphadenopathia, skin eruptions, coagulopathia	Serum level monitoring (100–300 µmol/L, 23–30 µg/mL)	10,24,25,47,60,61,62
Diazepam	0.2–2 mg/kg q8–24h	Sedation, PU/PD/PP, hepatic failure	Liver function monitoring is advisable	9,10,13,25,47,63,64
Potassium bromide	30–40 mg/kg q24h	PU/PD, vomiting, eosinophilic bronchopneumonia	Serum level monitoring	10,25,47,65
Clorazepate	3.75–7.5 mg/kg q6–12h	As diazepam		47
Levetiracetam	10–20 mg/kg q8h	Inappetence, sedation, hypersalivation		66
Gabapentin	5–20 mg/kg q6–12h	Sedation, ataxia	No clinical studies available	67
Zonisamide	5–10 mg/kg q12–24h	Sedation, inappetence, vomiting, diarrhea		68,c
Pregabalin	1–2 mg/kg q12h	Sedation	No clinical studies available	4
Propentophyllin	5 mg/kg q12h		No clinical studies available	10
Taurine	100–400 mg/cat q24h		Inhibitory aminoacid	69
Topiramate	12.5–25 mg q8–12h	Sedation, inappetence	No clinical studies available	70

PU, polyuria; PD, polydipsia; PP, polyphagia.

rationale for its usage is based on its low price, relatively long elimination time, tolerability, and long history of chronic use. More detailed descriptions of the pharmacologic properties of antiepileptic drugs can be found elsewhere.⁴⁹ The ILAE has developed evidence-based guidelines for human treatment studies with four classes of quality. Class I and II studies include only placebo-controlled, randomized, double-blind trials with a large number of cases. Class III evidence can be an open-label trial, whereas class IV represents expert opinion and case reports.⁵⁰ A few double-blind, placebo-controlled trials in dogs have recently been published.^{51–53} However, there is no comparable high-evidence treatment study available for cats and the literature contains only case reports, case series, and expert opinions. Human epileptologists have made a major effort to bring knowledge about epilepsy out of the shadow of expert opinion, thereby improving the management of the condition and the outcome for patients. Unfortunately, epilepsy in cats is still a long way from this stage. Clinicians should be aware of the limitation as knowledge of epilepsy in cats is generally based on the weakest class (IV) of evidence.

Outcome

The prognosis is based on the underlying etiology and its treatment. It was observed that with phenobarbital or diazepam, 40% of cats with IE become seizure-free, 40% show decreases of over 50% in frequency of seizure, and 20% are resistant to treatment.⁹ Others stated that the prognosis varies widely depending on the diagnosis and the response to treatment; however, despite severe seizures, the outcome can be good to excellent in most cases.⁴⁶ Another study concluded that cats with seizures, but no other neurologic abnormalities could have a good prognosis.¹² In a recent study, the majority of cats (50–80%

depending on the period examined) with suspected IE showed excellent or good seizure control (fewer than 6 seizures per year) with phenobarbital treatment, although some cases proved resistant. Nearly 50% of cats remained seizure-free for years, although cessation of treatment led to recurrence in 75% of cats.²⁵ A similar result, with 50% of cats becoming seizure-free, was reported in another study.^d

Future Perspectives

Abnormal, excessive, or synchronous neuronal activity in the brain is the essence of epilepsy. As changes could be subtle and difficult to detect, improvements in current EEG diagnostic procedures will be crucial for advances in our understanding of epilepsy in cats. Only through systematic studies on various aspects of EEG (including electrode placement, type of electrode, restraint techniques, and standardization) will we be able to define diagnostic methods that can be recommended for practical clinical use.

It seems reasonable to establish clinical syndromes to define various forms of epilepsy and this study has already been started for feline temporal lobe epilepsy. Based on work with human patients, such syndromes “are identifiable on the basis of a typical age onset, specific EEG characteristic, seizure types, and often other features which, when taken together, permit specific diagnosis.”²⁷ Modern neuroimaging techniques, which allow the functional examination of the brain, can also help put the field on a more precise footing.

Footnotes

^a Cizinauskas S, Fatzer R, Schenkel M, et al. Can idiopathic epilepsy be confirmed in cats? *J Vet Intern Med* 2003;17:246 (abstract)

- ^b Fors S, Jeserevics J, Cizinauskas S. Idiopathic epilepsy resulting in hippocampal and piriform lobe necrosis in three cats. ECVN/ESCVN 23rd annual symposium. Cambridge 2010;69 (abstract)
- ^c Brewer DM, Cerda-Gonzalez S, Dewey CW. Zonisamide treatment for refractory seizures in five cats with presumptive idiopathic epilepsy. Abstract ACVIM 2010 Annual Forum. J Vet Intern Med 2010;24(3):739 (abstract)
- ^d Szelecsenyi A, Steffen F, Golini L. Idiopathic epilepsy in 66 cats: survival time and owner perception of quality of life. J Vet Int Med Proc. 25th ECVN/ESVN Congress, Ghent, Belgium Sept 14–15. 2013:405 (abstract)

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