Update on Feline Epilepsy
John Rossmeisl, DVM, MS, DACVIM (SAIM and Neurology)
Virginia-Maryland College of Veterinary Medicine, Virginia Tech
Blacksburg, VA

While there exists a robust body of literature regarding canine epilepsy, until recently there has been a relative informational void regarding feline seizure disorders. This review will focus on recent developments in the classification of feline epilepsies, newly identified etiologies for feline seizures, and practical approaches to the management of cats with epilepsy.

Paradigm Shifts in Feline Epilepsies
The classification of epilepsy is a constantly evolving process, and thus is subject to continuous scrutiny and controversy. There are four main categories of epilepsy including genetic (primary/idiopathic), structural/metabolic (symptomatic), unknown (cryptogenic), and presumptive unknown. Although some breeds of cats have been reported as predisposed to developing epilepsy, and a feline familial epilepsy syndrome has been described, there is currently a lack of definitive evidence establishing a genetic basis of epilepsy in cats.1,2 Thus, some consider it inappropriate to apply the term genetic epilepsy to cats, which is the term proposed by the International League Against Epilepsy to replace the older ‘idiopathic’ terminology. This forms the basis for the use of the term unknown epilepsy in cats with recurrent seizures that have no abnormalities identified during diagnostic evaluations.

In the mid to late 1990’s, the preponderance of evidence with respect to the etiologies of feline seizures indicated that unknown, or idiopathic, epilepsy was rare. In the study by Quesnel et al. in 1997, 100% of cats with seizures were diagnosed with structural epilepsy.3 However, subsequent studies have demonstrated that cats meeting the diagnostic criteria for unknown epilepsy comprise 33-50% of all felines with epileptic seizures.4-6

Evolving Etiologies of Feline Seizure Disorders
Hippocampal Lesions in Feline Epilepsy
A syndrome consisting of necrosis of the hippocampus (HN) and piriform lobes of the brain was initially identified in cats from the European Union and later in North America.7 The neuropathological features of this disease are similar to those described in epileptic humans with hippocampal sclerosis. These cats classically presented with cluster complex partial seizures (CPS), facial twitching, orofacial automatisms, as well as potential behavioral changes.7,8 There is abundant evidence in the literature that indicates similar orofacial phenotypic manifestations and electroencephalographic epileptiform discharges can be experimentally induced in cats by lesioning the hippocampus. The MR characteristics of this condition have been described in a limited number of cats, and indicate that hippocampal and piriform changes manifest as T1 hypointensity and T2 and FLAIR hyperintensity, which may be bilateral or unilateral.
The clinician currently faces a diagnostic dilemma when presented with a cat with a seizure semiology or MRI findings consistent with HN, as HN can be a primary/idiopathic entity, or can occur secondary to a number of neoplastic, vascular, or inflammatory brain diseases (Table 1).

**Table 1- Potential Causes of Feline Hippocampal Lesions**

<table>
<thead>
<tr>
<th>DAMNIT-V Category</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neoplastic</strong></td>
<td>Lymphoma, oligodendroglioma</td>
</tr>
<tr>
<td><strong>Idiopathic</strong></td>
<td>Prolonged seizure activity</td>
</tr>
<tr>
<td></td>
<td>Idiopathic hippocampal necrosis</td>
</tr>
<tr>
<td><strong>Inflammatory</strong></td>
<td>VGKC Antibody-associated encephalitis*</td>
</tr>
<tr>
<td></td>
<td>Infectious encephalitis</td>
</tr>
<tr>
<td><strong>Toxic</strong></td>
<td>Many</td>
</tr>
<tr>
<td><strong>Vascular</strong></td>
<td>Feline ischemic encephalopathy</td>
</tr>
<tr>
<td></td>
<td>Ischemic infarction</td>
</tr>
<tr>
<td></td>
<td>Global brain ischemia</td>
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**Voltage-Gated Potassium Channel (VGKC) Antibody-Associated Limbic Encephalitis**

Feline complex partial seizures (CPS) with orofacial involvement and hippocampal pathology also shares similarities to humans with limbic encephalitis and voltage-gated potassium channel (VGKC) complex antibody. A recent study evaluated cats with CPS and orofacial involvement for the presence of VGKC-complex antibodies. Five of 19 cats affected with CPS, but no control cats were identified as having serum VGKC-complex antibodies directed against leucine-rich glioma inactivated 1 (LG11) protein, which is also a major target of VGKC-complex antibodies in humans. Follow-up serological testing of affected cats in remission demonstrated a return of VGKC-complex antibody concentrations to within the reference ranges following treatment with antiepileptic drugs (AED) and corticosteroids. Results of this study demonstrate that autoimmune limbic encephalitis exists in cats and that VGKC-complex/LG11 antibodies may participate in the pathogenesis of this disorder, as they do in humans.

**Feline Audiogenic Reflex Seizures (FARS)**

Reflex seizures are defined as those seizures that are objectively and consistently precipitated by an environmental or internal stimulus. FARS is a recently described, geriatric onset seizure disorder in cats, with a median age of onset of 15 years. The Birman breed appears to be over-represented. The seizure triggers in FARS are various high-pitched noises, although 20% of cats with FARS will experience spontaneous seizures. Myoclonic seizures are the predominant seizure phenotype in this syndrome, and frequently progress to generalized tonic-clonic seizures. In the study by Lowrie et al, 50% of the cats were reported to be deaf. No underlying structural etiology for the seizures was
observed on diagnostic imaging examinations of the brains of affected cats. Levetiracetam treatment provided satisfactory seizure control in most cats. The natural history course of the epilepsy was non-progressive in 70% of cats. However, more than 50% of cats owners experienced an insidious decline in their overall health following diagnosis, which manifested principally as becoming less responsive, reluctance to jumping, developing pelvic limb ataxia or paresis, and/or exhibiting dramatic weight loss. These constitutional signs were exclusively reported in cats experiencing seizures for >2 years.

**Etiologies of Structural/Metabolic Epilepsy in Cats**

Intracranial neoplasia is the most common etiology of structural epilepsy cats, with meningeomas and lymphoma being commonly reported neoplasms associated with seizures.\(^1,6\) Meningoencephalitis of unknown etiology, feline infectious peritonitis, and toxicoses are also frequently reported etiologies of feline structural and metabolic epilepsies.\(^1\) However, recent studies have suggested that HN and possibly autoimmune limbic encephalitis are also common, with one reporting HN second only to intracranial neoplasia as an etiology for feline structural epilepsy.\(^1,7\)

**Management of Feline Seizure Disorders**

Similar to dogs, structural/metabolic epilepsy should be strongly suspected in cats that have status epilepticus, an abnormal interictal neurological examination, or an onset of seizures at greater than 7 years of age. A complete diagnostic workup including MRI imaging of the brain and cerebrospinal fluid analysis should be recommended in patients with any of these characteristics. Conversely, cats with unknown epilepsy are typically <7 years of age, are more likely to have seizures while resting, or display ictal fits of running.\(^1\) It is reasonable to assume that many with seizures < 7 years of age with a normal interictal examination, no evidence of significant disease on physical examination, and an unremarkable laboratory minimum data base will have unknown epilepsy.

There is no currently no consensus regarding when AED treatment should be started in cats. One feline study claimed that early initiation of phenobarbital treatment can be associated with a better outcome.\(^4\) An approach used by the author and other veterinary neurologists is to recommend treatment when an structural epilepsy is present, the cat has experienced status epilepticus, ≥2 seizures have occurred within 6-weeks period, or seizure activity was observed within 1 week of a traumatic episode.

**Antiepileptic Drug Response and Prognosis in Cats with Epilepsy**

The current veterinary literature contains purely low-level evidence (case reports, case series, and expert opinion) with regards to feline responses to AED. While there are numerous AED that can be used in cats, the existing evidence suggests that with the exception of FARS, phenobarbital is the drug of choice for epileptic cats, irrespective of the etiology the epileptic seizures.\(^10,11\) Compared to dogs cats also have a lower incidence of clinically intolerable phenobarbital
associated adverse effects. Early studies have indicated that nearly 80% of cats can achieve satisfactory seizure control with phenobarbital or diazepam therapy. Reviews of feline case series suggest that approximately 40-50% of cats can achieve seizure freedom, and greater than 90% of cats will have a satisfactory response to chronic phenobarbital therapy. However, a recent study reported seizure recurrence following phenobarbital withdrawal in 75% of cats that had experienced long term seizure control.¹

The prognosis associated with structural/metabolic epilepsy is heavily dependent on the underlying etiology. Studies to date indicate that the prognosis for cats with unremarkable interictal neurologic examinations and unknown/idiopathic epilepsy generally have a favorable prognosis.¹,⁴,⁶

References