Review
J Vet Intern Med 2017;31:633–640

Feline Temporal Lobe Epilepsy: Review of the Experimental Literature

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Accumulating evidence suggests that epileptic seizures originating from the temporal lobe (TL) occur in cats. Clinically, affected cats experience focal seizures (FS) with orofacial automatism including salivation, facial twitching, lip smacking, chewing, licking, and swallowing (Fig 1). Motor arrest and autonomic and behavioral signs also may occur. Many affected cats have clinical and behavioral signs of TL epileptic seizures in cats. Furthermore, the research data supports the idea that TL epilepsy represents a unique clinical entity with a specific seizure type and origin in cats.

Key words: Electrical stimulation; cat; Kindling model; Review; Temporal lobe.

Abbreviations:
AD after discharge
CPA complex partial seizure
ECS electroconvulsive shock
EEG electroencephalography
FTLE feline temporal lobe epilepsy
MRI magnetic resonance imaging
NE norepinephrine
NREM nonrapid eye movement
TL temporal lobe

The goal of our review was to emphasize the importance of experimental research in FTLE in veterinary medicine in order to gain additional and better knowledge about the anatomical and functional mechanisms underlying the disease. Consequently, we summarized the literature on experimental research regarding FTLE. The years from 1950 to 1980 received special focus, however, important basic knowledge about epilepsy was acquired experimentally from cats. Better knowledge of these experimental results may help clinicians to understand more about FTLE.

The database search

Our review is based on literature searches in online medical databases, as well as a few selected specialized books on epilepsy and the important anatomical

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A poster abstract was published: Pakozdy A., Klang A., Kitz S., Wrzosek M., Halasz P. Feline temporal lobe epilepsy. What can we learn from early experimental research? Proceedings 26th Symposium ESMN-ECVIN. Journal of Veterinary Internal Medicine. 2014;28(3):944–975. doi:10.1111/jvim.12333.

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Submitted July 8, 2016; Revised January 12, 2017; Accepted February 23, 2017.

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DOI: 10.1111/jvim.14699

The TL is the main source of epileptic discharges, but electroencephalographic confirmation usually is absent. Feline temporal lobe epilepsy (FTLE) is a well-known model based on experimental research. Until recently, very little knowledge from experimental research in FTLE was used in clinical veterinary epilepsy. However, important basic knowledge about epilepsy was acquired experimentally from cats. Better knowledge of these experimental results may help clinicians to understand more about FTLE.

The database search

Our review is based on literature searches in online medical databases, as well as a few selected specialized books on epilepsy and the important anatomical
structures involved. The research involved medical databases such as PubMed, Europe PubMed Central, Scopus, Ovid, and ScienceDirect. The following search criteria were used: “epilepsy cat,” “TL epilepsy cat,” “FTLE,” “experimental research cat epilepsy,” and “experimental research TL epilepsy cat.” To increase the specificity, “kindling TL cat,” “kindling kitten,” “electrical stimulation TL cat,” and “chemical stimulation TL cat” were added. Finally, the references of each publication were reviewed.

Electrical Stimulation Studies of Temporal Lobe Epilepsy in Cats

Amygdala Stimulation

Ursin and Kaada described the “attention response” as one of the most common reactions after amygdala, as well as hippocampal, stimulation in cats. Kaada (1951) called it “arrest,” and others called it “searching” or “attention response.” At the beginning of stimulation, cats stopped all spontaneous activities. Their facial expression and behavior changed to attention or alertness. Cats frequently seemed surprised and behaved as if they expected something to happen. The response usually included initial respiratory arrest, strikingly in expiration. The initial inhibition was followed by a movement resembling orientation. The cats raised their heads and sometimes their forelimbs as well. They seemed to be anxiously searching for something and looked backwards, usually contralateral to the stimulation side but ipsilateral turning also occurred. The eyes were widely opened, the pupils dilated, and directional movement of the ears sometimes occurred. Occasionally, sniffing movements were observed. During this period, cats reacted appropriately to different stimuli. The initial apnea was followed by tachypnea of low amplitude. The contralateral searching sometimes continued into contralateral circling. The attention response sometimes was combined with other motor and autonomic signs. Most frequently, licking and ipsilateral facial twitching were observed (Fig 2).

Studies from Delgado et al. showed a clear correlation between electrical stimulation of the amygdala and direct ipsilateral facial motor effects. Similarly, Kaada et al. showed that electrical stimulation of distinct parts of the amygdala in unanesthetized cats resulted in an immediate and strong contraversive turning of the head, eyes, and cranial part of the body. It usually was combined with backward-upward movement of the head and tonic extension of the forelimbs, culminating in a spiral movement of the head and upper body parts.

Kaada et al. stated that both motor and autonomic responses were obtained mainly from the same phylogenetically old anteromedial division of the amygdaloid nuclei. The animals also were looking or staring at a certain body area, which was interpreted as a change of bodily sensation. These responses were obtained mainly from the phylogenetically younger basolateral division. Furthermore, a study by Kesner and Doty identified a link between electroconvulsive shocks (ECS) applied to the amygdala and some state of amnesia.

Hippocampal Stimulation

Delgado and Sevillano observed the so-called “attention response,” similar to the amygdala stimulation. When stimulation was carried out during sleep or dozing, animals opened their eyes, looked around, and stared. In contrast, in completely awake animals, there were no obvious effects, and spontaneous activity, such as walking, continued, seemingly undisturbed. Only with longer stimulation (>5 seconds) did the spontaneous activity of the animals stop and the typical “attention response” appeared, which lasted until the stimulation was finished. Afterward, the cats were frequently hyperactive, walking, or running around with increased vocalization. Approximately 10% of stimulations with recordable after discharges (ADs, discharges of neural impulses after an initiating stimulus) were asymptomatic in the hippocampus.

The hippocampal stimulation generally also had autonomic, motor, and behavioral effects. The most frequently observed autonomic effects were mydriasis, salivation, gagging, and piloerection (Fig 2). The main motor responses were arrest, staring, head turning, vocalization, facial twitching, and clonus. Behavioral effects were attention or apprehensiveness, signs of fear or anger, searching behavior, and sniffing. Immediately after hippocampal stimulation,
motor signs similar to a “wet dog shaking” may occur.\textsuperscript{13,14} The hippocampus generally is considered to have striking electrical features within the brain because discharges may be elicited easily after an initial electrical stimulation elsewhere.\textsuperscript{9} Elul et al.\textsuperscript{15} also found a regional differentiation of the hippocampus. The dorsal hippocampus exhibited lower AD thresholds than did the ventral part.\textsuperscript{16}

In 1936, a study concerning the convulsion threshold of various parts of the feline brain noted that points with rather low thresholds were found along the course of the fornix, in the gyrus cinguli and in the TL.\textsuperscript{17} The low threshold points close to the amygdaloid nucleus are of interest because the fornix and taenia semicircularis connect the amygdaloid nucleus and adjacent structures with the TL, and there is evidence that fiber connections to the gyrus cinguli run through the fornix.\textsuperscript{17}

### Insular Stimulation

The insula and peri-insular regions of the feline brain are thought to be substantially less developed than those of humans. Studies concerning the role of the insula and peri-insula in experimental epilepsy in cats were carried out in the early 1960s.\textsuperscript{18} The main effects after stimulation of the insular region also can be divided into autonomic, motor, and behavioral. The

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**Fig 2.** Seizure features in experimental temporal lobe (TL) epilepsy in cats using tungstic acid injection into the different TL regions according to Blum et al.\textsuperscript{18}
most frequent autonomic responses were mydriasis and salivation. Motor effects included head turning, looking sideways, jumping, and swallowing. Behavioral responses were apprehensiveness, searching, and vocalization (Table 1, Fig 2).\textsuperscript{19,20}

**Staging Systems in Feline Temporal Lobe Epilepsy by Kindling**

A classification of certain stages emerged throughout the years of research in this field, and systems of the chronological development of seizure patterns were developed (Table 2). The early stages of 0–3 represent motionless staring, autonomic manifestations such as salivation and dilatation of pupils, focal (partial) seizures, and head turning. With progressive kindling and recruitment of more distant structures, stages 4 and 5 evolve and are represented by forelimb clonus and extension, and generalized seizures of different severity with falling and tonic-clonic convulsions. Some researchers even extended evaluation to stages 6–8, which occur after more intense stimulation and lead to progressively more severe seizures.\textsuperscript{21} Most researchers continued stimulation until a stage 5 seizure state was achieved.\textsuperscript{22} Wada et al.\textsuperscript{23} used a similar classification system for their amygdala-kindled cats.

**Table 1.** Effects of hippocampal, amygdaloid, and insular stimulation.

| Effects of Stimulation | Hippocampus | Amygdala | Insula |
|------------------------|-------------|----------|--------|
| Autonomic              |             |          |        |
| Mydriasis              | Mydriasis   | Mydriasis|        |
| Gagging                | Salivation  | Defecation| Salivation|
| Piloerection           | Urimination |           |        |
| Motor                  | Head turn   | Head turn| Head turn|
| Facial twitching       | Facial      | Facial   |        |
| Facial twitching       | Licking     |          |        |
| Arrest                 | Sniffing    |          |        |
| Staring                | Chewing     |          |        |
| Vocalization           | Tonic stiffening | Apnea |        |
| Behavioral             | Attention   | Attention| Apprehensiveness |
| Searching              | Searching   | Searching| Searching |
| behavior               | behavior    | Body sensation | behavior |
| Anger                  |             |          |        |
| Sniffing               |             |          |        |

**Table 2.** Two different staging systems of experimentally induced seizures and clinical observations of naturally occurring temporal lobe seizures.\textsuperscript{1,30,32}

| Wada et al.\textsuperscript{23} (Experimentally Induced Seizures) | Sato et al.\textsuperscript{12} (Experimentally Induced Seizures) | Pakozdy et al.\textsuperscript{1} (Naturally Occurring Seizures; Did Not Use Staging but Retrospectively Recognizable) |
|-------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Stage 1 Unilateral ipsilateral face twitching                     | Attention response, looking around, sniffing                      | Arrest                                                                                                                                 |
| Stage 2 Bilateral facial twitching                                 | Immobility (staring and arrest)                                   | Hypersalivation, oro facial automatism, mydriasis, licking, lip smacking                                                     |
| Stage 3 Head nodding                                              | Autonomic manifestation: salivation, licking, pupillary dilatation | Masticatory movements, facial twitching                                                                                       |
| Stage 4 Contralateral head turning, tonic extension of contralateral forepaw | Facial twitching, masticatory movements                           |                                                                                                                               |
| Stage 5 Generalized clonic jerking while standing                  | Tonic extension of contralateral forepaw, head nodding, head turning |                                                                                                                               |
| Stage 6 Falling down with generalized convulsive seizure           | Generalized clonic convulsions in lateral recumbency              | May evolve into generalized convulsive seizures                                                                                 |

**Kindling Model**

Kindling is a widely accepted experimental animal model of epilepsy with a progressive and permanent character. It is used mainly as a model to study epilepsies\textsuperscript{24} and as a method to study physiological changes in epilepsies. Kindling studies initially were performed in rats, but other mammalian species, such as dogs, cats, and primates,\textsuperscript{25} and even amphibians,\textsuperscript{26} soon followed. Kindling is based on repeated, low-intensity, initially subconvulsive, daily electric stimulation, resulting in focal AD at the electrode tip but without seizures.\textsuperscript{27,28} Complex, widespread functional reorganization of the brain\textsuperscript{29} and alternation of neuronal responses take place after kindling without gross morphological damage.\textsuperscript{5,30} The repetition leads to a lengthening of ADs, which gradually elicits seizure activity. Once an animal has been successfully kindled, the increased response to the stimulus seems to be permanent, and spontaneous seizures can occur within a short period of time.\textsuperscript{6} Once generalized seizures occur, the excitability of the stimulated brain area stays altered.\textsuperscript{28} Kindling also can be induced by...
Tetanus Toxin Model

The tetanus neurotoxin, produced by the gram-positive bacteria Clostridium tetani, was first used as an experimental model for recurrent chronic focal (partial) seizures in the 1960s. It's effect involves the synaptic blocking of the release of inhibitory neurotransmitters such as γ-aminobutyric acid (GABA), as shown when applied experimentally to hippocampal slices. In 2 studies by Louis et al., tetanus toxin was applied to the cerebral cortex of 60 dogs and the left primary motor cortex of 5 cats. In both studies, the administration of tetanus toxin induced epileptogenic foci, which lasted up to 2 months. A clinical and electroencephalographic (EEG) onset occurred after a relatively short latency period that varied from hours to several weeks and remained chronically active. In the 5 cats with tetanus toxin lesions of the motor cortex, clonic motion of contralateral shoulder and forepaw initially occurred. When the tetanus toxin was injected into the hippocampus, behavioral, autonomic, and motor signs were observed similarly to those described during direct electrical stimulation of the hippocampus. The toxin seemed to be an ideal agent for producing highly localized lesions after local injection, because of its large molecular size and its rapid binding to receptors. Tetanus toxin lesions are relatively small and well confined, consisting of necrosis and reactive gliosis. Another advantage of tetanus toxin is the wide range of susceptible telencephalic application areas (e.g., the hippocampus, substantia nigra, thalamus, orbital frontal cortex, cerebral cortex, and motor cortex).

Tungstic Acid Model

In the studies of Blum et al., a characteristic TL type of epilepsy was induced by the unilateral injection of tungstic acid in the hippocampus and lateral amygdala of cats. In the new tungstic acid method, by the injection of minute quantities of tungstic acid gel, discrete lesions in 3 selected areas of the TL were produced: the ventral hippocampus, the amygdala, and the insula. The pathological findings were the same in the different parts of the TL. Epilepsy with different clinical signs occurred within 12–24 hours after the injection, but generalized seizures only were observed after amygdaloid injection. Both the hippocampal and insula-perinsula-type seizures were described as being behavioral and autonomic. The clinical signs after injection of the 3 different sites overlapped, which is not surprising because they all belong to the limbic system. With unilateral ablation of the amygdala in cats, ipsilateral motor manifestations disappeared and did not return, even during kindled generalized seizures.

Sleep and Epilepsy in Cats

From 1980 to 2005, Shouse performed FTLE studies using a different premise. She proposed that studying sleep and arousal disorders coexisting with FTLE might identify common underlying mechanisms.
for the onset or expression of secondary generalized seizures. She produced 3 major sets of findings:

1. Temporal lobe epilepsy in humans and cats shows similar, sleep-related timing of secondary generalized TLE seizures and of sleep disorders. Peak TLE seizure manifestations occur in nonrapid eye movement (NREM), also called slow-wave sleep (SWS) in cats. Shouse was the first to show the physiological factors for rapid eye movement (REM) suppression and NREM activation of generalized seizure manifestations when compared to waking. Identical findings were obtained in evoked seizure measures using feline models of primary generalized epilepsy (PGE) (ECS and systemic penicillin epilepsy) and TLE (amygdala kindling). Atropinized cats displayed REM sleep with a selective presence of a synchronized, NREM-like EEG and selective increase in seizure discharge generalization without motor seizure accompaniment. The epileptic spikes usually originated from the amygdala and could be recognized during stages 1 and 2 seizures. After stage 3, the EEG discharges were so pervasive that no distinction was possible. Independent interictal spikes also occurred not only arising from the amygdala but also the locus coeruleus, motor cortex, piriform and entorhinal cortex, and lateral geniculate nucleus. Interestingly, these multifocal interictal discharges were very prominent during SWS and during cluster seizures between the convulsive periods. Strikingly, in some cases, such interictal spikes were completely absent in kittens with severe spontaneous seizures, even during SWS. The absence of motor signs was attributed to profound lower motor inhibition, also called atonia, in REM. This was confirmed by lesions of the pontine tegmentum which selectively abolished the atonia of REM. Cats without atonia had motor seizures in REM as readily as in waking.

2. Lastly, Shouse’s group discovered the first model of developmental FTLE and of spontaneous, convulsive “sleep” epilepsy by amygdala kindling in kittens. Microdialysis showed early postkindling depletion of norepinephrine (NE) in the brainstem and amygdala and subsequent increase of NE with low concentrations predicting evoked and spontaneous seizures and sleep disorders in cats kindled as kittens. Also, microinjection of NE agonists delayed, whereas antagonists accelerated, kindling in kittens.

From the 1950s to the 1980s, cats frequently were used as animal models for neurophysiological experiments and electrophysiological studies. Electrical discharges are easily elicited in the hippocampus within the TL. For functional testing of the TL, different methods were used in cats. The most frequent method to investigate TL function was electrical stimulation. Stimulation electrodes were placed in different parts of the TL, and the behavioral, motor, or EEG changes were documented. Other studies involved injections of different chemical substrates into discrete TL structures, usually the amygdala, hippocampus, or TL cortex. Another type of research involved a special kind of stimulation called “kindling.” Based on the experimental data, it can be concluded that epileptic activity within the TL in cats has characteristic ictal signs. Experimentally elicited ictal signs were best described in a staging system by Sato et al. Knowledge on that literature is important because there is accumulating evidence that epileptic seizures originating from the TL occur spontaneously in cats worldwide. The initial signs can be summarized as orofacial automatism, which is the main clinical feature of the TL seizure in cats. This is so characteristic that it can be recognized clinically, and it is very likely that these early stages (1–3) were observed by clinicians. Looking more closely at the different stages: arrest (stage 2), orofacial automatism (stage 3), facial twitching (stage 4), and generalized clonic convulsions (stage 6) were recognizable as epileptic by Pákozdy et al. Based on clinical observation, tonic extension of the contralateral forelimb (stage 5) was not observed clinically because it is less obvious and it could have been overlooked. More importantly, the clinical recognition of stage 1 signs (looking around, attention response, sniffing movement) is more challenging. However, knowledge of the experimental literature may enable recognition in the future. The clinical rediscovery of the experimentally well-known TLE in cats is summarized in Table 2.

The clinical postmortem diagnosis of TLE in cats can be supported by magnetic resonance imaging (MRI) changes, but electrophysiological confirmation, usually is lacking. Epileptic discharges, however, were detected in experimental cats, and detailed clinical observations were provided. The experimental studies clearly show that orofacial automatism is the main feature of TL epilepsy, which sequentially can evolve into generalized motor convulsions. However, orofacial automatism is not necessarily always an epileptic phenomenon and obsessive-compulsive disorder may be a differential diagnosis. Furthermore, many epileptic discharges may not manifest themselves clinically.

Abnormal, excessive, or synchronous neuronal activity in the brain is the main feature of epilepsy. Epileptic discharges can be detected by EEG, which is the main diagnostic procedure in the study of epilepsy in people, whereas in cats it is rarely used.

A drawback in the study of epilepsy in animals is that EEG data are not consistent and there is neither agreement about the appropriate technique and sedation protocol nor about the EEG features that are associated with epileptic seizures. The consequence of these limitations is 2-fold. First, it is usually not possible to diagnose epilepsy in clinical practice. Secondly, localization of the epileptic discharge within the brain cannot be achieved. Consequently, whether an episodic event is epileptic and where it is localized can only be suspected based on clinical, laboratory, and neuroimaging findings. This limitation underlines the importance of knowledge about the ictal signs of experimental epilepsies in cats.
This feature was widely studied during early experimental research. The EEG recording usually was a central part of the studies, and epileptic discharges were recorded and simultaneous behavioral changes were observed and noted. The electrodes used frequently were intracranial, and were able to detect epileptic discharges in deep brain structures. For this reason, this method is more sensitive than the EEG with its surface electrodes. These data are important for clinicians because the evidence for epileptic discharge is much higher than in clinical cases. On the other hand, it is not clear whether these epileptic discharges reach the cerebral surface and are recordable by surface EEG during sedation or general anesthesia.

Temporal lobe epilepsy seizures occur most frequently in SWS in amygdala-kindled cats, but these aspects were not investigated in clinical cases. However, different aspects could be interesting in the future. Electroencephalography could be performed in a subgroup of cats during natural sleep, which could help in understanding more about sleep and awake states in this species. Secondly, sleep (REM versus SWS) could be influenced by different drugs, increasing diagnostic value in epileptic animals.

In conclusion, early experimental research data are in agreement with recent clinical observations regarding the ictal clinical signs of TL epileptic seizures in cats. When summarizing these results, it seems that TLE represents a unique clinical entity with a specific seizure type that can be recognized clinically. Knowledge of the earlier research supports the recognition and interpretation of epileptic signs. However, challenging cases still may occur, and confirmation usually is not possible.

Acknowledgments

The authors thank Zs. Demeter for her help with graphics.

Grant support: This work received financial support from the Vicerectorate for Research and International Relations of the University of Veterinary Medicine Vienna (grant number: Pp13011230) and Richter Pharma AG.

Conflict of Interest Declaration: Authors declare no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

References

1. Pakozdy A, Gruber A, Kneissl S, et al. Complex partial cluster seizures in cats with orofacial involvement. J Feline Med Surg 2011;13:687–693.
2. Marioni-Henry K, Monteiro R, Behr S. Complex partial orofacial seizures in English cats. Vet Rec 2012;170:471.
3. Vanhaesebroeck AE, Posch B, Baker S, et al. Temporal lobe epilepsy in a cat with a pyriform lobe oligodendroglioma and hippocampal necrosis. J Feline Med Surg 2012;14:932–937.
4. Yanai H, Palus V, Caine A, et al. Feline idiopathic hippocampal necrosis: Findings in a UK case. Vet Times 2013;11:19–20.
5. Schwartzkroin P. Epilepsy: Models, Mechanisms and Concepts, 1 ed. Cambridge: Cambridge University Press; 2007:560.
6. Andersen P, Morris R, Amaral D, et al. The Hippocampus Book, 1 ed. Oxford: Oxford University Press; 2006:872.
7. Ursin H, Kaada BR. Functional localization within the amygdaloid complex in the cat. Electroencephalogr Clin Neurophysiol 1960;12:1–20.
8. Gastaut H, Meyer A. Experimental psychomotor epilepsy in the cat electro-clinical and anatomo-pathological correlations. J Neuropath Exp Neurol 1959;18:270–293.
9. Delgado JR, Sevillano M. Evolution of repeated hippocampal seizures in the cat. Electroencephalogr Clin Neurophysiol 1961;13:722–733.
10. Kaada BR, Andersen P, Jansen J. Stimulation of the amygdaloid nuclear complex in unanesthetized cats. Neurology 1954;4:48–64.
11. Kesner R, Doty R. Amnesia produced in cats by local seizure activity initiated from the amygdala. Exp Neurol 1968;21:58–68.
12. Kaada B, Jansen J, Andersen P. Stimulation of the hip- pocampus and medial cortical areas in unanesthetized cats. Neurology 1953;3:844–857.
13. Haas KZ, Sperber EF, Moshe SL. Kindling in developing animals: Expression of severe seizures and enhanced development of bilateral foci. Dev Brain Res 1990;56:275–280.
14. Haas KZ, Sperber EF, Moshe SL. Kindling in developing animals: Interactions between ipsilateral foci. Dev Brain Res 1992;68:140–143.
15. Elul R. Regional differences in the hippocampus of the cat. Specific discharge patterns of the dorsal and ventral hippocampus and their role in generalized seizures. Electroencephalogr Clin Neurophysiol 1964;16:470–488.
16. Wada JA, Sato M. The generalized convulsive seizure state induced by daily electrical stimulation of the amygdala in split brain cats. Epilepsia 1975;16:417–430.
17. Gibbs FA. The convulsion threshold of various parts of the cat’s brain. Arch Neurol Psychiatry 1936;35:109–116.
18. Blum B, Liban E. Autonomic-psychic experimental epilepsy in the cat due to insular and circum-insular lesions. Epilepsia 1961;2:243–250.
19. Blum B, Liban E. Experimental basotemporal epilepsy in the cat: Discrete epileptogenic lesions produced in the hippocampus or amygdaloid by tungstic acid. Neurology 1960;10:546–554.
20. Blum B, Liban E. Experience with experimental temporal lobe epilepsies produced by the tungstic acid method. Isr J Exp Med 1963;11:7–17.
21. Pilton JPF, Rovner LI. Experimental epileptogenesis: Kindling-induced epilepsy in rats. Exp Neurol 1978;58:190–202.
22. Racine R, Okujava V, Chipushvili S. Modification of seizure activity by electrical stimulation. 3. Mechanisms. Electroencephalogr Clin Neurophysiol 1972;32:295–299.
23. Wada JA, Sato M, Corcoran ME. Persistent seizure susceptibility and recurrent spontaneous seizures in kindled cats. Epilepsia 1974;15:465–478.
24. Wauquier A, Ashton D, Melis W. Behavioral analysis of amygdaloid kindling in beagle dogs and the effects of clonazepam, diazepam, phenobarbital, diphenylhydantoin, and flunarizine on seizure manifestation. Exp Neurol 1979;64:579–586.
25. McNamara JO, Constant Byrne M, Dusheiff RM, Gregory Fitz J. The kindling model of epilepsy: A review. Prog Neurobiol 1980;15:139–159.
26. Morrell F, Tsuru N, Hoeppner TJ, et al. Secondary epileptogenesis in forebrain: Effect of inhibition of protein synthesis. Can J Neuro Sci 1975;2:407–416.
27. Goddard G. Development of epileptic seizures through brain stimulation at low intensity. Nature 1967;214:1020–1021.
28. Magdaleno-Madrigal VM, Valdés-Cruz A, Martínez-Vargas D, et al. Effect of electrical stimulation of the nucleus of the solitary tract on the development of electrical amygdaloid kindling in the cat. Epilepsia 2002;43:964–969.
29. Goddard GV, McIntyre DC, Leech CK. A permanent change in brain function resulting from daily electrical stimulation. Exp Neurol 1969;25:295–330.
30. Wada JA. Kindling. New York, NY: Raven Press; 1976:61–83.
31. Wake A, Wada JA. Frontal cortical kindling in cats. Can J Neurol Sci 1975;2:493–499.
32. Sato M. Hippocampal seizure and secondary epileptogenesis in the “kindled” cat preparations. Psychiatry Clin Neurosci 1975;29:239–250.
33. Louis E, Williamson P, Darcey T. Experimental models of chronic focal epilepsy: A critical review of four models. Yale J Biol Med 1987;60:255–272.
34. McGeer EG, Olney JW, McGeer PL. Kainic Acid as a Tool in Neurobiology. New York: Raven Press; 1978.
35. Mellanby J, George G. Tetanus toxin and experimental epilepsy in rats. Adv Cytopharmacol 1979;3:401–408.
36. De Deyn PP, D’Hooge R, Marescau B, Pei YQ. Chemical models of epilepsy with some reference to their applicability in the development of anticonvulsants. Epilepsy Res 1992;12:87–110.
37. McMahon HT, Foran P, Dolly JO, et al. Tetanus toxin and botulinum toxins type A and B inhibit glutamate, gamma-aminobutyric acid, aspartate, and met-enkephalin release from synaptosomes. Clues to the locus of action. J Biol Chem 1992;267:21338–21343.
38. Louis ED, Williamson PD, Darcey TM. Chronic focal epilepsy induced by microinjection of tetanus toxin into the cat motor cortex. Electroencephalogr Clin Neurophysiol 1990;75:548–557.
39. Glaser GH, Yu RK. A model of hippocampal epilepsy produced by tetanus toxin. Neurology 1977;27:337.
40. Shouse MN, Staba RJ, Ko PY, et al. Monoamines and seizures: Microdialysis findings in locus ceruleus and amygdala before and during amygdala kindling. Brain Res 2001;892:176–192.
41. Shouse MN, Scordato JC, Farber PR. Sleep and arousal mechanisms in experimental epilepsy: Epileptic components of NREM and antiepileptic components of REM sleep. Ment Retard Dev Disabil Res Rev 2004;10:117–121.
42. Shouse MN, Siegel JM, Wu MF, et al. Mechanisms of seizure suppression during rapid-eye-movement (REM) sleep in cats. Brain Res 1989;505:271–282.
43. Shouse MN, Scordato JC, Farber PR, de Lanerolle N. The alpha2 adrenoceptor agonist clonidine suppresses evoked and spontaneous seizures, whereas the alpha2 adrenoceptor antagonist idazoxan promotes seizures in amygdala-kindled kittens. Brain Res 2007;1137:58–68.
44. Shouse MN, Scordato JC, Farber PR. Ontogeny of feline temporal lobe epilepsy in amygdala-kindled kittens: An update. Brain Res 2004;1027:126–143.
45. Dichter MA, Hauser WA, Vinters HV, Pedley TA. Epimyology, pathology, and genetics of epilepsy. In: Engel J, Pedley TA, Aicardi J, eds. Epilepsy: a comprehensive textbook. Philadelphia: Lippincott Williams and Wilkins; 2008:9–216.
46. Fatzer R, Gandini G, Jaggy A, et al. Necrosis of hippocampus and piriform lobe in 38 domestic cats with seizures: A retrospective study on clinical and pathologic findings. J Vet Intern Med 2000;14:100–104.
47. Schwartz-Porsche D, Kaiser E. Feline epilepsy. Probl Vet Med 1989;1:628–649.
48. Parent JM, Quesnel AD. Seizures in cats. Vet Clin North Am 1996;26:811–825.
49. Fisher RS, van Emde Boas W, Blume W, et al. Comment on epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia 2005;46:470–472.
50. Pakozdy A, Halasz P, Klang A. Epilepsy in cats: Theory and practice. J Vet Intern Med 2014;28:255–263.