Stiftung Tierärztliche Hochschule Hannover
University of Veterinary Medicine Hannover, Foundation

Klinik für Kleintiere

Katzen sind keine kleinen Hunde – modernes Epilepsiemanagement bei der Katze

Prof. **Holger A. Volk** *DipECVN, PhD, PGCAP, FHEA, FRCVS*
Direktor der Klinik für Kleintiere, Tierärztliche Hochschule Hannover
RCVS & EBVS® European Specialist in Veterinary Neurology
Honorary Professor of Veterinary Neurology and Neurosurgery -Royal Veterinary College
Affiliate Professor of Neurology, University of Copenhagen

1

Wieviele epileptische Katzen sehen Sie?

1. > 1 Fall pro Tag
2. 1 Fall pro Tag
3. ~ 1 Fall pro Woche
4. ~ 1 Fall alle 2 Wochen
5. ~ 1 Fall pro Woche

2

Definition von Krampfanfällen

Was ist ein epileptischer Anfall?

- Normale Gehirnaktivität
- Krampfanfall

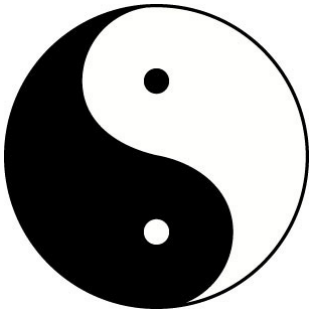
3

Definition von Krampfanfällen

Was ist ein epileptischer Anfall?

- Normale Gehirnaktivität
- Krampfanfall

4



Dr. Holger A. Volk, 2010

5

Exzitation versus Inhibition

6

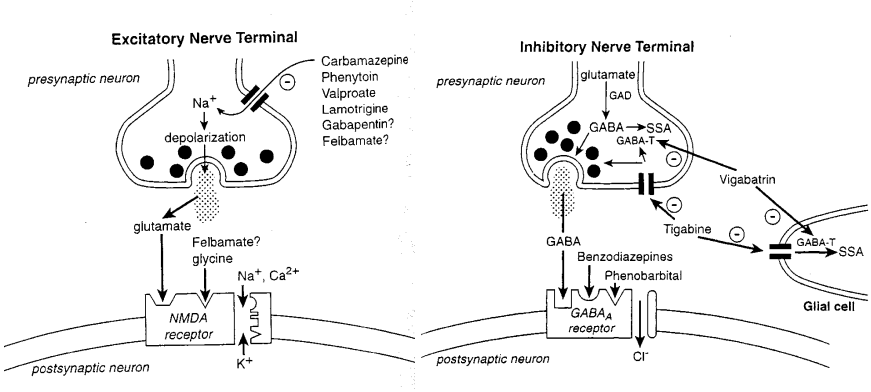
7

Exzitation versus Inhibition

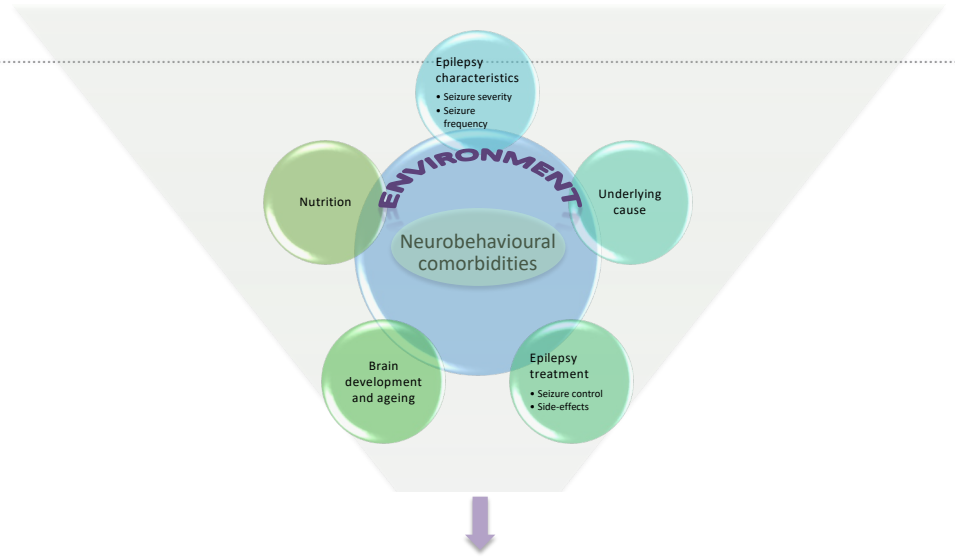
8

9

Therapy – Mode of action



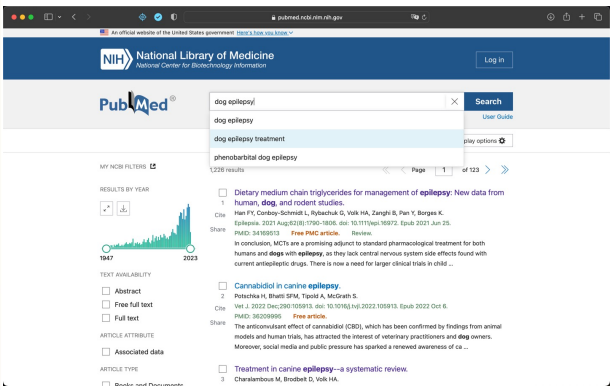
10

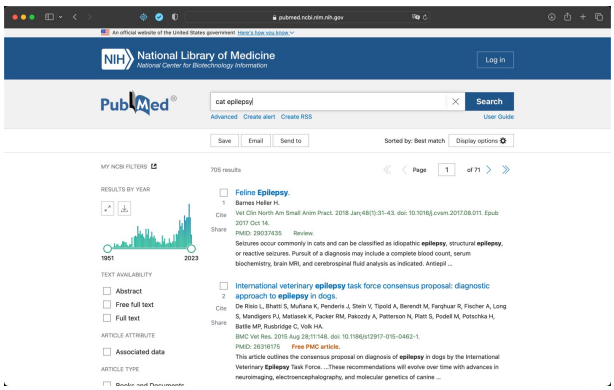


Quality of life

11

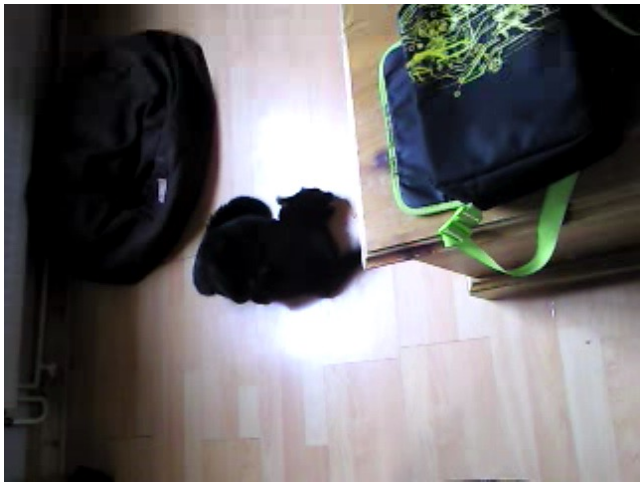
Evidenz?





12

?



13

?

14

Clinical characteristics of episodic disorders

1. Syncope
2. Neuromuscular weakness
3. **Feline Oestrus Behaviour**
4. Paroxysmal Behaviour changes
5. Vestibular attack
6. **Feline hyperaesthesia syndrome**
7. **Feline cognitive dysfunction**
8. Epileptic seizure

15

Berendt *et al. BMC Veterinary Research* (2015) 11:182
DOI 10.1186/s12917-015-0461-2

BMC Veterinary Research

Early terminology	Terminology currently in use	Suggested veterinary terminology 2015
Primary Epilepsy - Epilepsy where no structural cerebral pathology is suspected	Idiopathic Epilepsy - Epilepsy where no structural cerebral pathology is suspected. A genetic component may be involved	Idiopathic Epilepsy 1. Proven genetic background 2. Suspected genetic background 3. Unknown cause and no indication of structural epilepsy
Secondary or Acquired epilepsy - Epilepsy caused by identified cerebral pathology	Symptomatic Epilepsy - Epilepsy caused by identified cerebral pathology	Structural epilepsy - Epilepsy caused by identified cerebral pathology
Cryptogenic - Meaning hidden	Probably or possibly symptomatic epilepsy - A suspected symptomatic cause, which however remains obscure	Unknown cause

16

Intracranial structural asymmetrical lesions
Predictors for structural asymmetrical lesions include age of seizure onset >6years, the occurrence of cluster seizures, asymmetrical seizure episodes, a symmetrically abnormal interictal neurological examination and an asymmetrically abnormal interictal neurological examination

Variable	Maximum Odds ratio		SE	95% CI	*t* Value	*P*-Value
Seizure onset >6years	17.81	±	0.28	9.80-32.39	10.21	<0.0001
Cluster seizure	2.44	±	0.26	1.41-4.21	3.45	0.003
Asymmetrical seizure	3.23	±	0.39	1.41-7.36	3.01	0.008
Neuro exam abnormal symmetrical	9.50	±	0.31	4.94-18.28	7.30	<0.0001
Neuro exam abnormal asymmetrical	27.97	±	0.35	13.38-58.50	9.57	<0.0001

Intracranial structural symmetrical lesions
Predictors for a symmetrical structural lesions are the age of seizure onset and an abnormal symmetrical neurologic examination.

Variable	Maximum Odds ratio		SE	95% CI	*t* Value	*P*-Value
Age of seizure onset	1.06	±	0.02	1.01-1.10	2.69	0.008
Neuro exam abnormal symmetrical	6.06	±	0.64	1.71-21.44	2.81	0.05

Intracranial functional lesions
Predictors for functional intracranial lesions are: age of seizure <6years, occurrence of a single and symmetrical seizure episode and normal interictal neurological examination Combined, these factors can predict the presence on a functional intracranial lesion with a sensitivity of 82.1% and a specificity of 83.9%.

Variable	Maximum Odds ratio		SE	95% CI	*t* Value	*P*-Value
Seizure onset <6years	13.55	±	0.28	7.47-24.58	9.75	<0.0001
Single seizure	1.92	±	0.27	1.06-3.39	2.44	0.035
Symmetrical seizure	2.30	±	0.38	1.00-5.31	2.22	0.051
Neuro exam normal	15.4	±	0.25	8.72 -27.02	10.8	<0.0001

17

The Veterinary Journal 225 (2017) 9–12

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Short communication

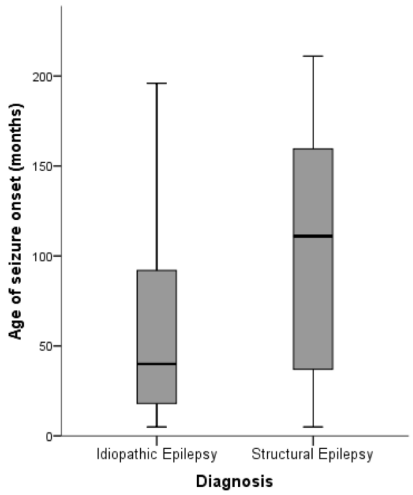
Clinical reasoning in feline epilepsy: Which combination of clinical information is useful?

Gabriela-Dumitrita Stanciu[a,b], Rowena Mary Anne Packer[a], Akos Pakozdy[c], Gheorghe Solcan[b], Holger Andreas Volk[a,1,*]

[a] Department of Clinical Science and Services, Royal Veterinary College, Hatfield AL9 7TA, UK
[b] University of Agricultural Sciences and Veterinary Medicine "Ion Ionescu de la Brad", Faculty of Veterinary Medicine, Department of Internal Medicine/Neurology, Iasi, 8 M. Sadoveanu Alley, 700489, Iasi, Romania
[c] Clinic for Internal Medicine and Infectious Diseases, University of Veterinary Medicine, Neurology Service, Veterinarplatz 1, A-1210 Vienna, Austria

18

Alter

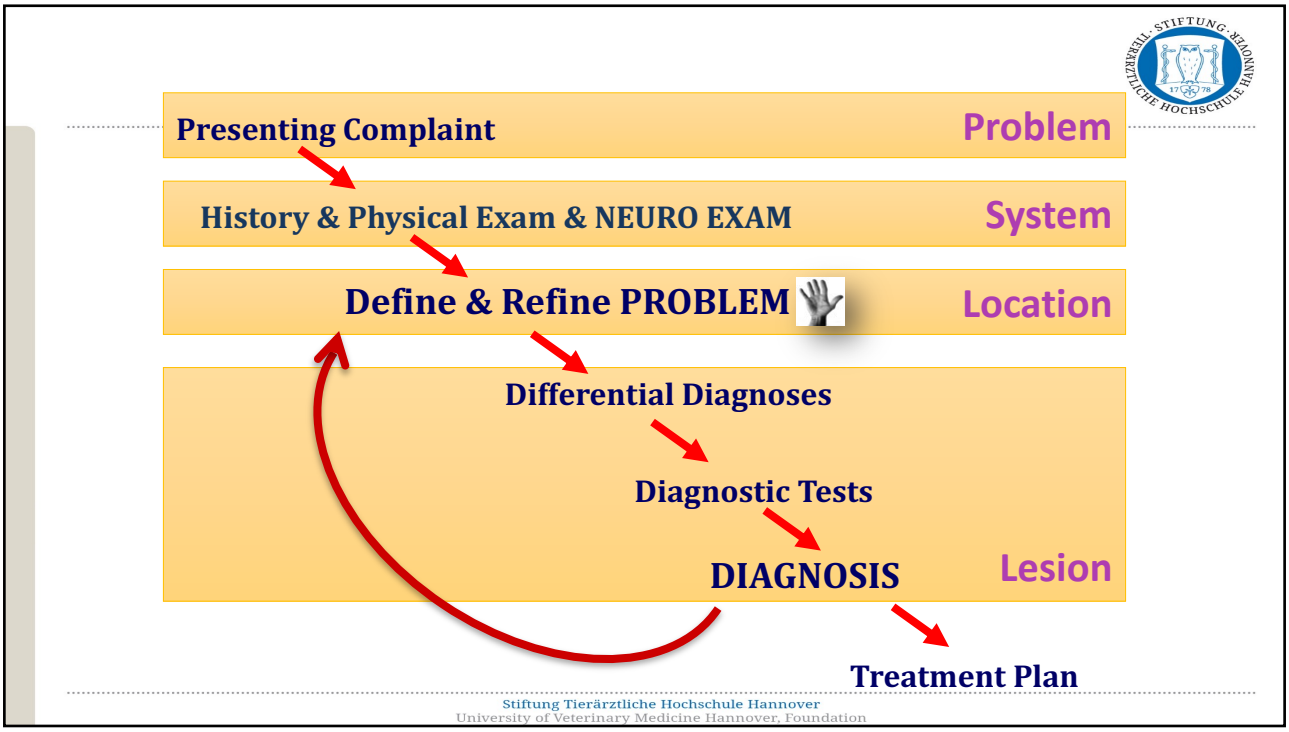


19

Statistical Modelling

- Katzen, die älter sind als 7 Jahre -> 5fach mehr wahrscheinlich -> Strukturelle Epilepsie.
- Abnormale neurologisch Untersuchung -> 3fach mehr wahrscheinlich -> Strukturelle Epilepsie.

20



21

Diseases to be considered in cats presenting with seizures

Category	Subcategory	Possible aetiologies	Interictal neurological deficits possible? Progressive? Symmetrical/Asymmetrical
Idiopathic	Genetic?	- / Gene defect (susceptibility/causative)	-
Structural	Degenerative	Hippocampal necrosis* Storage diseases	- Yes & Progressive & Symmetrical
	Anomalous	Hydrocephalus Lissencephaly	Yes & Progressive & Symmetrical Yes & Progressive & Asymmetrical
	Neoplastic	Primary (e.g. Meningioma, glioma [rare], lymphoma [rare]) Secondary/metastatic (e.g. lymphoma)	Yes & Progressive & Asymmetrical
	Inflammatory	VGKC-associated limbic encephalitis	- / can have behaviour changes
		Meningoencephalitis of unknown aetiology	Yes & Progressive & Asymmetrical
	Infectious	*Toxoplasma gondii* Feline immunodeficiency virus Feline infectious peritonitis Rabies Fungal infections	Yes & Progressive & Asymmetrical
	Traumatic	Trauma	Yes & Static/Improving & Asymmetrical

Stiftung Tierärztliche Hochschule Hannover
University of Veterinary Medicine Hannover, Foundation

22

Ancillary tests

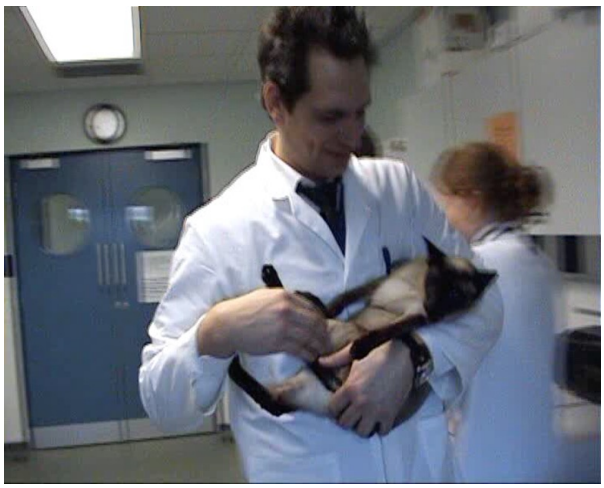
Diagnostics to be considered for cats presenting with seizures.

Extracranial Work-up	Intracranial Work-up

• Complete Blood Cell count
• Serum biochemistry
• Urinalysis
• Dynamic bile acids testing/Ammonia
• Depending on age and clinical presentation
  • Blood pressure and/or ECG
  • Serology/PCR for *Toxoplasma gondii*, FeLV/FIV, FCoV (also consider Albumin:Globulin ratio, 1- α-acid glycoprotein, haematology for diagnosis of FIP)
  • Thyroxine
	• Advanced Imaging
	  • MRI (CT less ideal)
	• Cerebrospinal fluid analysis
	  • Nucleated cell count
	  • Protein concentration
	  • PCR (*Toxoplasma gondii*, FCoV)
	• EEG

23

?



24

Check for updates

Case Series

Feline hyperaesthesia syndrome with self-trauma to the tail: retrospective study of seven cases and proposal for integrated multidisciplinary diagnostic approach

Journal of Feline Medicine and Surgery
1–8

DOI: 10.1177/1098612X18764246
journals.sagepub.com/home/jfms
This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS*
SAGE

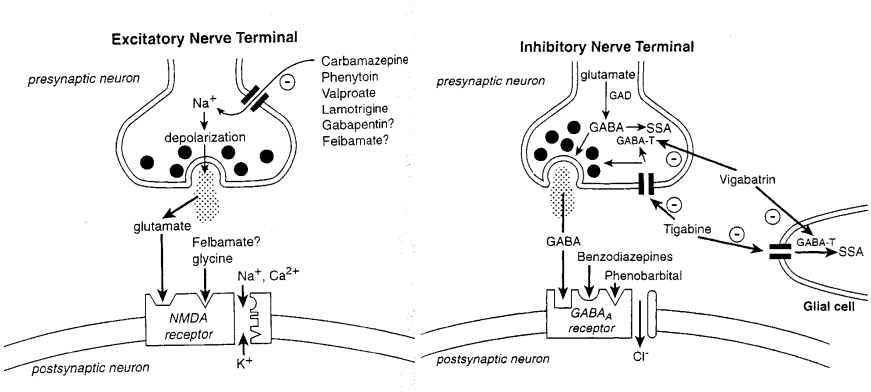
Pablo Amengual Batle[1], Clare Rusbridge[2,3], Tim Nuttall[1], Sarah Heath[4] and Katia Marioni-Henry[1]

- Median age of 1 year
- Multiple daily episodes of tail chasing and self-trauma
- Vocalisation during the episodes and rippling of lumbar skin
- Gabapentin effective in 6/7 cases

Welches Medikament?

1. Phenobarbital
2. Imepitoin
3. Kaliumbromide
4. Levetiracetam
5. Gabapentin
6. Zonisamide

Therapy – Mode of action



Charalambous *et al. BMC Veterinary Research* (2018) 14:64
https://doi.org/10.1186/s12917-018-1386-3

BMC Veterinary Research

RESEARCH ARTICLE Open Access

Systematic review of antiepileptic drugs' safety and effectiveness in feline epilepsy

Marios Charalambous[1*], Akos Pakozdy[2], Sofie F. M. Bhatti[1] and Holger A. Volk[3]

29

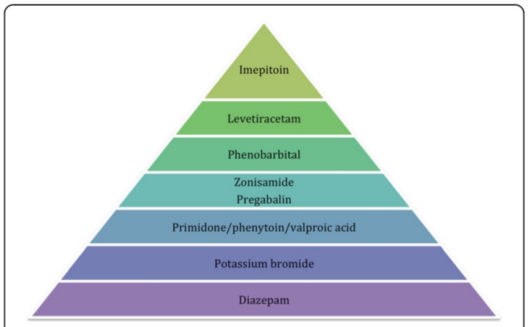


Fig. 6 Pyramid of AEDs' safety hierarchy based on the quality of evidence and outcomes assessment

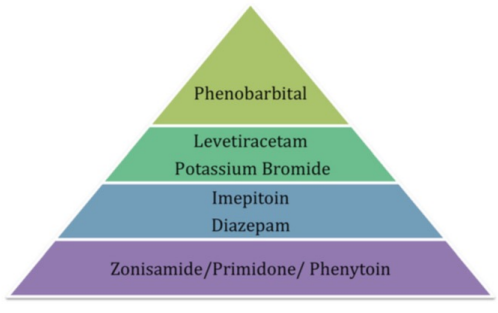


Fig. 5 Pyramid of AEDs' efficacy hierarchy based on the quality of evidence and outcomes assessment

30

Summary of the antiepileptic drugs available to treat epilepsy in cats.

Antiepileptic drug	Initial dose	Therapeutic range	Potential adverse effects	Comments
Phenobarbital	2-3 mg/kg q 12-24 hrs	10-30 mg/dl	Sedation, ataxia, hepatotoxicity, blood dyscrasias, skin eruptions	Currently considered 1st line antiepileptic drug in the UK
Diazepam	5-10 mg q 8-12 hrs	500-700 ng/ml (nordiazepam)	Acute hepatic necrosis, sedation	Currently not recommended for chronic treatment, should only be used for acute seizures*
Levetiracetam	10-20 mg/kg q 8-12 hrs	?	Inappetance, sedation, hypersalivation	Considered 2nd line*
Zonisamide	5-10 mg/kg q 12-24 hrs	?	Sedation, vomiting, diarrhoea, hepatotoxicity	
Gabapentin	5-10 mg/kg q 8-12 hrs	?	Sedation, ataxia	No clinical studies published
Pregabalin	2 mg/kg q 12 hrs	?	Sedation, ataxia	No clinical studies published
Topiramate	12.5-25 mg q 8-12 hrs	?	Sedation, inappetence, weight loss	No clinical studies published

*authors opinion; Please consider the cascade regulation when prescribing antiepileptic drugs. Imepitoin might be an alternative drug to be considered in the future as we continue to increase our knowledge about the efficacy and safety of imepitoin in cats.

Imepitoin….20-30mg/kg zweimal täglich?

Original Article

Treatment and long-term follow-up of cats with suspected primary epilepsy

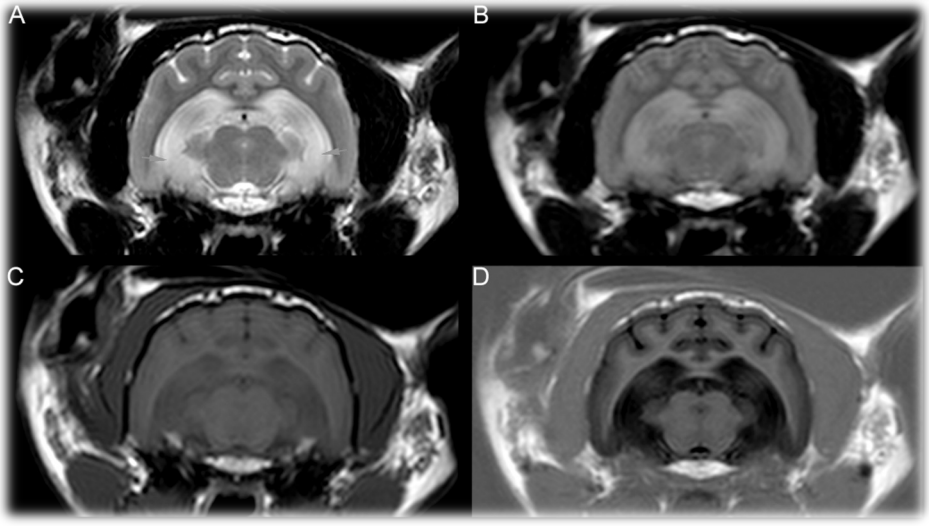
Journal of Feline Medicine and Surgery
15(4) 267–273
© ISFM and AAFP 2012
Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/1098612X12464627
jfms.com
SAGE

Akos Pakozdy[1], Ali Asghar Sarchahi[2], Michael Leschnik[1], Alexander G Tichy[3], Peter Halasz[4] and Johann G Thalhammer[1]

- 40–50% -> Anfallsfrei
- 20–30% gut kontrolliert
- 20-30% schlecht kontrolliert

33

Hippocampal changes



34

J Vet Intern Med 2013;27:212–214

Suspected Limbic Encephalitis and Seizure in Cats Associated with Voltage-Gated Potassium Channel (VGKC) Complex Antibody

A. Pakozdy, P. Halasz, A. Klang, J. Bauer, M. Leschnik, A. Tichy, J.G. Thalhammer, B. Lang, and A. Vincent

Background: Treatment-resistant complex partial seizures (CPS) with orofacial involvement recently were reported in cats in association with hippocampal pathology. The features had some similarity to those described in humans with limbic encephalitis and voltage-gated potassium channel (VGKC) complex antibody.

Hypothesis/Objectives: The purpose of this pilot study was to evaluate cats with CPS and orofacial involvement for the presence of VGKC-complex antibody.

Animals: Client-owned cats with acute orofacial CPS and control cats were investigated.

Methods: Prospective study. Serum was collected from 14 cats in the acute stage of the disease and compared with 19 controls. VGKC-complex antibodies were determined by routine immunoprecipitation and by binding to leucine-rich glioma inactivated 1 (LGI1) and contactin-associated protein-like 2 (CASPR2), the 2 main targets of VGKC-complex antibodies in humans.

Results: Five of the 14 affected cats, but none of the 19 controls, had VGKC-complex antibody concentrations above the cut-off concentration (>100 pmol/L) based on control samples and similar to those found in humans. Antibodies in 4 cats were directed against LGI1, and none were directed against CASPR2. Follow-up sera were available for 5 cats in remission and all antibody concentrations were within the reference range.

Conclusion and Clinical Importance: Our study suggests that an autoimmune limbic encephalitis exists in cats and that VGKC-complex/LGI1 antibodies may play a role in this disorder, as they are thought to in humans.

Key words: Autoimmune limbic epilepsy; Feline.

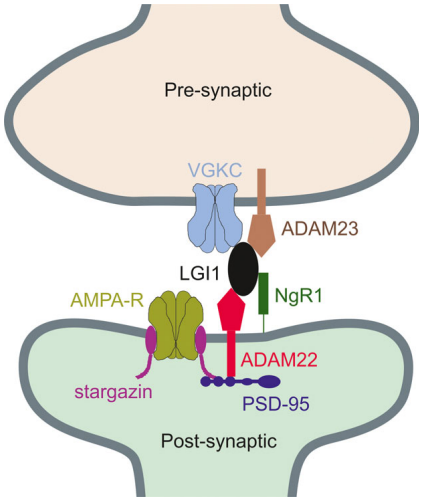
35

Journal of Veterinary Internal Medicine
Open Access

Review
J Vet Intern Med 2015;29:997–1005

LGI Proteins and Epilepsy in Human and Animals

A. Pakozdy, M. Patzl, L. Zimmermann, T.S. Jokinen, U. Glantschnigg, A. Kelemen, and D. Hasegawa



36

Original Article

Levetiracetam in the management of feline audiogenic reflex seizures: a randomised, controlled, open-label study

Mark Lowrie[1]*, Sarah Thomson[1], Claire Bessant[2], Andrew Sparkes[2], Robert J Harvey[3] and Laurent Garosi[1]

Journal of Feline Medicine and Surgery
2017, Vol. 19(2) 200–206

DOI: 10.1177/1098612X15622806
jfms.com
SAGE

Table 1 Baseline characteristics of cats allocated to each treatment group

	Levetiracetam (n = 34)	Phenobarbital (n = 34)	*P* value
Age (years)	18 (12–23)	19 (13–22)	0.09
Weight (kg)	4 (2–8)	4 (1–10)	0.29
Breed (n)			0.97
DSH	17	19	
DLH	2	1	
Birman	8	9	
Other	7	5	
Sex (n)			0.70
F	17	15	
FN	13	9	
M	17	19	
MN	11	14	
Age at onset of seizures (years)	15 (10–19)	16 (10–19)	0.10
Time from first seizure to study start point (years)	3 (2–4)	3 (2–4)	1.00

Table 3 Efficacy of levetiracetam and phenobarbital in the management of feline audiogenic reflex myoclonic seizures

	Levetiracetam group (n = 28)	Phenobarbital group (n = 29)	*P* value
Number of cats achieving ⩾50% reduction from baseline in the number of myoclonic seizure days per week	28 (100)	1 (3)	<0.001
Mean percentage reduction from baseline in the number of myoclonic seizure days per week	98.8 ± 4.7	2.8 ± 23.3	<0.001
Number of cats achieving myoclonic seizure freedom	14 (50)	0 (0)	<0.001
Mean percentage increase in myoclonic seizure-free days	95.7 ± 8.8	–57.0 ± 54.5	<0.001

Data are n (%) or mean ± SD

37

Epilepsy Research (2010) 92, 85–88

ELSEVIER
journal homepage: www.elsevier.com/locate/epilepsyres

SHORT COMMUNICATION

A familial spontaneous epileptic feline strain: A novel model of idiopathic/genetic epilepsy

Takayuki Kuwabara[a,1], Daisuke Hasegawa[a,*,1], Fukie Ogawa[c], Masanori Kobayashi[a,d], Michio Fujita[a], Hiroetsu Suzuki[b], Naoaki Matsuki[c], Hiromitsu Orima[a]

- focal limbic seizure with secondary generalization.
- generalized seizures **were induced by vestibular stimulation**

38

SHORT COMMUNICATION

A familial spontaneous epileptic feline strain: A novel model of idiopathic/genetic epilepsy

Takayuki Kuwabara[a,1], Daisuke Hasegawa[a,b,*,1], Fukie Ogawa[c], Masanori Kobayashi[a,d], Michio Fujita[a], Hiroetsu Suzuki[b], Naoaki Matsuki[b], Hiromitsu Orima[a]

39

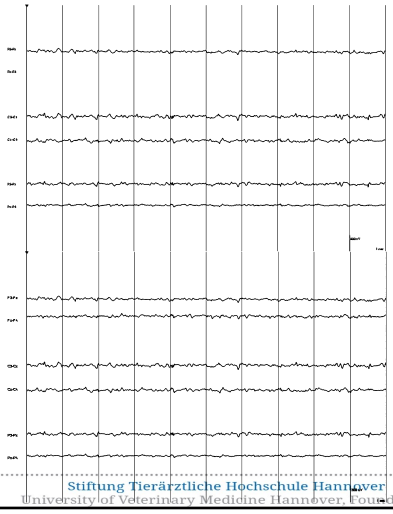
40

Case Report

J Vet Intern Med 2009;23:200–205

Seizure-Like Episodes in 3 Cats with Intermittent High-Grade Atrioventricular Dysfunction

V.A. Penning, D.J. Connolly, I. Gajanayake, L.A. McMahon, V. Luis Fuentes, K.E. Chandler, and H.A. Volk



41

Pseudoresistant

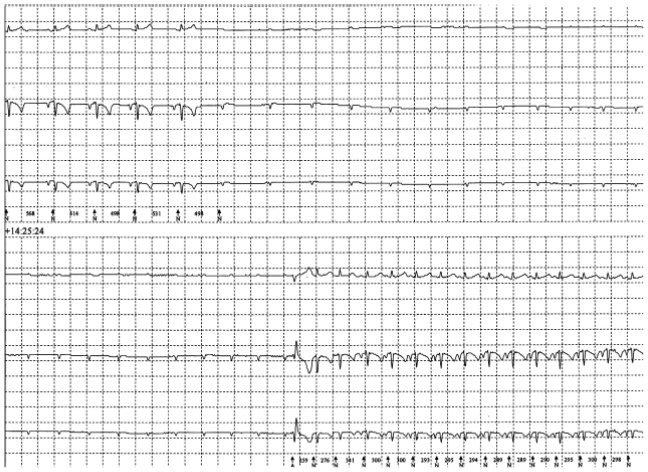
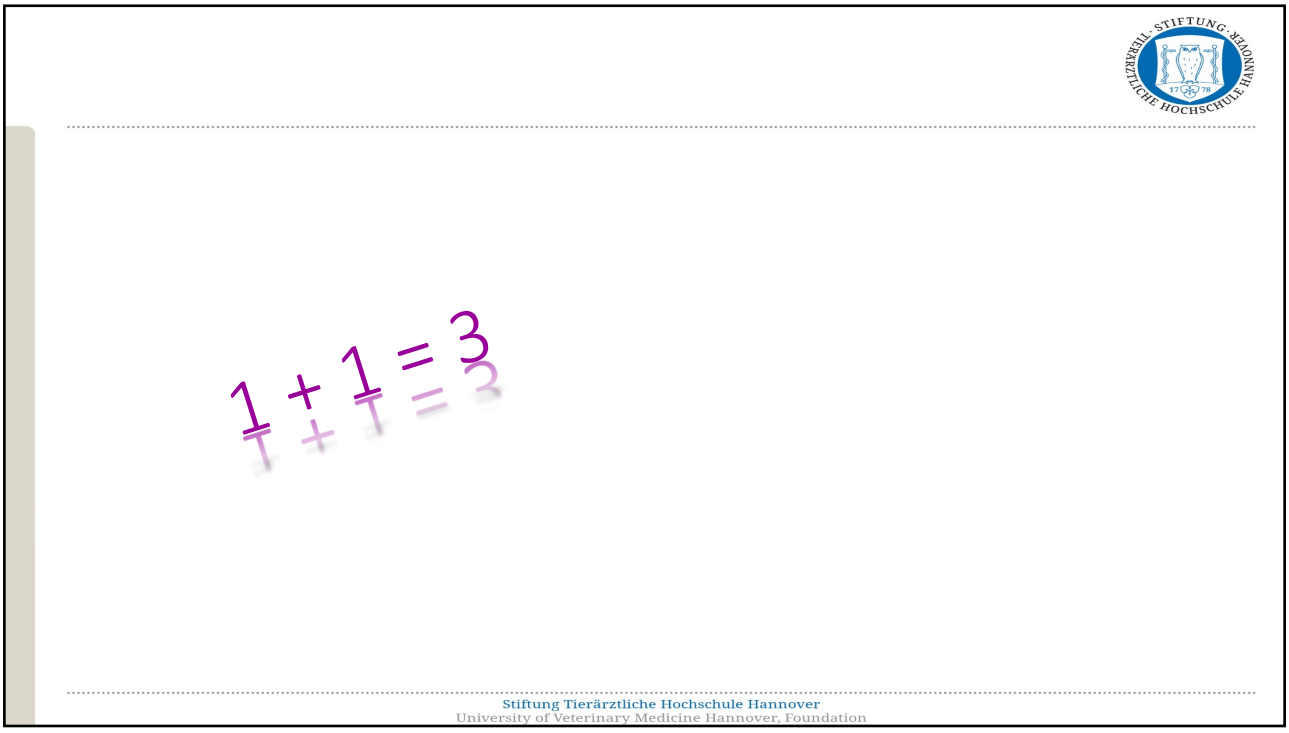


Fig 1. ECG from "Case 1" showing nonconducted P waves followed by a wide and bizarre complex consistent with a ventricular escape complex before returning to sinus rhythm.

42


1 + 1 = 3
Stiftung Tierärztliche Hochschule Hannover
University of Veterinary Medicine Hannover, Foundation

43