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Short communication

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

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ABSTRACT

We sought to identify the association between clinical risk factors and the diagnosis of idiopathic epilepsy (IE) or structural epilepsy (SE) in cats, using statistical models to identify combinations of discrete parameters from the patient signalment, history and neurological examination findings that could suggest the most likely diagnosis. Data for 138 cats with recurrent seizures were reviewed, of which 110 were valid for inclusion. Seizure aetiology was classified as IE in 57% and SE in 43% of cats. Binomial logistic regression analyses demonstrated that pedigree status, older age at seizure onset (particularly >7 years old), abnormal neurological examinations, and ictal vocalisation were associated with a diagnosis of SE compared to IE, and that ictal salivation was more likely to be associated with a diagnosis of IE than SE. These findings support the importance of considering inter-ictal neurological deficits and seizure history in clinical reasoning.

Epileptic seizures affect 1–2% of the general feline population (Schriefl et al., 2008). Seizure manifestations can differ from those typically seen in dogs, but the underlying causes of seizure activity appear to be similar and include both idiopathic (IE) and structural epilepsies (SE). Despite many references and controversial data published about feline IE (Schriefl et al., 2008), only one large-scale study has examined the aetiology and classification of feline epilepsy (Pakozdy et al., 2010). The aim of this study was to evaluate aetiology in a population of cats, and to provide information to improve clinical reasoning when investigating seizures in cats.

We reviewed medical records of 138 cats with a history of recurrent epileptic seizures that had been presented for investigation between 2006 and 2016 at the Royal Veterinary College Small Animal Referral Hospital. The following data were extracted for each cat: signalment, history and neurological examination, seizure characteristics, magnetic resonance imaging (MRI) changes and cerebrospinal fluid results. All cats included in the study were required to have a complete epilepsy questionnaire and history, a neurological examination and a comprehensive investigation (complete serum biochemistry and haematology; and MRI of the brain −1.5 T Gyroscan NT, Philips Medical Systems). We classified seizure aetiology as IE or SE using an adapted version of the classification system published by the International Veterinary Epilepsy Task Force for dogs (IVETF tier II; De Risio et al., 2015). The IVETF classification system of IE is based upon seizure history, age at seizure onset, neurological examination, blood tests and urinalysis at the tier I confidence level, with the addition of MRI and CSF at tier II confidence level. Because we were investigating age at seizure onset and neurological examination status as predictors of IE vs. SE diagnosis, we omitted these factors from the initial classification. As such, cats were diagnosed with IE if they had a history of two or more unprovoked epileptic seizures occurring at least 24 h apart, no clinically significant abnormalities on minimum data base blood tests and urinalysis, unremarkable MRI of the brain and CSF analysis. The diagnosis of SE was based on the history of seizures and confirmed pathological findings in haematology, serum biochemistry, CSF analysis and/or morphological changes of the brain as identified by MRI. Hippocampal changes identified on MRI (in conjunction with clinical and ictal characteristics associated with hippocampal pathology) were considered as SE, as limbic encephalitis could not be ruled out (Pakozdy et al., 2013).

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Data were first analysed at the univariable level using the Chi-squared (X^2) test for categorical variables and Mann-Whitney test for continuous variables, based on the non-normal distribution of the data (Table 1). The following variables were analysed: age at first seizure (continuous), gender, breed, type of seizure, ictal signs (salivation, vocalisation, rapid running, urination, defaecation, orofacial motor signs and mydriasis), presence/absence of the postictal signs and neurological examination status (normal/abnormal). Variables identified as being broadly associated with the outcome (IE vs. SE, $P \leq 0.2$) were taken forward for multivariable analysis using binary logistic regression models (SPSS, Version 22, IBM). A manual forward selection step-wise construction method was taken for model building. Two-way interactions were tested for between all variables in the final model. The final model was evaluated with the Hosmer-Lemeshow goodness-of-fit test. Results of univariate analyses were corrected for multiple comparisons using the False Discovery Rate (FDR), and $P < 0.05$ was considered statistically significant for all results.

One-hundred and ten cats met the inclusion criteria. We excluded 28 cases because of the lack of accurate examination/incomplete follow-up information ($n = 20$) or a metabolic/toxic cause of epileptic seizures ($n = 8$). Cats with SE were diagnosed with intracranial neoplasia ($n = 24$), meningoencephalitis ($n = 11$), degenerative diseases ($n = 6$), vascular disorders ($n = 4$), anomalous ($n = 4$), or brain trauma ($n = 2$). Both pedigree and non-pedigree (17.4% vs. 82.6%) cats were included, both sexes (56% male vs. 44% female), and there was a median age and interquartile range (IQR) of 68 months (IQR, 23.0 to 144.0). The median age at first seizure was 65.0 (IQR, 21.0 to 142.5); cats with SE were older than cats with IE at the age of first seizure (IE, 40.9 [IQR, 17.8 to 40.0]; SE, 111.0 [IQR: 36.0 to 160.0]; $P = 0.001$; FDR-corrected, 0.004; Fig. 1). Several categorical factors were liberally associated with type of epilepsy at the univariable level ($P < 0.20$): age at seizure onset (under/over 7 years), ictal salivation and vocalisation, seizure type (focal), pedigree status and neurological examination findings. These were included in multivariable modelling (Table 1).

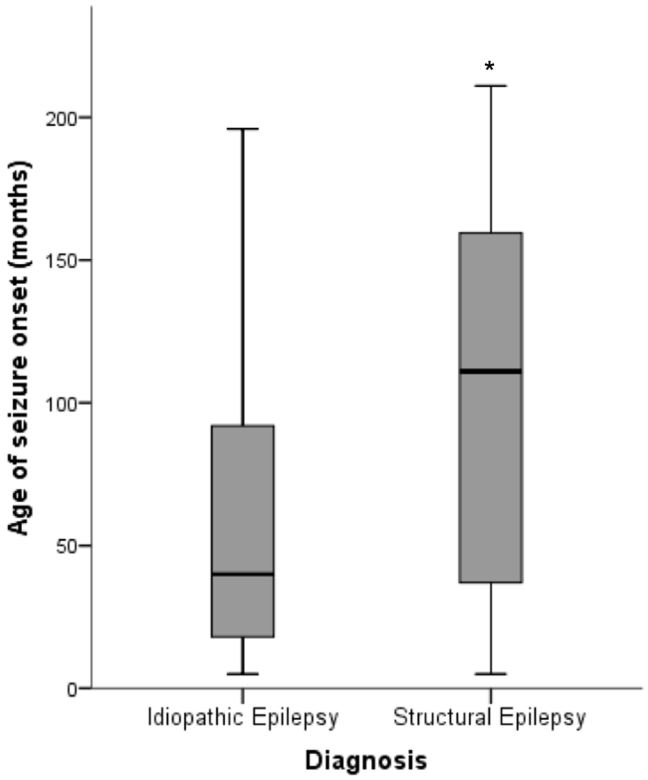

Fig. 1. Boxplot of age of seizure onset (months) for cats with idiopathic epilepsy ($n = 62$) and structural epilepsy ($n = 47$). The middle line of the boxplot represents the median, and the whiskers represent the range ($^*P < 0.05$).

Five factors remained significant in the final model (Table 2): one continuous (age at first seizure), and four categorical (neurological examination findings, the presence of ictal salivation ictal vocalisation, and pedigree status). No two-way interactions

Table 1
Comparison of sex, breed, type of seizure, ictal or postictal signs and neurological examination findings between cats with idiopathic epilepsy (IE) or structural epilepsy (SE; $n = 110$).

Main variable	Parameter	IE		SE		X^2	P	FDR corrected
		n	%	n	%			
Age at onset	≤7 years old	45	72.6	19	40.4	11.4	0.001	0.004
	>7 years old	17	27.4	28	59.6			
Sex	Female	27	43.5	22	46.8	0.12	0.735	0.840
	Male	35	56.5	25	53.2			
Breed	Pedigree	6	9.7	13	27.7	6.01	0.014 [a]	0.037 [a]
	Non-pedigree	56	90.3	34	72.3			
Type of seizure	Focal seizure	14	22.6	19	40.4	4.03	0.045 [a]	0.103
	Generalized seizure	41	66.1	23	48.9	3.26	0.071	0.128
	Focal seizure with secondary generalisation	7	11.3	4	8.5	0.23	0.633	0.780
Ictal signs	Salivation	25	40.3	8	17.0	6.88	0.009 [a]	0.029 [a]
	Vocalisation	4	6.5	14	29.8	10.56	0.001 [a]	0.004 [a]
	Rapid running	3	4.8	7	14.9	3.24	0.072	0.128
	Urination	37	57.8	27	42.2	0.15	0.873	0.873
	Defaecation	7	53.8	6	46.2	0.10	0.799	0.852
	Orofacial motor signs	13	48.1	14	51.9	0.52	0.283	0.411
	Mydriasis	8	50	8	50	0.28	0.535	0.713
Neuro exam findings	Normal	49	79.0	23	48.9	10.80	<0.001 [a]	0.005 [a]
	Abnormal	13	21.0	24	51.1			
Postictal signs	Present	37	59.7	33	70.2	1.29	0.204	0.326
	Absent	25	40.3	14	29.8			

[a] $P < 0.05$