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Article *in* The Veterinary Journal · November 2018

DOI: 10.1016/j.tvjl.2018.11.009

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PII: S1090-0233(18)30189-8
DOI: https://doi.org/10.1016/j.tvjl.2018.11.009
Reference: YTVJL 5228

To appear in:

Received date: 19 May 2018
Revised date: 11 November 2018
Accepted date: 15 November 2018

Please cite this article as: M.Kwiatkowska, S.Hoppe, A.Pomianowski, A.Tipold, Reactive seizures in cats: A retrospective study of 64 cases (2018), https://doi.org/10.1016/j.tvjl.2018.11.009

Reactive seizures in cats: A retrospective study of 64 cases

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Highlights

- Reactive seizures were diagnosed in 62 (7.9%) of 789 feline patients referred for seizure evaluation
- The most common identified cause of reactive seizures was presumed or confirmed intoxication
- Other causes included hepatic/renal encephalopathy, hypertension, hyperthyroidism, hypo/hyperglycaemia, thrombocytopenia
- The most common presentation among cats with reactive seizures was generalised, tonic-clonic seizures
- Status epilepticus, cluster seizures, and partial seizures were also observed as presenting complaints

Abstract

Epileptic seizures are a common indication for neurological evaluation. This retrospective study reviewed 789 cats referred for epileptic seizure evaluation to the Department of Small Animal Medicine and Surgery of the University of Veterinary Medicine in Hannover, between 1998 and 2017. The aim of this study was to determine common causes for reactive seizures (RS) in cats.

Reactive seizures were diagnosed in 62 (7.9%) of 789 feline patients. The most common cause of RS was presumptive or confirmed intoxication (*n*=34/62; 54.8%). Toxins included permethrin (*n*=5/62; 8.1%), fipronil (*n*=1/62; 1.6%), and pesticide (*n*= 1/62; 1.6%). Other common causes were hepatic and renal encephalopathy (n=6/62; 9.7% each),

hypertension (*n*= 5/62; 8.1%), hyperthyroidism (*n*=3/62; 4.8%), hypoglycaemia (*n*=3/62; 4.8%), and hyperglycaemia (*n*= 1/62; 1.6%). Most commonly, cats with RS presented with generalised tonic-clonic seizures (*n*=25/62; 40.3%). A single status epilepticus was observed in 9.7% (*n*=6/62) and 4.8% (*n*=3/62) presented only with cluster seizures. Focal seizures were the only presenting sign in 3.2% (*n*=2/62) of cases, however in 4.8% (*n*=3/62) they were accompanied by tonic- clonic seizures. The mean age of all cats presented for RS was 10.8 years. In the intoxication group, the mean age was 2.9 years. Intoxication (confirmed or presumptive) was the most common cause of RS identified. Clinicians should suspect intoxication when other causes of RS are excluded; when there are appropriate historical findings; when the cat is frequently unobserved by the owner; when symptomatic treatment leads to cessation of epileptic seizures; and when seizures do not recur after treatment has been discontinued.

Keywords: Cats; Intoxication; Reactive seizures

Introduction

Epilepsy is a common neurologic disorder in cats (Smith et al., 2009; Stanciu et al., 2017). Although epileptic seizures are reported less frequently in cats than in dogs, they are still one of the most commonly seen neurologic disorders in cats, with an overall reported prevalence of 2.1% (Schriefl et al., 2008). Epileptic seizures in cats can be a diagnostic challenge for clinicians, due to difficulties in obtaining a detailed history, the wide variety of clinical signs, including focal seizures which produce orofacial twitches and aggression (Pazkozdy et al., 2010), and because less data are available on treatment protocols and their efficacy in comparison to dogs. Additionally, unique magnetic resonance imaging (MRI) findings, such as hippocampal necrosis have been reported (Fatzer et al., 2000; Brini et al., 2004).

One potential cause of epileptic seizures in cats is idiopathic epilepsy (IE). This is a diagnosis of exclusion, based in dogs upon normal interictal neurological examination, normal blood test results (tier 1 confidence level), normal magnetic resonance imaging (MRI) (Raimondi et al., 2017) and cerebrospinal fluid (CSF) results (tier 2 confidence level), and interictal or ictal electroencephalography (EEG) findings (tier 3 confidence level; De Risio et al., 2015). Historically, IE in cats was believed to be rare, however, more recent studies have reported that approximately 30% of cats with epileptic seizures have idiopathic epilepsy (Barnes et al., 2004; Schriefl et al., 2008; Pakozdy et al., 2010). In comparison to canines, genetic epilepsy in cats is rare. However, feline familial spontaneous epileptic cats (FSECs) have been reported in Japan (Kuwabara et al., 2010; Mizoguchi et al., 2014; Hamamoto et al., 2017).

Epileptic seizures in cats can also be caused by structural brain disease, such as intracranial neoplasia, immune-mediated or infectious encephalitides, vascular diseases, traumatic brain injury, or anatomic anomalies. Recurrent seizures triggered by these disease categories are diagnosed as structural epilepsy (StE; Smith Bailey et al., 2009; Pakozdy et al. 2010; Stanciu et al., 2017).

Epileptic seizures can also be a reaction of the normal brain to transient disturbances in function. These disturbances can be metabolic (e.g. renal or hepatic encephalopathy, hepatic lipidosis, hyperthyroidism, polycythaemia, hyperosmolality), or toxic in nature and are reversible when the cause of disturbance is treated successfully. Such seizures are classified as reactive seizures (RS; Smith et al., 2009; Pakozdy et al., 2010; Berendt et al., 2015; Stanciu et al., 2017; Barnes, 2018).

In animals presented with a sudden onset of epileptic seizures, it is important to distinguish between IE, StE and RS in order to initiate appropriate treatment and control seizure activity. However, arriving at a confirmed or presumed diagnosis in cats can be challenging due to incomplete history, especially when the cat lacks owner supervision. Diagnosing intoxications in such cases remains a great challenge. One published study has reported causes for reactive seizures in dogs (Brauer et al., 2011), but no similar studies in cats have been performed thus far. The main aim of this retrospective study was to summarise common causes for reactive seizures in cats, to facilitate the diagnostic process.

Materials and methods

This is a retrospective study, conducted in a university neurology referral service. The records of 789 cats, referred to the Department of Small Animal Medicine and Surgery of the

University of Veterinary Medicine in Hannover between 1998 and 2017 for evaluation of epileptic seizures, were reviewed. The owners consented to the use of clinical data for research purposes.

The database was searched for ‘epileptic seizure,’ ‘epilepsy,’ ‘status epilepticus,’ ‘reactive seizures,’ ‘cluster seizures,’ and ‘cats.’ Among 789 cases, 87 were diagnosed with reactive seizures. Sixty-two cats were included in the current study, based on completeness of our database information. The minimum database included a clear description of the epileptic seizure event in the history, physical examination, neurological examination, haematology and serum biochemistry (urea, creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, albumin and total protein values, sodium, potassium, chloride, calcium, and glucose concentration). Additional diagnostic tests performed at the discretion of the clinician included bile acid stimulation test, total serum thyroxine concentration (tT4), urine examination, cerebrospinal fluid examination (CSF), magnetic resonance imaging examination (MRI), electrocardiography, and echocardiography examination (Table 1).

Epileptic seizures were defined as sudden, transient neurologic events (Berendt et al., 2015). Reactive seizures were defined as seizures occurring as a natural response of the normal brain to a transient disturbance in function (metabolic or toxic in nature), which is reversible when the disturbance is rectified.

When intoxication was suspected, additional examinations included determination of cholinesterase activity and screening urine, blood, and the stomach contents or faeces for toxin presence when possible (GIZ-Nord Poisons Centre; Table 1). A diagnosis of confirmed

intoxication was made when the owner witnessed the cat ingesting a toxic substance or when the owner applied a toxic substance on the animal himself (e.g. permethrin). In questionable cases (screening for toxins negative or unavailable), a diagnosis of presumptive intoxication was made when seizures did not recur after symptomatic and supportive treatment, and when other causes for seizures were excluded (structural epilepsy, idiopathic epilepsy, metabolic causes for reactive seizures).

Renal encephalopathy was diagnosed in cases with a serum urea concentration > 65 mg/dL (reference range, 20-65 mg/dL), creatinine concentration > 1.6 mg/dL (reference range, 0.6–1.6 mg/dL), and urine protein:creatinine ratio (UPC) > 0.4 (reference value, <0.2). These findings were consistent with IRIS stage 3 and 4 kidney disease, which are most commonly associated with concurrent systemic diseases signs as lethargy, obtundation, hypertension, retinopathy, and encephalopathy (Brown et al., 2016).

Hepatic encephalopathy was diagnosed when marked hyperammonaemia (>100 µg/dL) was observed, and/or markedly increased bile acid concentrations after a bile acid stimulation test (>25 µmol/L). Hepatic encephalopathy was confirmed via diagnostic imaging of the liver and its vasculature with ultrasound or computed tomography (CT; Lidbury et al., 2016; Gow, 2017).

Hypoglycaemia was diagnosed when serum glucose concentrations were < 2.8 mmol/L (range, 4.8–6.6 mmol/L). Diagnosis of hyperglycaemia was made when serum glucose concentration was persistently >10 mmol/L (range 4.8–6.6 mmol/L) and glucosuria was present (Thomovsky, 2017; Viebrock and Dennis, 2017).

Hyperthyroidism was diagnosed when a combination of findings was found – clinical signs of disease (increased appetite, weight loss), palpable nodules in the thyroid region, and increased tT4 value measured using the homogeneous enzyme immunoassay (EIA) method and was >1.6–5.0µg/dL (Peterson, 2013).

Hypertension was diagnosed when indirect systolic blood pressure (SBP) measured at antebrachial region was >160 mmHg (reference range, 120–160 mmHg) on three consecutive measurements (Vet Blood Pressure Doppler, Eickermeyer) on the same day. Measurements were performed in a separate room when the cat was calm and quiet (Stephen, 2011).

Results

Reactive seizures were diagnosed in 87 of the 789 cats referred to the Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover for evaluation of epileptic seizures. Only 62 of these animals, however, fulfilled the study inclusion criteria (7.9%).

Most commonly, cats with RS presented with generalised tonic-clonic seizures (*n*=25/62, 40.3%). In 24.2% (*n*=15/62), a mixture of isolated tonic-clonic seizures and status epilepticus was the reason for presentation in the clinic; whereas 11.3% (*n*=7/62) of cats experienced tonic-clonic seizures and cluster seizures. A single status epilepticus was observed in 9.7% (*n*=6/62) and 4.8% (*n*=3/62) presented only with cluster seizures. Focal seizures were the only presenting sign in 3.2% (*n*=2/62) of cases, however in 4.8% (*n*=3/62) they were accompanied by tonic- clonic seizures.

The mean age of cats presented for reactive seizures was 10.4 years (range, 8 months – 16 years). However, when only cats with intoxication were analysed, the mean age was 2.9 years (range, 8 months – 7 years). The mean age of cats diagnosed with portosystemic shunt was 1.7 years (range, 8 months – 6 years). The mean age of cats with other metabolic (renal encephalopathy, hyperthyroidism) and cardiac diseases was 11.4 years (range, 3–18 years).

Of the cats with RS, 80.6% (*n*=50/62) were Domestic shorthair cats, four were British shorthair cats (*n*=4/62; 6.5%), three were Persian cats (*n*=3/62; 4.8%), and there were two (n=2/62; 3.2%) Birman cats, two Norwegian Forest cats and one reach of the following breeds: Russian blue, Siamese, Siamese mix, Ragdoll and Maine Coon.

The most common cause of reactive seizures in the current study was intoxication (*n*=34/62; 54.8%), either confirmed or presumptive. In 79.4% cases (*n*=27/34; Fig. 1), no toxic substance could be identified on diagnostic screening (blood and urine examination, gastric contents, acetyl cholinesterase activity, faeces content). However, after symptomatic treatment consisting of fluid therapy, anti-seizure medications, and intravenous intralipid emulsion (Baxter), seizures did not recur, leading to a presumed diagnosis of intoxication. Cats were monitored for epileptic seizures recurrence for 4-14 months. Seven of the 34 cats had confirmed intoxication (*n*=7/34, 20.6%); five cats had permethrin intoxication *(n*=5/34; 14.7%), one from fipronil intoxication (*n*=1/34; 2.9%), and one from pesticide intoxication (*n*=1/34; 2,94%) (organophosphate). All cats with permethrin intoxication presented in status epilepticus, as did cats with fipronil and pesticide poisoning. Most cats with intoxication of unknown origin presented with a single generalised tonic-clonic seizure (*n*= 17/27; 63.0%), while seven cases presented with cluster seizures (*n*=7/27; 25.9%) and three with focal seizures (*n*=3/27; 11.1%; Fig. 1).

Hepatic encephalopathy due to portosystemic shunt (PSS) was found in six cases (n=6/62; 9.7%), with a mean ammonia concentration of 260.4 µg/dL (range 134–325 µg/dL; reference value, <100 µg/dL) and ultrasound or CT confirmation. In two cases *(n*=2/62; 3.2%), increased serum ammonia concentrations were detected (124 and 257 µg/dL, respectively), but the suspected shunt could not be confirmed on CT or ultrasound. Cats were treated with lactulose, metronidazole and a commercial diet produced for cats with hepatic diseases. Only two cases were treated with levetiracetam, as the remaining cases were referred before this medication was recommended to treat cats. Described treatment led to rapid improvement and resolution of epileptic seizures, therefore, a presumptive diagnosis of vascular hepatopathy was made. The mean age of diagnosis for cats with confirmed PSS was 1.69 years (range, 8 months – 6.5 years) and for cats with suspected hepatopathy the age at the time of presentation was 6.5 years. Among the cats with PSS, there was one Siamese, one Ragdoll, one Norwegian Forest cat, and the remaining cases were Domestic shorthair cats.

Renal encephalopathy was diagnosed in six cases (*n*=6/62; 9.7%). The mean concentration of urea was 111 mg/dL (range, 89–148 mg/dL; reference range 20–65 mg/dL). All cats had chronic kidney disease (Stage 3 or Stage 4), with a mean creatinine value of 2.9 mg/dL (range 3.1–5.7 mg/dL; reference range, 0.6–1.6 mg/dL), documented hypertension with mean arterial blood pressure of 174 mmHg (range 168–180 mmHg; reference range, 120–160 mmHg), and proteinuria with a mean UPC of 0.55 (range 0.4–0.89; reference value, <0.2). The mean age at presentation was 10.7 years (range, 7–15 years).

Hypoglycaemia was diagnosed in three cats (*n*=3/62; 4.8%) with a mean age of 8.9 years and a mean glucose value of 2.2 mmol/dL (range, 1.8–2.8 mmol/dL; reference range,

4.8–6.6 mmol/dL). All cats had been under therapy for diabetes mellitus, the suspected reason of hypoglycaemia was insulin overdose. All cats presented in status epilepticus.

One cat (*n*=1/62; 1.6%) presented with hyperglycaemia, with a glucose concentration of 11 mmol/dL (range, 9.2–13.2 mmol/dL; reference range, 4.8–6.6 mmol/dL), and concurrent signs of diabetic ketoacidosis. This cat presented with focal seizures at the age of 6 years. Increased serum fructosamine concentration and glucosuria confirmed diabetes mellitus.

Hyperthyroidism was diagnosed in three cats (*n*=3/62; 4.8%) at a mean age of 9.8 years (range, 8–12 years). Diagnosis was based on a combination of clinical signs (weight loss, normal to increased appetite, palpable nodule in the ventral neck region) with a mean total T4 value of 6.4 µg/dL (reference range, 1.6–5.0 µg/dL). All cats had concurrent hypertension, with a mean value of 178 mmHg (range, 170–198 mmHg; reference range, 120–160 mmHg).

In five cats (*n*=5/62; 8.1%) hypertension with a mean systolic BP of 173 mmHg (range, 170–186 mmHg; reference range, 120–160 mmHg) might have been the cause of epileptic seizures. Four of these cats had concurrent cardiomyopathy, one additionally arrhythmia, but no chronic kidney disease or hyperthyroidism was diagnosed in this group. All cats were treated with amlodipine additionally to cardiac medications. Satisfactory seizure control was achieved in three cats (*n*=3/62; 4.8%; Fig.2).

Discussion

In a retrospective study conducted by Schriefl at al. (2008) reactive seizures were diagnosed in 22.0% (*n*=20/91) of cats presented for epileptic seizure evaluation within a 5-year period, in another study performed by Pakozdy et al. (2010) secondary epilepsy was diagnosed in 62% of cats (*n*=78/125) presented with recurrent seizures; however, no detailed data regarding most common causes for reactive seizures are available.

Knowledge regarding the potential and most common causes for reactive seizures will facilitate rapid and accurate diagnosis and may point the clinician towards additional appropriate examinations, e.g. measuring blood pressure, serum tT4 concentration etc. Moreover, the ability to accurately differentiate between IE and RS is essential for appropriate treatment to be initiated.

In the case of reactive seizures, the most effective way to control seizure activity is to instigate appropriate treatment of the underlying cause. Therefore, a specific diagnostic workup is of utmost importance. In the current study, confirmed or presumed intoxication was the most common cause of reactive seizures, however in most cases, toxin presence could not be detected or confirmed. Considering that commercial, rapid toxin screening tests are unavailable for cats, clinicians should commence symptomatic treatment. In the current study, satisfactory improvement in most of the cases was achieved.

In metabolic and toxic diseases, seizures arise due to an inability to maintain the cell membrane resting potential. Seizure activity may occur regardless of anticonvulsant drugs used in an attempt to increase inhibition (Barnes et al., 2004; Schriefl et al., 2008; Bailey and Dewey, 2009; Brauer et al., 2011, Lidbury and Cook, 2016; Gow, 2017; Viebrock and Dennis, 2017; Barnes, 2018). In these cats, treating the underlying disease (e.g. administering

glucose, managing hyperthyroidism, renal or hepatic encephalopathy) is essential to providing adequate seizure control.

History taking for feline patients can be more challenging than that for dogs, as demonstrated in our study, because over 60% of cats spent the majority of their time without owner observation. This can make the diagnosis of intoxications a greater diagnostic challenge in cats than in dogs. Clinicians must be aware that they are unlikely to obtain information regarding potential toxin ingestion in the history, unless the owner applied permethrin. We failed to identify the toxin in most cases, despite the fact that intoxications accounted for 43% of cases. Our results are similar to those obtained in dogs, where intoxications were reported in 38.5% of dogs diagnosed with reactive seizures (Bauer et al., 2011). This finding was unexpected, since dogs are expected to ingest potentially toxic agents more frequently than cats.

In the same canine study (Bauer et al., 2011), the second most common reason for reactive seizures in dogs was hypoglycaemia (32.3% of cases), whereas we found hypoglycaemia in only 4.8% of our feline cases. Additionally, the underlying cause of hypoglycaemia differs between canine and feline patients. In dogs, the most common cause of hypoglycaemic seizures was insulinoma, while in cats, hypoglycaemia was caused by human error and insulin overdose. All hypoglycaemic cats in our study were diabetic. Our finding was similar to that obtained by Viebrock and Dennis (2017), which confirmed that symptomatic hypoglycaemia is a common cause for emergency presentation in diabetic cats under therapy. Glucose is a primary energy source of the brain and the brain is highly susceptible to hypoglycaemic damage, triggering seizure activity but also further nervous tissue damage, e.g. transient blindness and cognitive dysfunction (Thomovsky, 2017;

Viebrock and Dennis, 2017). In human medicine, it has been reported that hypoglycaemic events in neonates may lead to brain injury, and neurodevelopmental impairment (Burns et al., 2008). Therefore, both early recognition and treatment are important. Clinicians should consider hypoglycaemia when a cat with diabetes mellitus presents on emergency due to epileptic seizures.

In our study, the second most common reason for seizures was renal encephalopathy due to chronic kidney disease, with concurrent hypertension, and hepatic encephalopathy due to a portosystemic shunt. In the case of hepatic encephalopathy, clinical signs may vary from subtle behavioural changes (apathy) to seizures and a comatose state, which is the 4th stage according to West Haven grading scale modified for veterinary medicine (Gow, 2017). Neurologic abnormalities are caused by altered glutamine and glutamate transmission, increase in gamma-amino butyric acid agonists, alterations of serotonergic system and amino acid metabolism, potential manganese toxic effects, and high serum ammonia concentration that develop as a result of lack of its conversion (Gow, 2017). The reference standard for the diagnosis of hepatic encephalopathy is ammonia concentration, however, a bile acid stimulation test can also be used for a diagnosis (Lidbury et al., 2016; Gow, 2017). Portosystemic shunt should be suspected in the case of younger cats (most commonly <1 year) and copper-coloured eyes, especially when neurologic signs are reported by the owner between the seizure episodes (dysphoria, lethargy, ataxia). Portosystemic shunts are common in domestic shorthair cats, however, there may be a mild breed predisposition in Siamese and Persian cats (Barnes et al., 2004; Gow, 2017). In our study only one Siamese cat was diagnosed with PSS, other were domestic short hair cats, Ragdoll and Norwegian forest cat.

Epileptic seizures and coma are complications of both acute and chronic renal insufficiency. Failure to excrete metabolic products (urea) causes accumulation and leads to severe intoxication. Neurological signs can be further exacerbated by electrolyte disturbances (Lidbury et al., 2016). Feline patients in this study were diagnosed with stage 3 and 4 chronic kidney disease (CKD) with a subsequent hypertension of 168–180 mmHg, increasing the risk for target organ (brain) damage (Schwartz, 2002; Elliot et al., 2007; O'Neill et al., 2013; Brown et al., 2016).

Hypertension, as a clinical sign co-existing with hyperthyroidism, cardiac disease and chronic kidney disease was found in 19.3% of cases (n=12/62), when all cases are summarised. Hypertension is a common finding in the above-mentioned diseases, as previously reported in cats (Elliot et al., 2007; Stephen, 2011; Peterson et al., 2013; Brown et al. 2016). Arterial blood flow is typically maintained at a relatively constant level despite changes in blood pressure. Failure of autoregulatory mechanisms leads to hypertension, causing pathologic changes in the walls of small diameter cerebral arteries. This leads to barotrauma, brain oedema during periods of elevated blood pressure, and also to ischemic or haemorrhagic strokes which can result in seizure activity. The pathologic effect of systemic hypertension is most severe on tissues with a rich arteriolar supply, known as target organ damage (TOD). A variety of tissues can be affected, including the retina, kidney, myocardium and brain. Brain damage occurs when autoregulatory mechanisms fail, leading to brain oedema and arteriosclerosis (Schwartz, 2002; O'Neill et al., 2013).

Diagnosis of hypertension in cats can be challenging. However, if measurements are performed repeatedly, results can be reproducible and coincident with neurological signs (e.g. seizures, apathy, stupor), and neurologic signs resolve after appropriate antihypertensive

treatment, we think that hypertension may be diagnosed as a cause for reactive seizures. In the published literature, there is a case series of two cats and two dogs with hypertensive encephalopathy (O'Neill et al., 2013). The report describes hypertensive encephalopathy in older animals (a 19-year-old Domestic short haired cat and a 7-year-old Siamese cat), similar to our case series, confirming that seizures are a common presenting sign. Acute blindness and altered mentation were reported to be coexisting signs, attributed to diffuse prosencephalon abnormalities observed on MRI imaging (bilateral, symmetric lesions in the white matter, T2 and FLAIR hypertensive, T1 isointense, with no contrast enhancement) (O'Neill et al., 2013). Among the cats in our study, five underwent MRI, but only one had similar MRI findings to those described by O'Neill et al. (2013). Surprisingly, hypertension associated with renal, thyroid and cardiac disease was diagnosed in 19.3% of cats (n=12/62) in this study, making it a common reason for reactive seizures. A question remains whether the seizures were caused by the hypertension itself or by the coexisting disease (renal disease, cardiac disease, hyperthyroidism). Regardless, it is important to carefully evaluate blood pressure in cats presenting with seizures, especially cats over 8 years of age.

The most common cause of reactive seizures was presumptive or confirmed intoxication. Toxicologic blood examinations are often not readily available and, if they are, it may take several days to receive the results. Therefore, these cases may be challenging to diagnose. Clinicians should suspect intoxication when metabolic diseases (hepatic encephalopathy, renal encephalopathy, hypoglycaemia, hyperthyroidism, hypertension) are excluded, when there is an indication in the history, if the cat is frequently unobserved by the owner, and if a response to symptomatic treatment (anticonvulsive therapy, intravenous fluid, intralipid therapy) is observed.

Our study has several limitations. Given the retrospective nature of the study, we relied on historical data obtained over 17-year period. In this time, seizure investigation protocols and treatments have been constantly changing. Another limitation is the fact that we failed to identify the toxin in most of our cases. The presumptive diagnosis of intoxication was made based on the fact that seizure activity has not reoccurred after symptomatic treatment.

Conclusions

Seizures can be a life-threatening condition, but control is feasible when effective treatment is introduced. Seizures in cats are both a diagnostic and treatment challenge for the clinician. In comparison to dogs, feline seizures have been less commonly investigated and there is less information present in the literature. In our study, reactive seizures occurred in 62 (7.9%) of 789 cats referred for seizure evaluation. This study could inform clinicians regarding the most commonly seen causes for reactive seizures in cats and help guide treatment choices.

Conflict of interest statement

None of the authors of this paper have financial or personal relationship with people or organisations that could inappropriately influence or bias the content of the paper.

References

Barnes, H.L., Chrisman, C.L., Mariani, C.L., Sims, M., Alleman, A.R., 2004. Clinical signs, underlying cause, and outcome in cats with seizures: 17 cases (1997-2002). Journal of American Veterinary Medical Association 225, 1723-1726.

Barnes, H.L.,2018. Feline epilepsy. Veterinary clinics of North America Small Animal Practice 48, 31-43.

Berendt, M., Farquhar, R.G., Mandigers, P.J., Pakozdy, A., Bhatti S. F., De Risio, L., Fischer, A., Long, S., Matiasek, K., Muñana, K., et al., 2015. International veterinary epilepsy

task force consensus report on epilepsy definition, classification and terminology in companion animals. BMC Veterinary Research 11, 182.

Brauer, C.H., Jambroszyk, M., Tipold, A., 2011. Metabolic and toxic causes of canine seizure disorders: A retrospective study of 96 cases. The Veterinary Journal 187, 272-275.

Brini, E., Gandini, G., Crescio, I., 2004. Necrosis of hippocampus and piriform lobe: Clinical and neuropathological findings in two Italian cats. Journal of Feline Medicine and Surgery 6, 377-381.

Brown, C.A., Elliot, J., Schmiedt, C.W., Brown, S.A., 2016. Chronic Kidney disease in aged cats; clinical features, morphology, and Proposed pathogenesis. Veterinary Pathology 29, 1495-1501.

Burns, C.M., Rutherford, J.P., Broadman, F.M., Cowan, F.M., 2008. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycaemia. American Academy of Paediatrics 122, 65-74.

De Risio, L., Bhatti, S., Muñana, K., Penderis, J., Stein, V., Tipold, A., Berendt, M., Farqhuar, R., Fischer, A., Long, S., et al., 2015. International veterinary epilepsy task force consensus proposal: Diagnostic approach to epilepsy in dogs. BMC Veterinary Research 11, 148.

Elliot, J., Barber, P.J., Syme, H.M., Rawlings, J.M., Markwell, P.J., 2007. Feline hypertension; clinical findings and response to antihypertensive treatment in 30 cases. Journal of Small Animal Practice 21, 402-409.

Fatzer, R., Gandini, G., Jaggy, A., Dohher, M., Vandevelde, M., 2000. Necrosis of hippocampus and piriform lobe in 38 domestic cats with seizures. A retrospective study on clinical and pathologic findings. Journal of Veterinary Internal Medicine 14, 100-104.

Gow, A.G., 2017. Hepatic encephalopathy. Veterinary clinics of North America: Small Animal Practice 47, 585-599.

Hamamoto, Y., Hasegawa, D., Mizoguchi, S., Yu, Y., Wada, M., Kuwabara, T., Fujiwara-Igarashi, A., Fujita, M., 2017. Changes in the interictal and early postictal diffusion and perfusion magnetic resonance parameters in familial spontaneous epileptic cats. Epilepsy Research 133, 76-82.

Kuwabara, T., Hasegawa, D., Ogawa, F., Kobayashi, M., Fujita, M., Suzuki, H., Matsuki, N., Orima, H., 2010. A familial spontaneous epileptic feline strain: a novel model of idiopathic/genetic epilepsy. Epilepsy Research 92, 85-88.

Lamy, C., Domingo, V., Semach. F., Arquizan, C., Trystram, D., Coste, J., Mas, J.L., 2003. Early and late seizures after cryptogenic ischemic stroke in young adults. Epilepsia. 35, 959-964.

Lidbury, J.A., Cook, A.K., Steiner J.M., 2016. Hepatic encephalopathy in dogs and cats. Journal of Veterinary Emergency and Critical Care (San Antonio) 25, 455-473.

Lin, C.H., Yan, C.J., Lien, Y.H., Huang, H.P., 2006. Systolic blood pressure of clinically normal and conscious cats determined by an indirect Doppler method in a clinical setting. Journal of Veterinary Medicine Science 68, 827-32.

Mizoguchi, S., Hasegawa, D., Kuwabara, T., Hamamoto, Y., Ogawa, F., Fujiwara, A., Matsuki, N., Fujita, M., 2014. Magnetic resonance volumetry of the hippocampus in familial spontaneous epileptic cats. Epilepsy Research 108, 1940-1944.

O'Neill, J., Kent, M., Glass, E.N., Platt, S.R., 2013. Clinicopathological and MRI characteristics of presumptive hypertensive encephalopathy in cats and dogs. Journal of the American Animal Hospital Association 49, 412-420.

Pakozdy, A., Sarchachii, A., Leschnik, M., Tichy, A.G., Thalhammer, J.G., 2010. Clinical comparison of primary versus secondary epilepsy in 125 cats. Journal of Feline Medicine and Surgery 12, 910-916.

Peterson, M.E., 2013. Diagnostic testing for hyperthyroidism in cats. Journal of Feline Medicine and Surgery 15, 765-777.

Podell, M., Potschka, M., Batlle, M.P., Rusbridge, C., Volk., H., 2015. International veterinary epilepsy task force consensus proposal: diagnostic approach to epilepsy in dogs. BMC Veterinary Research 11, 148.

Raimondi, F., Shihab, N., Gutierrez-Quintana, R., Smith, A., Trevail, R., Sanchez-Masian, D., Smith, P.M., 2017. Magnetic resonance imaging findings in epileptic cats with a normal interictal neurological examination: 188 cases. Veterinary Record, 180(25):610.

Schriefl, S., Steinberg, T.A., Matiasek, K., Ossig, A., Fenske N., Fischer A., 2008. Etiologic classification of seizures, signalment, clinical signs and outcome in cats with seizures disorders: 91 cases (2000-2004). Journal of American Veterinary Medical Association 233, 1591-1597.

Schwartz, R.B., 2002. Hyperperfusion encephalopathies: hypertensive encephalopathy and related conditions. The Neurology 8, 22-34.

Smith Bailey K., Dewey C.W., 2009. The seizuring cat. Journal of Feline Medicine and Surgery 11, 385-394.

Stanciu, G.D., Packer, R., Pakozdy, A., Solcan, G., Volk, H.A., 2017. Clinical reasoning in feline epilepsy: which combination of clinical information is useful. The Veterinary Journal 225, 9-12.

Stepien, R.L., 2011. Feline systemic hypertension: diagnosis and management. Journal of Feline of Medicine and Surgery 13, 25-34.

Thomovsky, E., 2017. Fluid and Electrolyte therapy in diabetic ketoacidosis. Veterinary Clinics of North America: Small Animal Practice 47, 491-503.

Viebrock, K.A., Dennis J., 2017. Hypoglycaemic episodes in cats with diabetes mellitus: 30 cases (2013-2015). Journal of Feline Medicine and Surgery 21, 278-281.

Table 1

Additional diagnostic examinations performed in cats diagnosed with reactive seizures

Additional examinations	Reasons for reactive seizures							
	Presumed intoxication (*n*=27)	Verified intoxication (*n*=7)	Renal encephalopathy (*n*=6)	Hepatic encephalopathy (*n*=6)	Hypoglycaemia (*n*=3)	Hyperthyroidism (*n*=3)	Hyperglycaemia (*n*=1)	Hypertension (*n*=5)
Blood analysis [a]	27	7	3	6	3	5	3	5
Serum ammonia concentration	20	7	3	6	6	5	3	5
Urine examination	27	7	3	6	6	5	3	5
Faecal examination	7	2	0	0	0	0	0	0
Gastric content examination	1	0	0	0	0	0	0	0
MRI examination	14	0	0	0	0	1	0	0
CSF examination	14	0	1	0	0	0	0	0
Cardiology [b]	3	0	2	0	0	2	0	5
Blood pressure measurement	1	0	6	0	0	3	1	5
Thyroxine concentration	5	1	4	3	1	3	1	5
Cholinesterase activity	12	2	0	1	1	0	0	0
Abdomen CT	0	0	0	6	0	0	0	0
Abdominal ultrasound	20	0	6	2	3	3	1	0

MRI, magnetic resonance imaging; CSF, Cerebrospinal fluid; CT, Computed tomography

[a] Haematology and serum biochemistry. Biochemistry profile included aspartate aminotransferase, alanine aminotransferase, urea, creatinine, albumin, total protein, alkaline phosphatase, glucose, calcium, potassium, chloride, sodium, bilirubin, ammonia, bile acid stimulation test, fructosamine.

[b] Electrocardiography and echocardiography

Figure legends

Fig. 1. Differential diagnoses for confirmed or presumed intoxications in cats with seizures (*n*=34). In most cases, the toxin was not found in the blood, urine, or gastric contents. Diagnosis was made based on history, sudden onset of seizures, and rapid cessation of clinical signs with symptomatic treatment (*n*=27/34; 79.4%). The second most common cause for intoxication was permethrin application (*n*=5/34; 14.7%), and subsequently fipronil and pesticide intoxication.

Fig. 2. Occurrence of seizures due to metabolic and toxic disturbances (*n*=64). Proven and presumptive intoxications were the most common causes, followed by renal encephalopathy and portosystemic shunts. CKD, chronic kidney disease; PSS, portosystemic shunt.

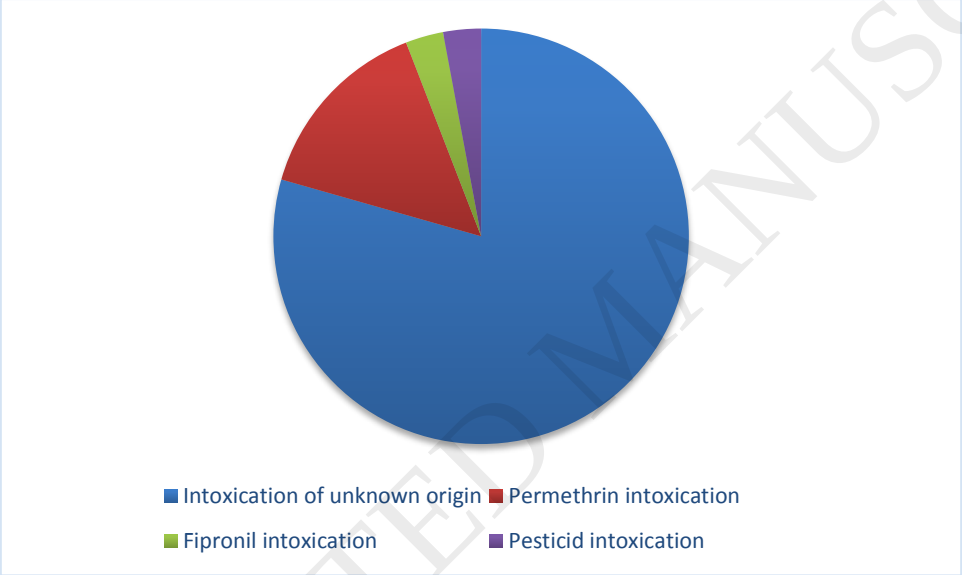

Fig 1.

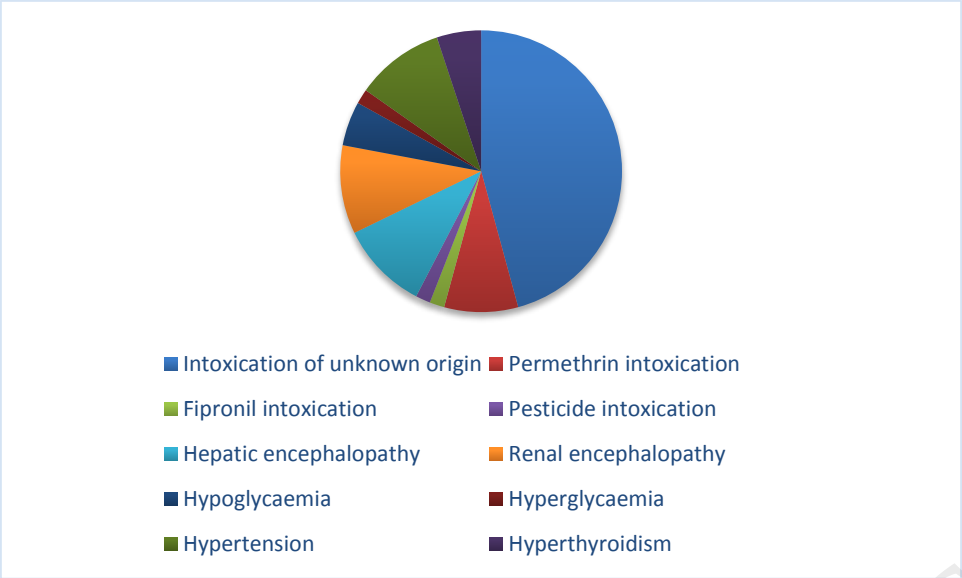

Fig.2