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A retrospective study of MR imaging in dogs with seizures

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1. Introduction

Epilepsy is the most common chronic neurological condition encountered in dogs; it is estimated to affect 0.5–5.7 % of all dogs. Seizures accounts for 10 % of all neurological disorders, and it occurs in all ages, genders and breeds of dogs (Jaggy and Bernardini 1998). It is estimated that 30% of epileptic dogs have seizures that cannot be controlled by anticonvulsant medication. This raises a great difficulty for owners and small animal clinicians (Buckmaster et.al. 2002). Proper identification of the underlying aetiology has distinct implications on therapeutic prognosis (Podell 1998).

Every dog can have an epileptic seizure if the stimulus is strong enough, but the term epilepsy should technically only be applied in the case of idiopathic epilepsy; where seizures occur without any neurological or non-neurological abnormality (Knowles 1998). Idiopathic epilepsy is observed more frequent in certain breeds, where the first seizure occurs in a young age (between six months and six years) (Chandler 2006). Symptomatic epilepsy is when an intracranial abnormality is the cause of seizures; some examples of this can be neoplasia or inflammatory brain diseases. MRI is the modality of choice when looking for underlying brain abnormality in patients with seizures due to its superior soft tissue contrast resolution (Leigh et al. 2008). Cryptogenic epilepsy is where seizures are thought to be symptomatic, but the underlying cause is not yet identified. Reactive seizures are when the cause is outside the central nervous system; such as metabolic disease like diabetes mellitus, hepatoencephalopathy due to liver failure, or toxicosis (Chandler 2006).

In this study 74 dogs with seizures that had undergone MRI examination was analysed retrospectively. The primary aim was to determine the number of dogs with normal vs. abnormal MR image, and the prevalence of different abnormalities compared to the literature. Another goal was to compare the dogs with normal MRI to the ones with abnormal MRI in regards to age, gender and breeds.

2. Literature review

2.1. Terminology and Classification of Epilepsy

According to Fisher et al. (2005), epilepsy is the name of a brain disorder characterized by recurrent and unpredictable interruptions of normal brain function, called epileptic seizures. Thus it is not a singular disease entity but a variety of disorders reflecting an underlying brain dysfunction that may result from many different causes.

New Terminology

The International League against Epilepsy (ILAE) proposed a new terminology in human epilepsy in 2011. This new terminology is due to major technological and scientific advances of the last several years in human epilepsy. According to Berg and Scheffer (2011), recent insights into the molecular genetics and pathophysiology of idiopathic epilepsies have threatened to make the term 'idiopathic' obsolete. Due to the new tools available when studying epilepsy the ILAE suggests moving away from the old classification system of symptomatic, cryptogenic and idiopathic epilepsy to "a more accurate classification". A summary of the new classification of epilepsy can be seen in the **table 1**.

Since most of the articles concerning epilepsy in veterinary medicine use the old terminology, and the old terminology cannot be directly transferred to the new classifications, I will use the old terminology when discussing different types of epilepsy.

Table 1: Comparison of major changes between the 1989 classification and terminology and the newly proposed terminology and concepts (adapted from Berg and Scheffer 2011).

Old terminology and concepts	Recommended new terminology and concepts
Idiopathic: there is no underlying cause other than a possible hereditary predisposition ***Symptomatic:*** the epilepsy is the consequence of a known or suspected disorder of the CNS ***Cryptogenic:*** this refers to a disorder whose cause is hidden or occult. Cryptogenic epilepsies are presumed to be symptomatic	***Genetic:*** the epilepsy is, as best understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder. This attribution must be supported by specific forms of evidence ***Structural/metabolic:*** there is a distinct other structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy. These disorders may be of acquired or genetic origin. When of genetic origin, there is a separate disorder interposed between the gene defect and the epilepsy ***Unknown***: the nature of the underlying cause is unknown; it may have a fundamental genetic basis (e.g., a previously unrecognized channelopathy) or it may be the consequence of an unrecognized structural or metabolic disorder not yet identified

Old Terminology

Epilepsy can be classified into 3 categories that are characterised by their underlying cause; symptomatic, cryptogenic and idiopathic epilepsy.

Symptomatic epilepsy is secondary to an intracranial structural brain lesion. Trauma, malformation, inflammation, degeneration and neoplasm are examples of these structural abnormalities, where neoplasia is the most common (March 1998, DeLahunta and Glass 2009). It can occur at any stage in life, but it is more frequent in dogs older than 6 years. Symptomatic epilepsy can be characterized by partial seizures with or without secondary generalization (Berendt and Gram 1999). Cryptogenic epilepsy (crypto=hidden) is where seizures are thought to be symptomatic, but the underlying cause is not yet known, also termed "probably symptomatic" (Engel 2001). Idiopathic (primary) epilepsy refers to epilepsy without any known underlying cause. Idiopathic epilepsy is associated with generalised

seizures and commonly occurs between six months and six years of age (Berendt and Gram 1999). It is suggested to be hereditary since the incidence is higher in a number of pedigree dogs.

Reactive seizures can also be mentioned here. This occurs as a consequence of extracranial disorder. Hypoglycaemia, hepatic encephalopathy, electrolyte imbalance, and uraemia are some examples of disorders that may cause seizures, but are not classified as epilepsy (Chandler 2006).

2.2. Classification of Seizures

An epileptic seizure is defined, according to the ILAE, as a "transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity of the brain" (Fisher et al. 2005).

Seizures are categorized according to their onset in the brain. The two main categories are partial (focal) or generalized seizures (Chandler 2006). Clinical appearance of the seizure can give us clues about what part of the brain is involved and where the seizure focus is located (March 1998).

Partial Seizures

A partial seizure is when the initial activation is in one part of the cerebral hemispheres or in a specific region of the forebrain. An example of this is when the initial activation occurs first in the hippocampus, which is the case in temporal lobe epilepsy in humans (Engelborghs et al. 2000). Partial seizures are associated with symptomatic epilepsy, and dogs with partial seizures are likely to have an intracranial pathology (Podell et al. 1995).

A *simple partial seizure* is characterized by an asymmetrical appearance without loss of consciousness. Many different forms of manifestation exist, since this depends on which cortical area is affected. Simple partial seizures can be with motor, somatosensory, special sensory, autonomic or behavioural signs (LeCouteur and Child 1989).

A *complex partial seizure* is manifested by stereotypical bizarre behaviour; e.g. fly biting, jaw clenching, vocalization, gastrointestinal signs, running or even aggression. Also called psychomotor seizure, there is usually some impairment of consciousness. This impairment of consciousness can have been present at onset or progressed from a simple partial seizure.

Complex partial seizures have a temporal or a frontotemporal origin where the epileptiform discharges are frequently bilateral (LeCouteur and Child 1989, March 1998).

Both simple and complex partial seizures can spread which results in secondary generalisation and may have a tonic-clonic appearance.

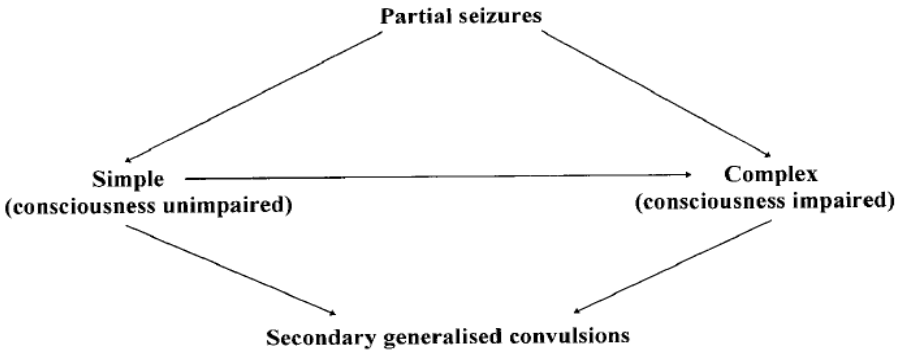


Figure 1: Way for a partial seizure to develop into secondary generalization (Adaption from Berendt and Gram 1999)

Generalised Seizures

When both cerebral hemispheres are initially involved in seizure activity it is called a generalized seizure. Generalized seizures are symmetrical from the onset. The generalized tonic-clonic (grand mal) seizures are the most recognized type in animals and are usually associated with the idiopathic form of epilepsy (Knowles 1998). Generalized seizures can occur in a non-convulsive (previously known as petit mal) and convulsive (previously known as grand mal) form. Non-convulsive generalised seizures are also called “absence seizure” because of the transient loss of consciousness and lack of motor activity. This form is not commonly recognized in cats and dogs, but this can possibly be due to the fact that they are clinically difficult to detect (Chandler 2006).

Convulsive generalised seizures have one or more of the following clinical appearances;

1) Tonic: increased muscle contraction that is sustained.
2) Clonic: regular repetitive prolonged myoclonus which involves the same muscle group.
3) Myoclonic: a sudden brief involuntarily muscle contraction that can be single or multiple.
4) Tonic-clonic: consisting of a tonic phase and then followed by a clonic phase. The animal becomes recumbent in the tonic phase.
5) Atonic: sudden loss of muscle tone which lasts 1-2 seconds or more

Recent studies show that what were believed to be primary generalised seizures really are partial seizures with secondary generalization (Berendt and Gram 1999). This indicates that partial seizures in dogs are much more common than was previously thought. These partial seizures with secondary generalisation have a focal onset, which can be observed as an aura like event (Chandler 2006).

Large breed dogs such as German shepherds, Saint Bernard and Irish setter often have severe seizures that appear in clusters. Miniature and toy poodles have a milder form of generalised seizures, but without loss of consciousness, where they act disoriented, have spasticity of limbs, neck and trunk, and diffuse trembling. Labrador retrievers often have simple partial seizures which are diagnosed as idiopathic epilepsy; this is also seen in Finish spitz dogs with normal MR imaging (DeLahunta and Glass 2009).

Table 2: Classification of seizures (adapted from LeCouteur and Childs 1989)

I. **Partial Seizures** (Local, Focal)

a) Simple Partial seizures
   1. With motor signs
   2. With somatosensory or special sensory signs
   3. With autonomic signs
   4. With behavioural signs

b) Complex Partial Seizures
   1. Beginning as a simple partial seizure and progressing to impairment of consciousness
   2. With impairment of consciousness at onset

c) Partial seizures with 2nd generalization

II. **Primary Generalised Seizures** (bilaterally symmetrical without local onset: with or without loss of consciousness)

1. Absence seizures
2. Myoclonic seizures
3. Clonic seizures
4. Tonic seizures
5. Tonic-clonic seizures
6. Atonic seizures

Phases of Seizures

An epileptic seizure can be described as a sequence of events; the prodromal, preictal (aura), ictus and postictus phase. These four phases can have an important diagnostic significance when we want to distinguish a seizure from other episodic events like syncope.

In humans the *prodrome* is described as a long lasting phase occurring hours to days before the "actual" seizure. It has been described as mood changes, anxiety, irritability or other emotionally irregularities. Prodromes are not considered to be part of the seizure since abnormal electrical activity cannot be observed during an EEG in this period (Berendt and Gram 1999). The *pre-ictus phase*, also known as the aura, is the part of the seizure that occurs before loss of consciousness. In humans this event is considered as an ictal manifestation with sensory, psychosensory and experiential symptoms (Luders et al. 1998). It has been described as a warning sign before the seizure, and it is a feeling of fear, déjà vu or a strange taste. Due to the nature of these "feelings", the pre-ictus is difficult to detect in dogs. However, many owners have reported behavioural changes before the occurrence of a seizure, which may indicate that dogs also experience some sort of aura (Chandler 2006).

Ictus is the seizure event itself where loss of consciousness occurs.

Post-Ictus phase follows ictus, and can be a period of disorientation, confusion, or deep sleep (Berendt and Gram 1999).

Interictal phase is the period between two seizures (McNamara 1994).

Table 3: The four phases of a seizure (adapted from Chandler 2006)

Prodrome	Behaviour changes that occur hours or days before the seizure
Aura	Event prior to seizure characterised by sensory, psychosensory and experiential symptoms in humans, and indicative of a sensory focal seizure. Can last seconds to minutes.
Ictus	The seizure event itself
Post-ictal phase	Behavioural changes hours or days after the seizure

2.3. Pathophysiology of Epilepsy

The pathophysiology of epileptic seizures is not well understood, but increased knowledge in the field has given us a partial understanding of the underlying mechanisms (March 1998).

There are two important phenomena that play a role in the ictogenesis of seizures; hyperexcitabilty and hypersynchronization of neurons. Even though many different epilepsy syndromes occur it seems that the increased neuronal excitability and synchronicity are common to all (Engelborghs et al. 2000).

Excitation and Inhibition of Neurons

Imbalance between excitation and inhibition of neurons may lead to epileptiform activity in the brain. Neurotransmitters and ion-channels are important in the development of neuronal excitability. Main excitatory neurotransmitter is glutamate and main inhibitory neurotransmitter is ɤ -amino-butyric-acid (GABA) (Engelborghs et al. 2000). GABA inhibits depolarization by opening of chlorine channels, causing an influx of chloride, consequently leading to hyperpolarization. It has been shown that blocking GABAergic inhibition produces seizures. This indicates that loss of GABAergic inhibition can be an important factor in epileptogenesis. Glutamate stimulates depolarization by activating sodium and calcium

channels through N-methyl-D-asparate (NMDA) receptors, which results in an influx of sodium and calcium. This will contribute to the development of an excitatory postsynaptic potential (EPSP) (action potential). Following brain injuries the glutamate receptor can change in type, number, spatial distribution or sensitivity, which can induce a change in the fixed excitability of the glutamatergic neurons, thus decreasing the seizure threshold. These changes in brain tissue haven been demonstrated in humans suffering from temporal lobe epilepsy where there was an increase in glutamate receptor sensitivity and density (March 1998).

In dogs with epilepsy significantly less GABA and more glutamate was found in CSF compared to the normal control group (Podell and Hadjiconstatinou 1997, Loscher and Schwartz-Porsche 1986).

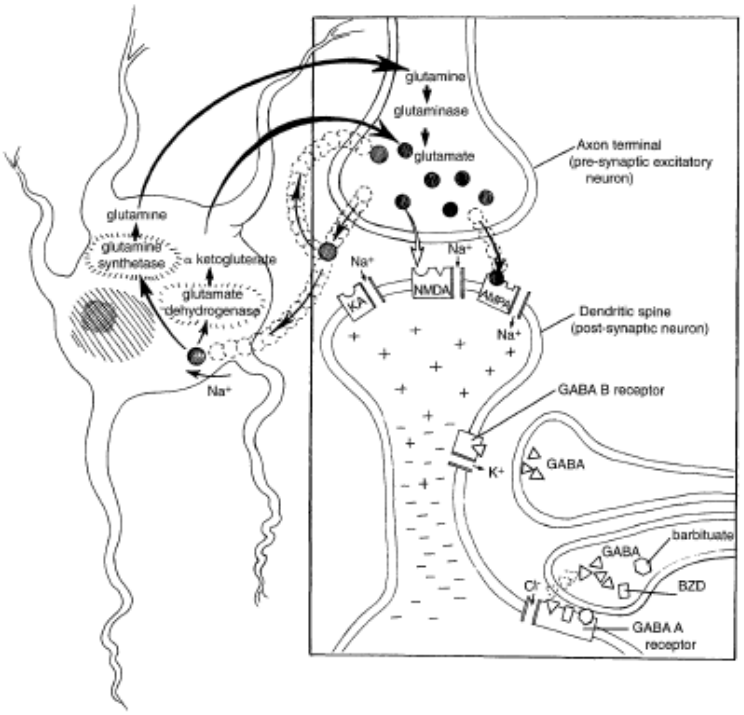


Figure 2: Glutamatergic and GABAergic synapses. Glutamate is released presynaptically by excitatory neurons to activate postsynaptic NMDA, AMPA and/or Kainate (KA) receptors which results in influx of sodium. GABA inhibits depolarization by opening of chlorine ($GABA_A$ receptors) and potassium ($GABA_B$ receptor) channels, causing influx of chloride and outflow of potassium (adapted from March 1998).

Synchronization and Recruitment of Neurons

Neurons fire in a hypersynchronous way during an epileptic seizure. This is possible due to the intrinsic properties and high connectivity of the cell. Hyperexcited neurons may synchronize other pyramidal neurons by using anatomical pathways and abnormal collateral connections. Direct electrical communication through gap junctions are a form of non-synaptic synchronization which contributes to the local recruitment of neurons. During excessive neuronal activity there is an outward movement of potassium as result of repolarization, which results in high extracellular (EC) concentration of potassium. Increased EC potassium can cause depolarization of neighbouring axon terminals and decrease the efflux of potassium during hyperpolarization. Also pacemaker neurons generate large depolarizing currents that can spread to surrounding neurons by ephaptic transmission (direct current flow between closely apposed unconnected cells). All of these mentioned factors can lead to synchronized, high frequency epileptiform discharge of neurons (March 1998).

Partial vs. Generalized seizures

As mentioned earlier, partial (focal) seizures can secondary generalise. In this case normal anatomical pathways help relay the impulse to distant locations. Intra- and interhemispheric pathways are used when a partial seizure is generalized to ipsilateral and contralateral cortical areas. Idiopathic primary generalised seizure pathogenesis is less understood than partial seizures. The main obstacle in understanding this disorder is the lack of macroscopic and microscopic lesions in the brain. However, the fact that this is lacking suggests that the abnormality is rather functional than anatomical, probably at a neurochemical or cellular level, such as when a neurotransmitter imbalance occurs due to a defect in synthesis, release or reuptake of glutamate or GABA (March 1998).

2.4. Aetiology

With the right stimuli, either from within (intracranial) or from outside (extracranial) the CNS, every brain is capable of epileptic activity. Consequently the causes of seizures are many (LeCouteur and Childs 1989).

2.4.1. Extracranial causes of seizures

There are many extracranial disorders that can cause seizures in dogs. Any disorder which causes an alteration in the metabolism of neurons of the CNS, can potentially lead to a seizure.

In dogs hypoglycemia, hepatic encephalopathy, electrolyte imbalance, uremia, hypoxia, hyperlipidemia, hyperthermia and intestinal parasites in puppies are known to cause seizures. Several toxins can also cause seizures. The most common are organophosphates, lead, ethylene glycol, and metaldehyde (Chandler and Volk 2008). In patients with an extracranial cause of seizures the interictal neurological findings are usually normal; however the physical examination may show signs of a systemic abnormality (DeLahunta and Glass 2009).

If cost is not an issue, diagnostic work necessary to exclude extracranial causes of seizures is (Chandler and Volk 2008):

1. Complete blood cell count (CBC)
2. Biochemistry, including glucose, electrolytes (especially Ca, Na, and K) and serum triglycerides
3. Pre- and postprandial bile acids
4. Urinalysis
5. Blood pressure

Depending on signalment, history and physical findings, further tests include:

6. Antibodies for Neospora Caninum and Toxoplasma Gondii
7. Thyroxine and thyroid-stimulating hormone
8. Serum lead concentration

Table 4: Seizures due to extracranial disease (adapted from Volk and Chandler 2008)

Extracranial causes of Epilepsy	Due to electrolyte imbalance, such as:	Hypernatraemia
		Hypocalcaemia
		Hyponatraemia
	Due to energy deprivation	Thiamine deficiency
		Hypoglycaemia*
	Due to organ dysfunction	Uraemic encephalopathy
		Hepatic encephalopathy*

* Most commonly seen in practice

2.4.2. Intracranial causes of seizures

Seizures are a common clinical sign of a number of intracranial physiologic disorders in dogs. Intracranial disorders include malformation (e.g. hydrocephalus), inflammatory disorders (e.g. granulomatous meningoenchephalitis), cranial trauma, neoplasia, degeneration (e.g. storage disease) and cerebral infarction.

Patients affected with structural intracranial disorders may often show progressively worsening and lateralised signs, head pressing and partial seizures. Intracranial cause of epilepsy is often associated with seizures that are refractory to medication (Chandler and Volk 2008).

Anomalies

The most common malformation causing seizures seen in dogs are obstructive hydrocephalus. Lissencephaly is another, where the onset of seizures usually occurs when the dog is a few years of age. Hydranencephaly (condition where the brain cerebral hemispheres are absent and replaced by sacs filled with cerebrospinal fluid) is quite rare, but have been observed in poodles. More subtle changes can be abnormalities in neuronal migration that causes various cerebrocortical dysplasias (DeLahunta and Glass 2009).

Neoplastic

Tumours are the most common intracranial lesions that cause seizures. Seizures are usually the initial or only sign of brain neoplasia, and cannot be excluded without advanced imaging (Chandler and Volk 2008). In a retrospective study with 95 dogs with brain tumours, 46

(47%) had seizures. Tumour location is the most important factor in epileptogenesis, tumours located in the cerebral hemispheres and diencephalon is most commonly associated with seizures (Bagley and Gavin 2008).

Infectious

Encephalitis that involves the proencephalon commonly causes seizures. This includes viral, bacterial, fungal, parasitic, protozoal and rickettsial agents (Chandler and Volk 2008).

Inflammatory

Autoimmune disorders such as granulomatouse meningoencephalomyelitis, necrotizing leukoencephalitis, eosinophilic meningoencephalomyelitis and other meningoencephalitides (e.g. pug encephalitis) are all known to cause seizures (Chandler and Volk 2008).

Traumatic

Seizures caused by head trauma can start immediately, weeks, months or years following injury due to scar tissue formation. The believed pathogenesis behind this is the astrocytic proliferation, neuronal reorganization and formation of new synapses that are all part of the normal healing process of brain tissue. This may serve as seizure focus when it occurs in the prosencephalon (DeLahunta and Glass 2009).

Vascular

With increased availability of CT and MRI in veterinary medicine, it is clear that cerebrovascular disease also occur in dogs. Historically this was thought to be rare. Even though seizures are said to be an uncommon sign of ischemic and haemorrhagic strokes in both humans and dogs, they do occur. MRI of an ischemic stroke is characterized as a triangular, sharply demarcated lesion. Like after a trauma, seizure does not necessarily occur immediately after the cerebrovascular insult, but can present itself weeks, months or years later due to changes in molecular and cellular network causing increased neuron excitability (Chandler and Volk 2008).

Degenerative

Neural degeneration in the prosenchephalon is caused by several different disorders (e.g. storage diseases). In adult humans temporal lobe epilepsy is common; it is characterized by recurrent complex partial seizures and hippocampal sclerosis (Buckmaster et al. 2002, Engelbourghs et al. 2000). Temporal lobe epilepsy is correlated with specific type of pathological lesions in the hippocampus. Histology of the dentate gyrus shows loss of

neurons, gliosis and axon reorganization (mossy fiber sprouting). Hippocampal sclerosis can be seen during a MR examination. It is recognized as atrophy on the affected side shown as hyperintensity on image (Takayuki et al. 2010). The neural loss can also be measured by MR volumetry in cases with significant reduction in hippocampal volume (Buckmaster et al. 2002). In dogs, presence of hippocampal sclerosis in connection with epilepsy is still controversial. However, recent reports in veterinary medicine suggest that this also occur in dogs. A study where 58 dogs with idiopathic epilepsy underwent brain MR volumetry of the hippocampus concluded that hippocampal atrophy also occur in dogs, even though less frequent than in humans (Takayuki et al. 2010).

2.4.3. Idiopathic epilepsy

Idiopathic epilepsy (IE) is the most common cause of seizures in dogs and is defined as "recurrent seizures for which no underlying abnormality can be identified (Chandler and Volk 2008)". In dogs with IE the first seizures usually present itself between the ages of six months and six years, and the IE seizures are usually generalised and symmetrical from onset. IE seizures are mainly seen at home after a period of rest or sleep and rarely occur when animals are active (Jaggy and Bernardini 1998). The seizure can last from 30 seconds to 30 minutes, and the interval between the seizures can vary from one week to months. There is a tendency that frequency of seizures increases with age. Dogs may occasionally develop status epilepticus which might be lethal (DeLahunta and Glass, 2009).

Typically, dogs with IE are neurologically normal in the interictal period. However it is common that dogs show cerebral dysfunction as a residual neurological deficit due to seizure activity. This can be blindness, ataxia/paresis, mentation changes and miosis. They generally last a few hours to days following a cluster of seizures or status epilepticus (Chandler and Volk 2008)

The change in neuronal environment in patients with IE which causes the seizure threshold to decrease has not been identified by any laboratory or microscopic examination of the brain. Such change in the prosencephalon is believed to be genetically determined. In humans, a genetic basis for several IE cases has been recognized. Even though there are cases of IE in both mixed breed dogs and pure bred dogs, it is suggested to be hereditary due to a high correlation between certain breeds and epilepsy. Test mating in controlled situations with a

few dogs has revealed definite evidence that IE is genetically linked. Dog breeds that show a high prevalence of epilepsy include; German shepherds, Belgian Tervueren, Keeshounds, Beagles, Dachshunds, Hungarian Vizsla, Bernese Mountain dog, Irish Wolfhound, Golden Retriever, standard Poodle, Labrador Retriever, miniature Schnauzer, Saint Bernard, Siberian Huskies, Fox Terriers, Cocker and Springer spaniel. Some studies support an autosomal recessive or polygenic recessive inheritance (Knowles 1998).

The diagnosis of IE is done by exclusion of all other known causes, where MR imaging plays a crucial role (DeLahunta and Glass 2009).

2.5. MRI diagnosis of intracranial disease related to seizures

According to Mellema et al. (1999), magnetic resonance imaging (MRI) is frequently used for evaluation of patients with seizure disorder to look for evidence of underlying structural abnormalities.

2.5.1. Anatomical areas of interest

The areas of interest when trying to detect or rule out an intracranial disease in association with epileptogenesis, are the cerebral hemispheres, basal nuclei, diencephalon, and the rostral portion of the mesencephalon, also referred to as the prosencephalon or forebrain. In terms of MRI these regions of the brain are called the supratentorial central nervous system, due to the rostral position of an imaginary line drawn parallel to the tentorium cerebelli (Bagley and Gavin 2009).

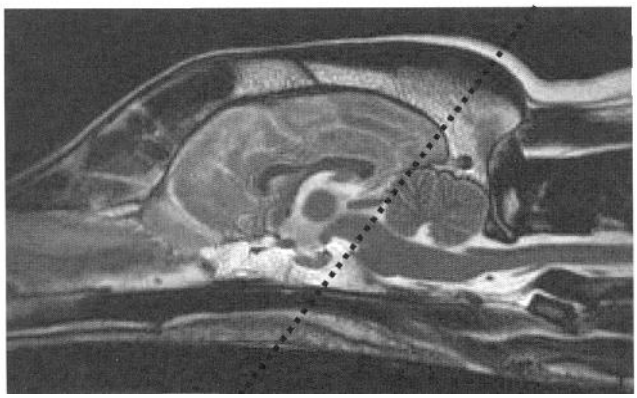


Figure 3: Sagittal, T2-weighted MR image of a dog brain. The dotted line represents the imaginary anatomical division between the supra- and infratentorial structures at the level of the tentorium cerebelli (adapted from Bagley and Gavin 2009, p. 24).

Lesions in the cerebrum are often found to be the cause of seizures, unless cerebral dysfunction is of indirect origin, like in increased intracranial pressure. It is therefore unlikely that a lesion found elsewhere in the brain is the cause of the seizure. The probability of finding intracranial lesions in dogs presented with recurrent seizures increases significantly in dogs older than five years. CT and/or MRI in these patients are much more important than in young patients without any neurological deficits, since it is unlikely to find evidence of structural brain disease in these young dogs (Smith et al. 2008). Most common found lesions under MR examinations in dogs with recurrent seizures are intracranial neoplasia (e.g. meningioma or glioma) and CNS inflammation involving the cerebrum (GME, neosporosis, toxoplasmosis) (Chandler and Volk 2008). All image appearances are compared with a standard or reference tissue at the time of imaging, and it is important to determine this standard when describing image characteristics. As a general rule when imaging the brain, the cerebral cortical elements are used as the standard tissue to which other anatomical structures and intracranial abnormalities are compared. This cortical or neuronal element is often relatively isointense (Bagley and Gavin, 2009).

2.5.2. Different sequences used in intracranial MRI

Standard high-field spin-echo sequences provides good contrast and spatial resolution for identification of most clinically relevant brain anatomy on selected images in transverse, sagittal and dorsal planes. Examples of such high-field spin-echo sequences are turbo spin echo (TSE) T2 and T1-weighted imaging (Leigh et al. 2008). In an article concerning reversible MRI abnormalities in dogs following seizures, the preferred sequences were T1 and T2-weighted images (Mellema et al. 1999). These were also the preferred sequences in a study on 76 dogs with epilepsy where they used a low field MR scanner (0.2T permanent magnet) (Smith et al. 2008). T2-weighted, fluid attenuated inversion recovery (FLAIR) and T1-weighted contrast enhanced (Gadolinium-DTPA – 0.1 mmol/kg) sequences in a 1.5T MR system were used when screening for hippocampal sclerosis in 58 dogs presented with epilepsy (Takayuki et al. 2010).

In summary, T2-weighted images are good as a general screening sequence for a variety of intracranial diseases. This is because most intracranial diseases are associated with edema that appears hyperintense on the T2-weighted image. Many intracranial diseases change the water content of the affected tissues, which can be either focal or diffuse. These changes may not be apparent in T1-weighted images.

FLAIR is used to null out the signals from fluids, which is useful to suppress signals from CSF. This makes lesions that are periventricular easier to detect. Free fluid when using FLAIR sequencing will appear dark while edematous tissue appears bright. FLAIR is used subsequently to T2 (and T1) weighted images (Bagley and Gavin 2009).

2.5.3. Intracranial MRI findings in dogs with seizures

Anomalous

In hydrocephalus the MR image will show the ventricular system filled with CSF as hypointense (darker) on the T1-weighted, and hyperintense (whiter) on T2-weighted imaging sequence.

MR is the image modality of choice when diagnosing canine lissencephaly antemortem. The image shows a smooth cerebral surface and a thick neocortex with corona radiata absent (Bagley and Gavin 2009).

Neoplasia

Space-occupying lesion, such as intracranial neoplastic disease, alters the anatomical structure of the brain. Brain tumours can be diagnosed using advanced imaging modalities such as CT or MRI. Specific tumour types will show a variety of imaging characteristics.

The most common brain tumour found in dogs is meningioma. These usually appear as broad based, extraaxial, contrast enhanced masses on MRI. They may contain hemorrhagic or mineralized regions. Meningiomas may have a varied appearance on the T1- and T2 weighted images. However, as a general rule they will appear hypointense/ isointense pior to administration of IV-contrast in the T1-weighted image, and hyperintense prior to contrast in T2-weighted images. Meningiomas usually appear as a solitary abnormality in dogs.

Gliomas include astrocytes and oligodendrogliocytes that arise from the supporting cells of the brain parenchyma. The MRI appearance of gliomas varies and enhancement after contrast is inconsistent. Commonly they appear hyperintense in T2- weighted images and hypointense in T1- weighted image.

Choroid plexus tumours are usually isointense on T1-weighted images and hyperintense on T2-weighted images. They tend to be located in and around the ventricular system, and may therefore cause an obstruction, which can result in obstructive hydrocephalus.

Tumours are often associated with cerebral edema which tends to follow the cerebral white matter that results in a crown like appearance of the lesion (Bagley and Gavin 2008).

Inflammatory and Degenerative

Encephalitis and meningitis of both infectious and non-infectious origin are often most obvious on T2-weighted and FLAIR imaging sequences. Here they appear as hyperintense regions. On T1-weighted images they appear iso-/hypointense before administration of contrast. In Infectious diseases such as toxoplasmosis, the lesion may be seen on T2-weighted and FLAIR images, but administration of contrast does not enhance the lesion. This can also be the case in GME where focal inflammatory mass lesion can resemble focal neoplastic disease on MR sequences (Bagley and Gavin 2009).

Degenerative diseases, like hippocampal sclerosis, can be seen as unilateral or bilateral atrophy of hippocampus and hyperintensity on T2-weighted and FLAIR images. These appear as hypointense regions on the T1-weighted images (Takayuki et al. 2010).

Reversible abnormalities following seizures

Reports in human medicine have shown that reversible MR imaging lesions follow seizure activity. Mellema et al. (1999) did a study of dogs presented with seizures; MRI was performed within 14 days of the last seizure and 10-16 weeks after starting anticonvulsant therapy. Lesions were found in the piriform/temporal lobes, characterized by variable degree of hyperintesity on T2-weighted images and hypointensity on T1-weighted images. The lesions identified in these dogs initially had a similar appearance on images, and on re-evaluation showed partial to complete resolution once seizure control was achieved (without use of anti-inflammatory or anti-microbial medication). This study therefore concludes that these lesions were a result of seizures activity and not the cause (Mellema et al. 1999).

2.6. Previously done retrospective studies on epilepsy

2.6.1. Jaggy and Bernardini (1998)

In this study 125 well documented cases of confirmed idiopathic epilepsy were evaluated retrospectively. A total of 2224 dogs with neurological symptoms that were referred to the small animal clinic at the University of Berne, 235 dogs with a history of seizures were selected. Out of these 235 dogs, 115 (49%) was diagnosed with idiopathic epilepsy. This diagnosis was based on a history of more than two seizures in the absence of other medical problems, normal physical and neurological examination, as well as clinicopathological analyses. Also a thorough knowledge of signalment, age of onset, incidence rate and classification of seizures was available. Owners was given a questionnaire were they gave a detailed description of the seizures, including preictal, ictal and postictal phases.

The mean age of the first seizure was 32 months with a peak value between one and five years. 83 of the dogs were male (8 neutered) and 42 females (17 neutered). There were 46 different breeds included in the study; 27 Labrador Retrievers, nine Golden Retrievers, seven German Shepards, four Malinois, four Border Collies, four St. Bernards and four Dachshunds.

2.6.2. Bush et al. (2002)

The aim of this retrospective study was to determine whether neurological examination findings, CSF analysis, or age at onset of seizures could be used to predict the result of MRI examination with respects to a normal or abnormal image. 115 dogs with seizures were included, all of which had undergone a neurological examination, CSF analysis and MRI examination. Age of onset of first seizure was also known. Dogs with abnormal CBC or serum biochemistry that could suggest an extracranial cause of seizures were excluded from the study.

The dogs ranged from six months to 15 years of age, average being 6.7 years. There were 57 males (38 neutered) and 58 females (46 neutered). Results of MRI was 54 (46%) normal and 61 (53%) abnormal. Results of neurological examination and CSF analysis in correlation with the MRI results can be seen summarized in **table 5**.

Table 5: Cross-correlation of results of a neurologic examination, results of CSF analysis, and results of MRI in 115 dogs examined because of seizures (Bush et al. 2000).

		No. of dogs (%)	
Neurological examination result	**CSF analysis results**	**Abnormal MRI results**	**Normal MRI results**
Abnormal	Abnormal	36 (97)	1 (3)
Abnormal	Normal	11 (73)	4 (27)
Normal	Abnormal	12 (43)	16 (57)
Normal	Normal	2 (6)	33 (94)

2.6.3. Smith et al. (2008)

In this study the main aim was to estimate the prevalence of intracranial abnormalities in 76 dogs with epilepsy, which were interictally normal, in a low field MR (0.2T). The results were 16 (21%) dogs with abnormal MRI, seven which were classified as incidental. In the remaining nine, six had space occupying lesions with characteristics of neoplasia, one with an arachnoid cyst, one with T2-hyperintense lesion near the mesencephalic aqueduct, with associated hydrocephalus. The last one had marked ventricular asymmetry with ipsilateral cortical atrophy.

When the dogs were subdivided into two groups, according to age; five of the 46 dogs (10.9%) was under the age of six, and 11 of the 30 dogs (37.7%) was older than six years, had

abnormal MRI scans. However, when they excluded the dogs with incidental abnormalities, only 1/46 (2.2%) dogs younger than six years was found to have a "significant" lesion on MRI, compared to 8/30 (26.7%) dogs older than six years. The age distribution is summarized in **table 6**.

Table 6: The table shows the number of dogs with normal and abnormal MRI scan in different age group (adapted from Smith et al. 2008).

Age	Normal	Abnormal
0-1	7	0
1-2	12	1
2-3	7	0
3-4	6	0
4-5	11	0
5-6	2	0
6-7	8	0
7-8	3	1
8-9	0	2
9-10	3	0
10-11	5	2
11-12	1	0
12-13	1	2
13-14	1	0
14-15	0	1
TOTAL	67	9

2.6.3. Pakozdy et al. (2008)

In this study 240 dogs with seizures were analysed retrospectively. The aim was to examine underlying aetiology and compare idiopathic epilepsy (IE) with symptomatic epilepsy (SE) concerning signalment, history, ictal patterns, clinical and neurological findings.

The diagnosis of SE was based on abnormal findings in CBC, serum biochemistry, CSF analysis, and structural changes in brain detected by CT/MRI. When possible histopathological examinations was also preformed.

The results of this study concluded that 115 dogs were diagnosed with IE, and 125 dogs with SE. The results are summarized in **table 7**.

Table 7: Classification and cause of seizure in dogs (n = 240)
(Adapted from Pakozdy et al. 2008)

Cause of seizures	Number of dogs	Percentage (%)
Idiopathic epilepsy	115	48
Intracranial neoplasm	39	16
Encephalitis	23	10
Brain anomaly	10	4.16
Brain degeneration	9	3.75
Toxicosis	9	3.75
Hepatoencephalopathy	8	3.33
Hypoglycaemia	7	2.91
Brain vascular disorder	7	2.91
Other extracranial disorder	5	2.08
Head trauma	3	1.25
Uremic encephalopathy	3	1.25
Electrolyte imbalance	2	0.83

3. Materials and Methods

3.1. Study population

This was a retrospective study of magnetic resonance imaging (MRI) of the brain, preformed on 74 dogs with a history of recurrent seizures. The MR examinations were conducted between March 2001 and February 2013 at the Institute of Diagnostic Imaging and Radiation Oncology, Kaposvar University. The aim of the MRI examination was to diagnose intracranial structural abnormalities as the possible underlying cause of the seizure disorder.

The study population consisted of 74 dogs, were six was mixed breeds, and 68 were pure breeds, (most common was the Labrador retriever). The represented breeds are summarized in the table below (**table 8**).

Table 8: Number of the different breeds included in this study.

Breed	**Number**
Labrador Retriever	10
Mongrels	6
Hungarian Vizsla	5
French bulldog, Bichon Bolognese, Dachshund, Beagle, Yorkshire Terrier	4
German Shepard, Bernese Mountain Dog, Cocker Spaniel	3
Pug, Boxer, Pekingese.	2
Malthese, Tervueren, Cavalier King Charles Spaniel, Caucasian Shepard, Pumi, Puli, Cane Corso, Dalmatian, Miniature Schnauzer, Mudi, Parson Russel Terrier, Skye Terrier, Westland Highland White Terrier, Bichon Havananese, Golden Retriever, Border Collie, Spitz, Hungarian Greyhound.	1

Of the 74 dogs there were 42 males, of which two were castrated and 32 females, of which two had undergone ovariohysterectomy. The age of the dogs ranged from six months to 13 years (average; 5.0 years). All dogs had recurrent epileptic seizures and were referred to Kaposvar from local veterinarians for a MRI examination.

3.2. Anaesthesia protocol

General anaesthesia was preformed for the whole duration of the MRI examination. Midazolam (Dormicum:EGIS, Hungary) at 0.5 ml/10 kgbw and 1% propofol at 6 ml/10 kgbw, both administrated intravenously, was used for induction. The patients were intubated to administer oxygen (1-2 l/min, depending on bodyweight) and positioned in sternal recumbency. For maintenance 1-3 vol % Sevoflurane was used.

3.3. MR imaging protocol

The MRI examinations were performed in a 1.5T field strength Siemens Magnetom Avanto MR equipment with owners consent. The MR sequences were acquired with the patient in sternal recumbency and followed the institute protocol for imaging of epileptic dogs;

- T2-weighted spin echo sequences in sagittal and transversal planes.
- 3D MP-RAGE T1 weighted sequences in sagittal plane.
- Reconstruction in transversal and coronal planes (slim slice reconstruction).
- FLAIR in transversal plane, and MRI-angiography.

Contrast used was 0.1 mmol of gadolinium-DTPA/kg. All the images have been interpreted by the radiologists employed at the institute, and were considered abnormal if abnormal anatomy or signal intensity or contrast enhancement was identified.

3.4. Data analyses

We retrospectively analysed the data of the study population (breed, age, gender) and the results of the MRI examinations (normal or abnormal, lesion type). We then compared our results with results of similar studies in the available scientific veterinarian publications. According to literature, the incidence of seizures due to intracranial abnormalities is increased if the dog is six years or older. We therefore compared the number of dogs with abnormal versus normal MRI after dividing them into two groups; dogs younger than six years and dogs six years or older.

4. Results

4.1. Population traits

Results of the MRI examinations gave 51 (69%) normal and 23 abnormal (31%) scans, the results are summarized in the **table 9**. We classified the dogs with a normal MRI with idiopathic epilepsy (IE), and the dogs with an abnormal MRI with symptomatic epilepsy (SE).

4.2. Aetiology

Of the 23 dogs with SE, there were 10 dogs with brain tumour, four with hydrocephalus, where one of these also had syringomyelia, two with Chiari-like malformation (**Fig 10**), two with dilated ventricles (**Fig 5**), and five dogs with the following; cerebral hernia, syringomyelia, frontal lobe atrophy (**Fig 8**), cerebellar infarct and encephalitis (**Fig 9**). Breed, age and gender for these 23 dogs are summarized in **table 10**. Of the ten dogs with brain tumour, six of them were Labrador retrievers (**Fig 4**).

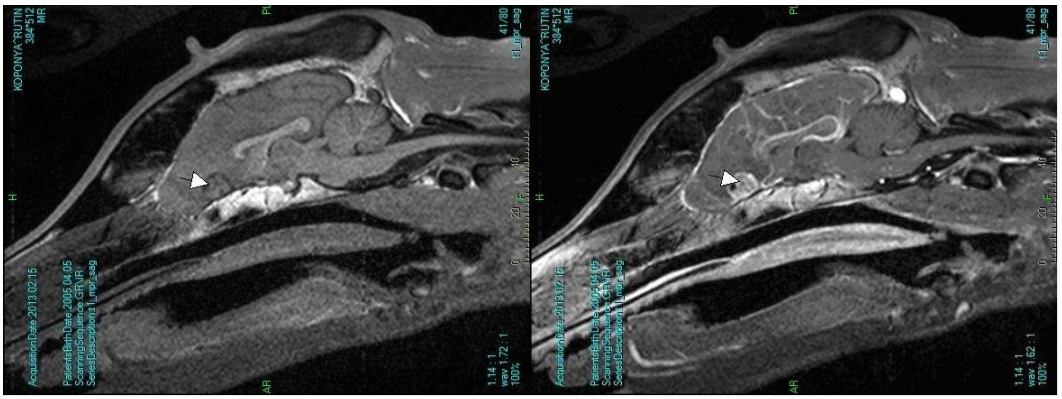


Figure 4a: before contrast administration b: after contrast administration

Figure 4a & b: Sagittal, T2-weighted MRI of an 11-year-old female Labrador retriever with a brain tumour (arrow).

Table 9: Dogs included in the study with result of MRI

Cases	Breed	Sex	Age	Clinical signs	Result
1	Beagle	M	0.8	seizures	Negative
2	Yorkshire terrier	Fs	1	seizures	Positive
3	Hungarian greyhound	F	1	seizures	Negative
4	WHWT	M	1.5	seizures	Positive
5	Boxer	F	1.5	seizures	Positive
6	Hungarian Vizsla	F	1.5	seizures	Negative
7	Labrador retriever	M	1.5	seizures	Negative
8	Mongrel	M	1.5	seizures	Negative
9	Pekinese	M	1.5	seizures	Negative
10	Yorkshire terrier	M	2	seizures	Positive
11	Dachshound	M	2	seizures	Positive
12	Bernese	F	2	seizures	Negative
13	Border Collie	F	2	seizures	Negative
14	Dachshound	F	2	seizures	Negative
15	Dalmatian	F	2	seizures	Negative
16	Mongrel	Fs	2	seizures	Negative
17	Dachshound	M	2.5	seizures	Positive
18	Yorkshire terrier	M	2.5	seizures	Positive
19	Hungarian Vizsla	F	2.5	seizure	Negative
20	Mongrel	F	2.5	seizures	Negative
21	Bichon Bolognese	M	2.5	seizures	Negative
22	Labrador retriever	M	2.5	seizures	Negative
23	Labrador retriever	M	2.5	seizures	Negative
24	Cocker spaniel	F	3	seizures	Negative
25	German shepard	F	3	seizures	Negative
26	Parson russel terrier	F	3	seizures	Negative
27	Beagle	F	3	seizures	Negative
28	Cane Corso	M	3	seizures	Negative
29	Maltese	M	3.5	seizures	Positive
30	Boxer	F	3.5	seizures	Negative
31	Dachshound	F	4	seizures	Negative
32	Beagle	M	4	seizures	Negative
33	Cocker spaniel	M	4	seizures, aggression	Negative
34	French bulldog	M	4	seizures	Negative
35	Pumi	M	4	seizures, aggression	Negative
36	CKCS	F	4	seizures	Positive
37	Pug	F	4.5	seizures	Positive
38	Bichon Havanese	F	4.5	seizures	Negative
39	Miniature Schnauzer	F	5	seizures	Positive
40	Caucasian shepard	M	5	seizures	Positive
41	French bulldog	M	5	seizures, stiffness	Positive
42	Puli	F	5	seizures	Negative
43	Skye terrier	F	5	seizures	Negative
44	French bulldog	M	5	seizures	Negative
45	Labrador retriever	M	5	seizures	Negative
46	Golden retriver	F	5.5	seizures, ↑ liver enzymes	Negative
47	Yorkshire terrier	M	5.5	seizures	Negative
48	Labrador retriever	M	6	seizures	Positive
49	Bichon Bolognese	M	6	seizures	Positive
50	Mudi	F	6	seizures	Negative
51	German shepard	M	6	seizures	Negative
52	Hungarian Vizsla	M	6	seizures	Negative
53	Mongrel	M	6	seizures	Negative
54	Pekinese	M	6	seizures	Negative
55	Spitz	M	6	seizures	Negative
56	Labrador retriever	M	6.5	seizures, paraesthesia	Positive
57	Labrador retriever	F	7	seizures	Positive
58	Bichon Bolognese	M	7	seizures	Negative
59	Pug	M	7	seizures	Negative
60	Hungarian Vizsla	M	7.5	seizures	Positive
61	Bichon Bolognese	M	8	seizures	Negative
62	Hungarian Vizsla	Mc	8	seizures	Negative
63	French bulldog	F	9	seizures	Negative
64	German shepard	M	9	seizures	Negative
65	Mongrel	M	10	seizures	Negative
66	Tevueren	M	10	seizures	Positive
67	Labrador retriever	Mc	10.5	seizures	Positive
68	Bernese	F	10.5	seizures	Negative
69	Labrador retriever	F	11	seizures	Positive
70	Labrador retriever	M	11	Seizures, ataxia	Positive
71	Bernese	M	11	seizures	Negative
72	Mongrel	F	12	seizures	Positive
73	Beagle	F	12	seizures	Negative
74	Cocker spaniel	F	13	seizures, excitement	Negative

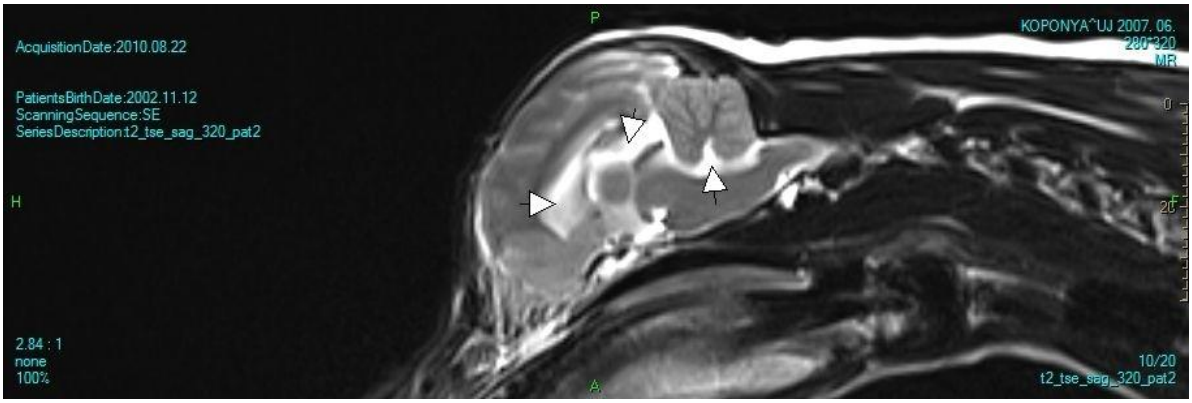


Figure 5: Sagittal, T2-weighted MRI in a 8 year old male Bichon Bolognese. All the ventricles (lateral, third and fourth and the aqueduct) are enlarged (arrows).

Table 10: Details of abnormal findings on MRI

Breed	Sex	Age (years)	Lesion
Yorkshire terrier	Fs	1	Chiari-like malformation
West Highland White Terrier	M	1.5	Cerebral hernia
Boxer	Fi	1.5	Hydrocephalus
Yorkshire Terrier	Mi	2	Hydrocephalus
Dachshound	Mi	2	Mild dialation of lateral ventricles
Dachshound	Mi	2.5	Hydrocephalus
Yorkshire Terrier	Mi	2.5	Hydrocephalus, syringiomyelia
Maltese	Mi	3.5	Left lateral ventrical enlargement
Cavalier King Charles Spaniel	Fi	4	Syringomyelia
Pug	Fi	4.5	Frontal lobe atrophy
Miniature Schnauzer	Fi	5	Brain tumour
Caucasian shepard	Mi	5	Brain tumour
French bulldog	Mi	5	Chiari-like malformation
Labrador retriever	Mi	6	Brain tumour
Bichon Bolognese	Mi	6	Encephalitis
Labrador retriever	Mi	6.5	Brain tumour
Labrador retriever	Fi	7	Brain tumour
Hungarian Vizsla	Mi	7.5	Cerebellar infarct
Tevueren	Mi	10	Brain tumour
Labrador retriever	Mc	10.5	Brain tumour
Labrador retriever	Fi	11	Brain tumour
Labrador retriever	Mi	11	Brain tumour
Mongrel	Fi	12	Brain tumour

Fi/Fs - Female intact/Female spayed.
Mi/Mc - Male intact/Male castrated.

In summary the abnormal MRI findings can be classified as 10 intracranial neoplasm, nine brain anomalies (hydrocephalus, chiari-like malformation and dilated lateral ventricles, cerebral hernia), one encephalitis, one brain degeneration (frontal lobe atrophy) and one brain vascular disorder (cerebellar infarct).

4.3. Age

When categorizing the dogs with normal scans (IE) according to age, we see a much higher frequency of dogs in the younger age groups (**Fig 6**). Were 34 of 51 dogs are younger than six years. The average age of the dogs with normal MRI scan was 4.8 years.

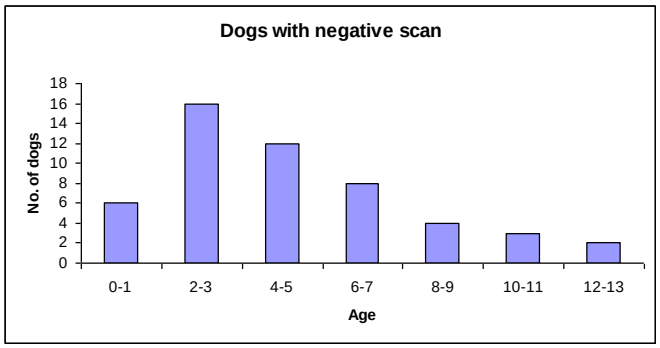
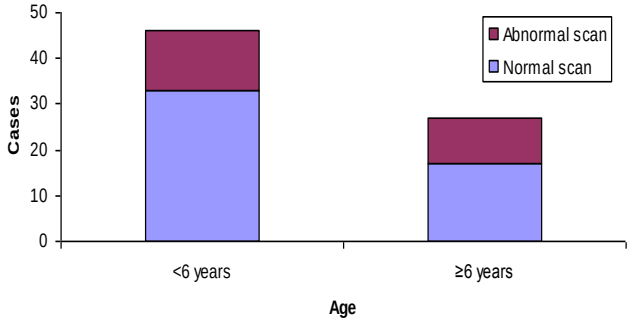


Figure 6: Graph showing the distribution of dogs with normal scans according to age.

Subdividing the dogs with abnormal MRI scan according to age revealed that 13/46 (27.6 %) dogs was less than six years old, and 10/27 (37%) dogs were six years or older (**Table 11**). Average age in dogs with abnormal MRI scan was 5.5 years.

Table 11: Table showing number of normal and abnormal scans in different age groups

AGE	NORMAL	ABNORMAL
0-1	2	1
1-2	9	4
2-3	10	2
3-4	6	2
4-5	5	4
5-6	8	2
6-7	2	2
7-8	2	1
8-9	2	0
9-10	1	1
10-11	2	3
11-12	1	1
12-13	1	0
TOTAL	51	23



4.4. Breeds

When studying the breeds that were represented with three or more individuals, we observe that there is four Labrador Retrievers, four Beagles, four Hungarian Vizslas, three German Shepards, three Bernese Mountain dogs, three Bichon Bolognese, three French Bulldogs and three Cocker Spaniel all with normal MRI (idiopathic epilepsy).

4.5. Gender

When analysing our data according to gender distribution we found that the IE group was made up of 28 (55%) males (one castrated) and 23 (45%) females (one spayed). The SE group consisted of 15 (65%) males (one castrated) and 8 (35%) females (one spayed) (**Fig 7**).

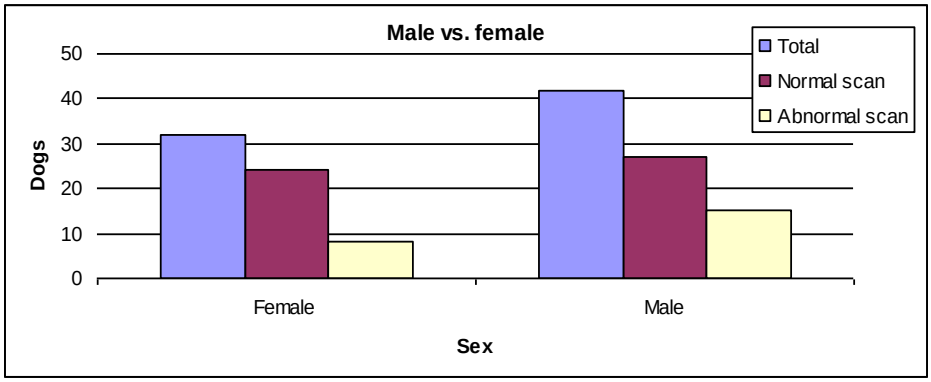


Figure 7: Graph showing the total male and female dogs, the number of normal scans and abnormal scans.

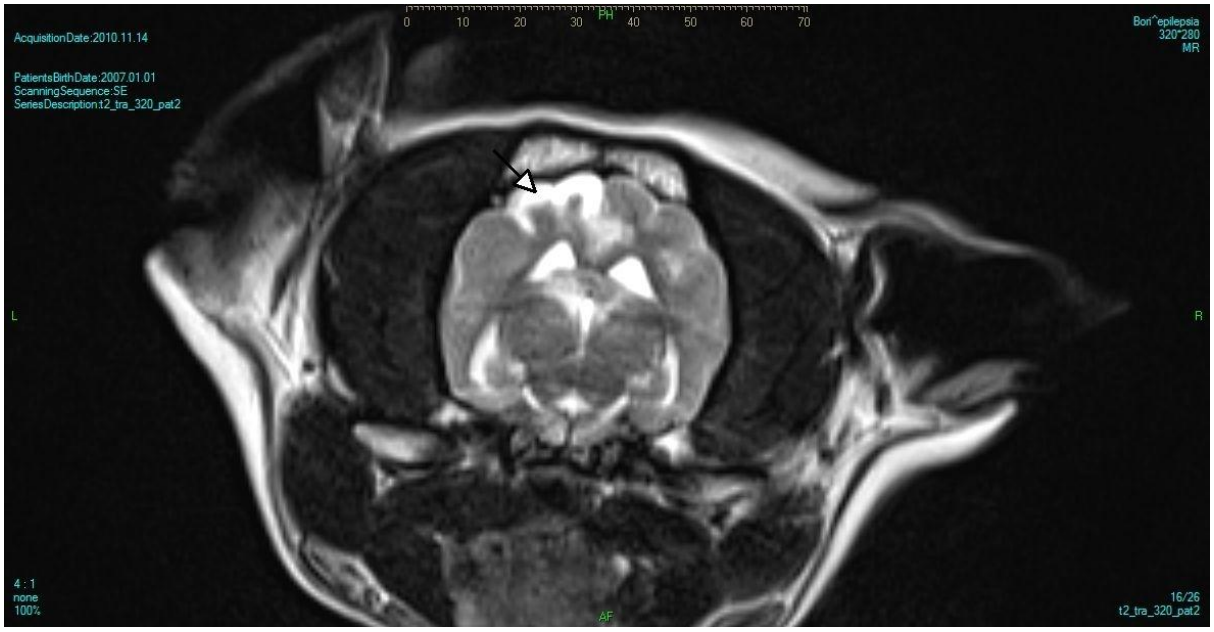


Figure 8: Transverse, T2-weighted MRI of a 4 year old pug with frontal lobe atrophy and consequential liquor filling (arrow).

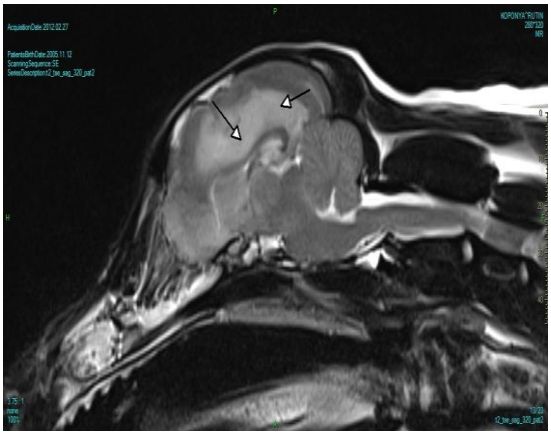


Figure 9: Sagittal, T2-weighted MRI of six year old male Bichon Bolognese with encephalitis, seen as higher signal intensity on image (arrows).

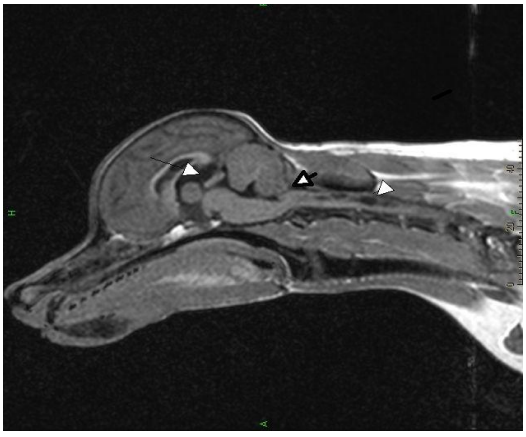


Figure 10: Sagittal, T1 weighted MRI of a one year old Yorkshire terrier with chiari-like malformation cisterna magna obstruction due to occipital hypoplasia (black arrow), hydrocephalus (white arrow) and syringomyelia (arrowhead).

5. Discussion

The diagnosis of idiopathic epilepsy is done by exclusion of all other known causes. This is done by a thorough history, clinical signs, negative laboratory (CBC, biochemistry, urinalysis, and CSF), EEG and different imaging techniques, where MRI plays a crucial role (DeLahunta and Glass 2009).

An important purpose of our study was to determine the ratio of idiopathic epilepsy (IE) and symptomatic epilepsy (SE) in our patient population compared to previously done studies.

In our study, 51 out of 74 dogs (69%) were suffering from IE. Jaggy and Bernardini (1998) found a much lower precentage, 125/235 (53%), of IE among dogs with seizures. Pakozdy et al. (2008) reported a similar proportion, 115/240 (48%), of IE among dogs. In these two studies IE was considered when the results of a physical and interictal neurological examination was normal and no underlying cause of the seizures had been identified in routine serum biochemistry, haematology, CSF analysis, computed tomography (CT) or MRI. All the dogs with IE were re-evaluated 6-24 months later where no abnormalities could be identified. The reason of the higher ratio of the idiopathic epilepsy in our study is unknown. One reason can be that the Hungarian dog population differs from those in other countries with regards to the prevalence of different breeds, but there are probably other more likely explanations. Since the institute of Diagnostic Imaging and Radiation Oncology in Kaposvar is not a veterinary clinic, and therefore only gets referral patients for MRI examination, no examinations or ancillary diagnostics test are done here. Due to this the results or accuracy of the diagnostic work up (if any) on the dogs included in this study is unknown. Also a detailed history and signalment of the seizures is lacking. The consequence of this may be that some of the dogs included in our study may suffer from an extracranial cause of seizures, and been wrongly diagnosed with IE. This might be a reason for the high percentage of dogs with IE in our study.

SE was diagnosed in 23 (31 %) dogs in or study based on an abnormal MRI. Pakozdy et al. (2008) reported a much higher incidence of SE, 125 out of 240 dogs (52%). This might be because they categorized extracranial causes of seizures as SE, and when excluding these dogs the number with SE is 91 (38%), which is still higher but more similar to our results.

Typically IE occurs between the age of six month and six years (Jaggy and Bernardini 1998). In this study we observed a higher prevalence of normal MRI scans in dogs between these ages, 34/51 (66.7%) (**fig. 6**). The average age was 4.8 years (range 9 months to 13 years) in the IE group, compared to 5.5 years (range 1 to 12 years) in the dogs with SE. Dogs between the age six months and six years in the SE group was 12/23 (52%). One reason for the high average age among the dogs with IE can be, as mentioned above, due to the missing diagnostic work up, resulting in dogs with extracranial cause of seizures to be included in the IE group. As the age of onset of the *first* seizure is important, and this information is lacking in our study, one can ask if our result would differ if this information was available. It is common practice that veterinarians refer only the problematic cases for further diagnostic imaging, and therefore the dogs in our study might have had seizures for a longer period when the MRI was preformed.

The average age of the SE group was lower (5.5 years) than expected when we compare it to Pakozdy et al. (2008) results, 7.38 years. This might be due to the high incidence of brain anomalies in our study, symptoms of brain anomalies (e.g. Chiari-like malformation and hydrocephalus) usually occur between six months and three years of age, with more severely affected dogs presenting before two years of age (Cagle 2010). In conclusion, similar to the results of other studies, the dogs with idiopathic epilepsy are generally younger than the dogs with symptomatic epilepsy.

Certain breeds are predisposed to IE, and a genetic inheritance is suggested. In our study we observed a higher incidence of Beagles (4/4), Hungarian Vizslas (4/5), German Shepards (3/3), Bernese Mountaindogs (3/3), and Cocker Spaniels (3/3) with IE. Except for the Hungarian Vizslas, all of the participants in the study of these mentioned breeds were diagnosed with idiopathic epilepsy. In the case of the Hungarian Vizsla that was diagnosed with cerebellar infarct it can be argued that this was an incidental finding since lesions in the cerebellum rarely cause seizures (Smith et al. 2008). If this is the case then all of the Vizslas included in this study had IE. The low number of each studied breed did not allow for a precise conclusion, but the result in this study is supported by the literature where Beagles (Bielfelt et al. 1971), Hungarian Vizslas (Patterson et al. 2003), German Shepards (Falcon et. al 2008), Bernese Mountain dogs (Kathman et al. 1999) and Cocker Spaniels (Baker et al. 1973) are among the breeds that show a predisposition of IE.

In our study population there were more male (43) than female (31) dogs. This was also the case in the IE group, with 28 males (55%) and 23 females (45%). We can find similar results in other studies (Jaggy and Bernardini 1998, Pakozdy 2008), but the difference between the number of male and female dogs is too insignificant to draw a conclusion. In our SE group the difference between male and female dogs is high, with 15 males (65%) and eight females (35%). There was no literature that supported this finding, and we concluded that this was a coincidental finding due to the few number of dogs taking part in this study.

We also analysed the prevalence of different abnormalities found in the 23 (31%) dogs diagnosed with SE. The most common aetiology was intracranial neoplasia, which occurred in 10 of the 23 dogs (43.4%), which is 13.5% of the total study population. This is similar to the results of previous studies. Pakozdy et al. (2008) reported that 38% of 240 dogs with seizures had an underlying brain abnormality. As in our study, neoplasia was the most common abnormality with 42.8%, making the incidence 16.2% of the total study population. Smith et al. (2008) reported that out of 76 interictal normal epileptic dogs, 21% was found to have brain abnormalities, 37.5% out of them were neoplasia. The number of abnormal MR images was lower than what we found in our study, but this was to be expected since the aim of that study was performing MRI on dogs that had been diagnosed with idiopathic epilepsy. This diagnosis was based on a normal physical and neurological examination, and normal ancillary diagnostic tests. Another reason for the relative lower number in that study can be that the MRI scanner used had a 0.2 T permanent magnet. While the images using this instrument are excellent for identifying large structural lesions, subtle lesions are likely to go undetected (Smith et al. 2008), though this is unlikely since the abnormal changes in our study was large structural lesions.

The occurrence of intracranial neoplasm increases significantly in dogs five years or older, and are uncommon in dogs less than five years of age (Bagley et al. 1999). This was in accordance to our results, as all 10 dogs with brain tumour was five years or older (average, 8.4 years). Interestingly, in our study we found a high number of Labrador retrievers with brain tumours. Out of the 10 dogs that had brain tumours, six of them were Labrador retrievers, while there were only 10 Labradors in total in our study. Labradors are among the dog breeds that are predisposed to IE (Jaggy et al. 1998), but this does not explain the overrepresentation of Labradors with brain tumours in our study. Snyder et al. (2006) suggest that intracranial neoplasm occurs more often in Labradors (11/173), though compared with other breeds like mixed breeds (56/173), golden retrievers (21/173) and boxers (18/173) they

are not the most predisposed breed. Though our finding was much higher than the result in the Snyder et al (2006) study, this can be due to the few cases of intracranial neoplasia in our study. Also, if we had a larger study population the result might show a more even distribution among the different breeds.

In our study hydrocephalus was the second most common intracranial abnormality with four cases. The affected breeds were two yorkshire terriers (one which also had syringomyelia) one boxer and a dachshund. Toy and brachycephalic breeds are predisposed to congenital hydrocephalus (Chandler and Volk 2008). Our result differs from the literature, where the second most common intracranial cause of seizures is inflammatory brain disorders of infectious or non-infectious origin (Chandler and Volk 2008). Pakozdy et al. (2008) reports the same as the literature, were 23 of 91 dogs (25%) with symptomatic epilepsy had encephalitis. Only 10 out of 91 dogs (11 %) had a brain anomaly, compared to our study's nine out of 23 (39%). Since inflammatory brain disease usually has a rapid progression with severe clinical signs and a poor prognosis, the availability of the MRI is important. The MRI used in the current study is located at a human research facility 200 km outside Budapest and is mainly used for animals on Sundays. This may be a contributing reason for the low number of inflammatory brain disorders in our study.

Chiari-like malformation was found in two dogs, both without syrinx. This is most common in Cavalier King Charles Spaniel (CKCS) where the incidence can be as high as 95%. Surprisingly the only CKCS in our study had a normal MRI of the brain, but on the MRI of the spine it was found to have syringomyelia. CKCS has an increased incidence of syringomyelia, but usually in connection with Chiari-like malformaion. Syringomyelia can be an incidental finding, since it usually does not cause seizures. Idiopathic epilepsy is also common in this breed (Rusbrigde et al. 2006). The two dogs that did have Chiari-like malformation were a French bulldog and a Yorkshire terrier. According to literature this disease is common in dogs with shortened foreskulls, which includes brachycephalic and miniature breeds, like French bulldog and Yorkshires terrier (Cagle 2010).

The high number of brain anomalies in this current study might be incidental. Smith et al. (2008) classified seven of their abnormal MRI scans as incidental since further diagnostic tests did not support a clinical significance to the seizure activity. Among these were two Chiari-like malformations, without concurrent syringomyelia, due to the implausible cause of seizures in view of which part of the brain that is affected. They also argued that since

asymmetry and/or mild enlargement of the lateral ventricles are relatively common in many breeds, when it occurs without forebrain deficits it is reasonable to consider these as non-significant findings.

The main limitation with this study was, as mentioned above, the lack of, or unknown, diagnostic work-up of dogs included. In similar retrospective studies of dogs with seizures, a thorough general and neurological examination, ancillary diagnostic test like CBC, serum biochemistry, urinalysis and abdominal and thoracic imaging done by x-ray and/or US was a prerequisite for dogs to be included. CSF has also been performed in these studies (Smith et al. 2008, Pakozdy et al. 2008, Jaggy and Bernardini 1998, Bush et al. 2002). In Bush et al. (2002) the MR images were examined by at least one board-certified neurologist, and the image was re-evaluated if the result of the neurological examination and/or CSF was considered abnormal. Due to this limitation, dogs with extracranial cause of seizures were unlikely to be identified and were therefore diagnosed as having IE. This will increase our number of dogs diagnosed with IE.

6. Conclusion

Based on the result of our study idiopathic epilepsy occurs more frequent that symptomatic epilepsy. Dogs that are diagnosed with idiopathic epilepsy are usually younger than six years. Certain breeds have a higher incidence of idiopathic epilepsy, in our study the Hungarian Vizsla, Beagle, German Shepard, Bernese mountain dogs and Cocker spaniel were more likely to have a normal MRI scan.

In older dogs the incidence of symptomatic epilepsy is increased, especially if the dog presents with other neurological sign. The most common intracranial abnormality is neoplasia, and the prevalence increases significantly after five years of age.

In our study we also found that there were a higher prevalence of male dogs presented with seizures, and the presence of an intracranial abnormality was more frequent in male dogs. But this is believed to be incidental due to the few dogs taking part in the study.

The gold standard for brain imaging is MRI, but since the aetiology of seizures are so complex, an accurate diagnosis cannot be obtained with MRI alone. In our study, three dogs presented with other neurological signs, all of these dogs had intracranial structural abnormalities. This highlights the importance of a thorough neurological examination for the possible diagnosis/exclusion of IE. A thorough physical examination and ancillary diagnostic test, like haematology, biochemistry, urinalysis, and thoracic and abdominal imaging is also necessary to rule out extracranial cause of seizures.

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