




# Prevalence of seizures in dogs and cats with idiopathic internal hydrocephalus and seizure prevalence after implantation of a ventriculo-peritoneal shunt

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## Abstract

**Background:** Seizures are considered a clinical sign in dogs with internal hydrocephalus but are not found in recent studies. Seizure prevalence due to ventricular enlargement and the prevalence of postoperative seizures in animals is not known.

**Objectives:** To determine seizure prevalence in dogs and cats with idiopathic internal hydrocephalus, to identify risk factors for seizure development, and to determine seizure prevalence in a 2-year period after ventriculo-peritoneal shunting (VPS).

**Animals:** Records and MRIs of 197 animals from 2001 to December 2019 were investigated. A total of 121 animals (98 dogs and 23 cats) were included in the study.

**Methods:** A retrospective multicenter case cohort study was conducted. Databases were searched for dogs and cats with internal hydrocephalus. MRI and CSF examinations were evaluated for signs of additional underlying disorders. Prevalence of seizures was estimated for animals showing only hydrocephalus internus. Risk factors were evaluated according to age, morphometric and morphological findings in the brain. All animals that underwent surgery were reexamined 2 years after surgery.

**Results:** One hundred twenty-one animals (98 dogs and 23 cats) with internal hydrocephalus met the inclusion criteria. Seizure prevalence in dogs and cats with internal hydrocephalus was low (1.7%; <5.8% CI 95%). Seizures were not observed in the 2-year period after surgery.

**Conclusion and Clinical Importance:** Seizure prevalence in dogs and cats diagnosed with hydrocephalus internus is low. Seizures in association with VPS do not seem to be a complication of the procedure.

## KEYWORDS

canine, magnetic resonance imaging, ventriculomegaly, volumetry

**Abbreviations:** CSF, cerebrospinal fluid; FLAIR, fluid-attenuated inversion recovery; IVP, intraventricular pressure; MRI, magnetic resonance imaging; TE, echo time; TR, repetition time; VBR, ventricle brain ratio; VPS, ventriculo-peritoneal shunting.

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## 1 | INTRODUCTION

Internal hydrocephalus is 1 of the most common malformations of the central nervous system in dogs<sup>1-3</sup> characterized by accumulation of cerebrospinal fluid (CSF) and enlargement of the ventricular system.<sup>4-6</sup> Hydrocephalus can occur when the normal CSF flow pathway becomes obstructed, leading to a diagnosis of noncommunicating hydrocephalus. In contrast, communicating hydrocephalus is diagnosed with patent ventricular flow.<sup>7</sup> Obstruction to CSF flow can occur secondary to tumors, hemorrhage, inflammation, or malformations, but can also be present without any obvious cause (primary or idiopathic hydrocephalus).<sup>8</sup>

Diagnosis of hydrocephalus is more complex than radiological presentation of large ventricles.<sup>9</sup> It is important to note that ventriculomegaly can be seen in neurologically normal dogs.<sup>10-12</sup> The presence of clinical signs<sup>13</sup> and/or findings indicating high intraventricular pressure (IVP) on magnetic resonance imaging (MRI)<sup>14</sup> can help to support a diagnosis of clinically relevant hydrocephalus. As the presence of clinical signs is mandatory, the type of associated signs must be clearly characterized in order to avoid false diagnoses and inappropriate treatment. The most common clinical signs reported are visual impairment, obtundation, ataxia, behavioral changes, and strabismus. Head tilt and nystagmus can be associated with distension of the fourth ventricle.<sup>1-5</sup>

Hydrocephalus was also reported to carry the potential to evoke seizures in companion animals.<sup>13,15-18</sup> Prevalence of seizures in clinical investigations of hydrocephalus in dogs and cats varies between 16%<sup>19</sup> and 33%,<sup>20,21</sup> but these studies do not distinguish between the type of hydrocephalus (congenital vs acquired, communicating vs noncommunicating hydrocephalus) or evaluate the presence of additional brain disorders in these animals.<sup>22</sup> In contrast to other studies, seizures were not found in a recent investigation involving large case series.<sup>23</sup> Seizures are also not documented in experimental hydrocephalus in dogs and cats.<sup>24,25</sup>

Seizures occur in shunt-treated children with hydrocephalus.<sup>26,27</sup> The underlying mechanisms remain undetermined. Injury to brain tissue during penetration by the ventricular catheter through the cortex and the presence of an intracranial foreign body and associated immunologic reactions are thought to relate to seizure development.<sup>26,27</sup>

The first aim of this study was, therefore, to investigate seizure prevalence in dogs with internal hydrocephalus after careful exclusion of other diseases or morphological aberrations. The second aim of this study was to document the seizure prevalence that may occur after ventriculo-peritoneal shunting (VPS) in a large case series. We hypothesize that the prevalence of seizures is low in animals with internal hydrocephalus if meningoencephalitis of unknown origin (MUO) and other diseases are excluded, and we hypothesize that the prevalence of postoperative seizures is also low.

## 2 | MATERIALS AND METHODS

### 2.1 | Case selection and study criteria

Two clinics participated in this retrospective case control study; the Department of Veterinary Clinical Science, Small Animal Clinic,

Justus-Liebig-University Giessen, Germany and the Department of Internal Diseases with a Clinic for Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Wrocław, Poland. At each institution, medical record databases were searched for records with a diagnosis of internal hydrocephalus dated January 2001 to December 2019. Data collected from the records included the animals' age in months at the time of diagnosis, breed, sex, body weight, neutering status, clinical signs, CSF examination, and if surgery was performed after diagnosis. Data of the neurological status at initial examination and reexaminations were retrieved. If seizures had occurred, semiology and frequency of seizures were recorded. Results of further diagnostic tests including complete blood counts, serum biochemistries, or CSF analysis were obtained.

### 2.2 | Image analysis

All MRI datasets were retrieved from the relevant Picture Archiving and Communication System and evaluated retrospectively by a board-certified neurologist (MJS) and radiologist (SS). Study numbers were assigned to all animals so that the observers were blinded to the identity of the animals and their clinical history including the presence of seizures. All images were reanalyzed and the presence of any deviation from normal brain architecture beyond ventricular distension was recorded, if identified. Furthermore, the images were evaluated for morphological and morphometric criteria allowing grading of ventricular enlargement and the presence of IVP. These morphological criteria were the flattening of gyri and sulci, deformation of the interthalamic adhesion, disruption of the internal capsule, dilatation of the olfactory recess, and presence of periventricular edema. Corpus callosal height was measured and assessment of lateral ventricle size was performed using a ventricle/brain ratio (VBR).<sup>14</sup>

Approval from the ethics committee of the Justus-Liebig-University was not sought as retrospective studies of images and records stored in the archive are not subject to ethical review.

### 2.3 | Inclusion criteria

Animals with a complete history of clinical signs and onset (as well as the presence or absence of seizures) of seizure, signalment, medical record (including at least general and neurological examination), MRI and CSF examinations and a diagnosis of hydrocephalus internus were included in the study. Diagnosis of a hydrocephalus internus was based on the presence of any clinical signs and further morphological and morphometrical imaging criteria described by Laubner et al.<sup>14</sup> Hydrocephalus was diagnosed in dogs and cats with a VBR greater than 0.62 and if at least 2 or more of the following morphological criteria were present: flattening of gyri and sulci, deformation of the interthalamic adhesion, disruption of the internal capsule, dilatation of the olfactory recess, and presence of periventricular edema.<sup>14</sup> All owners were asked for the presence or absence of seizure events and seizure semiology, if they were present. Video records were also

evaluated if present. If seizure events were not documented in the medical history an absence of seizures was proposed.

In order to determine the true prevalence of seizures associated with hydrocephalus alone, dogs and cats were excluded when there were lesions anywhere in the brain with a hyperintense signal in T2 and fluid-attenuated inversion recovery (FLAIR) and a contrast uptake of these lesions after administration of intravenous Gadolinium. Animals with a lack of clinical history, signalment or incomplete medical records (general or neurological examination), or incomplete imaging studies were excluded. Series with inadequate image contrast and spatial resolution or incomplete series were excluded from the study. Finally, dogs and cats were excluded if there were abnormalities on routine CSF analysis (dogs: <5 cells/ $\mu$ L; protein: <300 g/L; cats: <8 cells/ $\mu$ L; protein: <300 g/L) or no CSF analysis was performed. Follow-up information was collected only from animals that underwent VPS placement.

## 2.4 | Magnetic resonance imaging

Imaging was performed using a 1.5 or 3.0 Tesla high field MRI scanner (Phillips Intera Gyroscan, Philips Healthcare, Hamburg Germany; Siemens Verio). Images included at least sagittal, transverse, and dorsal T2-weighted images (Turbo Spin Echo, repetition time [TR] 2900 ms, echo time [TE] 120 ms, slice thickness 3 mm), transverse FLAIR sequences, gradient echo-sequences as well as T1-weighted pre- and post-contrast medium administered images (TR 588, TE 15, slice thickness 1 mm). The field of view measured 180  $\times$  180 mm in small dogs and 210  $\times$  210 mm in large dogs. The matrix was 288  $\times$  288 in small dogs and 384  $\times$  384 in large dogs, leading to an in-plane pixel size between 0.625  $\times$  0.625 mm and 0.54  $\times$  0.54 mm.

Breed	Nr.	Breed	Nr.
Chihuahua	24	Dachshund	1
Mixed-breed	17	Keeshond	1
French Bulldog	9	Miniature Pinscher	1
English Bulldog	5	Miniature Schnauzer	1
Maltese	4	Peruvian Hairless Dog	1
Jack Russel Terrier	3	Pomeranian	1
German Shepherd	3	Pug	1
Golden Retriever	3	Rhodesian Ridgeback	1
Australian Shepherd	2	Rottweiler	1
Austrian Hound	2	Shih Tzu	1
Border Collie	2	Tibetan Spaniel	1
Bull Terrier	2	West Highland White Terrier	1
Labrador Retriever	2	Whippet	1
Russkiy Toy	2	Cats	
Yorkshire Terrier	2	Persian	14
Boston Terrier	1	European Shorthair	7
Boxer	1	British Shorthair	1
Cavalier King Charles Spaniel	1	Ragdoll	1

Abbreviation: Nr., number of animals included.

## 2.5 | Shunting procedures

VPS was performed using a commercially available shunt system (miniNAV and paediGav Miethke GmbH & Co KG, Potsdam, Germany) as described elsewhere.<sup>11</sup> The shunt system in all dogs and cats included a ball valve with variable opening pressures.

## 2.6 | Statistical analysis

Statistical analysis was performed using a commercial statistical software package (BMDP Statistical Software, Los Angeles, California). Seizure prevalence was assessed and a confidence interval of 95% was determined for animals diagnosed with hydrocephalus internus and for dogs and cats that underwent VPS. Multiple logistic regression was used to evaluate morphological and morphometric risk factors for seizures in dogs and cats with hydrocephalus internus.

## 3 | RESULTS

Records and MRIs of 197 animals from 2001 to December 2019 were investigated. From this cohort, 98 dogs and 23 cats had no relevant intracranial lesions on MRI other than communicating hydrocephalus and CSF results (cells <5/ $\mu$ L and protein <300 g/L), as well as blood examination were within normal limits. These animals were included in the study. Of the dogs, 32 were female (24 intact, 8 neutered) and 66 were male (54 intact, 12 neutered). A summary of the included breeds is listed in Table 1. The median age of the animals was 10 months (0.08-168 months). The median body weight of the dogs

**TABLE 1** Breeds of dogs and cats included in the study

**TABLE 2** Summary of animals with seizures, age, and morphometric measurements of the study group and excluded animals

Clinical signs	Study group (121 animals)	Excluded animals (76 animals)
Seizures	2 (1.7%)	26 (34.7%)
Median age (months)	10 (0.08–168)	32 (1–164)
Morphometric measurements		
Mean VBR	0.79	0.66
Mean CcH	11.6 mm	7.1 mm

Abbreviations: CcH, corpus callosal height; VBR, ventricle brain ratio.

was 5.6 kg (0.7–58 kg) and the median body weight of the cats was 2.9 kg (0.5–4.4 kg) (Table 2).

Seventy-six animals (63 dogs and 13 cats) were excluded due to missing CSF examination (33) and/or due to additional findings on MRI as follows: inflammatory lesions ( $n = 22$ ), neoplastic lesions ( $n = 13$ ), porencephaly ( $n = 6$ ), suspected storage disease ( $n = 2$ ), midline defects ( $n = 4$ ), ischemic midbrain infarct ( $n = 1$ ), epidermoid cyst ( $n = 1$ ). Seizures were observed in 26 (26/76) animals. They were excluded from further analysis due to missing morphological signs of increased IVP (10), missing CSF examination (7), inflammatory changes in CSF and/or MRI (6), neoplasia (3), porencephaly (2), brain atrophy with suspected storage disease (1), dermoid cyst (1), metabolic toxic changes (1). The number of seizures varied from 1 seizure before presentation (5), 1 to 10 seizures before presentation (12) and more than 10 seizures before presentation (9). Seizures were generalized tonic-clonic (19) and focal (7).

VPS was performed in 59 (47.1%) of the animals (53 dogs and 6 cats), all animals at 1 clinic. Follow-up information was available for 57 animals. None of the animals that experienced seizures underwent surgery.

### 3.1 | MRI findings in the study group

All 121 animals were diagnosed with a congenital, communicating hydrocephalus internus. Forty-three (35.5%) animals had dilatation of the lateral cerebral ventricles (biventricular hydrocephalus), and 49 (40.5%) additionally showed dilatation of the third ventricle (triventricular hydrocephalus). Twenty-nine (24%) animals had dilatation of all cerebral ventricles (tetra-ventricular hydrocephalus). Supracollicular fluid accumulation was present in 42 (34.7%) cases. Syringomyelia was found in 24 (19.8%) animals. Morphological signs of increased IVP were observed as follows: periventricular edema in 99/121 (81.8%), flattening of the gyri and sulci in 99/121 (81.8%), deformation of the interthalamic adhesion in 98/121 (81%), dilatation of the olfactory recess in 88/121 (72.7%), and disruption of the internal capsule in 86/121 (71.1%) of the dogs and cats. The median VBR was 0.79 (0.56–0.98) and the median corpus callosum height was 11.6 mm (3.5–30 mm) (Table 2). None of these morphometrical or

morphological parameters could be identified as possible risk factor of seizure development in dogs and cats with internal hydrocephalus ( $P > .05$ ).

### 3.2 | Clinical signs in the study group

The most common clinical signs at time of presentation were ataxia in 53 (43.8%) and vision deficits observed in the clinical neurological examination and by the owners in 45 (37.2%) animals. Seizures occurred in 2 (2/121) animals of the study group, this accounts for a seizure prevalence of 1.7% (<5.8% with a confidence interval of 95%). The first was a 10-months old female intact Chihuahua with idiopathic triventricular internal hydrocephalus and a history of seizures as the only clinical sign that started at 7 months of age with 1 seizure per month. Seizure type was generalized tonic-clonic with loss of consciousness lasting for 1 minute. Ventricular dimensions were moderately increased (VBR of 0.76), morphological criteria included a deformation of the interthalamic adhesion, flattening of the gyri and sulci of the cerebral hemispheres, disruption of the internal capsule and distention of the olfactory recess. The other dog was a 12-year-old Miniature schauzer with a history of acute onset of generalized tonic-clonic seizures. Seizures were the only clinical sign in this dog. MRI showed a triventricular hydrocephalus internus with a VBR of 0.79, the dog also showed a deformation of the interthalamic adhesion and flattening of the gyri and sulci as signs of increased intracranial pressure.

### 3.3 | Results of postoperative investigation

From 121 dogs and cats, 59 were treated with VPS. Two of the VPS treated animals were lost to follow-up. The remaining dogs (51) and cats (6) that underwent surgery were regularly reexamined after VPS placement. None of the dogs that underwent VPS experienced seizures during a follow-up time of at least 2 years (range 2–11 years).

## 4 | DISCUSSION

Seizures have been reported to be a common clinical sign in investigations of dogs and cats with internal hydrocephalus.<sup>13,15–18</sup> In contrast, seizures were not found in a more recent study.<sup>23</sup> A possible explanation for this discrepancy could be the presence of secondary undetected diseases in addition to hydrocephalus that are, in fact, the underlying cause for epileptogenesis. Here, we evaluated the true prevalence of seizures as a clinical sign in dogs and cats with idiopathic internal hydrocephalus after carefully ruling out additional brain diseases. This prevalence was 1.7%, which is far less than reported in previous studies.

The acute pathological effects on the brain and clinical signs in association with hydrocephalus are mediated through a combination of stretching of the periventricular white matter, as well as impaired

perfusion by periventricular blood vessels<sup>28,29</sup> and transependymal bulk flow of CSF into the brain tissue leading to interstitial edema and impaired parenchymal metabolism.<sup>30</sup> In the chronic state of the disease and even after VPS, delayed or impaired maturation of myelination<sup>31</sup> and maturation of inhibitory systems in the neuronal network can occur. A relationship between seizures and raised IVP has been proposed in children.<sup>32</sup> Dogs and cats have been animal models for the study of internal hydrocephalus in the past. Although the development of ventricular dilatation in this form of hydrocephalus is very progressive leading to an increase of IVP to 4-fold the normal level, seizures were never documented in these animals.<sup>33,34</sup> On the other hand, it was shown that dogs with internal hydrocephalus must not have increased IVP.<sup>35</sup> It must therefore be questioned whether increased IVP, ventricular distention and associated parenchymal damage alone can really evoke seizures in affected animals.

If seizures are not the consequence of IVP or ventricular changes, they might be associated to the underlying causes of hydrocephalus. Etiologies of hydrocephalus in dogs and cats include intrauterine infections, perinatal hemorrhage, and associated malformations that may impair CSF flow.<sup>8</sup> Hydrocephalus can be associated with “subclinical” periventricular bacterial encephalitis in dogs, which may trigger seizures.<sup>36,37</sup> Parainfluenza and Paramyxovirus have been shown to be capable of inducing encephalitis in neonatal dogs<sup>38</sup> and may lead to aqueductal stenosis. Seizures were also observed in some of these animals. Diagnosis of these different etiologies is hardly possible postpartum in a living animal and the influence of these underlying causes remains undetermined in dogs and cats.

In a young adult dog with hydrocephalus, seizures might have another cause. Meningoencephalitis of unknown origin (MUO) is very common in brachycephalic dogs,<sup>39,40</sup> and potentially underdiagnosed, especially if computed tomography or even low field MRI was used for diagnosis.<sup>41</sup> Enlarged ventricles are also a very common finding in brachycephalic dog breeds and have been referred to as “ventriculomegaly” to demarcate this finding from relevant internal hydrocephalus.<sup>14</sup> It is found in dogs of all age.<sup>8,11</sup> Differentiation of these 2 terms is important, because ventriculomegaly does not cause clinical signs.<sup>14</sup> The diagnosis of ventricular distention, which can be severe,<sup>14</sup> is obvious for the interpreter and might be falsely interpreted as the underlying cause for clinical signs in these animals. We have seen co-occurrence of profound ventriculomegaly and MUOs in numerous cases. In dogs that are referred for surgical treatment to our clinic, in which seizure activity is the only clinical sign, we consider idiopathic epilepsy and/or inflammatory brain disease the more likely cause of epileptic seizures until proven otherwise. The presence of underlying inflammatory/infectious diseases that were not detected might explain the discrepancy between the much higher prevalence of seizures found in other studies and the present investigation. Parenchymal changes associated with MUO might have been interpreted as periventricular edema, or were not visible at that stage of the disease. Contrast studies and CSF examination that could reveal inflammatory diseases were not always performed.<sup>19-21</sup>

In children with internal hydrocephalus, seizures are also associated with the etiologies of hydrocephalus, with associated pre- or

post-natal infections (50%) being the main risk factors,<sup>42</sup> or with malformations of the cerebral cortex in addition to ventricular distention (30%).<sup>42-44</sup> Hydrocephalus associated parenchymal changes alone are not recognized as epileptogenic lesions in pediatric neurology.<sup>42</sup>

On the other hand, children are very prone to develop seizures after implantation of VPS,<sup>43,45</sup> whereas postoperative seizures were not observed after surgery in the dogs and cats included in this investigation. In humans, shunt-related seizures are reported in up to 48% and are suggested to be due to infections or hemorrhage associated with the placement of the VPS.<sup>26,27</sup> Shunt-related infections are not commonly observed in dogs and cats treated with VPS<sup>20</sup> compared to humans,<sup>27</sup> which might also explain the differences in shunt-related seizure activity. However, in some children seizures were observed after VPS without a present infection or hemorrhage as the underlying cause.<sup>27</sup> Shunt placement allows the brain tissue to restore and potentially repair damage that occurred under ventricular distention.<sup>28</sup> The occurrence of shunt-related seizures might be associated with the reparation of the tissue, for example, reorganization of the neuronal network, synaptic regrowth, and alterations in neurotransmitter concentrations which was not possible before VPS implantation. Another explanation could be the injury to the brain parenchyma caused by the penetration of the ventricular catheter through the cortex or an immunologic reaction to the ventricular catheter itself.<sup>42</sup> A pediatric shunt system and more or less the same surgical technique in animals as described in children was used for the animals in our cohort, which makes a basic procedural difference unlikely. The reason for the absence of postoperative seizures in animals remains undetermined.

Although this study includes a large number of cases, it has some limitations. First, the retrospective character of the study and the fact that the cases were selected from different institutes means that there was no standardized procedure of questionnaire, or MRI protocol. However, the reevaluation of MRI data was obtained by the same persons using clear morphometric and morphological criteria to assess the presence or absence of hydrocephalus internus and other imaging findings. All dogs and cats that underwent VPS placement and had a complete follow-up were managed at the same institute. Another limitation is the lack of a standardized owner questionnaire and the definite documentation of the absence of seizures in all cases. The absence of seizures is defined by a lack in the clinical history and it is strongly dependent on the owner's recognition. Video data were evaluated if present, but were absent in most of the cases. It is therefore possible that owners did not recognize seizures in their animals. In dogs and cats that underwent VPS placement it seems unlikely that seizures were part of the clinical presentation as owners were interviewed at least 2 times without mentioning seizure events in any of these animals. It however cannot be excluded completely.

The rigorous criteria for exclusion of cases might have had an impact on the prevalence determined in the present study. Dogs with internal hydrocephalus and abnormalities in CSF examination or missing CSF analysis were excluded. There is limited data concerning CSF abnormalities in association with idiopathic internal hydrocephalus in animals. A mild increase in total nuclear cell counts (8 cells/ $\mu$ L) was

found in CSF of dogs with syringomyelia attributed to parenchymal damage of the spinal cord.<sup>46</sup> Damage of periventricular white matter could also lead to elevation in cell counts in absence of inflammatory diseases, however, cytological examination in humans with idiopathic hydrocephalus are essentially normal and idiopathic hydrocephalus is not considered to cause alteration in composition of the CSF.<sup>47,48</sup> The fact that 121 dogs and cats in the study group had CSF within normal limits suggests that internal hydrocephalus alone does not cause significant changes in CSF and dogs with CSF changes were rightly excluded. From the excluded dogs with internal hydrocephalus and seizures that showed CSF abnormalities, 3 were diagnosed with MUO that responded to immunosuppressive drugs. One Tibetan spaniel with severe hydrocephalus and CSF pleocytosis was euthanized due to increasing seizure frequency and granulomatous meningoencephalitis was proven histopathologically. This again supports our theory that inflammatory brain disease and not the hydrocephalus itself were the epileptogenic lesion.

Although internal hydrocephalus was previously diagnosed in some of the medical records, reevaluation of the data showed only mild to moderately enlarged ventricles in a lot of these cases, which rather meet the criteria of "ventriculomegaly."<sup>14</sup> Differentiation of these 2 terms is important, because ventriculomegaly does not cause any clinical signs.<sup>14</sup> Presence of ventriculomegaly is so frequent in brachycephalic dogs that it is considered incidental in dogs that present with seizures.<sup>49</sup> The determination of objective morphologic and morphometric parameters as described by Laubner et al<sup>14</sup> helped to differentiate between the 2 entities in this study and lead to the exclusion of dogs with ventriculomegaly. However, ventricular dilatation is a dynamic process and there was an overlap in some parameters between ventriculomegaly and hydrocephalus.<sup>14</sup> It can therefore not be ruled out that 4 of dogs with ventriculomegaly were falsely excluded. However, including these 4 dogs would increase the prevalence to 5%, which is still by far less than most other studies reported.

In this study, only 2 dogs with hydrocephalus and no evidence for another disease experienced seizures. Although the Chihuahua was diagnosed with internal hydrocephalus, the underlying cause cannot be determined with absolute certainty. Idiopathic epilepsy should also be considered.

The other dog was a 12 years old Miniature schnauzer with an acute onset history of generalized tonic-clonic seizures (VBR of 0.79). Based on the advanced age at the time of its first seizure event, it is likely that there is another unidentified underlying cause for the seizures.<sup>50-52</sup> Therefore the dog must be diagnosed with cryptogenic (likely to be symptomatic) epilepsy, not associated to internal hydrocephalus. It therefore remains undetermined as to whether internal hydrocephalus was the underlying cause for seizures or if there was another source of epileptogenesis in these dogs.

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## CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

## OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

## INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

The study was conducted according to the University's institutional guidelines and received ethical approval from the institutional Ethic Commissioners. Reevaluation using MRI was part of the standard operating procedure for the treatment of internal hydrocephalus, which is why approval from the Hessen state government (Regierungspräsidium) was not necessary.

## HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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