Presumptive spontaneous brain microhemorrhages in geriatric dogs: a comparative retrospective MRI study of dogs with and without evidence of canine cognitive dysfunction

Curtis W Dewey Corresp., 1, 2, 3, Mark Rishniw 1, Philippa J Johnson 1, Emma S Davies 1, Joseph J Sackman 2, Marissa O’Donnell 2

1 Clinical Sciences, Cornell University College of Veterinary Medicine, Ithaca, New York, United States
2 Long Island Veterinary Specialists, Plainview, New York, United States
3 Rochester Veterinary Specialists and Emergency Services, Rochester, New York, United States

Corresponding Author: Curtis W Dewey
Email address: cwd27@cornell.edu

The objective of this study was to compare specific brain MRI anatomic measurements between three groups of geriatric ( > 8yrs) dogs: 1) neurologically impaired dogs with presumptive spontaneous brain microhemorrhages and no clinical evidence of canine cognitive dysfunction 2) dogs with canine cognitive dysfunction 3) dogs without clinical evidence of cognitive impairment or abnormalities on neurologic examination (control dogs). MR images from 46 geriatric dogs were reviewed and measurements were obtained of interthalamic adhesion height (thickness) and mid-sagittal interthalamic adhesion area for all dogs, in addition to total brain volume. Interthalamic adhesion measurements, either absolute or normalized to total brain volume were compared between groups. Signalment (age, breed, sex), body weight, presence and number of SBMs, as well as other abnormal MRI findings were recorded for all dogs. All interthalamic adhesion measurement parameters were significantly (p<0.05) different between control dogs and affected dogs. Both dogs with cognitive dysfunction (12/13; 92 %) and dogs with isolated brain microhemorrhages had more microhemorrhages than control dogs (3/19; 16%). Affected dogs without cognitive dysfunction had more microhemorrhages than dogs with cognitive dysfunction. In addition to signs of cognitive impairment for the CCD group, main clinical complaints for SBM and CCD dogs were referable to central vestibular dysfunction, recent-onset seizure activity, or both. Geriatric dogs with spontaneous brain microhemorrhages without cognitive dysfunction have similar MRI abnormalities as dogs with cognitive dysfunction but may represent a distinct disease category.
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TITLE: PRESUMPTIVE SPONTANEOUS BRAIN MICROHEMORRHAGES IN GERIATRIC DOGS: A COMPARATIVE RETROSPECTIVE MRI STUDY OF DOGS WITH AND WITHOUT EVIDENCE OF CANINE COGNITIVE DYSFUNCTION

AUTHORS NAMES AND DEGREES:

Curtis Wells Dewey1,2,3, DVM, MS, CTCVMP, DACVIM (Neurology), DACVS; Mark Rishniw1, BVSc, MS, PhD, DACVIM (Internal Medicine, Cardiology); Philippa J. Johnson1, BVSc, CertVDI, DECVDI, MSc, MRCVS; Emma S. Davies1, BVSc, MSc, DECVN; Joseph Sackman3, AA, BS; Marissa O’Donnell3, BS

AUTHOR AFFILIATIONS: Department of Clinical Sciences1, College of Veterinary Medicine, Cornell University, Ithaca, NY; Rochester Veterinary Specialists and Emergency Services2, Rochester, NY; Long Island Veterinary Specialists3, Plainview, NY

AUTHOR CONTACT INFORMATION:

CW Dewey: C4 169 Clinical Programs Center, Cornell University College of Veterinary Medicine, Ithaca, NY 14853; cwd27@cornell.edu

M Rishniw: C2 015 Clinical Programs Center, Cornell University College of Veterinary Medicine, Ithaca, NY 14853; mr89@cornell.edu

PJ Johnson: Department of Clinical Sciences, Cornell University College of Veterinary Medicine, 930 Campus Road, Box 25, Ithaca, NY 14853; pjj43@cornell.edu
ES Davies: C4 107 Clinical Programs Center, Cornell University College of Veterinary Medicine, Ithaca, NY 14853; ed445@cornell.edu

J Sackman: Long Island Veterinary Specialists, 163 South Service Road, Plainview, NY 11803; jsackman@livs.org.

M O’Donnell: Long Island Veterinary Specialists, 163 South Service Road, Plainview, NY 11803; modonnell@livs.org.

CORRESPONDING AUTHOR: Curtis W Dewey: C4 169 Clinical Programs Center, Cornell University College of Veterinary Medicine, Ithaca, NY 14853; cwd27@cornell.edu

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OBJECTIVE: To compare specific brain MRI anatomic measurements between three groups of geriatric (>8 yrs) dogs: 1) neurologically impaired dogs with presumptive spontaneous brain microhemorrhages and no clinical evidence of canine cognitive dysfunction 2) dogs with canine cognitive dysfunction 3) dogs without clinical evidence of cognitive impairment or abnormalities on neurologic examination (control dogs). MR images from 46 geriatric dogs were reviewed and measurements were obtained of interthalamic adhesion height (thickness) and mid-sagittal interthalamic adhesion area for all dogs, in addition to total brain volume. Interthalamic adhesion measurements, either absolute or normalized to total brain volume were compared between groups. Signalment (age, breed, sex), body weight, presence and number of SBMs, as well as other abnormal MRI findings were recorded for all dogs.

RESULTS: All interthalamic adhesion measurement parameters were significantly (p<0.05) different between control dogs and affected dogs. Both dogs with cognitive dysfunction (12/13; 92%) and dogs with isolated brain microhemorrhages had more microhemorrhages than control dogs (3/19; 16%). Affected dogs without cognitive dysfunction had more microhemorrhages than dogs with cognitive dysfunction. In addition to signs of cognitive impairment for the CCD group, main clinical complaints for SBM and CCD dogs were referable to central vestibular dysfunction, recent-onset seizure activity, or both. Geriatric dogs with spontaneous brain microhemorrhages without cognitive dysfunction have similar MRI abnormalities as dogs with cognitive dysfunction but may represent a distinct disease category.

KEYWORDS: Canine, dog, brain, microhemorrhage, cognitive, dementia, MRI, beta-amyloid, Alzheimer’s, cerebral amyloid angiopathy
Introduction

Geriatric humans can suffer cerebral microbleeds, also referred to as cerebral microhemorrhages. These microbleeds are often detected by MRI in patients with both Alzheimer’s disease or cerebral amyloid angiopathy, although they occur in patients with stroke-like events without evidence of dementia and, less commonly, as incidental findings.\(^1-5\) Cerebral amyloid angiopathy refers to a specific brain vasculopathy of geriatric humans caused by the accumulation of β-amyloid protein in vessel walls of brain arterioles and capillaries. Cerebral amyloid angiopathy commonly causes spontaneous cerebral microbleeds in geriatric humans, either as an isolated disorder or as a component of Alzheimer’s disease. Cerebral amyloid angiopathy possibly represents a precursor stage to subsequent Alzheimer’s disease, because its presence in the absence of dementia is a risk factor for developing Alzheimer’s disease.\(^3-8\) Microbleeds in humans appear on MRI as circular, ovoid or “dot-like” parenchymal lesions, best identified with T2* gradient echo or susceptibility-weighted MR sequences.\(^1-5\)

Pathologists have identified both cerebral amyloid angiopathy and cerebral microbleeds in geriatric dogs\(^9-14\), and clinicians have described putative microbleeds in geriatric dogs undergoing MR imaging.\(^15-17\)

We have observed geriatric dogs with and without evidence of cognitive dysfunction occasionally presenting with recent onset seizure activity and/or central vestibular dysfunction. The vestibular dysfunction in these dogs is generally much milder than that displayed in dogs with “geriatric vestibular syndrome” and tends to improve more rapidly than the peripheral disorder. These dogs typically exhibit varying numbers of punctuate lesions on MRI similar to what is referred to as microbleeds or microhemorrhages in humans. As with human patients with
brain microhemorrhages associated with cerebral amyloid angiopathy, neurologists have not identified any metabolic cause for the microhemorrhages in geriatric dogs.

We hypothesized that geriatric dogs with microhemorrhages without evidence of cognitive dysfunction have a form of vascular-associated degenerative brain disease and that these dogs have similar, abnormal, brain MRI features as dogs with cognitive dysfunction. More specifically, we hypothesized that interthalamic adhesion measurements in affected dogs would be smaller than that of aging geriatric control dogs (without evidence of encephalopathy or cognitive dysfunction), similar to what previous investigators have documented in dogs with cognitive dysfunction.\textsuperscript{18,19}
Materials and Methods

We searched databases from three institutions (Cornell University Hospital for Animals, Long Island Veterinary Specialists, and Rochester Veterinary Specialists and Emergency Services) for brain MRI scans of geriatric (>8 yrs old) dogs with a diagnosis of cognitive dysfunction, geriatric dogs with spontaneous brain microhemorrhages, and geriatric dogs with normal neurologic examination findings (control dogs). Because few geriatric dogs without evidence of brain disease undergo brain MRI, we acquired additional control geriatric brain MR images from two sources: 10 mixed-breed retired sled dogs with normal neurologic examinations that had been imaged as part of another study and 7 neurologically normal small-breed dogs whose owners volunteered for a no-cost brain MRI prior to scheduled dentistry procedures.

We based our diagnosis of cognitive dysfunction on previously established historical and clinical findings in association with characteristic MRI abnormalities.20-23

We defined spontaneous brain microhemorrhages using the same criteria as had been previously proposed in humans and dogs; namely, as punctate areas of signal void in the brain parenchyma of dogs (Figure 1) with no underlying metabolic reason (e.g., coagulopathy, endocrine disorder, renal hypertension, vascular neoplasia, etc.) or associated intracranial reason (e.g., tumor, inflammatory brain disease, etc.) for intracranial bleeding.5-7,17

All MRIs were performed under general anesthesia with one of four magnets: 1) 1.5 T Siemens Avanto (Munich, Germany) 2) 1.5 T Toshiba Vantage Elan (Lake Forest CA, USA) 3) 3.0 T Philips Achieva (Nutley NJ, USA) or 4) 3.0 T GE Discovery MR750 (Chicago IL, USA). Imaging sequences acquired included the following: sagittal T2-weighted; transverse T2-and T1-weighted; transverse and dorsal plane T1-weighted post-gadolinium injection; transverse T2-
fluid attenuated inversion recovery (FLAIR); transverse T2* gradient-recalled echo (GRE); and transverse susceptibility-weighted images (SWI). For the 1.5-T MRI units, measurement parameters were as follows: slice thickness, 3.5 mm; slice gap, 3.5 mm; FOV, 185 mm; matrix size of images, 480 x 480. For the 3.0-T MRI units, measurement parameters were as follows: slice thickness, 2.0 mm; slice gap, 1.0-3.0 mm (depending on dog size); FOV, 1101 mm; matrix size of images, 400 x 400.

For each dog, two investigators (JS & MO) measured the interthalamic adhesion height on transverse T2-weighted images, as previously described (Figure 2). Additionally, these investigators measured the cross-sectional area of the interthalamic adhesion on mid-sagittal T2-weighted images (Figure 3), and total brain volume for each dog, using Mimics® software. Volumetric measurements for total brain volume were performed as previously described. Both investigators used previously published anatomic landmarks for all measurements and both were blinded to the clinical status of the dogs in the study. One investigator counted all microhemorrhages evident on MR images for each dog (CD), based on transverse T2* gradient echo or susceptibility-weighted sequences.

**Statistical analysis**

We used Kruskal Wallis tests, with subsequent multiple comparisons by the Conover method for all comparisons described below. We did not correct for any experiment-wise error rate. We first compared ages and body weights of the three groups of dogs to demonstrate similarity of cohorts.
We compared the heights and areas of the interthalamic adhesions between the three groups of dogs both as absolute values, and after indexing to total brain volume (under the assumption that the height of the interthalamic adhesion would be proportional to the size of the brain).

Finally, we compared the number of microhemorrhages between the three groups of dogs.
Results

Our study consisted of 46 dogs: 19 control geriatric dogs, 14 dogs with spontaneous brain hemorrhages without evidence of cognitive dysfunction, and 13 dogs with evidence of cognitive dysfunction. Control dogs (10 yrs) were younger than affected dogs (13 yrs; \(P<0.0001\)). Bodyweights of dogs in each group did not differ \((P=0.9)\). Breeds represented in the control dog group (CD) included mixed breed (11), Chihuahua (3), Dachshund (2) and one each of Yorkshire terrier, Boston terrier and Maltese. There were 4 female spayed, and 2 each of female intact, male castrated and male intact dogs in the control group. Breeds represented in the spontaneous brain microhemorrhage group without cognitive impairment (SBM) included Shih tzu (2), mixed breed (2) and one each of Maltese, Greyhound, Shetland Sheepdog, Boston terrier, Chihuahua, Golden retriever, Pug, Yorkshire terrier and Bichon Frise. There were 8 female spayed and 6 male castrated dogs. Breeds represented in the cognitive dysfunction (CCD) group included Shih tzu (2), Springer spaniel (2), and one each of Labrador retriever, Chihuahua, Miniature Poodle, Shetland Sheepdog, Cockapoo, Samoyed, Miniature Schnauzer and mixed breed. There were 6 female spayed, 5 male castrated and 2 male intact dogs.

For the SBM group, the main clinical complaints included central vestibular dysfunction (9), recent-onset seizures (3), or a combination of the two (2). For the CCD group, 5 dogs had cognitive dysfunction alone, 5 also had recent-onset seizures and 3 also had central vestibular dysfunction.

Control dogs had a taller sagittal interthalamic adhesion and a larger interthalamic adhesion area than dogs with microhemorrhages without cognitive impairment and dogs with cognitive dysfunction \((P=0.0001\) for both comparisons) (Figure 4 and Figure 5). The two groups of abnormal dogs did not differ from each other \((P>0.05)\). When indexed to total brain volume,
control dogs had a taller sagittal interthalamic adhesion than dogs with cognitive dysfunction, but
not dogs with microhemorrhages without cognitive dysfunction ($P=0.005$) (Figure 6). However,
when indexed to total brain volume, control dogs had a larger interthalamic adhesion area than
both groups of abnormal dogs ($P=0.0001$) (Figure 7). Again, the groups of dogs with
microhemorrhages without cognitive dysfunction and those with cognitive dysfunction did not
differ from each other ($P>0.05$).

Three control dogs (3/19; 16%) exhibited evidence of microhemorrhages, with 2 hemorrhages in
one dog and a single hemorrhagic lesion in the other two. Twelve of 13 dogs with cognitive
dysfunction (92%) had evidence of brain microhemorrhages. Control dogs had fewer
microhemorrhages than either group of abnormal dogs. Dogs with cognitive dysfunction had
fewer microhemorrhages than dogs without cognitive dysfunction ($P<0.0001$) (Figure 8).
Discussion

Our study demonstrates that geriatric dogs with spontaneous brain microhemorrhages, but without evidence of cognitive dysfunction have MRI features similar to dogs with spontaneous brain microhemorrhages and cognitive dysfunction. Both groups of dogs with spontaneous brain microhemorrhages had smaller interthalamic adhesions (both in height and area) than similarly sized and aged control dogs. The interthalamic adhesion measurements did not differ between the two neurologically affected groups of dogs. Somewhat surprisingly, dogs without cognitive dysfunction had more microhemorrhages than dogs with cognitive dysfunction. Our observations, coupled with the similarity in presenting clinical complaints (recent onset seizures, vestibular dysfunction), suggest that dogs with microhemorrhages, with or without cognitive dysfunction, might share pathophysiologic mechanisms and might be manifestations along a spectrum of severity of a common disorder. However, the apparent absence of cognitive dysfunction in the group of dogs with nearly twice the number of microhemorrhages as in the dogs with cognitive dysfunction suggests that other factors might exist between the two groups.

Our results support the observations of previous investigators, who also found smaller interthalamic adhesions in dogs with cognitive impairment than in control dogs.\textsuperscript{18,19} However, decreases in interthalamic adhesion size are not specific for canine cognitive dysfunction, and have been reported sporadically in other disorders that can cause brain atrophy.\textsuperscript{18} Because we could not corroborate our findings with histopathology, we can only speculate that the lesions we observed on MRI are indeed microhemorrhages. However, the shape, size and imaging characteristics we identified are consistent with previous reports of microhemorrhages in both humans and dogs.\textsuperscript{1-5,15-17}
What could be causing microhemorrhages in dogs? Currently, we can only speculate about the cause. Pathologists have described histopathologic features of cerebral amyloid angiopathy in dogs, and have noted the presence of cerebral hemorrhages in these cases. Therefore, we can reasonably hypothesize that the microhemorrhages in our cohorts might be the result of cerebral amyloid angiopathy. Similar microhemorrhages in people are characteristic for cerebral amyloid angiopathy, the diagnosis of which generally relies upon MRI findings and supporting clinical features. Indeed, according to the Boston criteria for diagnosing human cerebral amyloid angiopathy, supportive clinical data and MRI evidence of microhemorrhages, combined with the absence of any other identifiable cause for hemorrhage, supports a diagnosis of “probable cerebral amyloid angiopathy”. Could microhemorrhages in dogs be caused by cerebral amyloid angiopathy and could this, in turn, lead to cognitive dysfunction? In humans, the relationship between cerebral amyloid angiopathy and Alzheimer’s disease is well-established, but not straightforward; investigators have identified cerebral amyloid angiopathy as a risk factor for development of Alzheimer’s disease, and Alzheimer’s disease patients are commonly afflicted with concurrent cerebral amyloid angiopathy. Furthermore, patients with Alzheimer’s disease or cerebral amyloid angiopathy often display generalized cerebral atrophy. Despite the interrelationships between these two amyloid-related brain disorders, cerebral amyloid angiopathy also occurs in people as an isolated brain disorder, independent of Alzheimer’s disease. Additionally, cerebral amyloid angiopathy can lead to dementia without concurrent development of Alzheimer’s disease. In both people and dogs, the amyloid deposits that occur in the walls of blood vessels differ from those occurring around neurons in the brain parenchyma. Vessel-associated amyloid is a soluble protein composed of 40 amino acids (Aβ1-40), whereas the more insoluble neuronal-associated...
amyloid protein is typically 42 amino acids in length (Aβ1-42). There is evidence in people that the ratio of Aβ1-40/Aβ1-42 in the brain might determine whether cerebral amyloid angiopathy (higher ratio) or Alzheimer’s disease (lower ratio) is more likely to develop. In turn, the expression of these proteins is thought to be influenced by specific gene mutations, particularly those genes that deal with proteolytic cleavage of amyloid precursor protein; these genes are variants of the apolipoprotein E gene.

Similar to human amyloid-related brain disorders, studies in dogs suggest that different molecular mechanisms may be involved in determining the preponderance of vascular-associated Aβ1-40 versus parenchymal Aβ1-42 in an individual. One study demonstrated that brain parenchymal Aβ1-42 deposits correlated with behavioral abnormalities, while vascular Aβ1-40 deposits were not. Canine cognitive dysfunction is considered by some to be the canine analogue of Alzheimer’s disease, and has been described extensively as both a clinical and pathologic entity. Unlike canine cognitive dysfunction, however, cerebral amyloid angiopathy has not previously been described as a clinical entity in dogs, but only as a pathological finding. We suspect that the microhemorrhages evident in both groups of affected dogs reflect disorders of amyloid metabolism, a suspicion that will require further inquiry. Unfortunately, because the dogs in our study were not euthanized at the time of presentation (or shortly thereafter), we cannot confirm our suspicion of amyloid deposition, either perivascularly or perineuronally, in affected dogs.

Putative cerebral microhemorrhages in dogs were described in a previous MRI-based study. These investigators compared dogs with microhemorrhages to all dogs undergoing similar brain MRIs, regardless of the indications for pursuing imaging. They found that dogs with cerebral microhemorrhages were older and smaller, and presented more frequently for vestibular
dysfunction than the control group of dogs. Similar to this study, our populations of dogs with microhemorrhages were primarily small-breed dogs; because we age-matched our controls as much as possible, we could not comment on age distributions, although all of our dogs were geriatric (≥8 yo). It is also possible that smaller breeds would be expected to predominate because they live long enough to develop degenerative brain disease, compared with larger dog breeds.

Both cerebral amyloid angiopathy and cognitive dysfunction are well-established pathologies of elderly dogs. Our study suggests that the dogs with spontaneous brain microhemorrhages represent a distinct neurodegenerative brain disorder with some similarities to cognitive dysfunction, but other features more reminiscent of cerebral amyloid angiopathy. Our suspicion that these dogs have cerebral amyloid angiopathy will require future histopathologic examination of brain tissue from patients with similar MRI abnormalities.

In addition to the lack of histopathologic correlation with the imaging findings in this study, there are several other limitations to our investigation, most of which are a consequence of its retrospective nature. We made the diagnosis of cognitive dysfunction in all dogs via historical and clinical features consistent with cognitive impairment, combined with supportive MRI findings. While this manner of diagnosing cognitive dysfunction is common practice and adequate for a clinical diagnosis, it is likely to under-diagnose dogs with mild to moderate cognitive impairment. There are a number of accurate behavioral test protocols for dogs that provide more objective data regarding cognitive health. Although the dogs with isolated microhemorrhages did not appear to have cognitive dysfunction, it is possible that they exhibited some level of cognitive dysfunction that was not appreciable without specific behavioral testing. Ten of the geriatric control dogs were kennel-housed and therefore not part of a home
environment, unlike the remainder of the control dogs and all dogs with microhemorrhages. As such, cognitive dysfunction in some of these kennel-housed control dogs could have gone unrecognized. Two of these dogs did have small interthalamic adhesions, despite being deemed as cognitively normal. Ideally, all the control dogs would have been from home environments, in which subtle behavioral changes could have been observed by owners. Although measuring interthalamic adhesion thickness from a transaxial MR image slice is an accurate and easily applicable clinical tool for the diagnosis of canine cognitive dysfunction\textsuperscript{18,19}, some inherent error in this method exists. The image slice that appears to have the largest interthalamic adhesion measurement is chosen from the slices available, which introduces a level of variability in the resultant data. Since the mid-sagittal interthalamic adhesion area is more consistent, this is likely a more accurate mode of measuring the interthalamic adhesion.\textsuperscript{18} We found no differences between the two groups of dogs with microhemorrhages, but the sample sizes were small and might have failed to detect a difference.

Our main goal with this investigation was to compare MR imaging findings between two abnormal geriatric groups of dogs: those with presumptive spontaneous brain microhemorrhages and no cognitive impairment and those with evidence of canine cognitive dysfunction. We chose our geriatric control dogs based upon a lower age limit of 8 years of age. Although this lower limit is based on several reports dealing with canine cognitive dysfunction\textsuperscript{20-23,30} (one of the affected dogs in our study, without cognitive dysfunction, was 8 years old), the definition of what minimum age defines “geriatric” in dogs is somewhat arbitrary. Our control dogs were younger than the affected dogs, but only one was 8 years old (and four were 9 years old). There are several potential interpretations of this finding. One possibility is that both geriatric brain disorders investigated in this report are more likely to occur with increasing age. This
phenomenon has been documented with canine cognitive dysfunction. In one study of putative microhemorrhages in dogs, affected dogs were significantly older than unaffected dogs, but an increasing tendency for brain microhemorrhages to occur with aging has not yet been established in this species. Another possibility is that a lower age limit of 8 years is too low for a definition of “geriatric” in dogs. If this is the case, interthalamic adhesion measurements may be less discriminative for degenerative brain pathology if the lower age limit for geriatric control dogs is increased. In one study evaluating interthalamic adhesion thickness as an indicator of cognitive dysfunction in dogs, 9 years of age was chosen as a lower limit for defining geriatric status. These investigators found a significant difference in interthalamic adhesion thickness between aging non-cognitively impaired and cognitively impaired older dogs. They also found a significant difference in interthalamic adhesion thickness between older non-cognitively impaired dogs and younger dogs (< 9 years of age). However, this difference was negated when the interthalamic adhesion numbers were normalized to brain height. The overall effect of aging on interthalamic adhesion parameters in successfully aging dogs needs to be more fully evaluated.

Future investigation into geriatric dogs with spontaneous brain microhemorrhages will hopefully include correlating MR imaging findings with histopathology, as well as more objective assessment of cognitive status. In addition, comparing imaging features of larger cohorts of dogs with and without cognitive dysfunction might help discern whether these entities are distinct with respect to interthalamic adhesion measurements.

In conclusion, we have, for the first time, associated clinical signs in dogs, both with and without cognitive dysfunction, with MRI evidence of microhemorrhages. Dogs with microhemorrhages had smaller interthalamic adhesions than age-matched, weight-matched control dogs. Dogs
without cognitive had more hemorrhages than dogs with cognitive dysfunction, suggesting that the cognitive dysfunction is not associated with hemorrhage number. Our data support, but do not confirm the idea that spontaneous brain microhemorrhages in dogs might be a manifestation of amyloid angiopathy.
References


Figure Legends

Figure 1. Transverse T2* gradient echo MR images demonstrating typical appearance of presumptive brain microhemorrhages. A-multiple microhemorrhages at the diencephalon level. B-a single microhemorrhage in the left cerebellum.

Figure 2. Transverse T2-weighted MR image depicting method of measuring interthalamic adhesion height (thickness).

Figure 3. Mid-sagittal T2-weighted image depicting method of measuring interthalamic adhesion area.

Figure 4. Box and whisker plots of interthalamic adhesion thickness (height) for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD).

Figure 5. Box and whisker plots of interthalamic adhesion area for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD).

Figure 6. Box and whisker plots of interthalamic adhesion thickness (height) indexed to total brain volume (TBV) for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD).

Figure 7. Box and whisker plots of interthalamic adhesion area indexed to total brain volume (TBV) for control dogs, spontaneous brain microhemorrhage dogs.
without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD).

Figure 8. Box and whisker plots of microhemorrhage numbers for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD).
Figure 1

Transverse T2* gradient echo MR images demonstrating typical appearance of presumptive brain microhemorrhages. (A) Multiple microhemorrhages at the diencephalon level.
Figure 2

Transverse T2* gradient echo MR images demonstrating typical appearance of presumptive brain microhemorrhages. (B) A single microhemorrhage in the left cerebellum.
Figure 3

Transverse T2-weighted image depicting method of measuring interthalamic adhesion height.
Figure 4

Mid-sagittal T2-weighted image depicting method of measuring interthalamic adhesion area.
Figure 5

Box and whisker plots of interthalamic adhesion thickness (height) for control dogs, spontaneous microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD).
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Box and whisker plots of interthalamic adhesion area for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD)
Figure 7

Box and whisker plots of interthalamic adhesion thickness (height) indexed to total brain volume (TBV) for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction.
Figure 8

Box and whisker plots of interthalamic adhesion thickness area indexed to total brain volume (TBV) for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction.
Figure 9

Box and whisker plots of microhemorrhage numbers for control dogs, spontaneous brain microhemorrhage dogs without cognitive dysfunction (SBM) and dogs with cognitive dysfunction (CCD)