Quantitative analysis of brain perfusion in healthy dogs by means of magnetic resonance imaging

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OBJECTIVE
To determine values of perfusion parameters determined via MRI in the brains of healthy dogs.

ANIMALS
10 healthy adult Beagles.

PROCEDURES
Each dog was anesthetized for MRI examination of the brain, including standard sequences and a perfusion-weighted sequence. Gadoteric acid (0.2 mmol/kg) was injected IV at a rate of 5 mL/s. A dedicated workstation was used to measure the times from contrast medium injection to arrival at an ROI (T0) and peak contrast enhancement (TTP), mean contrast medium transport time (MTT), and cerebral blood flow (CBF) in the caudate nucleus, thalamus, piriform lobe, hippocampus, semioval center, and temporal cerebral cortex. A simple mathematical model was used to compare parameter values among the various brain regions.

RESULTS
T0 and time to peak contrast enhancement had a significant linear relationship. A significant negative correlation was identified between T0 and CBF and, to a lesser extent, between MTT and CBF. Differences among brain regions were significant for MTT and CBF. The CBF was lowest in the semioval center, and the piriform lobe had almost 2-fold the CBF of that region. No significant differences were identified between hemispheres of the brain.

CONCLUSIONS AND CLINICAL RELEVANCE
Findings obtained in this study involving healthy dogs may serve as a reference for MRI perfusion measurements in specific brain regions and may help in the characterization of various brain diseases in dogs. (Am J Vet Res 2016;77:1227–1235)

Magnetic resonance imaging is a common diagnostic tool in veterinary neurology, although it is mainly used to detect morphological changes in the brain. However, not all diseases of the CNS lead to morphological changes that can be detected with conventional pulse sequences.

Functional MRI includes various techniques that help to visualize physiologic processes. In the broader sense, functional MRI also includes perfusion-weighted imaging. Perfusion is used to describe the blood volume that passes through the capillary bed of a specific tissue during a certain period. Various techniques for perfusion measurement are available, involving endogenous or exogenous markers. The most commonly used exogenous markers are gadolinium chelates. Contrast medium is injected IV as a bolus. Dynamic images are acquired before, during, and after contrast medium injection. From the acquired images, signal intensity–time curves are generated, which allow for the calculation of concentration-versus-time curves.

Gadolinium chelates are nondiffusible contrast agents that do not cross the intact blood-brain barrier. However, although the contrast medium remains in the intravascular space, the effects of the contrast medium extend to the extravascular space as well because of susceptibility effects and water exchange between the blood and the brain tissue. Gadolinium chelates cause shortening of the T1 (spin-lattice) relaxation time by enhancing the relaxivity of the intrinsic blood water. They also lead to a reduction of the T2 (spin-spin) relaxation time, given that field inhomogeneities induced by the differing susceptibility of the contrast medium result in a more prominent spin dephasing.

Various hemodynamic variables can be calculated from these measurement statistics: T0, TTP, MTT,

ABBREVIATIONS
AIF  Arterial input function
CBF  Cerebral blood flow
CBV  Cerebral blood volume
FLAIR  Fluid-attenuated inversion recovery
MTT  Mean transit time of contrast medium
ROI  Region of interest
T0  Time of contrast medium arrival
TTP  Time to peak contrast enhancement
CBV, and CBF. The T0 is defined as the interval between the injection of the contrast medium and its arrival at an ROI. The TTP is defined as the interval between the injection of contrast medium and the time when its maximum concentration is achieved within an ROI. Both of these variables can be read directly from the concentration-versus-time curve. The MTT represents the mean amount of time the contrast medium takes to pass through the vasculature of the ROI in an examined brain region. The CBV can be calculated from the AIF and the concentration of contrast medium in an ROI. It is defined as the volume of blood in an ROI divided by the mass of the ROI. The CBF is defined as the rate of blood flow through an ROI divided by the mass of the ROI. The CBV can also be calculated as the product of MTT and CBF.

In veterinary medicine, perfusion-weighted imaging has been used for the evaluation of the pituitary gland in healthy dogs. This method has also been considered to have potential for use in dogs for differentiating brain tumors or evaluating brain infarcts in combination with diffusion-weighted imaging. In human medicine, perfusion-weighted imaging is used to diagnose various diseases, predominantly in the evaluation of brain infarcts. In combination with diffusion-weighted imaging, a differentiation between viable and nonviable tissue becomes possible, which influences the choice of treatment.

In neuro-oncology, perfusion-weighted imaging is helpful in the characterization and classification of brain tumors, planning the region used for biopsy, and controlling treatment. Additional applications are the evaluation of neurodegenerative diseases, such as Alzheimer disease and epilepsy. Alzheimer patients have a decrease in CBV in certain brain areas, which is considered a consequence of a generalized brain atrophy. In humans with epilepsy, results of perfusion-weighted imaging vary depending on the cause of the epilepsy.

Considering the broad application of perfusion-weighted imaging in human medicine, it would be reasonable to presume that the technique would also be helpful in the diagnosis of and treatment planning for various diseases in veterinary medicine. The purpose of the study reported here was to determine values of brain perfusion parameters in healthy dogs so that the data may serve as a basis for future studies involving diseased dogs.

Materials and Methods

Animals

Ten purpose-bred Beagles (8 males and 2 females) were used in the study. Mean ± SD age was 2.4 ± 0.6 years (range, 21 to 40 months), and mean body weight was 9.5 ± 1.6 kg. A general physical and neurologic examination and complete hematologic analysis were performed for each dog prior to induction of anesthesia for MRI examination. The study was conducted prospectively and was approved by the Committee on the Ethics of Animal Experiments of Justus-Liebig University and the local Hessian government (reference No. V54-19c2015[1]GI18/17 78/2011).

Preparation for MRI

Two venous catheters were placed in each dog: one in the right cephalic vein and the other in the right saphenous vein. Diazepam (0.5 mg/kg) was administered IV, and anesthesia was induced with propofol (2 to 4 mg/kg, IV). Afterward, dogs were endotracheally intubated and anesthesia was maintained with 1.5% to 2% isoflurane in oxygen. Dogs were mechanically ventilated throughout the MRI examination.

MRI examination

Magnetic resonance imaging was performed by use of a 1.0-T superconductive system and an imaging coil consisting of 2 elliptical elements. For the examination, dogs were positioned in sternal recumbency. The 2 elements of the coil were placed in a standardized manner on the right and left side of the head, and this position was fixed with foam cushions.

Dorsal and transverse T2-weighted images, transverse T2-weighted FLAIR images, and dorsal T1-weighted gradient echo images were acquired before and after contrast medium administration to exclude structural brain abnormalities (Appendix). Perfusion-weighted images were acquired by use of a dynamic multishot fast-field echo–echo-planar imaging sequence in the dorsal plane. The slices were oriented parallel to the base of the skull, with 1 slice (slice No. 6) going through the thickest part of the caudate nucleus. A total of 40 dynamics/slice were acquired, each 1.6 milliseconds apart from another.

At the 10th dynamic, with dynamics 1 to 9 serving as the baseline, contrast medium (gadoteric acid; 0.2 mmol/kg) was injected at 5 mL/s by use of a double-headed injection pump. This injection was followed by a 20-mL injection of isotonic Ringer solution.

Perfusion analysis

Image analysis was performed at a dedicated workstation. Values of perfusion parameter were extracted from the MRI scans by means of deconvolution techniques and variate fitting. The concentration of contrast medium in the incoming artery (as measured by the AIF) was compared with the concentration in the ROI, and their relationship determined the perfusion values. The chosen AIF was at the level of the medial cerebral artery. For determination of perfusion values, several ROIs were manually drawn around the caudate nucleus, thalamus, piriform lobe, hippocampus, semioval center, and temporal cerebral cortex lateral to the semioval center (Figures 1 and 2).

Each ROI was drawn on 1 representative slice; because of the slice thickness, most structures were visible on only 1 slice. Images of the other sequences were available at the time of the ROI placement and served as references for comparison of anatomic
structures. The ROIs were drawn as large as possible while avoiding the inclusion of other structures. The ROI drawings were repeated 5 times at different times, and the process of repeated ROI drawings is henceforward referred to as the ROI selection run. The integrated software was used to determine the values of T0, TTP, MTT, CBV, and CBF.

Mathematical model

The natural laws and parameters governing the transport of blood within the brain can be presumed to be constant over time. Hence, the characteristic shape of the time-dependent concentration curve should be the same, so only amplitude should be expected to change between the different ROIs. Therefore, a constant flow of blood was assumed for the study, independent of time. From this, the difference between T0 and TTP was inferred to be constant, as represented by the following relationship: TTP = T0 + offset.

Additionally, the flow within blood vessels of the brain was presumed to be laminar, given that small turbulences were averaged out in our setting. Laminar flow through tubes (capillaries) is described by the law of Hagen-Poiseuille, by which volume flow is related to the cross-sectional area of the tube.22 We further presumed that the gradient of the blood pressure would be proportional to the length of any capillary. Therefore, the velocity would be proportional to the cross-sectional area, whereas the flow would be proportional to its second power.23 Blood may course through many possible routes through a specific ROI; nevertheless, we believed it reasonable to presume that the probability of the blood taking a specific route would be proportional to the cross-sectional area of that route.

With the aforementioned considerations, the parameters T0 and MTT can be expressed by similar expressions: one dependent on the routes to the ROI, and the other dependent on routes through the ROI. Within an ROI in the brain, only small capillaries are present. We therefore expected that the variance in cross-sectional area of the capillaries among dogs and ROIs would be of a much smaller scale than the fluctuations in the mean length, suggesting that for MTT, the denominator could be kept constant. This then suggested that the MTT could be modeled as a random variable, depending on the ROI.

The CBF is given by the volume flow through the arterial inlet entering the ROI, scaled by the mass of the ROI. As indicated by the law of Hagen-Poiseuille, volume flow is proportional to the square of the cross-sectional area of the artery entering the ROI or, if multiple arteries enter the ROI, to the sum of squares of the cross sections.22 Any of these cross sections depend on the arterial inlet, which the blood passes on its way to the ROI. On the basis of this assumption, we expected that CBF would not depend strongly on the capillaries within a specific ROI. Instead, we expected it to be proportional to the volume flow to the ROI.

We consequently expected the CBF to be correlated with T0, but only slightly with MTT. This slight dependence was presumed to exist because the sum of the cross-sectional areas of routes through the ROI was expected to depend on the sum of cross-sectional areas of routes to the ROI because these capillaries are connected. The exact relationship between T0 and CBF remains to be understood. While developing the mathematical model for this study, we found...
that an inverse power (T₀² value of approx 1/CBF) described the situation sufficiently well. We chose to model CBF and hence also T₀ by a γ distribution, as our mathematical model suggested that both parameters are multiples of normally distributed random variables. According to the central volume theorem, the CBV within an ROI is given by the product of the CBF and MTT. Therefore, CBV was not evaluated further.

**Statistical analysis**

Statistical analysis was performed by use of statistical software. Several correlation tests were performed to verify suitability of the chosen modeling approach. The Pearson correlation test (r) was used to determine whether a linear relationship existed between T₀ and TTP. The Spearman correlation test (ρ) was used to determine whether the proposed nonlinear relationship existed between CBF and T₀ as well as between CBF and MTT.

Dependence of the brain perfusion parameters on anatomic or operator-dependent effects was then examined by fitting several linear mixed models with varying fixed and random terms. Specifically, to test for the significance of a given parameter (e.g., dependence on the ROI or the drawing of the ROI), 2 models were fitted: 1 including the parameter, and the other excluding it. To determine the significance of factors entering the model, the linear mixed models were tested against each other by use of the χ² test. Models were built by including normally distributed random effects for MTT, whereas for CBF and T₀, γ-distributed random effects were used.

For CBF, an additional cluster analysis was performed, dividing the data into clusters on the basis of the number of arterial inlets included in the ROI. Results of the associated Q-Q plots and Kolmogorov-Smirnov tests based on these distributions supported our hypotheses. Values of P ≤ 0.01 were considered significant for all tests.

**Results**

Values for T₀ and TTP were significantly (P < 0.001) correlated with each other (r = 0.81; Figure 3). The relationship between T₀ and TTP was almost perfectly linear, confirming the assumption of a constant flow independent of time. Given this strong correlation, the decision was made to use T₀ rather than TTP for further analysis with the understanding that findings for T₀ could be applied to TTP. Values for T₀ were also significantly (P <

![Figure 3 — Scatter plot showing the linear relationship between T₀ and TTP in the brains of 10 healthy Beagles as determined via perfusion-weighted MRI. The line represents the best linear fit.](image)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Caudate nucleus</th>
<th>Thalamus</th>
<th>Piriform lobe</th>
<th>Hippocampus</th>
<th>Semicircular</th>
<th>Temporal cerebral cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td>T₀ (s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>24.0 ± 1.8</td>
<td>24.6 ± 1.9</td>
<td>24.4 ± 1.9</td>
<td>25.2 ± 1.6</td>
<td>26.5 ± 2.0</td>
<td>24.0 ± 2.0</td>
</tr>
<tr>
<td>Left</td>
<td>24.0 ± 1.7</td>
<td>25.0 ± 1.8</td>
<td>23.8 ± 1.9</td>
<td>24.8 ± 1.8</td>
<td>25.6 ± 2.0</td>
<td>24.0 ± 2.0</td>
</tr>
<tr>
<td>Mean</td>
<td>24.0 ± 1.7</td>
<td>24.8 ± 1.9</td>
<td>24.1 ± 1.9</td>
<td>25.0 ± 1.7</td>
<td>26.0 ± 2.1</td>
<td>24.0 ± 1.9</td>
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<tr>
<td>MTT (s)</td>
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</tr>
<tr>
<td>Right</td>
<td>3.0 ± 0.7</td>
<td>3.7 ± 0.9</td>
<td>3.5 ± 0.5</td>
<td>4.4 ± 0.8</td>
<td>3.8 ± 1.3</td>
<td>2.9 ± 0.6</td>
</tr>
<tr>
<td>Left</td>
<td>3.4 ± 0.8</td>
<td>2.8 ± 0.6</td>
<td>3.9 ± 0.3</td>
<td>3.9 ± 1.1</td>
<td>3.9 ± 1.4</td>
<td>3.5 ± 0.9</td>
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<tr>
<td>Mean</td>
<td>3.2 ± 0.8</td>
<td>3.3 ± 0.9</td>
<td>3.7 ± 0.5</td>
<td>4.1 ± 1.0</td>
<td>3.9 ± 1.3</td>
<td>3.2 ± 0.8</td>
</tr>
<tr>
<td>CBF (mL/100 g/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>277.8 ± 90.4</td>
<td>235.4 ± 51.6</td>
<td>270.8 ± 52.6</td>
<td>233.4 ± 67.4</td>
<td>145.1 ± 28.6</td>
<td>274.7 ± 71.9</td>
</tr>
<tr>
<td>Left</td>
<td>232.2 ± 68.4</td>
<td>225.4 ± 50.9</td>
<td>286.3 ± 78.8</td>
<td>266.7 ± 83.0</td>
<td>148.6 ± 26.1</td>
<td>241.1 ± 68.9</td>
</tr>
<tr>
<td>Mean</td>
<td>255.0 ± 83.3</td>
<td>230.4 ± 51.5</td>
<td>278.5 ± 67.4</td>
<td>250.1 ± 77.4</td>
<td>146.8 ± 27.3</td>
<td>257.9 ± 72.4</td>
</tr>
</tbody>
</table>

Values for MTT were normally distributed, whereas values for CBF and T₀ were gamma distributed. However, the choice was made to report mean ± SD for all 3 parameters for ease of interpretation and because these statistics also uniquely specify the distribution.
Inclusion of CBF in the model for associations with T0 was essential. Results of statistical analysis supported the result from the mathematical model concerning the relationship between T0 and CBF, as revealed by comparing 2 models with this dependence absent or present. Results of this comparison indicated that the effect of CBF on T0 was significant ($P < 0.001$). No direct correlation between T0 and the ROI selection run (repeated, manual drawing of the ROI) or the AIF or ROI itself (meaning the anatomic region) was identified. However, because of the strong correlation between T0 and CBF, an indirect correlation existed between T0 and the ROI selection run, AIF, and ROI.

Values for MTT were also significantly ($P < 0.001$) negatively correlated with CBF, but this correlation was smaller than that between CBF and T0 ($\rho = -0.19$). The MTT was significantly ($P < 0.001$) influenced by ROI selection run as well as by AIF. Significant ($P < 0.001$) differences in MTT were also identified among the 6 ROIs. Side of the brain (right vs left) did not significantly influence the MTT.

Values for CBF were strongly dependent on the ROI selection run ($P < 0.001$). After data were clustered on the basis of the number of arterial inlets included in the ROI ($n = 2$ clusters), the model fit improved significantly ($P < 0.001$). Differences among the 6 ROIs in CBF were also highly significant ($P < 0.001$). No significant influence on CBF was identified for AIF or side of the brain.

The lowest CBF values were identified in the semioval center (mean ± SD, 146.8 ± 27.3 mL/100 g/min), and the highest were identified in the piriform lobe (278.5 ± 67.4 mL/100 g/min). Neither side of the brain had a systematically higher value than the other. Values for T0, MTT, and CBF for the 6 brain regions were summarized (Table 1).

Discussion

Magnetic resonance imaging of the head in veterinary medicine is generally limited to morphological assessment. The purpose of the present study was to obtain information about perfusion characteristics in various brain regions in healthy dogs. Brain regions were chosen on the basis of their visibility on perfusion-weighted MRI scans, their different functions, and their importance in various disease processes.

The caudate nucleus is part of the motor system of the brain and is active during movement processes and learning. Its proximity to the lateral ventricles renders the caudate nucleus prone to compression resulting from hydrocephalus. Detection of changes in brain perfusion may aid in the earlier diagnosis of clinically relevant hydrocephalus and its differentiation from clinically unimportant ventriculomegaly. However, this possibility remains to be evaluated.

The thalamus is also involved in the coordination of movement and is important to emotions and affective behavior. Lesions of the thalamus can lead to focal or generalized seizures, pleurothotonus, or so-called hemi-inattention or thalamic pain syndromes. The piriform lobe is involved in conscious olfaction. Reversible and irreversible changes in the piriform and temporal lobes reportedly occur as consequence of seizures in humans, dogs, and cats.

As part of the limbic system, the hippocampus is important for memorization and coordination of emotional behavior and is involved in various other regulatory processes. The hippocampus is of particular interest in the evaluation of epilepsy. In human medicine, a connection is suspected between hippocampal sclerosis and temporal lobe epilepsy. However, it remains unknown whether the sclerosis is the cause of or a sequel to temporal lobe epilepsy. Whether temporal lobe epilepsy exists in small animals is a subject of debate. Some investigators suspect that a connection between hippocampal sclerosis and temporal lobe epilepsy exists in small animals, particularly cats, which is similar to that in human medicine. The semioval center contains connecting nerve fibers. The temporal cerebral cortex contains motoric and sensory areas. Conscious perception, interpretation, and linking of information take place in the cerebral cortex. The semioval center and cerebral cortex were included in the present study because they may serve as reference structures for white and gray matter, respectively, to allow normalization of perfusion values for other brain regions. Brain white matter is commonly used for this purpose in human medicine.

In human medicine, alterations in brain perfusion patterns have been identified for various brain diseases. A complete general, neurologic, and hematologic examination was performed prior to performance of MRI in the present study, and additional MRI sequences (T2-weighted, T2-weighted FLAIR, T2-weighted gradient echo, and T1-weighted images before and after contrast medium administration) were acquired to rule out subclinical disease in the study dogs. Because of the invasiveness and possible hazards of CSF sample collection, such samples were not obtained and analyzed to confirm the absence of disease.

The dogs in the present study ranged in age from 21 to 40 months. Congenital diseases should have already become clinically apparent in these dogs, and the risk of age-related degenerative or neoplastic diseases was expected to be low. Additionally, CBF is known to decrease with increasing age in humans, and this decrease has been attributed to overall brain atrophy. Reduced synaptic density as well as reduced neuronal size leading to reduced metabolic activity and therefore reduced perfusion have also been associated with increasing age. Others believe that diminished neuronal activity without any reduction in the number or size of neurons is a possible cause of reduced perfusion. Reduced CBF with increasing age has also been reported for dogs. In a
study involving single photon–emission CT, dogs older than 96 months had significantly decreased CBF in the frontal and temporal lobes as well as in subcortical nuclei, relative to values in younger control dogs.

Additionally, CBF is higher in women than in men. Possible explanations are sex differences in Hct, blood viscosity, or circulating estrogen concentrations. We found no differences in perfusion values between male and female dogs in the present study, but the study sample was limited to 10 dogs, 8 of which were female, reducing the statistical power to detect such differences.

In contrast to the situation in human medicine, MRI of the brain in dogs requires that the dogs be anesthetized. Evaluation of brain perfusion in rats has revealed an increased CBF when isoflurane rather than pentobarbital or fentanyl is used as an anesthetic. The increase in CBF is attributable to intracerebral vasodilation, which is particularly pronounced in the subcortical areas as well as in the thalamus. Therefore, we expected that the results of the present study would be influenced by the anesthesia, which was unavoidable. All dogs received the same anesthetic protocol; therefore, the effect of anesthesia could be presumed to be similar among the dogs.

Some technical factors influencing brain perfusion are strength of the magnetic field, concentration and dose of contrast medium, rate of contrast medium injection, pulse sequence, and method of data analysis. All MRI scans in the present study were acquired, processed, and analyzed by use of identical settings to control for these potential influences on the results.

A linear relationship was identified between T0 and TTP, confirming our assumption of a constant CBF independent of time. The T0 was also strongly correlated with CBF, whereas the MTT and CBF had a weaker correlation. The stronger correlation between CBF and T0 versus MTT was expected, given that both T0 and CBF are mainly influenced by the possible routes to the ROI, whereas MTT is mainly influenced by what is happening inside the ROI.

The significant influence of the ROI selection run, thus of the exact choice of the region, on MTT was also expected, given that different choices of the same ROI probably would have led to slightly different borders or volume of the ROI, which then would have affected the MTT by changing the length of possible routes through the ROI. The ROI selection run also had a strong influence on the calculated CBF. These results were not unexpected, given that CBF is influenced by 2 variables: the mass of the ROI and the volume flow on the routes to the ROI. Selecting different borders for a given ROI would alter its mass, thereby influencing the number of arteries measured and leading to a clustering of the data into different groups.

The T0 is independent of AIF, and it can be extracted from the concentration-versus-time curve without further processing. Calculations of MTT and CBF require the AIF; therefore, an influence on both was expected. However, a significant influence of AIF was identified for only MTT and not CBF in the present study, and we are unable to explain why CBF was not influenced as well.

A significant difference among the examined ROIs was identified for MTT and CBF in the study dogs. The hippocampus had the highest mean MTT (4.1 ± 1.0 seconds), indicating the time required for blood to pass through that region was the longest of the ROIs evaluated. We can only guess at the reason underlying this finding. The size of the ROI in the hippocampus is typically smaller than in other gray matter structures such as the caudate nucleus or cerebral cortex; therefore, the size of the ROI can be excluded as a cause for an increase in MTT. The capillaries within the hippocampus might be more tortuous or ramified than in other regions, leading to an increased distance the blood needs to travel within the hippocampus. However, because of the small size of the hippocampus, the possibility existed that structures not belonging to the hippocampus were included in the ROI on dorsal perfusion-weighted images in the present study, leading to alterations in the measured MTT.

The MTT of the semi-oval center had the second highest mean value (3.9 ± 1.3 seconds). The semi-oval center consists of white matter that has a wide-meshed capillary net and lower blood flow than the gray matter structures. Although the piriform lobe belongs to the gray matter (allocortex), the mean MTT (3.7 ± 0.5 seconds) in that region was much higher than that of the other gray matter structures. The most likely explanation is the larger size of the ROI drawn in the piriform lobe. The caudate nucleus, thalamus, and temporal gray matter had similar mean MTTs (3.2 ± 0.8 seconds, 3.3 ± 0.9 seconds, and 3.2 ± 0.8 seconds, respectively). The slightly higher MTT in the thalamus could have been attributable to this region being composed of white and gray matter and to the slower blood flow in white matter, leading to an increased time needed for the blood to pass through the thalamus than in other structures composed solely of gray matter.

The lowest mean CBF was identified in the semi-oval center (146.8 ± 27.3 mL/100 g/min). This finding was consistent with data from human medicine that indicate decreased blood flow in white matter versus gray matter structures. However, our CBF values for dogs were much higher than published CBF values for humans. Mean ± SD values for healthy white matter in humans vary between 24 ± 5 mL/100 g/min to 35 ± 13 mL/100 g/min and for healthy gray matter are approximately 70 mL/100 g/min. Studies of CBF in the brains of rats have revealed greater values than in humans as well, with rates varying between 105 ± 16 mL/100 g/min to 139 ± 19 mL/100 g/min. One might therefore presume that CBF is similarly greater in dogs than in humans. Another explanation for the discrepancy might be the use of isoflurane for the anesthesia or the method of data analysis.
Another study \(^{58}\) in which brain perfusion was examined in dogs by means of single photon emission CT, revealing significantly greater perfusion in the left versus right cerebral hemisphere. Similar findings have been identified in humans, \(^{59-61}\) and these have been attributed to volume differences. \(^{59}\) However, no significant difference was identified between perfusion of the left and right cerebral hemispheres in another study \(^{62}\) involving dogs in which single photon emission CT was used.

Perfusion values obtained in the present study by means of perfusion-weighted MRI should, theoretically, be comparable to values obtained with other MRI systems. However, because many elements of the imaging process can influence perfusion parameters, the data reported here must be considered specific to the study conditions. In addition, consideration should also be given to the small number of dogs used, which were of similar size, age, and breed. Consequently, additional studies involving a more diverse and larger sized sample of dogs are necessary to strengthen our findings.

Regardless of any limitations, results of the study reported here provided a first insight into the differences and similarities in brain perfusion parameters within various brain regions of dogs as identified via MRI. Similar to results in humans, perfusion in the white matter of the brain of the study dogs was on a lower scale than in gray matter, as suggested by a lower CBF and higher MTT. The relationships between the various brain regions examined should be comparable to relationships identified in different experimental circumstances, regardless of whether the obtained values may differ between settings. However, in addition to known technical factors influencing measured perfusion parameters, the ROI selection run and AIF each had a significant influence on those parameters. In human medicine, perfusion-weighted MRI is used to identify or characterize brain infarctions and various other diseases. Information obtained in the present study may therefore help to better understand healthy brain function in dogs, potentially leading to the earlier diagnosis and improved treatment of brain disease.

Acknowledgments
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The authors thank Prof. Patrick Kircher and Dr. Matthias Dennler for technical assistance.

Footnotes
b. MR WorkSpace 2.6.3.5, Philips Medical System, Hamburg, Germany.
c. Dotarem, Guerbet GmbH, Sulzbach, Germany.
d. SENSE-flex M coil, Philips Healthcare, Hamburg, Germany.

References


Appendix

Settings used for various MRI sequences to evaluate brain perfusion in healthy dogs.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dorsal T2-weighted</th>
<th>Transverse T2-weighted</th>
<th>Transverse FLAIR</th>
<th>Dorsal T1-weighted gradient echo</th>
<th>Dorsal perfusion-weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field of view (mm)</td>
<td>180</td>
<td>180</td>
<td>180</td>
<td>140</td>
<td>190</td>
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<tr>
<td>Rectangular field of view (%)</td>
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<td>80</td>
<td>100</td>
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<td>2.0</td>
<td>5.0</td>
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<td>-</td>
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<td>Scan matrix (pixels²)</td>
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<td>256</td>
<td>256</td>
<td>320</td>
<td>128</td>
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<td>Voxel size (mm)</td>
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<td>0.7 X 0.7 X 4.0</td>
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<td>0.65 X 0.65 X 1.0</td>
<td>-</td>
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<tr>
<td>Time of echo (ms)</td>
<td>85</td>
<td>85</td>
<td>97.5</td>
<td>6.9</td>
<td>30</td>
</tr>
<tr>
<td>Time of inversion (ms)</td>
<td>—</td>
<td>—</td>
<td>2.000</td>
<td>—</td>
<td>-</td>
</tr>
<tr>
<td>Time of repetition (ms)</td>
<td>4,000</td>
<td>4,000</td>
<td>3,962</td>
<td>25</td>
<td>806.5</td>
</tr>
<tr>
<td>No. of excitations</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>

*Values represent frequency encoding direction X phase encoding direction X slice thickness.
— = Not applicable.