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Morphometric analysis of ventricular indexes and intracranial cerebrospinal fluid spaces in the brain using magnetic resonance imaging healthy in Van cats

Veysel Delibaş^{1*} and Cemil Göya²

Abstract

Background Ventricular indexes are defined as a numerical marker of ventricular dimensions in domestic mammals. The anatomical size of the brain ventricles has been the subject of many studies so far and has been accepted as a potential indicator of many brain disorders in the clinical field. Currently, the number of studies describing the morphometry of the brain ventricular system in cats is limited. Furthermore, no studies have been conducted specifically on indexes characterizing the numerical compatibility of the brain and brain ventricles in cats. The aim of this study was to reveal the morphometric status of intracranial cerebrospinal fluid spaces and ventricular indexes in healthy Van cats by magnetic resonance imaging method.

Results For this retrospective study, T2-weighted magnetic resonance imaging (MRI) scans were performed at 1.5 T on 20 (10 male and 10 female) Van cats, under general anaesthesia. The animals were at the age of mean 4 (3–5 age). All Van cats were selected from individuals who had not undergone any surgical procedures, were not neutered, and had no visible anomalies. The statistical analysis of first, descriptive statistics such as mean and standard deviation were calculated. In line with the mean results obtained, the difference between sex was examined statistically. 'A Mann-Whitney U test' was applied to detect sex differences in measurement parameters in the study. The results are as follows (mean \pm standard deviation): Intracranial cerebrospinal fluid spaces measurements: R-fs: 1.02 ± 0.19 mm, L-fs: 1.03 ± 0.18 mm, A-if: 1.06 ± 0.26 mm, R-sf: 1.38 ± 0.32 mm, L-sf: 1.37 ± 0.27 , V_1 : 4.26 ± 0.53 mm. Indexes: Fourth ventricle: $15.95 \pm 1.73\%$, Bifrontal: $17.45 \pm 1.78\%$, Bioccipital: $47.53 \pm 9.36\%$, Evans: $13.76 \pm 2.93\%$, Lateral ventricle: $35.41 \pm 2.50\%$, Callosal angle: $85.06^\circ \pm 4.42^\circ$.

Conclusions The present study provides baseline values of intracranial cerebrospinal fluid spaces and linear indexes of the ventricles in the Van cats. The acquisition of these data contributes to filling the knowledge void on important anatomical and morphological features of the Van cats brain.

Keywords Cat, Cerebrospinal fluid, Morphometric, MRI, Ventricular index

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Background

Ventricular indexes are numerical markers used to assess the dimensions of the brain ventricles in domestic mammals [1]. In various studies, these indexes are calculated separately, including the evans index, bifrontal index, bioccipital index, and fourth ventricle index [1–4]. Linear measurements of intracranial cerebrospinal fluid (CSF) spaces are similarly assessed, including the maximum width of the frontal subarachnoid space, the maximum width of the sylvian fissure, the maximum width of the anterior interhemispheric fissure and the maximum width of the fourth ventricle [1–4].

The anatomical size of the brain ventricles has been extensively studied and is recognized as a potential indicator for various brain disorders in the clinical field [5–8]. Research in humans indicates that ventricular indexes can provide valuable insights into the reduction of brain volume in atrophy-related disorders beyond normal aging [9, 10]. Additionally, enlargement of CSF spaces is reported in conditions such as Alzheimer's disease, schizophrenia, Parkinson's disease, and particularly hydrocephalus [2, 10].

Hydrocephalus, often referred to as overt or progressive ventriculomegaly, is categorized into internal and external types. Internal hydrocephalus results from excessive accumulation of CSF within the cerebral ventricles [11–13], while external hydrocephalus involves CSF accumulation between the cerebral hemispheres and the overlying arachnoid membrane, rather than within the lateral ventricles [14]. Numerous cases of hydrocephalus, caused by pathological processes such as infection or tumors, have been reported in domestic animals [12, 13, 15]. In veterinary practice, magnetic resonance imaging (MRI) of the brain is routinely employed in cats to investigate suspected intracranial diseases. The causes of ventriculomegaly and the assessment of ventricular enlargement remain active areas of research in veterinary medicine [16–18]. In addition, the use of the cat species in studies on mathematical modeling of the cerebral ventricular system is of interest [19].

Currently, there are studies describing the morphometry of the brain ventricular system in cats [20, 21].

However, there are no studies specifically focusing on the indexes that characterize the numerical relationship between the brain and its ventricles in cats. In the veterinary field, the only existing research on ventricular indexes pertains to healthy sheep [22]. Furthermore, there is a lack of studies addressing the morphometry of intracranial cerebrospinal fluid spaces in domestic animals.

The aim of this study is to morphometric characterize ventricular indexes and cerebrospinal fluid spaces using MRI images in healthy Van cats.

Results

Intracranial cerebrospinal fluid (CSF) spaces were clearly delineated in the dorsal T2 MRI sections acquired for this study, with anatomical borders accurately identified. The measurements for the maximum width of the right frontal subarachnoid space (R-fss), maximum width of the left frontal subarachnoid space (L-fss), maximum width of the anterior interhemispheric fissure (A-if), maximum width of the right sylvian fissure (R-sf), maximum width of the left sylvian fissure (L-sf), and dorsal width of the fourth ventricle (V_1) are reported in millimeters (Table 1). These measurements were analyzed separately for male and female cats, and the statistical comparison between sex is presented in Table 1. It was found that R-fss, L-fss, and A-if measurements were significantly greater in males compared to females ($p < 0.05$) (Table 1). In contrast, no significant differences were observed between sex for the R-sf, L-sf, and V_1 measurements ($p > 0.05$) (Table 1).

Anatomical measurements from the dorsal MRI images were used to calculate various ventricular indexes. The indexes computed include the fourth ventricle index (VQ-indx), bifrontal index (BF-indx), bioccipital index (BO-indx), Evans index (EV-indx), and lateral ventricular index (LV-indx). Additionally, callosal angle (CL-ang) measurements were obtained from T2 weighted transversely MRI images. As with the previous measurements, the ventricular indexes were analyzed separately for males and females, with statistical comparisons shown in Table 2. The BO-indx and CL-ang measurements were significantly higher in males ($p < 0.05$) (Table 2). Conversely, the EV-indx measurement was significantly higher in females ($p = 0.023$) (Table 2). No significant differences between sex were found for the VQ-indx, BF-indx, and LV-indx measurements ($p > 0.05$) (Table 2).

Discussion

Ventricular indexes are well-established indicators of changes in brain parenchymal volume, atrophy, and neurological conditions related to ventricular expansion [23–25]. Neuroimaging techniques such as MRI and computed tomography (CT) are crucial for analyzing

Table 1 Mean and statistical results of measurements of the intracranial cerebrospinal fluid space

| Measure | Mean values of all cats (n = 20) | Mean values of female cats (n = 10) | Mean values of male cats (n = 10) | p |
|------------|----------------------------------|-------------------------------------|-----------------------------------|--------|
| R-fss (mm) | 1.02 ± 0.19 | 0.93 ± 0.18 | 1.11 ± 0.16 | 0.032* |
| L-fss (mm) | 1.03 ± 0.18 | 0.94 ± 0.18 | 1.11 ± 0.15 | 0.034* |
| A-if (mm) | 1.06 ± 0.26 | 0.83 ± 0.12 | 1.30 ± 0.08 | 0.001* |
| R-sf (mm) | 1.38 ± 0.32 | 1.36 ± 0.42 | 1.41 ± 0.20 | 0.726 |
| L-sf (mm) | 1.37 ± 0.27 | 1.28 ± 0.31 | 1.46 ± 0.18 | 0.097 |
| V_1 (mm) | 4.26 ± 0.53 | 4.12 ± 0.50 | 4.40 ± 0.53 | 0.083 |

(*) $p < 0.05$ statistical significance value

Table 2 Mean and statistical results of measurements of the ventricular indexes

| Measure | Mean values of all cats (n=20) | Mean values of female cats (n=10) | Mean values of male cats (n=10) | p |
|-------------|--------------------------------|-----------------------------------|---------------------------------|--------|
| VQ-indx (%) | 15.95±1.73 | 15.19±1.70 | 16.72±1.76 | 0.530 |
| BF-indx (%) | 17.45±1.78 | 17.77±2.06 | 17.14±1.48 | 0.443 |
| BO-indx (%) | 47.53±9.36 | 41.78±9.74 | 53.29±4.05 | 0.003* |
| EV-indx (%) | 13.76±2.93 | 15.20±2.48 | 12.32±2.70 | 0.023* |
| LV-indx (%) | 35.41±2.50 | 34.85±2.99 | 35.97±1.90 | 0.333 |
| CL-ang (°) | 85.06±4.42 | 81.58±3.19 | 88.54±2.04 | 0.001* |

(*) $p < 0.05$ statistical significance value

alterations in brain size and ventricular volumes in these pathologies.

HDR-MRI combines multiple suboptimal images that highlight different features into a single image that displays all features simultaneously. However, the wider dynamic range sacrifices quantitative contrast between samples since the absolute range of pixel intensities is fixed [26]. Therefore, in this study, HDR MRI method was used to precisely examine anatomical structures and determine measurements.

Age is a critical factor influencing the volume of intracranial cerebrospinal fluid spaces [4]. Studies in humans have indicated that subarachnoid space variability is greater before the age of two [10]. As individuals age, brain atrophy typically presents as a decrease in gray matter and an increase in the size of the third, fourth, and lateral ventricles [27]. Similarly, ventricular enlargement is observed in conditions such as hydrocephalus and cerebral atrophy [2, 28]. To establish a baseline for intracranial CSF volumes in adult cats, our study focused exclusively on cats with an mean age of four years.

Weight is an important factor affecting intracranial cerebrospinal fluid (CSF) volume [29–31]. Many studies have shown that the correlation between body weight and CSF volume in dogs is linear but not directly proportional [29–31]. Although our study did not directly examine the relationship between weight and CSF space measurements, we think there may be a significant relationship between weight and cerebrospinal fluid (CSF) spaces in this study. In our study, male Van cats weigh more than female Van cats. Additionally, when cerebrospinal fluid area measurements are examined, it is seen that male Van cats have larger dimensions than female Van cats (Table 1). Based on this, we hypothesize that there may be a connection between weight and CSF areas. However, since the effect of the weight factor on CSF area measurement values was not statistically examined in our this study, we cannot reach a definitive conclusion.

Sex also significantly affects the volume of intracranial cerebrospinal fluid spaces and ventricular index measurements [32, 33]. Human studies have found that males tend to have higher measurement values compared to

females [32, 33]. In our study, we accounted for sex differences and found that R-fss, L-fss, and A-if measurements were higher in males. Similarly, the BO-indx and CL-ang measurements were also elevated in males. In contrast, the EV-indx was higher in females, which differs from the patterns observed in humans.

Bourne et al. [8] reported a linear correlation between ventricular volumes and ventricular measurements. Therefore, ventricular indexes can serve as practical diagnostic tools, potentially replacing the need for separate volume calculations in clinical settings [4, 8, 34]. The mean bifrontal index in humans is typically around 30% [4, 35], while the mean bifrontal index in sheep is 33.8% [22]. Our study found that the mean value bifrontal index in healthy Van cats was $17.45 \pm 1.78\%$. In some studies, the ventricular-brain index (calculated by dividing the maximum continuous distance between the inner borders of the ventricles in the same image by the maximum width of the brain parenchyma) was assessed in dogs [17, 36]. One such study reported an average ventricular-brain index value of 54% in a group of dogs with ventriculomegaly and 73% in a group of dogs with hydrocephalus [17]. In our study, this index corresponds to the bioccipital index. The mean bioccipital index in humans is approximately 69% [37, 38], whereas in healthy Van cats, it was $47.53 \pm 9.36\%$.

The Evans index, first established by Willem Evans, remains a widely used ventricular index in clinical research [39]. In humans, this index mean between 20% and 25% [38], and in sheep, it is around 21% [22]. Our study determined that the mean evans index in healthy Van cats is $13.76 \pm 2.93\%$.

The fourth ventricle index, which reflects the ratio of the transverse diameter of the fourth ventricle to the total diameter of the brain at the same level, is a key marker of ventricular dilation [40]. The mean of this index in humans is $12.11 \pm 1.81\%$ [10], whereas in healthy Van cats, it was $15.95 \pm 1.73\%$.

The lateral ventricular index, calculated by dividing the craniocaudal length of the brain by the craniocaudal length of the right or left lateral ventricle, has been strongly associated with dementia diagnoses in clinical studies [41–43]. In our study, the mean lateral ventricular index in healthy Van cats was $35.41 \pm 2.50\%$. The callosal angle, defined as the angle between the lateral ventricles in transverse view, is an important indicator of ventricular dilation [44, 45]. Our data showed that the callosal angle in healthy Van cats was $85.06^\circ \pm 4.42^\circ$ degrees.

Among the limitations of this study are the lack of sufficient reference studies for making species-specific comparisons, the age of the Van cats used in the study, and the head conformation of the Van cat breed being different from other cat breeds. The landmarks used to define our measurements naturally vary between species.

Therefore, the comparison of results obtained from cats with those from humans has significantly limited our study. There are studies indicating that age is correlated with the morphometry of brain ventricles. However, the preference for Van cats with an mean value age of 4 years is another limitation of our study. There are studies related to the correlation between ventricular enlargement and the degree of brachycephaly. However, an important limitation of our study is that only data on the Van cat breed is presented. Additionally, the head structure of Van cats is not specified. This causes our results to be inadequate to explain the relationship between ventricular enlargement and head structure. Another important limitation of our study is the use of ketamine as an anesthetic. Previous studies have shown that chemicals used for sedation and anesthesia can affect cerebrospinal fluid pressure [46, 47]. In this context, ketamine used in our study may have affected cerebrospinal fluid pressure, which in turn may have affected the measurements of cerebrospinal fluid spaces in our study. To more accurately determine the reliability of these measurements and to better explain the morphometry of cerebrospinal fluid spaces and ventricular indices in healthy Van cats, studies involving different cat breeds, various age ranges, and a larger population of animals are recommended.

Conclusion

This study provides the first comprehensive morphometric analysis of intracranial cerebrospinal fluid spaces and ventricular indexes in healthy Van cats. We present normative values for these measurements, offering valuable reference points for research involving neurological and behavior disorders (anxiety, obsessive-compulsive disorder, and aggression) associated with ventriculomegaly or neurodegeneration in cats. Our findings establish a foundational reference for neuroscientists and veterinarians seeking to use cats as preclinical models in neurological research.

Methods

Animals

This study was conducted with approval from the Van Yuzuncu Yil University Animal Experiments Local Ethics Committee, dated February 29, 2024, under decision number 2024/02–01. The study involved 20 healthy adult Van cats, comprising 10 males and 10 females. The animals were at the age of mean 4 (min: 3–max: 5). The mean weights were 3300 ± 0.49 (2.700–4.300) g for females and 4340 ± 0.98 (2.800–5.700) g for males. All Van cats were selected from individuals who had not undergone any surgical procedures, were not neutered, and had no visible anomalies and no physical or neurological disorders.

Anesthesia and imaging

In accordance with the animal welfare guidelines of the local ethics committee, Van cats were given ad libitum to food prior to anesthesia. In order to minimize the risk of aspiration pneumonia during the anesthetic procedure, food was completely withheld approximately 12 h before the anesthetic procedure and water was completely withheld approximately 3 h before the anesthetic procedure. Subsequently, they were transferred to the anesthesia room and restrained. General anesthesia was induced to immobilize the Van cats during the MRI scan. Anesthesia was administered via an intramuscular (IM) injection of a combination of Ketamine (15 mg/kg body weight, IM, Ketazol® 10% injectable, Interhas Veterinary Pharmaceuticals, Ankara) and Xylazine (1–2 mg/kg body weight, IM, Alfazyne® 2% injectable, Ege Vet Veterinary Pharmaceuticals, Izmir). During anesthesia, the depth of anesthesia was monitored using a hands-on monitoring method. Key indicators included the presence of corneal reflexes, mucous membrane color, and jaw tone.

A 1.5 Tesla magnetic resonance imaging (MRI) device (SIEMENS Healthineers-MAGNETOM Altea, Germany) was used for imaging. The Van cats were positioned in a supine posture within the MRI machine. The images obtained were recorded in DICOM (Digital Imaging and Communications in Medicine) format. Anatomical images were acquired in T2-weighted sequences, including dorsal and transverse planes. To overcome the feature loss caused by low signal-to-noise ratio, and to improve contrast differentiation of tissues, High Dynamic Range (HDR) processing was applied to the T2-weighted images. Therefore, HDR-MRI images were generated (B in Figs. 1, 2, 3, 4 and 5). Parameters for dorsal and transverse images of the head were obtained using T2-weighted turbo (fast) spin echo (TSE) sequences with a repetition time (TR) of 4010 ms and an echo time (TE) of 90 ms. The slice thickness was set to 2 mm with no gap. The field of view (FoV) was 150 mm, and the matrix was 256×256 .

Dataset preparation

Morphometric measurements were performed on the MRI images following the methodologies outlined by Özdikiçi [10] and Trovatelli et al. [22]. The evaluation of MRI images and the taking of morphometric measurements in this study were performed by two observers, a PhD veterinary anatomist with a background in veterinary radiology and a PhD radiologist. All measurements were taken by each one separately. The images were analyzed to obtain various measurements as detailed below. Intracranial cerebrospinal fluid measurements (Fig. 1) were taken as follows:

R-fss: Maximum width of the right frontal subarachnoid space.



Fig. 1 Intracranial cerebrospinal fluid spaces and measurement parameters in T2 dorsal MRI images. **(A)** T2-weighted dorsal MRI section passing through the lateral ventricles in the center and the Sylvian fissure level in the periphery: (1) right and left frontal subarachnoid space, (2) anterior interhemispheric fissure, (3) right and left Sylvian fissure, (4) olfactory bulb, (VL) lateral ventricles; **(B)** T2-weighted HDR image dorsal MRI section passing through the lateral ventricles in the center and the level of the Sylvian fissure in the periphery: (A-if) maximum width of anterior interhemispheric fissure, (R-fss) maximum width of the right frontal subarachnoid space, (L-fss) maximum width of the left frontal subarachnoid space, (R-sf) maximum width of the right Sylvian fissure, (L-sf) maximum width of the left Sylvian fissure

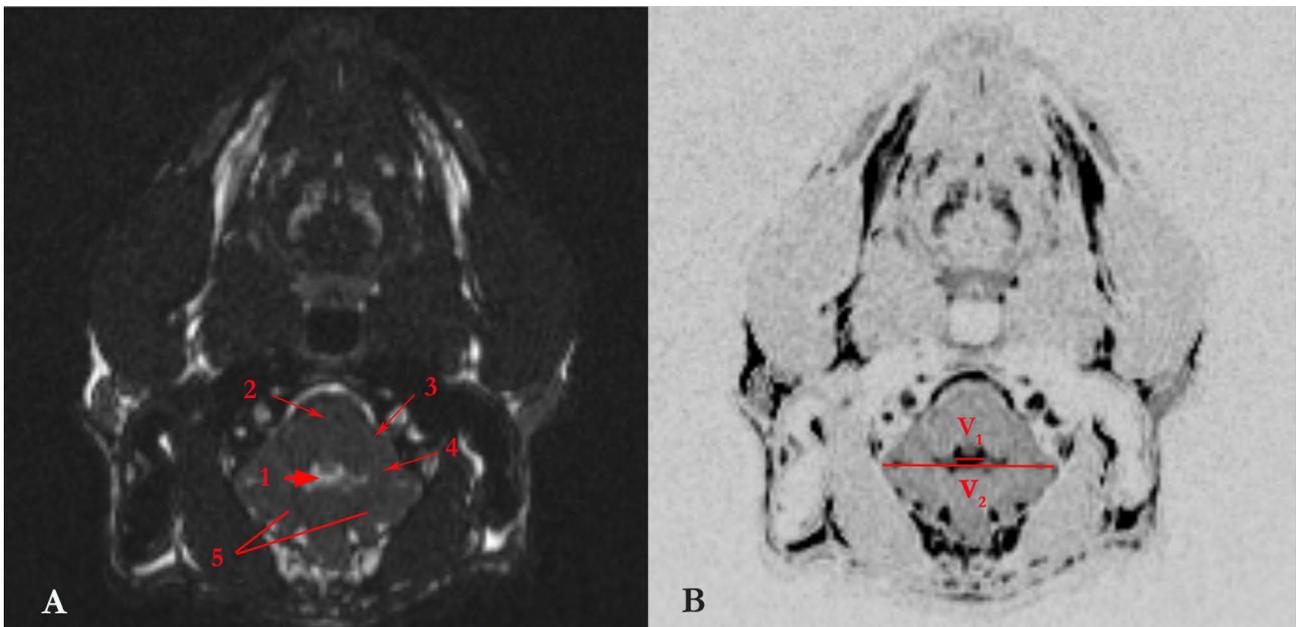


Fig. 2 Fourth ventricle and index measurement parameters in T2 dorsal MRI images. **(A)** T2-weighted dorsal MRI section passing through the level of the fourth ventricle: (1) fourth ventricle, (2) pons, (3) cerebello pontine angle (4) middle cerebellar peduncle (5) cerebellar hemisphere; **(B)** T2-weighted HDR image dorsal MRI section passing through the level of the fourth ventricle: (V₁) maximum width of fourth ventricle, (V₂) Internal diameter of the skull at the level of the measurement parameter V₁

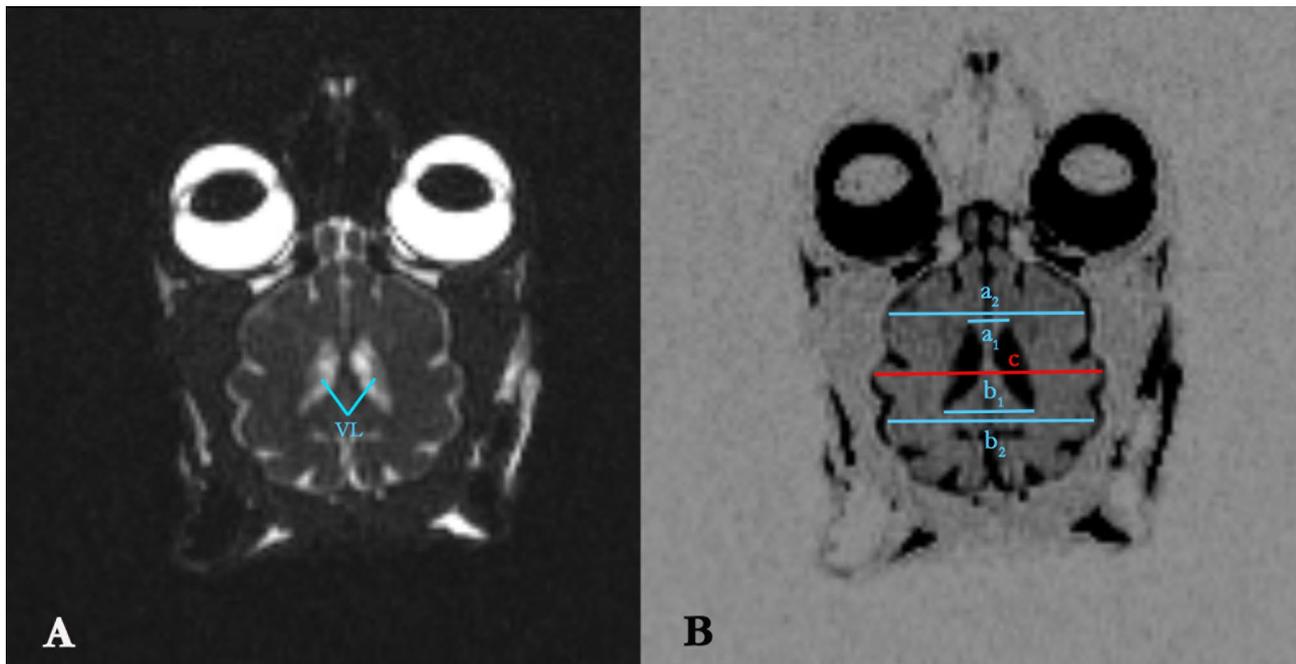


Fig. 3 Measurement parameters for ventricular indexes in T2 dorsal MRI images. **(A)** T2-weighted dorsal MRI section passing through the lateral ventricles in the center and the sylvian fissure level in the periphery: (VL) lateral ventricles; **(B)** T2-weighted HDR image dorsal MRI section passing through the lateral ventricles in the center and the level of the sylvian fissure in the periphery: (a_1) the largest distance between the anterior horns of the lateral ventricles, (a_2) internal diameter of the skull at the level of the measurement parameter a_1 , (c) the maximum diameter of the cavum cranii in dorsal section, (b_1) the posterior lateral ventricles the largest distance between the horns, (b_2) internal diameter of the skull at the level of the measurement parameter b_1

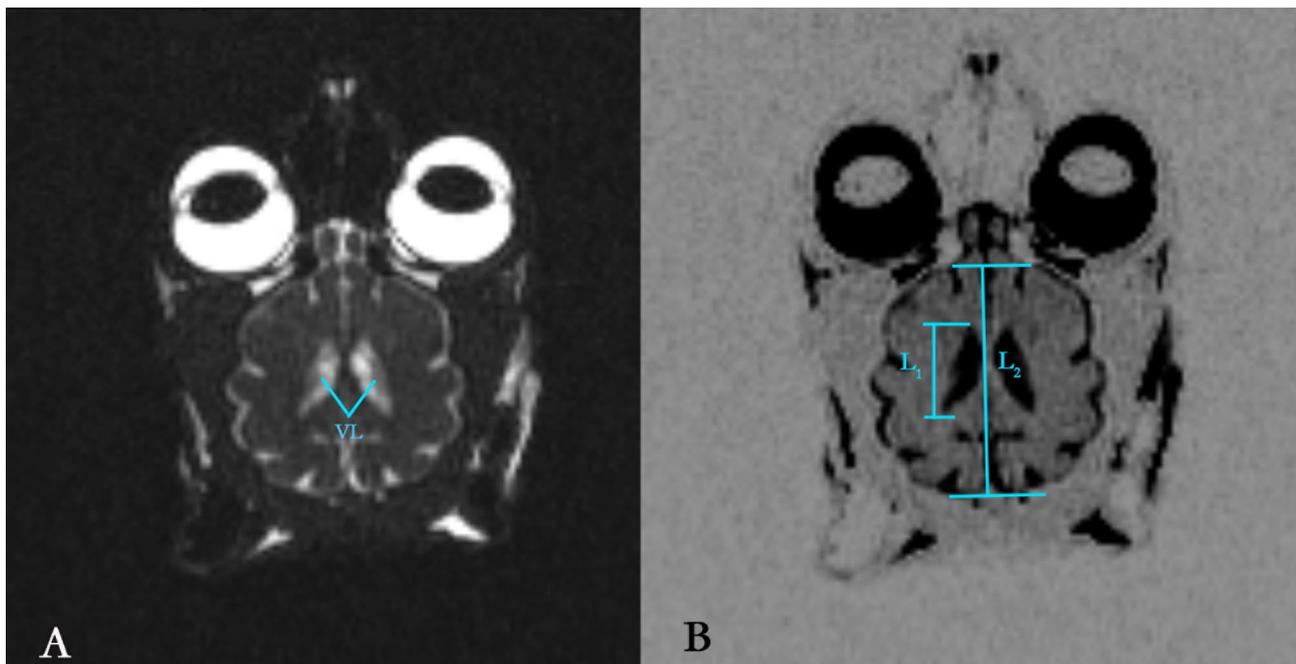


Fig. 4 Measurement parameters for lateral ventricular index on T2 dorsal MRI images. **(A)** T2-weighted dorsal MRI section passing through the lateral ventricles in the center and the sylvian fissure level in the periphery: (VL) lateral ventricles; **(B)** T2-weighted HDR image dorsal MRI section passing through the lateral ventricles in the center and the level of the sylvian fissure in the periphery: (L_1) maximum craniocaudal length of lateral ventricle, (L_2) craniocaudal diameter of cavum cranii

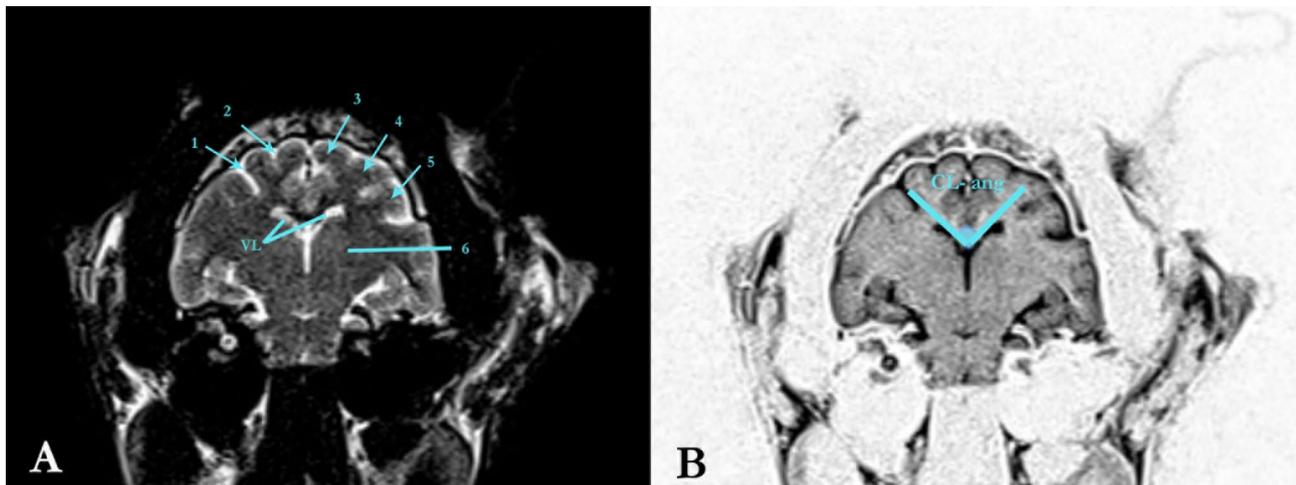


Fig. 5 Callosal angle measurement parameter in T2 transversal MRI images. **(A)** T2 transversal MRI section passing through the caudal thalamus level: (VL) lateral ventricles, (1) suprasylvian sulcus, (2) lateral sulcus, (3) suprasplenial gyrus, (4) suprasylvian gyrus, (5) ectosylvian gyrus, (6) thalamus; **(B)** T2-weighted HDR image transversal MRI section passing through the caudal thalamus level: (CL-ang) callosal angle

L-fss: Maximum width of the left frontal subarachnoid space.

A-if: Maximum width of the anterior interhemispheric fissure.

R-sf: Maximum width of the right sylvian fissure.

L-sf: Maximum width of the left sylvian fissure.

V_1 : Dorsal width of the fourth ventricle.

The following indexes were calculated:

VQ-idx: Fourth ventricle index = $(V_1 / V_2) \times 100$.

V_1 : Maximum width of the fourth ventricle (Fig. 2B).

V_2 : Internal diameter of the skull at the level of V_1 (Fig. 2B).

BF-idx: Bifrontal index = $(a_1 / a_2) \times 100$.

a_1 : Maximum distance between the anterior horns of the lateral ventricle (Fig. 3B).

a_2 : Internal diameter of the skull at the level of a_1 (Fig. 3B).

BO-idx: Bioccipital index = $(b_1 / b_2) \times 100$.

b_1 : Maximum distance between the posterior horns of the lateral ventricle (Fig. 3B).

b_2 : Internal diameter of the skull at the level of b_1 (Fig. 3B).

EV-idx: Evans index = $(a_1 / c) \times 100$.

a_1 : Maximum distance between the anterior horns of the lateral ventricle (Fig. 3B).

c : Maximum diameter of the cavum cranii in the dorsal section (Fig. 3B).

LV-idx: Lateral ventricle index = $(L_1 / L_2) \times 100$.

L_1 : Maximum craniocaudal length of the lateral ventricle (Fig. 4B).

L_2 : Craniocaudal diameter of the cavum cranii (Fig. 4B).

CL-ang: Callosal angle = The angle is defined as the angle formed between the left and right parts of the corpus callosum (the upper walls of the ventricles) in a

coronal section passing through the posterior commissure (PC) and perpendicular to the anterior commissure-posterior commissure (AC-PC) plane.

CL-ang: Callosal angle (Fig. 5B).

Statistical analysis

Descriptive statistics, including mean and standard deviation, were calculated for all measurements. To assess differences between sex, the Mann-Whitney U test was applied to detect any significant variations in measurement parameters. All statistical analyses were conducted using SPSS (version 21).

Abbreviations

| | |
|-------|--|
| AC | Anterior commissure |
| CSF | Cerebrospinal Fluid |
| CT | Computed Tomography |
| DICOM | Digital Imaging and Communications in Medicine |
| FoV | Field of View |
| HDR | High Dynamic Range |
| IM | Intramuscular |
| MRI | Magnetic Resonance Imaging |
| PC | Posterior commissure |
| PhD | Doctor of Philosophy |
| SPSS | Statistical Package for the Social Sciences |
| TE | Echo Time |
| TR | Repetition Time |
| TSE | Turbo Spin Echo |

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Author contributions

V.D.: Conceptualisation, methodology, software, validation, formal analysis, investigation, resources, data curation, visualisation, writing – original draft, writing – review and editing, and project administration. C.G.: Conceptualisation, methodology, software, validation, formal analysis, investigation, resources, data curation, visualisation, writing – review and editing, project administration, and supervision.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

This study was conducted with the decision No. 2024/02 – 01 of Van Yüzüncü Yil University Animal Experiments Local Ethics Committee

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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