Radiological Investigation of the Rat Cavernous Sinus and Surrounding Channels

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With 3 figures. **Received in March, accepted March 2024**

Abstract

The anatomy of the rat cavernous sinus has been reported inconsistently in the literature. In the present study, we aimed to investigate the rat cavernous sinus and surrounding venous channels using radiological methods. Four adult Sprague Dawley rats underwent computed tomography venography following the injection of a contrast agent via the tail vein. In all rats, the cavernous sinus was consistently identified laterally adjacent to the internal carotid arteries and pituitary glands. Intracranially, the cavernous sinus extended along the floor of the skull base, from the orbito-rotundum foramen to the posterior edge of the basisphenoid. It had inferior continuity with the interpterygoid veins via the midline osseous venous component, anterior continuity with the superior and inferior orbital veins, superior continuity with the basal vein, and posterior continuity with the superior and inferior petrosal sinuses. Our findings were generally consistent across all rats, although minor variations in tributaries were noted. The present findings update our anatomical understanding of the cavernous sinus in rats and potentially resolve inconsistencies from past reports. Furthermore, we have provided a detailed radiological visualization of the cavernous sinus and its surrounding venous structures through computed tomography venography, which may serve as an atlas of venous anatomy in this region. This improved understanding will aid in the interpretation of in vivo rat studies involving the cavernous sinus, and will contribute to the field of comparative neuroanatomy.

Keywords: rat, CTV, cavernous sinus

Introduction

The rat is a widely used experimental animal, and our knowledge of its anatomy greatly influences the results of the animal studies and their subsequent interpretation. From the perspective of comparative anatomy, detailed macro-anatomical studies facilitate our understanding of tissue phylogenic and embryologic backgrounds. However, our knowledge of the basic anatomy of the rats in specific regions is sometimes far less than that of humans.

The cavernous sinus is a complex of vascular structures located in the skull base of reptiles Porter et al. (2016) , birds (Porter and Witmer, 2016), and mammals (Butler, 1967). Although the documentation of rat cavernous sinus anatomy has been limited to a few articles (Butler, 1967; Bleys et al., 1996; Szabó, 1990; Paxinos, 2014), human cavernous sinus anatomy has been described in detail in numerous radiological (Tanoue, 2006 and Gailloud, 2000), and cadaveric studies (Harris and Rhoton, 1976). Notably, these articles have used inconsistent terminology and anatomical descriptions, particularly when describing the intercavernous sinus and its extent. In the present study, we therefore aimed to investigate the venous anatomy of rats using micro-computed tomography venography (CTV). We then integrated the current findings with past anatomical research, thus providing a detailed venous atlas for future studies.

Materials and methods

The current study was a retrospective radiological analysis and examination of CT angiography images obtained from the sham group of another study with other aims. This previous study was conducted according to a protocol that was reviewed and approved by the laboratory animal center of KEIO University (Permit No. A2023-031). The present study included four adult Sprague Dawley rats (150–250 g, 7–12 weeks of age) purchased from Japan SLC (Shizuoka, Japan). The rats were anesthetized by peritoneal injection of medetomidine hydrochloride (0.15 mg/kg), midazolam (2 mg/kg), and butorphanol (2.5 mg/kg). Next, a contrast agent (0.03–0.045 mL/g) was injected via the tail vein for approximately 15–30 seconds. The head of each rat was then positioned and scanned using micro-CT (RmCT2; Rigaku, Tokyo, Japan). The scan parameters were as follows: tube voltage, 90 kV; tube current, 20 μA; field of view, 30 mm; rotation time, 3 minutes; and spatial resolution, 10 µm. Axial source images and reconstructed coronal, sagittal, and oblique images were used for the analyses, which were conducted using a three-dimensional image analysis software (Synapse Vincent; Fujifilm, Tokyo, Japan). In this way, we investigated the anatomical features of the cavernous sinus and adjacent venous channels. The continuity of vessels enabled us to distinguish between arteries and veins.

Results

Coronal and axial CTV images are shown in Figs. (1, 2). Schematic illustrations superimposed on bone CT are shown in Fig. (3). In rats, the cavernous sinus was located laterally to the internal carotid artery and pituitary gland; it was identified in all four rats. The cavernous sinus extended intracranially along the floor of the skull base, from the orbito-rotundum foramen to the posterior edge of the basisphenoid. Posteriorly, it was continuous with the superior and inferior petrosal sinus. The horizontal intercavernous sinus connected the cavernous sinuses on both sides at the junction between the cavernous and superior petrosal sinus. Superiorly, the cavernous sinus connected with the basal vein, which drained the anterior cerebral and middle cerebral veins. The basal veins also had a tributary connecting the basal veins on both sides; this was a pial vein that we termed a “posterior communicating vein”. Inferiorly, the posteroinferior osseous tributary of the cavernous sinus (the caverno-ophthalmic vein (Szabó, 1990) on each side anteriorly reached the midline osseous venous compartment of the ectopterygoid vein within the basisphenoid. The osseous compartment was continuous with an interpterygoid vein on each side, which further emptied into an internal maxillary vein. The compartment also received another tributary via the anterior lacerate foramen, from the anterior part of the cavernous sinus. Anteriorly, the cavernous sinus was connected with the superior and inferior orbital veins via the orbito-rotundum foramen; it has sometimes been considered a direct continuation of the orbital veins, and was referred to as the “ophthalmic vein” in previous literature (Szabó, 1990). The branch perioptic vein of the superior orbital vein was an anterior emissary vein via the optic canal, and drained the midline interperioptic sinus at the anterior cranial base (Szabó, 1990). The midline sinus was continuous with the left and right anterior cerebral veins and was involved in basal drainage in the rat brain. The findings regarding these veins were consistent among all rats with the exception of the small posterior communicating vein, which was identified in only two rats.

Discussion

In the present report, we described the venous anatomy adjacent to the cavernous sinus using CTV. Although earlier studies have reported the dissection and histological investigation of the cavernous sinus (Bleys, 1996; Szabó, 1990, Paxinos, 2014), radiological investigation using CTV has not been previously reported. Although anatomical dissection is generally considered the gold standard for anatomical studies, radiological methods enable the observation and analysis of structures without destroying tissues. Given that the cavernous sinus is located adjacent to bony tissues, and that the surrounding venous structure is connected via a bony canal and a foramen, anatomical studies using CTV are likely beneficial for this specific region. Indeed, our radiological study allowed us to describe the detailed anatomy of the venous channels in this area as well as the surrounding bony structures, and will likely serve as an atlas of venous anatomy in this region.

The venous anatomy adjacent to the cavernous sinus develops differently in rats than in humans. According to an important textbook (Paxinos, 2014), the main difference is the two-story venous structure in rats; its intracranial upper floor is situated in the parasellar region and connects with the basal vein and superior and inferior petrosal sinuses, and is comparable with the human cavernous sinus. The lower osseous segment comprises a midline structure connected with both the upper intracranial compartment and the bilateral interpterygoid veins, which are further emptied into internal maxillary veins. Depending on the study, the midline osseous compartment is either considered an extension of the cavernous and intercavernous sinuses (Paxinos, 2014) or the basisphenoid sinus (Szabó, 1990) .

The venous anatomy described in the present CTV study was mostly consistent with a study by Szabó (1990), in which exact anatomical and embryological analyses were conducted using corrosion cast and histological sections. The major novel finding of the current study was the continuity of the cavernous sinus from the anterior cranial base (where it connects with the superior and inferior orbital veins) to the parasellar region (where it connects with the superior and inferior petrosal sinus). This continuity has not previously been clearly reported in the literature. This may be because the connection is relatively small compared with the connection with the basisphenoid osseous veins, meaning that it might have failed to be recognized in previous studies. Furthermore, our findings suggest that the term "cavernous sinus" should be limited to the intracranial parasellar and anterior cranial base segments. This is because anatomical terminology should be defined according to strict anatomical dispositions. In humans, the "sinus" represents the venous channels within the dura mater, and consistency of terminology among species is essential from a comparative neuroanatomy viewpoint. Moreover, as a general perception, the cavernous sinus—either in rats or humans—is a channel that is directly connected with the ophthalmic and pterygoid veins. Past articles have mistakenly considered the osseous compartment to be a part of the cavernous sinus, without recognizing the direct connection between the ophthalmic veins and parasellar cavernous sinus. We therefore propose that the midline osseous compartment should be considered an osseous extension of the interpterygoid veins rather than a part of the intercavernous sinus (as it has been referred to in past literature) (Paxinos, 2014). The "true" intercavernous sinus is thus a channel connecting the bilateral parasellar cavernous sinus just above the basisphenoid, as mentioned in a previous report (Szabó, 1990).

In the present study, we made another major finding regarding the caverno-ophthalmic vein, which was initially described in the corrosion study by Szabó (1990). In his illustration, the vein joins the basisphenoid vein anteriorly to the pterygoid veins after running through the so-called "caverno-ophthalmic" osseous canal. However, in our rats, the connection was always posterior to the pterygoid veins. The previous corrosion study may have failed to recognize the precise location of the connection within the basisphenoid bone; by contrast, the current CTV study enabled us to observe vessels without destroying relationships among tissues, which likely contributed to our finding. The caverno-ophthalmic vein is named after its connection between the midline osseous component of the interpterygoid vein and the cavernous sinus, because Szabó (1990) considered that the osseous component is a direct continuation of the ophthalmic vein (the superior/inferior orbital veins). However, given that our study demonstrates a direct intracranial connection between the cavernous sinus and the ophthalmic vein (the anterior part of the cavernous sinus), we believe that the term “caverno-pterygoid vein” may better represents the anatomical features of this vein, rather than the original—relatively confusing—name.

As demonstrated in the present study, the rat cavernous sinus is a relatively less developed channel, and from the viewpoint of blood flow, the greatest amount of venous flow from the orbital veins seems to be directed to the interptery-goid vein rather than to the parasellar segment of the cavernous sinus. A study by Butler (1967) indicates that, at the early embryological stage, the ophthalmic vein (the primitive maxillary vein) is originally continuous with the pro-otic sinus (the precursor of the cavernous sinus). The primitive maxillary veins have many connections with the facial tributaries of the external jugular vein, across the orbital margin. Later, the growth of the posterior dural sinuses leads to a shift in venous flow to the posterior dural sinuses, with reduced venous flow in the pro-otic sinus, whereas the connection between the ophthalmic and facial veins increases in size. One of these anastomoses may later represent the connection between the ophthalmic and interpterygoid veins via the midline osseous venous channel. This embryological configuration might explain the relatively small size of the cavernous sinus in rats, as well as the well-developed ophthalmic, basisphenoid osseous, and pterygoid veins.

Our study has a few limitations. For example, our results and discussion were based solely on imaging findings, and may not be entirely consistent with the true anatomy of rats. Additionally, this study retrospectively reviewed CTV data from rats in another study, which had a different aim. Accordingly, a direct dissection and microscopic investigation was not performed in the rats in the present study. Furthermore, we must note that images obtained using contrast agent are always influenced by the experimental protocol as well as by the age, weight, and cardiac function of the experimental subjects. In addition, rat strain may influence venous channel anatomy; the anatomy presented in the current study may thus not correspond to that of rats of different strains.

Conclusions

The present findings update our anatomical understanding of the cavernous sinus in rats, and potentially resolve inconsistencies from past reports. Furthermore, we have provided a detailed radiological visualization of the cavernous sinus and its surrounding venous structures through CTV, which may serve as an atlas of venous anatomy in this region. This improved under-standing will aid in the interpretation of *in vivo* rat studies involving the cavernous sinus, and will contribute to the field of comparative neuroanatomy.

Acknowledgment

We thank Bronwen Gardner, PhD, from Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

Conflict of interest statement

The authors declare no conflict of interest.

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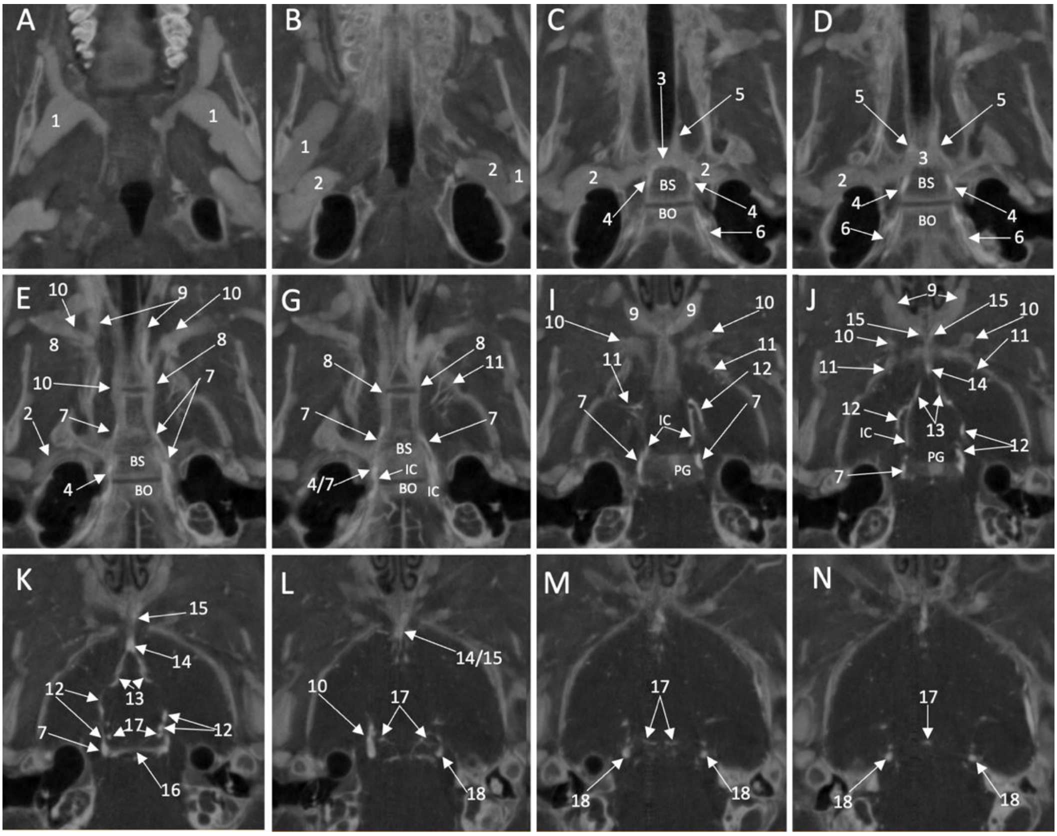

Fig. (1): Coronal images of the rat cavernous sinus in computed tomography venography. A to N, arranged ventral to dorsal.

1, Internal maxillary vein; 2, interpterygoid vein; 3, midline osseous compartment of the interpterygoid vein; 4, caverno-ophthalmic vein; 5, anastomosis via the anterior lacerated foramen; 6, inferior petrosal sinus; 7, cavernous sinus; 8, anterior part of the cavernous sinus (ophthalmic vein); 9, superior orbital vein; 10, inferior orbital vein; 11, middle cerebral vein; 12, basal vein; 13, anterior cerebral vein; 14, interperioptic sinus; 15, perioptic vein; 16, intercavernous sinus; 17, posterior communicating vein; 18, superior petrosal sinus; BO, basioccipital; BS, basisphenoid; IC, internal carotid artery; PG, pituitary gland

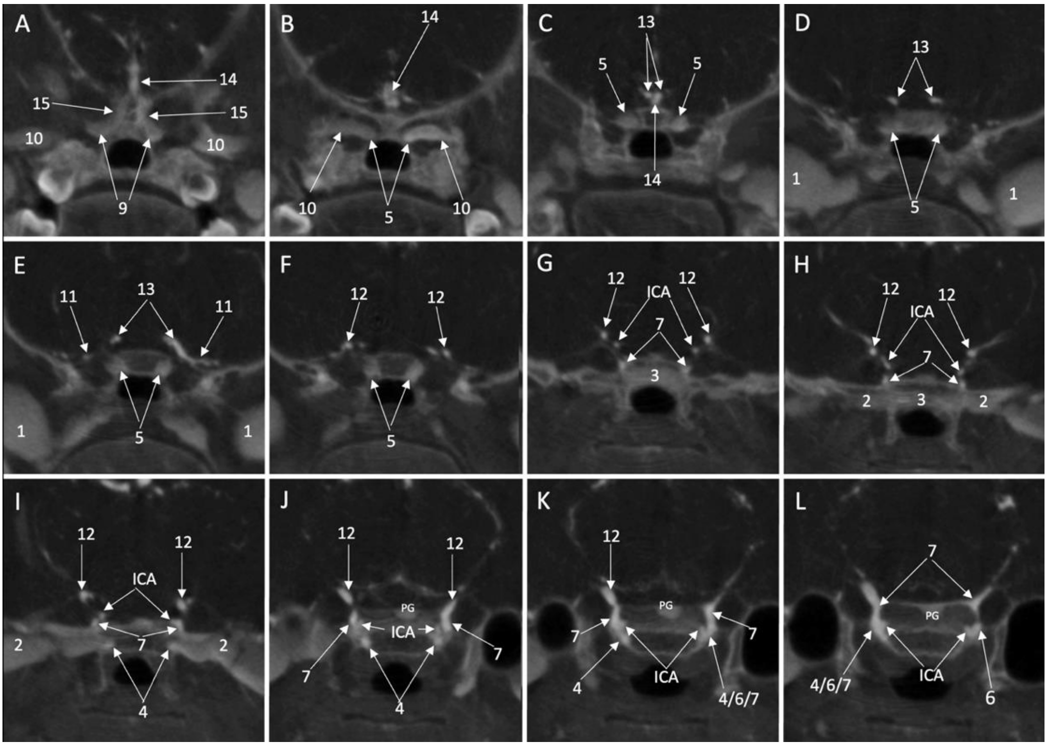

Fig. (2): Axial images of the rat cavernous sinus in computed tomography venography. A to N, arranged cranial to caudal.

The veins are numbered in the same order as in Figure (1).

1, Internal maxillary vein; 2, Interpterygoid vein; 3, midline osseous compartment of the interpterygoid vein; 4, caverno-ophthalmic vein; 5, anastomosis via the anterior lacerated foramen; 6, inferior petrosal sinus; 7, cavernous sinus; 8, anterior part of the cavernous sinus (ophthalmic vein); 9, superior orbital vein; 10, inferior orbital vein; 11, middle cerebral vein; 12, basal vein; 13, anterior cerebral vein; 14, interperioptic sinus; 15, perioptic vein; IC, internal carotid artery; PG, pituitary gland

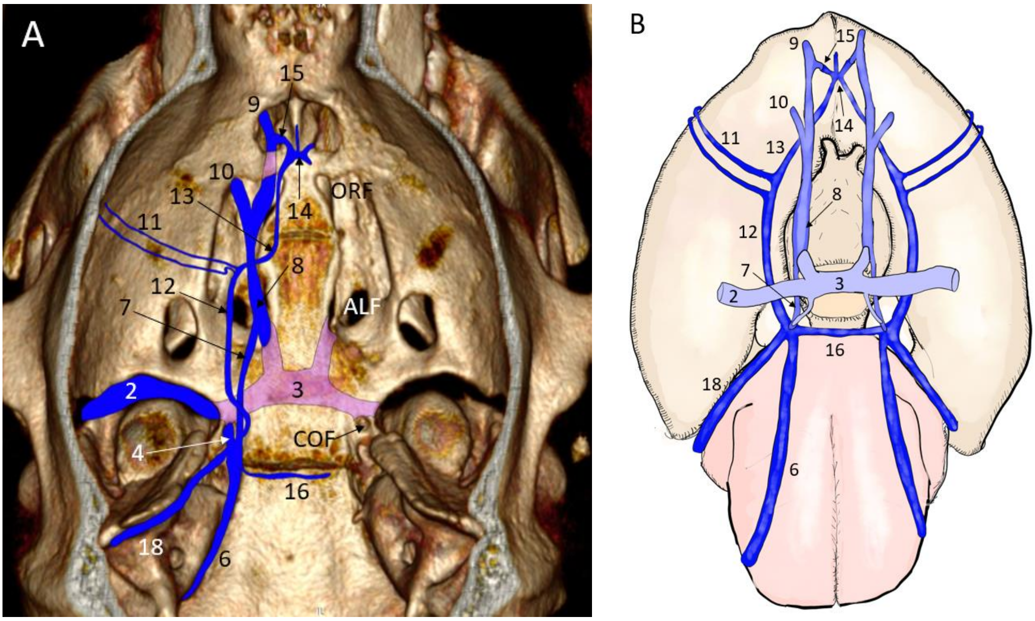

Fig. (3): The cavernous sinus and adjacent channels (A, superior view; B, inferior view).

A; To facilitate the recognition of bone landmark, only the left venous channels are illustrated in this rendered rat bone computed tomography image. Channels within or behind bones are displayed in purple.

B; The ventral view of venous channels is illustrated with the brain.

The veins are numbered in the same order as in Figure (1).

2, Interpterygoid vein; 3, midline osseous compartment of the interpterygoid vein; 4, caverno-ophthalmic vein; 6, inferior petrosal sinus; 7, cavernous sinus; 8, anterior part of the cavernous sinus (ophthalmic vein); 9, superior orbital vein; 10, inferior orbital vein; 11, middle cerebral vein; 12, basal vein; 13, anterior cerebral vein; 14, interperioptic sinus; 15, perioptic vein; 16, intercavernous sinus ;18 superior petrosal sinus ; ALF, anterior lacerated foramen; COF, caverno-ophthalmic canal; ORF, orbito-rotundum foramen.

Animal species in this Issue

Sprague Dawley

A laboratory rat is a rat of the species Rattus norvegicus (brown rat), which is bred and kept for scientific research. Laboratory rats have served as an important animal model for research in psychology, medi-cine, and other fields.

The **Sprague Dawley** rat is an outbred multipurpose breed of albino rat used extensively in medical and nutritional research, Its main advantage is its calmness and ease of handling. This breed of rat was first pro-duced by the Sprague-Dawley farms (later to become the Sprague-Dawley Animal Company), in Madison, Wisconsin in 1925. The name was originally hyphenated, although the brand styling today (Sprague Dawley®, Envigo, Inc) is not. The average litter size of the Sprague Dawley rat is 11.0.
These rats typically have increased tail to body length ratio compared with Wistar rats.

Ideal For:
General multipurpose model, safety and efficacy testing, aging, nutrition, diet-induced obesity, oncology, surgical model

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