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Variations in Origin of Arteries Supplying the Brain in Rabbit and Their Impact on Total Cerebral Ischemia

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1. Introduction

1.1 Laboratory animals

Animal testing, also known as animal experimentation, is the use of non-human animals in experiments. Worldwide it is estimated that the number of vertebrate animals—from zebrafish to non-human primates—ranges from the tens of millions to more than 100 million used annually (Cohn, 2010). The number of mice and rats used in the United States alone in 2001 was 80 million. Most animals are euthanized after being used in an experiment (Carbone, 2004).

It includes pure research such as genetics, developmental biology, behavioral studies, as well as applied research such as biomedical research, xenotransplantation, drug testing and toxicology tests, including cosmetics testing. Animals are also used for education, breeding and defense research. The practice is regulated to various degrees in different countries.

The earliest references to animal testing are found in the writings of the Greeks in the 2nd and 4th centuries BCE. Aristotle (384–322 BCE) and Erasistratus (304–258 BCE) were among the first to perform experiments on living animals (Cohen & Loew, 1984).

The ability of humans to change the genetics of animals took a large step forwards in 1974 when Rudolf Jaenisch was able to produce the first transgenic mammal, by integrating DNA from the SV40 virus into the genome of mice (Jaenisch & Mintz, 1974). This genetic research progressed rapidly and in 1996 Dolly the sheep was born, the first mammal to be cloned from an adult cell (Wilmut et al., 1997).

Toxicology testing became important in the 20th century. In the 19th century laws regulating drugs were more relaxed. For example, in the U.S. the government could only ban a drug after a company had been prosecuted for selling products that harmed customers. In the 1960s, in reaction to the Thalidomide tragedy, further laws were passed requiring safety testing on pregnant animals before a drug can be sold (Burkholz, 1997).

Albino rabbits are used in eye irritancy tests because rabbits have less tear flow than other animals and the lack of eye pigment in albinos make the effects easier to visualize. Rabbits are also frequently used for the production of polyclonal antibodies.

1.2 Cerebral ischemia

It is the deficiency of blood and metabolic substrates in the brain due to insufficient arterial supply or venous drainage, causing disruption of cerebral functions and partially reversible or irreversible damage to neurons.

Ischemia leads to alterations in brain metabolism, reduction in metabolic rates and energy crisis (Vespa et al., 2005).

There are two types of ischemia: focal ischemia, which is confined to a specific region of the brain; and global ischemia, which encompasses wide areas of brain tissue.

The main symptoms involve impairments in vision, body movement, and speaking. The causes of brain ischemia vary from sickle cell anemia to congenital heart defects. Symptoms of brain ischemia can include unconsciousness, blindness, problems with coordination, and weakness in the body. Other effects that may result from brain ischemia are stroke, cardiorespiratory arrest and irreversible brain damage.

An interruption of blood flow to the brain for more 10 seconds causes unconsciousness and an interruption in flow for more than a few minutes generally results in irreversible brain damage. In 1974, Hossmann and Zimmerman demonstrated that ischemia induced in mammalian brains for up to an hour can be at least partially recovered. Accordingly, this discovery raised the possibility of intervening after brain ischemia before the damage becomes irreversible.

Global brain ischemia occurs when blood flow to the brain is halted or drastically reduced. This is commonly caused by cardiac arrest. If sufficient circulation is restored within a short period of time, symptoms may be transient. However, if a significant amount of time passes before restoration, brain damage may be permanent. While reperfusion may be essential to protecting as much brain tissue as possible, it may also lead to reperfusion injury. Reperfusion injury is classified as the damage that ensues after restoration of blood supply to ischemic tissue.

1.3 Anatomy of the arteries supplying the brain in the rabbit

1.3.1 Aorta ascendens

The aorta ascendens arises almost linearly and dorsally in the midline. It extends from the cranial margin of the second rib cartilage to the cranial margin of the first rib cartilage. At first runs inside the pericard, left to beginning of the pulmonary trunk, to the left and cranially to the dorsal part of the right auricle and to the left and cranially to the right ventricle. Then it runs inside the thymus dorsally to the left side of the v. cava cranialis dextra (vena) and continues to the arcus aortae (Nejedlý, 1965).

1.3.2 Arcus aortae

The arcus aortae is running from the right to the left transversally and also a little caudally from the point of the second thoracic vertebra. Its dorsal wall is convex, the ventral wall is concave. It lies to the left from the v. cava cranialis dextra. The left part turns around the bronchus principalis sinister and ends on the left side of the third thoracic vertebra behind the v. cava cranialis sinistra. Very close to the midline of the body from its arise to the right the truncus brachiocephalicus and to the left the a. subclavia sinistra (arteria) (Popesko et al., 1990; Fig. 1). The truncus brachiocephalicus, the a. carotis communis sinistra and the a. subclavia dextra as branches of the arcus aortae were described by Nejedlý (1965). Nellie (1930) described the a. subclavia dextra and the a. subclavia sinistra as branches of the arcus

aortae. Ding (2006) found the origin of the a. subclavia dextra in 1.5% of cases and the origin of the a. carotis communis sinistra in 4% of cases from the arcus aortae. White (1893) by studying 700 rabbits found in one case the a. carotis communis dextra et sinistra and the a. subclavia dextra et sinistra as independent branches of the arcus aortae.

1.3.3 Truncus brachiocephalicus

The truncus brachiocephalicus runs behind the cartilage of the first rib and the v. cava cranialis dextra on the left side of the trachea. Near the midline it courses to the right and then partly dorsally. Immediately after its origin gives off the a. carotis communis sinistra. The truncus brachiocephalicus is very short and divides into the a. carotis communis dextra and the a. subclavia dextra (Nejedlý, 1965). By other author the a. subclavia dextra was described as the first branch of the truncus brachiocephalicus (Popesko et al., 1990).

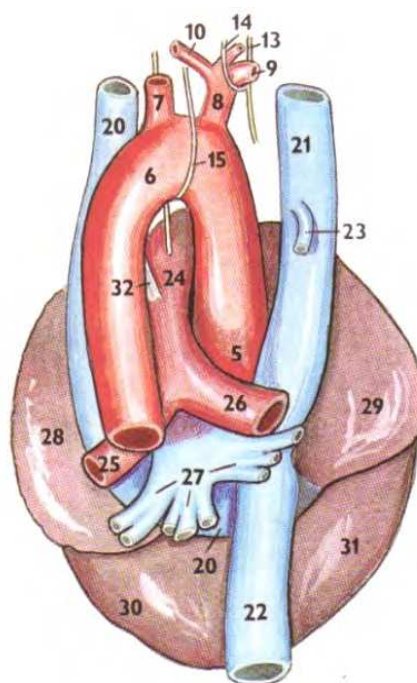


Fig. 1. Basis cordis

7. a. subclavia sinistra; 8. truncus brachiocephalicus; 9. a. subclavia dextra; 10. truncus bicaroticus; 13. n. vagus dexter; 14. n. recurrens dexter; 15. n. recurrens sinister; 20. v. cava cranialis sinistra; 21. v. cava cranialis dextra; 22. v. cava caudalis; 23. v. azygos dextra; 24. truncus pulmonalis; 25. a. pulmonalis sinistra; 26. a. pulmonalis dextra; 27. vv. pulmonales; 28. atrium sinistrum; 29. atrium dextrum; 30. ventriculus sinister; 31. ventriculus dexter; 32. ligamentum arteriosum; 33. lymphonodi thoracici aortici; 34. a. bronchialis. v. Vena. Vv. Venae. n. Nervus. a. Arteria. Dorsal view (Popesko et al., 1990)

1.3.4 Arteria carotis communis

In the neck region the a. carotis communis is covered by m. sternohyoideus (musculus), more cranially also by the m. sternothyroideus. It lies on the lateral surface of the trachea. The a. carotis communis lies dorsally to the esophagus, then laterally to the larynx. It reaches the maxillar angle laterally from the cranial end of the m. sternohyoideus and under the parotid gland. In this area it divides into the a. carotis interna and a. carotis externa (Nejedlý, 1965).

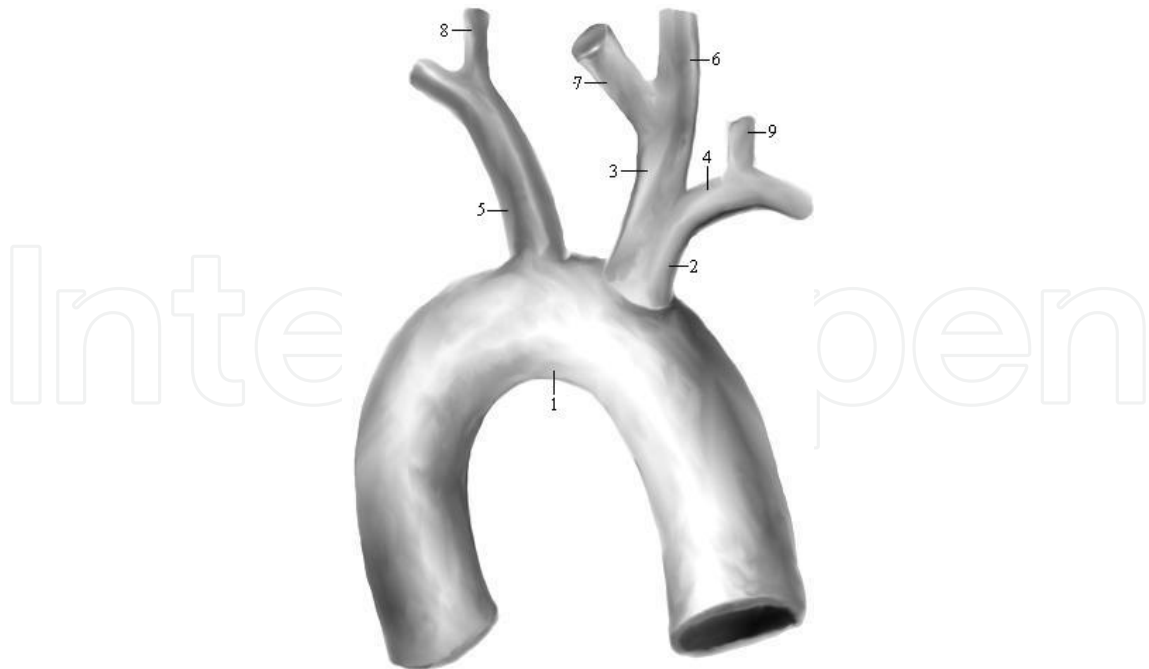


Fig. 2. Scheme of the origin of the large arteries supplying the brain in the rabbit
 1. arcus aortae; 2. truncus brachiocephalicus; 3. truncus bicaroticus; 4. a. subclavia dextra; 5. a. subclavia sinistra; 6. a. carotis communis dextra; 7. a. carotis communis sinistra; 8. a. vertebralis sinistra; 9. a. vertebralis dextra. a. Arteria. Lateral view

1.3.5 Arteria carotis interna

The a. carotis interna as poorly developed artery it arises by the division of the a. carotis communis into the a. carotis externa and the a. carotis interna. From the a. carotis externa it is divided by m. styloglossus and m. stylopharyngeus. It is running dorsally on the medial side of the bulla tympanica ossis temporalis. It enters the canalis caroticus ossis temporalis and inside this canal continues into the skull cavity. It is running rostrally on the medial surface of the n. trigeminus (nervus) and on the lateral surface of the corpus ossis basisphenoidalis is directed into the sulcus caroticus. It turns dorsally on the medial surface on the place of the entrance of the n. oculomotorius into the fissura orbitalis. It crosses the n. oculomotorius to the right. In this way it makes three bends. After this it enters the ventral end of the canalis caroticus. Here it gives off the a. communicans caudalis and a. ophthalmica dorsalis and subsequently is divided into the a. cerebri rostralis and a. cerebri media (Nejedlý, 1965).

1.3.6 Arteria subclavia

The a. subclavia runs caudally and dorsally to the v. subclavia, above the n. cervicalis VIII., behind the origin of the m. sternomastoideus and m. pectoralis superficialis. The branches of a. subclavia are: truncus costocervicalis, a. vertebralis, a. cervicalis superficialis, a. mammaria interna, a. intercostalis suprema, a. cervicalis profunda and a. transversa colli. The direct continuation is a. axillaris (Nejedlý, 1965).

1.3.7 Arteria vertebralis

The a. vertebralis enters the foramen transversarium of the sixth cervical vertebra. It gives off rr. musculares (rami) and rr. spinales. It continues inside the canalis transversarius of the

cervical vertebrae cranially. It passes through the foramen transversarium of the atlas, courses medially, then cranially and a little dorsally. It runs through the foramen vertebrale laterale of the atlas and gives off the a. spinalis dorsalis and ventralis. After this it penetrates the dura mater and continues to the cranial part of the medulla oblongata. On the caudal margin of the dorsal surface of the pars basilaris ossis occipitalis it is fused together with the contralateral a. vertebralis. This fusion forms the a. basilaris (Fig. 3). A. basilaris continues rostrally on the ventral surface of the medulla oblongata and pons. This artery gives off some branches which participate on the formation of the circle of Willis and by this way it participates on the arterial supplying of the brain (Nejedlý, 1965).

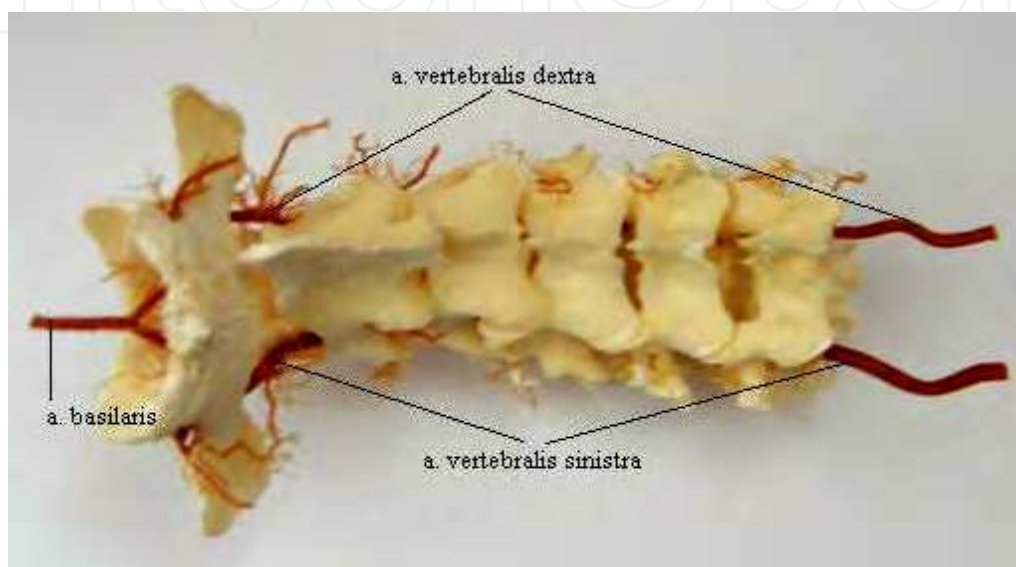


Fig. 3. Corrosion cast of the vertebral arteries

A. vertebralis dextra et sinistra located inside canalis transversarius of the cervical vertebrae. The fusion of the bilateral aa. vertebrales to the a. basilaris. a. Arteria. Dorsal view

1.3.8 The arteries of the brain

The arteries of the brain may be described on its ventral surface as follows:

- a. A. cerebelli caudalis is the largest of the transverse branches arising from the a. basilaris on the ventral surface of the hindbrain. It originates about half way along the a. basilaris and passes laterally and up the side of the caudal part of the cerebellum
- b. A. cerebri caudalis is a paired vessel formed at the level of the rostral margin of the pons by the bifurcation of the a. basilaris. It passes at each side laterally and dorsally to the caudal portion of the cerebral hemisphere, giving secondary branches to the diencephalon
- c. A. cerebelli rostralis is a relatively large branch of the a. cerebri caudalis, arising near the origin of the latter and passing to the rostral portion of the cerebellum after giving branches to the midbrain
- d. The end of the a. carotis interna lies on either side of the tuber cinereum. It turns forward, but is connected backwards with the a. cerebri caudalis by an a. communicans caudalis
- e. A. cerebri media is given off from the a. carotis interna, branching over the middle portion of the hemisphere to supply most of its lateral and dorsal surfaces

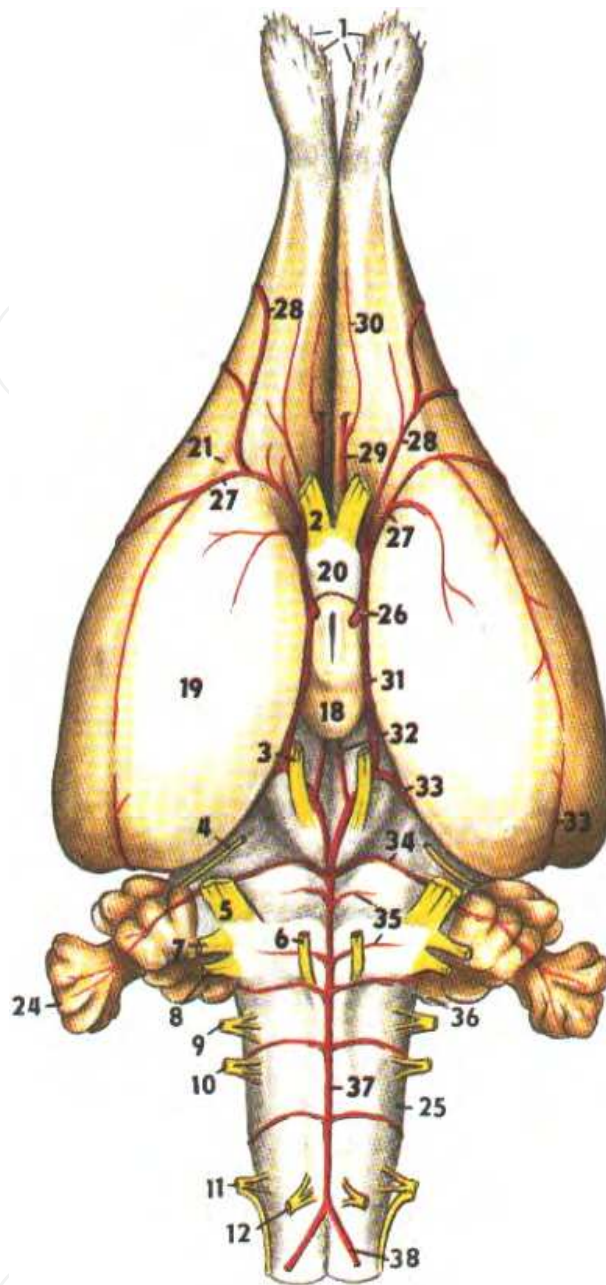


Fig. 4. The arteries of the brain

1. bulbus olfactorius; 2 n. opticus; 3. n. oculomotorius; 4. n. trochlearis; 5. n. trigeminus; 6. n. abducens; 7. n. facialis; 8. n. vestibulocochlearis; 9. n. glossopharyngeus; 10. n. vagus; 11. n. accessorius; 12. n. hypoglossus; 18. corpus mamillare; 19. lobus piriformis; 20. chiasma opticum; 21. sulcus rhinalis lateralis; 24. paraflocculus; 26. a. carotis interna; 27., 28. a. cerebri media; 27. r. caudalis; 28. r. rostralis; 29. a. cerebri rostralis; 30. a. ethmoidalis interna; 31. a. communicans caudalis; 32. r. corporis mamillaris; 33. a. cerebri caudalis; 34. a. cerebelli rostralis; 35. rami ad pontem; 36. a. cerebelli caudalis; 37. a. basilaris; 38. a. vertebralis. a. Arteria. r. Ramus. Ventral View (Popesko et al., 1990)

- f. A. cerebri rostralis is the continuation of the a. carotis interna after the origin of the a. cerebri media. It passes to the rostral portion of the ventral surface of the cerebral hemisphere and to the olfactory bulb.

The a. cerebri rostralis unites with that of the other side to form a short common trunk between the hemispheres, which redivides into the paired vessels supplying the medial surfaces. A complete anastomotic loop is thus formed round the hypothalamus by the a. carotis interna, a. cerebri rostralis, a. communicans caudalis and a. cerebri caudalis. This is the circle of Willis or the circulus arteriosus cerebri (Popesko et al., 1990). Nejedlý (1965) described the a. communicans rostralis as a connection between the bilateral aa. cerebri rostrales.

1.4 Rabbit as experimental animal of the brain ischemia

Over 20,000 rabbits were used for animal testing only in the UK in 2004. Examples include restricting blood flow to the brain to induce cerebral ischemia (Tolwani et al., 1999). This is most often carried out by ligation of major vessels, e.g. the truncus brachiocephalicus and the a. subclavia sinistra, in their place of origin (Hossmann 1998; Iwama et al., 2000; Pluta 1987). Harukuni and Bhardwaj (2006) reported ligation of the truncus brachiocephalicus and the a. subclavia sinistra as one way to induce total cerebral ischemia. Ischemia within the arteries branching from the vertebral arteries in the back of the brain may result in symptoms such as dizziness, vertigo, double vision, or weakness on both sides of the body. Other symptoms include, difficulty speaking, slurred speech and the loss of coordination (Beers et al., 2003). The aim of this study was to verify whether experimentally induced total cerebral ischemia in rabbits actually corresponds to total ischemia on the basis of the origin of certain vessels. We observed morphological variations in the origin and course of the arteries supplying the brain with blood in the rabbit.

2. Material and methods

2.1 Experimental animals

The study was carried out on 50 adult (age=140 days) New Zealand white rabbits (breed HY+), females (n=25) and males (n=25) of weight range 2.5-3 kg in an accredited experimental laboratory at the University of Veterinary Medicine in Kosice, Slovak Republic. The animals were kept in cages under standard conditions (temperature 15-20 °C, relative humidity 45 %, 12 hours light period) and fed granular mixed feed (O-10 NORM TYP, Spišské krmné zmesi, Spišské Vlasy, Slovak Republic). Drinking water was provided ad libitum.

2.2 Material

The Batson's No. 17 Plastic Replica and Corrosion Kit (Polysciences Europe GmbH, Germany) was used as a casting medium. This consists of Base Solution A (2-Propenoic acid, 2-methyl-, 1,2-ethanediyl 1 ester, Dibutyl phthalate, Methyl methacrylate, Polymethyl methacrylate), Catalyst (Acetone, Benzoyl peroxide, Dibutyl phthalate), Promoter C (Dibutyl 1 phthalate, N,N-Dimethyl-4-toluidine) and red pigment (1,2-Benzenedicarboxylic acid, bis[2-ethylhexyl ester], epoxidized soybean oil and 2-Naphthenecarboxylic acid).

2.3 Methods

2.3.1 Surgical preparation of the rabbit

The animals were injected intravenously with heparine (50,000 UI/kg) 30 minutes before they were sacrificed with intravenous injection of Embutramide (T-61, 0.3 mL/kg). The skin

was subsequently removed as far as possible to prevent it from sticking to the corrosive cast in the maceration process. The thoracic cavity was opened from the left side by removing of the ribs. After the opening of the pericardial cavity a ligature was introduced to the ascending aorta. The aorta was cannulated through the left ventricle. The perfusion started after the fixation of the cannula in the ascending aorta with the ligature. The right vestibule was opened to lower the pressure in the vessels to ensure good injection. The vascular network was manually perfused through the fixed cannula in the ascending aorta for approximately 15-20 minutes with 2.5-3 l of warm (37 °C), 0.9 % NaOH in 0.01 M phosphate, pH 7.3 (Hossler & Monson, 1995).

2.3.2 Preparation of the casting medium

The red pigment was added to the Base solution A prior to mixing the catalyst and promoter. The pigment was added in the amount of 5 %. It was mixed and divided into two equal parts (each part=25 mL). To the first half Catalyst in amount of 12 mL was added and mixed. To the second half Promoter C in amount of 12 drops was added and mixed. Then these two parts were mixed together.

2.3.3 Application of the casting medium

The arterial network was filled with the casting medium manually through the same cannula inserted in the ascending aorta. Adequate filling was determined by the visualization of an even distribution of the casting medium (red) throughout the superficial vessels of the body. After the vascular casting is complete, the animals must not be manipulated for at least 30 minutes and then must be submersed in water at a temperature ranging from 40 °C to 60 °C for a period of 24 hours for full polymerization of the casting medium (Lametschwandtner et al., 1990).

2.3.4 Corrosion

The corrosion as the dissolution of tissues surrounding the cast was performed by potassium hydroxide (KOH) at the concentration of solution 2-4 % for a period of 2 days. For the corrosion to be faster, the solution must remain at a constant temperature of 40 °C (Lametschwandtner et al., 1990). The solution for the corrosion was changed every 12 hours. After the surrounding tissue was dissolved vascular castings were rinsed in running water for removing the rests of the soft tissues. Specimens were dried at the room temperature by air exposure (Flešárová et al., 2003).

3. Results and discussion

3.1 Variations in origin

3.1.1 A. carotis communis

Vascular corrosion cast of the rabbit aortic arch displaying the origin of the truncus brachiocephalicus and the a. subclavia sinistra from the arcus aortae in 92 % of cases (46 animals). a. Arteria. Ventral view. Macroscopic image

Vascular corrosion cast of the rabbit aortic arch displaying the origin of the truncus brachiocephalicus, the a. subclavia sinistra and the a. carotis communis sinistra from the arcus aortae in 6 % (3 animals). a. Arteria. Ventral view. Macroscopic image

In 92 % of cases (46 animals) the a. carotis communis sinistra originated as the first branch from the truncus brachiocephalicus. The a. carotis communis dextra arise together with the

a. subclavia dextra by terminal division of truncus brachiocephalicus (Fig. 5). The a. carotis communis sinistra originated from arcus aortae in 6 % (3 animals; Fig. 6).

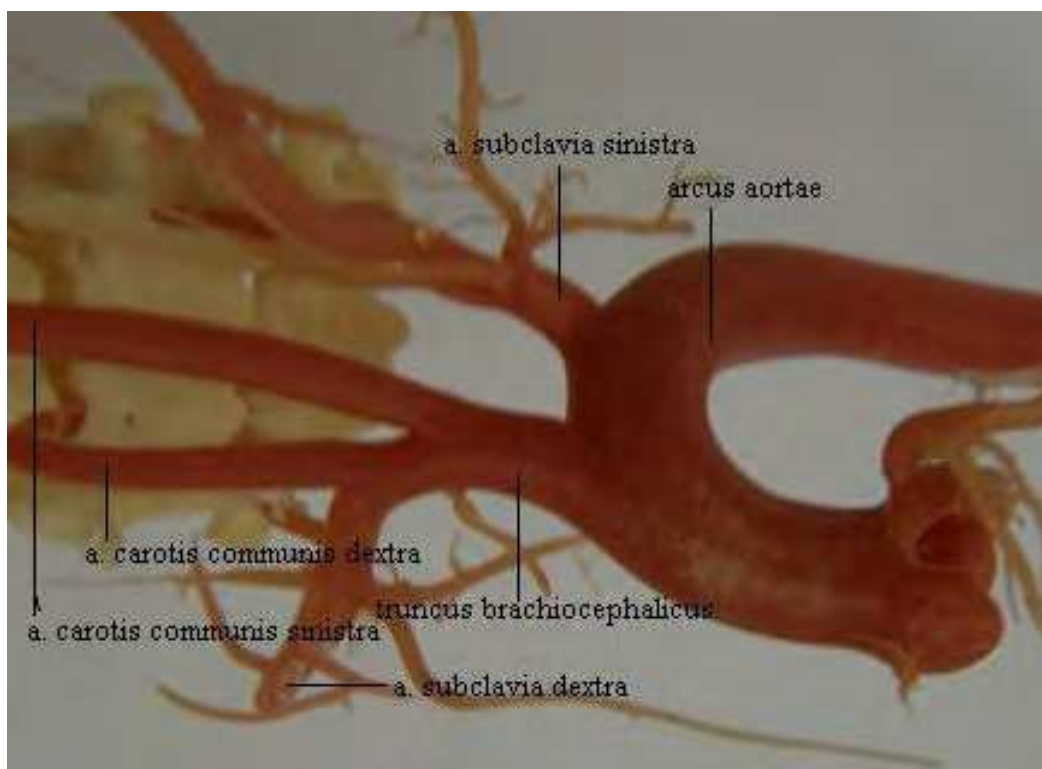


Fig. 5. Aortic arch of the rabbit without variations

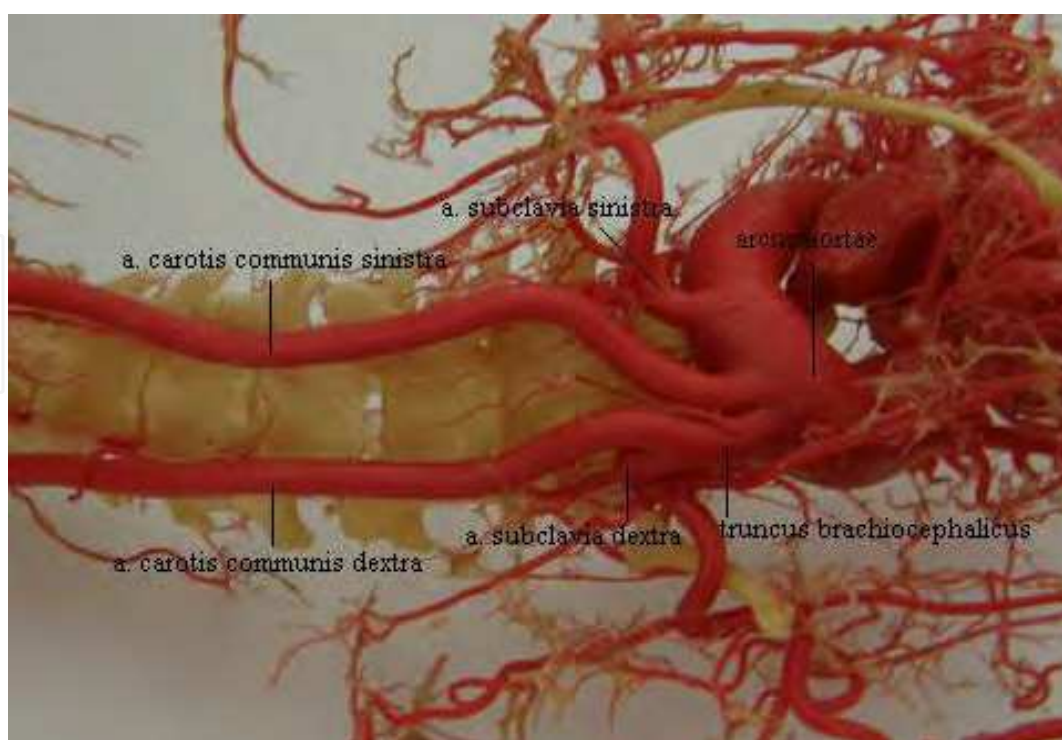


Fig. 6. Aortic arch of the rabbit with variation in origin of a. carotis communis sinistra

3.1.2 A. subclavia

In 98 % of cases (49 animals) the a. subclavia sinistra originated from the arcus aortae (Fig. 5). In 2 % (1 animal) originated from the arcus aortae the truncus bicaroticus, the a. subclavia dextra and the a. subclavia sinistra (Fig. 6).

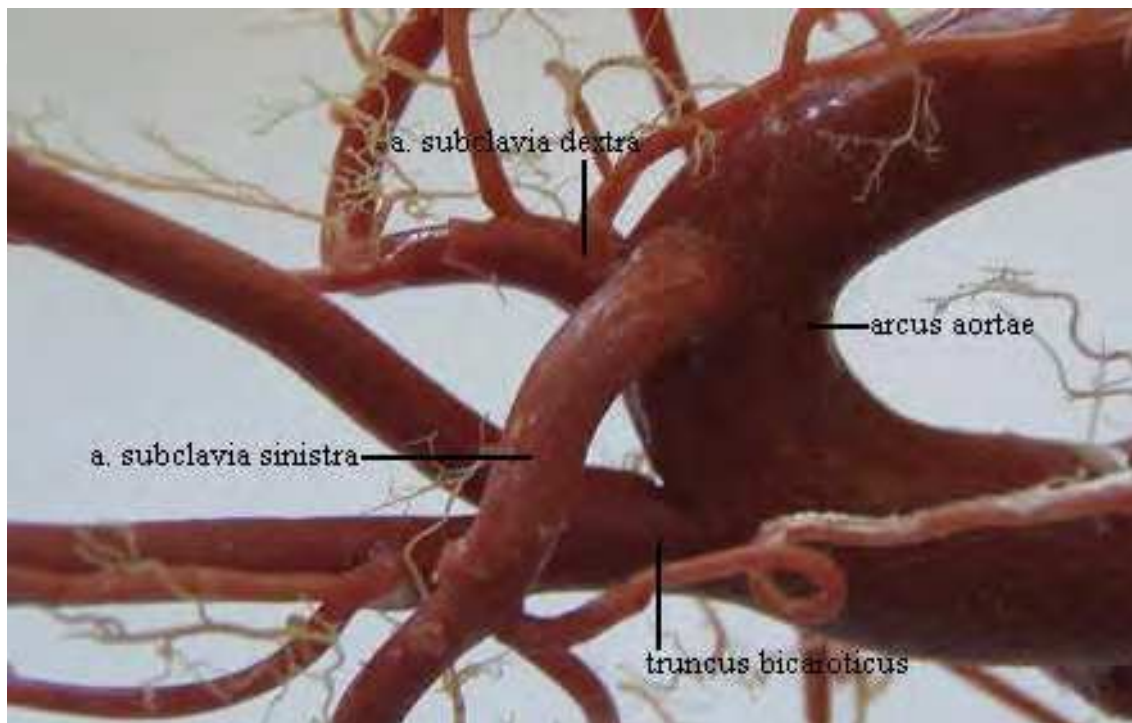


Fig. 7. Aortic arch of the rabbit with variation in origin of a. subclavia dextra

Vascular corrosion cast of the rabbit aortic arch displaying the origin of the truncus bicaroticus, the a. subclavia dextra and the a. subclavia sinistra from the arcus aortae in 2 % (1 animal). a. Arteria. Dorsolateral view. Macroscopic image

3.1.3 A. vertebralis

In 86 % of cases (43 animals) the a. vertebralis sinistra originated directly from the a. subclavia sinistra (Fig. 8) in 10 % of cases (5 animals) it originated from the arcus aortae as an independent branch (Fig. 9) and in 4 % of cases (2 animals) it arose from the arcus aortae as a common trunk with the a. scapularis descendens. The a. vertebralis dextra originated from the a. subclavia dextra in 98 % (49 animals) of cases. In that case we observed two aa. vertebralis dextrae (arteriae) with two different origins.

The a. vertebralis dextra I originated from the a. subclavia dextra and the a. vertebralis dextra II arose from the common trunk with the a. cervicalis superficialis dextra that originated from the a. carotis communis dextra.

After a short distance, they merged between the fifth and sixth cervical vertebrae into a single a. vertebralis dextra, which then entered the canalis transversarius at the level of the fifth cervical vertebra (Fig. 10). In summary, the origin of both aa. vertebrales varied in 16 % of cases (8 animals). In 8 % (4 animals) we found a bypass between the a. vertebralis sinistra and the a. basilaris (Fig. 11). This a. basilaris was also formed by the fusion of the a. vertebralis dextra et sinistra.

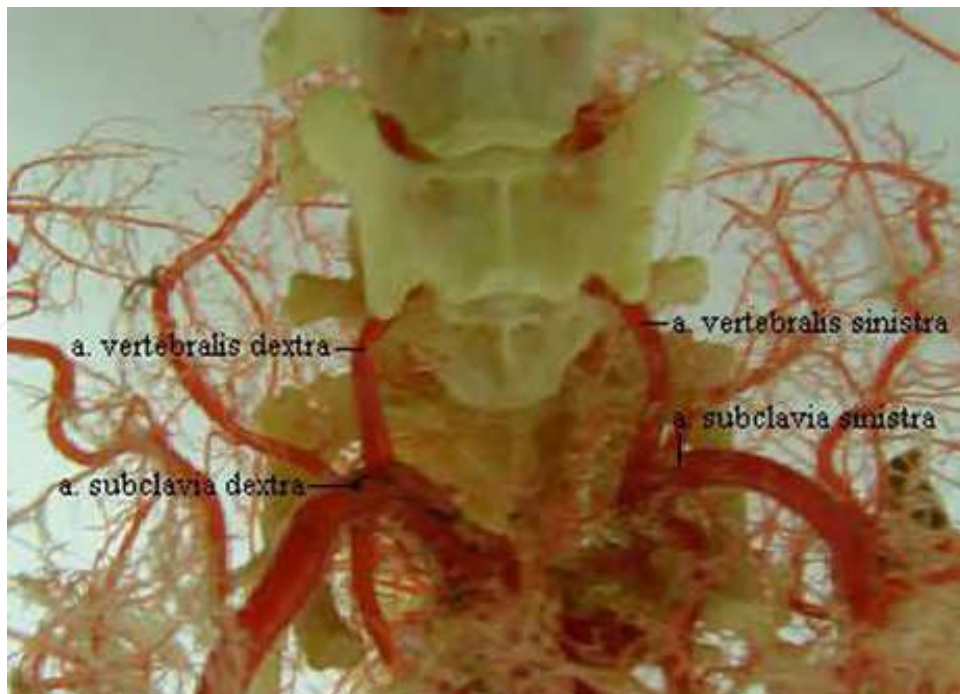


Fig. 8. A. vertebralis with its typical origin

Vascular corrosion cast displaying the origin of the a. vertebralis dextra et sinistra from the a. subclavia dextra et sinistra in 86 % of cases (43 animals). a. Arteria. Ventral view. Macroscopic image

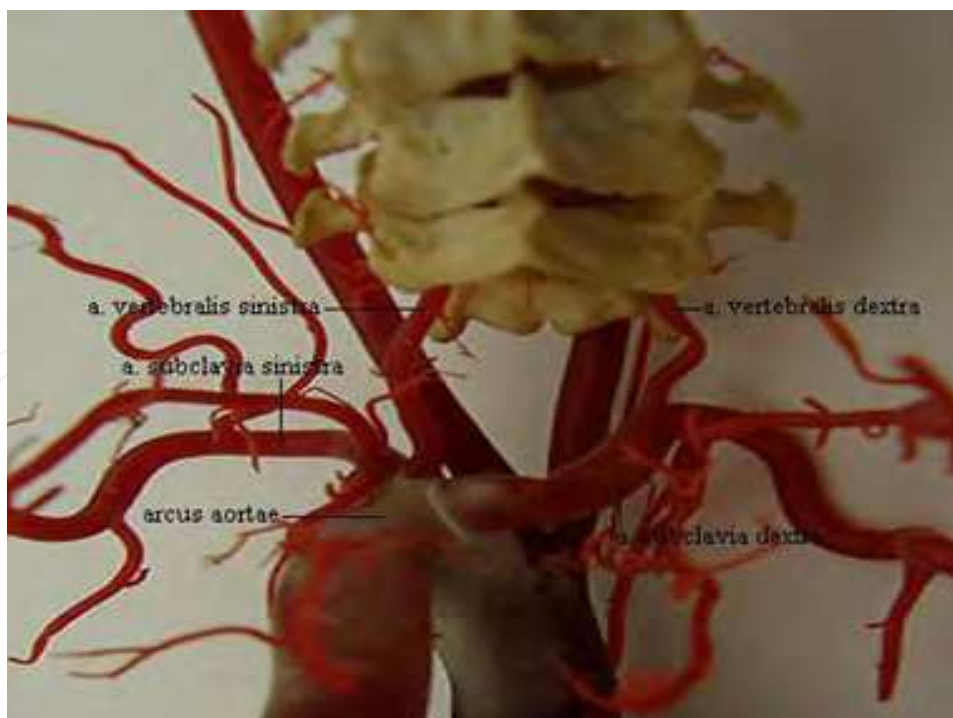


Fig. 9. Atypical origin of the a. vertebralis

Vascular corrosion cast displaying the origin of the a. vertebralis sinistra from the arcus aortae in 10 % of cases (5 animals). a. Arteria. Dorsal view. Macroscopic image

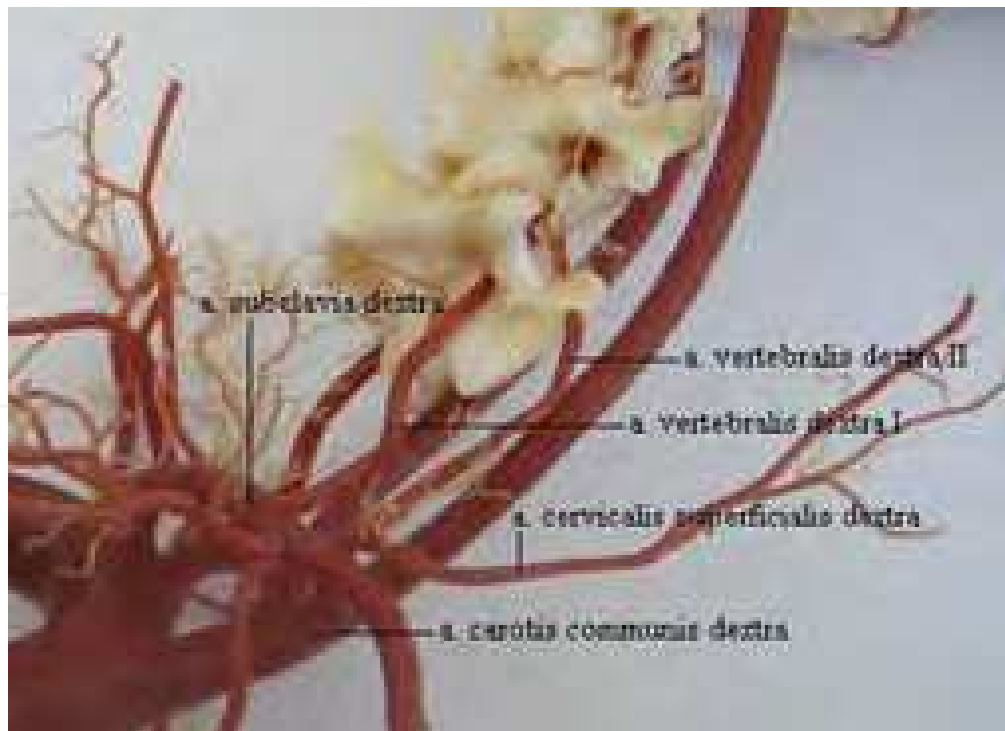


Fig. 10. Doubled a. vertebralis

Vascular corrosion cast displaying two aa. vertebrales dextrae. Note merging of the two arteriae into a single vessel. a. Arteria. aa. Arteriae. Lateral view. Macroscopic image

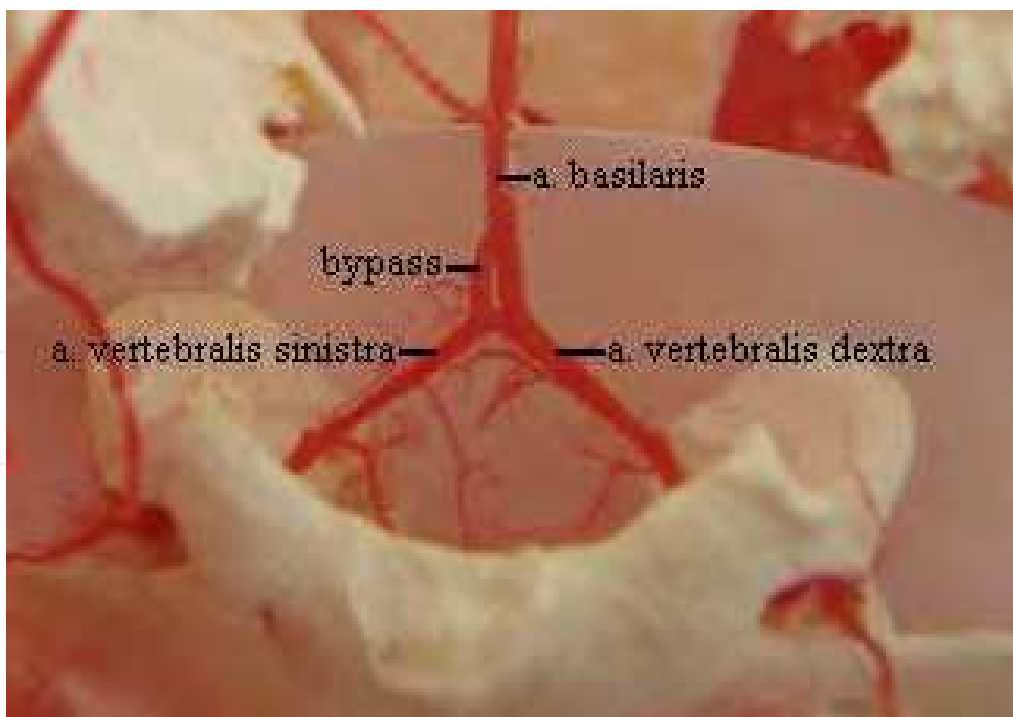


Fig. 11. Variation in formation of a. basilaris

Vascular corrosion cast displaying the bypass between the a. vertebralis sinistra and a. basilaris in 8 % (4 animals). a. Arteria. Dorsal view. Macroscopic image

3.1.4 A. carotis interna

Vascular corrosion cast of the cephalic and neck region displaying the origin of the a. carotis interna by the terminal division of the a. carotis communis together with the a. carotis externa in 94 % (47 animals). Note the entrance of the a. carotis interna to the canalis caroticus. a. Arteria. Ventrolateral view. Macroscopic image

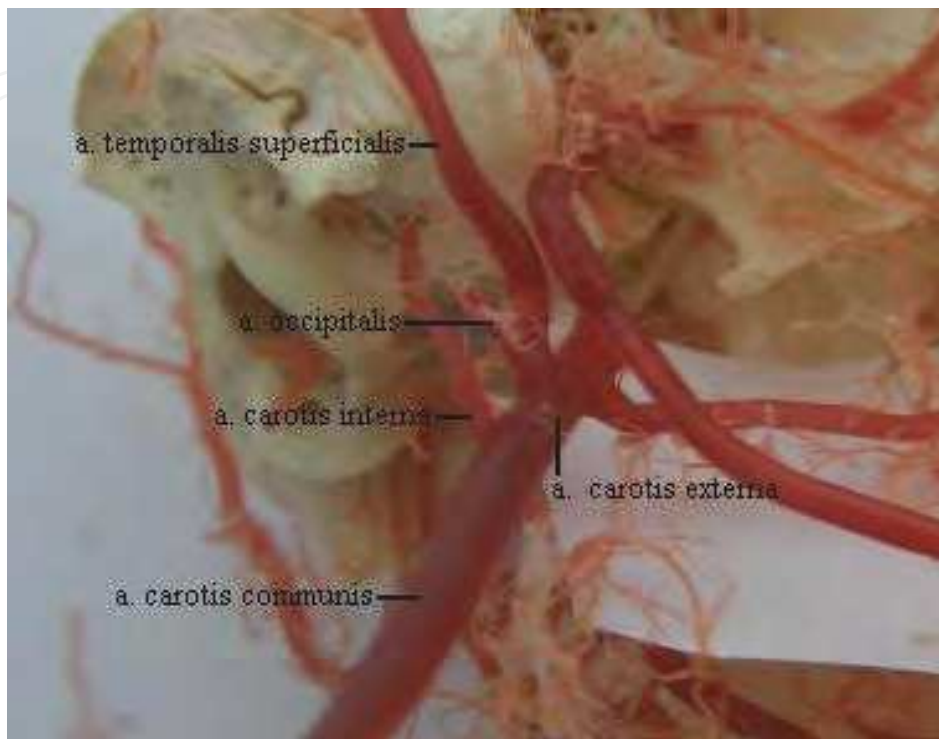


Fig. 12. Typical origin of a. carotis interna

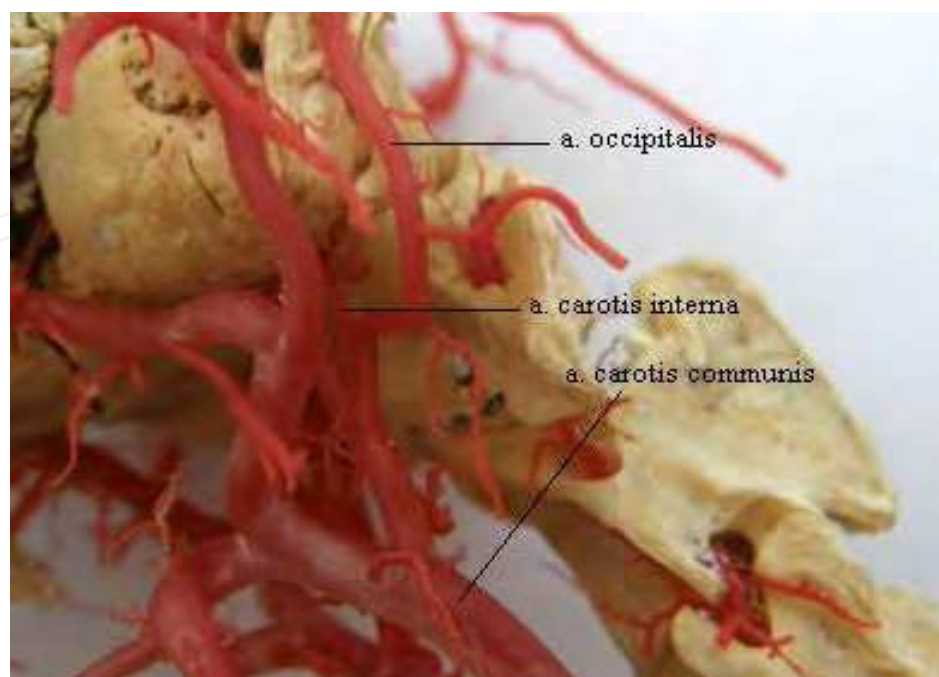


Fig. 13. Atypical origin of a. carotis interna

Vascular corrosion cast of the cephalic and neck region displaying the origin of the a. carotis interna from the common trunk with the a. occipitalis in 6 % (3 animals). a. Arteria. Caudoventral view. Macroscopic image

In 94 % (47 animals) the a. carotis interna arised by terminal division of the a. carotis communis together with the a. carotis externa (Fig. 12). In 6 % (3 animals) the a. carotis interna originated from a common trunk with the a. occipitalis (Fig. 13). The trunk is a branch of the a. carotis communis.

3.1.5 The arteries of the brain

In 40 % (20 animals) the a. cerebelli caudalis dextra et sinistra originated at the same level (Fig. 14). In 40 % (20 animals) the a. cerebelli caudalis dextra originated from the a. basilaris more rostrally than the a. cerebelli caudalis sinistra (Fig. 15). In 20 % (10 animals) the a. cerebelli caudalis sinistra originated more rostrally than the a. cerebelli caudalis dextra.

The a. cerebri caudalis dextra et sinistra originated from the a. basilaris at the same level in all studied animals (100 %).

The a. cerebri media dextra et sinistra originated from the a. carotis interna at the same level in all studied animals (100 %).

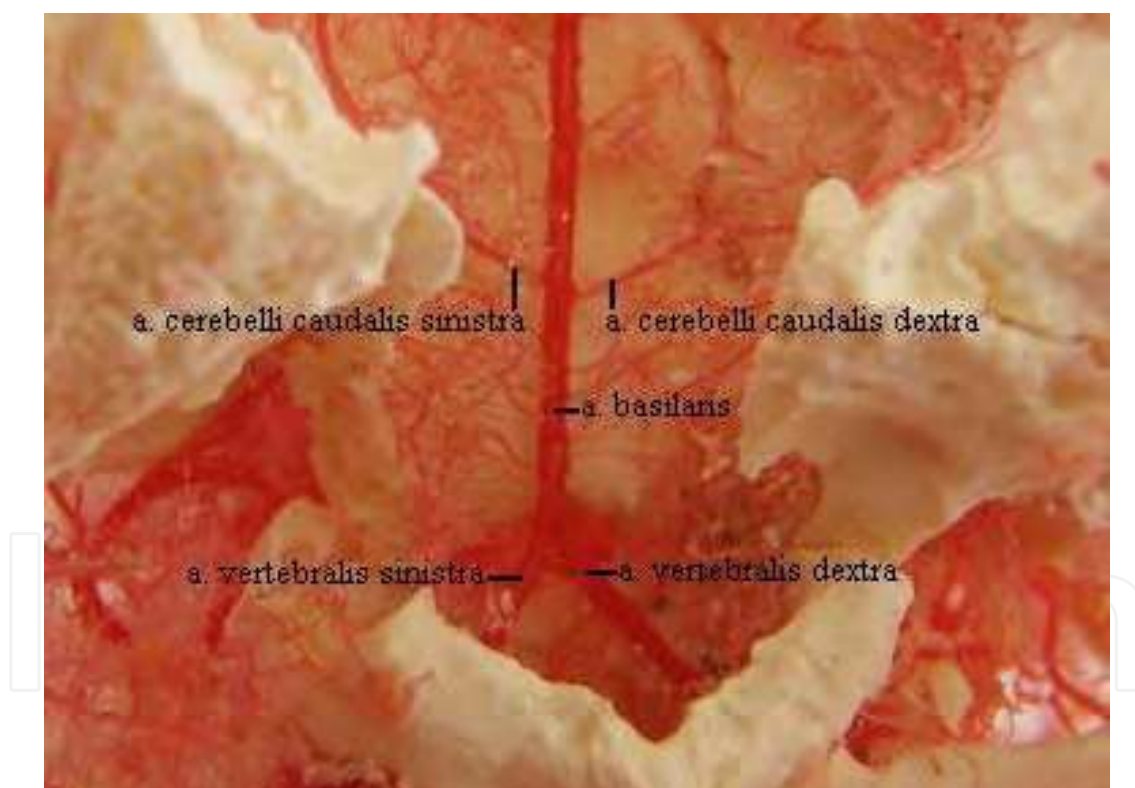


Fig. 14. Typical arrangement of a. cerebelli caudalis

Vascular corrosion cast. In 40 % (20 animals) the a. cerebelli caudalis dextra et sinistra originated at the same level from the a. basilaris. Dorsal view. Macroscopic image

The a. cerebri rostralis dextra et sinistra as the direct continuation from the a. carotis interna originated at the same level in all studied animals (100 %).

These all arteries were divided into the r. rostralis and r. caudalis. In 10 % (5 animals) the a. cerebri caudalis sinistra was divided into the r. rostralis, r. medius and r. caudalis.

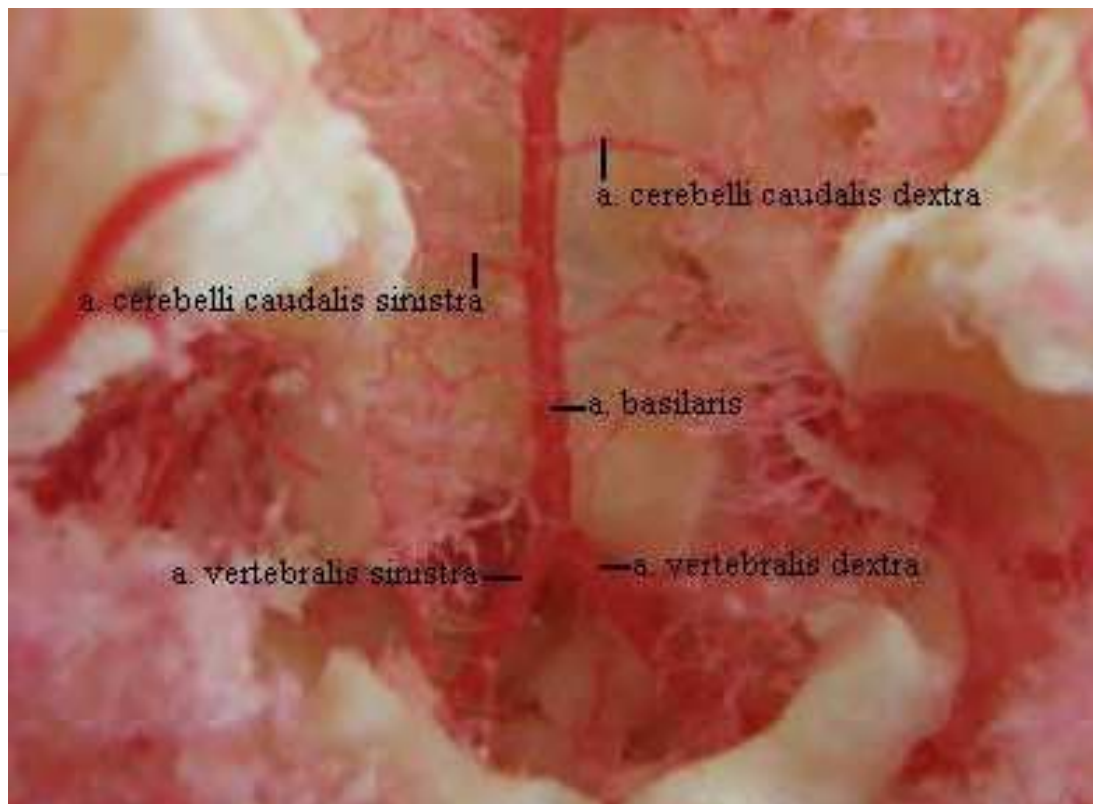


Fig. 15. Variation in arrangement of a. cerebelli caudalis
Vascular corrosion cast. The a. cerebelli rostralis dextra et sinistra originated from the a. basilaris at the same level in all studied animals (100 %). Dorsal view. Macroscopic image

3.2 Discussion

3.2.1 A. carotis communis

In 92 % of cases (46 animals) the a. carotis communis sinistra originated as first branch from the truncus brachiocephalicus. The a. carotis communis dextra arise together with the a. subclavia dextra by the terminal division of the truncus brachiocephalicus. Popesko et al. (1990) described a. carotis communis dextra et sinistra as branches arising from truncus bicaroticus by its terminal division. Truncus bicaroticus was described as the direct continuation of the truncus brachiocephalicus. The a. carotis communis sinistra as branch of the arcus aortae in 4 % (2 animals) was also described by Ding (2006). By Nejedlý (1965) the origin of the a. carotis communis sinistra from the arcus aortae was described as a typical arrangement of branches of the arcus aortae. In 2 % (1 animal) originated from the arcus aortae the truncus bicaroticus. Nellie (1930) described this arrangement in all studied animals. White (1893) by studying 700 rabbits found in one case the a. carotis communis dextra et sinistra as independent branches of the arcus aortae.

3.2.2 A. subclavia

In 98 % (49 animals) the a. subclavia dextra arise together with the a. carotis communis dextra by the terminal division of the truncus brachiocephalicus. By some authors the a.

subclavia dextra was described as the first branch arising from the truncus brachiocephalicus (Popesko et al., 1990). Nellie (1930) described the a. subclavia dextra and the a. subclavia sinistra as branches of the arcus aortae. Ding (2006) found the origin of the a. subclavia dextra in 1.5% of cases from the arcus aortae and Nejedlý (1965) described it as typical arrangement of the branches of the arcus aortae. White (1893) by studying 700 pieces rabbits found in one case a. subclavia dextra et sinistra as independent branches of the arcus aortae.

3.2.3 A. vertebralis

Until now the scientific literature has cited almost exclusively the uniform origin of the a. vertebralis from the a. subclavia (Nejedlý, 1965; Popesko et al., 1990). It was not described independent origin from the arcus aortae or the doubled a. vertebralis like in our cases. In 8 % (4 animals) we found the bypass between the a. vertebralis sinistra and the a. basilaris at the place of fusion of the a. vertebralis dextra et sinistra to the a. basilaris.

3.2.4 A. carotis interna

We found the origin of the a. carotis interna and the a. carotis externa by the terminal division of the a. carotis communis in 92 % (46 animals). The same origin was described by Nejedlý (1965) and Popesko et al. (1990). But we found except this typical arrangement the origin of the a. carotis interna from the a. occipitalis in 8 % (4 animals).

3.2.5 The arteries of the brain

Until now the origin of the bilateral a. cerebri rostralis et caudalis and a. cerebelli rostralis et caudalis was described at the same level from the a. basilaris and the a. carotis interna (Nejedlý, 1965; Popesko et al., 1990). We found that in 40 % (20 animals) the a. cerebelli caudalis dextra originated from the a. basilaris more rostrally than the a. cerebelli caudalis sinistra. In 20 % (10 animals) the a. cerebelli caudalis sinistra originated more rostrally than the a. cerebelli caudalis dextra.

These all arteries were divided into the r. rostralis and r. caudalis (Nejedlý, 1965; Popesko et al., 1990). In 10 % (5 animals) the a. cerebri caudalis sinistra was divided into the r. rostralis, r. medius and r. caudalis.

The bilateral aa. cerebri rostrales are fused together. The same arrangement was described by Popesko et al. (1990). The a. communicans rostralis as a connection between bilateral aa. cerebri rostrales was described by Nejedlý (1965).

4. Conclusion

The effect of various chemical substances (Cantu & Hegsted, 1970) on the brain nerve tissue damaged by ischemia as well as various pathological and pathophysiological changes induced by the total cerebral ischemia in rabbits and other laboratory animals are the subject of many studies (Ishiyama et al., 2010).

The place of origin of the truncus brachiocephalicus and the a. subclavia sinistra are most commonly used to induce the total cerebral ischemia by ligation (Hossmann 1998; Iwama et al., 2000; Pluta, 1987). Harukuni and Bhardwaj (2006) present also the ligation of the truncus brachiocephalicus and the a. subclavia sinistra as a possible way to induce the total cerebral ischemia. The question is, whether this method of induction of the total cerebral ischemia is correct.

The variations in the origin of arteries supplying the brain which we found point to the possibility of inducing only a partial brain ischemia in a given set of animals. The probability of causing the partial brain ischemia may be the same as the percentage of the occurrence of found variations.

One way to avoid obtaining of distorted results is the ligation of the arteries before their entering to the target organ, in this case to the brain. These arteries can be the a. basilaris or the a. carotis interna. The best results probably would have been achieved by ligation of the arteries on the ventral surface of the brain that are directly involved in the blood supply of the nerve tissue. However, this method is time consuming and surgically very difficult in. Another possibility is the detailed preparation of arteries in the place of their origin to avoid possible variations.

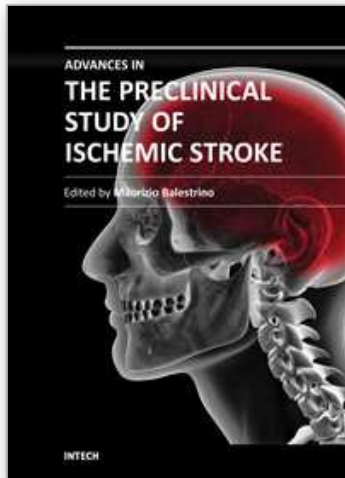
With this work we tried to emphasize the need for more detailed knowledge of the circulatory system of the rabbit, which is one of the ways to achieve more objective results also in a smaller number of animals used in experiments.

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This book reports innovations in the preclinical study of stroke, including - novel tools and findings in animal models of stroke, - novel biochemical mechanisms through which ischemic damage may be both generated and limited, - novel pathways to neuroprotection. Although hypothermia has been so far the sole "neuroprotection" treatment that has survived the translation from preclinical to clinical studies, progress in both preclinical studies and in the design of clinical trials will hopefully provide more and better treatments for ischemic stroke. This book aims at providing the preclinical scientist with innovative knowledge and tools to investigate novel mechanisms of, and treatments for, ischemic brain damage.

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