Quantitative Morphology of Human Retrolaminar Optic Nerve Vasculature

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Purpose. To quantify the variation in the blood supply of the retrolaminar optic nerve in humans. The retrolaminar anterior optic nerve is supplied by an elliptical arterial "circle" of Haller and Zinn formed by anastomoses around the optic nerve between medial and lateral paraoptic short posterior ciliary arteries (PO-SPCAs). The frequency with which complete perioptic nerve arteriolar anastomoses (PONAA) occur is unknown, yet they form the basis for many postulated pathophysiological mechanisms.

Methods. Scanning electron microscopy was performed on 25 orbital and ocular microvascular corrosion casts (methyl methacrylate) from 20 human cadavers of subjects 21 to 97 years of age without known ocular disease.

Results. Eighteen casts were examined in detail after microdissection (the analysis of seven casts was limited because of their fragility). In 15/18 (83%) casts, the PONAA were supplied by branches of a medial and lateral PO-SPCA; in 2/18, they were supplied by one (lateral) PO-SPCA; and in 1/18, they were supplied by a superior PO-SPCA and two horizontal PO-SPCAs. The PONAA had intact superior and inferior anastomoses in 8/18 (44%) casts, complete anastomoses with narrowed portions in 6/18 (33%), and incomplete in 4/18 (23%). Narrowed portions were not preferentially distributed to either superior or inferior anastomoses.

Conclusions. Complete PONAA was found in more than 75% of casts, including anastomoses with narrow portions in 33% of casts. Invest Ophthalmol Vis Sci. 1994;35:3858-3866.

The vascular structure of the retrolaminar optic nerve in humans after histologic serial sectioning, methyl methacrylate casts, and other injection techniques has been described.1-7 We have shown that anastomoses between medial and lateral paraoptic short posterior ciliary arteries (PO-SPCAs)6,7 form an elliptical "circle" consisting of superior and inferior parts around the optic nerve. The perioptic nerve arteriolar anastomoses (PONAA) are similar to the circle originally described by Haller and Zinn in 1755.8 In humans, the retrolaminar and laminar optic nerves receive their blood supply from pial arterioles, direct centripetal arterioles, and centripetal branches of recurrent choroidal arterioles derived from the PONAA.6 Such anastomoses are absent in subhuman primates.9-11 Variations in the blood supply of the anterior optic nerve have been noted in humans.12 In this study, we examined the variation in origin and form of the PONAA using methyl methacrylate techniques. Quantitative analysis may help establish whether variations in vascular structure determine patterns of visual field loss in conditions such as anterior ischemic optic neuropathy.

METHODS

Microvascular Casting Techniques in Humans

Complete orbital and ocular microvascular corrosion casts were prepared from 25 adult human autopsy specimens (20 cadavers) obtained 36 to 48 hours after death using our standard techniques.13 The autopsy specimens were collected from St. Thomas' Hospital. Hospital ethical committee approval was granted for
TABLE 1. Short Posterior Ciliary Artery Supply of the PONAA ("Circle" of Haller and Zinn)

<table>
<thead>
<tr>
<th>Number of Casts</th>
<th>Percentage of Casts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial and lateral para-optic SPCAs</td>
<td>15</td>
</tr>
<tr>
<td>Lateral para-optic SPCA</td>
<td>2</td>
</tr>
<tr>
<td>Medial, lateral, and superior SPCAs</td>
<td>1</td>
</tr>
</tbody>
</table>

TABLE 2. Composition of the PONAA ("Circle" of Haller and Zinn)

<table>
<thead>
<tr>
<th>Number of Casts</th>
<th>Percentage of Casts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete anastomoses</td>
<td>8</td>
</tr>
<tr>
<td>Complete with narrowed sections</td>
<td>6</td>
</tr>
<tr>
<td>Incomplete anastomoses (including 1 fractured anastomosis)</td>
<td>4</td>
</tr>
</tbody>
</table>

The term perioptic nerve arteriolar anastomoses (PONAA) is used instead of circle of Haller and Zinn in the text. Here, the PONAA is complete but has narrowed sections.

taya's method was used, and in four eyes Fahrenbach's method was used. All the surrounding tissue was corroded in 6 M potassium hydroxide, and the casts were thoroughly washed in distilled water and then air dried.

Examination of Vascular Casts

Each cast was examined under a binocular dissecting microscope to orientate the specimen and to identify the posterior ciliary bundles and perioptic nerve arteriolar anastomoses (PONAA). Microdissection was performed to reveal details of the blood supply to the retrolaminar and laminar optic nerve regions. The dissected specimens were mounted on aluminum stubs and were coated with gold sputter (50 µm gold) for examination under scanning electron microscopy at 20 kV. Photographic documentation of nine different views of each microvascular cast was made at magnifications X20 and X25 by rotating and tilting the specimen within the scanner. Detailed documentation of features of interest was made at higher magnification.

RESULTS

Full analysis of 7/25 casts was limited by fragility on sequential microdissection; therefore, the findings for these casts are not included.

There were 14 white subjects—five men and nine women, 21 to 97 years of age (mean, 71 years; median, 76.5 years). In 10 of these subjects, only one eye was studied. All eyes were from subjects without known ocular disease, as determined by telephone discussions with relatives and by hospital records if available, with full ethical committee approval from St. Thomas' Hospital. Refractive errors were not recorded. Morphometric findings are summarized in Tables 1 and 2.

Overview of Short Posterior Ciliary Circulation

A montage depicting the medial and lateral short posterior ciliary artery bundles is shown in Figure 1. Each
FIGURE 2. (A) Scanning electron micrograph of a methyl methacrylate cast of a right human eye (same eye as in Fig. 3, eye 1R, but viewed obliquely from a 90° angle). This is an oblique view of part of the medial SPCA bundle (on left), with the inferior branch of the medial paraoptic SPCA branch contributing to the inferior anastomosis (boxed). Bar = 600 μm. (B) Higher magnification of boxed part of (A) showing pial arteriole (asterisk [*]) and its branches encircling and entering the anterior optic nerve (arrow) supplying the retrolaminar optic nerve. Solid circles indicate a pial vein. Bar = 100 μm.

bundle is composed of many distal short posterior ciliary arteries (D-SPCAs) and one paraoptic short posterior ciliary artery (PO-SPCA) lying closest to the optic nerve. The lateral PO-SPCA most commonly divides proximal to the medial PO-SPCA (estimated extrascleral), adjacent to the anterior optic nerve, with a characteristic gap between it and the more numerous D-SPCAs in the lateral bundle (Fig. 1). The medial PO-SPCA branches more distally (estimated to be either just outside the sclera or within the sclera), close to the D-SPCAs, without a discernible gap (Fig. 1). The location of branching in relation to the sclera is estimated by the distance posterior to the choroid because all tissue landmarks are corroded in vascular casting. The medial and lateral PO-SPCA branches form a “circle” of Haller and Zinn composed, in effect, of two anastomotic parts, one superior and one inferior to the anterior optic nerve, which are better termed perioptic nerve arteriolar anastomoses (PONAA). The retrolaminar optic nerve is supplied by pial arterioles arising from the PONAA (Fig. 2). Other branches from the PONAA include recurrent choroidal arterioles and centripetal arterioles.

Specific Vascular Findings

Scanning electron micrographs from one view of five of the 18 casts (each cast was examined from nine different angles) are shown in Figure 3. Scanning electron micrographs of one cast seen from two different angles, including magnified details of branches, are shown in Figure 4.

In 15/18 (83%) of casts, the PONAA was supplied by both a medial and a lateral PO-SPCA, whereas in 2/18 (11%) casts it was supplied by a lateral PO-SPCA (Fig. 5) and in one eye it was supplied by a superior SPCA and two horizontal PO-SPCAs (see Table 1).

The PONAA was complete in 14/18 (77%) of casts with both superior and inferior anastomotic parts. However, in six (33%) of these casts, narrowed sections (Figs. 1 and 6) were noted that were not restricted preferentially to either the superior or the inferior parts (see Table 2). For example, in the left eye of subject 3 (Fig. 1), there were narrow sections along both the superior and the inferior anastomotic parts, and in the right eye of subject 8 (Fig. 6), there was a narrow section in only the inferior part of the anastomosis. A narrow portion was defined as a small, interconnecting vessel of regular but narrow caliber (20 to 30 μm intraluminal diameter) completing the PONAA. Pial arterioles and direct centripetal branches still arose from narrow portions. Narrowings were not noted elsewhere in the casts.

In 4/18 (22%) casts, the PONAA was incom-
FIGURE 3. Five scanning electron micrograph "miniatures" at various stages of microdissection, each viewed posteriorly. Patient number and laterality are marked on the micrograph. Original magnification, x20. Eyes 2R and 3R show PONAA detached from the choroid and the optic nerve. Eye 3R is viewed anteriorly. An iatrogenic break is seen along the anastomosis in the upper figure. Bar = 1200 μ. All casts were examined from eight additional views to establish the supply and form of the PONAA, which cannot always be seen from this one view.
FIGURE 4. (A) Inferior view of left eye of subject 7 (same as Fig. 3, no. 7L) showing complete inferior anastomosis (large solid white arrow) between vertically orientated lateral paraoptic SPCA (small white arrows) and flatter orientated medial paraoptic SPCA branches (black arrows). Bar = 600 μm. (B) Posterior view of the same eye showing branches of medial paraoptic SPCA (black arrows). On the left lies part of the optic nerve with both the central retinal vein (V) and the artery (A). Bar = 325 μm. (C) Lateral view of same eye showing lateral paraoptic SPCA in foreground (star) dividing into three branches, one superior (white solid arrow) and two inferior branches (solid black cone arrow). Central retinal artery (A), central retinal vein (V) in center of optic nerve capillaries. Bar = 325 μm. (D) Higher magnification of part of inferior anastomosis (lying horizontally in lower picture) with pial arterioles (asterisks [*]), direct centripetal branches (small open arrows), and centripetal branches (small solid black arrows) off recurrent choroidal arterioles supplying the retrolaminar and laminar optic nerve. Bar = 100 μm.
FIGURE 5. Complete PONAA dissected from the posterior choroid and anterior optic nerve (same cast as Fig. 3, eye 2L). It is supplied by only one lateral paraoptic SPCA (open arrow). Although this appears to be similar to a circle, it could not function as one. Bar = 750 μm.

FIGURE 5. Complete PONAA dissected from the posterior choroid and anterior optic nerve (same cast as Fig. 3, eye 2L). It is supplied by only one lateral paraoptic SPCA (open arrow). Although this appears to be similar to a circle, it could not function as one. Bar = 750 μm.

DISCUSSION

This methyl methacrylate vascular casting study of human eyes (without known ocular disease) clearly demonstrates the variation in the blood supply to the retro-laminar and laminar regions of the anterior optic nerve. Although the “circle” of Haller and Zinn was originally described in 1755 from meticulous dissections of human cadaver eyes, the frequency of its existence and its form has remained unclear. In this study, perioptic nerve arteriolar anastomoses between PO-SPCAs were present with intact superior and inferior parts in 77% of the casts examined, although in several of these the anastomoses had narrow portions. Branches of two PO-SPCAs (medial and lateral) most commonly formed the anastomoses, but in a small proportion (12%) either one or three paraoptic short posterior ciliary arteries contributed. Although the anterior optic nerve in humans is largely supplied by the short posterior ciliary circulation, apart from the surface nerve fiber layer, most of the short posterior ciliary circulation supplies the choroid; the anterior optic nerve is usually supplied by two paraoptic SPCAs, which also supply the peripapillary choroid, whereas the 10 to 20 distal SPCAs supply only the choroid. On the rare occasions when only one PO-SPCA supplies the anterior optic nerve, there may be potential vascular vulnerability, similar to a “circle” of Willis (circulus arteriosus of Willis) with only one internal carotid artery.

The casting techniques used in this study involve complete tissue corrosion and extensive manipulation and therefore are limited by fragility, making accurate quantitative analysis of smaller vessels, particularly capillary densities, difficult. Although the low viscosity of the mixture appears to give a good capillary and venous fill, such vessels may be lost again during processing and dissection. For instance, in this series, one of the four casts (22%) in which the “circle” was incomplete had an apparent iatrogenic fracture, with loss of a small section of the circle of Haller and Zinn. These fractures are usually apparent from the shape of the broken ends on scanning electron microscopy. Care must be taken in interpreting empty areas in casts, particularly when specimens with suspected disease are being examined. Comment can only be made on microvascular casts that are present. The cast with an obvious fracture and a missing segment may have had complete anastomosis.

Other methyl methacrylate casting studies have confirmed the presence of some form of arterial circle around the anterior optic nerve in humans. Investigations of latex casts of human eyes were not primarily designed to examine the anterior optic nerve, which was often discarded to allow for choroidal and anterior uveal studies. Interpretation of latex casts was hampered by the low magnification and depth of focus of dissecting microscopes and by the difficulty in distinguishing accurately between arteries and veins and the lack of rigidity of the cast. These problems have been redressed in methyl methacrylate casting, wherein high magnification and depth of focus of dissecting microscopes and by the difficulty in distinguishing accurately between arteries and veins and the lack of rigidity of the cast. These problems have been redressed in methyl methacrylate casting, wherein high magnification and depth of focusing are available with scanning electron microscopy and the type of vessel is identifiable by the characteristic endothelial nuclear impressions made on the rigid cast.

Findings from studies using histologic serial sections are difficult to interpret because the PONAA lies in different planes anteroposteriorly (like a hammock) and has both extrasceral and intrasceral portions. The three branches derived from the PONAA are pial, recurrent choroidal, and direct cen-
tripetal. It is not possible to distinguish between arteri-ies, arterioles, and terminal arterioles other than by the cast diameter, which represents the vessel lumen diameter because all tissue has been corroded. The histologic distinction between a small artery and a large arteriole is arbitrary, and we have named the pial branches arterioles and recurrent choroidal branches arterioles by their cast diameters. Three-dimensional reconstruction of these from histologic serial sections is difficult because the blood vessels branch in different directions from the anastomotic parts of the circle (Fig. 4d). The pial arterioles pass first centripetally, then proximally, along the pia, supplying the retro-laminar optic nerve (Figs. 2, 4, and 6). The recurrent choroidal arterioles are so named because they pass centripetally and anteriorly before bending sharply to travel in a centrifugal anterior direction to supply the peripapillary choroid. Pial and direct centripetal arterioles from both the PONAA and the elbow of the recurrent choroidal arterioles supply the retrolaminar and laminar optic nerves. Neither the numbers of pial arterioles derived from each part of the PONAA nor the capillary densities of retrolaminar and laminar optic nerves were quantified for this study.

Levitzky and Henkind,22 from studies combining histologic sectioning and ink injection techniques, suggested that the circle of Haller and Zinn was incomplete in most instances. Lieberman et al1 commented that intrascleral anastomoses were variable in extent and number and did not report a complete circle in humans. Using dissection and latex casts, Hayreh12,23 examined large numbers of human cadaver orbits and concluded that the circle of Haller and Zinn was most commonly incomplete. Some studies failed to differentiate clearly between findings from humans and other primates.21,22 Anderson and Braver-
man10 clarified this by showing that some form of anas-
tomotic intrascleral circle was found in human speci-
mens, but not in subhuman primates. Risco et al,11 working with methyl methacrylate casts of cynomolgus monkeys, confirmed that SPCA branches supplied the distal optic nerve, without any anastomoses between SPCAs. A review of the literature and the results of this study show that although morphologic findings in humans are similar to those found in other primates, caution should remain in extrapolating findings from subhuman primates to man. Such comparisons may also be limited because subhuman primate studies have usually been undertaken on live or freshly killed young healthy animals, whereas most human anatomic studies are autopsy specimens from older subjects with a range of ages (and hence arteriosclerosis) examined many hours after death. Increasing age did not appear, in this study, to be related to incompleteness of the circle because some of the complete anastomoses were found in older subjects.

The term circle of Haller and Zinn may imply both an anatomic and a functional vascular circle. The “circle” is an ellipse consisting of two separate anatomic anastomoses between branches of a medial and a lateral PO-SPCA, and the patterns of vascular branching and reduction of intraluminal diameter along the anastomoses do not suggest that these vascular anastomoses function as a circle. A similar semantic argument can be applied to the term circle of Willis (circulus arteriosus of Willis), which also does not function as a circle. We are, therefore, increasingly using the term perioptic nerve arteriolar anastomoses. Under normal physiological conditions, it appears unlikely that blood would flow into one PO-SPCA, cross the anastomosis, and exit through the other PO-SPCA. It is likely that an arterial front exists along each anasto-
tomosis, where blood from each of the two PO-SPCAs meets, then runs off in the branches to the retrolami-
lar and laminar optic nerves, and to the peripapillary choroid. This zone of functional separation of flow from the medial and lateral PO-SPCA may be regarded as a functional watershed zone, which may shift along each of the anastomoses according to the relative perfusion pressures, varying, for instance, with eye move-
ments even though there is anatomic continuity along the vascular anastomoses. It is interesting that in one third of the casts studied, narrow segments were found along one or both vascular anastomoses that were shown to be continuous with vessels from the other PO-SPCA when the specimen was tilted and rotated in the scanning electron microscope. It should be noted that these attenuated sections were located to one side of the midline, the significance of which is unclear. These narrow portions probably do not repre-
sent vessel spasm in view of the timing of casting after death. Neither do they represent postmortem clot by their morphologic appearance. An artefact cannot be excluded. The PONAA were often anatomically complete, but this does not mean they were functionally complete.

Although the pathogenesis of anterior ischemic optic neuropathy is unknown, an understanding of the blood supply of the retrolaminar optic nerve may help in understanding the different clinical and fluo-
rescein angiographic appearances of arteritic and nonarteritic anterior ischemic optic neuropathy.24-26 In nonarteritic anterior ischemic optic neuropathy, hypoperfusion within the microvasculature of the anterior optic nerve affects the microperfusion of the retrolaminar optic nerve.6 Ischemia may occur in an anatomically crowded disc with a tight scleral canal and a thickened sclera.27 There may be associated peri-
papillary choroidal perfusion delay on fluorescein an-
giography.28 In contrast, occlusion of the posterior and short posterior ciliary arteries from arteritis29 not only causes an infarct in the optic disc, it also produces
extensive choroidal hypoperfusion, a common feature of arteritic ischemic optic neuropathy. This study does not provide an anatomic basis for the preferential inferior visual field loss seen in nonarteritic anterior ischemic optic neuropathy because constant structural asymmetry between the superior and inferior parts of the PONAA could not be demonstrated. A possible explanation for this may be that, if there is hypoperfusion of the anterior optic nerve, more proximal pial collaterals from the central retinal artery at its entry into the nerve may provide preferential sparing of inferior optic nerve axons.

In summary, this study of human cadaver eyes demonstrates the variation in normal blood supply to the retrolaminar and laminar optic nerves. Periopic nerve arteriolar anastomoses, usually described as the circle of Haller and Zinn, could be identified in some form in 77% of methyl methacrylate casts studied, with variations in supply from the PO-SPCAs and in the structure of the anastomoses.

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Key Words
optic nerve, human, microvasculature, corrosion casting

References


