

Intraocular Projections From the Pterygopalatine Ganglion in the Cat

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ABSTRACT

The intraocular projection of the cat pterygopalatine (sphenopalatine) ganglion was examined by using retrograde axoplasmic transport techniques in order to investigate the possibility of the involvement of the facial nerve in ocular parasympathetic innervation. Following an injection of horseradish peroxidase (HRP) or wheat germ agglutinin-HRP into the eye, retrogradely labeled cells were observed in the ipsilateral pterygopalatine ganglion, principally in the caudal part. By dissection of silver-impregnated, acetylcholinesterase- and cholinesterase-stained orbital preparations, it was determined that two different nerve pathways link the pterygopalatine ganglion and the eye. One took a retrograde course to join the retro-orbital plexus and then traveled forward accompanying the ciliary artery, the long ciliary nerve, the short ciliary nerve, and/or the optic nerve sheath. The other entered the orbit directly, fused with the ethmoidal nerve or the infratrochlear nerve in a retrograde fashion, and then turned forward along the long ciliary nerve to enter the eye. All these nerves arose from the caudal part of the ganglion. These results are discussed in relation to recent biochemical and histochemical data demonstrating the involvement of the facial nerve in the control of ocular blood flow and intraocular pressure.

Key words: ganglia, parasympathetic nervous system, eye, intraocular pressure, facial nerve

Parasympathetic fibers in the eye arise chiefly from the main and the accessory ciliary ganglia and from scattered ganglion cells in the ciliary nerves (Gabella, '76; Kuchiwa et al., '88b, '89; Kuchiwa, '90). Recent studies suggest that the pterygopalatine (sphenopalatine) ganglion is an additional source of ocular parasympathetic innervation.

The pterygopalatine ganglion contains many vasoactive intestinal polypeptide (VIP)-like immunoreactive neurons (Uddman et al., '80a; Hara et al., '85). Axons showing immunoreactivity to VIP are to be found in various cephalic structures (Gibbins et al., '84; Hara et al., '85), including the ocular tissues. VIP axons have been demonstrated by immunohistochemistry and radioimmunoassay in the posterior uvea and ciliary body of the cat (Uddman et al., '80b), rabbit (Unger et al., '81; Butler et al., '84), guinea pig (Terenghi et al., '82), and human (Miller et al., '83). VIP axons in the posterior uvea and ciliary body disappear after ablation of the pterygopalatine ganglion (Uddman et al., '80b; Butler et al., '84), but levels of VIP-like immunoreactivity are unaffected by sensory or sympathetic denervation (Butler et al., '80, '84; Unger et al., '81). This strongly suggests an association of the pterygopalatine ganglion cells with VIP immunoreactivity with ocular parasympathetic innervation.

Linkage of the eye with the pterygopalatine ganglion has been suggested by micro-dissection methods in several species of mammals (Ruskell, '65, '70a; Kuwayama et al.,

'87; Lin et al., '88). The innervation to the eye by this ganglion is documented by degeneration studies in the rabbit and monkey (Ruskell, '65, '70a; Butler et al., '84). However, in other animals, including the cat, direct evidence of this projection has not been provided by recent hodological techniques.

The purpose of this work was to establish, by intraaxonal transport techniques and micro-dissection of selectively stained preparations, the eye innervation by fibers of facial nerve origin in the cat, so as to complement the findings of previous dissection studies.

MATERIALS AND METHODS

Axoplasmic transport studies

Nine adult cats (body weight = 1.5–4.5 kg) were used in the retrograde axoplasmic transport experiments. The cats were anesthetized by intramuscular injection of ketamine hydrochloride (20–40 mg/kg) and placed in a stereotaxic head holder. Local anesthesia (Xylocaine) was applied at all pressure points of one eyeball. The needle of a 100 μ l microsyringe was inserted through the sclera approxi-

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mately 4 mm posterior to the limbus, and 100 μ l of 30% HRP (Toyobo, Grade IC) dissolved in saline or 50 μ l of 5% wheat germ agglutinin-HRP (WGA-HRP; prepared in the author's laboratory; Kuchiiwa et al., '88a) was injected into the chambers of the eye. The surface of the eyeball was flushed with saline immediately after puncture and withdrawal to minimize extraocular leakage of HRP/WGA-HRP. In addition, the puncture site was plugged with a surgical binding agent, Aron Alpha A (alkyl- α -cyanoacrylate monomer; Sankyo) to minimize possible backflow of HRP/WGA-HRP from the eyeball. After a postinjection period of 43–51 hours, the cats were re-anesthetized deeply and perfused through the ascending aorta with 1,000 ml of saline followed by 2,000 ml of 2.5% formalin and 1.25% glutaraldehyde in 0.1 M sodium phosphate buffer at pH 7.4. The pterygopalatine, accessory and main ciliary ganglia, and brains were removed and immersed in cold buffer containing 30% sucrose, and 40 μ m or 100- μ m-thick sections were cut on a freezing microtome. In several cases the pterygopalatine ganglion was prepared as a wholemount. All sections of the ganglia and every third section of the brain, and whole preparations of the pterygopalatine ganglia were prepared for peroxidase histochemistry by the tetramethylbenzidine reaction method (Mesulam, '78). A part of each section was counterstained with neutral red. Light and polarized illuminations were employed to identify HRP/WGA-HRP labeled cells.

Dissection

A total of 10 adult cats (b.w. = 1.5–4.5 kg) were dissected to trace fiber bundles associated with the ganglion. The cats were deeply anesthetized with ketamine hydrochloride (50 mg/kg) and perfused through the ascending aorta with physiological saline followed by 10% buffered formalin (pH 7.4). In some cases the cranial vascular system was injected with a 1% Berlin blue solution. A preliminary dissection was performed to expose the appropriate nerves in the orbit and the floor of the cranial cavity. Extraocular muscles were partially resected without damage to the underlying nerves and adipose tissue was removed under a binocular microscope.

In four cases silver impregnation of the nerves was accomplished using the method of Christensen ('35-'36) as modified by Grimes and von Sallmann ('60) in order to facilitate observation of the fine nerve connections. In two cases the preparation was stained using the thiocholine method for the histochemical demonstration of cholinesterase (ChE) as described by Kuwayama et al. ('87). In the

other four cases the tissue was treated by a slight modification of the acetylcholinesterase (AChE) staining method of Hardy et al. ('76). The selectively stained preparations were then dissected under binocular microscope with special attention to the course of the fine autonomic nerves.

The procedure of AChE staining was as follows. The tissue was immersed in a 20% phosphate-buffered sodium sulfate solution (pH 7.4) at 37°C for 2 hours and incubated in a 0.05 M acetate buffer solution (pH 5.0) containing 4 mM of acetylthiocholine iodide, 10 mM of glycine, 7.5 mM of copper sulfate, at 37°C for 1 hour. It was then rinsed five times in distilled water, transferred to 1.25% sodium sulfite solution for 3 minutes, and again rinsed five times. The specimen was then placed in a solution of 1% silver nitrate for 2 to 5 minutes depending upon the degree of staining desired. It was subsequently rinsed in distilled water twice and treated in 5% sodium thiosulfate for approximately 10 minutes. Finally the preparation was thoroughly rinsed. These steps were carried out at room temperature and the solutions were well stirred during the procedure. The stained preparation was stored in distilled water at 4°C. When necessary, a small part of tissue was dissected out, dehydrated in graded alcohol, cleared in xylene, mounted on a slide, and observed with a light microscope.

RESULTS

Axoplasmic transport studies

In all cases HRP/WGA-HRP labeled cells were identified in the pterygopalatine ganglion and in the main and accessory ciliary ganglia ipsilaterally following injection of HRP or WGA-HRP into the eye.

In this experiment cases in which the retrogradely labeled neurons were observed in the oculomotor, trochlear, abducens, trigeminal, or facial nucleus were excluded, because in these cases it was considered that the injected enzyme had leaked from the eyeball into the orbit (2 cases). In the remaining cases, many labeled cells were observed in the pterygopalatine ganglion (Fig. 1A–C). The pterygopalatine ganglion of the cat consists of several cell masses along a forward extension of the nerve of the pterygoid canal (Fig. 1A). The greatest number of labeled cells were located in the masses in the caudal part of the ganglion and a few in the middle part. Most labeled cells were rounded or oval in shape. The total number of labeled neurons, counted in five wholemount preparations, ranged from 38 to 53 with an average of 46.8. Most cells observed in this ganglion were weakly labeled both in the sectioned and in the wholemount

Abbreviations

III	oculomotor nerve	Mx	maxillary nerve
ACG	accessory ciliary ganglion	Nc	nasociliary nerve
CA	ciliary artery	Oc	<i>rami oculares</i> from the retro-orbital plexus
CG	ciliary ganglion	ON	optic nerve
ER	external rete	Or	<i>rami orbitales</i> of the pterygopalatine ganglion
Et	ethmoidal nerve	Pa	palatine nerve
IC	internal carotid nerve	Ph	pharyngeal nerve
IO	nerve to the inferior oblique muscle	PC	nerve of pterygoid canal
Io	infraorbital nerve	Pp	pterygopalatine nerve
IR	nerve to the inferior rectus muscle	PPG	pterygopalatine ganglion
It	infratrochlear nerve	R	retinal artery
LC	long ciliary nerve	RO	retro-orbital plexus
LP	nerve to the levator muscle of the palpebra	SCI	lateral short ciliary nerve
LPCI	lateral long posterior ciliary artery	SCm	medial short ciliary nerve
LPCm	medial long posterior ciliary artery	Sp	sphenopalatine nerve
MR	nerve to the medial rectus muscle	SR	nerve to the superior rectus muscle

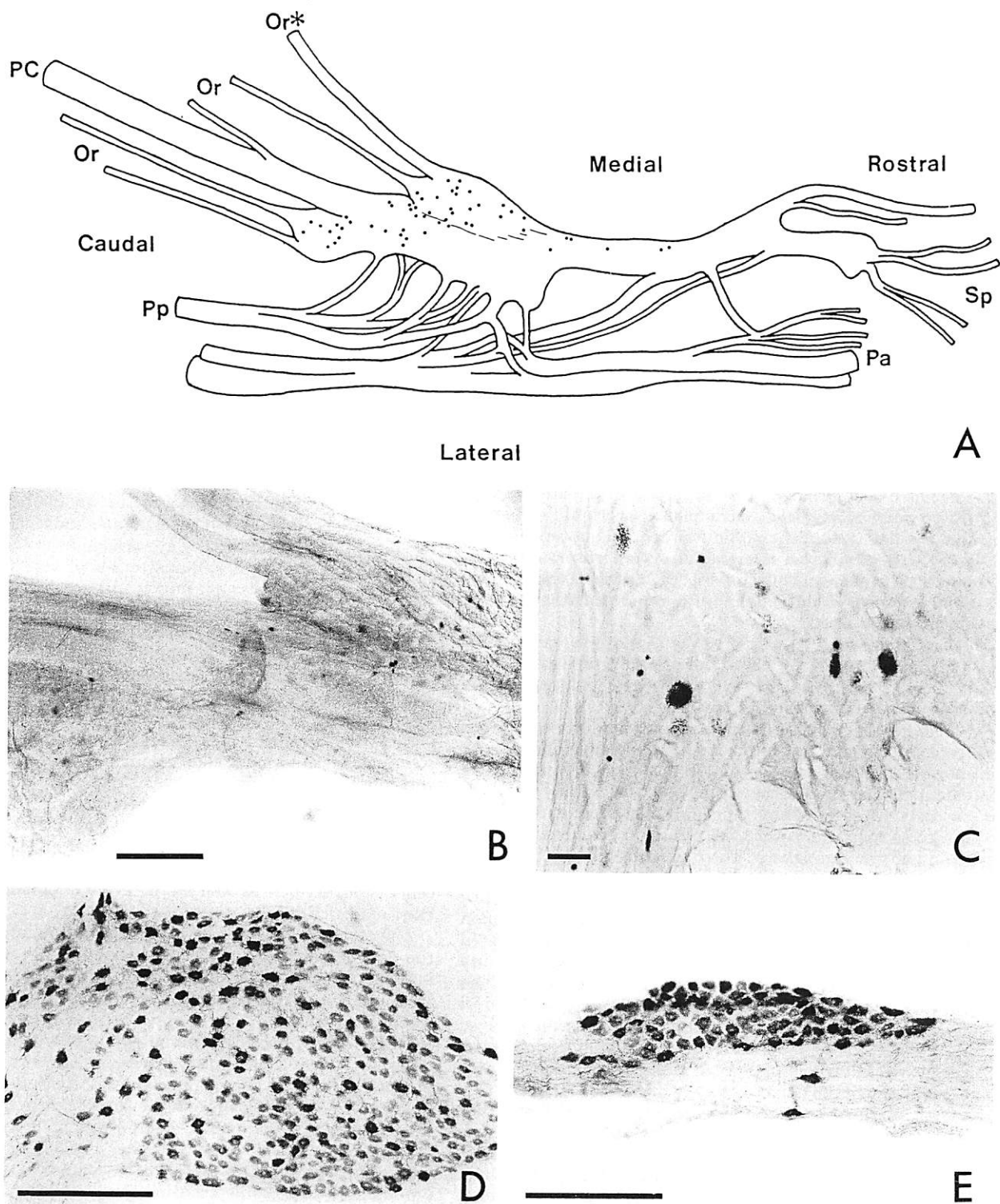


Fig. 1. A. Diagram of a wholemount preparation of the pterygopalatine ganglion illustrating HRP-labeled cells (dots) following application of HRP into the eye. Asterisk indicates the *ramus orbitalis* directly entering the orbit to join the ethmoidal or infratrochlear nerve. B-E. Photomicrographs showing HRP-labeled neurons after an injection of HRP into the eye: B, low power photomicrograph of the wholemount

preparation of the pterygopalatine ganglion, the same preparation as in A, scale 1 mm; C, the pterygopalatine ganglion in another case, 40- μ m-thick sectioned preparation, scale 100 μ m; D, the main ciliary ganglion, the same animal as B, 40- μ m-thick section, scale 0.5 mm; E, the accessory ciliary ganglion, the same animal as B and D, 100- μ m-thick section, scale 0.5 mm.

preparations. By contrast, in the main and accessory ciliary ganglia, the great majority of ganglion cells were labeled and the labeling was extremely heavy (Fig. 1D-E).

Dissection

In the silver-impregnation method, motor and somatic sensory nerves were stained dark brown, fine unmyelinated nerves pale brown, and other tissues remained unstained. The histochemical methods for the detection of AChE and ChE activity applied to the partially dissected preparations effectively stained postganglionic nerves arising from the pterygopalatine ganglion. The short ciliary nerves were also stained for AChE but not for ChE. Motor and somatic sensory nerves were not stained by these histochemical staining procedures.

The pterygopalatine ganglion of the cat lay on the superior surface of the pterygoid muscle and abutted onto the inferior surface of the periorbita. The ganglion was positioned between the medial orbital wall and the infra-orbital nerve. The nerve of the pterygoid canal entered the caudal end of the ganglion (Fig. 1A). The sphenopalatine nerves supplying the nose branched from the rostral part and the pterygopalatine nerves entered the lateral edge. The retro-orbital plexus was situated in the external rete (Fig. 2). It was formed by a complex network of fine nerves that divided and anastomosed frequently between the rete vessels. A number of microganglia were observed at the junction points of the plexus (Fig. 3A). Besides these, a few small but prominent ganglia were found near the nerve of the pterygoid canal.

Two different nerve pathways to the eye were determined; one traveled by way of the retro-orbital plexus or the small ganglia near the nerve of the pterygoid canal, the other entered the orbit directly.

The former pathway contained several nerves that arose from the caudal part of the ganglion, or occasionally one or more arose from the nerve of the pterygoid canal or the small ganglia near the nerve (Fig. 3A). They traveled caudally in a fanlike arrangement, divided and anastomosed as they ran toward the orbital apex and sometimes included small ganglia at their junction points (Fig. 3B). They then entered the external rete and joined a fine nerve network and microganglia in the retro-orbital plexus. A few branches that arose from the superior cervical ganglion coursed forward beneath the trigeminal ganglion, entered the external rete at its caudal end (Fig. 3A), divided into many fine filaments, and mixed with the nerve plexus. The nerves from the plexus to the eyeball (*rami oculares* of Ruskell, '70a) were several in number, generally derived from the plexus, often directly from the small ganglia near the nerve of the pterygoid canal. Most of them took a course accompanying the ciliary artery, which arose from the rete (illustrated in Fig. 2). Some entered the eyeball together with the artery; others left the artery to reach the dural sheath of the optic nerve where they divided and anastomosed to form a plexus in the sheath (Fig. 3C). Others joined the long or short ciliary nerves or other filaments from the retro-orbital plexus and then traveled to the eye (Fig. 2). Besides these, a few nerves not accompanying the ciliary artery were observed. Some coursed along with the long ciliary nerve passing through the rete; others traveled backward to enter the dural sheath of the optic nerve and mixed with the plexus in the sheath (Fig. 3A,C). The latter optic nerve sheath branches occasionally arose from the small ganglia near the nerve of the pterygoid canal.

The latter pathway consisted of one or more fine nerve branches that arose from the mediocaudal part of the pterygopalatine ganglion, traveled mediocaudally and then medially around the extraocular muscle cone, and penetrated the periorbita. They ran upward on the nasal surface of the medial rectus muscle and fused with the ethmoidal nerve or, in a few preparations, with the infratrochlear nerve in a retrograde fashion. The pathway is illustrated schematically in Figure 3A. Occasionally an ansa, indicated with arrowheads in the figure, was observed between the ethmoidal nerve and the long ciliary nerve. These orbital branches were considered to take a retrograde course along the ethmoidal or infratrochlear nerve and then turn to the eyeball accompanying the long ciliary nerve.

In a few preparations another orbital branch was observed. It derived from the rostral part of the ganglion, traveled upward, invaded the orbit, and took a retrograde course to join the ciliary ganglion or the nerve to the inferior oblique muscle (Fig. 3A).

DISCUSSION

From the present study it is apparent that the intraocular projection from the pterygopalatine ganglion originates in the caudal cell masses of the ganglion and that there are two different pathways to the eye arising from the masses. This study is the first demonstration of this projection using the retrograde axoplasmic transport technique. The findings obtained here support the results of the degeneration studies of Ruskell ('65, '70a) in the rabbit and monkey and Butler et al. ('84) in the rabbit.

In the axoplasmic transport study most of the HRP/WGA-HRP positive cells in the pterygopalatine ganglion were weakly labeled both in the sectioned and in the wholemount preparations. In the same animals the great majority of the accessory and the main ciliary ganglion cells were labeled very intensely, indicating that the uptake of the enzyme was maximal in the intraocular structures. This weak labeling of the pterygopalatine ganglion is presumably the result of the possible complex ramifications of the postganglionic fibers of the ganglion, which distribute widely to the cephalic structures as well as the eye (Gibbins et al., '84; Hara et al., '85).

The *rami orbitales* from the pterygopalatine ganglion join the network of the retro-orbital plexus in the rat, rabbit, monkey, and human (Ruskell, '65, '70b, Kuwayama et al., '87), and fine nerves from this plexus supply the eye (*rami oculares* of Ruskell, '70a) in the rat, rabbit, and monkey (Ruskell, '65, '70a,b; Kuwayama et al., '87). The ramifications of the internal carotid nerves are also mixed in the plexus, however, in the monkey at least, the *rami orbitales* to the retro-orbital plexus and the *rami oculares* to the eye are composed predominantly of unmyelinated parasympathetic fibers arising from the pterygopalatine ganglion (Ruskell, '70a). In the cat as in the monkey, the *rami orbitales* of the pterygopalatine ganglion constitute the parasympathetic roots of the retro-orbital plexus, and the *rami oculares* are presumably principally composed of parasympathetic fibers originating in the pterygopalatine ganglion. The small ganglia located near the nerve of the pterygoid canal, the small ganglia in the *rami orbitales*, and the microganglia within the retro-orbital plexus are assumed to be accessory ganglia of the pterygopalatine ganglion.

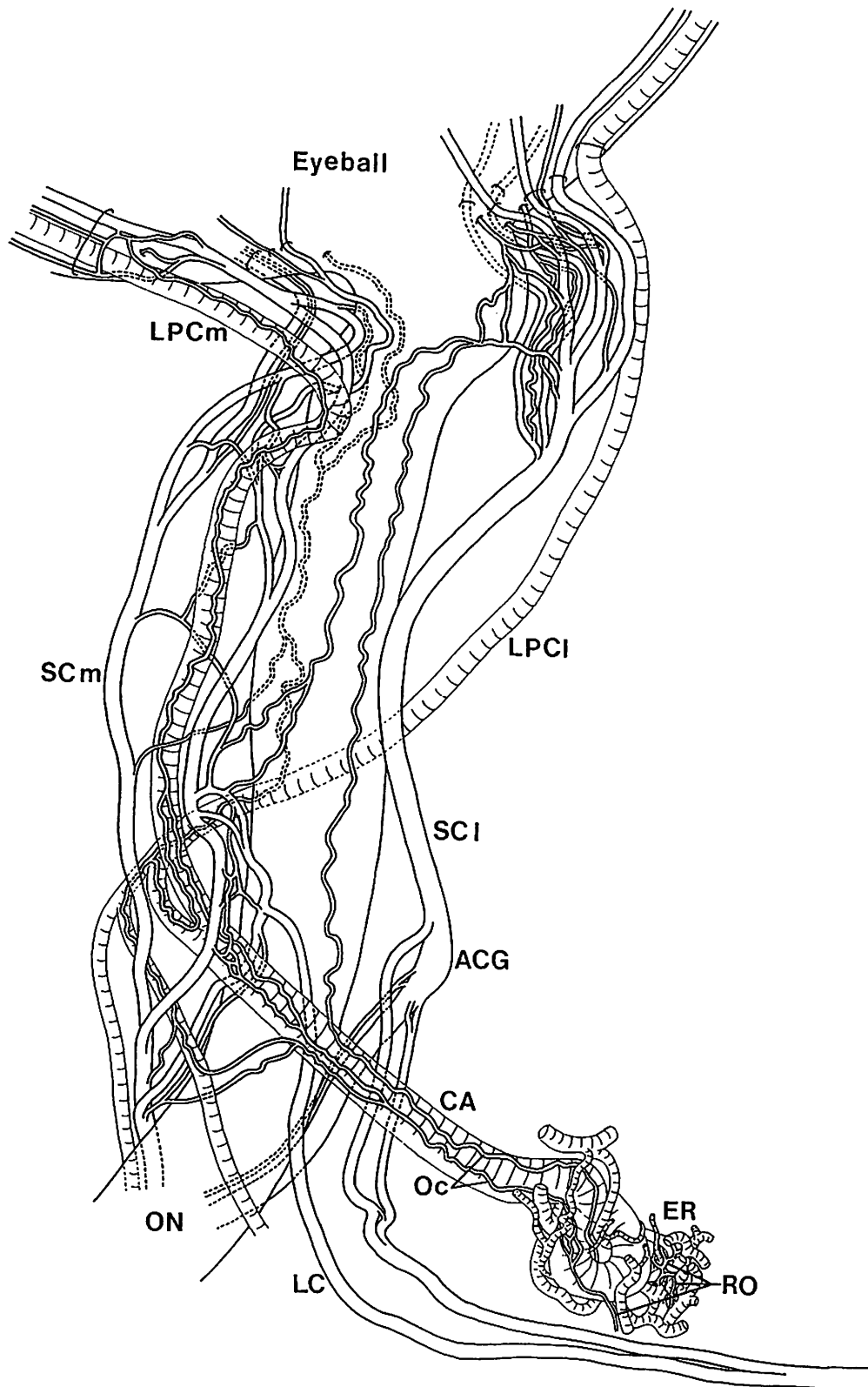


Fig. 2. A sketch of the silver-impregnated wholemount preparation showing the *rami oculares* arising from the retro-orbital plexus to the eyeball. Only small parts of the external rete and the retro-orbital plexus are illustrated. Right orbit, viewed from above with the globe to the top.

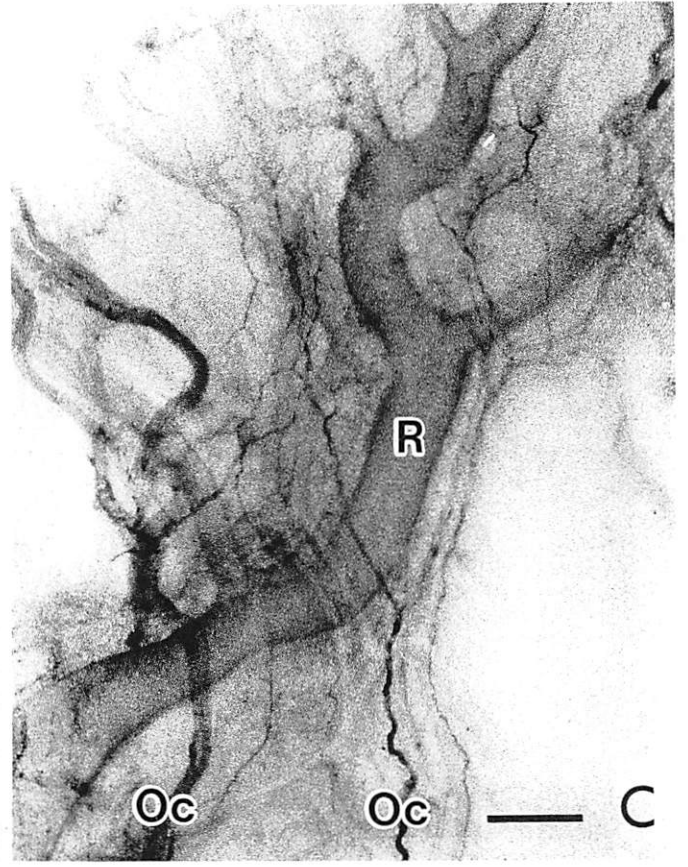
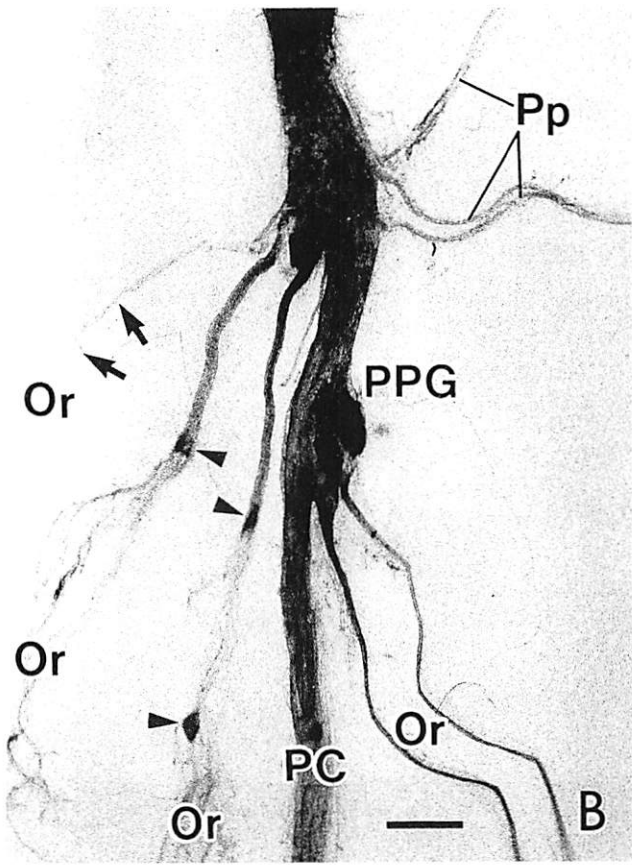
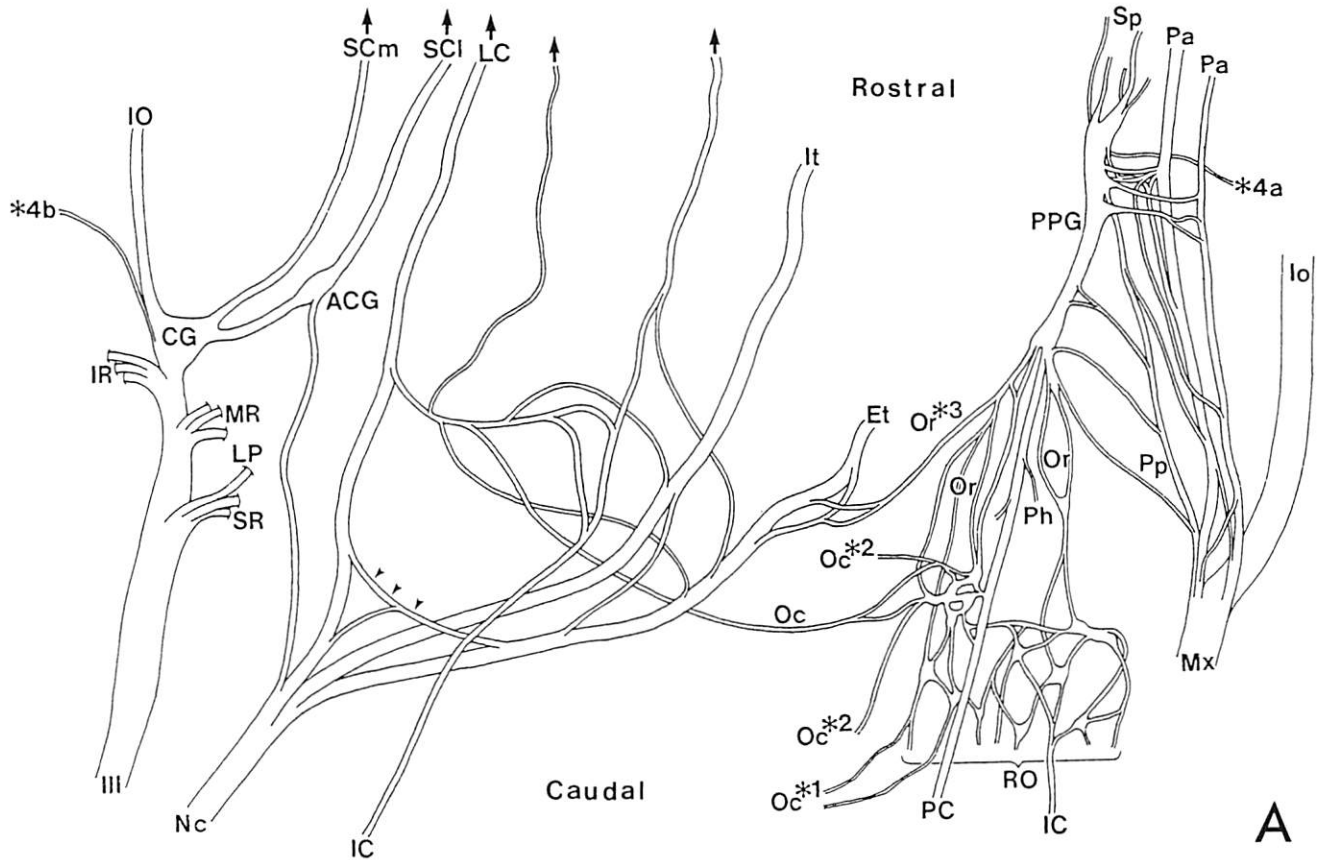


Figure 3

The pterygopalatine ganglion contains many VIP-like immunoreactive cells, and the uvea contains abundant VIP-like immunoreactive fibers (Uddman et al., '80a,b). The ablation of the ganglion results in the disappearance of VIP-like immunoreactive fibers (Uddman et al., '80b; Hara et al., '85) or in a fall in VIP level (Butler et al., '84) in the uvea. Ganglion cells (Castro-Correia, '67) and, more recently, VIP-immunoreactive cell bodies (Terenghi et al., '82; Miller et al., '83; Stone et al., '86) have been observed in the choroid of several species, but the innervation is believed to be principally extrinsic because choroid nerve degeneration occurs following damage of the ganglion (Ruskell, '65, '70a; Butler et al., '84). The pterygopalatine ganglion is the most likely source of the VIP-like immunoreactive fibers that reach the eye.

Vasoactive intestinal polypeptide is a potent vasodilator in many vascular beds (Larsson et al., '76; Uddman et al., '81), including the ocular arteries. VIP-like immunoreactive nerve fibers in the eye are seen in close association with blood vessels, chiefly in the choroid (Uddman et al., '80b; Unger et al., '81; Terenghi et al., '82; Miller et al., '83; Butler et al., '84). Intravenous injection of VIP results in a vasodilation in the choroid, and injection into the anterior chamber causes a marked vasodilation in the anterior uvea (Nilsson and Bill, '79). Both these injections can also cause a rise in intraocular pressure (Nilsson and Bill, '79; Butler et al., '84). Moreover, Gloster ('61) and Stjernschantz and Bill ('80) have observed an increase in uveal blood flow and intraocular pressure after intracranial facial nerve stimulation. Interruption of the greater petrosal nerve or ablation of the pterygopalatine ganglion causes a fall in the intraocular pressure (Golding-Wood, '64; Ruskell, '70a). These results substantiate the facial VIP nerve supply to the eye controlling the intraocular blood flow and the intraocular pressure.

Concerning the pupillomotor functions, it is believed that there must be two separate efferent pathways, one subserving the light reflex that passes through the ciliary ganglion, the other concerned in the contraction of the pupil that accompanies convergence and accommodation, probably mediated in the accessory ciliary ganglion (Kuchiiwa et al., '88b, '89; Kuchiiwa, '90). With regard to the latter pathway, Phillips ('73) cited the degeneration studies of Ruskell ('65, '70a), which demonstrated projection of the pterygopalatine ganglion to the eye, and he proposed that the pterygopalatine ganglion might be a station for the convergence-accommodation synkinetic contraction rather than the

accessory ganglia of Axenfeld ('07)—they are nothing more than the accessory ciliary ganglia located adjacent to the sclera; see Kuchiiwa et al., '89—because he found the accessory ganglia of Axenfeld only in a few mammalian species. Indeed, anterograde WGA-HRP labeling has been observed in the rostral part of the pterygopalatine ganglion following an injection into the rostral part of the midbrain including the oculomotor nucleus in some cats (T. Kuchiiwa, personal communication), and the present study indicated that there was a communicating pathway linking the rostral part of the pterygopalatine ganglion and the ciliary ganglion in a few cats. But the intraocular projection from the pterygopalatine ganglion originates in the caudal part but not the rostral part. Since it is difficult to believe that there is a connection between the rostral and the caudal parts through the internuncial cells, it therefore seems very improbable that the pterygopalatine ganglion plays a functional role in mediating the pupillary contraction associated with convergence and accommodation.

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Fig. 3. A. Diagram showing the connection between the pterygopalatine ganglion and the eyeball: Oc*1, *rami oculares* traveling by way of the ciliary artery to the eye, to be continued in Figure 2; Oc*2, *rami oculares* taking a course along the dural sheath of the optic nerve, to be continued in Figure 3C; Or*3, *ramus orbitalis* joining the ethmoidal nerve or infratrochlear nerve to take a retrograde course to the long ciliary nerve; *4a, the communicating branch to the ciliary ganglion, to be continued to *4b. Arrowheads indicate the ansa between the ethmoidal nerve and the long ciliary nerve. Arrows indicate nerve penetration into the sclera. B. Photomicrograph of the caudal part of the right pterygopalatine ganglion, wholemount preparation stained with ChE method. Arrowheads indicate the small ganglia in the *rami orbitales* to the retro-orbital plexus. Arrows indicate the *ramus orbitalis* joining the ethmoidal nerve or infratrochlear nerve in the orbit. Dorsal view. Scale 1 mm. C. Photomicrograph of flatmount preparation of the optic nerve sheath showing fine autonomic nerves originating in the retro-orbital plexus, with the eye to the top. Stained with AChE method, scale 1 mm.

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