
Control of intraocular blood flow.

II. Effects of sympathetic tone

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The effects of sympathetic tone on ocular blood flow have not been adequately studied in the past. Recent experimental work has contradicted earlier observations. We have used nuclide-labeled microspheres to measure the intraocular blood flow. The results of the study demonstrate that the ocular vascular beds are responsive to sympathetic tone. Cervical sympathectomy increased ocular blood flow, and sympathetic stimulation caused a decreased blood flow.

Key words: sympathectomy, sympathetic stimulation, intraocular blood flow, nuclide-labeled microspheres, sympathetic vasomotor tone.

The regulation of ocular blood flow is dependent upon multiple factors. In a previous paper we demonstrated the effects of intraocular pressure on ocular blood flow.¹ The effects of sympathetic tone have not been adequately studied. Previous authors have implied that cervical sympathectomy increased ciliary body blood flow.²⁻⁴ Other studies have shown that sympathetic stimulation reduces blood flow to the uvea.^{5, 6} However, most of these studies have measured ocular blood flow by indirect methods and have demonstrated the effects in only one subdivision of the uvea at a given time. The purpose of this present study is

to demonstrate the role of sympathetic vasomotor tone in regulating intraocular blood flow using the nuclide-labeled microsphere technique.

Methods and materials

In Part I of this study, adult cats weighing 2 to 3 kilograms and of both sexes were used. The animals were anesthetized with pentobarbital sodium, intraperitoneally, 30 mg. per kilogram. Six cats had preganglionic section of the cervical sympathetic nerve. Section of the nerve was made 1 to 2 cm. proximal to the ganglion and a 1 cm. segment was extirpated. The side of sympathectomy was alternated in the cats. The cats were allowed to convalesce for seven days. The existence of the sympathectomy was determined by the presence of miosis and partial covering of the eye by the nictitating membrane on the side of the sympathectomy. The cats were anesthetized a second time, a tracheotomy was performed and the cats were artificially respired with a respirator. Intraocular pressure was controlled by cannulating the anterior chamber at the limbus with a 21-gauge needle connected to a saline reservoir.

In part II of the study, the animals were anesthetized, had a tracheotomy, and the intraocular pressure was controlled, as described above, at 17 mm. Hg. Using a midline cervical incision, the

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sternohyoid and omohyoid muscles were separated exposing the carotid artery, the vagus, and the sympathetic nerve. The sympathetic nerve was carefully separated from the vagus. A two-pronged platinum electrode, insulated to approximately 1 mm. from the tip, was placed 2 cm. proximal to the superior cervical ganglion. A drop of mineral oil was placed on the nerve to prevent drying. The nerve was stimulated with an electronic stimulator (Grass Model S4) for 5 minutes before, and during injection of the microspheres. The stimulus parameters of 4 volts, 10 cycles per second and 2 msec. duration were used.

The blood-flow measurements were obtained as previously described.¹ In brief, the left hemithorax of the cat was opened and 0.5 c.c. of labeled microspheres per kilogram of body weight were injected into the left heart. The eyes were enucleated and dissected into iris, ciliary body, choroid with tapetum, choroid without tapetum, and retina. The tissues were air dried and weighed and the radioactivity was determined.

Results

Cervical sympathectomy increased ocular blood flow more than 30 per cent (Table I). The increase in blood flow was approximately equal in both the uveal subdivisions and the retina. Sympathetic stimulation decreased ocular blood flow. The blood flow was decreased by 56 per cent in the ciliary body, 45 per cent in the choroid, and 41 per cent in the retina. The results were similar when the control vs. experimental eye was alternated.

Discussion

The use of microspheres as a valid and quantitative method for studying ocular blood flow was discussed in a previous paper.¹ In this present study the intraocular pressure was held constant because of the inverse relationship between intraocular pressure and ocular blood flow. These experimental results demonstrate an inverse correlation between sympathetic vasomotor tonus and ocular blood flow. All of the ocular vascular beds appear to be equally responsive to sympathetic tonus as evidenced by change in blood flow.

Cervical sympathectomy increased ocular blood flow to the various ocular vascular beds. This is in good agreement with similar findings by Alm.⁷ An extraocular

Table I. The effect of sympathetic tone on ocular blood flow*

	Sympathectomy	Sympathetic stimulation
Retina	1.32	0.59
Choroid with tapetum	1.30	0.40
Choroid without tapetum	1.45	0.46
Ciliary body	1.36	0.44
Iris	1.30	0.44
Nictitating membrane	1.31	

*Results are expressed as a ratio of the value in the experimental eye compared to the control eye. Each number is the mean of the results from six sympathectomized animals and three animals having sympathetic stimulation.

orbital tissue, the nictitating membrane, was used to study whether there was preferential sympathetic tonus to the intraocular vessels. The good agreement between blood flow changes in both the nictitating membrane and intraocular tissues implies equal sensitivity to sympathetic tonus.

The decrease in blood flow to the ciliary body (45 per cent) caused by sympathetic stimulation was consistent with the values obtained by Langham and Rosenthal⁵ using the ascorbic acid clearance technique after sympathetic stimulation. In the iris and choroid we found that sympathetic stimulation decreased blood flow by approximately 45 per cent.

Recent work has suggested that alterations in uveal blood flow after cervical sympathetic stimulation occur passively in response to changes in ocular vascular perfusion pressure.⁸ Cervical sympathetic stimulation could increase systemic blood pressure, and this would increase blood flow to a given vascular bed. We measured the change in blood flow to paired vascular beds, in which one served as the control. Any systemic change would therefore effect both vascular beds equally.

The exact points in the arterial system where the sympathetic vasomotor tonus is exerted are not shown conclusively by this experiment. Evidence accumulated from both anatomic methods^{9, 10} and labeled catecholamine uptake studies¹¹ have demonstrated adrenergic innervation of iris, ciliary body, and choroidal blood vessels.

In the case of the retina, this vasomotor control has to be external to the cribriform plate, because there is no evidence of sympathetic innervation to the retinal vessels.⁹ We presently have studies underway to determine the site in the vascular bed where this sympathetic control is localized.

REFERENCES

1. Weiter, J. J., Schachar, R. A., and Ernest, J. T.: Control of ocular blood flow. I. Intraocular pressure, *INVEST. OPHTHALMOL.* **12**: 327, 1973.
2. Langham, M. E., and Taylor, C. B.: The influence of superior cervical ganglionectomy on intraocular dynamics, *J. Physiol.* **152**: 447, 1960.
3. Becker, B., and Linner, E.: Ascorbic acid as a test substance for measuring relative changes in the rate of plasma flow through the ciliary processes, *Acta Physiol. Scand.* **26**: 79, 1952.
4. Perkins, E. S.: *Int. Ophthalmol. Cong., Acta XVII, Montreal-N. Y.* **2**: 1157, 1954.
5. Langham, M. E., and Rosenthal, A. R.: Role of cervical sympathetic nerve in regulating intraocular pressure and circulation, *Am. J. Physiol.* **210**: 786, 1966.
6. Cole, O. F., and Rumble, R.: Responses of iris blood flow to stimulation of the cervical sympathetic in the rabbit, *Exp. Eye Res.* **10**: 183, 1970.
7. Alm, A.: Aspects of physiological and pharmacological regulation of blood flow through retina and uvea. Doctoral dissertation, Uppsala University, Uppsala, Sweden, 1972.
8. Best, M., Masket, S., and Ravinowitz, A. Z.: Effect of sympathetic stimulation on ocular hemodynamics, *INVEST. OPHTHALMOL.* **11**: 211, 1972.
9. Laties, A. M., and Jacobowitz, D.: A comparative study of the autonomic innervation of the eye in monkey, cat, and rabbit, *Anat. Rec.* **156**: 383, 1966.
10. Wolter, J.: Nerves of the normal human choroid, *Arch. Ophthalmol.* **64**: 120, 1960.
11. Kramer, S. G., and Potts, A. M.: Iris uptake of catecholamines in experimental Horner's syndrome, *Am. J. Ophthalmol.* **67**: 705, 1969.