Effect of cervical sympathetic stimulation on accommodation in guanethidine-treated monkeys

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The ciliary muscle of monkeys is unusual in that its adrenergic receptors seem to be exclusively of the β type. Stimulation of its sympathetic nerves decreases cholinergically induced accommodation. This effect is completely blocked by guanethidine.

Key words: guanethidine, accommodation, β-receptors, monkeys, sympathetic nerve stimulation.

Guanethidine is known to inhibit the responses to sympathetic nerve activity. This inhibition mainly results from a decreased release of transmitter substance. Since the ciliary muscle in monkeys has been shown to have only β-adrenergic receptors which inhibit the cholinergically elicited accommodation,[1, 2] it was interesting to examine the effect of guanethidine in this system. There seem to be no reports on the action of guanethidine in a pure β-adrenergic situation.

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This work was supported by United States Public Health Service Grant EY-00231, made to Dr. E. Bárány, and by a research grant from Magnus Bergvalls Stiftelse, Stockholm, Sweden.

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Manuscript submitted April 22, 1970; revised manuscript accepted Aug. 6, 1970.

Material and methods

Young cynomolgus monkeys (*Macaca irus*) of both sexes, weighing 2.4 to 3.0 kilograms, were used in the experiments. The method of studying refractive state and intraocular blood volume changes has been described in detail elsewhere.[2, 3]

Monkeys iridectomized on one eye were anesthetized with pentobarbital (30 mg. per kilogram of body weight) intraperitoneally, the cervical sympathetic nerve (preganglionic) on the side of the iridectomized eye was dissected free, and insulated silver electrodes were applied. A square-wave stimulator generated the stimuli which had a width of 1 msec. and were of supramaximal voltage (50 V.). The frequencies used were 1 to 5 stimuli per second. Stimulations were performed during periods of 1 to 1.5 min. The refractive state of the iridectomized eye was read with an optometer. During the critical phases of an experiment, about 15 refraction readings were taken per minute. To make these readings as exact as possible a negative corneal contact lens was used, which explains the hypermetropic readings given in Fig. 1. The influence of such a lens on changes in refraction is negligible. In all experiments the change in intraocular blood volume was recorded by cannulating the anterior chamber of the eye and connecting it to a perfusion fluid container, the weight of which was

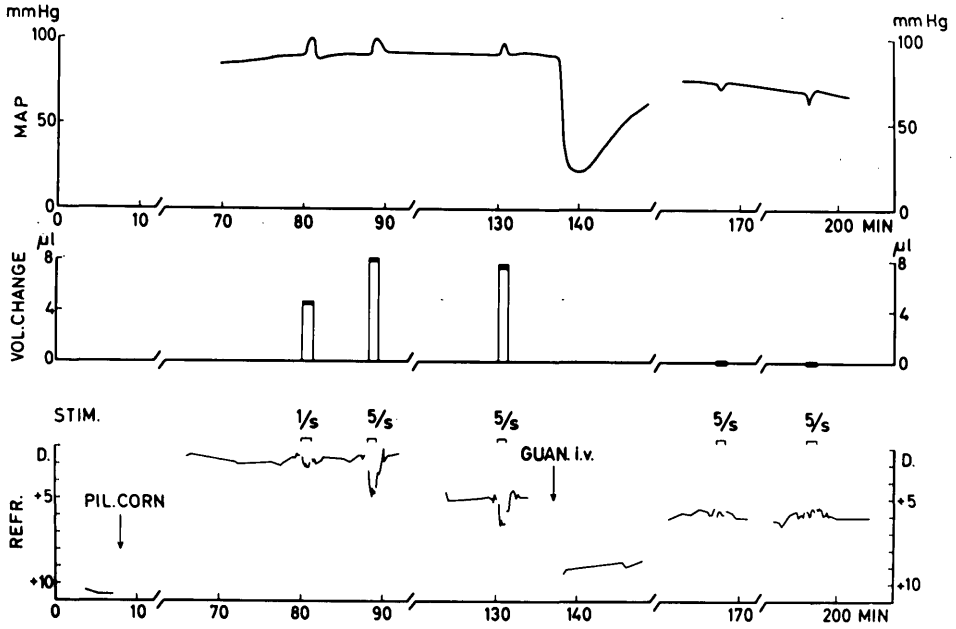

Fig. 1. Effect of cervical sympathetic stimulation on refractive state, intraocular blood volume (same eye), and mean arterial blood pressure before and after guanethidine (20 mg. per kilogram intravenously). The monkey's eye was made myopic by 1 mg. of pilocarpine applied to the cornea. A negative corneal contact lens was used during the experiment which explains the hypermetropic starting values.

constantly recorded.[4] Rapid volume changes as small as 0.5 µl could thus be recorded.

The blood pressure was taken in every monkey (femoral artery transducer recorder).

The results are given in time-response diagrams (Fig. 1). In these, two consecutive refraction readings, in diopters (D), were grouped together, and the averages were plotted and joined by straight lines.

Results

Four animals were used for the experiments; all showed the same principal result, which is best described by Fig. 1. The inhibitory effect of sympathetic nerve stimulation on accommodation is easy to show in unstimulated muscle. It is even easier to see the effect in the presence of some ciliary muscle tone[5]; this is the reason pilocarpine (1 mg.) was applied to the cornea. One stimulus per second to the cervical sympathetic nerve gave only a small decrease in accommodation (less than 0.5 D). But 5 stimuli per second, which can be considered an intense but physiological stimulation rate, always gave a distinct response (decrease in accommodation, 1 to 2 D) before guanethidine was given. Together with the decrease in accommodation there was also a clearcut change in blood volume at every stimulation period; this was especially so when the higher stimulation frequency was used. The volume decrease at stimulations with 5 per second was on an average 5.5 µl with a range of 3.0 to 8.0 µl. Other signs of sympathetic nerve activity such as piloerection and lid retraction were also observed during stimulation.

When guanethidine (20 mg. per kilogram intravenously as sulfate) was given there was an immediate decrease in mean arterial blood pressure to rather low values (25 to 45 mm. Hg). Together with this there was a decrease in the pilocarpine-induced accommodation. This dependence of accommodation on a sufficiently high blood pressure has earlier been described.[6] When, after 5 to 20 min., the

blood pressure had stabilized on levels above those being critical, the accommodation had also returned to preguanethidine values. It has been shown[2, 5] that as soon as there is some tone in the ciliary muscle (also after the blood pressure has been low) it is possible to elicit inhibition with sympathetic nerve stimulation.

After guanethidine had been given, at least two stimulations with 5 per second were performed. There was never any accommodation response on stimulation, nor was there any change in intraocular blood volume; this was true for all monkeys examined. Also, the signs of lid retraction and piloerection could not be seen after guanethidine.

Discussion

The recorded changes in eye blood volume during stimulations are of the order reported earlier. These changes are mediated by intraocular α-receptors[2, 7] and are totally blocked by guanethidine.

The present investigation shows that the neuron-blocking agent guanethidine completely inhibits the β-adrenergic effect of sympathetic nerve stimulation on accommodation. There seems to be only one earlier report in the literature of a similar condition, i.e., guanethidine blocking a nerve-stimulation effect on a pharmacologically classified β-receptor. Edvardsen[8] found the detrusor muscle of the urinary bladder of cats to have both α- and β-receptors which could be blocked by Dibenzyline and propranolol, respectively. Guanethidine was also found to block the effects of hypogastric nerve stimulation on these receptors.

In the detrusor of the cat, as in many other tissues, both α- and β-receptors are present together. The ciliary muscle of monkeys, on the other hand, is unique, not only because it is a smooth muscle which can be contracted voluntarily, but also because it is supplied with adrenergic receptors of the β-type only. These receptors can be excited via the cervical sympathetic nerves.[2] α-Adrenergic activity, which by means of blocking agents can be dissociated from β-activity,[2] has not been found to play any part in the accommodation mechanism. This means that vascular effects (via α-adrenergic vessels in the ciliary body) are of no importance for accommodation in monkeys.[2] Though the adrenergic innervation of the ciliary muscle may be rather unimportant for accommodation[5] it makes the accommodation of monkeys a very interesting test system.

Guanethidine has been found by several authors[9-12] to reduce the intraocular pressure in patients with simplex glaucoma. It has not been established if this effect is accomplished by an increase of facility[11] and/or a reduction of aqueous humor secretion.[10, 12] In some of these studies,[10-12] as well as in one describing the effect of guanethidine in patients with monocular diplopia,[13] it has been stated that guanethidine does not affect accommodation. From the present and former investigations,[2] one would have expected it to slightly increase the accommodation amplitude by inhibiting the sympathetic (accommodation-decreasing) tonus. The failure of the above-mentioned investigators to see any effect of guanethidine on human accommodation could depend on (1) different adrenergic innervation in man and monkeys, (2) investigation methods which are not accurate enough, or (3) small physiological importance of the sympathetics for accommodation also in human subjects. The last possibility, or a combination of the last two, seems the most probable explanation.

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