The relative importance of the parasympathetic and sympathetic nervous systems for accommodation in monkeys

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The refractive state of monkeys was followed during preganglionic oculomotor nerve stimulation and during preganglionic sympathetic nerve stimulation performed against a background of oculomotor stimulation. It was found that oculomotor stimulation rates of 2 to 5 per second gave accommodative responses of about 1 to 3 D, and 20 to 50 stimuli per second gave about 6 to 11 D of accommodation. Accommodation followed changes in oculomotor stimulation within 1 to 2 seconds. The effect of sympathetic stimulation performed against a parasympathetic background was small and developed and vanished much more slowly. If it is permissible to draw conclusions from nerve stimulation experiments, it seems that sympathetic nerve activity is of very small importance for desaccommodation. There is a proportion of individuals who would gain from a sympathetic distance accommodation, but because of the slowness of the effect its importance remains questionable.

That not only parasympathetic but also sympathetic nerves influence accommodation was first shown by Morat and Doyon in 1891. Their results could not be confirmed and authorities of those days denied any influence of the sympathetic nervous system on accommodation. However, after several later investigations, it is now generally accepted that sympathetic activity decreases accommodation. The size of the effect has been found to be different by different authors; this is probably dependent upon the species of animal used. The present investigation was performed in monkeys because they have a large accommodation amplitude and because their eyes have anatomical and physiological similarities to those of humans.

In a previous paper it was shown that decrease in accommodation on sympathetic stimulation developed rather slowly (maximal effect after 10 to 40 seconds). Even in strongly accommodating eyes, where the stimulation of the sympathetics had a larger effect, maximal stimulation gave rather small responses. In these experiments accommodation was induced by pilocarpine or eserine which was applied onto the cornea. To study the influence of the sympathetic nervous system on accommodation in monkeys in a more physiological manner the following experiments were performed where the cervical sympathetic nerves were stimulated against a background of oculomotor stimulation.
background of electrically induced parasympathetic activity. In this connection the effect of different stimulation frequencies of the oculomotor nerve on accommodation was also studied.

Materials and methods

Five young adult cynomolgus monkeys (Macaca irus) of both sexes were used in the experiments. The method of following the refractive state of the eye has been described elsewhere in detail. In essence the procedure was as follows: At least 1 to 2 months prior to the experiments double iridectomies had been performed on one eye to prevent miosis during oculomotor nerve stimulation. During the experiments the animals were anesthetized with pentobarbital, 30 mg. per kilogram bodyweight, given intraperitoneally. The cervical sympathetic nerve (preganglionic) on the side with the iridectomies was dissected free up to the superior cervical ganglion, and the thin connections to the vagus nerve were cut. Electrodes were not applied to the sympathetic nerve until the oculomotor nerve preparation was finished. To reach this latter nerve, access was gained through the temporal and parietal bones. The temporal brain lobe was elevated with a speculum and the oculomotor nerve cut immediately after its exit from the brain. To free a longer part of the nerve the dura was split for 1 to 2 mm. at the point of passage of the oculomotor nerve. The nerve was then placed on silver electrodes connected to a square wave stimulator (American Electrical Laboratories, model 104 A).

The monkey was now placed prone on a table and kept warm by infra-red lamps. The cervical sympathetic nerve (earlier dissected free) was cut and the peripheral (cranial) part was placed on silver electrodes connected to another square wave stimulator (H 44, C.F. Palmer Ltd.). The integrity of the sympathetic nerve was tested at the beginning and end of the experiments by checking the response of the pupil. Stimulations of both the oculomotor and the sympathetic nerves were performed with supramaximal voltage (50 v.) and with a pulse width of 1 msec. The frequency varied from 1.0 to 100 stimuli per sec. for oculomotor stimulation and from 1 to 20 for sympathetic stimulation. Stimulations of the cervical sympathetic nerves were performed during continuous oculomotor nerve stimulation, and often several periods of sympathetic stimulation were performed during one period of oculomotor stimulation. The refractive state of a horizontal meridian was followed on the eyes which had iridectomies with a Thorner optometer. This instrument gives the axial spectacle plane refraction in diopters (0.25 D increments). To save time the observed values as well as time for stimulations and other manipulations were read to a tape recorder during the experiments. Ten to sixteen readings were obtained per minute but it was quite possible to have one reading within a second after the beginning or the end of a stimulation period.

To increase the sensitivity of the refraction measurements and to prevent corneal drying during prolonged opening periods of the eye a corneal contact lens was often used. The same lens was used with all animals and the data of the

Fig. 1. Effect on refractive state of oculomotor nerve stimulation and of sympathetic nerve stimulation. The latter was performed against a background of oculomotor stimulation. Shorter periods of sympathetic stimulation (5/sec.) were performed during longer periods of oculomotor stimulations (10, 5, and 20/sec.). A corneal contact lens was used during the experiment.
lens were: power −5.0 D, inner radius of curvature 6.0 mm, and axial thickness 0.12 mm. Of course the principal results were the same whether the measurements were performed with or without a contact lens. It can be calculated that a constant refractive change inside the eye gives a slightly smaller response, measured as change in spectacle plane refraction, if the contact lens is present. This could be verified in 13 monkeys where the accommodation response to topically given drugs was measured both with and without the lens at the same experimental occasion. The mean accommodation was 10.7 D with the contact lens and 11.3 D without it.

The reliability of the method has earlier been shown to be good. In the present experiments the standard deviation of single readings caused by error of the methods was calculated with successive differences between single readings before stimulation began, pooled with similar successive differences obtained more than one minute after stimulation (both sympathetic and parasympathetic) had ended. This standard deviation was 0.15 D (320 readings) when the contact lens was used. The small scatter of observations is also obvious from Fig. 1.

By means of a polyethylene tubing introduced into the femoral artery and with a pressure transducer, the blood pressure was monitored in all experiments.

Before the beginning of the experiments eye movements as the result of oculomotor stimulation were expected to cause trouble. This was not the case. Certainly eye movements occurred. At low stimulation frequencies small oscillating adduction movements were seen, and at higher frequencies (10 per second and more) steady adduction occurred but was easily compensated for by moving the optometer and realigning it with the optical axis of the eye.

Results

The blood pressure recordings were made because ciliary muscle contraction has been shown to be very sensitive to blood supply. In the present investigation no important blood pressure changes occurred during the stimulation experiments.

To study the effect of the various oculomotor stimulation frequencies on accommodation, all animals were examined without the contact lens. The results are given in Table I. One to two stimuli per second gave only small responses whereas 50 per second gave very large effects. Increasing the stimulation frequency to 100 per second caused no further increase of accommodation. The accommodation response was fully developed already in 1 to 2 seconds (Fig. 1). Thereafter accommodation sometimes decreased for 10 to 30 seconds until a steady state was reached. The decrease in accommodation during continuous oculomotor nerve stimulation was more obvious for the high stimulation frequencies, where sometimes a decrease of 1 or 2 D was seen (Fig. 1). At the cessation of oculomotor stimulation accommodation ended completely in 1 to 2 seconds.

The results of Table I permitted us to choose a suitable oculomotor stimulation frequency for a background for the sympathetic nerve stimulations. Five, 10, and 20 stimuli per second seemed to give "physiological" accommodative responses and these were the parasympathetic stimulation rates most often used.

To evaluate the effect of the sympathetic innervation against that of the parasympathetic, the cervical sympathetic nerve was stimulated, most often with 5 stimuli per

Table I. Effect of different oculomotor stimulation rates on accommodation

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<th>Monkey No.</th>
<th>Dioptic effect of different stimulation frequencies</th>
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<td>1</td>
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The accommodation values were calculated as the difference between the mean of all readings within 30 seconds before and the mean of all readings within 30 seconds after stimulation started. All values without contact lens.

*Mean of three stimulations.
†Mean of two stimulations.
second (maximal or almost maximal frequency) during continuous oculomotor nerve stimulation (steady state). The effect was the same in all animals in that 5 to 10 seconds after the start of sympathetic stimulation, accommodation began to decrease and this decrease became maximal in 10 to 40 seconds, and Fig. 1 illustrates a typical experiment. The largest decreases were seen when high parasympathetic background stimulation was used, but the decreases in accommodation were never greater than 1.5 D (measured with contact lens), not even when large sympathetic stimulation frequencies (20 per second, 4 experiments) were used. After the end of sympathetic stimulation 5 to 20 seconds elapsed until the effect had ended completely.

Discussion

According to Folkow the upper limit for the "physiological" discharge rate in vasoconstrictor nerves is 6 to 8 stimuli per second, and 10 to 15 stimuli per second seem to give maximal responses. Slightly higher frequencies for maximal effect (15 to 20 per second) have been found for pilomotors, nictitating membrane, and uterus. In a previous study of the effect of sympathetic stimulation on accommodation, maximal effects were found with 5 to 10 stimuli per second. Thus 5 per second was chosen as a high physiological sympathetic stimulation frequency in the present investigation. Four experiments with 20 stimuli per second showed no definite increase in effects.

The physiological discharge rate in the parasympathetic system seems generally to be somewhat higher than in the sympathetic. Maximal effects on salivary glands and stomach have been found at 25 to 35 stimuli per second and for iris contraction in the cat at 25 per second. In a paper on accommodation in the cat Ripps and associates found 14 stimuli per second to give maximal response. In the present investigation maximal effects were reached with the increase from 20 to 50 stimuli per second and thus the results grossly agree with those previously mentioned.

From unsophisticated observations of their behavior (eating, grooming, etc.) one would expect monkeys of this species to need an accommodative amplitude of 5 to 10 D. As the monkeys used here were all emmetropic, stimulation frequencies at least up to 20 per second (Table I) seem to be "physiological."

In the present investigation accommodation of 10 to 12 D but not more could be maintained for short periods. Previously, young monkeys with pharmacological stimulation have been able to accommodate 15 to 20 D and more for very long periods. This would indicate that the pharmacologically induced accommodation can be increased beyond the physiological maximum, as shown for man by Fincham. Unfortunately the maximal accommodation amplitude after drugs was not tested in the monkeys used in the present experiments.

Though nowadays there is general agreement that the sympathetic system influences accommodation, the mechanism of this influence is not agreed upon. It has been suggested that the sympathetic nerves affect accommodation by a vascular mechanism, changing the ciliary body volume. However, the evidence for this is only indirect: vasoconstriction and hyperopic changes in refraction were found to occur at the same time. In the present and in a former investigation on monkeys there is one finding which speaks in favor of a vascular mechanism, and this is the comparatively slow development of the decrease in accommodation on stimulation. However, there is much evidence against a vascular mechanism. With the use of adrenergic receptor antagonists it was possible to block eye volume changes without affecting the accommodation decrease on sympathetic stimulation (α-blockers) or to block accommodation decrease but not eye volume changes (β-blockers). (Stimulation of β-adrenergic receptors of many smooth muscles is known to inhibit activity, whereas α-activity as a rule is excitatory.)
The main reason for performing the experiments reported here was to evaluate the importance of the sympathetic innervation of the ciliary body for accommodation. There are two facts which should be stressed. One is the small effect of sympathetic stimulation in monkeys. In lower animals effects have been larger, which possibly is due to the (excitatory) α-adrenergic innervation of the ciliary muscle in these animals.

The other fact, which even more strongly speaks against any important influence of the sympathetic system on accommodation is the very slow development of the sympathetic response. It is hard to believe that a refractive change which needs about 10 seconds or more to develop or end has any physiological significance. On the other hand the response to parasympathetic stimulation is fully developed within 1 or 2 seconds in the monkey. This is in good agreement with the results of Campbell and Westheimer who in humans found the time necessary to obtain a reasonably stable level of accommodation to be about 1 second from the onset of stimulus (reaction time 0.37 second). It was also found in the present experiments that after cessation of the third nerve stimulation the accommodation ended with the same velocity: in 1 to 2 seconds the refractive state was at pre-stimulation values.

Considering the small effect and its slow onset and disappearance, it thus seems probable that the importance of the sympathetic system for desaccommodation (relaxation of accommodation) is very minor at least in the species of monkey studied. Desaccommodation was accomplished effectively and rapidly by cessation of oculomotor stimulation without the aid of sympathetic stimulation.

The importance of the sympathetic system for distance accommodation (here defined as accommodation from resting position to distance) is more difficult to evaluate. Also in nonaccommodating monkeys the effect of sympathetic stimulation develops slowly. In 9 animals, given no other drug than pentobarbital, 5 stimuli per second gave an average hyperopic change of 0.6 D, which was fully developed in 14 seconds (range 5 to 30 seconds). After atropine, 1.0 mg. per kilogram intravenously, no response to sympathetic stimulation occurred. Applying the experimental results to physiological conditions, this means that if it is possible for an individual to stop all parasympathetic nerve activity, sympathetic activity would have no hyperopic effect, possibly because the β-adrenergic inhibitory mechanism has nothing to inhibit.

On the other hand, if it is impossible to stop all parasympathetic activity, there still is a small margin for the sympathetic system to act. A sympathetic mechanism helping distance accommodation would have importance only if it could act from a state of slight myopia. The refraction of *Rhesus macaques* has been studied by Young. After topical cyclopentolate administration he found the median refractive error for 299 wild monkeys to be +0.79 D, and the mean was +0.63 D with a σ = 0.72 D. Since probably there always is some parasympathetic activity during the physiological resting condition, quite a considerable part of the macaque population is in a position to derive some benefit from sympathetic distance accommodation. For those monkeys which were hyperopic also at accommodative rest, and for those myopic by more than 1 to 1.5 D, the sympathetic system seems to have no practical effect in distance accommodation. But, as stated above, the sympathetic effect develops very slowly and this makes its physiological importance questionable for all individuals.

REFERENCES

Oculomotor stimulation and accommodation