

**ACCOMMODATIVE RESPONSE OF THE CATS EYE
TO ELECTRICAL STIMULATION OF THE CILIARY GANGLION**

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FOREWORD

This report was prepared in the Aero Medical Laboratory, Directorate of Research, Wright Air Development Center, under a Vision Section project, RDO No. 696-67, "Aircraft Visual Requirements," with Lt Colonel Elwin Marg, USAF serving as project engineer. This work was completed in December 1952.

The animal experimentation as reported herein was carried out under the provisions of the American Medical Association governing these procedures.

ABSTRACT

The purpose of this study was to obtain background information on the neural innervation of accommodation of the eye. This was obtained by electrically stimulating the ciliary ganglion in cats with biphasic pulses of varying voltage and frequency from a Grass stimulator, and measuring the refractive state of the eye with an eye refractometer (Rodenstock). Varying the electromotive force (EMF) of the stimulus produces a graded response, presumably by the number of fibers made active (spatial summation). Varying the frequency of the stimulus (temporal summation) produced a threshold response at about 4 cycles per second and a linearly graded response from 20 to 35 cycles, depending upon the EMF, after which it remained constant. The slope of the linear frequency response (frequency sensitivity) increases with the EMF. Within a certain central range of frequency and EMF, either of the parameters may be substituted for the other to provide a given level of accommodative response. A fifteen year old cat also was studied and the accommodative response to electrical stimulation of the ciliary ganglion was measured and graphed. The accommodative amplitude of the aged cat was found to be lower than the mean amplitude of a group of young cats, but not significantly so. The cat was estimated to have an age equivalent to a man of 75-90 years. Since man shows little or no accommodative amplitude (absolute presbyopia) at this age, it is apparent that no similar phenomenon occurred in the aged cat.

Evidence is offered to support the Hess theory of a physiological reserve of accommodative amplitude.

The significance of the findings in relation to the ratio between accommodative convergence and accommodation (AC/A) is discussed.

PUBLICATION REVIEW

This report has been reviewed and is approved.

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SECTION I

ACCOMMODATIVE RESPONSE OF THE EYE TO ELECTRICAL STIMULATION OF THE CILIARY GANGLION IN CATS

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INTRODUCTION

The peripheral parasympathetic pathway for the control of accommodation is well known. The preganglionic fibers appear to originate in the Edinger-Westphal nucleus of the IIIrd nerve center. These fibers help form the oculomotor trunk and go to the ciliary ganglion in the orbit. After a cell station, the medullated postganglionic fibers emerge from the ganglion in numerous short ciliary nerves which pierce the sclera in a ring around the optic nerve. Losing their medullary sheath, the fibers course through the sclera to the ciliary plexus, thence to the ciliary muscle.

The smooth ciliary muscle contracts in sphincter-fashion and, through the zonule fibers releases the tension on the capsule of the crystalline lens. In response to the contraction of the capsule, the lens takes on a higher curvature, thus increasing the refractive power of the eye.

Up to the present time studies of the nervous pathways controlling accommodation, reviewed by Morgan (Ref. 1), have been concerned not with the mechanism of accommodative gradation but with the pathways for parasympathetic and sympathetic control of accommodation and their relative roles. These findings indicate that in general only the parasympathetic should be considered of practical significance since the sympathetic, through the long ciliary nerves to the eye, controls only about 1/10 of the total dioptric range, and this in a negative direction.

The general purpose of this study is to investigate the peripheral parasympathetic mechanism for the graded control of accommodation. Specifically, this paper is concerned with the accommodative response of the cat's eye to electrical stimulation of the ciliary ganglion. This is, perhaps, a first step in the study of the neural mechanism controlling accommodation.

How is accommodation controlled by parasympathetic impulses? It is generally believed that the gradation of maintained motor function depends on two characteristics of nerve propagation:

1. The number (and perhaps distribution) of fibers active in the nerve bundle.
2. The frequency of discharge of these active fibers.

These characteristics of motor gradation have been studied in voluntary motor systems (Ref. 2) and in autonomic effectors (Ref. 3) such as the sympathetically controlled nictitating membrane of the cat and the parasympathetic vagus control of the heart. In so far as we have been able to determine, no one has investigated these control characteristics in the parasympathetic accommodation of the eye.

APPARATUS AND PROCEDURE

A Grass Stimulator (Model 3C) provided the electrical stimulus. This oscillator generates monophasic or biphasic wave forms with variable voltage, frequency and pulse duration. The stimulus was applied to the ciliary ganglion by two polyethylene-insulated solid silver wires (No. 24) held together by a larger polyethylene tube. The electrodes were bared at the tip for about 2 mm and separated by about 1 mm. The electrodes were either hooked around the ciliary ganglion or placed astride it. Generally, biphasic pulses were used. (Two stimulus pulses, one positive and one negative, were presented in each cycle. These were spaced only one msec. apart and therefore were considered to be a single stimulus pulse. The biphasic wave forms were used to minimize polarization.) These were obtained by differentiation of rectangular waves so that zero potential was reached just at the end of each rectangle. The pulse duration of the rectangular waves from which the biphasic pulses were derived was fixed at one msec. Exploratory data with pulse duration as a variable indicated that 1 msec gave an optimum response. Calibration of the stimulator with a cathode-ray oscilloscope against standard laboratory oscillators and the 60 cycle power mains indicated that the stimulator scale readings were 20% high for peak voltage (without a load), 5% high for frequency and 18% high for the pulse duration used. These errors are not considered serious and are not corrected in the following data and graphs.

The ciliary ganglion was exposed following the procedure of Shen and Cannon (Ref. 4). Nembutal was generally used, but in some instances decerebration provided the anesthesia. A portion of the zygomatic process and orbital wall was cut away and the inferior oblique muscle exposed. The nerve innervating this muscle was followed back to the ciliary ganglion which was found between the lateral rectus and the optic nerve. After the electrode was fixed on the ganglion, the wound was closed with metal Michel suture clips which also held the electrode in place. In order to avoid eye movements upon stimulation, two or more of the extraocular muscles usually were severed.

Circulation to the eye usually was not seriously disturbed. Only a few of the anterior ciliary arteries and veins which accompany the recti muscles were severed. Generally only two muscles were cut so that even these vessels were not all disrupted. The ciliary body was still served by its usual primary supply, the long posterior ciliary arteries and the venous return through the vortex veins.

A Rodenstock Eye Refractometer provided an objective measure of the state of refraction of the eye. The spectacle plane refraction in diopters was read directly from the instrument dial after the target on the fundus was optically focused. A few drops of 1-1/2% sodium bicarbonate solution were dropped on the cornea after each three measurements. This maintained its good optical quality and prevented it from drying.

Young, fully grown cats were partially iridectomized from several weeks to several months before they were used for measurements. This surgery was necessary since stimulation of the ciliary ganglion would close the normal slit pupil, making optical measurement impossible. It was convenient to have a piece of intact iris which by a slight contraction following stimulation provided a check on adequate placement of the electrode on the ciliary ganglion. There was no need to employ an artificial pupil as would be necessary in a skiascopic determination of the refractive state since the entrance pupil of the eye-refractometer was smaller than the exit pupil of the eye. Thus no difficulty was experienced because of the increase of optical aberrations arising from the large pupil of the partially iridectomized eye.

The stimulus was applied for about two seconds, just long enough to obtain a measurement of the refraction. This was read and recorded, again taking about two seconds during which time no stimulation was applied to the ciliary ganglion. Each stimulus value was used three times and the corresponding refractions averaged. Stimulus values were applied in ascending order.

RESULTS

Figure 1 shows the relation between the stimulus electromotive force (EMF) in volts applied to the electrodes at the ciliary ganglion and the refractive state of the eye as measured at the spectacle plane in diopters. A graded response of accommodation as seen in Curve A is produced by varying the voltage of the stimulus. Grading is probably effected by the increasing number of neural elements brought into action by the increasing voltage. (We have no way of determining in this experiment the effect of EMF, nor of frequency on the individual structures responding to the stimulus or in turn on the individual nerve fibers and motor units. Such data could be obtained by microelectrode recording techniques and is left for future research. As a first assumption the following two points seem reasonable: (1) The frequency threshold of the individual structures responding to the stimulus is generally of the same order; and gradation is effected by the frequency response of the individual effectors pari passu with that of the stimulus; (2) The EMF threshold varies over the full range of voltage sensitivity and the number of structures activated provides gradation. This is necessary to remain within the framework of the all-or-none law. However, no such limitation is required for the frequency mechanism where it is reasonable that the individual structures responding to the stimulus will follow the stimulus pulses up to their maximum response frequency which is certainly not reached in this experiment.) Curve B, shows substantially the same result for another eye. It is worth noting that the accommodative amplitude appears to be about 2 diopters (D.). One interesting difference in Figure 1 is the apparent initial dip in Curve B before the rise. Although the dip in this curve is based on only one point, it may be significant as it occurred frequently in similar curves for a large number of cats. However, it must, for the time being, be considered an artifact since there appears to be no likely explanation in terms of present accepted knowledge of the physiology of the eye. (For example, one could hypothesize that there are some sympathetic fibers in the cat's ciliary ganglion from the third nerve which have a lower electrical threshold than the parasympathetic fibers and are therefore stimulated first. However this hypothesis would be pure speculation.)

Not infrequently the gradation portion of the EMF response curve tended to be linear as seen in Figure 1, Curve A, but generally this function was curved.

Figure 2 illustrates the effect on accommodation of varying the frequency of the stimulus to the ciliary ganglion. The open circles represent the data from one eye of one cat and the closed circles from one eye of another cat. The ordinates were adjusted to provide superposition of the curves as may be seen from the two scales, one on the left and the other on the right. The stimulus frequency threshold appears to be at about 4 cycles per second and from other curves not shown here it may vary between 2 and 6 cycles. After the threshold, there appears to be a linear relationship between frequency of stimulation and accommodation in diopters. At about 21 cycles (with a 5 volt stimulus) accommodation appears to reach its maximum and increasing the frequency does not appear to have further effect. The effect of frequency on accommodation can be expressed as the slope of the active linear portion of the curve which, in these instances at 5 volts is 0.10 diopter per cycle. It may be noted that the amplitude of accommodation for both curves in Figure 2 is the same as for both curves in Figure 1, about 2 D. Each of these four curves was obtained from different eyes.

In order to determine the importance of the anesthesia used in the present experiment, the curve in Figure 2 corresponding to the ordinate scale on the left (closed circles) was taken after the animal had been decerebrated under ether anesthesia. The other curve (open circles) was taken under nembutal anesthesia. It does not appear that nembutal anesthesia interferes with the experiment and was therefore used generally. The 2.50 D. difference in the ordinates is due to the basic refractive state of these two eyes, not to the anesthesia.

The interrelationship of frequency and EMF on the refractive state of the eye is demonstrated in Figure 3 by a family of frequency curves taken at different voltages. The lower three curves (1, 1-1/2, and 2 volts), are measured from one eye and the upper three curves (3, 5, and 10 volts) are measured from the other eye of the same cat. Each curve has been arbitrarily raised 0.50 D. more on the ordinate than the curve directly below it, with the exception of the 3 volt curve where the step is 1.00 D. In other words, the 1 volt curve is as measured; the 1-1/2 volt curve is shifted 0.50 D. upward on the ordinate; the 2 volt curve, 1.00 D.; the 3 volt curves, 2.00 D.; the 5 volt curve 2.50 D.; and finally the 10 volt curve 3.00 D. This separation was made for clarity of presentation by avoiding interlacing of the distribution.

It seems clear that the frequency threshold, independent of voltage, is 4 cycles per second. It also appears that the sensitivity of the frequency gradation mechanism increases with increasing voltage. This is seen in the slopes of the linear central portion of the curves. As the EMF increases through 1, 1-1/2, 3, 5, and 10 volts, the frequency sensitivity increases

through 0.02, 0.04, 0.06, 0.08, 0.10, and 0.12 diopters per cycle respectively. The maximum accommodative response, regardless of frequency, appears to be 2 D. However, this maximum, as already suggested by Figure 1 is not reached until the EMF is raised to between 3 and 5 volts. Within a certain central range of frequency and voltage, these two parameters may be substituted for each other to provide a given level of accommodative response.

DISCUSSION

Bozler (Ref. 5), in his classification of muscle, calls smooth muscle "multiunit" when it is motor nerve controlled and has many units (not syncytial) and hence acts somewhat like skeletal muscle. The nictitating membrane and blood vessel musculature are included in this class. Allen (Ref. 6), has provided further evidence, based on the latent period of, and temporal summation in the ciliary muscle of an enucleated eye, which puts the ciliary muscle in this group. Further, as Allen points out, the ability to grade accommodation is additional evidence that accommodation is effected by multiunit smooth muscle. The fine mechanism of accommodative gradation has been quantitatively investigated in the present paper.

The gradation of function of an effector, as already mentioned, is controlled by changing either the number of active units or their frequency of discharge. Lindsley (Ref. 2), in an investigation of the electrical activity of human motor units during voluntary contraction, found that changes in both the number and frequency of units operate together throughout the range of contraction intensities. He concluded that change in frequency is probably the more delicate grading mechanism and change in number the more effective. The lowest regular frequency of response that he found in striated muscle was 3 cycles per second, and the highest 50 cycles per second.

The results illustrated in Figure 3, showing a stimulus frequency gradation sensitivity from 4 to at least 37 (35 corrected) cycles per second make it appear that smooth ciliary muscle has a frequency innervational pattern similar to that of striated muscle. (However, it should be noted that skeletal muscle will respond to frequencies of less than 4 cycles per second although the response may not be tetanic.) It seems, further, that either the number of fibers, or the frequency of discharge can control the state of accommodation anywhere within its full amplitude provided a certain minimum frequency (about 20 cycles per second) or a certain minimum number of units (corresponding to about 3 volts) is maintained.

Unfortunately, there is no simple way to determine the quantitative relationship between the EMF and the relative number of active fibers in the pathway between the ciliary ganglion and the ciliary muscle. However, it is clear that with a constant EMF (i.e. with a given number of units active) the state of accommodation in diopters is directly proportional to the frequency of stimulation. One might use the term "neurodiopter" to express that unit of neural innervation which changes accommodation 1 diopter, a term similar to the myod diopter of Flieringa and van der Hoeve (Ref. 7). Assuming that the frequency of stimulation may be considered the degree of neural innervation,

Figure 3 shows that the neurodiopter is a linear unit when frequency is the gradation mechanism in cycles per second (the reciprocal of the sensitivity) and becomes a smaller unit as the EMF (i.e. number of active fibers) increases and Figure 3 shows a decrease of neurodiopters from 52 cycles to 8 cycles. In other words, the sensitivity of the frequency mechanism (the reciprocal of the neurodioptric value) is a function of the stimulus EMF (or the number of active fibers). Contrariwise, it appears that the sensitivity of gradation regulated by varying the number of active fibers is a function of the frequency.

Are the frequency and number mechanisms independent of each other? This appears to be true at the low frequency threshold where the value is 4 cycles regardless of the EMF. However, there is a significant deviation from independence at the high frequencies where the maximum frequency which increases the response appears to decrease as the number of fibers increases.

Figure 4 is a redrawing of the curves of Figure 3 with the base line of each curve put at the same level on the ordinate. The solid lines show the actual curves, which at the 3, 5, and 10 volt level appear to be prevented from reaching their full height, i.e., amplitude of accommodation. The broken lines in Figure 4 are obtained by extrapolation based on the distance between the curves and the shift of the inflection point of each curve. They indicate as Hess and others (Ref. 8,9,10) believe, that the neuromuscular phase of accommodation (physiological accommodation) is greater than that limited by the suppleness of the crystalline lens (physical accommodation). In Figure 4, the physical accommodation is 2 D., and the physiological accommodation is presumably about 3 D. This could also be checked by using homatropine as a partial cycloplegic as did Flieringa and van der Hoeve but using the length of the slope as an indication of the full elicitation of the frequency mechanism. In other words, the lower voltage curves appear to show the full function or amplitude of the frequency mechanism. If this full frequency amplitude could be shown with the higher voltages with homatropinization of the eye further justification would be provided for the extrapolation of the curves in Figure 4.

As mentioned earlier, there has been considerable study of the frequency response of autonomic effectors. A summary of these investigations has been published by Rosenblueth (Ref. 3). Generally, autonomic frequency-response curves measured in degrees by the angle of movement of pilomotor action in a cat's tail or the isometric or isotonic contraction of the nictitating membrane of a cat's eye are rectangular hyperbolas. The frequency gradation mechanism of accommodation, however, becomes linear when measured in diopters after being transformed into the sphincter-like action of the ciliary muscle and then into dioptric power by changes in the physical configuration of the crystalline lens. (This function is hyperbolic when accommodation is measured in linear units, i.e. meters.) This is indeed a wonder. It brings to mind another interesting linearity, the relationship between accommodative-convergence expressed in angular measure such as degrees or centrad and accommodation expressed in diopters (Ref. 11, 12). This relationship is abbreviated

AC/A. If, as has been demonstrated here, the relationship between the frequency of accommodative stimulus and accommodation is linear, and if the AC/A is linear, then it can be concluded that the relationship between convergence and the frequency of convergence innervation is linear. This could be confirmed directly by a similar experiment stimulating the extraocular muscles.

The fact that the peripheral mechanism of accommodation appears to have a linear gradation system would seem to imply that the whole AC/A neuromuscular innervational chain is composed of linear links. For if one link in an innervational chain is linear and the system as a whole is linear, then it seems likely that each separate section of the system is also linear.

Figure 1. Stimulus-response curves varying the stimulus EMF. Curve A - One eye. Curve B - Contralateral eye of the same cat. Frequently this type of curve plateaus at 3 volts rather than at 5 volts as illustrated.

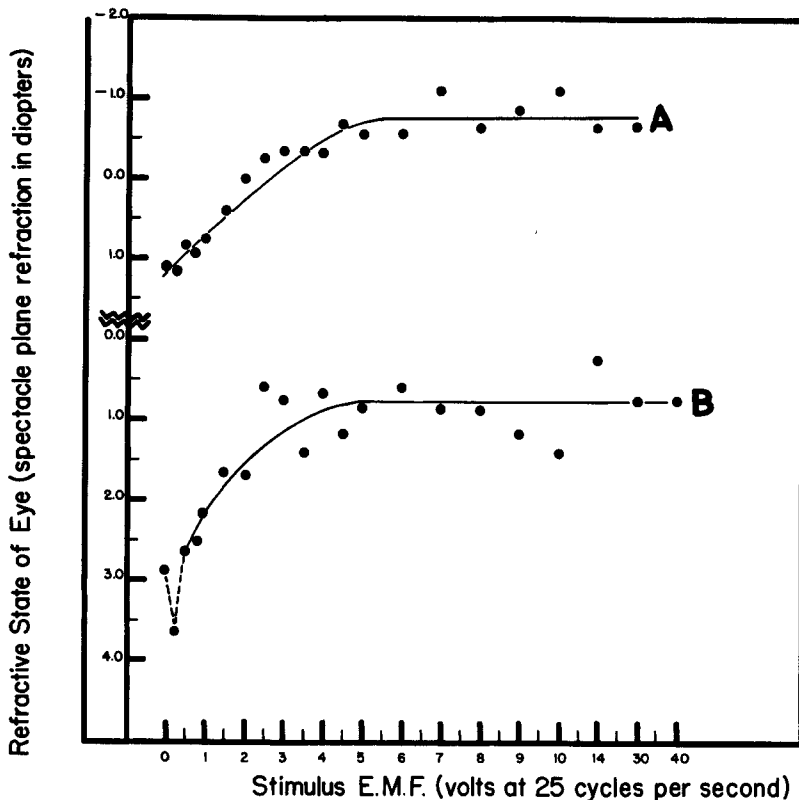
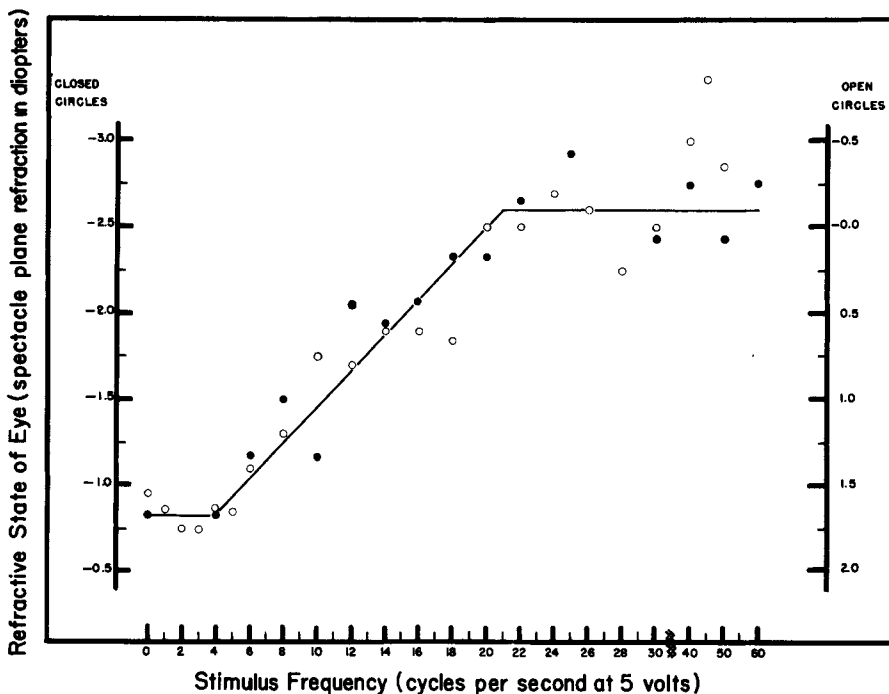


Figure 2. Stimulus-response curves varying the stimulus frequency. Open circles and scale on the right represent cat under nembutal; closed circles and scale on the left with decerebration.



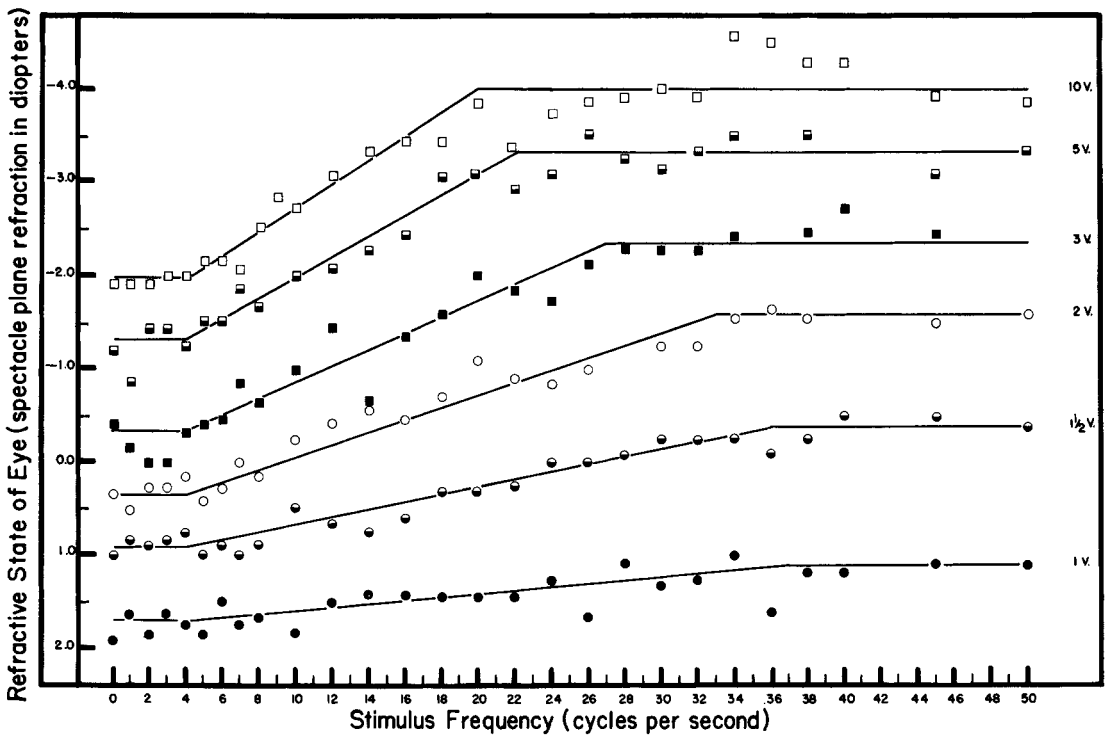


Figure 3. Family of frequency stimulus-response curves taken at different voltages as noted by numbers at the extreme right. Each curve has been arbitrarily raised 0.50 D. on the ordinate above the curve below it, except for the 3 volt curve which has been raised 1.00 D. The shifts were made for clarity of presentation. For fuller explanation, see text.

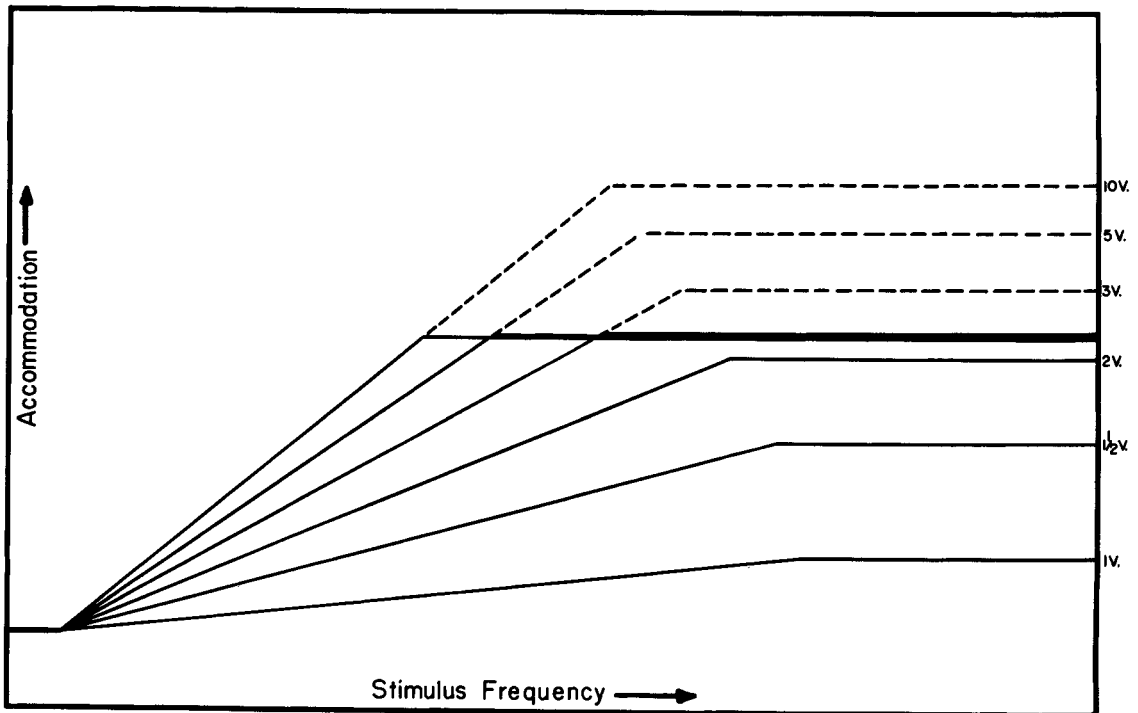


Figure 4. Solid lines are the curves from the previous figure with all base lines set together on the ordinate. Broken lines are extrapolations. For interpretation, see text.

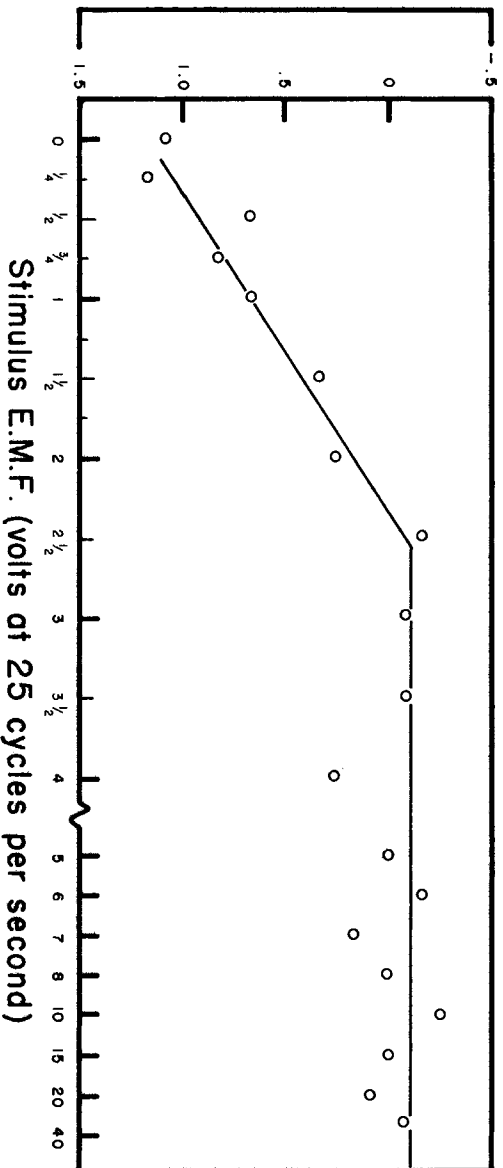


Figure 5. Stimulus-response curve varying the stimulus EMF (aged cat)

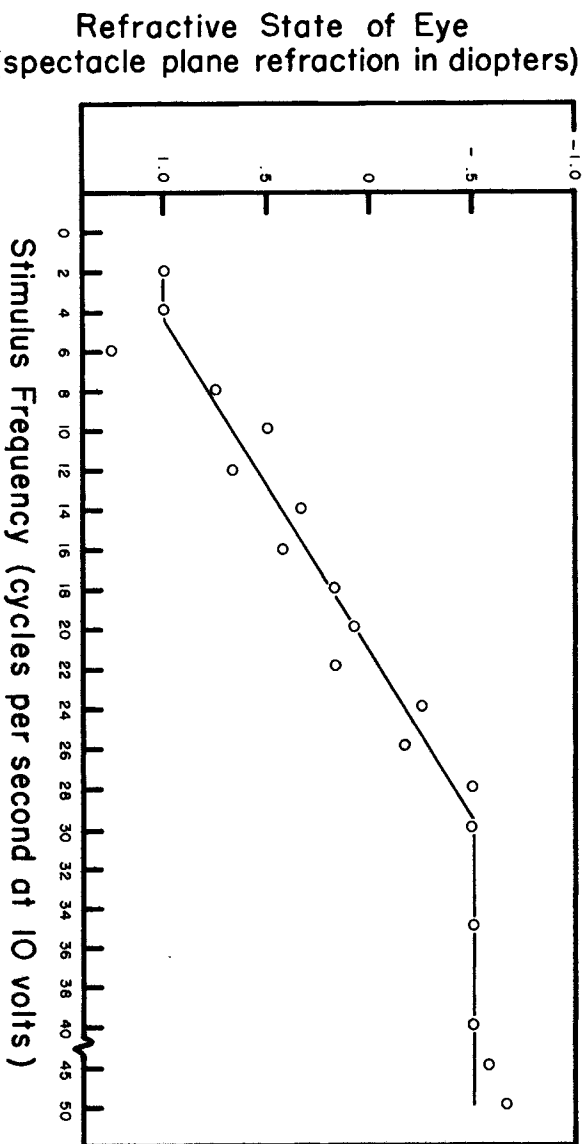


Figure 6. Stimulus-response curve varying the stimulus frequency (aged cat)

SECTION II

ACCOMMODATIVE RESPONSE OF THE EYE OF AN AGED CAT TO ELECTRICAL STIMULATION OF THE CILIARY GANGLION

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INTRODUCTION

It is well known that man's power of accommodation is progressively and continuously reduced throughout most of his life. He is born with almost 18 diopters (D.) of potential accommodative amplitude. At 10 years of age the amplitude is about 15 D.; and it is generally believed that it reaches a minimum of 1 D. or less at about 60 years.

What is known about accommodative amplitude and age in animals other than man? Although the ability to accommodate is well established in various mammals from stimulation experiments, there is no experimental evidence available as yet to show that mammals other than the primates actually accommodate in the course of their normal activity. Although reference to presbyopic animals, indicating a reduction of accommodation with age, may be found in the literature, it appears to be based on anthropomorphism rather than experimentation. We have been able to find no evidence that animals other than man exhibit a reduction of accommodation with age.

We were fortunate in obtaining for experimental use a cat unquestionably known to be 15 years old. This animal was used in an experiment similar to those of the previous study on a group of young cats (Section I). The question was, does the accommodative amplitude in the aged cat differ significantly from that in young cats? If the aged cat's amplitude is significantly lower, then perhaps the process which reduces accommodative amplitude is similar to that in man. If the amplitude is not significantly reduced, it might be of interest to future investigators of presbyopia in man to determine why cats do not suffer a similar affliction.

PROCEDURE

The subject was a 15 year old neutered domestic short-haired cat which had been in excellent health except for several infected teeth extracted some months previously. The eyes were partially iridectomized; and the experimentation was done after the animal had completely recovered from this surgery. Under nembutal anesthesia the ciliary ganglion was exposed. The inferior rectus and inferior oblique were severed to prevent eye movement upon stimulation. The silver bipolar electrode was placed across the ganglion and the wound was clamped shut. Stimulation was provided by a Grass Stimulator set at 1 msec pulse duration with biphasic waves. This is essentially a differentiated rectangular wave with the discharge timed so that the zero potential is reached at the time the negative phase or latter half of the cycle begins. The pulse duration is the duration of an original square wave.

RESULTS

Figure 5 shows the relation between stimulus voltage at 25 cycles per second and the refractive state of the eye in diopters referred to the spectacle plane. It appears to be essentially linear over its gradation length of 2-1/2 volts and then levels off. The accommodative amplitude is about 1.3 D.

Figure 6 shows the results of varying stimulus frequency at 10 volts. With the exception of one stray point at 6 cycles, the relationship is essentially linear over its gradation range from 4 to 30 cycles. The amplitude of accommodation is 1.5 D.

DISCUSSION

The stimulus voltage curve (Fig. 5) of the aged cat has no obvious characteristics that distinguish it from similar curves of younger cats. Although the maximum gradation voltage of 2-1/2 is low compared to that of 5 volts for the young cats (Fig. 1), the value appears to be within the range of normal variation, since some young cats also showed higher voltage sensitivity. Furthermore, the voltage sensitivity may be dependent, in part, on the placement of electrodes and the short-circuiting effect of surrounding tissue and fluids, so that it cannot be depended upon as a reliable absolute measure between two different preparations. The accommodative amplitude is low compared with the approximate 2 D. values from young cats seen in figures 1 and 3. Hence there may be a reduced amplitude of accommodation in the aged cat indicated by this curve. This topic will be discussed in detail later.

The stimulus frequency curve (Fig. 6) of the old cat has no obvious characteristics that distinguish it from similar curves of younger cats. The lower frequency threshold at 4 cycles per second does not appear to differ in the two sets of data; and the upper frequency threshold, considering the possible unreliability of comparing absolute voltages from one preparation to another seems to be within normal limits for young cats. The amplitude of accommodation is 1.5 D., which is low when compared to that shown in the curves for young cats in figures 1 and 3.

The only important feature of the data from the old cat compared to that of young cats appears to be a reduction in the amplitude of accommodation. The next and obvious question is how significant is this apparent reduction? In other words, is it likely that the difference in accommodation in the two experiments is due to experimental variation rather than being a real, significant difference?

Significance of the Apparently Reduced Amplitude

The original raw data from young cats were studied with a view to determining the limits of the amplitude of accommodation. Where different curves obtained from the same eye did not agree as to amplitude, the highest value was chosen on the assumption that it was probably closer to the real amplitude. This seems reasonable since poor electrode placement, injury from the surgery or the stimulation, or fatigue, may cause a decrease in the apparent amplitude. Seventeen sets of data showed a mean accommodative amplitude of 1.9 D. with a standard deviation of ± 0.4 D. The range was from 1.2 to 2.6 D. Using the same criterion for the amplitude on the curves of the aged cat, the 1.5 D. value would be used for comparison. This value is only one standard deviation from the mean amplitude for young cats; and therefore cannot be considered significantly low.

Comparison of Amplitude in Cats and Man

It is generally believed that the average man's amplitude of accommodation

is reduced to 1 D. or less by the age of 60 and does not change after that*. This is less than one-tenth the amplitude of youth. If a parallel phenomenon took place in cats, one would expect to find 0.2 D. or less of amplitude in a cat which had the equivalent age of a 60 year old human being. What is then the equivalent age of a 15 year old cat? There appears to be no experimental evidence that would indicate this relationship. Veterinary clinical experience indicates that one year of a cat's life is equal to five or six years of a man's life (Ref. 13). On this basis our aged cat would have an age equivalent to a man 75 to 90 years! Hence little, if any, accommodation would be expected if the course of man's amplitude were paralleled by that of the cat.

SUMMARY AND CONCLUSIONS

The accommodative response of the eye of a 15 year old cat to electrical stimulation of the ciliary ganglion was measured. The data were compared with those of a previous similar study on young cats. The accommodative amplitude of the aged cat was lower than that of the average young cat, but not significantly so. When compared with the decrease of accommodative amplitude with age in man (which gives rise to presbyopia) it is clear that the aged cat exhibited no similar phenomenon.

* These data are obtained by using stimulus values (subjective blur) rather than response values (as obtained by stigmatoscopy) which are more valid. Unpublished preliminary results of Marg, E. and Ong, J. indicate that the accommodative amplitude is generally zero after the age of 52.

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