ACCOMMODATIVE RANGE IN AMBLYOPIC MONKEYS (MACACA NEMESTRINA)

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Abstract—Three naturally strabismic and two chronic bilaterally atropinized monkeys were tested for spatial contrast sensitivity and range of accommodation. All eyes that showed deficits in contrast sensitivity also showed deficits in accommodation. The strabismic monkeys all showed interocular differences in their CSFs and in their accommodative ranges. The atropine monkeys had no interocular differences on either measure. However, one had depressed contrast sensitivity relative to normal and also showed a reduced accommodative range. A statistically significant correlation was found between the high frequency cutoffs of the CSFs and accommodative ranges. These deficits in accommodative range that accompany contrast sensitivity losses in the monkey are similar to the deficits in accommodative range that accompany amblyopia in humans.

Strabismus Accommodation Accommodative amplitude Contrast sensitivity Amblyopia Atropine Monkey

INTRODUCTION

In recent years our laboratory has been working to establish and study non-human primate models of strabismic amblyopia (Kiorpes and Boothe, 1980, 1981) and anisometropic amblyopia (Boothe et al., 1982; Boothe et al., 1984). These experiments have demonstrated that it is possible to produce acuity and contrast sensitivity deficits in monkeys that are similar to those found in human strabismic and anisometropic amblyopes.

There is increasing evidence that human amblyopes have a weakened or variable accommodative response in addition to their well-studied deficits in acuity and contrast sensitivity (Urist, 1959; Abraham, 1961; Sherman, 1970; Wood and Tomlinson, 1975; Otto and Safra, 1978; Hokoda and Cuiffreda, 1982). It is not clear, though, how the accommodative deficits are related to the amblyopia. An animal model could be useful for studying this relationship. If the conditions that lead to decreased acuity and contrast sensitivity in monkeys also lead to accommodative deficits, then the monkey could provide a means for studying the interaction between the development of amblyopia and the accommodation control system.

Smith and Harwerth (1984) used a modified clinical procedure to measure accommodative amplitudes of normal macaque monkeys. In the present study, we have used a similar procedure to assess accommodative ranges of monkeys that have contrast sensitivity deficits.

METHODS

Subjects

We tested five pigtailed macaques (Macaca nemestrina) ranging in age from 68 to 117 weeks. All of the animals had been tested extensively on contrast sensitivity measurements and hence were wellpracticed observers. Descriptions of the individual animals are given in Table 1. Retinoscopy was conducted by an ophthalmologist while the monkeys were lightly anesthetized with ketamine hydrochloride. Pupils were dilated and accommodation paralyzed by instilling 1 drop each of 1% cyclopentolate and 10% phenylephrine in each eye every

Monkey identification	Age (months)	Visual status	Refraction	CSF cutoff (c/deg)	Accommodative range (D)
K.F.	29	Esotrope	OD + 4.00	22.7	8.0
			OS + 4.25 + 0.50 × 80	15.7	6.0
K.Y.	27	Esotrope	$OD + 4.00 + 0.50 \times 90$	8.8	3.5
			OS + 5.00	9.3	6.5
V.P.	20	Esotrope	$OD + 3.00 + 1.50 \times 150$	17.6	4.5
			$OS + 2.00 + 1.00 \times 30$	22.7	9.5
N.U.	19	Atropine reared	OD + 1.50	43.7	14.0
C.L.	17	Atropine	OD + 3.75	18.2	5.0

5 min for 15 min. The last drops were administered one-half hour prior to examination. All of the animals exhibited hyperopia which could have been related to the animals' other visual abnormalities.

Three of the monkey subjects were naturally occurring esotropes (K.Y., K.F., V.P.). The remaining two monkeys, N.U. and C.L., had been reared with daily administration of 1% atropine sulfate to both eyes. This rearing condition produced chronically blurred retinal images during the first six postnatal months.

Behavioral testing methods

The monkeys were tested on an operant twoalternative forced-choice discrimination task (Boothe, 1981; Williams *et al.*, 1981) while they were free-roaming in a face-mask cage (Sackett *et al.*, 1971). The animal's task was to discriminate sinusoidally modulated gratings from a homogeneous field of equal average luminance. Correct responses were rewarded with 0.3 cm^3 of apple juice and wrong responses triggered a 10–15 sec delay before the onset of the next trial.

Stimuli were displayed on a pair of CRT screens (Tektronix 602 with P31 phosphor) at a luminance of 26 cd/m^2 . The CRT screens subtended 3 deg at a viewing distance of 120 cm and were surrounded by a screen of approximately equal color and luminance. The surrounding screen provided a constant stimulus for accommodation. Further details about stimulus generation and calibration have been presented elsewhere (Williams *et al.*, 1981).

Shutters on the front of the face-mask were used to select the test eye. Standard trial lenses and 6 mm apertures were mounted in lens wells in front of the selected eye hole, at a vertex distance of approx. 7 mm. The 6 mm apertures were used to ensure that the monkey viewed through the optical center of the lens. The animals viewed with their natural pupils which are about 5.5 mm in our testing situation.

Accommodative range was determined in our monkeys by a method analogous to the minus-lens technique that is used clinically. In a standard minus-lens procedure, the subject attempts to maintain clear focus of a high-contrast target while progressively higher minus lenses are introduced in the spectacle plane. The end point of accommodation is taken to be that point where the subject can no longer maintain clear focus. The procedure used in the present study involved determination of contrast threshold for a designated grating stimulus as a function of lens values. Lens power was changed in 0.5 or 1.0 diopter (D) steps until contrast threshold became elevated by 1 log unit or until performance became too variable to obtain a reliable estimate of contrast threshold. The series was then repeated in descending order. A procedure similar to this has been used by Smith and Harwerth (1984) to measure accommodative ranges in normal monkeys.

Contrast thresholds were determined by the method of constant stimuli. Forty to sixty trials were

collected at each of four to six contrast levels, separated by 0.2 log unit steps. The contrast levels were chosen such that performance at the highest contrast was near 100% and performance at the lowest contrast was near chance. For contrast sensitivity functions (CSFs), contrast thresholds were determined for each of a number of spatial frequencies, whereas for accommodative range testing, only one spatial frequency was used. (The criteria used for choosing this frequency are described below.) The data were subjected to probit analysis (Finney, 1977) to obtain a median contrast threshold value and standard errors of that estimate at each spatial frequency.

There were several considerations in choosing the spatial frequency to be used for testing accommodative range. The stimulus spatial frequency needed to be high enough so that defocus would cause reasonably large changes in contrast threshold. According to the data of Williams and Boothe (1983) a 1 log unit change in contrast sensitivity can be effected by 2-3 D of defocus in a cycloplegic monkey eye at spatial frequencies from 6.3 to 12.6 c/deg. At lower frequencies a comparable change in contrast threshold would require 4-6 D of defocus. On the other hand, the spatial frequency needed to be low enough so that contrast thresholds were fairly similar for the two eyes of the amblyopes. If contrast sensitivity was substantially different for the two eyes of an animal at a particular spatial frequency then differences in accommodative amplitude could simply be due to the inability of one eve to detect the stimulus. Given these considerations, the designated frequency for a given monkey was always chosen to be higher than the peak of the CSF but within 1.5 octaves of the peaks of the CSFs for both eyes. The frequencies chosen for individual monkeys ranged from 4.5 to 12.6 c/deg, and were necessarily not the same for all monkeys.

In order to quantify the extent of the accommodative range for these monkeys' eyes, we calculated the lens powers for which the fiducial limits (99%) confidence intervals) of contrast threshold no longer overlapped those of the threshold at the best corrected lens value. The first of two consecutive points that fell outside of the fiducial limits at the best lens in both the hyperopic and myopic directions were taken as the end points. However, in two cases performance became too variable at one end of the range to obtain an accurate estimate of contrast threshold. In those cases, we took the end point to be $0.5\,D$ higher than the highest lens value for which reliable data were obtained. The range of lens powers falling between the end points is considered to be the accommodative range.

RESULTS

Contrast sensitivity functions (CSFs) and accommodative range data for each of the monkey subjects are shown in Figs 1-5. The three naturally strabismic



Fig. 1. Data for strabismic monkey K.F. (a) Contrast sensitivity functions (CSFs) for the right (triangles) and left (circles) eye. The curves fitted to the data points are exponential functions, as described by Williams *et al.*, (1981). High frequency cutoffs are the points where the extrapolated high frequency portions of the curves meet the abscissa. The arrow points to the frequency chosen for testing accommodative range. (b) Accommodative range data for the right (triangles) and left (circles) eye. Contrast sensitivity (1/threshold) +/-1 SE is plotted for each lens power tested. The end points, determined as stated in the text, are indicated by the letters on the abscissa for each accommodation function.



Fig. 2. CSFs (a) and accommodative ranges (b) for both eyes of strabismic monkey V.P. Symbols as described for Fig. 1.



Fig. 3. CSFs (a) and accommodative ranges (b) for both eyes of strabismic monkey K.Y. Symbols as described for Fig. 1. Note that the ordinate in (b) is expanded, covering only 2 log units.



Fig. 4. CSF (a) and accommodative range (b) for the right eye of atropine monkey N.U. Symbols as described for Fig. 1.



Fig. 5. CSF (a) and accommodative range (b) for the right eye of atropine monkey C.L. Symbols as described for Fig. 1. Note that the ordinate in (b) is expanded, covering only 2 log units.

monkeys each showed clear interocular differences in their CSFs whereas the bilateral atropine monkeys exhibited no such interocular differences. Thus, CSFs for both eyes of each of the strabismic monkeys (Figs 1a, 2a and 3a) and one eye of each of the atropine monkeys (Figs 4a and 5a) are presented. The arrows above the CSFs in each monkey's plot point to the frequency chosen for accommodative range testing. (The criteria for choosing the test frequency are described in the methods section.)

Qualitative inspection of the accommodation data reveals that shortened accommodative ranges were found for all eyes that demonstrated reduced contrast sensitivity. For each, of the strabismic monkeys, the accommodative ranges of the amblyopic eyes were shorter than those for the fellow better eyes (Figs 1b, 2b and 3b). For the atropine monkeys, C.L. showed depressed contrast sensitivity relative to N.U. (compare Figs 4a and 5a) and, accordingly, C.L. showed a shortened accommodative range relative to N.U. (Figs 4b and 5b).

The quantitative estimates of accommodative range, obtained as described in the methods section,

for all tested eyes are listed in Table I. Comparison of the two eyes of each of the strabismic monkeys reveals that K.F. and K.Y., had interocular differences in accommodative range of at least 2 and 3 D, respectively, whereas V.P. showed a larger difference of about 5D. Atropine monkey N.U. showed the greatest accommodative range, 14 D, whereas atropine monkey C.L. had a range of 5 D, which was similar in extent to that of the amblyopic eyes of the strabismic monkeys.

Examination of the data from these monkeys suggests that a quantitative correlation may exist between contrast sensitivity and accommodative range. We calculated the correlation coefficient between high spatial frequency cutoff of the CSF and the estimated extent of the accommodative range for all eyes tested. The correlation (r = 0.902) was found to be statistically significant (P < 0.005).

DISCUSSION

The results of this study demonstrate that monkey eyes that have depressed contrast sensitivity also show reduced ranges of accommodation. This was not only true for the amblyopic eyes of the strabismic animals but also for the eyes of our atropine animal who exhibited depressed sensitivity bilaterally.

All of the monkeys clearly demonstrated that they could accommodate by the fact that the decrease in contrast sensitivity with increasing hyperopic defocus was less than would be predicted on the basis of optical defocus. Williams and Boothe (1983) have shown that, in cycloplegic monkey eyes, contrast sensitivity falls off at a minimum rate of 0.24 log units per diopter of defocus for the spatial frequency range used in this study. Only one monkey's data show a fall-off of contrast sensitivity that is nearly as steep as shown by Williams and Boothe (1983). The right eye of K.Y. showed a decrease in contrast sensitivity of 0.15 to 0.20 log units per diopter. On the other hand, if the animals were accommodating perfectly the plateau portion of the accommodation functions would be flat, whereas for our animals they were sloped. This gradual decline in contrast sensitivity with increasing lens power was most likely due to increasing fatigue as the animals attempted to maintain a clear image of increasingly defocussed stimuli for extended periods of time.

The deficits in accommodative range found for the amblyopic eyes of our strabismic monkeys are similar to those reported for amblyopic humans. Hokoda and Ciuffreda (1982) reported finding a range of 1 to 5 D difference between the eyes of human amblyopes using the standard minus-lens technique. All of the three strabismic monkeys in this study showed differences within that range K.F. and K.Y. had at least 2 and 3 D difference, respectively, whereas V.P. had a somewhat larger 5 D difference.

Our primary interest in this study was to compare the relative accommodative ranges of normal and amblyopic eyes. Our estimates of the absolute extent of the accommodative ranges should be considered to be conservative. Although the animals were wellmotivated and well-practiced at the task, we were obviously measuring the range of voluntary accommodation. Physiological accommodative range in young macaque monkeys, as assessed by administration of a maximally effective dose of a cholinomimetic, is over 30 D, which is substantially larger than our behaviorally measured range (Bito et al., 1982). In two particular cases our monkeys' performance became too variable to allow a reliable estimate of the end point to be obtained (Fig. 1b, right eye plus-lens end point; Fig. 3b, left eye minus-lens end point). In those cases, our estimate of the measured range may be somewhat shorter than the actual capability of the monkey. However, in both cases for which this occurred in this study it was with the non-amblyopic eye of a strabismic monkey and, if anything, the measured difference between the eyes in these animals would be an underestimate.

Accepting that the estimated extent of the accommodative range in our monkeys is conservative, we can attempt to compare our monkey data to data from other studies of humans and monkeys. Clinically, the endpoint of accommodation is the first lens value for which sustained blur (that which cannot be cleared by accommodative effort) occurs. Our test procedure does not allow us to directly measure this point. However, given that blur reduces the contrast of an image, a significant elevation in contrast threshold would be expected to occur at the point of sustained blur. Thus our criterion was chosen to determine the point at which threshold was significantly elevated from the normal corrected level. Assuming that the methods are somewhat analogous, then, we find that the extents of our monkeys' ranges are at least similar to those reported by Hokoda and Ciuffreda (1982) with the minus-lens technique. They found accommodative ranges that lay between 4.13 and 11.40 for amblyopic eyes and 8.05 and 12.24 for non-amblyopic eyes of strabismic patients. Our strabismic monkeys' ranges lie between 3.5 and 6.5 for eyes with depressed sensitivity and 8.0 and 9.5 for eves with normal contrast sensitivity.

Smith and Harwerth (1984) measured accommodative amplitudes for normal monkeys using a technique similar to ours. The ranges found for our monkey' eyes that had normal CSFs appear to be shorter than those found by Smith and Harwerth (1984). This apparent difference is purely a function of a difference in choice of end points. If we scored our data by their criterion, that is, an overlap of standard deviations rather than an overlap of the 99% fiducial limits, the normal eyes' ranges would extend from 15 to 17 D which is similar to their findings of 17 to 18 D. Thus we feel that the data from the two labs are comparable even though we used different psychophysical paradigms for testing.

In summary, we have found deficits in accommodative ability in monkeys who also exhibited deficits in contrast sensitivity. The estimated extent of the accommodative ranges in our monkeys' eyes was highly correlated with their high spatial frequency sensitivities. The existence of such a relationship has been suggested by human studies although it has not been examined quantitatively. The macaque monkey appears to be an appropriate animal model for studying some aspects of the accommodative control system in normal and amblyopic eyes.

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