Arch. Soc. amer. oftal. optom. (1959) - II - 73

IDENTIFICATION OF ROD AND CONE RECEPTOR MECHANISMS IN ATYPICAL CONGENITAL ACHROMATOPSIA

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Introduction

In recent years, there has been a renewed interest in congenital achromatopsia, in part because of the discovery of what have been designated "atypical cases". (Ref. 1, 2, 3). A few of these atypical cases exhibit normal or supranormal visual acuity and yet reveal a total absence of chromatic discrimination. However, most of the cases of atypical achromatopsia exhibit greatly reduced visual acuity, but demostrate some remnant of chromatic discrimination. Both classes of patients show evidence of an hereditary transmittance of the abnormality. In contrast to both classes of atypical cases, cases of atypical achromatopsia reveal both a total absence of chromatic discrimination and greatly reduced visual acuity.

In view of obvions differences between these two broad categories of atypical congenital achromatopsia, the present authors suggested recently (Ref. 4) that patients with achromatopsia be described by compound terms, the first describing the number of cone receptor systems found to be operative, the second describing the type of chromatic discriminations which the patient was capable of making. Thus, for example, there may be tri-cone monochromacy in which red, green, and blue cones are present but the patient still has a monochromatic funtional system. Or, there may be di-cone monochromacy in which two cone systems are present, or mono-cone monochromacy in which only one cone system is in operation.

The suggested use of this compound nomenclature implies, of course, that sources of evidence other than chromatic discriminations can be found which will identify the number and spectral characteristics of the cone systems present. The literature suggests that luminosity (Ref. 5), the acuity function of luminance

(Ref. 6), and the effect of chromatic adaptation on acuity (Ref. 7) provide useful indices of the number of cone mechanisms in operation, independent of the patient's ability to make chromatic discriminations.

We have initiated a study of atypical achromatopsia with the objective of identifyng the cone mechanisms in operation as well as the chromatic discriminations of which the patients are capable. The results to be reported here are concerned with three cases of atypical congenital achromatopsia with reduced visual acuity and some chromatic discriminations. Further data on these and similar patients will be reported in more detail subsequently.

The present patients were refered to us by Dr. Harold F. Falls of the Department of Ophthalmology, the University of Michigan, and our measurements were made while we were working in the Vision Research Laboratories of that institution. Analysis of the data has been made possible in part by a grant from The Knights Templar Fund at the University of Michigan, in part by support from Dr. William H. Havener, Chairman of the Department of Ophthalmology at The Ohio State University, and in the largest part by generous support from The Ohio Lions Eye Research Foundation.

Experimental Data

A. Medical Findings

The three patients were brothers; the quantitative data are so nearly identical for the three that in most instances it will be sufficient to present average data. The ages of the three patients at the various times at which we studied them varied within the following limits: 16 to 19, 20 to 23, and 23 to 26. The visual abnormality was known to be congenital, having been reported in other male members of the family. The was no evidence of change in the abnormality observed in the brothers since birth.

The pedigree obtained by the University of Michigan Heredity Clinic consists of forty related persons. The three affected brothers had one sister who was tested and found to be normal. The father was tested and found to be normal. All his relatives were reported to be normal. The mother was normal except for foveal dark adaptation which showed some evidence of rod function. One of the mother's three brothers was reported by the patients to have the same defect as they both with regard to visual acuity and color vision. The maternal grandfather of the patient's mother was also reported individuals were known. Thus the inheritance of the patients' color vision defect appears to follow the classical sex-linked pattern.

Ophthalmological examinations by Dr. Falls gave the following results. The patients had no chromatic discriminations under normal testing conditions but their visual acuity was correctable to about 20/60. There was an absence of gross nystagmus, no photophobia, and no evidence of retinal degeneration. There was no evidence of suppression or of eccentric fixation. The only fundus abnormality was a faint "stippling" of the choroidal pigment in the macular region, combined with a slight baring of the peripheral choroidal vasculature.

We assessed the patients' chromatic discriminations with the Farnsworth-Munsell 100-hue test, administered under a Macbeth Illuminant C easel lamp. Numerous errors were made throughout the spectrum, with the fewest errors at R and YYG. The patients showed somewhat better discrimination than typical achromats, who generally show a pattern of errors at and beyond the extremes of the graph. Measurements on a Nagel-type anomaloscope indicated that the patients were dichromatic or monochromatic, with the brightness even more depressed in the red than is found in protanopia.

B. Psychophysiological Measurements

Special equipment was constructed to enable us to measure luminosity and chromatic discriminations, dark adaptation, and visual acuity at various luminance levels.

1. Luminosity

Visual luminosity, or apparent brightness of various parts of the visible spectrum, was measured in a spectral comparator based upon a Hilger prism monochromator (Ref. 8). Radiometric measurements were made of the output of the device at various wavelengths, and cut-off filters were used to eliminate the spectral stray light which would otherwise have invalidated our measurements. This device was used first (Ref. 9) to measure luminosity functions on normal observers, and an optimal technique was developed. A standard source of 402 millimicrons was usually used and each subject was required to match other wavelengths of the spectrum in turn to this standard. Matches were always verified after adaptation to a white light of matched luminance, to minimize the possibility of chromatic adaptation. For normal subjects, it was found desirable to reduce color differences between the standard and comparison fields by use of a series of standards spaced across the spectrum. For the present patients, initial use of this procedure demonstrated that the patients had no difficulty matching all wavelengths against a single standard. Subsequent tests required the patients to match all wavelengths against the 402 millimicron standard. It was shown that the measurements obtained with the two methods were equivalent and they have been used interchangeably through the present report.

In our spectral comparator, the photometric comparator is of the concentric ring variety. In our device, the diameter of the inner field, which contained the standard, subtended 30 minutes. The diameter of the outer field, containing the spectral comparison, subtanded 1 degree. Thus, the entire field will fall within the supposedly rod-free fovea centralis if the subject fixates the precise center of the comparator as he is instructed to do. The device incorporates an artificial pupil so that it is possible to compute the retinal illuminance produced by the standard when set at various radiance levels. A special lens is used (Ref. 10) to reduce difficulties due to the chromatic abberration of the human eye.

During the luminosity measurements, it was a simple matter to ask the patients if they could obtain a perfect match between various spectral stimuli and the 402 millimicron standard. Insofar as they were able to obtain a perfect match, it could be concluded that the patients were without chromatic discrimination.

Luminosity measurements were first made at the maximum intensity of the 402 millimicron standard. Utilizing the 1951 photopic luminosity values proposed by Judd (Ref. 11), the retinal illuminance was computed as 1.76 trolands for normal subjects. The data for the three patients are shown in Figure 1, together with average data on 10 normal subjects obtained under the same conditions.

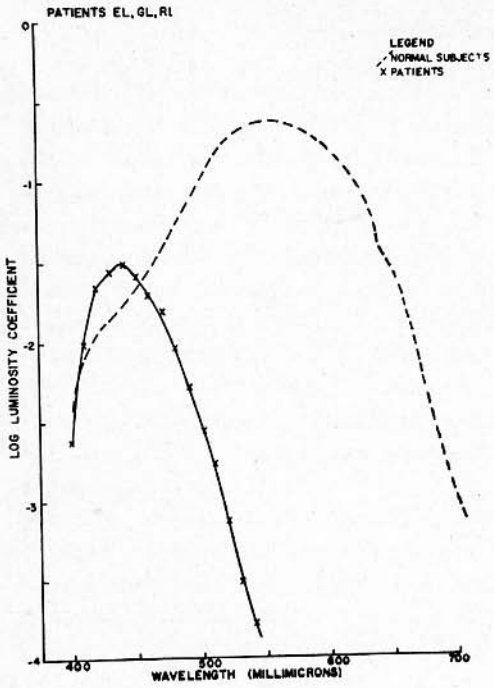


Fig. 2. Luminosity data for the patients and for normal subjects at a retinal illuminance of 1.76 trolands.

The luminosity coefficients are defined by the relation:

$$\text{Luminosity Coefficient} = \frac{N\hat{\lambda}}{N\lambda} \; V\hat{\lambda}$$

where $N\hat{\lambda}$ = radiance of 402 millimicron standard;

$N\lambda$ = radiance of comparison wavelength; and

$V\hat{\lambda}$ = CIE photopic luminosity coefficient at 402 millimicrons.

By this definition, each luminosity coefficient should agree with the standard photopic luminosity value if the luminosity function is normal. The data obtained on our 10 normal subjects agree in general with the standard values, exhibiting a peak luminosity at about 555 millimicrons, and substantial luminosity between the limits of 400 and 700 millimicrons. In contrast, the data on our patients show a very narrow luminosity function with a peak at 440 millimicrons. The extent of difference between our patients and the normal subjects is perhaps concealed by the use of a logarithmic scale of luminosity coefficients. In fact, the luminosity function for our patients is less than one-thousandth normal at 540 millimicrons, and indefinitely less at longer wavelengths!

The patients were able to obtain perfect matches between all comparison stimuli and the 402 millimicron standard. Thus, we may conclude that they were functionally monochromatic under these conditions. For what it is worth, it should be reported that the patients all referred to the color of the photometric field as "blue". One of them stated that the field looked "like a blue sweater in a black room". Because of the narrowness of this luminosity function and the great resemblance of this curve to the z function in the C. I. E. colorimetric system, we have concluded tentatively that only one cone receptor system is present and that it may be designated the blue cone system. It was on this basis that these patients were originally designated blue monocone monochromats (Ref. 4).

Measurements were next made under identical conditions except that the intensity of the 402 millimicron standard was reduced so that it provided only 0.0754 trolands. The data obtained on the three patients under these conditions are presented in Figure 2. Data obtained on the 10 normal subjects at the lower luminance level are presented for comparison. Note that the luminosity function is now considerably broader than before, with the peak value at about 520 millimicrons. Thus, our patients exhibited a massive "anti-Purkinje" shift, the luminosity shifting to longer wavelengths as the luminance is reduced. It is still

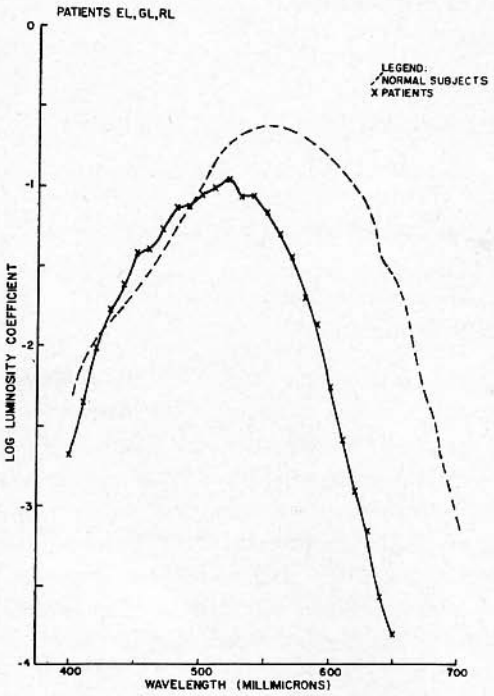


Fig. 2. Luminosity data for the patients and for normal subjects at a retinal illuminance of 0.0754 trolands.

apparent, however, that the luminosity function is far from normal. The patients were able to obtain perfect matches between all spectral comparison stimuli and the 402 millimicron standard. In this case, they reported the photometric field as "colorless". Thus, again they may be considered monochromatic.

The luminosity curve obviously bears some resemblance to the scotopic luminosity curve, which is known to be produced by the action of rod receptors. This resemblance creates at once an interesting possibility. It is to be remembered that our patients were instructed to make these luminosity settings with foveal fixation and that they believed they were following these instructions. If this is the case, and assuming the patients did not exhibit an unaccustomed nystagmus, the rod-like luminosity curve we have obtained was produced by receptors located in the fovea centralis.

A quantitative comparison of these data and the standard 1951 CIE scotopic luminosity function (Ref. 11) is presented in Figure 3. This comparison can only be made in relative terms so that all we can judge is the similarity of shape of the two luminosity curves. It is apparent that there is good agreement at wavelengths longer than 550 millimicrons but that there is a considerable depart-

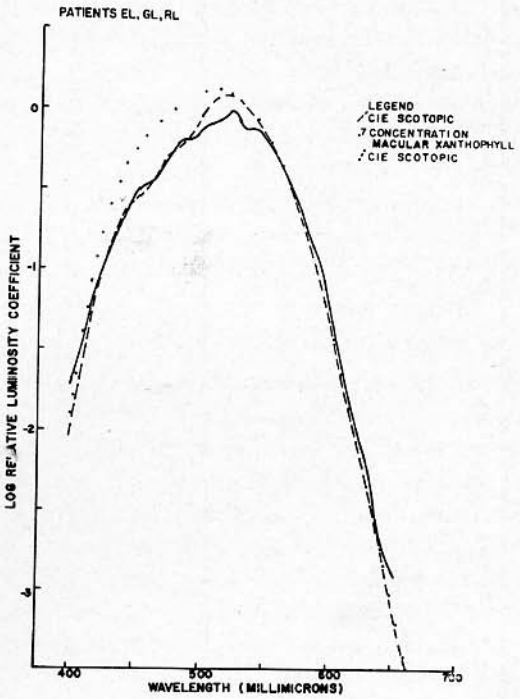


Fig. 3. Luminosity data for the patients at a retinal illuminance of 0.0754 trolands in comparison with theoretical curves.

ure between the curves in the range from 420 to 540 millimicrons. Initially, we postulated that the relative loss in luminosity exhibited by the patients at the short wave end of the spectrum reflected an inhibitory effect of blue cones.

While discussing these data with W. S. Stiles of the National Physical Laboratory, Teddington, Great Britain, an alternative explanation occurred to us. We begin by noting that Wald (Ref. 12) has reported the existence of an inert yellow pigment which exists in relatively high concentration in the macular retina, and which reduces the sensitivity of macular receptors in the short wave end of the spectrum. This pigment has an absorption spectrum which closely resembles crystalline leaf xanthophyll. It exists also in the peripheral retina, in concentrations no greater than one-fifteenth those found in the macular retina.

If we assume that this xanthophyll exists in the macular retinae of our patients, then the luminosity function of the underlying receptors will be altered at the short end of the spectrum by absorption due to macular xanthophyll. We have postulated that rods exist in the fovea centralis of these patients, and that their absorption spectrum was indeed modified by the presence of macular xanthophyll.

It is necessary to construct theoretical scotopic luminosity curves modified by various concentrations of macular xanthophyll, since the concentration can easily vary among patients, and is known to vary with retinal location. The dashed curve in igure 3 represents modification of the CIE scotopic luminosity function by a concentration of macular xanthophyll 70% as great as that reported by Wald. We believe the agreement between this modified luminosity function and our luminosity data is quite good. Thus, we feel that we have probably established the existence of a foveal rod luminosity function, to be distinguished from the usual scotopic curve, which may well be considered a peripheral rod luminosity function.

It is known that the standard scotopic luminosity function closely resembles the absorption spectrum of rhodopsin. This is not surprising, since the concentration of macular xanthophyll is known to be low at the retinal locations used to determine the scotopic luminosity function. The fact that the concentration of macular xanthophyll presumably decreases gradually from a maximum at the fovea would seem to imply that there should be various scotopic luminosity curves for different retinal locations, modified by different concentrations of macular xanthophyll. If this is reasonable, then the precise shape of the scotopic luminosity curve can perhaps be used to determine to some extent the retinal location used by the patients in making psychophysiological measurements. We shall have occasion to make use of this notion in subsequent analysis of our data.

After discovering the presence of the blue cone and foveal rod receptor systems, each producing monochromatic vision at one luminance level, we measured luminosity curves at various luminance levels between the two values originally studied. We generally obtained what must be regarded as mixed luminosity curves, and we found a dichromatic color system in each case.

The solid curve in Figure 4 represents an example of the mixed curves. The data are for patient EL at a retinal illuminance level of 0.508 trolands. (It is necessary to present individual data in this case, since the mixed curves obtained by the three patients at a given luminance level differ to such an extent that averaging would not be advisable.) When these mixed curves were obtained, the patients were able to make perfect matches between the spectral lights and the 402 millimicron standard only from about 400-450 millimicrons. Otherwise, the spectral light was reported as chromatically different from the standard. In general, the patients reported a "neutral zone" in the region from about 450 to 510 millimicrons, in which the spectral light was reported as white or cream colored. Spectral lights beyond 510 millimicrons were invariably called "yellow". This result was obtained both when the patients were matching these wavelengths with the 402 millimicron standard and when they observed unknown wavelengths

singly and without reference to other color stimuli. Thus, at the luminance levels at which mixed luminosity curves were found, the patients clearly exhibited a dichromatic color system. It seems reasonable to suppose that the dichromatic color system was based upon blue cone and foveal rod receptor systems, since the dichromacy occurred at luminance levels at which both systems might reasonably be expected to be operative.

The constructions in Figure 4 are intended to demonstrate the reasonableness of this postulation. The blue cone curve shown in Figure 1 and the theoretical foveal rod curve shown in Figure 3 have been plotted in comparison with the mixed luminosity curve. These curves have been arbitrarily adjusted for good fit with the mixed luminosity curve, with the result shown in Figure 4. It is apparent that the mixed curve has sufficient width to be composed of blue cone and foveal rod mechanisms as postulated. It is also apparent that the form of the mixed curve conforms reasonably well to the blue cone and foveal rod curves at the ends of the spectrum where only one receptor system would be expected to be operative. The appearance of the mixed curve in the region from about 450 to 510 millimicrons could be interpreted as due to some kind of facilitation of the blue cone and foveal rod systems upon each other. The mixed luminosity

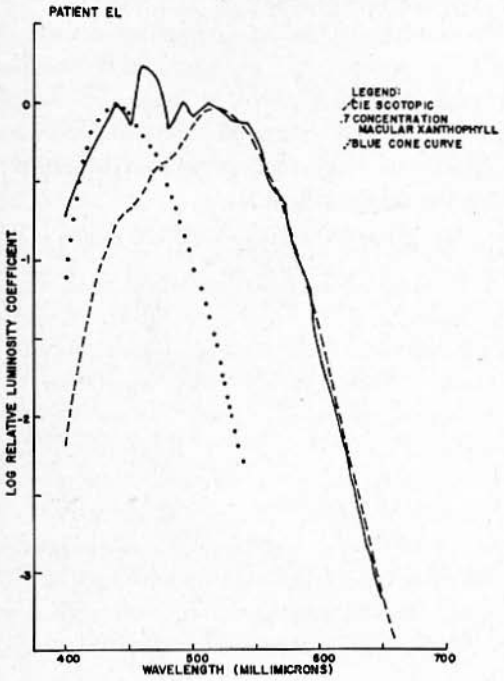


Fig. 4. Luminosity data for one patient at a retinal illuminance of 0.508 trolands in comparison with theoretical curves.

curves obtained on these patients almost invariably reveal this evidence for facilitation in the spectral region where the two receptor systems are presumably of about equal sensitivity. We cannot consider this point proved, of course, but the data can perhaps be interpreted in this manner.

We believe the luminosity data have revealed the presence of blue cone and foveal rod receptor systems in the foveal or near-foveal retinae of our patients, and have suggested that chromatic discriminations can be made whenever both these systems have about equal sensitivity. The implications of these results for color vision theory are of particular interest and we are continuing efforts to develop a theoretical model my means of which such a color discriminative system can operate.

2. Dark adaptation measurements

Foveal and peripheral dark adaptation were measured in a recording dark adaptometer constructed along the general lines of the instrument described by McLaughlin (Ref. 13). Basically, the device consists of a pre-adapting field of controllable luminance and duration, and a flashing test of continuosly variable intensity which the subjet maintains at a threshold level during dark adaptation by adjustment of a knob control linked to a circular neutral photometric wedge. For the present studies, the test light subtended 15 minutes of arc, and was presented intermittently during the entire test period in the following sequence: 2.4 seconds on, 1.2 seconds off, 2.4 seconds on, etc. Viewing was binocular and natural pupils were utilized. The experimental sequence consisted of a 900 second initial period of dark adaptation to was out effects of unknown previous adaptation, followed by a period of 500 second light adaptation to a luminance of 1280 foot-lamberts, followed by the dark adaptation test.

For tests of "foveal" adaptation, the test target was presented in the center of a diamond configuration composed of four white fixation lights. Each light subtended 4.6 minutes of arc, and the distance from the center of the configuration to the center of each light was 48 minutes. The test subject controlled the intensity of the fixation lights from time to time during dark adaptation by adjustment of a rheostat so that the lights remained clearly visible without becoming bright enough to have a deleterious effect upon the threshold of the test light. The results obtained by the patients with a white test stimulus are presented in Figure 5. Here we have plotted the logarithm of the luminance of the test stimulus required for it to be at threshold level during adaptation to darkness. Data on thirteen normal subjecs are present for comparison. (The data are not precisely comparable, since the light adaptation luminance was 1155 foot-lamberts rather than 1280. Ancillary experiments suggest, however,

that this difference in the pre-adaptation luminance does not affect the dark adaptation curve appreciably). It is obvious that the patients exhibit an initial deficiency in adaptation but that after some 12 minutes in the dark, they hace greater sensitivity than normal subjects. The initial deficiency in sensitivity is quite large, the threshold being as much as 50 times greater than normal. The dark adaptation curve obtained on the patients appears to have the change in slope usually attributed to a transition from cone to rod receptors (Ref. 14).

In order to identify the photoreceptor systems responsible for adaptation at different times in the dark, we utilized what might be called "spectrophysio-analysis. The basic idea is that we can identify receptor mechanisms responsible for visual function from data obtained with stimuli of different spectral quality, upon the basic of the known action spectra of the receptor systems. This idea has utilized previously (Ref. 15, 16, 17, 18) but deserves considerably more attention. In the present instance, we repeated our foveal dark adaptation measurement after insertion of a Wratten Nº 47B colored filter in the test stimulus beam. This filter has a peak transmittance at about 430 millimicrons and a half width of about $\pm$ 20 millimicrons. Now, we can compute the effective optical density of the Nº 47B filter, assuming a given photoreceptor sensitivity funtion, and test the extent to which this computed density brings the dark adapta-

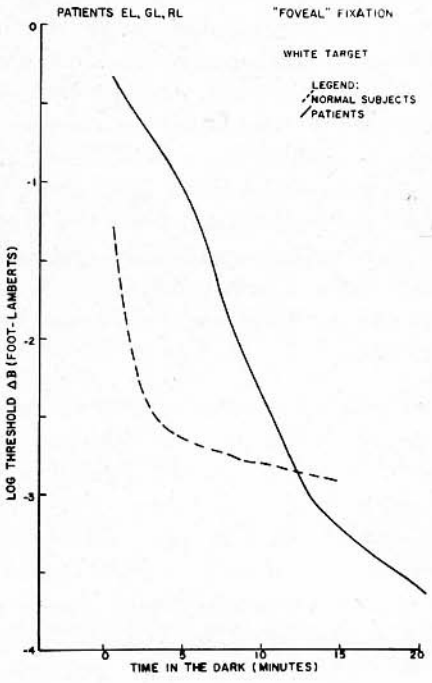


Fig. 5. "Foveal" dark adaptation data for the patients and for normal subjects with

tion funtion obtained with blue light into agreement with the original dark adaptation function obtained with white light. This analysis necessitates accurate radiometric data un the energy distribution of the light source used in the test stimulus. Measurements of the radiant energy emitted at various wavelengths by the test target system ware made by our associate B.S. Pritchard, utilizing a double grating monochromator previously calibrated against a standard lamp of known color temperature. It is also necessary to take account of the fact that the so-called neutral wedge used to adjust the test light to threshold, and other neutral filters usted to reduce the test light to near threshold, are spectrally selective and hence change their calibration when the blue filter is inserted. We measured the spectral transmittance of the various neutral materials with the double grating monochromator and computed the densities of these materials when the incident light was modified by insertion of the blue filter. The density changes were quite small but appropriate allowances have been made in the data.

Initially, we tested the assumption that either the ordinary scotopic or photopic receptor systems might have been involved. The density of the blue filter was found to be 1.45 for the standard scotopic function and 2.59 for the Judd 1951 photopic function. The test of the assumption that the entire foveal dark adaptation function is provided by a receptor system having the sensitivity of the CIE. scotopic function consists of computing the values of threshold AB on the assumption that the effective density of the blue filter is 1.145, and comparing the dark adaptation data for the blue and white test lights after making this correction. This procedure was followed, with the results shown in Figure 6. The dashed curve represents the data obtained with the test light, assuming that the density of the blue filter was indeed 1.45. The solid curve represents the data obtained with the white test light, as shown previously in Figure 5. We consider the data for the blue and white test stimuli after seven minutes in the dark to be in excellent agreement. This presumably means that the receptor system responsible for dark adaptation after seven minutes has the wavelength sensitivity of the CIE scotopic function. Presumably, this identifies the receptors as peripheral rods.

During the first seven minutes of dark adaptation, the blue light curve falls considerably below the white light curve. This presumably means that a receptor system more sensitive to blue light than peripheral rods is at work. It naturally occurred to us that the blue cone mechanism, previously identified in the luminosity data obtained at high luminance, was responsible for this portion of the dark adaptation curve. In order to make a quantitative check of this assumption, we computed the density of the blue filter for blue cone receptors, utilizing the average luminosity curve presented in Figure 1. The densitiy was found to be

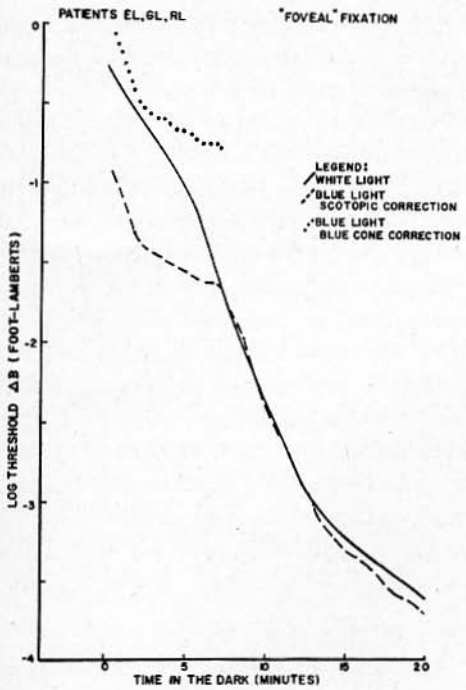


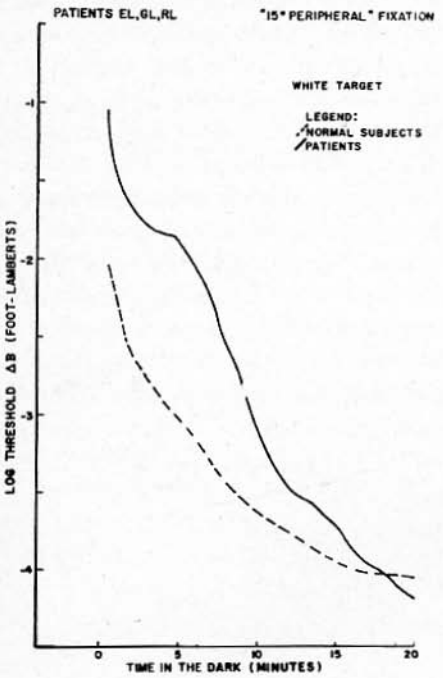
Fig. 6. Comparisons of "foveal" adaptation data obtained by the patients with white and blue test lights.

0.53. We must also remember that the neutral filters used during the blue light dark adaptation test have a different effective density for blue cone receptors than for peripheral rod receptors. It is possible to allow for this effect by computation. Allowances for this effect, and for the blue cone density of the blue filter, have been made in the blue light adaptation date obtained during the first seven minutes. The corrected data are plotted in Figure 6 as closed circles. The blue light data now fall somewhat above the white light data, indicating that the receptors responsible for this portion of the dark adaptation process are somewhat less blue-sensitive than the blue cones. It is perhaps most reasonable to suppose that both blue cones and rods are involved inthe adaptation process during the first seven minutes in the dark. The distance of the white light curve from the dotted and the dashed blue light data presumably reveals the relative contribution of the rods and blue cones at various moments. In general, the blue cones have the largest relative effect during the first three minutes, as might be expected. From these data it seems safe to assume that "foveal" dark adaptation represents the joint action of blue cones and rods, with the blue cones predominating during the first three minutes, and the rods contributing with increasing significance, until after seven minutes the funtion appears entirely dependent upon rods.

There is one small lack of consistency in our analysis which has not as yet been pointed out. The luminosity data shown in Figure 3 were used to demonstrate that foveal rod photoreceptors do not have the CIE scotopic function, but rather a modification of this function due to the absorption of macular xanthophyll. It would seem reasonable that we should use the modified CIE scotopic function in computing the effective density of the blue filter used to adjust the blue light data of Figure 6, rather than the CIE scotopic function which we used, since the patients were supposed to be using foveal fixation. The effective density of the blue filter for the CIE scotopic function modified by .7 concentration of macular xanthophyll is 1.67. This means that the blue light data should all be lowered in Figure 6 by .22 log units, if we assume that foveal rods are involved. It is apparent that this adjustment will markedly worsen the agreement between the blue and white light data obtained after seven minutes in the dark. It appears that this identifies the receptors responsible for the later part of dark adaptation as peripheral rather than foveal rods. Or more precisely, it appears that the rods responsible for adaptation following seven minutes in the dark are not overlaid with any appreciable amount of macular xanthophyll. This probably means that the patients shifted their fixation toward the peripheral retina during the latter phases of dark adaptation.

Dark adaptation measurements were also made by the patients, utilizing peripheral fixation. A single fixation point was provided which was separated by 15 degrees from the center of the test light. The fixation light was located to the right of the test light along the horizontal meridian. With binocular fixation, the test light fell on the blind spot in the left eye, and upon the temporal retina of the right eye. This procedure has the advantage that the patients use binocular fixation, which we have found more stable in the dark than monocular fixation, without having the disadvantage of our using a binocular peripheral test. (It is not uncommon for the two peripheral retinae to vary considerably in sensitivity, which produces a rather ambiguous test result. Our foveal test was of course binocular, but we have not found there to be important sensitivity differences between the two foveal retinae). The subjects continually adjusted the peripheral stimulus to threshold, carefully looking at the fixation light. They also adjusted the intensity of the fixation light from time to time to maintain it always clearly visible without allowing it to become bright enough to produce a deleterious effect upon the visibility of the test light.

The dark adaptation curve obtained with white light is presented as the solid line in Figure 7. For comparison, data on 13 normal subjects are presented as the dashed line. Unfortunately the data are not entirely comparable since the preadaptation luminance was 1078 foot-lamberts for the normal subjects and 1280



Fifg. 7. 15° peripheral dark adaptation data for the patients and for normal subjects with a white test light.

for the patients. Ancillary experiments suggested that this difference in pre-adaptation luminance should have only a negligible effect on the data. It should be noted that peripheral dark adaptation data very so much from individual to individual that the patients' dark adaptation curve may be within normal limits.

The change in slope evident in the patients' data suggests the transition from one to a second receptor mechanism. In fact, various authors have concluded on more basis than the appearance of this curve that rod and cone photoreceptor systems are functioning during the dark adaptation process. As we shall see, this conclusion is not correct.

To identify the receptors operating during dark adaptation, we measured adaptation with a blue test stimulus, as before. The blue light data were initially corrected by the CIE scotopic funtion on the assumption that peripheral rods were involved, and compared with the white light data. The results are shown in Figure 8, where the corrected blue light data are represented by the dashed line. We consider the agreement between the two curves to be quite good over their entire course. This means that the receptors responsible for the entire course of peripheral dark adaptation have the wavelength sensitivity of peripheral rods.

The two curves in Figure 8 agree in exhibiting two segments with a change in slope after some five minutes in the dark. We cannot interpret this as due to receptor systems of different wavelength sensitivity, since the curves agree throughout. We must speculate that two receptor systems seem to be operative, with the same wavelength sensitivity, but with a different rate of dark adaptation. There may be two photosensitive pigments with different regenerative dynamics. Or, the two receptor systems may differ in terms of their neural connections. Receptors functioning primarily through polysynaptic neural networks may adapt at a different rate from receptors functioning primarily through directly coupled neural networks. Further research may well be expected to provide a basis for identifying the essential difference between the systems responsible for the two segments of these curves. It is interesting to note, of course, that there is very little evidence of two similar segments in the peripheal dark adaptation functions of the normal subjects.

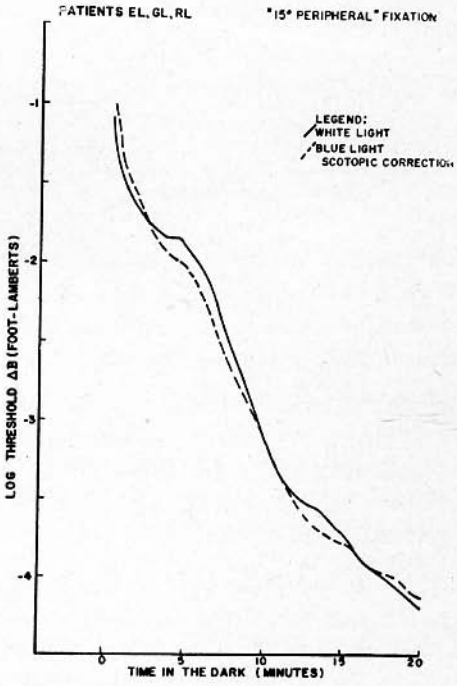


Fig. 8. Comparison of 15° peripheral dark adaptation data obtained by the patients with white and blue test lights.

We can reject the idea that the receptors responsible for the peripheral dark adaptation curves of the patients are rods whose sensitivity has been modified by macular xanthophyll. As before, if we assume what we have called foveal rods to be responsible for the adaptation curves, we must adjust the blue light data

downward by an additional .22 log units, which will clearly worsen the agreement between the blue and white light data. This result conforms to what might reasonably expect, since there should not be any macular xanthophyll at a location 15 degrees from the fovea.

3. Visual acuity measurements.

Visual acuity was measured at different luminance levels, utilizing a letter chart and projected illumination, which could be varied in level by means of neutral filters. The charts utilized involved letters developed by Sloan (Ref. 20). The subjects hand-held a 2 mm. artificial pupil over one eye, the other eye being covered with a translucent patch. He walked toward and away from the chart, until a given criterion letter was considered to be just resolvable. The letter selected was K. By selection of a suitable size letter on the Sloan Chart, the subjects were usually prevented from having to approach to less than 5 feet from the chart. Three measurements were made at a given illumination level, then the level was changed and three new settings were made. Measurements were usually made at luminance levels which were gradually reduced from highest to lowest, then a second set of measurements were made at luminance at luminance levels gradually increased from lowest to highest. Luminance levels were studied in 0.5 log unit steps. Values of retinal illuminance were computed on the basis of the measured luminance of the test chart and the area of the artificial pupil.

Data for the patients are presented in Figure 9 for white light allumination. Each patient had been refracted in the Department of Ophthalmology and wore the indicated opthalmic correction. No corrections exceeded three diopters. For comparison, data on two normal subjects are also presented. These data exhibit the change in slope usually attributed to the operation of rod and cone mechanisms at different luminances. Note that whereas the patients and the normals have essentially equal acuity at illuminance levels below 0.1 trolands, the acuity of the patients falls far below normal at higher luminances. The maximum acuity achieved by the patients was 20/63, whereas the normal subjects reached an acuity of 20/16. The change in slope of the acuity function of the patients, which occurs at about 20 trolands, is particularly interesting.

Acuity was measured also with blue light, in order to explore the significance of the duplex nature of the acuity function and to identify the receptors responsible for the two segments. The Wratten Nº 47B filter was either placed in the projector or hand-held by the subject. Measurements were first made to investigate whether or not a change in opthalmic correction should be made to compensate for possible effects of ocular chromatic aberration. Perhaps because of the reduced acuity of these patients, it was not possible to show any improvement

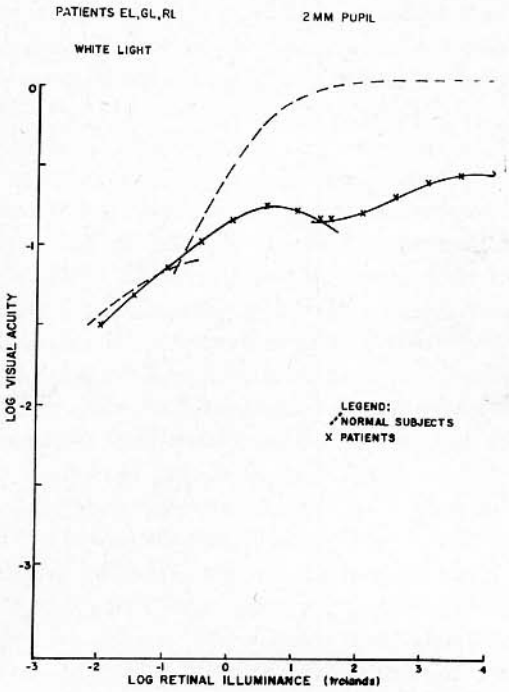


Fig. 9. The luminance function of acuity for the patients and for normal subjects with a white test light.

in the acuity function measured with blue light when changes in the ophthalmic correction were used. Hence, the patients' usual opthalmic corrections were worn.

The acuity data obtained with blue light are plotted in Figure 10, together with the data obtained with white light. It was initially assumed that peripheral rods were responsible for the acuity data overall. Accordingly, the blue light acuity data were adjusted along the retinal illuminance scale to correspond to a density of 1.37 for the blue filter. (This density was computed on the basis of the CIE scotopic function. It differs from the value of 1.45 reported in connection with the dark adaptation data because of a difference in the radiant emission spectrum of the light sources used in the two cases).

It is apparent from Figure 10 that there is excellent agreement between the white light and the corrected blue light data up a level of 10 trolands. Above that level, the blue light data fall systematically above the white light curve.

The blue light data taken alone show evidence of a small change in slope at about the 10 trolands level. Accordingly, it was assumed that the data for illuminances below 10 trolands are produced by one receptor system, those above 10

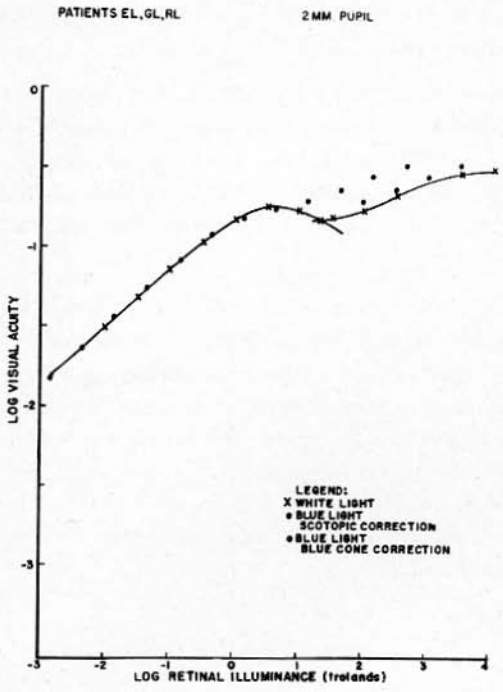


Fig. 10. Comparisons of the luminance function of acuity for the patients with white and blue test lights.

trolands level being produced by a second system. The agreement between the white and corrected blue light data below 10 trolands identifies the receptors system responsible for this portion of the acuity function as peripheral rods.

We next supposed that the upper section of the acuity function was produced by blue cones. This assumption was tested by adjusting the blue light acuity data at levels above 10 trolands to correspond to a density of the Nº 47B filter equal to 0.53, computed by utilizing the blue cone luminosity function shown in Figure 1. The points so adjusted are shown in Figure 10 to agree better with the white light data than before. This result probably justifies our assumption that blue cones are responsible for the upper segment of the acuity curve, although agreement is in this case somewhat less convincing thas in the other instances reported here.

The fact that the corrected blue light data points represent higher acuity than the white light data may be interpreted as follows. Rods may well normally "inhibit" blue cones, at illuminance levels at which the two receptor systems posses nearly equal sensitivity. The presence of this inhibition can explain the deep cusp found in the white light acuity data. Use of the blue filter minimizes the

role of peripheral rods with respect to blue cones. With blue light, the acuity in the region at which the blue cones are operative is therefore enhanced.

This explanation gains credence through an additional fact. The patients reported that the use of the blue filter removed "snow" from the acuity task. This "neural noise" could be produced by rods stimulated to the point of satiation. Another generally confirmatory fact is that the acuity function obtained in blue light fails to show the deep cusp exhibited so clearly in the acuity data obtained with white light.

As in the case of "foveal" dark adaptation, we find that we cannot accept the view that acuity at low luminances is due to what we have called foveal rods. If the blue light data are corrected on the assumption that the scotopic luminosity curve is modified by the presence of macular xanthophyll, they must be moved to the left by .22 log units which greatly worsens the agreement between the white and corrected blue light data. Thus, we must conclude that our patients performed their acuity task at low luminance with rod receptors unaffected by macular xanthophyll. This presumably means that the patients used eccentric fixation during the acuity measurements at low luminance.

SUMMARY AND CONCLUSIONS

Our investigations have led to the identification of a blue cone receptor mechanism never before found completely in isolation. As will be shown in a forthcoming publication, (Ref. 19) this mechanism closely resembles the hypothetical blue mechanism inferred from color mixture data and the blue mechanism isolated functionally by selected conditions of observation. This finding certainly emphasizes the value of psychophysiological study of clinical patients for the development of visual theory.

We have also isolated what we have called foveal rods, and shown that the action spectrum of this receptor system is modified by the absorption spectrum of macular xanthophyll. We have also shown that the action spectrum of various visual functions can be used to identify to some extent the fixation utilized, since the action spectra of foveal and peripheral rods are sufficiently different for differentiation to be made between them.

We have shown that chromatic discriminations can be made with a dichromatic color system based upon blue cones and foveal rods. This demostration that chromatic discriminations are not restricted to cone photoreceptors is also important to color vision theory.

We have shown that blue cones and foveal rods can summate their luminosity contributions, at least under conditions in which the contributions made by the two systems are of approximately equal magnitude.

We have shown that "foveal" dark adaptation in the patients studied consists initially of contributions of blue cones and rods, but that peripheral rods are responsible for adaptation after seven minutes. In peripheral dark adaptation, there are two sets of peripheral rod receptors with different time courses of adaptation.

In acuity at low luminances, our patients used peripheral rods. At high luminances, acuity is mediated by blue cones. At intermediate luminances, acuity is mediated by blue cones and rods, and the rods appear to reduce the acuity which otherwise be possible with the blue cones, perhaps by creating "neural noise".

The complex way in which the patients presumably sometimes used foveal and sometimes peripheral rods, in spite of our best efforts to control their fixation, suggests that future effots should be made to record the precise locus of ocular fixation during various psychophysiological measurements on patients of this type.

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