Sensitivity deficits consistent with aberrant crossed visual pathways in human albinos.

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There is both anatomical and electrophysiological evidence that human albinos have abnormally crossed visual pathways. The present study examined some perceptual consequences of such pathways on the visual abilities of 12 oculocutaneous albinos and one ocular albino.

Measurements were made of visual fields in all subjects. For seven subjects, contrast sensitivity functions were obtained for the central, nasal, and temporal retinas. There was a wide variation in the dimensions of the visual fields, but there was no evidence for a loss corresponding to the origin of the aberrant projections. On the basis of their contrast sensitivity functions, however, it was possible to classify the albinos into two groups. One group, with higher overall sensitivity, showed no differences between central, nasal, and temporal retina. The other group showed a marked depression in sensitivity for the temporal retina, indicating that in some albinos, information from the retinal region corresponding to the aberrant pathway is degraded. (INVEST OPHTHALMOL VIS SCI 21:873-877, 1981.)

An abnormal organization of the neuroanatomical connections of the visual pathways is associated with albinism. Instead of remaining ipsilateral, a proportion of ganglion-cell axons that originate in the temporal retina decussate at the optic chiasm and project to the contralateral lateral geniculate nucleus (LCN). The overrepresentation of decussating fibers is accompanied by disruptions of the laminar structure of the LCN and by functional abnormalities within the visual cortex.

The characteristic anatomical reorganization has been observed among albinos of all species, although extensive physiological and behavioral measures are available only for the Siamese cat. In the Siamese cat, single-unit recording from the visual cortex has revealed two broad classes of response profile. In one class, termed Midwestern, input from the aberrant pathway is suppressed so that there is minimal cortical representation of the region of the retina that extends from the midline to about 20° temporal. In the other class, termed Boston, this retinal area is represented in a small segment of cortex inserted at the boundary between areas 17 and 18. Recent evidence suggests that this dichotomy might represent two extremes of a continuum.

When tested behaviorally, Siamese cats exhibit a variety of visual deficits. Their visual acuity and contrast sensitivity is low compared with that of normal cats and they lack the ability to use binocular cues for depth perception. In addition, perimetric testing has shown that Midwestern Siamese cats show a loss in the nasal visual field corresponding to the site of origin of the anomalous projections from the temporal retina. Boston Siamese cats, in contrast, appear to have normal visual fields.

Guillery et al. have reported anatomical abnormalities within the LCN of human albinos, whereas other studies have demonstrated hemispheric asymmetries in the visual-evoked po-
Fig. 1. Extent of visual fields in two albino subjects. A, Data for subject with the largest fields, who was essentially indistinguishable from normal. B, Data for subject with the most restricted fields.

Such data are consistent with a reduction in the proportion of nondecussated fibers and suggest that human albinos suffer the same anatomical and physiological deficits observed in albinos of other species. It is important to determine, therefore, whether the visual capacities of albinos, assessed psychophysically, also reflect abnormal organization. Although it is well known that albinism is associated with several visual complaints, no attempt has been made yet to relate the deficiencies directly to anomalies of the visual pathways. The present work represents such an attempt. In this preliminary study, visual fields were measured and contrast sensitivity functions for the central, nasal, and temporal retina were obtained. We hoped to find evidence for selective visual losses consistent with a suppression of input from the abnormal retina.

Method

Subjects. The albinos were 13 adults who were solicited through the offices of local physicians and through the Canadian National Institute for the Blind. They included nine female and three male oculocutaneous albinos and one female ocular albino. Fifteen normally pigmented individuals served as controls. The albino subjects had monocular acuities ranging from 20/67 to 20/200. The
control subjects had normal or corrected to normal acuities.

Apparatus. Visual fields were measured with a 1 m² tangent screen viewed from a distance of 50 cm. The target was a bright red dot produced by a 0.5 mW helium-neon laser and back-projected onto the tangent screen. The dot subtended a visual angle of 12 min.

Contrast sensitivity functions were measured with sine-wave gratings generated conventionally on a Tektronix 608 display monitor with a white (P4) phosphor. Mean luminance was maintained at 30 cd/m², and contrast was varied by the experimenter by means of a decibel attenuator. A white screen restricted the view of the gratings to a rectangular 9° by 12°. Viewing distance was 57 cm. Screen luminance was matched approximately to that of the display. Two black fixation dots, each subtending 1°, were positioned 12° to the left and right of the center of the display.

Procedure. Prior to the experiment proper, each albino was tested for the ability to fuse targets presented dichoptically. The presence of stereopsis was ascertained by means of random dot stereograms presented as anaglyphs.

Visual fields were measured for each eye separately. The subject rested his or her head on a chin rest and fixated the center of the tangent screen while the experimenter swept the target slowly (~2.57 sec) across the field, beginning at the top and moving down in 5° steps. The subject indicated when the target was visible and when it disappeared. Scotomatous areas were explored systematically. Some variability might have been expected in the fields of the albino subjects because of a persistent nystagmus. However, repeated measurements of the blind spot suggested that the nystagmus produced only a small error.

Contrast sensitivity functions and high-frequency resolution limits were obtained for each eye for all the normal subjects and seven of the 13 albinos. Contrast thresholds were obtained with central fixation and with fixation at 12° to the left and right of the center of the display. An ascending method of limits was used to assess contrast threshold and two determinations were made at each spatial frequency for each viewing condition. On a given trial the grating contrast was set to a random value below threshold and subjects were required to fixate either the center of the screen or one of the fixation points. Contrast was then increased in 1 dB steps until the subject reported seeing stripes. After the subject had made a threshold judgment using each eye at all three fixation positions, the grating spatial frequency was changed and the sequence was repeated. Two threshold determinations were made at each spatial frequency tested. Before contrast sensitivity was measured, the estimate of high-frequency resolution was obtained by means of a grating with the contrast set at 70%. This was done by having the subject fixate the center of the screen while the spatial frequency of the grating was decreased from a high value to the point where the pattern was just visible.

Results. None of the albinos was able to fuse the dichoptic targets or to perceive depth in the stereograms.

Visual field size and shape varied among individual albino subjects; nine of the 13 had smaller fields than those of the normal controls. The largest fields (Fig. 1, A) were scarcely distinguishable from those of normals, whereas the worst subject (Fig. 1, B) had fields that were severely restricted. But in no case was there any indication of an inability to detect the dot target in the near nasal fields.

The high-frequency cutoff values for the albinos ranged from a low of 2.2 cy/deg to a high of 6.5 cy/deg. As one might expect, the average sensitivity of the albino subjects was well below that of the controls for all but the lowest spatial frequencies at all retinal positions. Closer examination of individual contrast sensitivity functions indicated, however, that the albinos could be subdivided into two groups on the basis of their relative sensitivities.

No formal criterion was used to distinguish the groups because there was no overlap between the functions; the peak sensitivity of the poorest subject in the high-sensitivity group (class 1, n = 4) was about twice that of the best subject in the low-sensitivity group (class 2, n = 3). Since there were no differences between the functions for each eye, data from both eyes of the subjects were pooled and the contrast sensitivity functions, averaged across subjects within groups (normal, albino class 1, albino class 2), are presented in Fig. 2.

Among the normal subjects, sensitivity was equal in the nasal and temporal retina and lower than that of the central retina. The same pattern was not observed for either of the albino groups. Class 1 albinos showed no threshold differences across retinal position. For those in class 2, in contrast, average sensitivity for the central retina was superior to that of the nasal retina. The sensitivity of the nasal retina was superior to that of the temporal retina. The pattern was consistent across all
spatial frequencies tested and all subjects in the groups showed a similar pattern of responses, although the magnitude of the differences varied widely.

**Discussion.** Studies on a variety of albino mammals have shown rather similar anatomical and electrophysiological abnormalities of their visual pathways. The psychophysical findings presented here indicate that the anatomical and electrophysiological anomalies found in human albinos may be reflected also in reduced contrast sensitivity. It is well established that most human albinos suffer from severely reduced visual acuity caused in part by a lack of ocular pigment and by a relatively undeveloped fovea. Such conditions account for the lack of a difference in sensitivity between the central and peripheral retina in some of the present subjects. The most striking aspect of the data, however, is that some albinos show their most severe loss in the temporal retina. Such a result is compatible with the view that input from this region is partially suppressed. The failure to observe a corresponding visual field loss when a bright target spot is used indicates that suppression is not complete.

The separation of albinos into two groups based on the psychophysical data is consistent with the results of previous studies of the visually evoked potential (VEP). These studies also found different response patterns for different subjects. For example, Creel et al. observed that only 14 of 20 human albinos showed an asymmetrical VEP after monocular stimulation. More recently, Creel et al. have obtained evidence for misrouted projections in a much higher percentage of cases by changing the VEP stimulus parameters. Such data suggest that the pathway anomalies may occur in varying amounts, requiring tests of differing sensitivity to demonstrate them.

The present findings, and those just discussed, resemble the two patterns of cortical organization that have been reported in the Siamese cat.
Such an analogy should not be pushed too far, however, given the limitations of sample size. Nevertheless, the cross-species similarity in the pattern of visual deficits and anatomical abnormalities suggests that albino animals could represent a valid model of the human albino condition.

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REFERENCES


The sensitivity to sine-wave flicker of a rod monochromat was compared with that of a normal subject at photopic and scotopic levels of luminance. The sensitivity of the rod monochromat in the low-frequency region (below 3 Hz at scotopic levels and below 12 to 14 Hz at photopic levels) was found to be superior to that of the control. This superiority was most pronounced at photopic levels, where the rod monochromat showed a two-peak sensitivity curve. (Invest Ophthalmol Vis Sci 21:877-879, 1981.)

In one previous study, the flicker sensitivity (temporal modulation transfer function, MTF) of a rod monochromat has been compared with that of a normal subject. The results suggest a close similarity to normal vision except for an overall reduction in sensitivity. We have performed similar experiments on another rod monochromat and have found that although the high-frequency sensitivity of the rod monochromat is inferior to that of a control with normal vision, low-frequency sensitivity is clearly superior.

Methods

Subject. Our subject (author K. N.) is a 35-year-old man who shows all signs of typical rod monochromacy: low visual acuity (0.1 on both eyes in conventional tests, 0.12 when tested with laser-interference gratings), small central scotoma (Goldman-Projection Perimeter, object I, intensities 2 and 3), achromacy (Nagel anomaloscope) and congenital nystagmus (electronystagmography performed). His dark-adaptation curve shows only one branch typical of rod vision, as previously shown.