Dark-adapted L/M-cone-specific Visual Function Measured with a Commercial Perimeter

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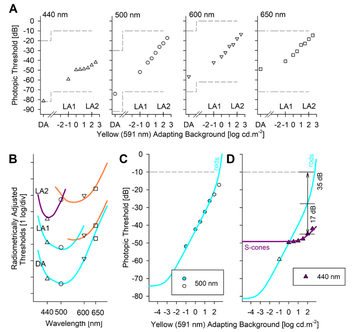
Introduction

Modern computerized static perimeters estimate the distribution of retinal disease severity in inherited retinal degenerations (IRDs) by stimulating focal regions with light across the retina. Sensitivity is defined by the dimmest light perceived at each location. To make sensitivity measures more specific, one takes advantage of differences between three types of photoreceptors: rods, L/M-cones and S-cones. Two-color dark-adapted perimetry[1] has been used to distinguish between rod and cone mediation in IRDs. Short-wavelength automated perimetry (SWAP)[2] using violet stimuli on yellow background has been used to probe S-cone function. There has been, however, little attention paid to L/M-cone specific perimetry. Standard perimetry uses a steady white light adaptation to desensitize the rods and allows measurement of L/M-cone function in normal eyes. In some IRDs such as blue cone monochromacy (BCM), achromatopsia (ACHM), or enhanced S-cone syndrome (ESCS), standard perimetric stimuli are often counterintuitively mediated by light-adapted rods, or S-cones, or both. In more common IRDs, such as retinitis pigmentosa (RP) or cone-rod dystrophy (CRD), there is often no information as to the source of photoreceptor mediation.

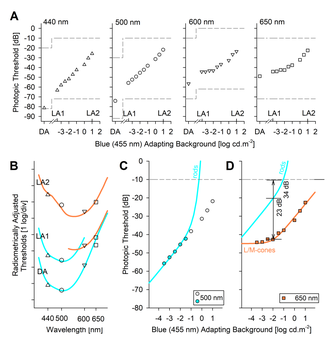
We used a turn-key commercial perimeter with built-in chromatic stimuli and chromatic adapting backgrounds to investigate stimulus and background parameters to define a perimetric outcome measure estimating L/M-cone-specific sensitivity which is effectively dark-adapted.

Adaptation to Yellow



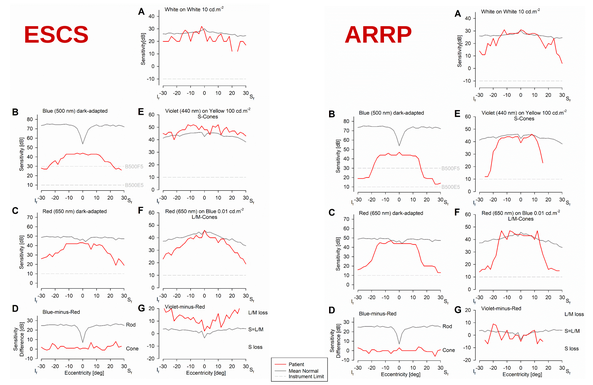
Normal chromatic thresholds obtained dark-adapted (DA) and on increasing yellow backgrounds in the perimacular region.
(**A**) Elevation of chromatic thresholds as a function of background luminance. DA, LA1, and LA2 represent conditions shown in panel B. (**B**) Radiometrically adjusted thresholds at DA, LA1, and LA2 conditions fit with scotopic (cyan), and photopic (orange) luminosity functions, and S-cone spectral sensitivity function (violet). (**C**) Light-adapted 500 nm thresholds mediated by rod (cyan filled circles) fit with rod adaptation model (cyan curve). (**D**) Light-adapted 440 nm thresholds mediated by S-cones (violet filled triangles) fit with S-cone adaptation model (violet curve); rod adaptation model shown to determine minimum effective dynamic range at the standard 100 cd.m^{-2} yellow background typically used for SWAP. Horizontal gray dotted lines indicate instrumental range.

Adaptation to Blue



Normal chromatic thresholds obtained dark-adapted (DA) and on increasing blue backgrounds in the perimacular region.
(**A**) Elevation of chromatic thresholds as a function of background luminance. DA, LA1, and LA2 represent conditions shown in panel B. (**B**) Radiometrically adjusted thresholds at DA, LA1, and LA2 conditions fit with scotopic (cyan), and photopic (orange) luminosity functions. (**C**) Light-adapted 500 nm thresholds mediated by rod (cyan filled circles) fit with rod adaptation model (cyan curve). (**D**) Light-adapted 650 nm thresholds mediated by L/M-cones (orange filled squares) fit with L/M-cone adaptation model (orange curve); rod adaptation model shown to determine minimum effective dynamic range at the optimal 0.01 cd.m^{-2} blue background. Horizontal gray dotted lines indicate instrumental range.

Inherited Retinal Degeneration (IRD) Examples



Enhanced S-cone syndrome (ESCS)[9,10] characterized by developmental absence of rods and increased S-cone. Standard perimetry shows near normal results (**A**). Both blue and red thresholds under DA condition are mediated by cones (**B-D**), as expected from the pathophysiology of the disease. S-cone thresholds with violet stimuli on yellow background are better than normal (**E**). L/M-cone thresholds with red stimuli on blue background are worse than normal in the perimacular region (**F**). Locus by locus subtraction of violet and red thresholds indicates relative increase of S-cone sensitivity or relative decrease of L/M-cone sensitivity (**G**).

Autosomal recessive retinitis pigmentosa (ARRP) typically shows progressive loss of photoreceptors that affect rods before cones. Standard perimetry shows normal results centrally[11] with a fall-off towards periphery (**A**). Both blue and red thresholds under DA condition are mediated by cones (**B-D**). S-cone thresholds with violet stimuli on yellow background (**E**) and L/M-cone thresholds with red stimuli on blue background (**F**) are near normal centrally and their difference is normal (**G**).

Summary

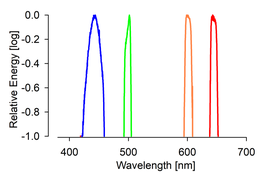
- A commercial turn-key perimeter can be used to perform a range of psychophysical measurements with high-dynamic range chromatic stimuli presented dark-adapted or on a range of chromatic backgrounds.
- Spectral sensitivity functions show expected results under dark-adaptation and counter-spectral light-adaptation.
- Optimal condition for probing dark-adapted L/M-cone-specific function is with red (650 nm) stimuli presented on dim (0.01 cd.m^{-2}) blue (455 nm) background. There is an effective dynamic range >23 dB before possible intrusion of normal rod function.
- A standard vertical perimetric profile using five conditions are proposed to distinguish between rods, L/M-, and S-cone mediated function across the macula and extramacular regions.
- These potential outcome measures are especially relevant for gene therapies in L/M-cone diseases where the aim is to improve long-wavelength sensitivity without disturbing rod and/or S-cone function.

Methods

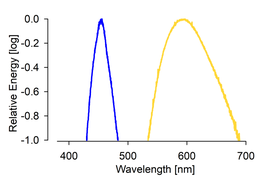
A commercial perimeter (MonCvONE, Metrovision, Perenchies, France) was used unmodified.[3,4] Manufacturer-provided stimulus choices were broad-band achromatic (white) and narrow-band 440 nm (violet), 500 nm (blue-green), 600 nm (orange), and 650 nm (red). All stimuli used in the current work were Goldmann size V equivalent in diameter and 200 ms in duration. Thresholds were measured in normal subjects and patients under dark-adapted (DA) or light-adapted conditions. Light-adaptation choices included broad-band achromatic (white), or yellow (591 nm), or blue (455 nm) with each available over a broad dynamic range. Testing was performed with no refractive correction in normal subjects and IRD patients with dilated eyes.

Chromatic stimuli were adjusted by radiometric differences and fit with spectral luminosity functions to determine mediation.[5,6] Two different mathematical equations were used for rods and cones to model the expected elevation of thresholds with increasing background luminance.[7,8]

Stimuli



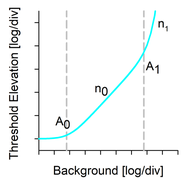
Backgrounds



Rod Background Adaptation Model

$$y = 10\left\{\log\left[\left(\frac{10^{x}+10^{A_0}}{10^{A_0}}\right)^{n_0}\right]+\log\left[\left(\frac{10^{x}+10^{A_1}}{10^{A_1}}\right)^{n_1}\right]\right\}$$

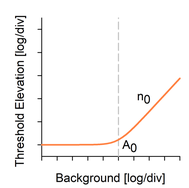
where y is the threshold elevation above the dark-adapted value in dB units, x is the background luminance in $\log_{10}$ units, A_0 is the low luminance knee-point in $\log_{10}$ units, n_0 is the slope of the low luminance section, A_1 is the saturation knee-point in $\log_{10}$ units, and n_1 is the slope describing the saturation section.



Cone Background Adaptation Model

$$y = 10\left[\log\left(\frac{10^{x}+10^{A_0}}{10^{A_0}}\right)^{n_0}\right]$$

where y is the cone threshold elevation above the cone plateau (dark-adapted) value in dB units, x is the background luminance in $\log_{10}$ units, A_0 is knee-point in $\log_{10}$ units, and n_0 is the slope.



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