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Major review

Acquired color vision deficiency

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ABSTRACT

Acquired color vision deficiency occurs as the result of ocular, neurologic, or systemic disease. A wide array of conditions may affect color vision, ranging from diseases of the ocular media through to pathology of the visual cortex. Traditionally, acquired color vision deficiency is considered a separate entity from congenital color vision deficiency, although emerging clinical and molecular genetic data would suggest a degree of overlap. We review the pathophysiology of acquired color vision deficiency, the data on its prevalence, theories for the preponderance of acquired S-mechanism (or tritan) deficiency, and discuss tests of color vision. We also briefly review the types of color vision deficiencies encountered in ocular disease, with an emphasis placed on larger or more detailed clinical investigations.

1. Introduction

Color vision deficiency secondary to ocular or visual pathway disease—known as acquired color vision deficiency—was perhaps the first recorded form of dyschromatopsia.[86] The English oculist, Dawbeney Turbervile, described a case of probable cerebral achromatopsia in a letter to the Royal Society published in 1684.[207] A similar—and most probably the same—case was elucidated by the natural philosopher, Robert Boyle, in his treatise *Uncommon observations about vitiated sight*[22] in 1688. Although these reports postdate by several centuries Albertus Magnus' description of a patient with probable cone dystrophy, the latter's report makes reference only to hemeralopia.[202] The traditional classification of color vision deficiency suggests that congenital and acquired deficiencies form 2 distinct entities.[66] Congenital color vision deficiency is said to be present from birth, stable, bilaterally symmetrical, and is thought to affect the entire field of vision. Acquired color vision deficiency, by contrast, may demonstrate progression or regression, may affect one eye or both eyes asymmetrically, and may affect only a portion of the visual field. In contrast to congenital color vision deficiency, acquired color vision deficiency is believed to be highly symptomatic.[66] Although acquired color vision deficiency may have a higher overall prevalence than congenital color vision deficiency,[43] there are limited data. With improved understanding of both the etiology of congenital color vision deficiency and of other congenital cone photoreceptor disorders, a degree of overlap is evident.[184] Acquired color vision deficiency may be classified by the site of pathology or by its

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clinical characteristics. Although congenital color vision deficiency has a predilection for affecting an individual cone class—and thereby a single subsystem of color vision—such characteristics are far less frequently encountered in acquired color vision deficiency.[184]

2. The substrate of color vision

2.1. *Receptoral*

Normal human color vision is trichromatic[127]; that is, any color can be matched by a mixture of 3 judiciously selected primary colors (provided that their wavelength may be varied or that color subtraction is permitted). The physiologic substrate of trichromatic color vision is the cone photoreceptor, of which there are 3 classes: the short- (S-), medium- (M-), and long- (L-) wavelength sensitive cones. The different classes of cone have overlapping, but distinct, spectral sensitivities (see Fig. 1). The peak sensitivities lie at about 419 nm, 531 nm, and at 558 nm for the S-, M-, and L-cones (see Fig. 1).[21] Under certain testing conditions[25]—and in certain pathologic states[161]—rods may influence, or participate in, the perception or discrimination of color. The response of any individual photoreceptor is unidimensional and cannot alone convey unambiguous information about the spectral nature of incident light (the so-called *principal of univariance*). Color vision is derived from a comparison of the rates of quantum catches signaled from the different classes of cone. The S-cones are absent from the foveola, comprise approximately 7%–10% of the cone photoreceptor population based on histologic observation,[2] and form 5.7 ± 0.7% (mean ± standard deviation) of the photoreceptor mosaic imaged *in vivo* about 1° from fixation.[72] The M- and L-cones share many similarities in terms of their known histology, physiology, and molecular genetics. These cone types comprise the remainder of the cone population, though considerable variability in the L-cone:M-cone ratio occurs among those with normal vision. Adaptive optics imaging suggests a range

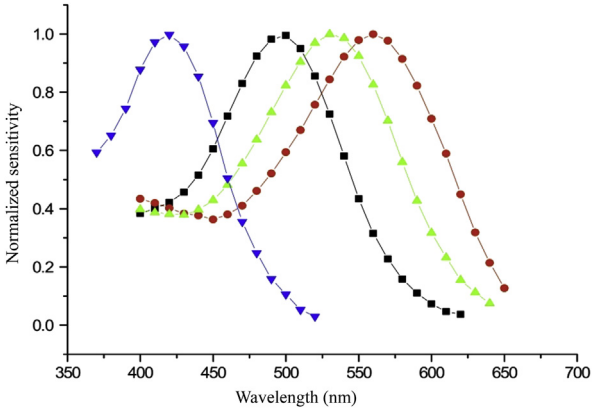

Fig. 1 – The spectral sensitivities of the 3 classes of cone photoreceptor (*S-cones, blue inverted triangles*; *M-cones, green triangles*; *L-cones, red circles*) and of the rods (*black squares*) plotted against wavelength in nm. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

in males from 1.1:1 to 16:1 (with more extreme ratios favoring M-cones occurring in female carriers of protanopia).[72] The spectral sensitivity of the photopigments is determined by the protein portion or "opsin." Opsins are heptahelical proteins that are bound to 11-cis-retinal and are members of the G-protein coupled superfamily of receptor molecules. The M- and L-cone photopigments are coded in an array on the X-chromosome and share a 96% similarity with each other in terms of primary structure, whereas the S-cone photopigment is coded on chromosome 7 and shares 43% identity with the M- and L-cone photopigments.[141]

2.2. *Postreceptoral*

There is evidence to suggest that the processing of spectral information from the visual scene is conducted *via* 2 subsystems of color vision that are phylogenetically distinct.[128] The first, and more ancient, system compares quantum catches in the S-cones to the M- and L-cones. The second, more recent, subsystem is thought to have partially commandeered a system initially specialized for spatial resolution. This is an important point in the context of acquired color vision deficiency as it has ramifications on the anticipated concomitant clinical features.

The S-cones synapse with S-cone bipolar cells and then with at least 4 different types of ganglion cell.[193] The most extensively studied of these is the small bistratified ganglion cell which receives "on" excitatory input from S-cone "on" bipolar cells with the "off" input derived from the M- and L-cones *via* diffuse "off" bipolar cells.[107] The details of the remaining ganglion cell types subserving the S-cones are yet to be fully elucidated, though at least one of these cell types receives an inhibitory S-cone input[107] (The existence of such inputs has been a matter of some controversy).[55] Ganglion cell axons subserving the S-cone system synapse in the intercalated layers of the lateral geniculate nucleus[71] and input into the lower echelons of layer 3 and 4A of the visual cortex.[193]

Spectral information from the M- and L-cones is carried by the midget ganglion cells. The center of the receptive field of the midget cells—at least in the central retina—is drawn from a single cone (*via* a single midget bipolar cell) and the surround from multiple cones, though there exists some controversy regarding the nature of such inputs (i.e., whether the surround is drawn from cones of a different class or indiscriminately from both).[193] The midget cells synapse in the parvocellular layers of the lateral geniculate nucleus (3, 4, 5, and 6) which in turn project to layer 4Cβ of the visual cortex.[193]

Like the responses from individual photoreceptor cells, the response from individual ganglion cells is unidimensional and does not alone convey an unambiguous signal regarding the spectral nature of a stimulus: this is in effect an extension of the principle of univariance. As a consequence, the spatial resolution of color vision is necessarily inferior to that for luminance discrimination.[55] For small targets, color vision is tritanopic.[131] Although there are fewer reliable data regarding the point discrimination acuity of the M/L-subsystem, other measures suggest that its resolution is superior to the S-cone system,[30,57] although the magnitude of this superiority is again a matter of conjecture.[120]