

10

NEURAL CHANGES IN VISION AFFECTING THE PRESBYOPIC EYE

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One of the major tasks of neural mechanisms in the human visual system is to undo problems created by the imperfect optics of the eye. With aging, the optics of the eye change (see Chapter 9) and the task of neural mechanisms becomes increasingly demanding. Here, we discuss neural factors affecting visual performance that occur in association with presbyopia. We briefly describe changes in chromatic, spatial, binocular, and temporal vision with respect to normal aging. More extensive reviews are available elsewhere.^{1,2} We do not describe visual disorders that, of course, occur more frequently after the onset of presbyopia. The final section describes visual adaptation mechanisms that mitigate some of the optical and early-stage neural changes associated with aging.

SENESCENT CHANGES IN SPECTRAL SENSITIVITY

The limits of visual sensitivity, approximately 400 to 700 nm, depend on the absorption characteristics of the eye's optics at short wavelengths and the photopigment absorption spectra at long wavelengths. Because the ocular media, primarily the lens, increase in density with age, the visible spectrum correspondingly decreases at short wavelengths. This change is continuous throughout one's lifespan but largely goes unnoticed until middle age when early signs occur,

such as more difficulty driving at night or more difficulty discriminating blues and violets.

Age-related changes in visual sensitivity have both an optical and a neural basis. These changes occur continuously throughout the lifespan so the terms *younger* and *older* are relative with respect to an average adult life from about 20 to 85 years. This is illustrated in Figures 10-1 and 10-2. Psychophysical studies have quantified the age-related losses in visual sensitivity under both scotopic (dark adapted) and photopic (light adapted) conditions. Early studies documented changes in dark adaptation (thresholds measured as a function of time) that affect both branches of the 2 scallop-shaped branches—the first branch being mediated by cone photoreceptors and the second being mediated by rods. Not only are the asymptotes of each of these branches elevated, but the rate of photopic and scotopic dark adaptation also decreases with increasing age (see Figure 10-1).³ More recent studies have separated the effects of reduced pupil area and increased optical density of the elderly eye from neural losses in sensitivity. It is clear from these studies that age-related losses in visual sensitivity are partly due to preretinal changes and partly due to neural losses that occur in the photoreceptors and neural pathways.

The importance of receptor changes in mediating age-related changes in dark adaptation is related, in part, to the changes in photopigment kinetics. That

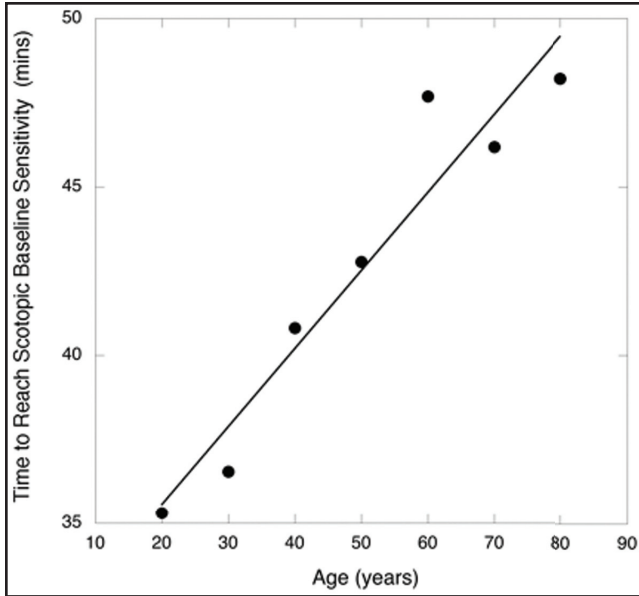


Figure 10-1. Time to reach within 0.3 log units of scotopic baseline sensitivity. Data from subjects grouped by age decade. Least-squares linear regression line was fitted to the data ($r = 0.96$). (Based on data compiled and replotted from Jackson GR, Owsley C, McGwin G Jr. Aging and dark adaptation. *Vision Res.* 1999;39(23):3975-3982.)

is, after photopigment bleaching, the recovery time is slower in the elderly eye. The amount of rhodopsin photopigment extractable from rods, however, seems not to change with age. This is curious because there is a substantial loss in rod numbers with age, implying that the remaining individual rods of the elderly eye contain more photopigment than in the younger eye. However, efficiency of receptor responses decreases in a manner that resembles losses in photon capture. This may be because elderly photoreceptors undergo morphological changes of the outer segments so that they become more convoluted in shape. These changes may contribute to losses in scotopic sensitivity because rhodopsin molecules now possess less-than-optimal orientations for absorbing light.

Under photopic conditions, vision is mediated by 3 different classes of photoreceptors, with each having maximal absorption at short (S-), middle (M-), or long (L-) wavelengths. There are several methods for isolating each cone type, and initial studies focused on age-related losses in sensitivity of the S-cone pathway. This choice was largely guided by evidence that S-cones are vulnerable to loss in retinal disease. In normal aging, S-cone pathways do lose sensitivity, but there are similar losses in the sensitivity of M- and L-cone pathways. Figure 10-2 shows sensitivity losses on the order of 0.13 log units (23%) for each decade of life beginning in adolescence and continuing for the entire lifespan.⁴

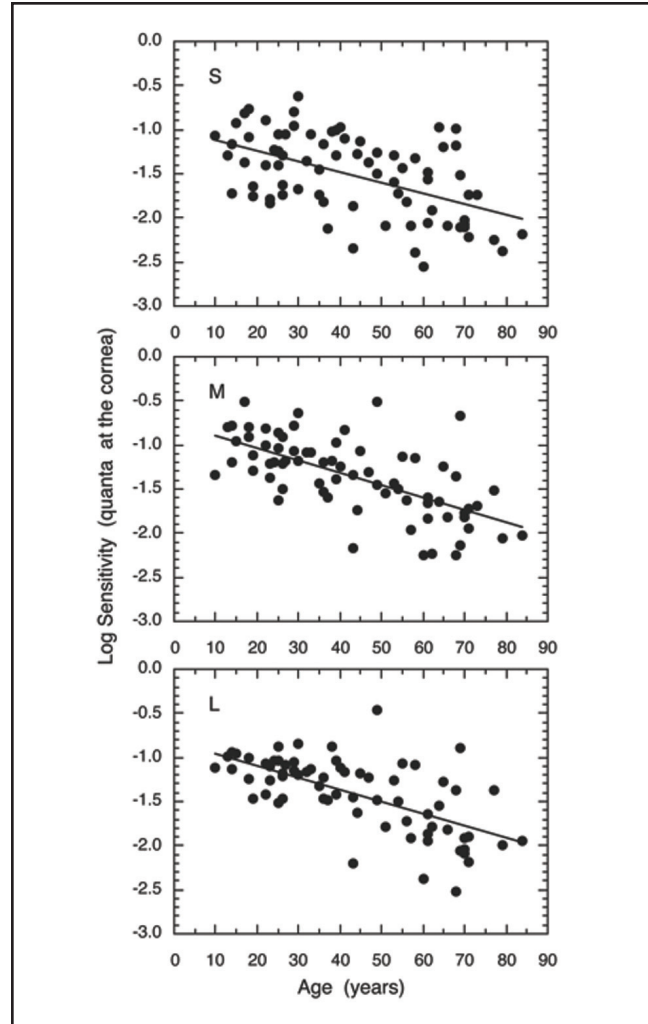


Figure 10-2. Log relative sensitivity (on a quantal basis) of S-, M-, and L- cone mechanisms is plotted as a function of age. (Based on data compiled from Werner JS, Steele VA. Sensitivity of human foveal color mechanisms throughout the life span. *J Opt Soc Am A Opt Image Sci.* 1988;5(12):2122-2130.)

It is clear that these losses in sensitivity are due to both optical and neural factors.

COLOR DISCRIMINATION AND APPEARANCE

Losses in visual sensitivity with age are due to reduced light reaching the retina and reduced sensitivity of photoreceptors. These changes are consistent with the idea that an older person is similar to a younger person, but operating effectively at a reduced light level. Because visual performance often depends on light level, some changes in the elderly eye may be simulated by a reduction in light level. This is the case for color discrimination.

As with cone sensitivity losses, hue discrimination measured with standardized arrangement tests declines with age, beginning in adolescence or early adulthood. On the Farnsworth-Munsell 100-hue test, these losses appear to be greater for tritan (S-cone) discriminations than for M- and L-cone discriminations. However, this effect is at least partly due to the construction of the test. When chromatic discrimination is tested under conditions that equate stimuli for individual subjects at the retina (ie, corrected for pupil size and ocular media density), losses are observed throughout the color space for both spectral and non-spectral stimuli. These studies demonstrate that age-related losses in chromatic discrimination are due, in part, to changes in neural pathways.

It is reasonable to expect that the effects of lens brunescence would be to shift color perception in the elderly, much like wearing yellow goggles in younger persons. In fact, color appearance of short-wave stimuli is initially modified by yellow filters. However, short-term effects of spectral filtering are not the same as the long-term adaptation to the slowly changing lens coloration associated with aging. A number of studies demonstrate that color perception is surprisingly stable across the lifespan when tested with color-naming methods using spectral lights, reflective surfaces, and simulated Munsell samples. In the latter case, as demonstrated by Figure 10-3, color naming of short-wave stimuli was shown to be independent of an individual's ocular media density.⁵ This is probably necessary for color nomenclature to be meaningful. Renormalization of color mechanisms to maintain color constancy throughout life is discussed further in the final section of this chapter.

SPATIAL VISION

In clinical settings, spatial vision is usually defined by visual acuity—the minimum angle of resolution measured with high-contrast symbols and moderate illumination. A wide range of results has been reported, with some older studies reporting that visual acuity is stable until approximately the age of 50 years and then progressively declines (see Chapter 9). When subjects are not screened for disease and are tested with their habitual refraction, visual acuity drops off more rapidly with age. More informative, however, are studies with careful screening for disease and optimized refraction for the test distance. These studies show better overall visual acuity with a slow

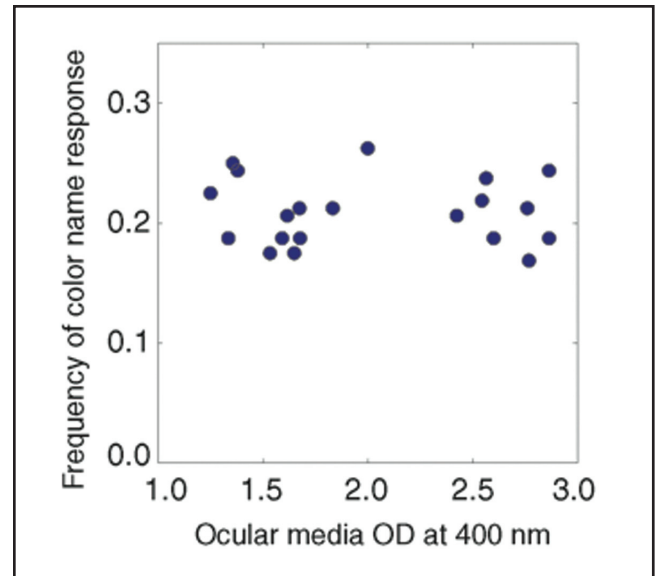


Figure 10-3. Proportion of blue responses to 40 simulated Munsell chips presented on a computer screen plotted as a function of ocular media density. The slope of the least-squares linear regression line did not differ significantly from zero. The range of ocular media density shown spans the lowest values typically found in an adult population to values typically diagnosed as early-stage cataract. (Hardy JL, Frederick CM, Kay P, Werner JS. *Psychol Sci*, 16(4), pp 321-327, copyright 2005 by SAGE Publications. Reprinted by permission of SAGE Publications.)

progressive decline after approximately age 25 years. It is not clear which data sets should be used to define what is meant by normal aging, but the higher values with optimized conditions of testing indicate that most normal individuals have the potential for much higher spatial resolution than suggested by earlier studies. Distance vision of 6/6 is not unusual for the entire lifespan. Vernier acuity (eg, alignment of 2 bars separated by distances less than a cone diameter), in contrast, exhibits little or no alteration with age.

A more complete characterization of spatial vision is provided by the contrast sensitivity function (CSF) measured with sinusoidal gratings of varying spatial frequency (number of cycles per degree [cpd]). With luminance-modulated stimuli under photopic conditions, several studies report greater age-related sensitivity loss for high compared with low spatial frequencies. As with most other performance characteristics, careful studies that refract subjects for the test distance and screen for ocular and retinal disease tend to reveal nearly linear changes as a function of age after adolescence or early adulthood. These losses are due to both optical (eg, smaller pupils, greater ocular media scatter and absorption) and neural factors.

To control for optical factors and, by default, assess neural factors responsible for age-related losses in the photopic CSF, high spatial frequency sensitivity has been measured using laser interferometry to bypass the eye's optics and reduce intraocular scatter. These results, which are limited, demonstrate that neural factors are responsible for approximately half of the age-related losses in high spatial frequency sensitivity. It is also possible to use adaptive optics (AO) to determine how much the higher-order aberrations contribute to age-related declines in the CSF. Figure 10-4 shows that higher-order aberration correction over a 6-mm pupil produces large improvements in the CSF.⁶ Older individuals typically have smaller pupils than young individuals; therefore, measurements were repeated with a 3-mm pupil to evaluate the influence of higher-order aberrations under more natural conditions. All observers exhibited higher contrast sensitivity with AO correction, but the benefit of this optical correction was less for both age groups compared with the 6-mm pupil condition. Interestingly, contrast sensitivity with AO compensation for the older observers was similar for both pupil sizes. This similarity could result from a balance of several optical factors; with a 6-mm pupil, higher retinal illuminance will improve sensitivity, but this may be offset by the presence of more residual aberrations. With a 3-mm pupil, the reduction in retinal illuminance may be balanced by the reduction in higher-order aberrations. Importantly, the quality of the eye's optics was better for older observers during AO compensation than for younger observers without AO compensation but, even under these conditions, contrast sensitivity was better for the younger observers. This clearly demonstrates that neural factors may set a hard upper limit on how much vision can be improved with compensation of higher-order aberrations in the elderly.

At any age, spatial vision is degraded under scotopic conditions, but the pattern of age-related loss is quite different than under photopic conditions.⁷ After 30 minutes of dark adaptation and retinal illuminance approximately equated for different age groups, the scotopic contrast sensitivity functions do not reveal greater losses for high spatial frequencies than for low spatial frequencies.

TEMPORAL VISION

Temporal resolution has been quantified historically by the critical flicker frequency (CFF)—the

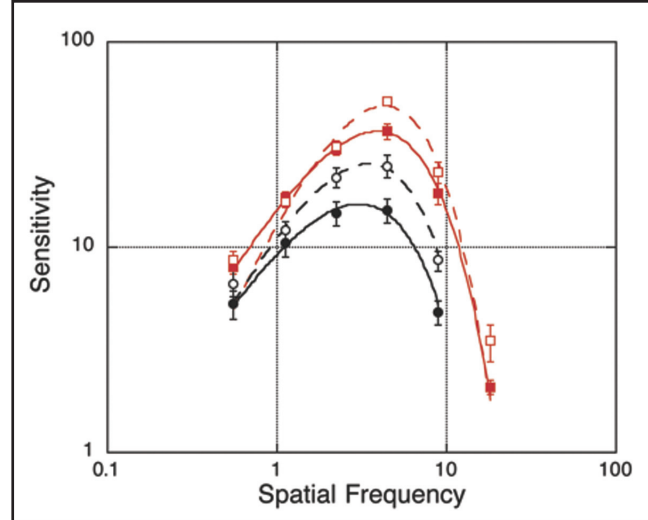


Figure 10-4. Average contrast sensitivity on a log-log scale for young observers (squares = mean age 23 years) and older observers (circles = mean age 76 years) with 6-mm pupils. Solid symbols and curves represent data without adaptive optics (AO) compensation; open symbols and dashed curves denote data with AO compensation. Curves were fitted using a double-exponential function. Error bars are ± 1 standard error of the mean. (Reprinted with permission from Elliott SL, Choi SS, Doble N, Hardy JL, Evans JW, Werner JS. Role of high-order aberrations in senescent changes in spatial vision. *J Vis.* 2009;9(2):24:1-24:16. Copyright Association for Research in Vision and Ophthalmology [ARVO].)

lowest frequency that is experienced as fused and therefore not discriminable from a steady stimulus. Because the CFF declines with retinal illuminance, studies that do not control for age-related changes in ocular media transmission invariably find losses in temporal resolution in the elderly. As with acuity in the spatial domain, CFF characterizes only the high temporal resolution of an individual. A more complete characterization of the visual system is provided by the temporal CSF.

Direct measurements of the temporal CSF reveal small age-related losses that are greater for higher temporal frequencies. These results are generally consistent with those quantifying temporal vision using a psychophysical measure of the temporal impulse response function—the theoretical response to a stimulus of infinitely short duration. The Fourier transform of the temporal impulse response function is directly related to the temporal CSF. The temporal impulse response function permits the theoretical derivation of both excitatory and inhibitory processes contributing to temporal response. This approach demonstrates that some elderly observers have a loss in temporal inhibition, which changes the shape of

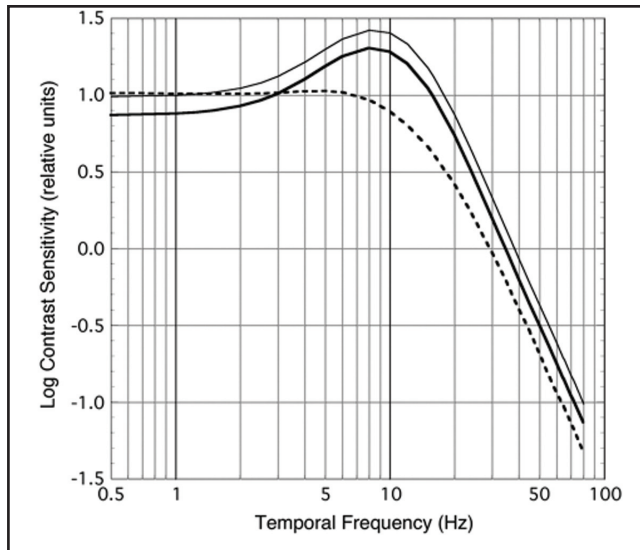


Figure 10-5. Temporal contrast sensitivity functions derived from impulse response functions. Theoretical observers were created based on average data for different age groups. Log contrast sensitivity is plotted as a function of temporal frequency for a theoretical 20-year-old subject (gray solid curve) and 80-year-old subjects with normal (black solid curve) or no inhibition (dashed curve). (Adapted from Shinomori K, Werner JS. Senescence of the temporal impulse response to a luminous pulse. *Vision Res.* 2003;43(6):617-627.)

the temporal contrast sensitivity,⁸ as shown in Figure 10-5. Because retinal illuminance was controlled in this experiment, the loss in high-frequency sensitivity of the elderly cannot be ascribed to optical factors. For many other individuals, however, temporal inhibition is not lost, and sensitivity to luminance-varying stimuli is only modestly affected by aging.

BINOCULAR VISION

Integration of signals from the 2 eyes begins in the visual cortex. Tests of binocular vision thus provide a valuable probe for evaluating age-related changes in cortical mechanisms. Clinically, it is important to understand binocular vision in relation to refractive corrections that affect the 2 eyes differently (eg, monovision), especially if aging has selective effects on binocular integration.

One index of binocular integration is based on summation of signals to the 2 eyes, such as the improvement in contrast sensitivity measured binocularly versus monocularly. Theoretically, binocular viewing is expected to improve contrast sensitivity by $\sim\sqrt{2}$ over monocular viewing. This value is attained for young individuals, but for elderly individuals,

binocular summation is significantly reduced,⁹ which represents a degradation in cortical binocular neurons at some level.

A more specialized function of cortical binocular mechanisms is to mediate stereopsis based on retinal disparity for objects at different distances from the point of fixation. With standardized tests such as the Verhoeff stereopter, stereo resolution (the minimum retinal disparity that can be detected) decreases with age. This could be due, in part, to changes in spatial vision at a monocular level. To control for this, Laframboise et al¹⁰ measured the binocular correlation required for thresholds. They found that the binocular correlation required to perceive stereo depth was significantly higher in older than in younger observers.

ADAPTATION MECHANISMS SUPPORTING STABILITY OF PERCEPTION IN VISUAL AGING

Given the dramatic sensitivity losses and changes in the spectral distribution of the retinal stimulus with normal aging, a surprising feature of the senescent visual system is how little change occurs in many aspects of visual appearance. That is, in many ways, the world appears to “look” the same to older observers despite evident and pronounced changes in their optics and neural processes. This suggests that visual coding is continuously recalibrated to maintain consistent perceptual experiences by compensating for sensitivity changes in the observer. Some of the best evidence for this perceptual constancy comes from studies of color appearance. As noted above, the older, brunescent lens severely restricts the intensity of short wavelength light reaching the retina and thus biases the average light spectrum the observer is exposed to. Yet, the stimulus that observers perceive as achromatic remains remarkably stable across the lifespan. Similarly, there is little change in the wavelengths chosen as spectral unique hues (pure blue, green, or yellow).

One likely mechanism contributing to this perceptual recalibration is visual adaptation. If the receptors or postreceptoral neurons adjust their sensitivity inversely with the level of stimulus exposure (eg, so that S-cones increase their gain when their average stimulation decreases), then this adaptation will act to discount biases in stimulation, and the spectrum that

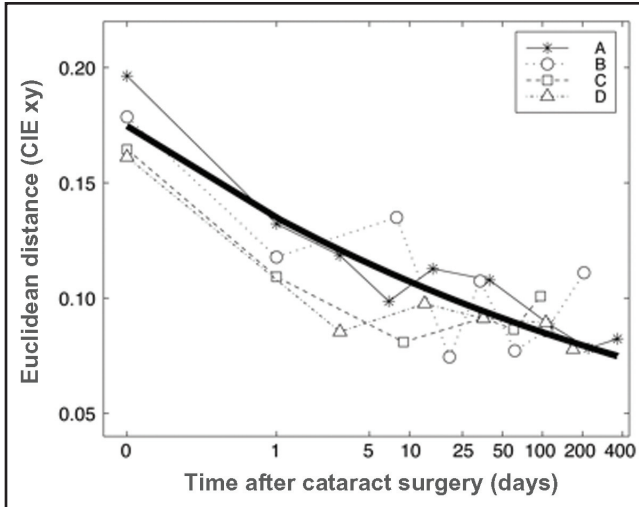


Figure 10-6. The shift in achromatic settings over time is plotted for 4 observers (A to D). The x-axis shows the days from surgery on a log scale. The y-axis shows the Euclidean distance in CIE x,y space from D65. The bold curve line shows the mean of the best fitting decaying exponential functions for each observer. (From Delahunt PB, Webster MA, Ma L, Werner JS. Long-term renormalization of chromatic mechanisms following cataract surgery. *Vis Neurosci.* 2004;21(3):301-307, reproduced with permission of Cambridge University Press.)

appears white will remain the average ambient spectrum in the observer's environment. Such adjustments are vividly illustrated by the changes in color appearance following cataract surgery, as shown in Figure 10-6. When the cataractous lens is first replaced, the retina is flooded with increased levels of short wavelength light, and the world appears noticeably brighter and blue. Yet, these after-effects gradually diminish as the observer adapts to the new average spectrum until the stimulus that appears gray again returns to close to the same stimulus chosen before surgery.¹¹ An intriguing aspect of this adjustment is that the perceptual changes occur gradually over a period of weeks or months, thus implying a form of adaptation that operates over much longer timescales than conventional light adaptation.

Such effects suggest that adaptation plays an important role in maintaining stable perceptions across the lifespan of the observer. But to what extent do the processes of adaptation themselves remain stable with aging? If the strength or form of adaptation is compromised, then this could underlie some age-related deficits in visual function. One case where this occurs is in the recovery of sensitivity during dark adaptation, which occurs at a slower rate in older observers (see Figure 10-1). Significant age-related changes have also been reported in a form of adaptation known as

“transient tritanopia,” which is a temporary loss in sensitivity to lights detected by S-cones after turning off a light that is visible only to the L- and M-cones.¹² This sensitivity loss is thought to result from a saturating rebound in the response of color-opponent channels and is larger in older observers, indicating that age-related changes in adaptation can occur beyond the receptors.

Adaptation itself probably occurs at multiple levels of the visual system.¹³ For example, adaptation effects on perceived movement or shape are well-known and must arise at cortical levels where pattern-selective attributes, such as motion and orientation, are first represented. Similarly, adaptation effects have been widely studied in the context of sensorimotor coordination (eg, how pointing or reaching is modified when the visual field is displaced while viewed through prisms). A number of studies have examined the influence of age on visuomotor adaptation. These have tended to show reduced adaptation in older adults, although this has been attributed to differences in control strategies rather than sensory recalibration. In contrast, surprisingly few studies have examined how aging impacts many of the visual after-effects associated with pattern perception. One such study reported weaker adaptation using a shape distortion after-effect chosen to reflect adaptation at high (extrastriate) levels of visual coding.¹⁴

In a study specifically relevant to presbyopia, Elliott et al¹⁵ examined age-related changes in adaptation to image blur. After viewing a blurred (or oversharpened) image, a physically focused image appears too sharp (or blurred; Figure 10-7). These blur after-effects presumably reflect sensitivity changes at cortical levels, which adjust to the spatial-frequency content of the images and have been shown to selectively adjust to the patterns of blur arising from different lower-order and possibly higher-order aberrations of the eye. They may, therefore, play a role analogous to normalizing the white point in color coding, in maintaining perceived image focus by compensating spatial coding for optically induced blur in the retinal image. The size of the blur after-effect was indistinguishable in younger and older observers, suggesting that the magnitude of neural adjustments to image blur remains largely intact with aging. However, it is not known whether there are changes in the dynamics of blur adaptation. Several studies have also demonstrated increases in acuity following adaptation to defocused images, although it has not been established whether these improvements occur to the same extent in older observers.^{16,17}

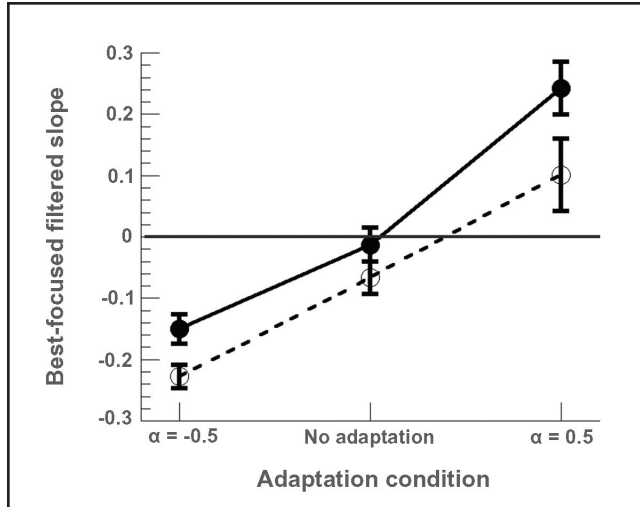


Figure 10-7. Physical blur level perceived as best-focused before or after adapting to blurred ($\alpha = -0.5$) or sharpened ($\alpha = +0.5$) images. Plots show the average settings for young adults (solid line) or older observer (dashed line). Values on the y-axis correspond to the slope of the filtered image spectrum (log amplitude versus log frequency), relative to the original unfiltered image. Negative or positive values correspond to blurred or sharpened spectra, respectively. (Reprinted with permission from Elliott SL, Hardy JL, Webster MA, Werner JS. Aging and blur adaptation. *J Vis.* 2007;7(6):8.1-8.9. Copyright Association for Research in Vision and Ophthalmology [ARVO].)

In presbyopes, adaptation to blur should tend to discount the increased blur in their retinal image so that the world continues to appear in focus. Correcting their vision should thus cause the stimulus to appear too sharp. Interestingly, Elliott et al¹⁵ observed some evidence for this recalibration. Older observers, whose defocus was corrected, chose significantly blurrier images as perceptually focused compared with young adults, which is consistent with habitual adaptation to the uncorrected level of blur. A further possibility is that the adaptation might be able to adjust perceived focus for the differences in blur with viewing distance. Depth-dependent blur after-effects have been demonstrated when distance is simulated as a size change, but it is not known whether the visual system can establish different adaptation states for near and far vision in natural viewing.

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