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Rapid method for assessing rod function using recovery of spatial contrast thresholds following a bleach

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ABSTRACT

Poor vision in low light is a common complaint of elderly people. This poorly understood phenomenon is likely to involve both receptoral and post receptoral mechanisms. We investigated the recovery of contrast thresholds for sine-wave gratings of low spatial frequencies and low mean luminance as a function of time in darkness after photo pigment bleaching. Thirteen subjects aged 30.4 (±10.7) years took part in the study. Contrast thresholds were measured for 15 min following almost complete photo pigment bleaching. The stimuli were achromatic sinusoidal gratings of 0.5, 1 and 2 cycle per degree (cpd) generated on a CRT monitor. They had mean luminance 0.01 cd m^{-2} and subtended 10° in diameter. The dynamics of the recovery at each spatial frequency were modelled using monophasic and biphasic exponential decay functions. The data were best modelled by a bi-phasic decay with a distinct transition point around 7 min after the bleach. Both phases followed an exponential decay. The time constant (mean, standard error) for the first phase was 0.35 (0.04) min while for the second phase it was 5.15 (0.27) min. This difference was statistically significant ($p < 0.001$). A control experiment revealed the second, slower phase was mediated by rod photoreceptors. Maximum contrast sensitivity was reached 15 min after a photic bleach. The dynamics of contrast sensitivity recovery follow two phases and these may be attributed to the cone and rod systems.

1. Introduction

The recovery of sensitivity to a luminance target following exposure to a photo-bleach has been known for many years (Hecht et al., 1937; Lamb and Pugh, 2004; Reuter, 2011). This classical recovery function, usually plotted in terms of time following a desensitising bleach, is composed of several kinetically distinct components and is divided in to rod- and cone-mediated sections (Lamb, 1981). Many systemic conditions, for example liver disease, adversely affect the kinetics of this recovery. Sensitivity recovery is slowed in later life (Jackson et al., 1999) and has been shown to be abnormal in the presence of ocular diseases including diabetic retinopathy (Henson and North, 1979) and Age Related Macular Degeneration (Brown et al., 1986; Owsley et al., 2000; Owsley et al., 2001; Owsley et al., 2007; Dimitrov et al., 2008).

The speed of dark adaptation is dependent on the regeneration of opsin to rhodopsin, the so-called retinoid cycle (Lamb and Pugh, 2004). However, it is still not clear whether rod-mediated functional deficits in AMD in particular, are primarily caused by a reduction in the number and/or sensitivity of photoreceptors, by post-receptoral abnormalities or by damage to other tissues, such as the Chorio-Bruch's RPE complex (CBRc) (Curcio et al., 1996). Feigl et al. (2007) proposed that most functional impairment in early AMD is post-receptoral, their findings were based on psychophysical and electrophysiological data. They suggested that changes in the CBRc induce a relative hypoxia in the intermediate layers of the retina. Bearing in mind this ischemia/post-receptoral hypothesis, it could be interesting to examine the recovery of the visual system to stimuli that depend on the activity of post-receptoral processing rather than the recovery of simple luminous thresholds as in the classical dark adaptation curve described above. Spatial contrast threshold detection is a good candidate for such a test, as it uses a stimulus with constant mean luminance and is mediated through post receptoral mechanisms via parvo-cellular (P) and magno-cellular (M) pathways (Lee, 2011).

It is thought the M pathway dominates detection of spatial patterns in the mesopic (rod- and cone-mediated) and scotopic (rod-dominated) ranges of retinal illumination. Purpura et al. (1988) used a primate model, to show that M cells, rather than P cells were sensitive to temporally modulated sine gratings at low

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spatial frequency (0.6–1.6 cpd) when the mean retinal illumination was lower than 0.43 td which is equivalent to the low mesopic range in humans. D'Zmura and Lennie (1986) using a technique to isolate rod and cone systems, found that over most of the mesopic range, the spatial contrast sensitivity of the cone system was lower than that of the rod system at low spatial frequencies (1–3 cpd). If this is so, then it could be expected that recovery in contrast sensitivity following a bleach, would contain rod- and cone-mediated components having different time courses.

To our knowledge there are very few studies that have used contrast threshold recovery after a photobleach to test this idea. Margrain and Thomson (1997) measured recovery of the luminance mechanism required to detect sinusoidal gratings (0.6–14 cpd) throughout the course of dark adaptation. The threshold over time for the lowest spatial frequency was qualitatively similar to a classical dark adaptation function, showing discrete rod and cone phases and for spatial frequencies above the rod spatial resolution limit (3.5 cpd), the rod phase was absent. Hahn and Geisler (1995) reported recovery of luminance sensitivity (log td) for sine-wave gratings targets (250 ms flash) ranging from 1 to 15 cpd during long-term dark adaptation following full bleaches. They found that the dark adaptation curves were similar in shape and time course throughout the course of long-term dark adaptation. Due to the experimental design, measurements were confined to the cone system. D'Zmura and Lennie, (1986) found that the recovery of contrast threshold after a bleach using a rod-isolating grating (1.38 cpd and mean illumination 9.3 td) had both cone and rod phases.

In this study, we ask the question, how do the post-receptoral contrast extracting mechanisms respond to a photic bleach? The issue is important because it may shed light on why sensitivity recovery involving rods is slowed in older eyes and vulnerable to a wide range of systemic and ocular conditions. Many patients complain of poor night vision, but its investigation is regarded as excessively time consuming. For this reason there are comparatively few studies concentrating on scotopic function. One of the major advantages of the technique described here, is that it is much faster than the more conventional luminance-based approach which takes around 30–35 min. By studying the recovery of contrast thresholds for grating stimuli after photopigment bleaching, we aim to determine the temporal characteristics of post-receptoral mechanisms in the dark adaptation process.

2. Methods

2.1. Apparatus

Sinusoidal gratings of 0.5, 1 and 2 cpd were generated on a calibrated, gamma-corrected high-resolution CRT monitor (Sony GDM-F500R, Tokyo, Japan). They were temporally modulated at 2 Hz. Michelson contrast ranged between 0.02 and 0.7 and was defined as

$$C = \frac{Lmax - Lmin}{Lmax + Lmin}$$

The stimuli subtended 10° at the viewing distance of 75 cm as illustrated in the inset in Fig. 1. The mean screen luminance was reduced from 12.5 cd m^{-2} to 1.3×10^{-2} cd m^{-2} using neutral density filters (four filters were used, three of type 211 (0.9 log units) and one of type 209 (0.3log units) [LEE Filters Worldwide, Andover, Hampshire, UK]). A ViSaGe unit (CRS, UK) and a desktop PC (Dell, USA) with Windows XP operating system (Microsoft, USA) were used to control the experiment. The hardware was controlled using a series of scripts written in MATLAB (2012b, The MathWorks, Inc., Natick, Mass, USA) and the psychophysics toolbox (Brainard, 1997). The scripts are available from the corresponding author.

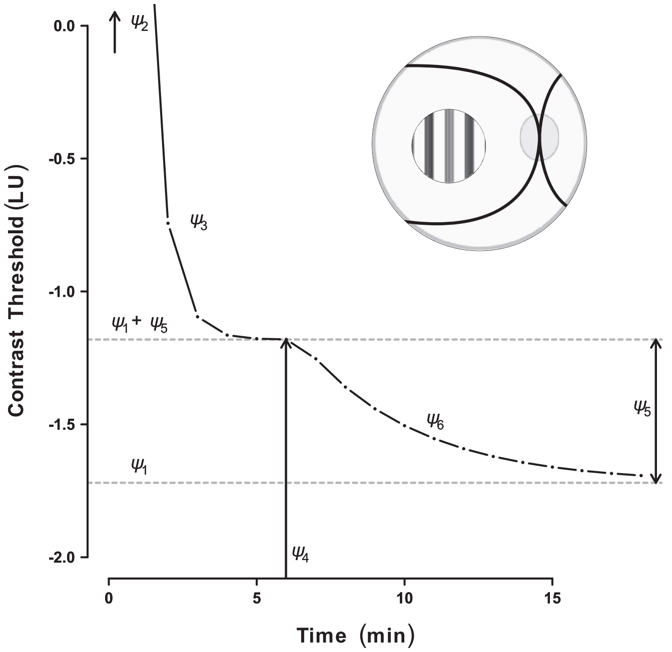

Fig. 1. The contrast sensitivity recovery function in log units (LU) as a function of time and the parameters of the bi exponential model. The parameters are explained in the text. Note the parameter ψ_5 is the offset from the final phase to the early phase. The inset illustrates the size and location of the stimulus.

2.2. Calibration of the monitor

The calibration followed a procedure described by Parry et al. (2006). Initially the screen was auto calibrated using a Colorcal photometer (CRS Ltd, UK) and its associated software, by testing 128 voltages to obtain a gamma correction curve.

The software used for stimulus generation (ViSaGe Desktop, CRS Ltd, UK) allows for correction values to compensate for intrinsic errors in the monitor for the red (R) green (G) and blue (B) phosphors and have default values of one.

The CIE coordinates of $x = 0.31$ and $y = 0.316$ with luminance 12.5 cd m^{-2} were entered into the software and the chromaticity coordinates at R, G and B were measured using the PR650 (Horiba UK). The voltages across the R, G and B guns were noted. The correction factors were adjusted until the monitor displayed the set luminance according to a PR1500 spot photometer (Photo Research USA).

Contrast calibration was checked using a Matlab script that used a look up table to present two squares on the monitor, each with sides of 100 pixels separated by 20 pixels. The luminance of each square was measured with the PR1500 and the contrast calculated for a range of different mean luminances. The $\log_{10}$ (contrast) was linear for the look up table index ($R^2 = 0.9996$).

2.3. Subjects

All observers had normal best-corrected visual acuity, no ocular pathology, established by an eye examination within the previous 12months. Thirteen naïve subjects were recruited (6 female) aged 30.4(22–55) yrs. They were given written and verbal information about the experiment and possible consequences of their