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The effect of eccentricity on the contrast response function of multifocal visual evoked potentials (mfVEPs)

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ABSTRACT

mfVEPs were recorded with a 22° radius, 60 sector pattern reversal dartboard stimulus (VERIS) at six contrast levels (10%, 25%, 35%, 50%, 75%, 95%). Contrast response functions (CRFs) based on response amplitudes were adequately described by a simple hyperbolic function. The effect of reducing contrast on the amplitude was most apparent in the central 1° radius, which had a C_{50} (contrast at 50% of the maximum response) in excess of 50%, compared to values for C_{50} in more eccentric regions that were 30% or lower. Mean latency increased 6 (±0.7SE) ms from the highest to the lowest contrast tested, and did not vary significantly with eccentricity.

1. Introduction

The multifocal visual evoked potential (mfVEP) is an objective measure of visual function that can be recorded non-invasively. The unique strength of the technique is that it allows simultaneous recording of local VEP responses from across the visual field, thereby providing spatially localized amplitude and latency information. Refinements in the analysis of mfVEP records have enhanced its clinical utility in the diagnosis of diseases affecting the optic nerve such as glaucoma and optic neuritis (Balachandran, Graham, Klistorner, & Goldberg, 2006; Fortune et al., 2007; Hood & Greenstein, 2003; Hood, Odel, & Zhang, 2000). As various peripheral ocular conditions such as refractive errors, lens opacities, corneal diseases or pre-ganglion cell abnormalities in the retina can cause a reduction in retinal image contrast, it is important to understand the relationship between the stimulus contrast and the mfVEP responses (Brown, 1993; Zadnik, Mannis, & Johnson, 1984).

Previous studies have investigated the effects of contrast on pattern reversal VEP or mfVEP responses (Baseler & Sutter, 1997; Hasegawa & Abe, 2001; Hood et al., 2006; Katsumi, Tanino, & Hirose, 1985; Klistorner, Crewther, & Crewther, 1997; Maddess, James, & Bowman, 2005; Park, Zhang, Ferrera, Hirsch, & Hood, 2008; Rudvin, Valberg, & Kilavik, 2000; Souza, Gomes, Saito, da Silva Filho, & Silveira, 2007; Zadnik et al., 1984), with attention to the stimulus location in some of the studies (e.g. Baseler & Sutter, 1997; Hasegawa & Abe, 2001; Maddess et al., 2005). However, these studies did not provide a complete analysis of the change in the contrast response function (CRF) with eccentricity. In theory, the effect of contrast on local VEP responses should vary across the visual field as the distribution of retinal ganglion cells with different contrast response characteristics changes with eccentricity (Curcio & Allen, 1990; Dacey, 1993; Kaplan & Shapley, 1986). To investigate whether the characteristics of the VEP CRF depend upon retinal eccentricity, we used the mfVEP technique to record 60 local VEP responses across a 22° radius of visual field in normal subjects for a range of stimulus contrasts. A report of this study has appeared previously in abstract form (Laron et al., Invest. Ophthalmol. Vis. Sci. 2008 49: E-Abstract 3311).

2. Methods

2.1. Subjects

Seven normal subjects participated in the study. Subjects ranged in age from 23 to 42 (mean ± SD: 28 ± 6), and had best corrected visual acuity of 20/25 or better. All subjects had a comprehensive eye examination and histories were taken prior to participating in the study, and were found to have no ocular or systemic conditions that could affect the visual system. Informed consent was obtained from all subjects. Procedures adhered to the tenets of Declaration of Helsinki, and the protocol was approved by the University of Houston Committee for the Protection of Human Subjects.

2.2. mfVEP procedures and data analysis

2.2.1. Stimulus (VERIS 5.1, mfVEP paradigm)

A dartboard pattern was presented on a 20" CRT monitor with a frame rate of 75 Hz. The pattern was comprised of 60 sectors scaled

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in size for cortical magnification (Fig. 1A). Each sector had 16 checks (8 black and 8 white), and followed a pseudorandom sequence of reversal (*m*-sequence) (Sutter, 2001). Mean luminance of the pattern was fixed at 66 cd/m^2, and the Michelson contrast was varied over six steps: 10%, 25%, 35%, 50%, 75%, and 95%. Photopic luminance (cd/m^2) of the stimulus was calibrated using a spot photometer (model LS-100, Minolta Camera Co., Ltd., Japan), and the Michelson contrast was calculated. The display was positioned so that the central 44.4° of the visual field were stimulated. Subjects viewed the display through their natural pupils with appropriate refractive corrections in place, and were instructed to maintain fixation at the stimulus center (marked as an "x"). The range of pupil sizes (4–5 mm in diameter) did not affect contrast sensitivity, because for photopic luminances, such as we used, and the low spatial frequency (here 2 cpd or lower), contrast sensitivity remains constant (De Valois, Morgan, & Snodderly, 1974). During recording, the eye position was monitored constantly by the examiner through the camera provided in the VERIS hardware.

2.2.2. Electrode placement and recordings

Three channels were recorded simultaneously and three additional channels were derived mathematically using customized software generously provided by Dr. Donald Hood's lab (Hood & Greenstein, 2003). The ground electrode was placed on the forehead, the reference electrode at the inion; the first channel electrode 4 cm above the inion; the second and third channel electrodes 1 cm above and 4 cm to the left and right of the inion. mfVEP was recorded for one eye from each subject with the other eye occluded. Stimuli were presented in order of increasing contrast to minimize adaptational effects. At each contrast level two 7-min recordings from each subject were averaged for offline analysis. Subjects rested between recordings as needed to avoid fatigue.

2.2.3. Data analysis

The first slice of second-order kernels for responses were calculated by VERIS 5.1 (Electro-Diagnostic Imaging, San Mateo, CA) software and exported. All data analyses were performed with a customized software based on the 'best channel' responses as previously described (Hood & Greenstein, 2003). 'Best channel' responses were used to improve response amplitudes over those from single channel recordings, as has been demonstrated previously (Hood & Greenstein, 2003; Klistorner & Graham, 2000). Use of 'best channels' has been shown to be particularly important for locations along the lower horizontal meridian and in central sectors (Hood & Greenstein, 2003), and clearly would be helpful for responses to low contrast stimuli. It is likely that for a particular field location (i.e., sector), the 'best channel' remained the same as contrast was varied. In theory, the relative strength (and waveform) of the local signals across the field is determined mainly by the position and orientation of the underlying dipole (i.e., anatomical convolution of the cortex) relative to the electrodes associated with particular channels, and this would not be expected to change with contrast. Further, basic waveforms at the same location were essentially unaffected by stimulus contrast, except in amplitude, in previous studies using 'best channel' responses (Hood & Greenstein, 2003) or 'single channel' recordings (Hasegawa & Abe, 2001).

The mfVEP response amplitude is reported in the present study as signal to noise ratio (SNR). A sector's SNR was calculated as the root-mean-square (RMS) amplitude of the signal window (45–150 ms) divided by the mean RMS amplitude of the noise window (325–430 ms in the record where stimulated activity was minimal) from all 60 sectors (Hood & Greenstein, 2003). Relative latency for the response in each sector was determined by calculating the cross-correlation of the subject's waveform and a template built on the basis of 100 norms (Devers Eye Institute, Portland, OR) (Fortune, Zhang, Hood, Demirel, & Johnson, 2004; Hood et al., 2004). The relative latency was the shift in milliseconds (ms) needed to achieve the best cross-correlation determined by the 'xcorr' function in MATLAB (The MathWorks Inc, Natick, MA).

2.2.4. Data analysis at different eccentricities

The mfVEP stimulus–response array was divided into six concentric rings of increasing eccentricity as shown in Fig. 1B. Ring 1 included the central four sectors within an eccentricity of 1° radius. Ring 2 included eight sectors which resided between 1° and 2.5°. Rings 3–6 included sectors with increasing eccentricity, up to those between 15° and 22° for ring 6. To evaluate the effects of eccentricity on contrast response characteristics, the SNRs or the latencies were pooled from all subjects for each ring and represented by the individual ring's mean or median values. This allowed sufficient data points for analysis, especially in the case of ring 1 which included only four sectors.

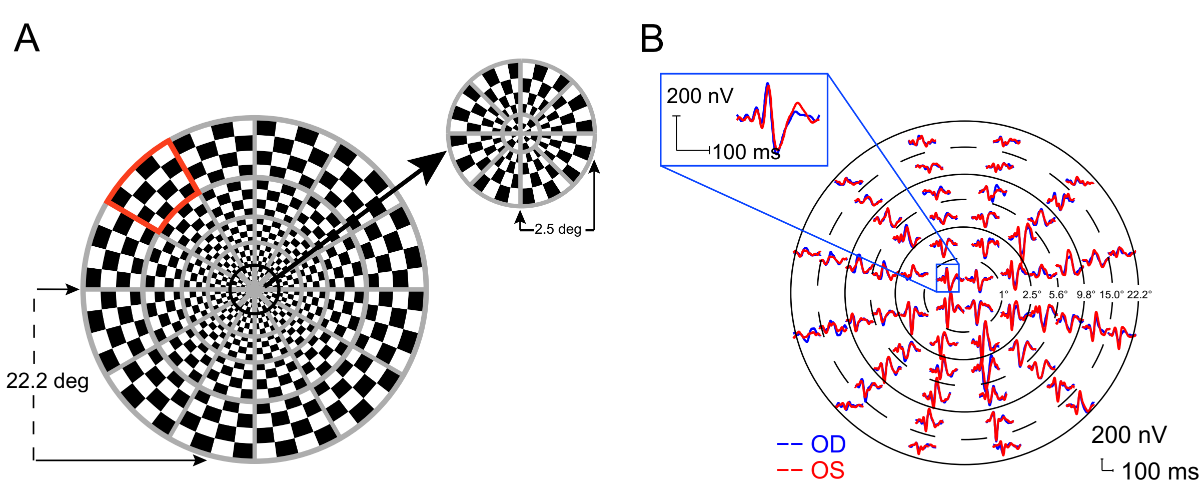

Fig. 1. (A) The mfVEP dartboard stimulus with one of the sectors marked in red. (B) mfVEP responses from the two eyes of a normal subject. The dashed and solid circles illustrate six concentric rings of increasing retinal eccentricity from 1° for the most central ring (ring 1), to 22.2° for the most peripheral ring (ring 6). The position of each of the 60 waveforms has been adjusted to enable better visualization. The inset shows the responses from one location on an expanded scale. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).