Assessing Spatial and Temporal Properties of Perimetric Stimuli for Resistance to Clinical Variations in Retinal Illumination

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PURPOSE. To develop perimetric stimuli for which sensitivities are more resistant to reduced retinal illumination than current clinical perimeters.

METHODS. Fifty-four people free of eye disease were dilated and tested monocularly. For each test, retinal illumination was attenuated with neutral density (ND) filters, and a standard adaptation model was fit to derive mean and SEM for the adaptation parameter (NDhalf). For different stimuli, t-tests on NDhalf were used to assess significance of differences in consistency with Weber’s law. Three experiments used custom Gaussian-windowed contrast sensitivity perimetry (CSP). Experiment 1 used CSP-1, with a Gaussian temporal pulse, a spatial frequency of 0.375 cyc/deg (cpd), and SD of 1.5°. Experiment 1 also used the Humphrey Matrix perimeter, with the N-30 test using 0.25 cpd and 25 Hz flicker. Experimenter 2 used a rectangular temporal pulse. SDs of 0.25° and 0.5°, and spatial frequencies of 0.0 and 1.0 cpd. Experiment 3 used CSP-2, with 5-Hz flicker, SDs from 0.5° to 1.8°, and spatial frequencies from 0.14 to 0.50 cpd.

RESULTS. In Experiment 1, CSP-1 was more consistent with Weber’s law (NDhalf ± SEM = 1.86 ± 0.08 log unit) than N-30 (NDhalf = 1.03 ± 0.03 log unit; t > 9, P < 0.0001). All stimuli used in Experiments 2 and 3 had comparable consistency with Weber’s law (NDhalf = 1.49–1.69 log unit; t < 2).

CONCLUSIONS. Perimetric sensitivities were consistent with Weber’s law when higher temporal frequencies were avoided.

Keywords: retinal illumination, temporal vision, perimetry
varied spatial and temporal properties of potential CSP stimuli in order to develop a second generation, CSP-2, to increase mean normal contrast sensitivity relative to CSP-1, while remaining more consistent with Weber's law than frequency-doubling perimetry.

**METHODS**

Three experiments (Table) were conducted on healthy volunteers free of eye disease, to assess spatial and temporal factors affecting consistency with Weber's law, and to design sinusoidal stimuli that elicit high contrast sensitivities that have good adherence to Weber's law. Experiment 1 assessed effects of temporal presentation on adherence to Weber's law, and Experiment 2 assessed effects of spatial frequency content. The results of these two studies led to the design of stimuli for CSP-2, which was then used in Experiment 3.

**Participants**

Fifty-four subjects were recruited who were free of eye disease on a comprehensive evaluation within 2 years, had best corrected visual acuity of 20/20 or better, spherical refractive error within −6 to 2 diopter (D), astigmatism less than 3 D, clear ocular media, and IOP less than 22 mm Hg. Exclusion criteria were an ocular or systemic disease known to affect the visual field, a first-degree relative with glaucoma, and usage of medications known to affect vision. Each subject selected one eye to be tested, and the other eye was occluded with a translucent white patch. Data collected from left eyes were averaged for the right eye for Experiment 1 and for Experiment 2. The fixation target was a black cross with lines 1° long and 5 minutes of arc wide.

For Experiment 1, CSP-1 testing was at 26 locations across the central visual field. For Experiment 2, we investigated three different stimuli at each location: a Gabor stimulus in the background: 100 cd/m² for N-30 and 50 cd/m² for CSP-1. For Experiment 3, CSP-2 used a custom-built testing station with a motorized headrest that allowed better control of head position, and a 33-cm test distance. The display subtended 51° × 42° of visual angle, allowing testing of more peripheral locations, for a total of 57 locations across the central visual field. The resistance of these stimuli to effects of peripheral optics has recently been demonstrated. Two adjustable headrests allowed compensation for prominence of the brow, and custom 50-mm spherical lenses were held in place by magnets, so that the metal rim remained as a cue to head and eye position (a plain glass lens was used when no spherical correction was needed). The patient’s head was placed in the X-Y motorized chinrest and positioned so that their pupil was centered in the corrective lens (checked with webcam) that was centered on the fixation target at a distance of 33 cm. Subject’s distance refraction combined with a +3.00 add was used for Experiment 3. The fixation target was a black cross with lines 1.2° long and 6 minutes of arc wide.

**Stimuli**

Luminance profiles and the appearance of the stimuli are shown elsewhere. For Experiment 1, the Humphrey Matrix (Carl-Zeiss Meditec) was used with the N-30 program to present grating stimuli: vertical 0.25 cycle/degree (cpd) spatial frequency gratings within a square, sharp-edged 10° × 10° window, with 25 Hz counter-phase square wave temporal modulation. Contrast sensitivity perimetry-1 presented Gabor stimuli: 0.375 cpd horizontal gratings within a two-dimensional (2D), soft-edged circular Gaussian window (SD = 1.5°), presented with a slow temporal pulse (temporal Gaussian, SD = 100 msec). For both stimuli, the gratings were in sine phase so that the mean luminance was the same as the background: 100 cd/m² for N-30 and 50 cd/m² for CSP-1.

For Experiment 2, we investigated three different stimuli that cause an increase in mean luminance: a Gabor stimulus in cosine phase with a peak spatial frequency of 1.0 cpd and SD of 0.25°, and two Gaussian blobs with SDs of 0.25° and 0.50° (equivalent to 0 cpd Gabors with these SDs, in cosine phase). All three stimuli caused an increase in mean luminance, and only the Gabor provided oriented spatial content. For these stimuli the temporal presentation was a 200-msec hard-edged rectangular pulse, whose Fourier spectrum contains a wide
range of temporal frequencies. Background luminance was 18.7 cd/m² for the Gabor cosine and 10 cd/m² for the Gaussian blobs. For the Gaussian blobs, the background was chosen to be the same as the Humphrey Field Analyzer (HFA). For all stimuli, contrast was defined as (peak-mean)/mean, and contrast sensitivity was defined as the reciprocal of contrast threshold.

For Experiment 3, CSP-2 presented Gabor grating patches at 57 locations with varying magnification: spatial frequency was 0.25 cpd at fixation and decreased to 0.14 cpd at 21°, based on spatial scale. These Gabor patches were horizontal gratings in sine phase within a 2D Gaussian window whose size was increased as spatial frequency decreased so that stimuli were simply magnified as spatial frequency decreased (SD x spatial frequency = 0.25). Stimuli were presented with 5-Hz counterphase square wave flicker. The stimuli were in sine phase so that their mean luminance was the same as the background, 50 cd/m².

**Protocol**

One eye per subject was first tested with natural pupils to make sure the subjects would understand the requirements of the testing and also have some measure of practice. These data were discarded. For all three experiments the subjects were then dilated with 0.5% tropicamide ophthalmic solution. Following stable dilation and refraction and visual acuity testing at the testing distance, neutral density filters were introduced at the correcting lens plane in either ascending or descending order. For Experiments 1 and 2, the descending order started at 0 ND (no filter), then each subsequent test used the next filter: 0.6, 1.2, 1.6 ND. Under this condition, the subject was asked to fixate on the testing monitor for 2 minutes before initial testing and then after each change in filter. For the ascending order, subjects began with densest filter (1.6 ND), and were asked to adapt to the low light level by fixating on the testing monitor for 10 minutes prior to testing. With each subsequent filter (1.2, 0.6, no filter), subjects were asked to adapt by fixating for 2 minutes prior to testing. For Experiment 1, CSP testing and N-30 testing were on two different visits. All the stimulus conditions for Experiments 2 and 3 were tested on a single visit. For Experiment 3, the neutral density filters were 0.6, 1.2, and 1.8 log units. The ascending and descending adaptation periods were the same as for the first two experiments.

For our custom testing stations, contrast sensitivity was measured by having the subject fixate a target in the center of the display and click a button whenever a stimulus was seen, as stimuli were presented at the different visual field locations on a uniform gray background, in a darkened room. Experiments 1 and 2 used a staircase with a variable interstimulus interval averaging 1700 msec. Experiment 3 used a ZEST algorithm with a variable interstimulus interval averaging 1200 msec. Further details on strategies for assessing and managing fixation loss, false positives, false negatives, and other artifacts are described elsewhere.

### Statistical Design

The primary analysis was for change in mean sensitivity (MS), computed as the average sensitivity across all locations, for each stimulus and ND filter. Secondary analyses looked at potential effects of eccentricity, averaging MS across locations with similar eccentricities rather than across all locations.

A standard two-parameter adaptation model was used to fit change in MS versus illumination. The model was fitted by minimizing the two parameters using the Levenberg-Marquardt algorithm, with graphing and data analysis software (Igor Pro, version 6.22A; WaveMetrics, Portland, OR) that provides a mean and SEM for each parameter. The first parameter was a vertical scaling factor that allowed for imprecision in the normalization to the 0 ND condition, and the parameter of interest was the second parameter, $ND_{half}$, a horizontal scaling factor that characterized the relative resistance of the stimulus to reduction in retinal illumination. $ND_{half}$ is the ND value at which it is expected that contrast threshold will increase by a factor of 2 (corresponding to a 0.3-log unit decline in contrast sensitivity). The greater the value for $ND_{half}$, the wider the range of illuminations for which MS is consistent with Weber's law. In the figures that plot decrease in contrast sensitivity versus decrease in retinal illumination, $ND_{half}$ can be considered to be a measure of the flatness of the curve.

The primary analysis was for ND values from 0.0 to 1.2 log units, similar to the 1.3-log unit range expected clinically. At lower illumination levels rod intrusion could affect the fits. For instance, ND of 1.5 log units on a 10 cd/m² background produces 0.5 cd/m², and on a 50 cd/m² background for CSP-1 and CSP-2 produces 2.5 cd/m²; these are both mesopic. The data point below 1.5 log unit was compared with the predictions to assess the potential impact of rod intrusion. When this point was removed, only for historical HFA data did $ND_{half}$ decrease by more than 0.02 log unit, so this point was only removed for historical HFA data.

Experiment 1 tested the hypothesis that use of high temporal frequencies explains why sensitivities for N-30 are not consistent with Weber's law. N-30 uses frequency-doubling (FD) stimuli that have low spatial frequency content, so the prediction from Graham and Hood is that temporal frequency is the limiting factor for these stimuli. The primary difference in temporal frequencies of CSP-1 and N-30 is that for the FD stimulus most of the energy in the Fourier spectrum is near 25 Hz, while CSP-1 stimulus has no appreciable energy above 3 Hz. Therefore, the first prediction was that contrast sensitivity would be more adherent to Weber's law for CSP-1.
than N-30, meaning that for each age group \( ND_{half} \) would be larger for CSP-1 than for N-30. The second prediction was that effects of age-related lens density would make \( ND_{half} \) smaller for the older age group, meaning that, for both CSP-1 and N-30, \( ND_{half} \) would be greater for the younger group than for the older group.

These four one-tailed predictions were tested by comparing the difference in mean parameter values divided by the pooled SEM, equivalent to a \( t \)-test. Significance was set to alpha equals 0.0125 as a conservative Bonferroni adjustment for repeated questioning of the data, which yields a cutoff of \( t \) equals 2.6 for 10 \( df \) and 2.5 for 19 \( df \). Therefore 2.6 was the criterion used for significance.

Experiment 2 explored the role of size and spatial frequency with a fixed temporal presentation (rectangular pulse as in conventional perimetry), using Gaussian windows with SDs of 0.25° and 0.5°, and grating spatial frequencies of 0 and 1 cpd. The three stimuli were compared in terms of \( ND_{half} \), using \( P \) less than 0.05 to identify any possible trends. The 1.0 cpd Gabor had the highest spatial frequency content, followed by the 0.5 cpd Gabor, the 0.25° Gaussian blob, and finally the 0.5° Gaussian blob. The expectation was that \( ND_{half} \) would be similar for the three stimuli, with a mild effect of spatial frequency, and the greatest difference would be between the 1.0 cpd Gabor and the 0.5° Gaussian blob.

Experiment 3 explored the prediction that the effects of eccentricity would be lowest for CSP-2, which magnifies stimulus size by the Keltgen and Swanson\(^ {19} \) surface for spatial scale. For each test, a \( t \)-score was computed as the difference between maximum and minimum values across eccentricity, divided by the mean value for SEM across eccentricities. Six tests were evaluated, so we used a Bonferroni correction and required \( t \) greater than 2.8 for significance.

### RESULTS

Figure 1 shows decrease in contrast sensitivity with decrease in retinal illumination for CSP-1 and N-30, for the young subjects in Experiment 1, along with historical data\(^ {3} \) for size III perimetry at 1 cd/m\(^ 2 \) ("Octopus") and 10 cd/m\(^ 2 \) ("HFA"). Consistency with Weber’s law is represented by a horizontal line at 0.0, and the vertical line at 1.3-log unit decrease represents the lowest illumination expected in a clinical population with normal lens aging but not manifest cataract.\(^ {11} \) The vertical line intercepts the fit at \( /C_0 \) 0.03 log unit for CSP-1 data with younger and older groups, respectively, showing consistency with Weber’s law. By comparison, N-30 data departed from Weber’s law for a 2-mm pupil, decreasing by \( /C_0 \) 0.22 and \( /C_0 \) 0.29 log unit for young and older age groups.

Figure 2 shows data from young and older age groups in Experiment 1. The vertical, dashed lines show the equivalent decreases for pupil diameters of 3 (thin line) and 2 mm (thick line), where 0 ND corresponds to 8 mm.
law than N-30 with a high temporal frequency: for the young

\[ \text{ND}_{\text{half}} = 2.28 \pm 0.02 \text{ log unit for CSP-1 versus 1.03} \pm 0.02 \text{ log unit for N-30 (} t = 63, P < 0.0001), \]

and for the older group \( \text{ND}_{\text{half}} = 1.86 \pm 0.08 \text{ log unit for CSP-1 versus 0.82} \pm 0.02 \text{ log unit for N-30 (} t = 18, P < 0.0001). \)

The second prediction was also confirmed, that lens aging would make \( \text{ND}_{\text{half}} \) smaller for the older age group: mean \( \text{ND}_{\text{half}} \) was found to be smaller for the older group versus the younger group, by \( 0.42 \text{ log unit for CSP-1 and by 0.21 log unit for N-30 (} t > 7, P < 0.0001). \)

The historical data bracketed the N-30 data, yielding \( \text{ND}_{\text{half}} \) of \( 0.76 \pm 0.06 \text{ log unit for the Octopus at 1 cd/m}^2 \) and \( 1.25 \pm 0.07 \text{ log unit for the HFA at 10 cd/m}^2. \)

Figure 3 shows decrease in contrast sensitivity with decrease in retinal illumination for Experiments 2 and 3. Each of the four curves fits for the standard adaptation model showed approximately 0.1-log unit decrease for a 2-mm pupil, (corresponding to the dashed, vertical line at 0.9 log unit), and an approximately 0.2-log unit decrease at 1.3 log unit. All four curves had \( \text{ND}_{\text{half}} \) in the range \( 1.6 \pm 0.1 \), so all four curves showed comparable adherence to Weber’s law, better than for N-30 and size III, but not as much as CSP-1. This indicates that 5-Hz counter-phase flicker has similar effects to the rectangular pulses used in conventional perimetry, and that spatial frequency is a relatively minor factor for the stimuli we used.

Figure 4 shows the predicted effect on log contrast sensitivity for the clinical limit of a 1.3 log unit reduction in illumination, as a function of eccentricity, for data from Figures 1 and 3. Error bars show \( \pm 1 \text{ SEM}. \)

**DISCUSSION**

When a perimetric test is administered clinically, retinal illumination can vary 20-fold (1.3 log unit) across patients free of cataract, due to differences in pupil diameter and aging of the crystalline lens.\(^{11,20–22}\) If data for a perimetric test adhered to Weber’s law over this 20-fold range, then the test would be immune to effects of reduced illumination due to pupil diameter and lens aging, because both background illumination and maximum of stimulus illumination would be affected by the same amount, and the contrast would not change. Our data with FD stimuli, and historical data with size III stimuli, show substantial departures from Weber’s law over the clinically significant range (Figs. 1, 2). This means that normal variability in retinal illumination due to pupil diameter and lens aging will translate into sources of within-subject and between-subject variability for perimetric sensitivity. Using stimuli for which data are more consistent with Weber’s law has the potential to decrease variability. The use of high temporal frequencies was identified as the primary reason that FD data departed from Weber’s law. Adherence was much better for CSP-2, whose temporal Fourier spectrum has approximately six times lower amplitude than FD at 25 Hz. Contrast sensitivity perimetry–1 has amplitudes near zero above 3 Hz, and yielded data with the greatest adherence to Weber’s law.

These data gathered across the central visual field were consistent with the literature on foveal adaptation:\(^{12}\) adherence to Weber’s law improves when high frequency content of the stimulus (spatial or temporal) is reduced. Contrast sensitivity perimetry–2 (with 57 test locations) magnified stimuli with eccentricity based on estimates of local spatial...
which we predicted would minimize eccentricity effects. This prediction failed because only at fixation did CSP-2 data adhere to Weber’s law as well as stimuli with luminance increments (Gaussians and 1.0 cpd Gabor cosine). We suggest that the spatial scale estimates may need to be improved, as indicated by our recent study of blur effects with CSP-2.16 These results can be used to guide development of perimetric stimuli. For instance, low temporal frequencies can be used to ensure adherence with Weber’s law over the expected clinical range of retinal illuminations for a given test. However, this resulted in substantially lower mean normal contrast sensitivity for CSP-1 than for N-30 and CSP-2, as shown in Figure 5 where log contrast sensitivity is plotted as a function of retinal illumination.11 As retinal illumination increases, each fitted function approaches an asymptotic maximum. The asymptotic values for CSP-2 (5 Hz) and N-30 (25 Hz) were much greater than for CSP-1 (<3 Hz). Most of the CSP-2 stimuli were smaller than the CSP-1 stimulus, so the primary factor is not size but use of flicker. N-30 uses much larger stimuli than CSP-2, but employs a higher temporal frequency that has been shown to reduce contrast sensitivity.8 Size and temporal modulation interact in determining asymptotic contrast sensitivity, and use of 5-Hz flicker allowed us to use smaller stimuli than N-30, while maintaining higher contrast sensitivity than CSP-1.

The purpose of this study was to assess how spatial and temporal properties of perimetric stimuli affect adherence to Weber’s law. Over much of the range of stimulus sizes and spatial frequencies we used, adherence to Weber’s law was largely independent of spatial properties of the stimuli (Fig. 3) and highly dependent on temporal properties (Figs. 1, 2). For sinusoidal stimuli there is a tradeoff between adherence to Weber’s law and high contrast sensitivity, with CSP-1 at very low temporal frequencies yielding data with the greatest adherence to Weber’s law, but having much lower contrast sensitivity than for CSP-2 at 5 Hz or N-30 at 25 Hz. We developed CSP-2 for use in a longitudinal study, to test our hypothesis that ganglion cell saturation causes high test–retest variability.23 We had already chosen lower spatial frequencies to improve resistance to modest amounts of blur,16 and here we looked for a balance between Weber’s law and the high contrast sensitivities needed to reduce effects of ganglion cell saturation. We wanted stimuli for which contrast sensitivity adheres to Weber’s law, to minimize effects of fluctuations in pupil size within and between tests. The results of this study show that CSP-2 has sacrificed some consistency with Weber’s law in order to achieve higher contrast sensitivity than CSP-1, but at all eccentricities was much more consistent with Weber’s law than N-30.

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References


