Mechanisms Isolated by Frequency-Doubling Technology Perimetry

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Purpose. The frequency-doubling (FD) phenomenon describes the increase in apparent spatial frequency occurring when low-spatial-frequency sine wave gratings undergo rapid counterphase flicker. It is unclear whether the visual mechanisms isolated when pattern appearance is used as a threshold criterion are the same as when a simple detection criterion (as in FD perimetry) is used. It is also unclear whether the FD stimulus isolates mechanisms that differ from those isolated by spatially uniform flicker. In the current study, adaptation and spatiotemporal tuning functions were determined, using the FD stimulus, uniform flicker, and static (nonflickering) grating targets, to establish whether distinct mechanisms are isolated by the FD stimulus.

Methods. Spatiotemporal tuning functions were determined in six observers, using an FD stimulus under conditions of detection and resolution and using spatially uniform flickering stimuli and static grating stimuli. The effect of light adaptation on these stimulus classes was also assessed. All stimuli were 10°-wide squares.

Results. Spatiotemporal tuning functions and adaptation characteristics were identical for both the FD detection and resolution paradigms. Spatially uniform flicker gave indistinguishable tuning functions and adaptation characteristics to the FD stimulus at 25 Hz and higher, but differed below this frequency. Static grating stimuli differed from FD stimuli in both tuning functions and adaptation characteristics.

Conclusions. Absolute detection of the FD stimulus involves mechanisms that are indistinguishable from those involved when a criterion based on spatial form (i.e., resolution of a pattern) is used, indicating that a simple detection criterion can be used in FD perimetry. The FD stimulus isolates similar mechanisms to spatially uniform flickering stimuli at high temporal frequencies. (*Invest Ophthalmol Vis Sci.* 2002;43: 398–401)

The frequency-doubling (FD) phenomenon was first described by Kelly,[1] who observed that a low-spatial-frequency sine wave grating appeared to double in spatial frequency when its contrast was counterphase flickered at high rates. It has been shown that contrast sensitivity to FD stimuli (i.e., low-spatial-frequency gratings flickered at high temporal frequencies) is reduced in glaucoma,[2–5] and FD stimuli have therefore been used in the frequency-doubling technology (FDT) perimeter (Welch Allyn, Skaneateles Falls, NY; and Humphrey Instruments, San Leandro, CA).

Maddess and Henry[6] have proposed that FD stimuli are detected by M_y ganglion cells within the magnocellular (M-cell) pathway. This and subsequent[5] work used a method-of-adjustment psychophysical procedure to determine thresholds, wherein subjects were instructed to use the appearance of the FD pattern as a criterion. Suprathreshold targets have also been used.[7,8] A criterion based on the appearance of the FD pattern differs from that used in the FDT perimeter, in which subjects typically respond to the perception of any stimulus, irrespective of whether a frequency-doubled pattern is visible. Indeed, if the perception of the FD pattern is used as a criterion in FDT perimetry, abnormal results are frequently found in otherwise normal subjects,[9] suggesting that the normative values used in the perimeter are based on subjects responding to the perception of any stimulus. It is unclear whether the appearance of a spatially doubled pattern persists down to threshold for an FD stimulus, with some investigators reporting that this occurs,[1] whereas others suggest that a zone of amorphous flicker exists before the pattern becomes visible[6,10] or that the grating stimulus returns to close to its true spatial frequency.[11] As such, it is possible that subjects responding to any percept in FDT perimetry are obtaining flicker thresholds, which are also known to be reduced in glaucoma.[12–15]

Johnson and Demirel[14] used a uniform flickering patch of the same size as the FD stimuli in the FDT perimeter, and found sensitivities and specificities for the detection of glaucoma were only slightly lower than when the FD stimulus was used. Such a result may be interpreted in several ways. First, a large flickering stimulus and the FD stimulus may both be detected preferentially by M_y cells, as proposed by Maddess and Henry.[6] Alternatively, the FD stimulus may only isolate a discrete FD mechanism when a criterion based on spatial form is used (e.g., as used by Maddess and Severt[5] and Maddess and Henry[6]), with simple detection strategies (as used by Johnson and Demirel) isolating a different, flicker-sensitive mechanism. As a third alternative, it is possible that a number of spatiotemporally discrete stimuli (i.e., those containing a limited range of spatial and temporal frequencies) can be used to detect glaucomatous loss. In support of this latter alternative, Johnson and Demirel[14] found that contrast sensitivity to static (i.e., nonflickering), low-temporal-frequency sine wave gratings gave only slightly lower glaucoma detection sensitivities than both the FD and flickering stimulus. It is difficult to assess whether the small differences in glaucoma sensitivity found between FD, flickering, and nonflickering stimuli are significant, owing to the relatively small number of subjects ($n = 16$) investigated.[16]

Therefore, it is not clear that simple detection strategies for the FD stimulus isolate the same mechanism or mechanisms as when criteria based on the perception of a spatial pattern are used. In addition, it is not clear that the FD stimulus isolates a different mechanism or mechanisms from a flickering, spatially uniform target. In this study, we determined adaptation and spatiotemporal tuning functions using the FD stimulus, a uniform flickering patch, and static grating targets, to establish whether distinct mechanisms are isolated by the FD stimulus. In addition, we examined what effect detection versus pattern resolution criteria had on the mechanisms isolated by the FD stimulus.

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METHODS

Apparatus and Procedure

Stimuli were presented on a calibrated video system [VSG 2/4 graphics card (Cambridge Research Systems Ltd., Kent, UK) and monitor (CPD-G500, frame rate, 100 Hz; Sony, Tokyo, Japan)]. The monitor subtended 62° × 48° (width × height) at the 33-cm viewing distance. Ambient room illumination was dim.

Three stimulus classes were used: an FD stimulus (0.25–2 cyc/deg gratings, counterphase flickered at 10–40 Hz), a uniform flickering patch (0 cyc/deg, 10–40 Hz), and nonflickering (static) gratings (0.25–2 cyc/deg). Stimulus contrasts were specified as Michelson contrasts, presented in a raised cosine window of 1000 msec. The minimum time between the offset of one stimulus and the onset of another was 500 msec. All grating stimuli were oriented at 90°, unless otherwise stated, and the spatial phase was random for each presentation. All stimuli were 10°-wide squares, as used in the FDT perimeter, and were presented centrally or at 15° eccentricity, as measured from the center of the stimulus.

The FD stimulus was used in both a detection and an orientation resolution paradigm. In the detection paradigm (FD detection), subjects were permitted to respond to any attribute of the FD stimulus, irrespective of whether spatial form was visible, hereinafter referred to as a simple-detection criterion. In the orientation resolution paradigm (FD resolution), subjects were forced to choose whether the bars in the FD stimulus were oriented at 45° or 135°. Comparison of the results from these two paradigms allows the effect that detection versus pattern resolution criteria has on the mechanisms isolated by the FD stimulus to be determined. For the principal author, detection thresholds were measured using a two-interval, forced-choice paradigm, and discrimination thresholds were measured using a two-alternative, forced-choice paradigm. Forced-choice experiments were used to eliminate any bias in this non-naïve observer. A ZEST (zippy estimation by sequential testing) procedure[17] of 30 trials, which converged at the 88% correct level, was used to manipulate contrast. In the remaining five observers, detection thresholds were measured using a yes/no paradigm of eight trials, with the ZEST procedure converging at the 78% correct level, and discrimination thresholds were measured as for the principal author. Thresholds from each subject were the geometric mean of at least two measurements. Although the difference in convergence levels between the forced-choice and yes/no paradigms would be expected to have a small effect on absolute thresholds (0.05 log units, using a typical model of the psychometric function[17]), there is no effect on the relative thresholds used in all the analyses presented in this article. Paradigm (detection or discrimination) and background luminance were kept constant during each experimental run, whereas spatial frequencies were interleaved.

Subjects

Six subjects, aged 29 to 51 years and with corrected vision better than or equal to 20/20, participated in the experiments. All subjects had no history of eye disease. Each subject viewed the monitor monocularly with his or her preferred eye and natural pupils, and fixation was maintained with a small, dark marker in the center of the monitor. Three subjects had a history of migraine, but all were required to have normal field results on the FDT perimeter. The study complied with the tenets of the Declaration of Helsinki and was approved by our institutional human experimentation committee, with all subjects giving informed consent before participation.

Analysis

Slopes of the curves presented in the figures were compared using a one-way repeated-measures ANOVA, with the Dunnett method used to compare each group with the FD simple-detection group. The criterion for significance was $P \leq 0.05$. A one-way repeated-measures ANOVA on ranks was performed when data were not normally distributed or were of unequal variance ($P \leq 0.05$). All statistical testing was performed on computer (SigmaStat 2.0; SPSS Science, Chicago, IL).

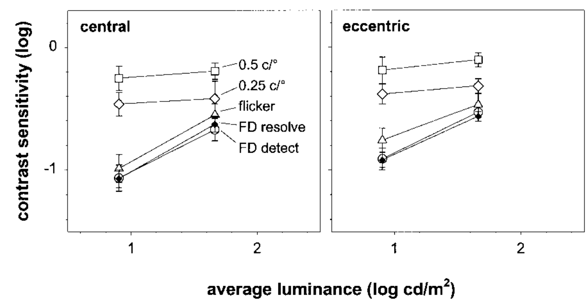

FIGURE 1. Effect of background luminance on contrast sensitivity for a variety of stimulus classes: (□), 0.5 cyc/deg static grating; (◇), 0.25 cyc/deg static grating; (△), 25-Hz flickering squares; (○), detection thresholds for an FD (0.25 cyc/deg, 25 Hz) stimulus; (◆), resolution thresholds for the FD stimulus. Error bars, ±SEM.

Experiment 1: Effect of Adaptation

It is known that the light adaptation characteristics of the visual system change with the spatiotemporal characteristics of the stimulus.[18] We determined light adaptation characteristics using an FD stimulus (0.25 cyc/deg, 25 Hz) in both a simple-detection and a resolution task, to see whether they could be differentiated from the adaptation characteristics of static gratings (0.25 and 0.5 cyc/deg) and a spatially uniform flickering target (25 Hz).

Stimuli were presented on backgrounds of 8 and 46 cd/m^2. Different background conditions were not interleaved. In addition, stimuli were presented on a local increase in luminance (a luminance pedestal) of 4 and 42 cd/m^2 above a background luminance of 4 cd/m^2, because it has been found that such local increases produce different light adaptation characteristics to full-field backgrounds.[19,20] Luminance pedestals had the same time course and spatial extent as the stimuli.

Experiment 2: Spatial and Temporal Tuning Characteristics

There is substantial evidence that the visual system consists of multiple filters with characteristic spatiotemporal tuning.[25–30] In this experiment, we examined the spatiotemporal tuning characteristics obtained with the FD stimulus, using both simple-detection and resolution tasks, and compared them with functions using uniform flicker and static grating stimuli.

Temporal-frequency tuning functions were determined for the uniform flicker and FD stimuli, from 10 to 40 Hz. Spatial-frequency tuning functions were determined for static gratings (0.25–2 cyc/deg) and the FD stimulus (0.25–1 cyc/deg, 25 Hz). A uniform background luminance of 46 cd/m^2 was used.

RESULTS

Experiment 1

The results for the uniform background luminances are shown in Figure 1. Sensitivity to the two static gratings remained largely unaltered as background luminance increased, consistent with Weberian adaptation.[21–23] Sensitivity to the FD and flickering stimuli improved, however, as background luminance increased, suggesting increased linearity as temporal frequency increases.[21–23] A similar change in FD sensitivity with background luminance has been found previously.[24] Similar patterns were found both centrally and eccentrically (Fig. 1, left and right panels, respectively). A repeated-measures ANOVA showed that both static gratings (unfilled squares and

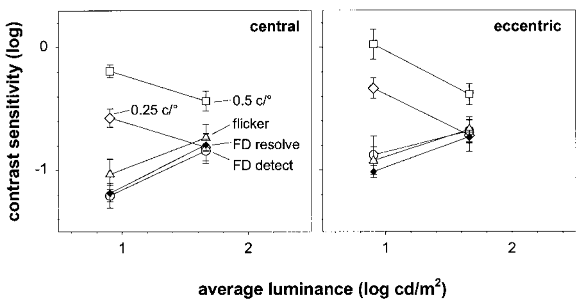

FIGURE 2. Effect of a local increase in luminance (a luminance pedestal) on contrast sensitivity. Stimulus classes are as in Figure 1. Error bars, ±SEM.

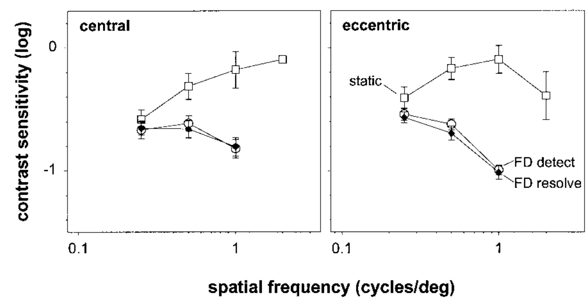

FIGURE 4. Spatial-sensitivity functions for a static grating patch (□) and for detection (○) and resolution (♦) of an FD stimulus. Error bars, ± SEM.

diamonds) had significantly ($P < 0.001$, central and eccentric) different adaptation characteristics from the FD simple-detection task, whereas the flickering and FD resolution stimuli were not significantly different from the FD simple-detection task.

The use of a luminance pedestal for adaptation (Fig. 2) resulted in negatively sloped adaptation curves for the static gratings and less positively sloped adaptation curves for the FD and flicker conditions, suggesting that the luminance pedestal partially defeats adaptation processes[19] and reduces contrast sensitivity. Despite this change in the absolute adaptation characteristic, comparison between groups is the same as found in Figure 1, with only the two static gratings having significantly ($P = 0.01$ and 0.001, central and eccentric, respectively) different adaptation characteristics from the FD simple-detection task.

Experiment 2

The temporal sensitivity tuning curves (Fig. 3) show that sensitivity decreased for all stimulus conditions as temporal frequency was increased. The high-frequency limbs (25–40 Hz) of all curves have indistinguishable slopes ($P = 0.28$ and 0.55, central and eccentric, respectively). At lower temporal frequencies (16–25 Hz), the flickering stimulus has a significantly shallower slope than the FD simple-detection stimulus ($P = 0.01$ and 0.001, central and eccentric), whereas the slope for the FD resolution task is indistinguishable from the FD simple-detection task.

The spatial sensitivity tuning curves (Fig. 4) show that sensitivity tended to increase with spatial frequency for the static grating, yet decreased for both FD tasks. Slopes for the functions both higher and lower than 0.5 cyc/deg are significantly different between the static grating and FD simple-detection task, but indistinguishable between the simple-detection and resolution paradigms for the FD stimulus ($P = 0.01$ and 0.001, below and above 0.5 cyc/deg centrally, and $P = 0.001$ and 0.001, below and above 0.5 cyc/deg eccentrically, respectively). Our results agree with similar experiments in which 10-Hz flickering gratings were used.[31]

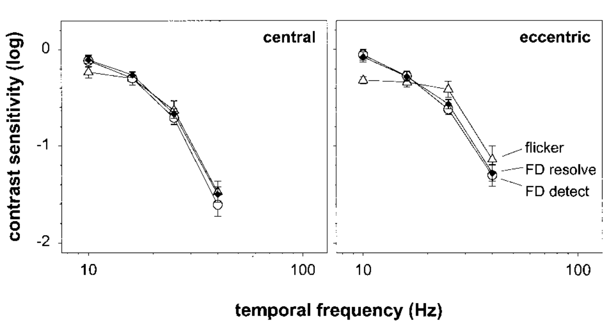

FIGURE 3. Temporal sensitivity functions for a flickering patch (△) and for detection (○) and resolution (♦) of an FD stimulus. Error bars, ± SEM.

DISCUSSION

Our results demonstrate that the mechanisms underlying sensitivity to the FD stimulus can be differentiated from those underlying spatially uniform flicker and static contrast sensitivity through the use of adaptation and spatiotemporal tuning characteristics.

The spatiotemporal tuning functions measured with an FD stimulus had identical shapes for both simple-detection and resolution criteria (Figs. 3, 4). This unity was preserved under differing levels of light adaptation, both when the entire field changed luminance (Fig. 1) and when only the stimulus area changed luminance (Fig. 2). These findings demonstrate that simple-detection strategies isolate the same mechanism or mechanisms as when criteria based on the appearance of spatial structure (as used by Maddess et al.,[4] Maddess and Henry,[6] and Bedford et al.[7]) are used. As such, subjects performing FDT perimetry should be instructed to respond to the perception of any target, which appears to be the criterion on which the normative database in the perimeter is based.[9] Although absolute sensitivity may vary, depending on the criterion used in FDT perimetry,[9,32] the mechanisms isolated do not. These findings also emphasize the importance of the instructions given to patients undergoing FDT perimetric testing, a result that has also been reported for standard automated perimetry.[33]

We found no evidence that spatially uniform flicker differs from an FD stimulus at 25 Hz and above, because both have indistinguishable adaptation and temporal tuning characteristics. We confirm therefore the hypothesis that FD stimuli and large, rapidly flickering targets isolate similar underlying mechanisms.[6] Given this, it is not surprising that spatially uniform flicker and an FD stimulus were found to have similar specificities and sensitivities for the detection of glaucoma.[14] The temporal-tuning characteristics of the two stimuli differed below 25 Hz (Fig. 3), however, suggesting a divergence in the mechanisms isolated at these lower temporal frequencies. It is known that the visibility of the FD phenomenon decreases as temporal frequency decreases,[7,10,34,35] and so it is possible that the spatial frequency of the FD stimulus ceased to appeared doubled at these lower temporal frequencies. This loss of the FD phenomenon may relate to the observed divergence between flicker and FD sensitivity, although this was not tested in our experiments.

Spatial-tuning characteristics (Fig. 4) and adaptation characteristics (Figs. 1, 2) were significantly different between the FD stimulus and static gratings, suggesting that the two stimuli isolate different mechanisms within the visual system. Despite this difference, Johnson and Demirel[14] found static gratings to have only slightly lower specificities and sensitivities for the detection of glaucoma than did the FD stimulus. These findings suggest that many spatiotemporally discrete stimuli that are preferentially detected by a single visual filter may successfully detect glaucomatous loss, because redundant filters do not exist to mask any small losses of sensitivity.[36] As such, the success of FDT perimetry in detecting glaucoma[2,3,37–40] may not be that its stimuli are detected by a pathway that is preferentially damaged by glaucoma,[6] but more that its stimuli are more spatiotemporally discrete than those used in conventional increment-threshold perimetry.

In conclusion, we found that the mechanism or mechanisms isolated by the FD stimulus were indistinguishable when subjects responded to any percept (simple-detection) from when they respond to a distinct spatial form (i.e., the appearance of a striped pattern). At a temporal frequency of 25 Hz or greater, we found evidence that that the FD stimulus isolated mechanisms similar to those isolated by a spatially uniform flickering patch.

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