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CLINICAL SCIENCE

The Hermann-Hering grid illusion demonstrates disruption of lateral inhibition processing in diabetes mellitus

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Background/aim: The Hermann-Hering grid illusion consists of dark illusory spots perceived at the intersections of horizontal and vertical white bars viewed against a dark background. The dark spots originate from lateral inhibition processing. This illusion was used to investigate the hypothesis that lateral inhibition may be disrupted in diabetes mellitus.

Method: A computer monitor based psychophysical test was developed to measure the threshold of perception of the illusion for different bar widths. The contrast threshold for illusion perception at seven bar widths (range 0.09° to 0.60°) was measured using a randomly interleaved double staircase. Convolution of Hermann-Hering grids with difference of Gaussian receptive fields was used to generate model sensitivity functions. The method of least squares was used to fit these to the experimental data. 14 diabetic patients and 12 control subjects of similar ages performed the test.

Results: The sensitivity to the illusion was significantly reduced in the diabetic group for bar widths 0.22°, 0.28°, and 0.35° ($p = 0.01$). The mean centre:surround ratio for the controls was 1:9.1 (SD 1.6) with a mean correlation coefficient of $R^2 = 0.80$ (SD 0.16). In the diabetic group, two subjects were unable to perceive the illusion. The mean centre:surround ratio for the 12 remaining diabetic patients was 1:8.6 (SD 2.1). However, the correlation coefficients were poor with a mean of $R^2 = 0.54$ (SD 0.27), $p = 0.04$ in comparison with the control group.

Conclusions: A difference of Gaussian receptive field model fits the experimental data well for the controls but does not fit the data obtained for the diabetics. This indicates dysfunction of the lateral inhibition processes in the post-receptoral pathway.

The presence of illusory light spots against a background of intersecting dark lines and light squares was first described by Brewster in 1844.¹ The illusion had been noticed while observing the bright sky against a leaded window frame. Hermann² and later Hering³ described the opposite effect, perception of dark spots at the intersections of light lines on a background of dark squares. Baumgartner⁴ suggested that the illusion results from circularly organised centre surround antagonism within the visual system, with overlapping centre surround receptive fields producing a depression of perceived brightness at the intersection of light bars.

The interconnections between horizontal cells, photoreceptors, and bipolar cells in the outer plexiform layer give rise to the bipolar cell receptive field, which has a circularly symmetric difference of two Gaussian shape.^{5–8} The interaction of amacrine cells, bipolar cells, and ganglion cells gives rise to the ganglion cell receptive field, which also has a circularly symmetric difference of two Gaussian configuration,^{9–14} whereas more complex field structures are seen in the higher processing centres.¹⁵ The Hermann-Hering grid illusion most probably originates in the middle and inner layers of the retina. Measurement of the illusory effect in humans is based on psychophysical responses and it is, therefore, more appropriate to discuss “perceptive fields,” particularly as although the origin of the illusion is clearly post-receptoral, the receptive fields of neurons throughout the visual system could contribute to the illusory perception, illustrated by changes in sensitivity as a function of orientation of the grid.^{16, 17}

Spillman¹⁸ developed a technique to allow use of the illusion to assess the size of the human perceptive field. A card printed with dark squares and light bars was viewed at different distances by an observer. The distance at which the illusion appeared maximal was measured and the visual angle subtended by the light bars at this distance was taken as the

measure of the size of the centre of the perceptive field. The card was subsequently moved further away from the subject until the illusion just disappeared, this angle taken as the size of the field surround. Using this technique the perceptive centre:surround ratio in a series of different observers was measured at different retinal eccentricities. He found that at the fovea the centre size was small, being approximately 4–5 minutes of arc, increasing to 1.7° at 15° eccentricity and 3.4° at 60° eccentricity.¹⁹

The main difficulty with this method is the judgment of illusory maxima by the observer. The human visual system lends itself well to detection of absolute thresholds and relative differences but not to absolute maxima. In our study a new experiment was developed based on measurement of the contrast threshold of perception of the illusion. This was accompanied by a computational analysis that allows estimation of the size of the centre and surrounds of the perceptive field.

Diabetic retinopathy is the most common form of diabetic eye disease²⁰ and the commonest cause of visual impairment in the diabetic population.²¹ The anatomical effects of diabetic retinopathy occur in the middle and inner retinal layers. Contrast sensitivity has been investigated in patients with diabetes and the results of different studies vary in terms of correlation with the extent of retinopathy as a function of spatial frequency.^{22–33} Diabetes, however, also has effects on the cornea,³⁴ lens,^{35–40} macular pigment,³⁷ and photoreceptors,⁴¹ which can also affect contrast sensitivity. The Hermann-Hering grid illusion originates in the middle and inner layers of the retina and is a useful tool for studying the function of this part of the visual system. This study tested two hypotheses—firstly, that the illusion can arise solely from a system using difference of two Gaussian detectors and, secondly, that perception of the illusion is altered in diabetes as a result of a disruption of the lateral inhibition processing.

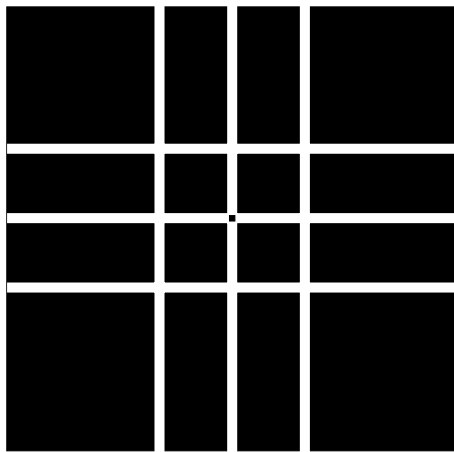


Figure 1 The Hermann-Hering grid used in the estimation of receptive field size in diabetic subjects and controls. When fixating the central marker, the grey "blobs" at the other eight intersections can be seen.

METHODS

The stimulus was presented on a calibrated monitor (Nokia 477xi) and generated by an IBM compatible PC. An 8 bit graphics card was used allowing the generation of 256 grey scale levels. The dot pitch of the monitor was 0.25 mm and the pixel window used by the computer was 1280 × 1024. The code for the stimulus presentation, data collection, and analysis was written in MATLAB V 5.2 (Mathworks Inc).

The test subject was seated at a distance of 1 metre from the monitor. An eye patch was worn over the left eye and the room darkened. The monitor displayed a grey square 10 cm × 10 cm in size, of luminance 30 cd/m² with a central black fixation spot, which was fixated with the right eye. The remainder of the screen was blanked off by a piece of black card. A grey on grey Hermann-Hering grid was then presented for a period of 1 second in a square wave temporal window at the same mean luminance (30 cd/m²) as the background. A total of eight grid intersections were viewed at 1 metre with an appropriate refractive correction if necessary, at an eccentricity of 1.7° at the apices and 1.2° at the sides (Fig 1). Following this, the screen returned to the background grey level, the central fixation marker remaining present. The subject responded "yes" if the illusion was seen or "no" if not. The operator (NPD in all cases) entered responses into the computer. The contrast threshold for detection of the illusion was assessed eight times for seven different bar widths using a randomly interleaved double staircase (visual angles 0.09, 0.16, 0.22, 0.28, 0.35, 0.47, and 0.60 degrees). The different bar widths were presented randomly to avoid afterimage effects.

Maintenance of a constant luminance throughout the experiment was achieved following a consideration of the Michelson contrast of the grid (see Appendix on *BJO* website). Analysis of the data collected gave mean log contrast sensitivity, with an accompanying standard error as a function of bar width in visual angle.

The study had approval from the research and ethics committee of St Mary's Hospital, London, and all patients gave written consent to be involved in the study. Fourteen diabetics and 12 controls performed the experiment. The control group had no ocular or systemic disease with ocular effects. The diabetic group had no other ocular or systemic disease with ocular effects. The level of retinopathy and grade of maculopathy were classified using the modified Airlie House classification.²⁰ Two of the diabetic subjects were unable to perceive the illusion, neither in the monitor, nor when viewing a printed card of the same stimulus under monocular or binocular conditions, at any distance of fixation, despite detailed

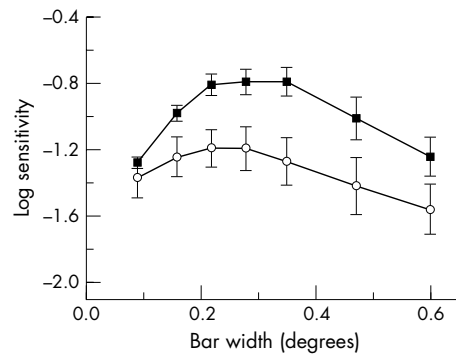


Figure 2 Plot of the mean sensitivity to the Hermann-Hering grid illusion for the diabetic group. The amplitude of the function for the diabetics is reduced in comparison with the controls. Error bars are plus or minus one standard error.

instructions and a description of the appearance of the illusion and they were excluded from the analysis. One patient had had focal macular laser treatment and had obvious laser scars temporal to the macula, but outside the area illuminated by the grid and had no macula oedema and a visual acuity of 0.00 logMAR at the time of the study. The second patient had had proliferative retinopathy treated with panretinal photocoagulation and had also had focal laser treatment to the macula, nasal to the fovea, but not temporally. This patient had grade 2 maculopathy and a visual acuity of 0.10 logMAR at the time of the study. The remainder of the subjects had no difficulty perceiving the illusion, first viewed on a printed card and subsequently viewed on the screen. The mean age of the diabetic group was 50.4 years (SD 8.5) and of the controls 45.8 (SD 12) years ($p=0.29$). Five of the diabetic patients had previously had macular photocoagulation for clinically significant macular oedema (of which three had also undergone panretinal photocoagulation). Seven patients had no maculopathy, four had grade 1 maculopathy, and one had grade 2 maculopathy. The mean logMAR acuity of the diabetic group assessed using the single letter scoring system was 0.03 log units (SD 0.05).

RESULTS

The results of each experiment are calculated as the mean log sensitivity and standard error derived from the eight threshold points measured as a function of visual angle. The overall mean sensitivities and standard deviations for both groups are plotted as a function of visual angle in Figure 2 and the results presented in Table 1. Analysis of variance shows a significant difference between the groups ($p = 0.004$). Multiple two sample comparisons between the sensitivities obtained at each bar width were performed. This shows a significant reduction in sensitivity to the illusion in the diabetic group for visual angles 0.22°, 0.28°, and 0.35° ($p=0.01$). Applying the Bonferroni correction for multiple tests suggests

Table 1 Mean log sensitivity of the data obtained with a statistical comparison between the two sets of data (Student's *t* test)

Bar width (degrees)	Controls	SD	Diabetics	SD	p Value
0.09	-1.28	0.11	-1.37	0.40	0.48
0.16	-0.98	0.15	-1.24	0.39	0.06
0.22	-0.81	0.20	-1.19	0.36	0.01
0.28	-0.79	0.24	-1.19	0.42	0.01
0.35	-0.79	0.27	-1.27	0.46	0.01
0.47	-1.01	0.41	-1.42	0.54	0.06
0.6	-1.24	0.38	-1.56	0.48	0.09

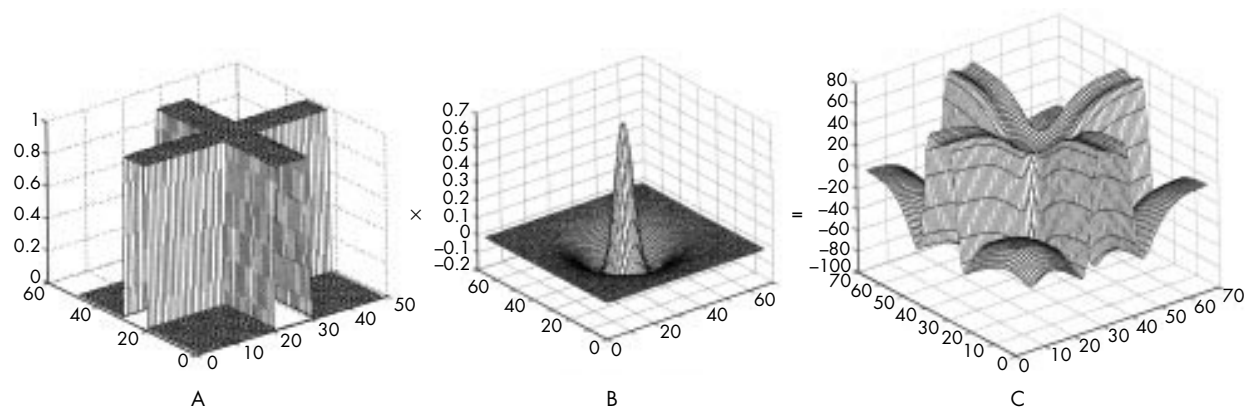


Figure 3 The convolution of the grid intersection (A) with the difference of Gaussian receptive field (B) gives the response (C).

that the p value for significance should be reduced to 0.007, but this adjustment method has been criticised⁴² and the reduction in sensitivities noted at these visual angles in the diabetics are probably sufficiently low to allow rejection of the null hypothesis.

There was no correlation between visual acuity and maximum sensitivity to the illusion ($r = -0.09$, $p = 0.80$) nor to overall amplitude of the illusory response ($r = 0.28$, $p = 0.42$).

Computational model of Hermann-Hering grid illusion

A model of the illusion was developed using two dimensional difference of two Gaussian (DOG) receptive fields. The centre to surround size was expressed in terms of the space constants in the DOG expression:

$$R(x,y) = A_c e^{-(x^2+y^2)/\sigma_c^2} - A_s e^{-(x^2+y^2)/\sigma_s^2} \quad (1)$$

where $R(x,y)$ is the receptive field, A^c and A^s are relative amplitudes, σ^c = central space constant, and σ^s = surround space constant.

Two dimensional difference of Gaussian (DOG) receptive fields were calculated for a large number of different centre to surround ratios in the range 1:1.1 to 1:30. The constants A^c and A^s were chosen to produce a zeroed response for uniform illumination. The information relayed to the higher processing centres from the retinal image can be modelled by calculating the convolution of the image with the detector function.⁴³ This can be represented by:

$$O(x,y) = I(x,y) \times R(x,y) \quad (2)$$

where $O(x,y)$ represents the retinal output, $I(x,y)$ the retinal image, and $R(x,y)$ the perceptive field structure. A single result is shown in Figure 3, where the illusory effect is seen in at the intersection. Using a linear processing model, sensitivity to the

Table 2 Best fit parameters for the difference of Gaussian model to the Hermann-Hering grid data. The centre and surround space constants are given in degrees

	Centre	Surround	Ratio	R ²
Control group	0.020	0.210	10.50	0.94
	0.015	0.205	13.67	0.76
	0.025	0.215	8.60	0.65
	0.025	0.215	8.60	0.43
	0.020	0.185	9.25	0.87
	0.020	0.145	7.25	0.92
	0.025	0.165	6.60	0.87
	0.025	0.180	7.20	0.92
	0.025	0.170	6.80	0.94
	0.025	0.215	8.60	0.50
	0.025	0.215	8.60	0.73
	0.020	0.205	10.25	0.82
	Diabetic group	0.025	0.160	6.40
0.015		0.205	13.67	0.28
0.020		0.210	10.50	0.12
0.020		0.210	10.50	0.90
0.010		0.200	20.00	0.31
0.015		0.065	4.33	0.83
0.025		0.215	8.60	0.40
0.010		0.155	15.50	0.80
0.025		0.175	7.00	0.64
0.010		0.090	9.00	0.94
0.025		0.215	8.60	0.56
0.010		0.200	20.00	0.14

Table 3 Comparison of the best fit data obtained for both groups of subjects and presented in Table 2

	Centre	Surround	Ratio	R ²
Control group				
Mean	0.023	0.194	8.83	0.78
SD	0.003	0.024	1.97	0.17
Diabetic group				
Mean	0.018	0.175	11.18	0.56
SD	0.007	0.050	5.10	0.30
p Value (t test)	0.03	0.26	0.16	0.04

illusion is proportional to the increment of the illusion in comparison with the light bars. This difference was calculated for each perceptive field size and bar width taking the mean of the four central pixels in the image as the illusion value and the mean of four pixels in the area of a light bar as the bar depth. This gives a sensitivity function for each DOG perceptive field of sensitivity to the illusion with respect to bar width.

Difference of two Gaussian model fitting

A curve fitting routine was written to find the best fit of the model sensitivity curves to the experimental data, using the method of least squares.

The result is expressed as the centre:surround ratio of the DOG perceptive field and the absolute visual angle of the central space constant that gives the best fit to the data. The R² correlation coefficient for the fit was also calculated as an indication of the variance in the data that can be explained by the model. The best fit of the model to the experimental data was calculated for each individual and the results is presented in Table 2. A comparison of the parameters obtained from the fitting between the two groups is given in Table 3, showing a significantly reduced goodness of fit for the diabetic group ($p=0.04$). Although the data also suggest a significant reduction in the central space constant for the diabetic group, the poor fit of the model indicates that the measure of centre size in the diabetics is not reliable. Examples of the best fits are shown in Figure 4 for the controls and in Figure 5 for the diabetics, showing abnormal responses to the illusion and a poor fit to the model.

DISCUSSION

The experiment developed above to assess the threshold of perception of the Hermann-Hering grid illusion shows abnormality in the diabetic group in comparison with the controls. Two of the diabetic patients were unable to perceive the illusion; none of the control subjects experienced this difficulty. The mean sensitivity of perception of the illusion was significantly reduced for the diabetic group at visual angles 0.22°, 0.28°, and 0.35° (Fig 2).

Visual acuity declines rapidly with eccentricity and by 1° has reached 60% of its maximum.⁴⁴ Foveal perceptive fields are very small (a finding illustrated by the absence of the illusion for foveally fixated grid intersections) and perceptive field size increases with increasing eccentricity.¹⁹ On the basis of this one would not expect a central visual acuity to correlate with sensitivity to the illusion as the two measures are made at different retinal locations, each with different functional attributes. No correlation between these variables is seen in our data.

The model developed using difference of Gaussian receptive fields gives a function that agrees qualitatively with the response obtained from normals by experiment. The sizes of centre and surround space constants agree with those obtained previously using psychophysical techniques.⁴⁵⁻⁴⁶ The centre:surround ratios are greater than the ratios obtained previously using electrophysiological techniques,¹¹⁻¹³⁻⁴⁷ although it has been shown that psychophysically measured field sizes are larger than those measured electrophysiologically by a factor of 1.3–2.⁴⁸ Model fitting to the data obtained from the diabetic patients is rather poor and shows that the illusory response is not satisfactorily explained by a detector system using difference of Gaussian perceptive fields.

The ocular media of diabetic subjects have been shown to be abnormal³⁴⁻⁴⁰ and there is the possibility that this could explain the differences observed between the patients and controls. Light loss in the ocular media (by absorption and reflection) does not, however, affect contrast at the retina, as long as the spectral distribution of light in the light bars and dark squares is the same, which is ensured by using a grey scale achromatic grid. Forward scattered light has the effect of reducing contrast in the retinal image, which itself would lead to an overestimation of the threshold for perception of the illusion. This would result in a global reduction in sensitivity to the illusion (see Appendix on *BJO* website), but no change in shape of the response function. Importantly, for the diabetic

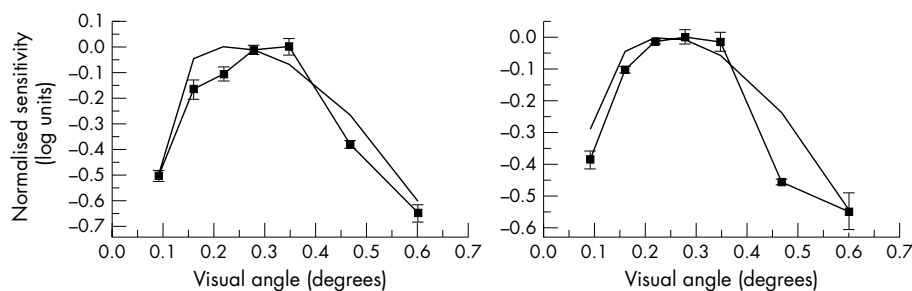


Figure 4 Best fit of model to experimental data obtained for two control subjects. The data are shown as black squares, the error bars are plus or minus one standard error. The model sensitivity curve is plotted as a solid line.

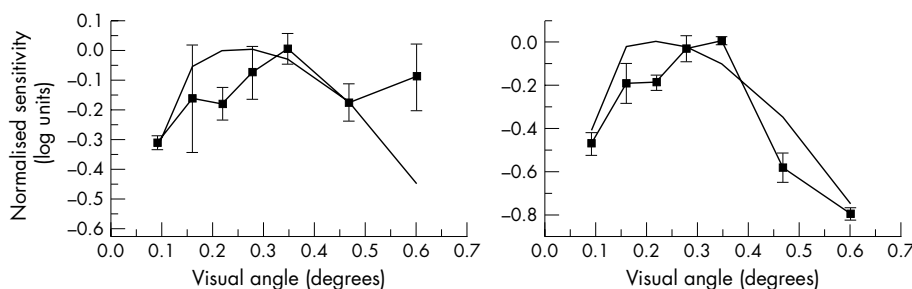


Figure 5 Best fit of model to experimental data obtained for two diabetic subjects. The data are shown as black squares, the error bars are plus or minus one standard error. The model sensitivity curve is plotted as a solid line.

patients the sensitivity to the illusion at the extremes tested is not different from that found in the normals (Table 1). Also for each individual the shape of the response is altered in a way that can not be explained by a simple increase in forward scattered light (confirmed by the poor fit to the computational model). It thus appears very unlikely that changes in the ocular media of the diabetic patients can explain the results observed.

Previous measurements of contrast sensitivity have identified deficits in spatial vision in patients with diabetes,^{22 24–33 49–54} although the results have been variable. Loss of sensitivity in retinopathic patients has been reported in some studies^{27 28} but not others.⁴⁹ Arden showed no difference between control subjects and diabetics without retinopathy,⁴⁹ but a difference in diabetics with retinopathy, whereas Ghafour *et al.*,²⁹ using the same test, found a significant difference in the contrast sensitivity of retinopathic diabetics in comparison with normals. Sokol *et al.*³² found that patients classified as having NIDDM without retinopathy had abnormal contrast sensitivity at high spatial frequencies and at all spatial frequencies in the presence of retinopathy. Trick *et al.*³³ noted loss of contrast sensitivity in mid to high range spatial frequencies. The grating periodicities that revealed differences between normals and diabetics were different for different studies; 6 cpd in one study,⁵¹ 22.8 cpd in another,³² and a wide range of low frequencies in another.²⁷

Contrast sensitivity is sensitive to changes in the preretinal ocular filters as well as neurosensory dysfunction. Correcting contrast sensitivity for Snellen acuity and for interferometric acuity, Chylack and co-workers²⁴ found that the degree of nuclear lens opacity could account for a portion of the loss of sensitivity at 6 and 12 cpd.

To assess the neural contribution to contrast sensitivity functions in diabetes, one study measured contrast sensitivity and lens optical density,²⁸ where no difference in the optical density of the lens was noted between diabetics and controls. Contrast sensitivity improved significantly after breathing 100% oxygen in patients with early background retinopathy⁵² and remains abnormal even when lens density is accounted for, in both retinopathic and aretinopathic patients.³⁰ Loss of contrast sensitivity has been correlated with decreased capillary blood velocity in diabetes, increased perifoveal capillary area, and also with increased extent of the foveal avascular zone at 12 cycles per degree.⁵³ The correlation of the sensitivity loss with the perifoveal intercapillary area and foveal avascular zone extent was, however, rather weak (with $R^2 = 0.29$ and 0.36). Although the findings of the above studies clearly show a neural origin of loss, the analysis of the contrast sensitivity functions obtained has been limited to comparisons at individual spatial frequencies and has not been extended to an estimation of perceptive field structure and extent. This is, however, difficult and requires several assumptions in the calculations.⁵⁶ Information regarding perceptive field size is relatively accessible when using the Hermann grid illusion as seen here. Our results suggest a post-receptor loss of spatial visual processing in diabetes that is consistent with the site of anatomical disruption caused by the disease. Further study of the Hermann grid illusion on a larger number of patients with different stages of retinopathy will allow a greater understanding of the effects of diabetes on lateral inhibition processing in the visual system.

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