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Individual differences in the shape of the nasal visual field

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ABSTRACT

Between-subject differences in the shape of the nasal visual field were assessed for 103 volunteers 21–85 years of age and free of visual disorder. Perimetry was conducted with a stimulus for which contrast sensitivity is minimally affected by peripheral defocus and decreased retinal illumination. One eye each was tested for 103 volunteers free of eye disease in a multi-center prospective longitudinal study. A peripheral deviation index was computed as the difference in log contrast sensitivity at outer (25–29° nasal) and inner (8° from fixation) locations. Values for this index ranged from 0.01 (outer sensitivity slightly greater than inner sensitivity) to −0.7 log unit (outer sensitivity much lower than inner sensitivity). Mean sensitivity for the inner locations was independent of the deviation index ($R^2 < 1\%$), while mean sensitivity for the outer locations was not ($R^2 = 38\%$, $p < 0.0005$). Age was only modestly related to the index, with a decline by 0.017 log unit per decade ($R^2 = 10\%$). Test-retest data for 21 volunteers who completed 7–10 visits yielded standard deviations for the index from 0.04 to 0.17 log unit, with a mean of 0.09 log unit. Between-subject differences in peripheral deviation persisted over two years of longitudinal testing. Peripheral deviation indices were correlated with indices for three other perimetric stimuli used in a subset of 24 volunteers (R^2 from 20% to 49%). Between-subject variability in shape of the visual field raises concerns about current clinical visual field indices, and further studies are needed to develop improved indices.
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1. Introduction

Scientists have studied the visual field since the time of Hippocrates and Euclid, and in modern perimetry the influential work of Traquair led to the concept of a "hill of vision" (Traquair, 1938). For the small stimuli used in perimetry, sensitivity declines monotonically with increased eccentricity, which gave the idea of a "hill." Contemporary perimetric methods use normative data derived from monocular testing of hundreds of people free from disease, documenting changes in the hill of vision with age and detecting visual field defects by comparing patient data with age norms (Bengtsson & Heijl, 1999). The emphasis is on the shape of the hill of vision, which becomes steeper with age, and an adjustment in the overall "height" of the hill of vision due to factors such as subject criterion and clarity of optical media (Heijl, Lindgren, Olsson, & Asman, 1989).

These normative values for the hill of vision are specific for the 0.4° diameter circular luminance increment that was introduced to perimetry in the first half of the 20th century (Goldmann, 1999) and became the clinical standard in the second half. It is now known that there are substantial between-subject differences in peripheral defocus, sufficient to affect contrast sensitivity for the small stimulus that was used to gather these norms (Horner, Dul, Swanson, Liu, & Tran, 2013). Furthermore, it has been found that the adapting luminance used to gather the norms was not high enough for Weber's law to hold, so variations in pupil size and lenticular density can affect sensitivity (Swanson, Dul, Horner, Liu, & Tran, 2014). It seems likely that some of the reported effects of age on the shape of the visual field measured with this small stimulus may be due to age-related optical factors such as pupillary miosis and increased lenticular density. Furthermore, with low-spatial-frequency sinusoidal stimuli it has been found

Abbreviations: CAP, conventional automated perimetry, Goldmann size III in the 24-2 test pattern; CSP, first generation of contrast sensitivity perimetry (Hot, Dul, & Swanson, 2008); CSP-2, second generation of contrast sensitivity perimetry (Swanson et al., 2014) where stimulus size varies with location; FDP, frequency-doubling perimetry in the 24-2 test pattern; MS, mean sensitivity, the average log contrast sensitivity across all locations tested with CSP; PDI, Peripheral deviation index. This is the difference in log contrast sensitivity for outer and central locations and is negative when outer sensitivity is lower than inner sensitivity.

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that the "hill" of vision can be rather flat (Anderson & Johnson, 2003; Pointer & Hess, 1989). The purpose of the current study was to assess between-subject differences in the shape of the monocular hill of vision, and the effects of age, using a low-spatial-frequency sinusoid that is resistant to peripheral defocus and an adapting luminance high enough that Weber's law holds even for small pupils.

The primary focus of this study was on the nasal visual field, because the asymmetric decline in perimetric sensitivity between the nasal and temporal visual field is the opposite of the corresponding decline in ganglion cell density (Keltgen & Swanson, 2012). We have modeled this in terms of local spatial scale (Watson, 1987) being determined by cortical rather than retinal factors (Pan & Swanson, 2006). With monocular perimetry, for a given vertical coordinate in the nasal visual field, horizontal location between 4° and 15° had little or no impact on local spatial scale (Keltgen & Swanson, 2012). With binocular perimetry, what is nasal in one eye is temporal in the other eye, so the region of the visual field that contains the physiological blind spot in one eye is part of this unusually flat region of the nasal visual field in the other eye. Horizontal location has been found to affect binocular contrast thresholds between 4° and 15° (Strasburger, Rentschler, & Juttner, 2011), so we wanted to know how much individuals varied from the mean shape of the nasal visual field. Furthermore, the region of the nasal visual field that we studied corresponds to the retinal region that includes the temporal raphe, where it is possible to image the beginnings of retinal nerve fiber bundles (Huang, Gast, & Burns, 2014; Huang et al., 2015). This region is therefore of interest in structure-function studies in patients with glaucoma. The combination of basic and clinical interest led us to focus on the nasal visual field, but results apply more broadly across the visual field.

2. Material and methods

2.1. Participants

Over the duration of the multi-center study, volunteers were tested at four different locations. Three locations were at Indiana University School of Optometry and one location was at State University of New York (SUNY) College of Optometry. The research for this study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review boards at Indiana University and SUNY College of Optometry. Informed consent was obtained from each participant after explanation of the procedures and goals of the study, before testing began.

Volunteers were recruited in the age range 21–85 years and were required to have regular eye exams, be free of visual disorder, have spherical equivalent refractive error between −6 D and +2 D, with cylinder $\leqslant -2.5$ D, and corrected visual acuity of 20/20 or better (20/25 over age 70). These volunteers were experienced and reliable on perimetric testing (Marin-Franch & Swanson, 2013; Swanson, Malinovsky, et al., 2014).

Volunteers were tested with contrast sensitivity perimetry (CSP), which refers to perimetry with Gabor stimuli (Harwerth et al., 2002). A reliable CSP test was defined as one with false negative rate no greater than 5%, false positive rate no greater than 10% and fixation loss no greater than 30%. These criteria removed 4 out of 107 people and 79 of 491 tests. The remaining 103 volunteers ranged in age from 21 to 85 years, median 53 years (mean ± standard deviation = 51 ± 18 years) and participated in testing from 1 to 10 times, median 3 tests (4.0 ± 2.6 tests), over periods ranging from 0.0 to 2.8 years, with 43% tested over at least 1 year and 29% tested over at least 2 years.

For the comparison of the CSP results with clinical perimetric sensitivities, data were analyzed for 24 of the volunteers who had participated in a published study in which conventional automated perimetry (CAP), a second generation of contrast sensitivity perimetry (CSP-2) and frequency doubling perimetry (FDP) were used. These volunteers ranged in age from 46 to 84 years, median 67 years (63 ± 11 years) and participated in CSP testing from 2 to 10 times, median 7 tests (6.1 ± 2.5 tests). Details of these methods are available elsewhere (Swanson, Malinovsky, et al., 2014).

2.2. Equipment

Two different designs for custom testing stations were used during the longitudinal investigation. Initially a 40 cm test distance was used (Hot, Dul, & Swanson, 2008), and this was later replaced by a 33 cm test distance (Swanson, Malinovsky, et al., 2014). The details of stimulus display, calibration, fixation monitoring, refractive correction for ametropia and test distance, stimulus configuration, test protocol and threshold algorithm for the CSP testing are available elsewhere (Hot et al., 2008; Horner et al., 2013; Swanson, Malinovsky, et al., 2014).

2.3. Stimuli

For the complete dataset of 103 volunteers, we used the CSP stimulus developed by Hot et al. (2008), a Gabor pattern (two-dimensional Gaussian multiplied by a sinusoidal grating) in sine phase with peak spatial frequency of 0.375 cycle/degree and a one-octave spatial bandwidth. The temporal presentation was a Gaussian pulse centered in a 600 msec window with a standard deviation (SD) of 100 msec. These spatial and temporal properties yield a stimulus resistant to variations in retinal illumination and peripheral defocus (Horner et al., 2013; Swanson, Dul, et al., 2014).

A second-generation CSP visual field test on the 33 cm testing stations used a broader spatial bandwidth for the Gabor stimuli and peak spatial frequency varying with visual field location. This is referred to as "CSP-2," and is described in detail elsewhere (Swanson, Malinovsky, et al., 2014). This was used with the subset of 24 volunteers tested with alternate forms of perimetry.

2.4. Analysis

This was an exploratory data analysis, so we examined effect size using correlation, linear regression, and F-tests (Wasserstein & Lazar, 2016). These statistical methods have good power to detect even modest effects: with 103 individuals, $p < 0.05$ is attained with $R^2 > 4\%$ and $F > 1.4$. P values are listed for any effects with $p < 0.05$ to provide a sense of likelihood that the result was due to chance.

A "mean sensitivity" (MS) index was computed as the average log contrast sensitivity across all 26 locations tested by CSP. A "peripheral deviation index" (PDI) was computed as the difference between outer and inner log contrast sensitivities. For the primary analysis, the outer value was computed as the average log contrast sensitivity for 4 locations 25–29° from fixation in the nasal visual field, and the inner value was computed as the average log contrast sensitivity for 4 locations 8° from fixation (Fig. 1, left panel). A negative value for PDI means that outer sensitivity was lower than inner sensitivity, and a PDI of zero or greater means that outer sensitivity was equal to or greater than inner sensitivity. For each volunteer, values for age, MS, inner sensitivity, outer sensitivity and PDI were averaged across all reliable tests, and these means were analyzed to assess individual differences.

Between-subject variability for the PDI was examined with non-parametric statistics (quartiles, box-and-whisker plot) and Gaussian statistics. Age effects were assessed by linear regression, and the remaining variability was expressed as the standard deviation (SD) of the residuals from the regression. Test-retest

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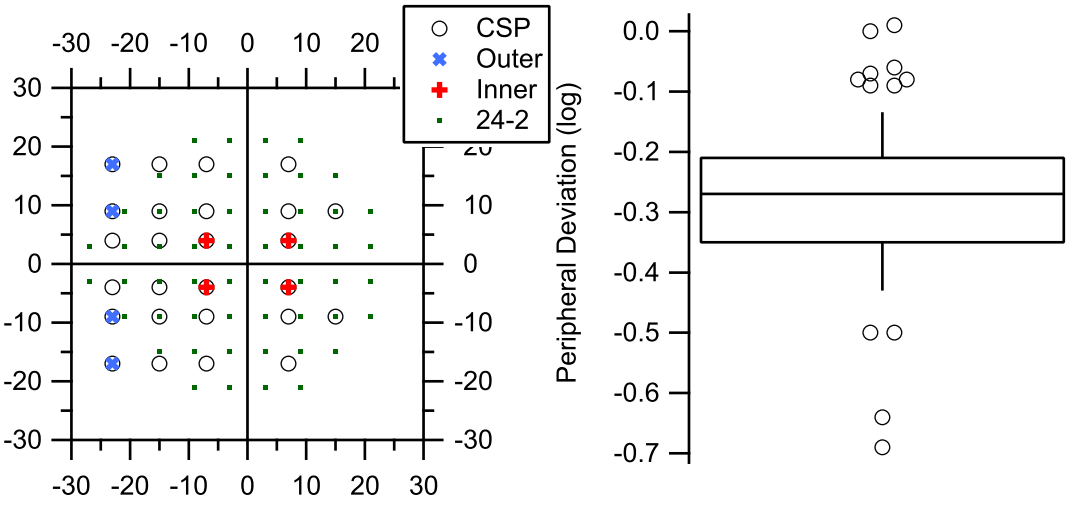

Fig. 1. Peripheral deviation index (PDI). Left panel: Stimulus locations used to compute the PDI, as the difference in log contrast sensitivity for outer and inner locations. Four locations at 8° from fixation were used for inner locations and four locations at 25–29° from fixation in the nasal visual field were used for outer locations. These are shown on a background map of the 26 locations for contrast sensitivity perimetry (CSP) and the locations of the 24-2 grid used in clinical perimetry. Right panel: Box-and-whisker plot for the peripheral deviation index (PDI) for the 103 volunteers. The boxes show the interquartile interval, the whiskers extend to the 10th and 90th percentiles, and the circles show 12 PDI values that fell beyond these computed percentiles.

variability was characterized as the SD across tests for each volunteer who had 7–10 reliable tests; Monte Carlo simulations indicated that on average this would be no more than 5% smaller than the true SD, and 95% of the time the underestimate would be no more than 15%.

3. Results

A total of 412 reliable CSP tests were completed by 103 volunteers over the 5 years of prospective testing. Fig. 1 (right panel) shows a box-and-whisker plot of the between-subject PDI values: the width of the interquartile interval was 0.14 log unit with a median PDI of −0.27 log unit. Two of the volunteers had no peripheral depression (PDI ⩾ 0.0), and two had deep peripheral depressions (PDI < −0.6). Fig. 2 shows Gaussians fit to histograms for MS and PDI; the standard deviation was 0.16 log unit for MS and 0.12 log unit for PDI ($F = 1.82$, $p < 0.005$).

Between-subject variability in PDI was only modestly due to effects of age, as shown in Fig. 3. There was a reduction in MS by 0.034 log unit per decade ($R^2 = 14\%$) and in PDI by 0.017 log unit per decade ($R^2 = 10\%$). The standard deviation of the residuals was 0.15 log unit for MS and 0.11 log unit for PDI ($F = 1.72$, $p < 0.005$).

Fig. 4 shows the two values used to compute PDI: mean sensitivity for the 4 locations nearest to fixation (inner, triangles) and mean sensitivity for the 4 most peripheral locations (outer, squares). These data are plotted as a function of their difference, which is the PDI. Between-subject variability was greater for outer sensitivities, with standard deviations of 0.16 log unit for inner sensitivities and 0.20 log unit for outer sensitivities ($F = 1.62$, $p < 0.01$). Mean sensitivity for the inner four locations was independent of PDI ($R^2 = 0.04\%$), while mean sensitivity for the outer 4 locations was not ($R^2 = 0.38\%$, $p < 0.0005$). The standard deviation of residuals was 0.16 log unit for both inner and outer sensitivities.

Fig. 5 shows test-retest variability for the 21 volunteers who had completed 7–10 CSP tests over both short-term (same day or 1 week later) and long-term (6 months later) intervals. For each volunteer, SDs are shown for PDI and its components (inner and outer sensitivities) as a function of mean PDI. Standard deviations

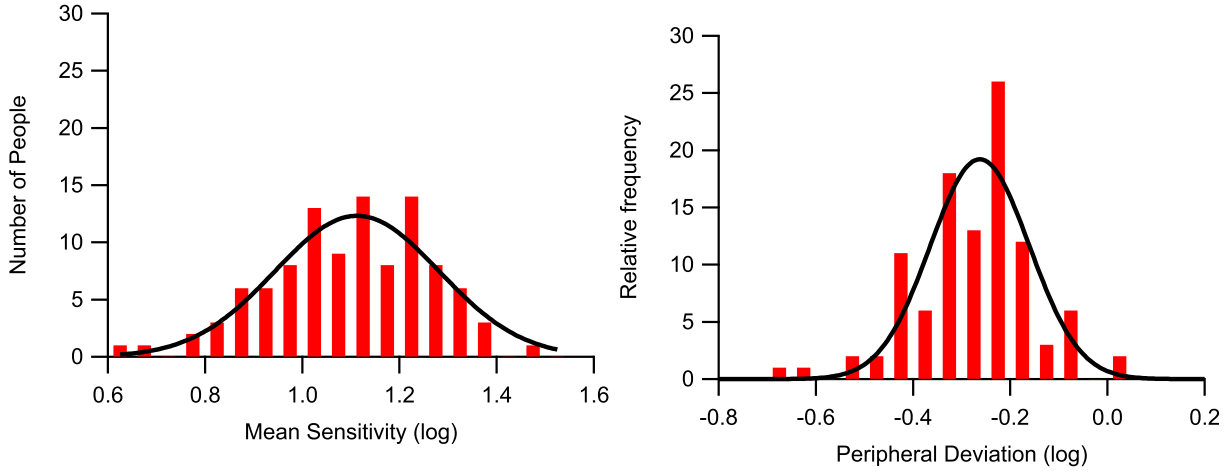

Fig. 2. Histograms for the 103 values for mean sensitivity (MS) and peripheral deviation index (PDI). The curves show Gaussian fits.

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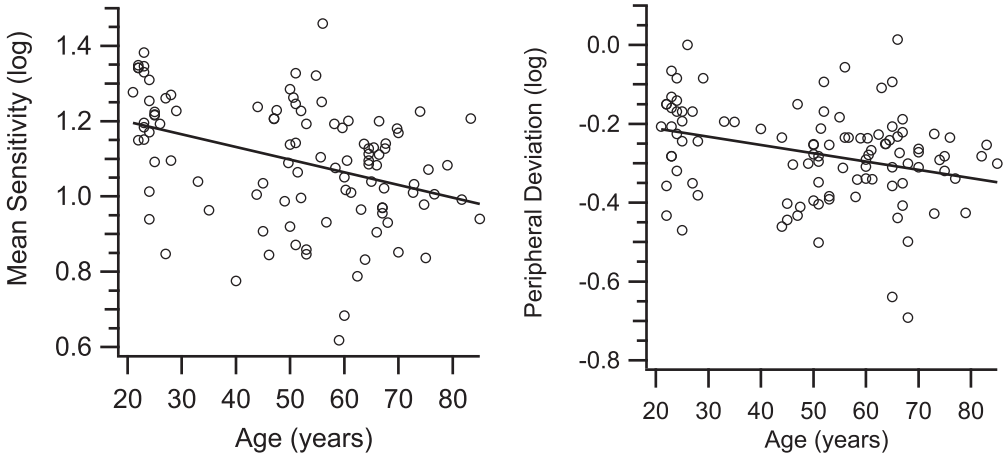

Fig. 3. Impact of age on mean sensitivity (MS) and peripheral deviation index (PDI). Lines show results of linear regression.

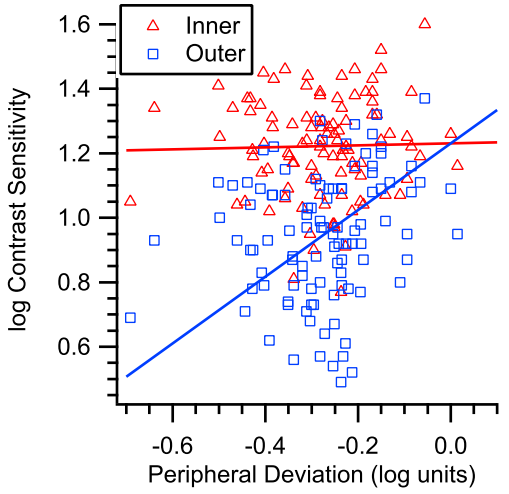

Fig. 4. Sensitivities at the inner and outer locations as a function of the peripheral deviation index (PDI). Lines show results of linear regression.

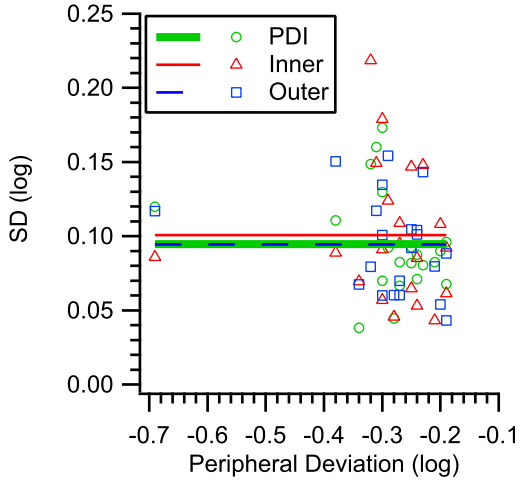

Fig. 5. Test-retest variability as standard deviation (SD) in log units for the 21 volunteers who had completed 7–10 visits. SDs are shown for sensitivities at inner and outer locations and for the peripheral deviation index (PDI), as a function of mean PDI value across the visits. Horizontal lines show means of SDs, which were similar for all three measures.

for PDI ranged from 0.04 to 0.17 log unit across volunteers, with a mean of 0.09 log unit. Fig. 6 shows individual longitudinal data for the two volunteers with the largest (#274) and smallest (#5018) PDI values, and two with PDI values near the upper bound of the interquartile interval. Subject #5018 had lower inner sensitivity than average, but this alone cannot account for the PDI because there were 17 people with inner sensitivities lower than for #5018, and their PDI values ranged from −0.50 to −0.11 (median −0.28) log unit.

Between-subject differences in PDI were related to between-subject differences for three other forms of perimetry, as shown in the right panel of Fig. 7. This comparison required that 2 of the outer locations used for the PDI be changed to be closer to the horizontal meridian, because CSP has two locations in the nasal visual field that fall outside the 24-2 pattern. The locations used to compute peripheral deviation for all 4 sets of test locations are shown in the left panel of Fig. 7. The correlation was stronger for CSP-2 (R^2 = 49%, $p < 0.0001$) than for FDP (R^2 = 21%, $p < 0.02$) and CAP (R^2 = 20%, $p < 0.02$).

4. Discussion

The shape of the monocular nasal visual field for contrast sensitivity perimetry (CSP) had between-subject variations that cannot be attributed to individual differences in peripheral defocus or retinal illumination, due to our choices for spatial and temporal properties of the stimulus. Much of the between-subject variability in shape of the nasal visual field that we measured was due to differences in peripheral sensitivity. This may reflect variability in how people distribute their attention when faced with uncertainty about visual field location of the stimulus they are to respond to. In traditional psychophysical studies the observer usually knows where the stimulus will occur, but in perimetric studies the observer must distribute attention across a very wide range of potential stimulus locations (Carrasco, 2011; Gardiner et al., 2008; Khuu & Kalloniatis, 2015; Pelli, 1985; Poggel, Treutwein, Calmanti, & Strasburger, 2012b; Wall, Woodward, & Brito, 2004).

This study focused on the nasal visual field because our lab has previously found that the nasal visual field shows a much more shallow decline in spatial scale than would be expected based on decline in ganglion cell density (Keltgen & Swanson, 2012), and that perimetric sensitivity is relatively constant across visual field locations once local spatial scale is accounted for (Pan & Swanson, 2006). These analyses related local spatial scale to cortical pooling

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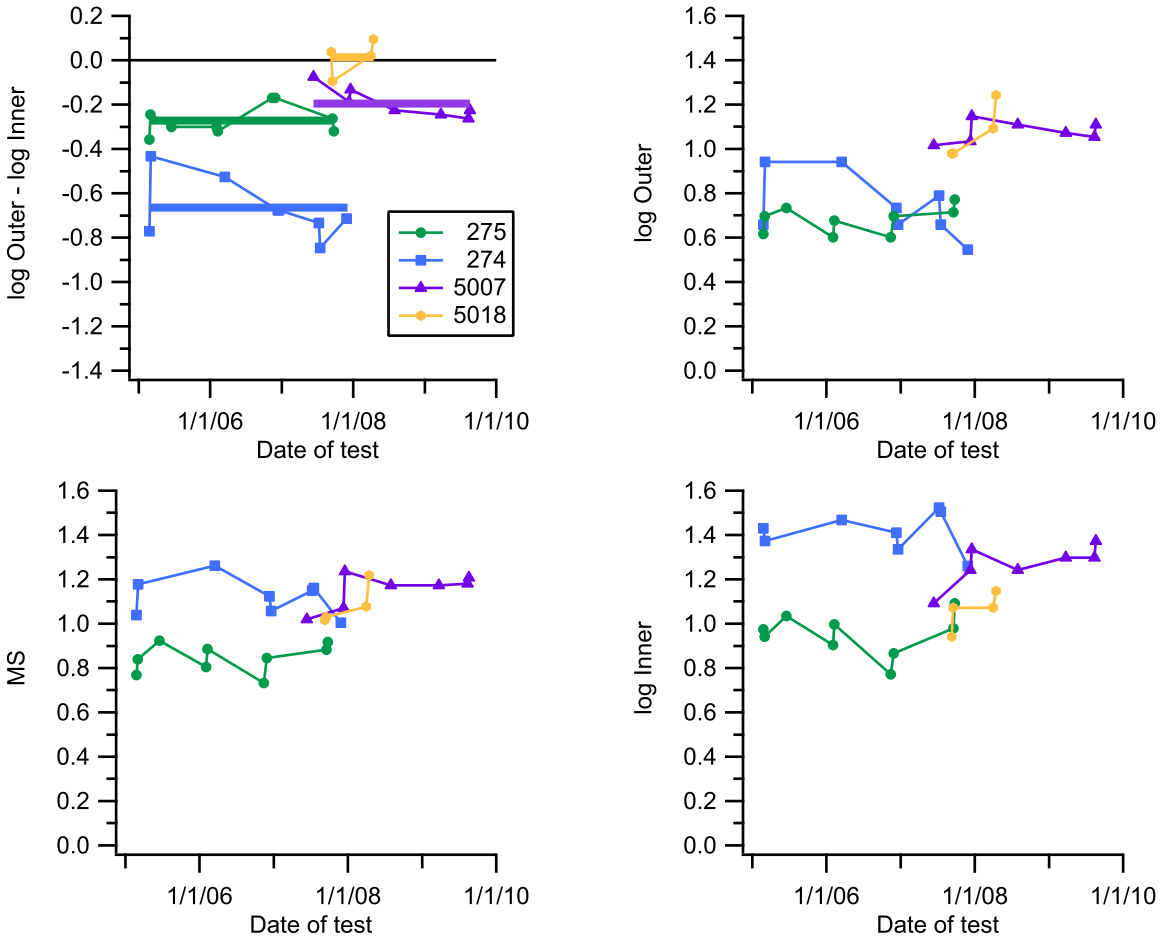

Fig. 6. Examples of individual longitudinal data. The upper left panel shows the peripheral deviation index (PDI), and the line segments show the mean PDI across visits. The lower left panel shows mean sensitivities (MS), the upper right panel shows sensitivities for outer locations, and the lower right panel shows sensitivities for inner locations.

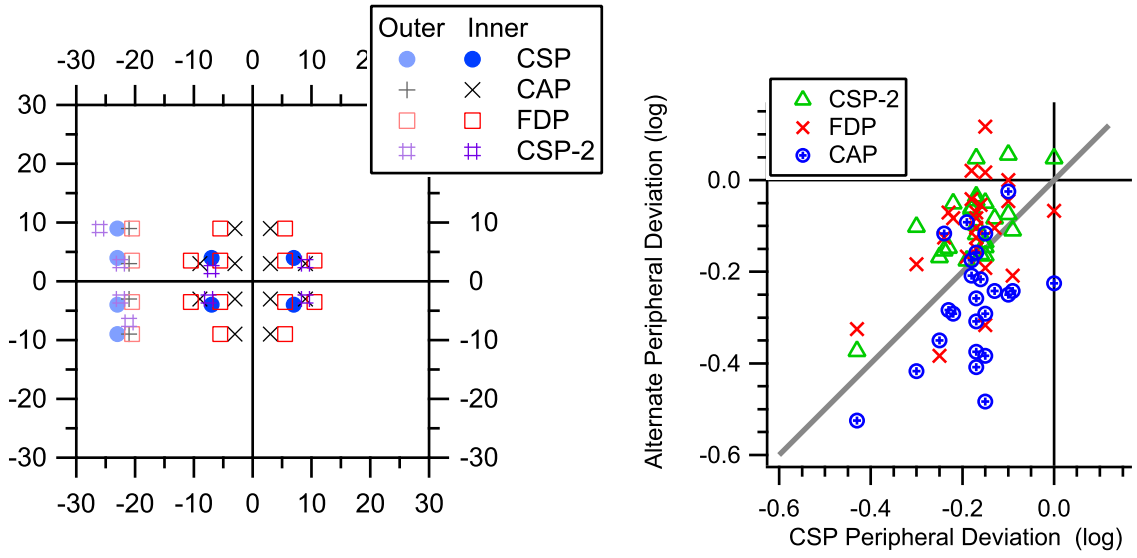

Fig. 7. Comparison of the peripheral deviation index (PDI) for CSP with PDI values for conventional automated perimetry (CAP), frequency-doubling perimetry (FDP) and revised contrast sensitivity perimetry (CSP-2). The left panel shows the locations used to compute inner and outer sensitivities for each of the four tests. The right panel shows the PDI values for CAP, FDP, and CSP-2 plotted as a function of each volunteer's PDI value for CSP.

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of ganglion cell responses (Swanson, Felius, & Pan, 2004; Swanson, Pan, & Lee, 2008), and it is possible that between-subject variability reflects differences in ganglion cell density and/or cortical pooling. Further research is needed to distinguish between-subject differences in how attention is distributed across the visual field from between-subject differences in numbers of ganglion cells and cortical pooling.

For conventional automated perimetry (CAP) with an 0.4° stimulus there is a stronger effect of age for peripheral than central locations (Heijl, Lindgren, & Olsson, 1987; Poggel et al., 2012a), but age had only a minor impact on the peripheral deviation index (PDI) that we used to characterize the shape of the nasal visual field. This was an exploratory study of age norms with CSP, so our emphasis is on results that had effect sizes of $R^2 > 33\%$ or $F > 1.5$: between-subject variability for PDI was lower than between-subject variability for MS, reflected greater variability for peripheral sensitivities than central sensitivities, and was correlated with between-subject variability for CSP-2. Other findings with smaller effect sizes we considered to be a guide for future hypothesis-based studies. For instance, the effect of age on mean sensitivity (MS) was −0.034 log unit per decade, with a standard error of the mean (SEM) of 0.008 log unit. By comparison, for CAP a slope of −0.064 log unit per decade has been reported for MS (Spry & Johnson, 2001). The shallower slope for CSP is an indication that the reported effects of age on perimetric sensitivities may be due in part to age-related optical factors reducing sensitivity to the small stimulus used to gather the normative data.

The finding that individual differences in the shape of the visual field were related to peripheral sensitivities but not central sensitivities led us to refer to the shape index as a "peripheral deviation" index. Basic psychophysical studies have found that eccentricity often depresses contrast sensitivity for sinusoids, but the use of low spatial frequencies can render the depression mild to non-existent (Pointer & Hess, 1989). Indeed, two of the people we tested had no peripheral depression with CSP, and for three more people FDP showed higher sensitivity for peripheral locations than for central locations.

CSP-2 was designed using stimuli magnified with visual field location based on estimates of local spatial scale (Keltgen & Swanson, 2012), with the expectation that on average there would be no peripheral depression. This expectation was not met: the median and mean values for peripheral deviation were equal at −0.1 log unit with CSP-2, and only three volunteers had values of zero or greater. Fig. 8 shows a map of mean sensitivities across the 55 visual field locations for CSP-2: the lowest sensitivities were in the peripheral nasal field and the highest were in central visual field and inferior visual field. The spatial scale estimates were derived from analysis of data gathered with a 40 cm test distance on a subset of 40 volunteers from the current study, and the most extreme eccentricities tested were 23° nasal and 17° vertical. The spatial scale estimates were fit with a two-dimensional parabola, and for CSP-2 at 33 cm were extrapolated out to 27° nasal and 21° vertical. This seems to have led to underestimating the magnification needed to equate spatial scale for stimuli in the peripheral nasal visual field, yielding a depression in that region. By comparison, there seems to be no depression in peripheral inferior visual field. Further studies are required to better assess spatial scale across the visual field, but the correlation between deviation indices for CSP and CSP-2 indicates that if spatial frequency were scaled so that mean sensitivity across volunteers were the same at all locations, individual variability in peripheral sensitivity would mean that some people would have peripheral depression and others would have central depression.

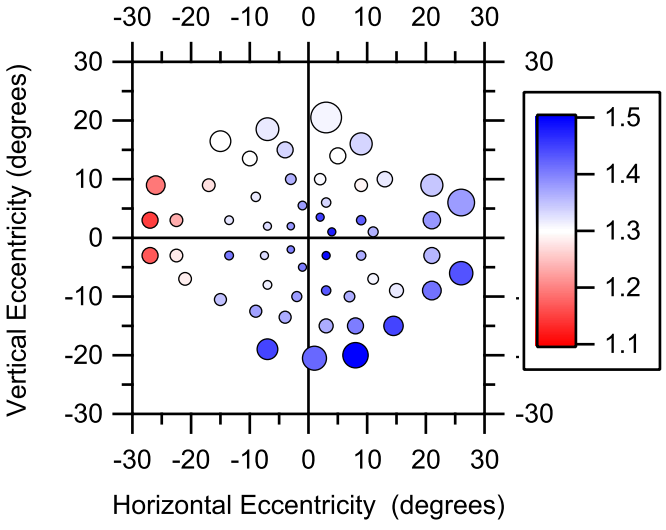

Fig. 8. Mean sensitivities for CSP-2 at 55 visual field locations. The size of the circle represents the size of the stimulus at that location, and the color represents the mean log contrast sensitivity.

Our analyses used test locations for CSP at 23° nasal, so the finding that peripheral depression for CSP-2 was only in the peripheral nasal visual field caused us to wonder whether our result was due to a local peripheral depression. To assess this possibility, we created a new index that added six more peripheral locations at vertical eccentricities of ±17° and horizontal eccentricities from 17° nasal to 7° temporal. A similar but less extreme pattern of results was seen for this new index: age slope −0.016 log unit/decade ($R^2 = 10\%$), SD of residuals 0.09 log unit, PDI correlated with mean sensitivity for the outer 10 locations PDI ($R^2 = 20\%$) but not the inner locations ($R^2 < 1\%$). We infer that the between-subject variability in our results was not due to our choice of far peripheral nasal locations for the deviation index.

Psychophysical studies often control for effects of variability in subjects' decision criteria for stimulus detection by using many blank trials, such as in signal detection theory and forced-choice methods (Swanson & Birch, 1992). Perimetry uses a different strategy for efficiency, and employs up to three indices for assessing the patient's criterion: false positive rate, rate of fixation losses, and false negative rate. When performance falls within clinical cutoffs for these indices, there can still be substantial effects of an individual's criterion on perimetric sensitivities at a given clinic visit. Clinical perimetry uses the "pattern deviation" plot that reduces between-subject variability due to differences in criteria by comparing the shape of an individual's visual field with the mean normal shape for their age (Heijl et al., 1989). The overall effect of the subject's criterion is reflected as the "height of the hill of vision", which is intended to be the difference between the height for the subject and the mean value for height from the age norms. This approach assumes that the shape of the hill of vision is similar for healthy individuals of a given age group, and can simply be adjusted in height. Our finding of substantial individual differences in the shape of the monocular visual field challenges the assumption behind the pattern deviation. Further research is needed to better understand how to control for effects of subject's criterion.

5. Conclusions

Using stimuli that are resistant to between-subject variability in peripheral defocus and retinal illumination, we found persistent individual differences in the shape of the "hill of vision." This has implications for perimetric researchers about pattern deviation analysis, and for basic psychophysics researchers about the effects of cortical pooling and distributed attention on peripheral sensitivity.

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