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Association of visual field pattern reversal with paracentral visual field loss

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Abstract

Purpose: Visual fields (VFs) that have more test points outside normal limits on the pattern deviation map than on the total deviation map have been assumed to be evidence of an unreliable VF. We propose the term “pattern reversal” to describe this VF finding and explore its association with paracentral loss.

Design: Retrospective cohort and case-control studies.

Subjects: Glaucoma and glaucoma suspect patients that completed VF testing in Veteran’s Affairs ophthalmology or optometry clinics.

Methods: In the cohort study VFs were included that demonstrated pattern reversal. The area of pattern reversal was categorized as peripheral, paracentral, or mixed (both peripheral and paracentral). In the case-control study, a group of patients with paracentral loss confirmed on 10–2 VFs were compared to a control group of VFs without paracentral loss.

Main Outcome Measures: In the cohort study the calculated false positive (FP) error rates were compared among groups categorized by area of pattern reversal. In the case-control study the rates of pattern reversal were compared between patients with and without paracentral loss.

Results: 217 eyes of 145 patients were included in the cohort study. VFs with pattern reversal and mixed loss had significantly higher FP rates compared to those with paracentral or peripheral loss only (16.25% vs 6.26% and 8.15%, respectively, $p<0.001$). 55 eyes of 41 patients were included in the case group and 55 eyes of 41 patients were included in the control group. Patients with paracentral loss were more likely to have history of pattern reversal compared to those without paracentral loss (58.2% vs 29.1%, $p=0.004$). Twelve eyes with paracentral loss had 24–2 VFs that showed defects on the pattern deviation map but not on the total deviation map

Conclusions: Pattern reversal may be associated with paracentral VF loss and is not always be associated with elevated FP rates.

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Precis:

Pattern reversal (i.e. visual fields with more test points outside normal limits on the pattern deviation map than on the total deviation map) can be associated with paracentral visual field loss.

Keywords

glaucoma; visual field; reliability

Introduction

Measurement of the visual field (VF) using standard automated perimetry (SAP) is a cornerstone of the diagnosis and management of glaucoma. When interpreting VF test results, assessments of test reliability are important for accurately differentiating stable from progressing VFs. An unreliable VF can mask true progression or suggest artifactual progression, either of which can lead to erroneous treatment decisions if unreliable test results are not recognized.[1–3] It has been common practice to evaluate VF reliability using standard reliability metrics. On the Humphrey Field Analyzer (HFA), these include false positive (FP) error rates, false negative (FN) error rates, and fixation loss (FL) rates. Gaze tracking records the degree of gaze deviation when a stimulus is presented during SAP and may serve as an additional measure of reliability.[4–7]

Patterns of VF loss, including total and pattern deviation plots, also can be used to assess reliability. The total deviation plot shows the significance of point-by-point deviations from age-corrected normal sensitivity values, while the pattern deviation plot is the total deviation plot after correction for generalized shifts in overall field sensitivity.[8,9] One may encounter, albeit infrequently, VF reports wherein the pattern deviation map shows more test points that are outside normal limits than is shown in the total deviation map (Figure 1). This has been referred to as a “reversed cataract pattern” because the pattern is the inverse of what may be seen in patients with media opacities. Such a pattern is commonly considered to suggest a “trigger-happy field” because the patient may have been responding even when no stimuli were actually seen.[10]

Although the described pattern is commonly interpreted as an artifact that may be associated with unreliable VFs, there have not been any prior studies to systematically evaluate the pattern. In an earlier study, we noted that paracentral loss was associated with this pattern.[11] That study included many patients with central VF abnormalities and the pattern was encountered far more frequently than is commonly seen in typical clinical settings. In this study, we further explore the association of this pattern with FP rates and paracentral loss, and propose “pattern reversal” as a descriptive term.

Methods

The study protocol was approved by the Veterans Administration San Diego Medical Center (VASDMC) Institutional Review Board and adhered to the tenets of the Declaration of Helsinki. A waiver of consent was obtained to review retrospective VF data.

Cohort study

Glaucoma and glaucoma suspect patients who were at least 18 years old and had undergone threshold VF testing in the Ophthalmology and Optometry clinics at the Veterans Administration San Diego Medical Center (VASDMC) from January 2018 to April 2018 were eligible for the study. Patients were included if they had a Humphrey Field Analyzer (HFA) 24–2 SITA Fast VF (Carl Zeiss Meditech Inc, Dublin, CA, USA) performed that demonstrated pattern reversal in one or both eyes. Pattern reversal was defined as at least 25% more test points reaching statistical significance of at least $p<0.02$ on the pattern deviation map compared to the total deviation map. The area of pattern reversal was further categorized as paracentral, mixed, or peripheral according to the location of the reversal defect on the pattern deviation map. Paracentral test points included the most central eight points, although it also could include an additional six nasal points. Peripheral defects did not contain paracentral points, and mixed defects contained points in both locations (Figure 2). There were no exclusion criteria based upon reliability indices. Data including patient age, gender, area of pattern reversal, and rate of FP errors were recorded for all included patients. If patients had three or more previous HFA 24–2 VFs available their prior VFs were also examined for additional instances of pattern reversal.

Case-control study

A case group was created of patients with isolated paracentral loss on HFA 24–2 VFs that was additionally confirmed by HFA 10–2 SITA Fast VF testing. Patients were included in the case group if they had an HFA 10–2 VF with three or more contiguous points reaching statistical significance of $p<0.05$ on the pattern deviation map. Patients with history of macular disease (e.g., macular degeneration, epiretinal membrane, etc) were excluded from the case group. Furthermore, patients in the case group had at least three prior HFA 24–2 VFs with no peripheral loss. Patients were randomly assigned to the control group if they had an HFA 24–2 VF without paracentral loss performed on the same day as the patients in the case group and at least three prior HFA 24–2 VFs. There were no exclusion criteria based upon reliability indices. Data including patient age, gender, and absence or presence of pattern reversal on prior HFA 24–2 VFs in both groups were recorded for all included patients.

Statistical Analysis

Statistical analyses were performed using SPSS version 27.0 (SPSS, Inc., Chicago, IL). The statistical significance of relationships between defect locations and patient and testing variables was determined with chi-squared tests and analysis of variance. The statistical significance of relationships between the case and control groups was determined with independent sample T tests, Fisher’s Exact Test, and chi-squared tests.

Results

Cohort study of pattern reversal

217 eyes of 145 patients were included in the cohort study. Patient demographics and VF characteristics are presented in Table 1. Patients had a mean age of 71.3 years and were

largely male (95.7%), as is typical for VA-based studies. A majority of eyes had pattern reversal over a mixed area (55.3%); 35.5% had paracentral loss and a minority of eyes had pattern reversal limited to the periphery (9.2%). There was no significant difference between the area of pattern reversal and age, sex, or eye ($p>0.05$ for all). Mean deviation was highest in the mixed group and lowest in the paracentral group (1.0 dB and −0.7 dB, respectively; $p<0.001$). The average FP error rate was 6.7% across all patients. Twenty-five percent of VFs had FP rates greater than 15%. FP error rates were significantly higher for VFs with mixed loss compared to paracentral or peripheral loss (16.25% vs 6.26% and 8.15%, respectively; $p<0.001$). In the 206 eyes that had three or more 24–2 VFs available for analysis, 69% of patients had prior instances of pattern reversal and there was no difference in the rates of prior pattern reversal between the three groups ($p=0.610$).

Case-control study of paracentral loss

55 eyes of 41 patients were included in the case group and 55 eyes of 41 patients were included in the control group. 35 eyes of 28 patients were included in both the cohort study and the case group of the case-control study. Patient demographics and VF characteristics are presented in Table 2. The patients' mean ages were 70.7 and 70.4 in the case and control groups, respectively, and largely male (92.7%) in both groups. The case and control groups were well matched with regards to age, sex, and eye laterality ($p>0.05$ for all). Patients with paracentral loss on HFA SITA Fast 10–2 VFs were more likely to demonstrate pattern reversal on prior 24–2 VFs than control patients without paracentral loss (58.2% vs 29.1%, $p=0.004$). Twelve eyes in the case group had 24–2 VFs that showed defects on the pattern deviation map but not on the total deviation map (Figure 3).

Discussion

In this study, we examined pattern reversal on 24–2 VFs through both cohort and case-control studies. Our cohort study demonstrated high FP rates in patients with mixed pattern reversal, consistent with what would be expected from a "trigger happy" patient. However, patients who only showed paracentral VF loss or peripheral VF loss showed significantly lower rates of FP responses. This suggests that paracentral pattern reversal is not always be associated with elevated FP rates, although "trigger happy" patients may not have elevated FP rates.[10,12] Patients with pattern reversal were likely to demonstrate this pattern repeatedly with almost 70% of patients having multiple VFs with pattern reversal irrespective of the location of VF loss. This high degree of recurrence may be due to patients repeating trigger-happy testing behaviors across multiple tests, an association with specific types and locations of defects, or additional unrecognized factors.

Our case-control study compared patients with 24–2 paracentral VF loss to a control group without such loss. Patients with paracentral 24–2 VF loss were significantly more likely to demonstrate pattern reversal when compared to the control group. In conjunction with those of the cohort study, these findings suggest that pattern reversal is not always a marker of an unreliable VF in patients with paracentral loss. Pattern reversal in patients with paracentral loss may be an artifact of the method used to calculate the pattern deviation map.[13] When a paracentral point is particularly depressed in comparison to the

periphery, the attempt to remove generalized depression for the pattern deviation map can cause an artifactual pattern reversal that highlights the paracentral defect. The normal significance limits for pattern deviation are also considerably more narrow in the macular field than in more peripheral points.[10,13] Thus, small adjustments for overall sensitivity when calculating pattern deviation results would be more likely to affect macular points compared to peripheral points.

Interestingly, more than 20% of eyes in the paracentral case group had VFs that demonstrated defects on only the pattern deviation map, not the total deviation map. Paracentral VF loss is particularly important to identify because paracentral defects are associated with decreased quality of life in glaucoma patients.[14–16] Recent studies have shown that 24–2 VFs frequently miss paracentral defects that can be identified on 10–2 VFs.[17,18] Unfortunately, undetected paracentral loss can have significant impact on quality of life in patients with glaucoma.[19] Clinicians should be aware that a paracentral defect that appears only on the pattern deviation map may be an early sign of paracentral VF loss as opposed to a sign of poor reliability. If repeatable after reinstructing a patient on VF test taking, such paracentral pattern reversal may be an indication for a 10–2 VF to evaluate for paracentral defects in greater detail. However, further research is needed to better differentiate true macular loss not seen on the total deviation map, patients with higher than average overall perimetric retinal sensitivity, and pattern reversal.

This study faces several limitations. First, the study sample was drawn from VA hospital outpatient veterans, so the patients enrolled were overwhelmingly male and may not be representative of other populations. Second, we defined the ratio of pattern reversal based on review of VFs initially collected for the study as there is no prior quantitative definition of this finding. Future studies of pattern reversal may modify this definition by regarding the ratio as a continuous variable and defining a more precise cutoff. Third, although elevated FP responses are now used as a surrogate marker for unreliable VFs, some patients with mixed VF patterns highly suggestive of a “trigger happy field” had normal FP rates. This supports suggestions that FP may not be as strong a measure of test result reliability as previously thought.[10,12,20] Fourth, not all patients with paracentral loss in the cohort study had 10–2 VFs available to differentiate between true paracentral loss versus artifactual loss. Finally, pattern reversal for the study was defined using points reaching statistical significance of $p<0.02$ or less and may not apply to VFs with pattern reversal of points reaching, for instance, statistical significance of $p<0.05$ or less. However, VFs with pattern reversal of points reaching statistical significance of $p<0.05$ alone were not encountered during data collection so this is likely a rarely encountered phenomenon.

Despite these limitations, this study suggests that paracentral pattern reversal may be associated with paracentral VF loss rather than always representing an artifact of an unreliable VF. For patients showing repeatable paracentral pattern reversal, one should consider macular structural imaging and/or obtaining a 10–2 VF to better ascertain whether or not there is significant macular damage.

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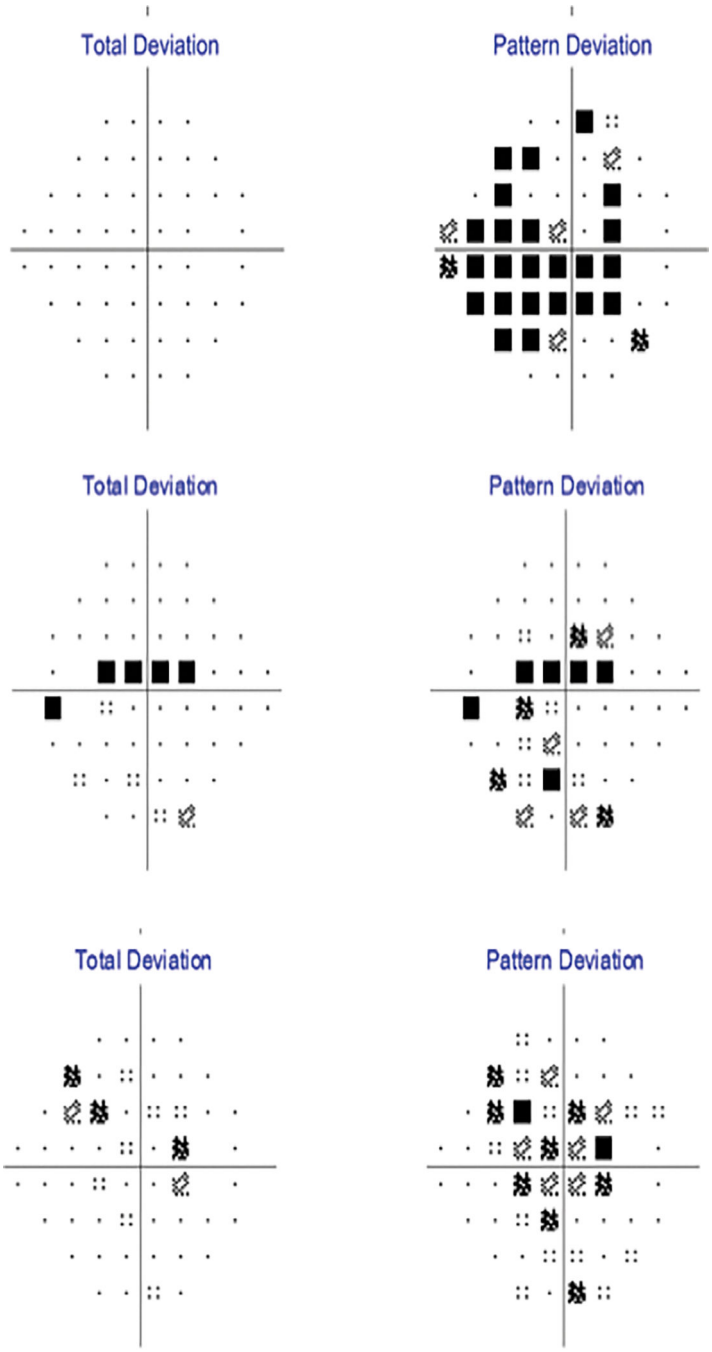

Figure 1.
Examples of pattern reversal in three patients.

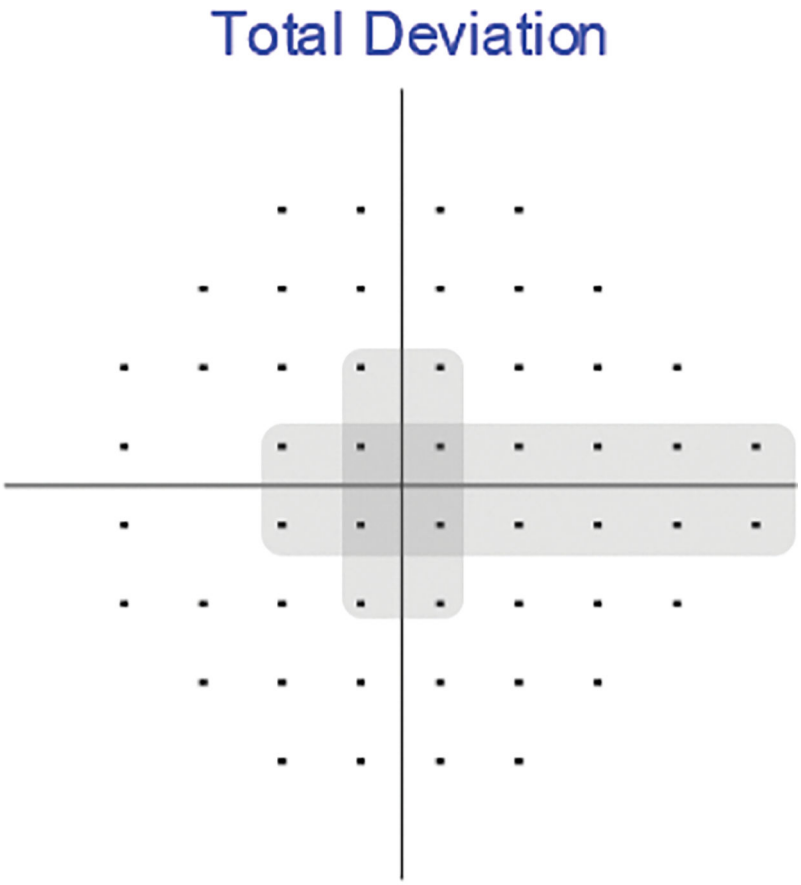

Figure 2.
Location of pattern reversal defect on total deviation map (left eye). Grey areas are paracentral, white are peripheral, and mixed contains points in both locations.

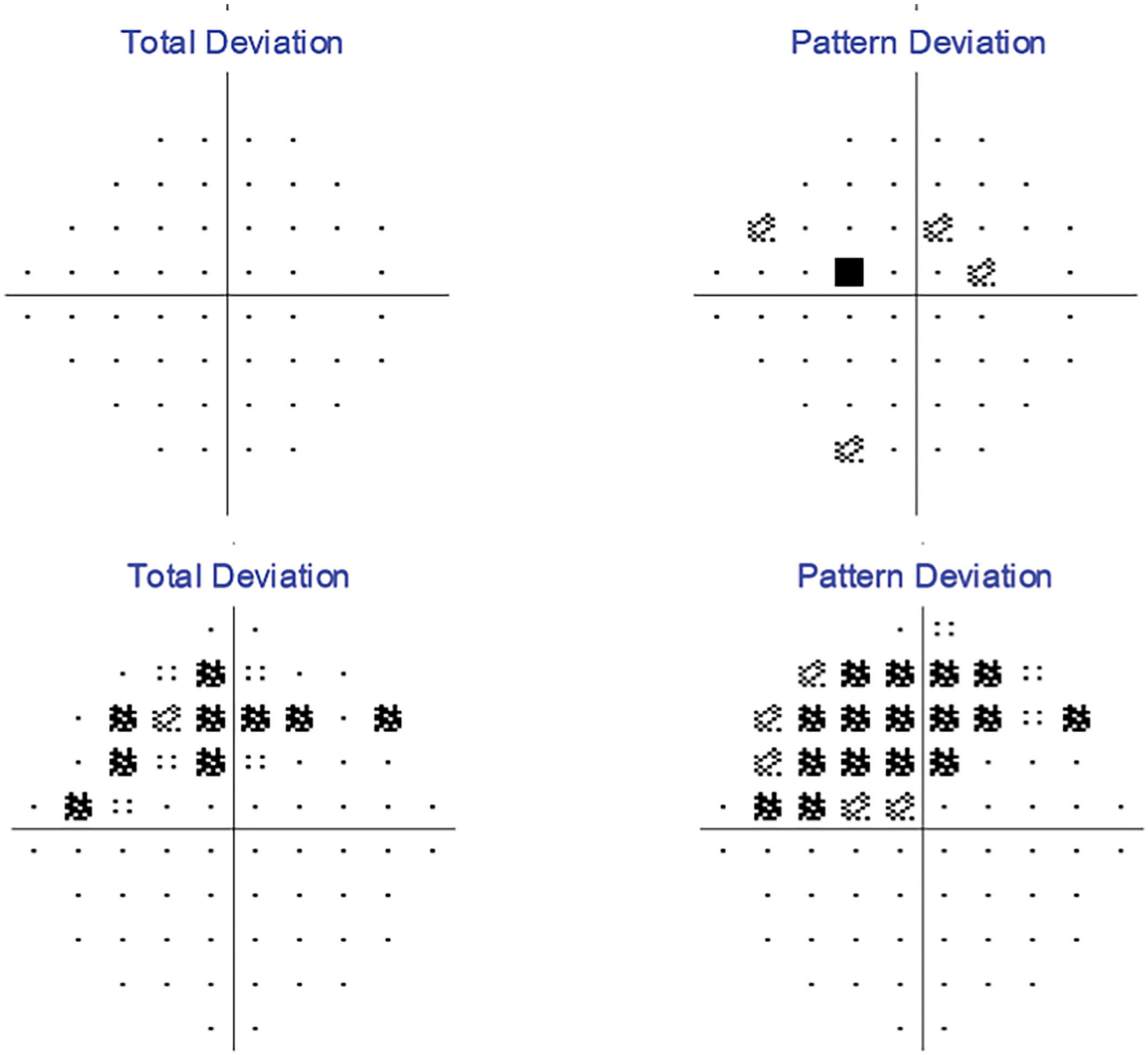

Figure 3.
Example of a patient with defects on the 24–2 visual field pattern deviation map but not on the total deviation map (A). The patient has a significant defect on the 10–2 visual field (B).

Table 1.

Cohort study patient and visual field characteristics.

	Paracentral (77 eyes)	Mixed (120 eyes)	Peripheral (20 eyes)	p-value
Age, mean (standard deviation)	70.5 (10.4)	72.7 (8.5)	67.8 (15.1)	0.185
Female, total (percent)	3 (3.9%)	3 (3.9%)	0 (0%)	0.683
Right eye, total (percent)	44 (57.1%)	59 (49.2%)	9 (45.0%)	0.454
Mean deviation, mean (standard deviation	−0.7 (1.5)	1.0 (2.4)	0.3 (1.7)	<0.001
False positive, mean (standard deviation)	6.3 (8.8)	16.25 (15.9)	8.2 (7.2)	<0.001

Table 2.

Case-control study of paracentral loss patient and visual field characteristics.

	Case	Control	p-value
Age, mean (standard deviation)	70.7 (13.8)	70.4 (14.9)	0.662
Female sex, total (percent)	3 (7.3%)	3 (7.3%)	1.000
Right eyes, total (percent)	27 (49.1%)	27 (49.1%)	1.000
Pattern reversal, total (percent)	32 (58.2%)	16 (29.1%)	0.004