Variability in Isopter Position and Fatigue during Semi-Automated Kinetic Perimetry

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Key Words

Semi-automated kinetic perimetry • Variability • Isopter • Fatigue effect • Reaction time

Abstract

Background: Assessment of factors influencing response variability to repeat presentations of III4e stimuli and the fatigue effect during semi-automated kinetic perimetry (SKP). **Design:** Prospective case series; setting: university hospital. **Participants:** 58 patients with severe visual field loss: 21 with glaucoma, 18 with retinitis pigmentosa, and 19 with post-chiasmal visual pathway lesions. **Methods:** Following initial testing with three isopters (I2e or V4e, I4e and III4e), presentations of the III4e stimulus were repeated four times during the same session along identical vectors. **Main Outcome Measures:** Variability in III4e-isopter position (scatter of kinetic threshold) and the difference of isopter area between the first and four subsequent sessions (fatigue effect) of SKP were analyzed by diagnosis, age, visual acuity and reaction time (RT). **Results:** The mean scatter of the kinetic threshold was 2.5 degrees (deg) in the glaucoma group, 1.5 deg in the group with retinitis pigmentosa, and 1.7 deg in the group of patients with postchiasmal lesions. The difference in the isopter area between a single examination and four times

repeated examination was 656 square degrees (deg²) in the glaucoma group, 104 deg² in the retinitis pigmentosa group and 227 deg² in the group of patients with postchiasmal lesions. Post-hoc regression analysis revealed that the variability of isopter position increased as the RT increased. **Conclusion:** The variability of III4e-isopter position and fatigue were most pronounced among glaucoma patients. RT is the most important factor influencing the variability of responses and fatigue during SKP, thus we propose that it can be used as a reliability indicator of SKP.

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Introduction

As in all psychophysical tests, response variability in perimetry is commonly observed during and between examinations [1]. Quantification of intra- and intertest variability has been widely studied for automated static perimetry [2–4] and for more recently developed techniques as high-pass resolution perimetry [5], motion perimetry [6], short-wavelength automated perimetry [7],

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frequency-doubling technology [8] and flicker perimetry [9]. However, only a few studies dealing with variability in manual and automated kinetic perimetry have been published [10–14]. Response variability during manual kinetic perimetry, as well as the fatigue effect and reaction time (RT) have not been as widely investigated as for static perimetry, in part because of difficulties in standardization of the procedure, substantial variability in administration of the test by different perimetrists and the need for processing to achieve numerical quantification of the results, e.g. digitization with calculation of the solid area subtended by each isopter [15]. With manual kinetic perimetry, the movement of stimuli is guided along the vector by hand, which cannot be kept constant [16]. However, kinetic perimetry using the Goldmann instrument [17] remains an accepted form of examination of the peripheral visual field in patients with advanced glaucoma [18], retinal diseases [19] and neurological disorders [20]. With semi-automated kinetic perimetry (SKP), the selected Goldmann test target is presented by the computer at a constant angular velocity [21, 22]. In addition, the area of each isopter can be measured in square degrees (deg²). Intrasubject variability can be assessed by repeated presentations of kinetic stimuli moving in random order along each given vector during the perimetric session. These repeated presentations enable assessment of the location and scatter of isopter position. Additionally, it is possible to measure the individual RT during SKP examination [23]. The applicability of SKP for normal subjects [24] and patients with advanced visual field loss and its comparability with manual kinetic Goldmann perimetry [25] and static automated perimetry [26] have already been demonstrated.

The purpose of this investigation was to assess factors influencing response variability to repeated presentations of III4e stimuli and fatigue during SKP examination in a group of patients with advanced visual field loss.

Method

Participants

SKP was performed on 58 patients (28 women, 30 men) with advanced visual field loss. Patients were recruited from the outpatient clinic and the study was conducted at the University Eye Hospital in Tübingen, Germany, in 2003. The participants consisted of 21 patients with advanced loss of retinal nerve fiber layer (RNFL) – greater than Aulhorn stage III [27] due to open angle glaucoma, 18 patients with concentric constriction of the visual field (with less than 30 deg of central field remaining) due to retinitis pigmentosa, and 19 patients with visual field defects that obeyed the vertical midline (hemianopia) and resulted from neu-

rological disorders affecting the postchiasmal visual pathway. Patients were experienced in performing static perimetry, but naive to kinetic perimetry. The study was a prospective observational case series. It was approved by the independent ethics committee and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consent was obtained from each individual after an explanation of the nature of the study.

Visual Field Examination

Only the eye with the better visual acuity was tested and the fellow eye was covered with an opaque occluder during examination. Patients were tested with the appropriate near correction for plotting the I2e isopter. All the examinations were performed by the same examiner.

First, the hill of vision was assessed in the routine manner by plotting three isopters once each with targets I4e, III4e and either I2e (27 visual fields) or V4e (31 visual fields) depending on the character of the visual field defect. Patients with concentric constriction ($n = 18$) and most of the patients with hemianopia ($n = 13$) were examined with V4e as these defects were very large and steeply bordered. The rest of the patients (6 with hemianopia and 21 with RNFL defects) were examined with I2e instead of I4e and III4e as these defects were not so severe and the visual acuity was better. Examinations were performed using SKP implemented on the Octopus 101 (Haag-Streit, Inc., Bern, Switzerland) instrument.

Origin, direction and length of the vectors were individually selected so that the stimulus was moved from nonseeing areas towards seeing areas almost perpendicularly towards the presumed scotoma border. Vectors were placed along 24 meridians and additionally perpendicular to the course of the anticipated isopter. The stimulus angular velocity was kept constant at the level of 3 deg/s, as a compromise between 4 deg/s as recommended by Johnson and Keltner [28] and Wabbels and Kolling [29] and 1–2 deg/s as proposed by Lachenmayr and Vivell [30]. Subsequently, four presentation sessions were performed in the course of which III4e vectors were presented in a random sequence at the same position as the initial III4e vector. The results of such repeated testing are presented in figure 1 as the mean $\pm$ SD local kinetic threshold. The III4e stimulus was chosen as this is the stimulus size in Germany for expert opinion and is the test target used to define ‘legal blindness’ in the USA. A break was given when needed. The locations of the mean local kinetic threshold were connected and the area enclosed by this isopter was measured in deg². The area of circumscribed absolute scotomas, when present, was subtracted from the total isopter area. The isopter area of the four repeat presentations was compared with the area of first (initial) SKP examination.

Additionally, the individual RT (time interval in milliseconds from the appearance of the stimulus to the patients response) was measured for each patient by using ‘RT vectors’ during the initial (single presentation) and four-times repeated subsequent examination (measurements of RT were repeated four times as well). As differences between RT values obtained in the center and periphery as well as nasal and horizontal parts of the visual field have been reported [31], two RT vectors were presented in the central and another two in the peripheral seeing area of the visual field (one in the superotemporal quadrant and one along the nasal horizontal meridian).

Fig. 1. The results of SKP for the left eye of a patient with an RNFL defect due to glaucoma. **a** Three isopters (III4e, I4e and I2e) obtained during the first presentations of the vectors. Shaded lines represent the age-correlated normative isopters for each stimulus. **b** III4e isopter positions obtained with SKP for the four repeat presentations. The variability in the local kinetic threshold is symbolized by the gray bars (mean $\pm$ 2 SDs local kinetic threshold).

Statistical Analysis

Statistical computations were carried out with Statistica 9.0 Software (StatSoft, Poland). The demographic data of the three groups of patients were compared using analysis of variance (ANOVA).

Variability in III4e-isopter position and the difference in isopter area between single and the subsequent four repeat presentations of the III4e stimulus were expressed in 95% confidence intervals (95% CI) for each vector of each patient and compared between three groups using ANOVA. Subsequently, these parameters were analyzed by diagnosis, age, gender and RT in an analysis of covariance (ANCOVA). Additionally, a post-hoc regression analysis was performed for variables displaying significant effects. The duration of the examination was automatically measured in minutes and was expressed as the median.

Results

Demographic Data

The mean age of all patients was 52 years (range 18–81 years). Subjects with glaucoma were significantly ($p < 0.000001$) older (mean age 67 years, range 51–81 years) than those with retinitis pigmentosa (mean age 38 years, range 18–61 years) or postchiasmal lesions (mean age

49 years, range 21–77 years). After age-matching of the group of patients with glaucoma, no significant relationship was found between age and variability in isopter position and difference in the isopter area (Pearson correlation).

Visual Acuity

The median visual acuity of all examined eyes was 0.8 [16/20; range 0.5 (10/20)–1.2 (24/20)]. The mean visual acuity was 0.95 [19/20; range 0.5 (10/20)–1.0 (20/20)] in the glaucoma group, 0.8 [16/20; range 0.5 (10/20)–1.2 (24/20)] in patients with severe field loss from retinitis pigmentosa and 1.0 [20/20; range 0.8 (16/20)–1.2 (24/20)] in patients with field defects as the result of a chiasmal lesion (ANOVA $p = 0.04$).

Reaction Time

The mean RT of all three groups of patients was 789 ms (95% CI, 703–874 ms). The mean RT was 905 ms (95% CI 752–1,058 ms) in the glaucoma group, 730 ms (95% CI 573–887 ms) in the group of patients with retinitis pigmentosa and 716 ms (95% CI 572–860 ms) in patients with field loss from chiasmal lesions (ANOVA n.s.).

Fig. 2. Variability in the III4e-isopter position (degrees) in the three groups of patients from four repeat presentations in the same session of SKP. Vertical bars represent 95% CIs. Only the glaucoma group showed a significant (*) increase in variability from repeated presentations.

Variability in Iopter Position

The mean scatter of the kinetic threshold was 1.9 deg (95% CI 1.7–2.2 deg) for the entire cohort. The mean scatter was 2.5 deg (95% CI 2.0–2.8 deg) in the glaucoma group, 1.5 deg (95% CI 1.1–2.0 deg) in the group of patients with concentric constriction of the visual field, and 1.7 deg (95% CI 1.3–2.2 deg) in the group of patients with field loss following chiasmal lesions (fig. 2). The variability in isopter position in the glaucoma group was significantly larger than in the group with retinitis pigmentosa and post-chiasmal lesion visual field loss ($p = 0.02$). Post-hoc analysis showed that the differences were significant between the group with glaucoma and retinitis pigmentosa ($p = 0.005$) and between glaucoma and postchiasmal lesions ($p = 0.03$).

The ANCOVA showed that only RT ($p = 0.04$) has a relevant effect whereas visual acuity and age did not play essential roles (table 1). Diagnosis was very close to significance ($p = 0.06$).

Regression analysis showed that an increase in RT increased the variability in isopter position ($p = 0.04$).

Iopter Area

The visual field area obtained by connecting the mean kinetic thresholds of the four repeated presentations of the III4e stimulus was 7,133 deg² (95% CI 6,023–8,242 deg²), which is significantly ($p < 0.001$) smaller than the

Fig. 3. Mean difference in isopter area in square degrees between the first and subsequent four repeat presentations of the III4e stimulus during the same SKP session in three groups of patients. Vertical bars represent 95% CIs. Only the glaucoma group showed a significant (*) increase in mean difference in isopter area from repeated presentations.

area of 7,469 deg² (95% CI 6,324–8,614 deg²) obtained by simple presentation of vectors inside the III4e isopter. The mean difference was –344 deg² (95% CI 153–535 deg²) or –4.5% of the area of the initially assessed III4e isopter for all the patients. Considering the three groups of patients separately, the difference was 656 deg² (95% CI 393–910 deg²) or 7.3% in the glaucoma group, 104 deg² (95% CI 54–263 deg²) or 2.5% in the retinitis pigmentosa group and 227 deg² (95% CI 259–713 deg²) or 2.5% in the group of patients with postchiasmal lesions (fig. 3). ANCOVA showed a relevant effect of RT ($p = 0.003$) on the difference of isopter area (table 2), whereas there were no significant effects of age and diagnosis. Diagnosis ($p = 0.06$) and visual acuity ($p = 0.05$) were very close to significance.

Regression analysis showed that an increase in RT increases the difference in isopter area between the single and the subsequent four repeat examinations ($p = 0.0007$).

Duration of the Examination

The median overall time of examination of three isopters with single stimuli was 15 min (range 5–28 min) and 14 min (range 5–25 min) with breaks. The automated examination (III4e-stimulus presentation repeated four times) of one eye took a median of 8 min (range 2–16 min) overall and 7 min (range 2–14 min) discounting breaks. The median break duration was 1 min (range 0–2 min).

Table 1. ANCOVA of the variability in isopter position testing effects of age, visual acuity, RT and diagnosis

Source of variation	Accounted variance, %	Degrees of freedom	Sum of squares	Mean square	F ratio	Probability
Age	0.0	1	0.0004	0.0004	0.001	0.98
Visual acuity	5.0	1	1.88	1.88	2.52	0.12
RT	8.0	1	3.47	3.47	4.67	0.04*
Diagnosis	10.0	2	4.41	2.21	2.97	0.06
Error		52	38.65	0.74		

* Significant.

Table 2. ANCOVA of the difference in isopter area between the first and the subsequent four repeat presentations of the III4e stimulus, testing for effects of age, visual acuity, RT and diagnosis

Source of variation	Accounted variance, %	Degrees of freedom	Sum of squares	Mean square	F ratio	Probability
Age	1.5	1	298,586	262,670	0.77	0.38
Visual acuity	7.5	1	1,628,735	298,586	4.19	0.05
RT	15.6	1	3,727,426	1,628,735	9.59	0.003*
Diagnosis	4.2	2	878,839	3,727,426	2.97	0.06
Error		52	20,218,363	439,419		

* Significant.

Discussion

In the present study, an attempt was made to assess variability and fatigue during SKP and factors influencing them. Our study showed that following a single SKP examination, variability in III4e-isopter position (scatter of the kinetic threshold) during repeated vector presentations was most pronounced among patients with advanced glaucomatous field loss. One possible explanation could be that visual field loss from glaucoma is not as steeply bordered as that present in advanced retinitis pigmentosa with markedly constricted fields, or in the visual field defects seen in postchiasmal visual pathway lesions. Another explanation could be that on average glaucoma patients were older. There were significant differences in mean age of patients within the three groups (glaucoma patients were the oldest). However, ANCOVA did not find that age was a relevant factor influencing the variability in isopter position. Interestingly, the variables diagnosis and RT were found to be important. Although glaucoma patients were overall more experienced in visual field testing than other patients, we do not suspect

that a learning effect could have counterbalanced the fatigue effect. Similarly, intratest variability (short-term fluctuations) of static perimetry has been reported to be larger in patients with glaucoma [2] and in optic neuritis [4].

The second finding of our study was that fatigue during SKP is most pronounced among glaucoma patients. In the present study, fatigue was defined as the difference between the first and the mean of the four subsequent tests. The area of the visual field obtained by repeated presentations of III4e vectors was significantly smaller than the area of the isopter obtained on the initial, single presentation of this stimulus. Thus, fatigue depends on the number of remaining tests.

Repeated examinations may have a twofold effect: they induce a learning effect on the one hand [32], whereby sensitivity increases during or between examinations, but repeat testing also introduces an element of fatigue, whereby sensitivity decreases during or between examinations. There is relative lack of information in the literature concerning the relationship between the learning and fatigue effects. It is hypothesized that these effects

oppose each other during any given examination. As the patient becomes more experienced, the learning effect diminishes and the fatigue component becomes more dominant [33]. However, several authors [34, 35] indicate that learning effects can occur over long time periods (even up to 5 years and longer).

It has been reported for static perimetry that fatigue increases in areas of field defects [3], with increasing eccentricity [36] and increasing age [37]. We did not find any influence of age on the fatigue effect.

The major finding of our SKP study was that RT is the most important factor influencing both variability and fatigue. Measurement of RT is an advantage of SKP. We have shown that with the increase in RT, the variability in isopter position and the difference in isopter area increased. Thus, it may be presumed that increased RT may be a predictor of increased variability and fatigue. In static perimetry, RT in glaucomatous visual field loss increases when the stimulus is closer to threshold [38] and it depends primarily on the slope of the frequency of the seeing curve for that test location and on the frequency of false-positive and false-negative responses [6]. RT, as determined by SKP, increases with increasing eccentricity of the origin of the vector in healthy individuals [24] and

in patients with advanced visual field loss [23]. The values of RT were larger than for normal subjects, but there were no relevant differences between groups of patients (advanced RNFL loss, concentric constriction of the visual field and hemianopia).

In summary, our results showed that the intrasubject, intra-session variability in SKP for the III4e stimulus is higher in glaucoma patients than in subjects with retinitis pigmentosa or postchiasmal visual pathway lesions. Repeated presentations of vectors resulted in delayed stimulus perception and, thus, smaller isopter areas, indicating a fatigue effect. Increase of RT increased both variability in isopter position and fatigue. Thus, it seems to be rational to use RT measurements as an indicator of reliability of SKP examination.

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