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Fixation pattern in healthy subjects during microperimetry with the scanning laser ophthalmoscope

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A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Visual field (VF) examinations provide important information about diagnosis and follow-up in many ocular and visual pathway disorders. Previous studies have shown that fixation stability can be measured very exactly around the center of the fixation point with SLO. The importance of measuring fixation during microperimetry in the absence of field defects is to learn more about the normal fixation pattern. This is of interest since changes in fixation pattern due to pathology can occur prior to detectable changes in the macula or visual pathway.

Material/Methods: Thirty-one adult subjects with healthy eyes were recruited from the staff of the Section of Ophthalmology and Vision, Department of Clinical Neuroscience, Karolinska Institutet. The fixation pattern in one randomly selected eye from each subject was investigated with the SLO using the fixation control function in the microperimetry technique.

Results: The results showed that the fixation pattern had a mean center of gravity located at a mean absolute distance of 0.27° from the fixation point (FP) and a directional predominance of the fixation pattern was found in that the fixations were more frequently distributed vertically than horizontally.

Conclusions: The computerized fixation control when performing microperimetry with the SLO provides information about the fixation pattern which cannot be obtained with standard clinical perimetry techniques.

key words: **microperimetry • fixation pattern • scanning laser ophthalmoscope • visual field**

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BACKGROUND

Visual field (VF) examinations provide important information about diagnosis and follow-up in many ocular and visual pathway disorders [1]. VF defect characteristics can thus be used to determine the location of a lesion affecting the visual pathways. Visual field examinations in a clinical setting are usually performed with conventional techniques such as differential light stimuli (DLS). However, since the accuracy of the conventional VF techniques relies on the assumption that the subject's fixation is kept foveal and stable during the examination [2–5], these conventional techniques are inadequate for accurate evaluation of the VF in macular and some retinal disorders. In these disorders, foveal vision is often compromised and thus the patients often have unstable or extrafoveal fixation [6]. If the fixation is not foveal, the VF will still be mapped as though fixation is in the center of the field, and all tested points will be shifted relative to their true retinal locations [7–10]. A way to compensate for this is to move the test chart according to the degree of extrafoveal fixation. The disadvantage of this strategy is the effect of cartographic deformation. Modern perimeters have devices to control fixation loss, but if the fixation is unstable and the eyes move significantly during testing, the size and location of a scotoma will be incorrectly plotted. In computerized DLS perimetry, fixation loss has been shown to be the most common cause of unreliability. Thus in normal subjects, fixation loss ranges from 9 to 16%, depending on the technique used [11]. Another study showed that fixation errors were not the major cause of the increased variability seen at locations with reduced sensitivity in glaucoma patients [12].

In recent years a perimetry technique has been introduced using the scanning laser ophthalmoscope (SLO), which is a computerized technique for measuring the response to light stimuli in the central VF. This technique thus eliminates some of the earlier problems occurring with conventional techniques, such as unstable fixation [10]. The use of SLO allows exact, repetitive measurements of the VF and the possibility to map scotomas, i.e. scotometry/microperimetry and fixation measurements, to verify the location and stability of fixation [13]. The human fixation system has a two-fold function during primary gaze: 1) to detect retinal image drift and thus preprogram corrective movements, i.e. saccades, and 2) to attend to or engage a certain target of interest. Failure to accomplish either of these functions will result in a disruption of steady fixation. It is necessary for these functions to work well under normal viewing conditions in order to achieve high-level vision. Previous studies have shown that fixation stability can be measured very exactly around the centre of the fixation point with SLO [14–17]. The importance of measuring fixation during microperimetry in the absence of field defects is to learn more about the normal fixation pattern, this to be able to detect changes earlier in the macula or visual pathways where the fixation pattern can often be one of the first signs of pathology. The aims of the present study were to investigate the fixation pattern in healthy subjects using the microperimetry technique obtained with the SLO and to calculate the fixation pattern with the "center of gravity" (CG) method using the x and y coordinates extracted from the SLO F00-files instead of the video grabbing technique commonly used.

MATERIAL AND METHODS

Subjects

Thirty-one subjects (14 men and 17 women, median age: 27.5 years, range: 22–39 years) were recruited from the staff at the Section of Ophthalmology and Vision, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. As age is a risk factor for eye disease, we did not recruit any subject older than 39 years. The inclusion criteria were: best corrected visual acuity equal to or better than 20/20, no earlier or present eye disease, and no ongoing medication. All subjects freely volunteered to participate in the study after the procedure and the aims had been explained to them. All subjects were informed about the SLO and test proceedings before the test. None of the subjects had any previous experience from perimetry sessions. The same examiner (FPK) performed all tests. One randomly selected eye from each subject was examined. The room where the SLO was located had no windows and there was no illumination in the room during the tests. The subject's head was fixed with a head and chin rest. The duration of each examination was approximately five minutes.

The laser scanning procedure

Microperimetry was performed with a Rodenstock SLO-101 using previously described methods [18–22]. The SLO obtains retinal images continuously with an infrared laser (780 nm) and scans/projects the stimuli on the retina with a modulated visible helium-neon laser (633 nm). Visual stimuli are produced in the laser beam raster by means of a microcomputer and graphics board connected to an acousto-optic modulator in the SLO. The acousto-optic modulator rapidly changes the intensity of the scanned laser beam in response to electronic signals from the graphics generator in the SLO computer. Any pattern produced by the SLO computer and projected onto the patient's retina is displayed simultaneously on a monitor.

The SLO provides a 32×22° image of the fundus with a minimum resolution of 4 minutes of arc (20 μm) for measurement and positioning of the stimuli. The graphics capabilities allow the investigator to determine the retinal location of visual stimuli directly on the retinal image in real time. The variables used for manual static visual field testing were those used in conventional perimetry, i.e. background illumination of 10 cd/m^2 and incremental test stimuli (brighter than the background) of 7×7 minutes of arc, which is approximately Goldman size 1. Stimulus duration was 200 msec. The helium-neon laser was also used as the light source for background illumination and the fixation aid. A fixation cross (0 dB) with a size of 36×36 minutes of arc was used and the subject was told to keep a steady fixation on the center of the fixation cross.

The stimuli were presented one at the time and the patient was asked to respond to every stimulus seen by pressing a hand-held button. A well-defined reference mark in the retina (i.e. a vascular branching point) was chosen by the experimenter. After every stimulus presentation, the reference mark was replaced on the same defined point as before the presentation. This ensured a correct alignment of the stimuli position on the retina and rejection of data points where the stimulus was presented during a saccadic eye movement.

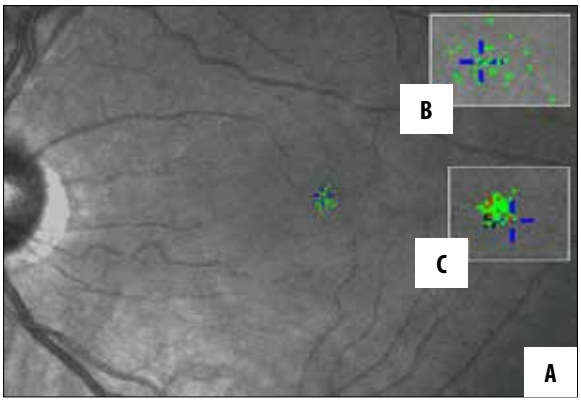

Figure 1. Ocular fundus from a representative SLO (Scanning Laser Ophthalmoscope) investigation with fixation distribution overlay. (**A**) Low magnification of the fundus where the fixations can be seen as green dots in the foveal area. The blue cross represents the fixation cross. (**B**) Enlargement of a typical fixation pattern of a subject with a wide distribution of the fixations. (**C**) Same enlargement as in B but from a subject with a more concentrated distribution of the fixations. The red dots in this picture represent the few fixation positions where the subject did not respond to the peripheral stimuli.

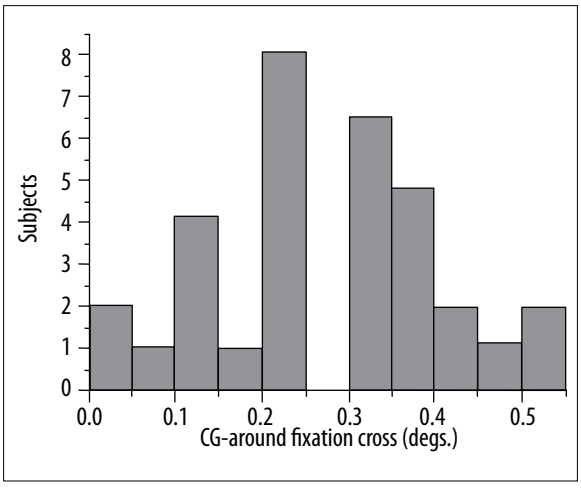

Figure 2. Histogram showing the mean distance between the fixation cross and the center of gravity (CG). Note that the CGs are distributed close to the fixation cross (mean: 0.27°).

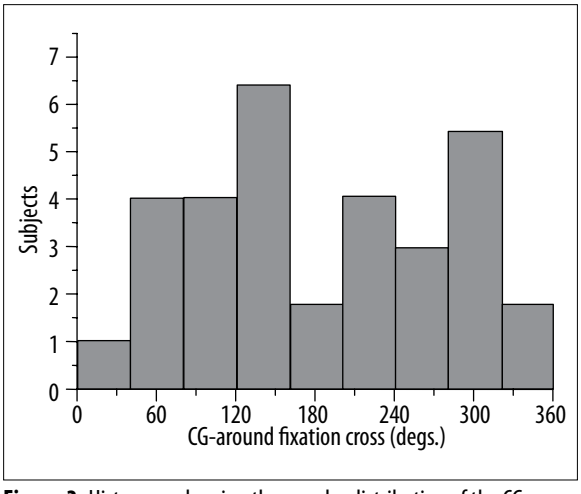

Figure 3. Histogram showing the angular distribution of the CGs (center of gravity) around the fixation crosses. Note a small directional preponderance in that more CGs are distributed in the vertical sectors (70–110° and 250–290°) than in the horizontal (340–320° and 160–200°).

Data collection and analysis

We performed a radial presentation of stimulus in order to get an acceptable cover of the central area in the macula that was of interest, similar to how the meridians in Goldman perimetry are presented. The peripheral stimuli were presented at different locations (0 to 15° from the center) along the orthogonal (0, 90, 180, and 270°) and oblique (45, 135, 225, and 315°) meridians. In total, between 30 and 90 stimuli were presented to each subject. The number of stimuli presented varied due to the ability of the subject to concentrate on the task. During each stimulus presentation the location of the fixation was saved in the computer (in x and y coordinates from the fixation cross location). These fixation locations, stored in the computer, were used to calculate the fixation pattern in each subject. Each fixation point and its x and y coordinates are represented in relation to the fixation cross. The results presented were obtained first by calculating each fixation point during a measurement (obtained simultaneously as the stimuli is presented) in relation to the fixation cross for each subject and then by taking the mean for each subject to obtain the results for the whole group.

The mean of the x and y coordinates in each subject were calculated to be used as a "center of gravity" (CG) for the fixation locations [23]. The distance and angular location of each CG relative to the fixation cross location was calculated in all subjects. All calculations and plots were performed with Origin Scientific Graphing and Analysis Software, version 7 (Microcal Inc.). One-way analyses of variance (ANOVA) were used for the statistical analysis.

Results

In all, between 30 and 90 fixation positions for each subject were obtained. The CG was calculated for each subject. There was no correlation found between the location of the presented stimuli and the fixation of each subject. In general, the fixation pattern varied among the subjects (Figure 1). The mean distance of the CGs in relation to the fixation cross was found to be 0.27° (*SD*: 0.13°, range: 0.04–0.50°) (Figure 2). There was also a slight tendency of a directional predominance of the CGs, more frequently distributed in the vertical sectors (70–110° and 250–290°) than in the horizontal (340–320° and 160–200°, Figure 3), but this tendency was not statistically significant. On an individual basis there where large differences in terms of fixation patterns. Some subjects showed a large area distribution of the fixation locations (Figure 4A), while others showed a much more concentrated distribution (Figure 4B). The angular distribution of the fixations was also found to vary between the subjects and some subjects showed a much more horizontal distribution of the fixation pattern than the more vertical distribution seen as the mean for the whole group (Figure 5).

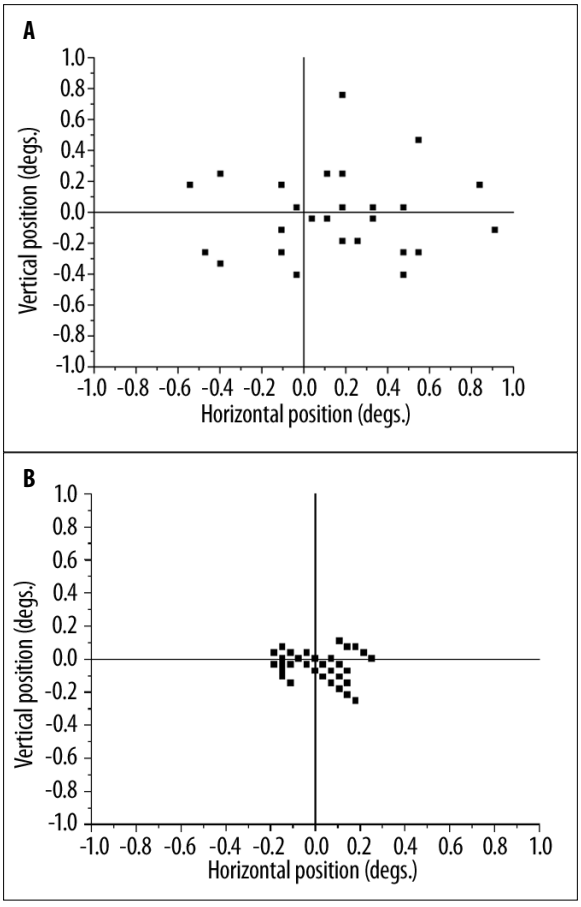

Figure 4. XY-plots showing fixations in two subjects representing different fixational distribution patterns. (**A**) showing a subject with a wide distribution of the fixations compared with (**B**) where the fixations are concentrated within a smaller area.

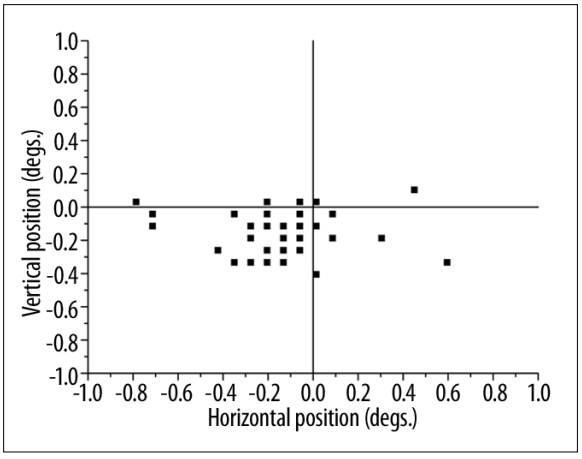

Figure 5. XY-plots showing fixation in a subject with a more pronounced horizontal distribution of the fixation pattern than the mean for whole group.

Discussion

Slight movements of the eyes are essential for good visual perception [24]. Three types of movements accompany fixation: drifts, tremor, and involuntary saccades [25,26]. Since fixation in normal subjects is not kept stationary, although efforts are made to fixate a stationary target, the term "fixation field" was suggested by Dog as early as 1907 [27].

Methodological considerations

Fixational eye movements have traditionally been measured by conventional methods such as the IR-reflection technique, scleral search coil, or the VOG technique [28,29]. However, the SLO microperimetry technique is the only perimetry method that allows exact mapping of the fixation position simultaneously with stimulus presentation during perimetry. Therefore the results from fixation mapping during microperimetry performed with the SLO are important when measuring the central VF in patients with unstable and/or extrafoveal fixation. However, it is important to note that since our results were obtained during perimetry, concentration on fixation may be disturbed by the effort to detect the peripheral light stimuli.

Since recent work shows no effect of abrupt onset location on the average pattern of eye movements during fixation, this implies that the oculomotor system is not obligatorily driven by events in the visual array [30]. The similarity of our results concerning the area of the central fixation pattern and those obtained with conventional methods for fixational eye movement analysis is interesting considering the differences in static and dynamic measurements. The ability of accurate measurement of the fixation pattern provides an estimate of the compliance during perimetry. The fixation can be quantified from video recordings [16] and defined as central if more than 50% of the fixation points were located within a predetermined area [17]. Others have used the Bivariate Contour Ellipse Area (BCEA) method for identifying the area used during fixation [31]. The BCEA method gives two orthogonal diameters describing the extent of the fixation distribution around a fixation mark, but the CG method can, as we have shown, also give further information in that the area around the fixation point is divided in eight sectors and the distribution of the fixation points within these sectors can easily be calculated and reported as we have done. The BCEA method relies on the assumption that the material is normally distributed, which is often not the case in this kind of measurement and can therefore cause misinterpretation of the data. If calculated with the CG method, however, no consideration is necessary to whether the material is normally distributed or not. We therefore consider the CG method more informative of fixation behavior in both normal subjects and subsequent patient groups to be investigated. The CG method has not, to our knowledge, been previously performed with the SLO. Our results are entirely built upon the hard data acquired from the SLO computer and the CG method to calculate the fixation location and could therefore limit the comparability between the results with others.

Fixation point distribution

For clear vision of higher spatial frequencies, e.g. a 20/20 Snellen optotype, the image should fall within the central 0.5° of the fovea. The results of the present study show that the mean distance from the fixation cross to the CG in our subjects was 0.27°, thus well within the retinal area for the highest visual resolution. The results of the present study thus have implications for the interpretation of the results ob-

tained from a conventional perimetry session where the fixation location can never be exactly measured. Rohrschneider and coworkers [14] found, using the SLO, an *SD* around the mean fixation point of 0.29°, thus comparable with the findings of the present study. Moller and coworkers [32] showed with SLO and video sequences recording of fixational eye movements that the mean amplitude for the fast and slow movements was 0.41 and 0.31°. respectively, this also comparable with our results. Earlier findings by Kosnik and coworkers concluded that there is no correlation between stability of fixation and age [33,34]. Notable in this study is that the angular direction of the location of fixation points with regard to the CG was found to have a tendency to be more pronounced in the vertical direction. To our knowledge, no other study has addressed the question of the angular distribution of fixations held. The explanation for the directional differences found in the present study is not yet fully known. This may be related to the sensitivity orientation of the ganglion cells in that the responses of most cells, to high spatial frequencies, depend on the grating orientation [35]. This indicates response fields that could be described by an ellipse. However, an effect of higher visual pathway processing cannot be excluded.

Conclusions

The abilities of the SLO make it a helpful diagnostic and data collection instrument that provides information complementary to standard clinical techniques. Together with knowledge about fixation in healthy subject, this technique may provide a possibility of early detection of macular pathology. This will be important in early intervention, lifestyle counseling, and insights into the development of diseases in the retina and the visual pathway due to the computerized registration of fixation that cannot be obtained with standard clinical perimetry techniques. This technique may provide better understanding of the real location of macular pathology in patients with unstable or extrafoveal fixation, which will be important in decisions regarding treatment and visual rehabilitation as well as in better explaining the visual fields in patients with many ocular and visual pathway disorders.

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