NEURO-OPHTHALMOLOGY

Pupil campimetry in patients with retinitis pigmentosa and functional visual field loss

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Abstract

Background The aim of our study was to test in a small series of cases if pupil perimetry can prove real concentric visual field loss in retinal degeneration and distinguish from feigned visual field loss.
Methods By means of infrared-video-pupillography, light responses to perimetric stimuli were recorded. The stimulus pattern consisted of 41 stimuli presented in the central 30° visual field. Stimulus intensity was 140 cd/m^2. 5 healthy subjects, 6 patients with retinitis pigmentosa and 2 patients with suspected functional visual field loss were examined.
Results Pupil perimetry was able to reproduce the visual field in retinitis pigmentosa very well. Normal subjects and patients with suspected feigned visual field loss showed normal pupillomotor fields, different from the findings in retinitis pigmentosa.
Conclusions This study provides sufficient evidence that pupil campimetry is applicable for differentiating between retinal dystrophy and functional concentric visual field loss. Possible residual light sensitivity of the blind retina due to melanopsin ganglion cells is obviously not sufficient to provide a pupillary light response to perimetric stimuli.

Keywords Pupil campimetry · Pupil perimetry ·
Retinitis pigmentosa · Concentric visual field loss ·
Functional visual field loss

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Introduction

To diagnose a retinal degeneration like retinitis pigmentosa (RP) is usually not a problem. However, there are occasionally patients with normal fundus appearance showing severely constricted fields. This might be non-organic visual loss, either feigned or psychogenic. To disclose non-organic visual field loss by objective methods may be a challenging issue in ophthalmology. If expert opinion is required, for example in social court issues, objective methods are necessary. At first an electroretino-gram would be done of course, however, reduced ERG does not necessarily imply visual field loss and blinking or otherwise poor compliance might produce reduced ERG responses. It is therefore desirable to have an additional tool. Also, in the light of the emerging gene therapy in ophthalmology an objective visual field test would be helpful.

Pupil perimetry or campimetry also represents an objective method of testing the visual field by examining the pupillary response to focal light stimuli projected onto the retina. It is therefore principally suited as a tool to distinguish organic from non-organic visual loss. Before applying pupil perimetry in cases with constricted visual fields it needs to be clarified that it is really possible to demonstrate organic constricted fields. Although it is not likely that the recently decribed melanopsin retinal ganglion cells would respond to short and dim stimuli [1, 2] one could argue that residual pupillary light reaction might be possible in blind areas of the visual field. The aim of our study was to show in a small series of cases that pupil perimetry can demonstrate real concentric visual field loss in retinal degeneration and distinguish from feigned visual field loss and normal visual fields.

Methods

For the purpose of this study, a group of 5 healthy subjects, 6 patients with retinitis pigmentosa and 2 patients with feigned concentric visual field loss were examined.

Patients with retinitis pigmentosa included in our study suffered from advanced disease of both eyes and had fulfilled the following inclusion criteria: visual field reduced to the central 10° or less; last ERG less than half a year ago, with a marked reduction of amplitudes and increase in latencies in both full-field and the multifocal ERG; typical ocular signs of RP; no other ocular disease which could interfere with the visual field or pupil light reaction. The study group of patients with RP consisted of 4 females and 2 males aged 29 to 71 years (median 48.5 years).

Two male patients with presumed concentric functional visual field loss aged 27 and 29 years were recruited from our neuro-ophthalmological clinic. Subjective visual acuity was bilateral light perception in one and 0.3 right and 0.5 left in the other patient. Both patients pretended to have markedly constricted visual field. The diagnosis of feigned visual loss was based on the absence of any objective sign of visual loss in any test including electrophysiologic testing and on inconsistency of vision and observed behaviour.

As control subjects served 5 healthy subjects with normal ophthalmological findings, normal pupil light reaction and normal visual field in both eyes. The control group consisted of 4 females and 1 male aged 26 to 56 years (median 27 years).

The study was approved by the local institutional ethics committee and followed the tenets of the Declaration of Helsinki. All participants received written information about the pupillometry and gave their written consent.

All subjects underwent a thorough ophthalmological examination including either static perimetry, using Tübingen Automatic Perimeter, or Goldmann 90° kinetic perimetry of both eyes. Finally, the computerized infrared (IR) pupil campimetry was performed. In all subjects both eyes were tested consecutively, one eye always being covered with a black eye patch during the test. The pupillographic device consisted of a computer, a 19 inch CRT screen for the stimulus presentation and a small fixation control display. Stimuli were presented on the computer screen at a distance of 20 cm from the subject's eye. Blinds around the device prevented straylight in the room from disturbing the measurement. The pupil reaction was recorded by means of an IR-sensitive video camera. The stimulus pattern consisted of 41 stimuli presented in the visual field centre and three concentric rings within the central 30° visual field. Stimulus diameter was 4°. For all stimuli white light was used, stimulus intensity was 140 cd/m^2 with a constant background luminance of 2.7 cd/m^2. Each stimu-lus was presented for 200 ms every 2000 ms. A small red spot was presented constantly for fixation. The perimetry program presented each stimulus at each tested location four times. If the pupil size could not be recorded four times without problems (e.g. of blinks), the stimulus was presented more often until four recordings of the pupil size were done for each stimulus. The pupillary response was analysed for each pupil record. Afterwards the four pupillary responses were averaged. Using these averaged values the further analysis was done.

In all groups the pupil fields were compared to the standard visual fields obtained on the same day both by a subjective assessment of an experienced observer and statistical evaluation. For statistical analysis the mean of the pupil light reaction in the centre of the visual field and at the eccentricity of 10, 20 and 30 degrees, was calculated in each subject. The median, mean, standard deviation, minimum and maximum were calculated in the control and RP group.

To compare the RP group with the control group, the pupil responses at individual eccentricities were analysed using a two-tailed Wilcoxon rank-sum test. Due to the small number of patients with non-organic visual field loss, their results were not evaluated by descriptive statistics or the non-parametric test, but the actual pupil response discussed in comparison to the other two groups.
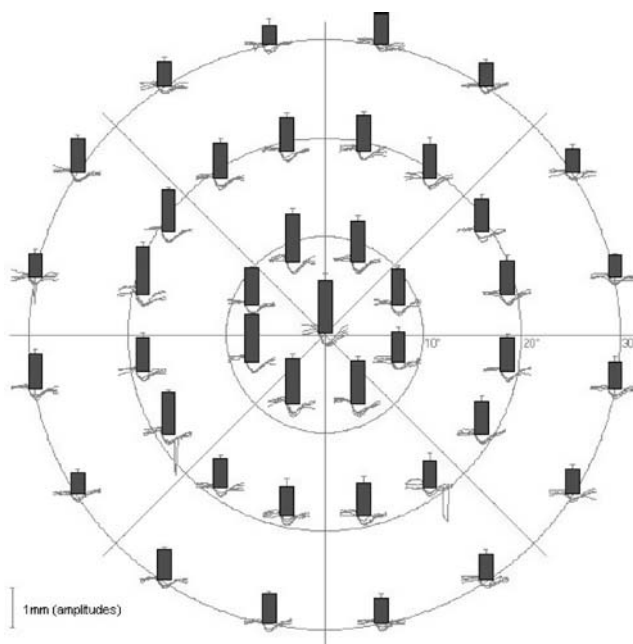
Fig. 1 Pupillomotor field in a healthy person. The column represents the mean value of pupil light response in mm at each tested location in the visual field. The mean value is calculated as an avarage of individual amplitudes of four displayed pupillographic curves. The error bar above the column represents the standard error (SE) of the mean value
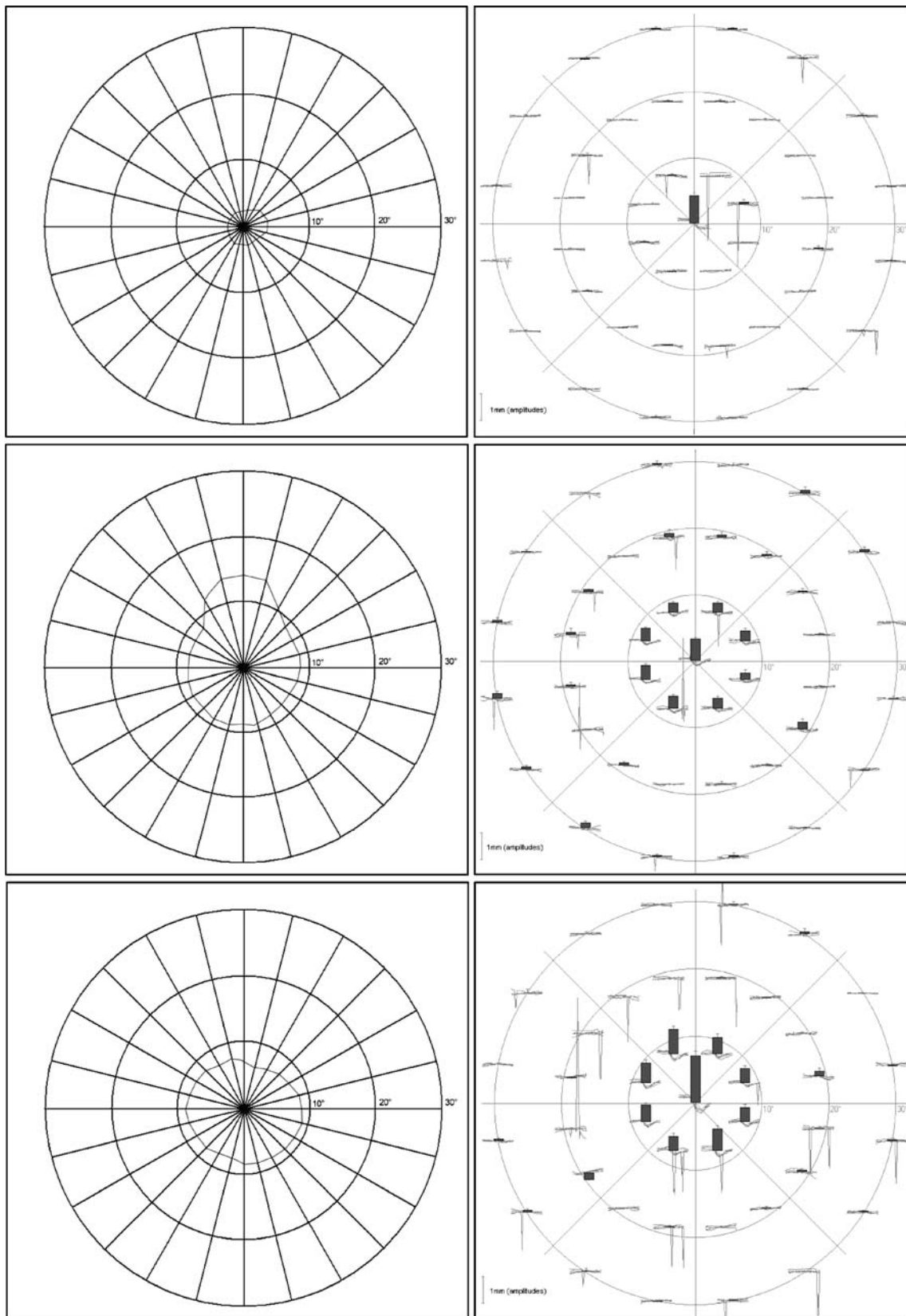
Fig. 2 Pupillomotor field in 6 patients with retinitis pigmentosa and the corresponding 30° visual field in Goldmann perimeter
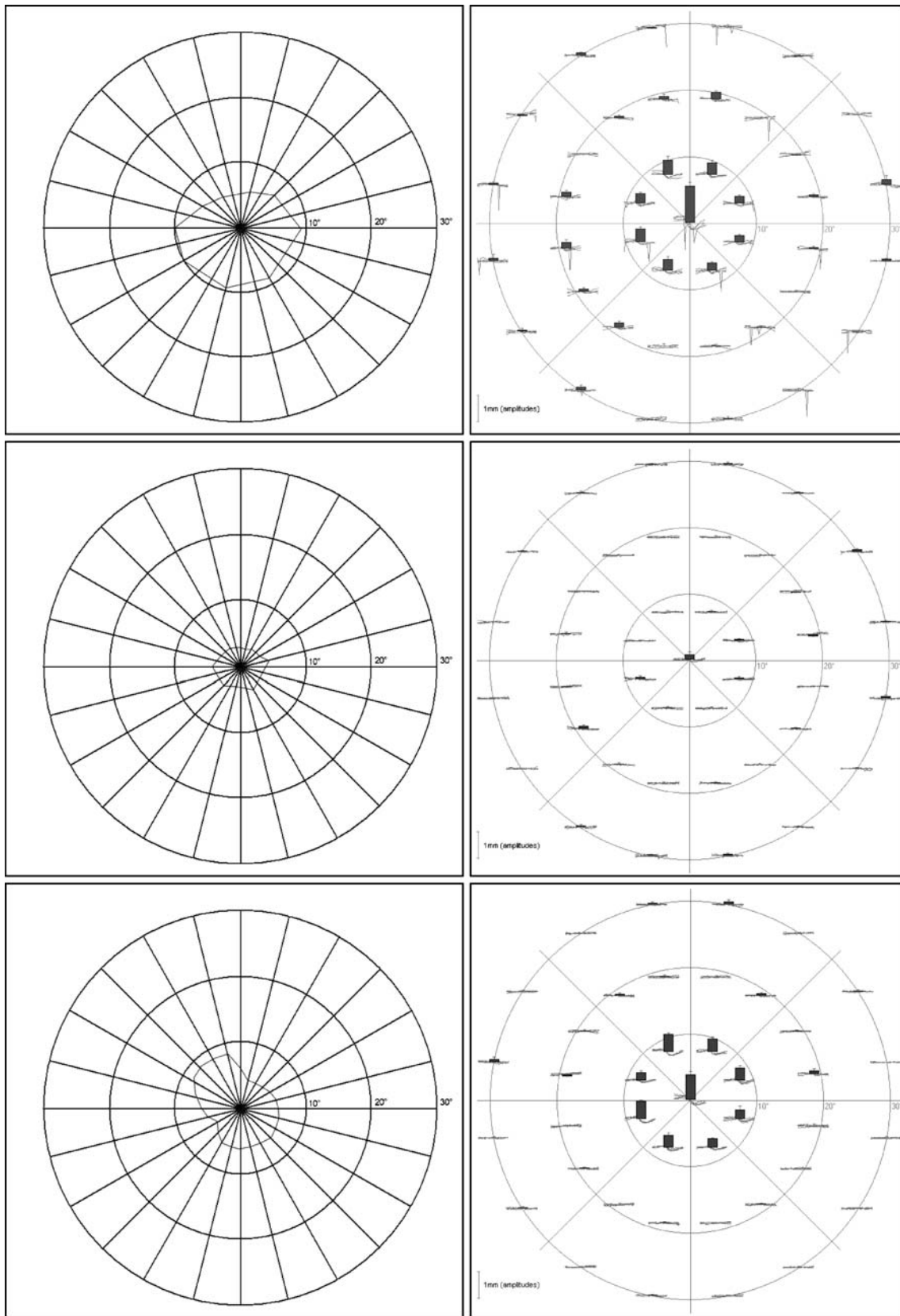
Fig. 2 (Continued)

Results

Pupil campimetry in control subjects showed pupil light reaction at all tested locations in the visual field with the highest amplitude in the centre of the visual field and a decrease towards periphery (Fig. 1). In patients with retinitis pigmentosa whose visual field was constricted to the central 3 to 10°, the pupil reaction was present only within the preserved visual field. No pupillary response could be recorded outside the area where Goldmann V4 was seen (Fig. 2). The median, mean, standard deviation, minimum and maximum of the pupil light reaction in the centre of the visual field and at the eccentricity of 10, 20 and 30 degrees in the control and RP groups, are listed in Table 1.

In the two patients with suspected feigned visual field loss one patient (1) pretented that he had a concentric visual field loss up to the central 10° on both eyes. There was no visible ocular pathology. The second patient (2) could identify only a few stimuli close to the centre of the visual field in both eyes during the visual field test. Ocular fundus of this patient showed only typical myopic changes. A relative afferent pupillary defect was not present with either of these patients. Magnetic resonance imaging scans of the brain and optic nerve had not revealed any pathology. Pupil campimetry in both patients showed a well evocable pupil reaction at all tested locations, with no evidence of any concentric constriction of the visual field in either eye (Fig. 3). The actual pupil reaction [mm] at defined eccentricities of the visual field for both patients is listed in Table 2.

The pupil responses differed significantly between the control subjects and the RP patients in the centre of the visual field (p=0.029), as well as at the eccentricity of 10, 20 and 30 degrees (all p=0.006). The pupil constriction amplitude of patients with feigned visual field loss resembled the results of the control subjects and differed

Table 1 Characteristics of pupil light reaction in the group of control subjects and RP patients

	Eccentricity	Median [mm]	Mean [mm]	SD	Minimum [mm]	Maximum [mm]
Control group	0°	1.80	1.76	0.36	1.25	2.26
	10°	1.23	1.22	0.27	0.91	1.65
	20°	1.04	1.03	0.24	0.71	1.33
	30°	0.81	0.87	0.22	0.56	1.09
RP group	0°	1.01	1.04	0.52	0.22	1.75
	10°	0.42	0.34	0.27	0.01	0.69
	20°	0.02	0.04	0.04	0.01	0.09
	30°	0.04	0.07	0.09	0.01	0.25

Median, mean, standard deviation, minimum and maximum are obtained from the mean values calculated for each subject at different eccentricities

from the results of RP patients especially at 10, 20 and 30 degrees eccentricity.

Discussion

Pupil perimetry was able to reproduce the visual field in retinitis pigmentosa very well. Pupil perimetry in patients with functional concentric visual field loss did not show a pattern similar to retinitis pigmentosa at all. On the contrary, it confirmed normal functions in allegedly blind areas of the visual field, thereby ruling out a severe retinal dystrophy.

This is in accordance with other studies dealing with the clinical applications of pupil perimetry which have shown that most diseases affecting the retina and the visual pathway cause pupil field scotomata which match the defects found in standard perimetry [3, 4, 5, 6]. Visual field defects in pupil campimetry can be recognized by a reduced or absent pupil light reaction within these areas.

Not much information exists about the pupillary visual field in retinitis pigmentosa. Alexandridis et al. [7] showed that it is possible to objectify visual loss in patients with retinitis pigmentosa by means of the pupillography. However, in his experiments he did not use pupil perimetry but central threshold measurement.
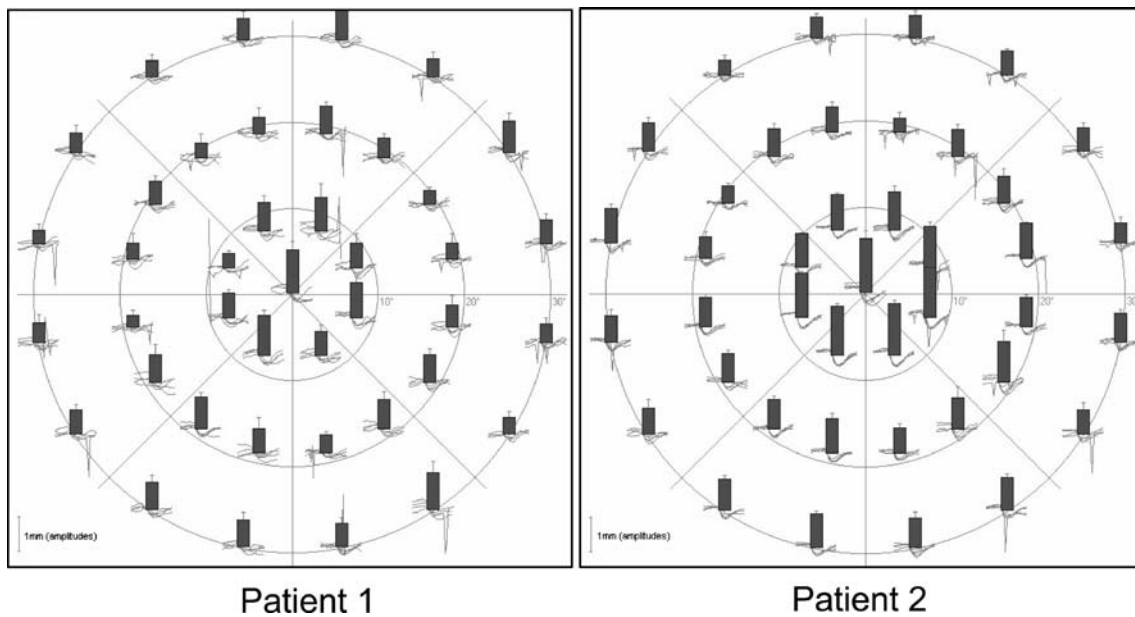
Use of pupil campimetry to test patients with functional visual loss has been investigated by other studies, as well [4, 5, 8, 9, 10]. To our knowledge, only two studies [8, 9] included a few patients with retinitis pigmentosa. Moore et al. [8] included 2 patients with retinitis pigmentosa, who showed no pupil response in the peripheral field, similar to ours. Based on the data of 17 patients with suspected functional visual field loss, the authors called pupil perimetry a method, which can objectively substantiate functional field loss when focal pupillary responses are normal but visual threshold is not. Yoshitomi et al. [9] also examined 2 patients with retinitis pigmentosa and found a congruence between conventional and pupil perimetry. Rajan et al. [10] conducted a study on 3 patients with presumed functional visual field loss respecting the mid-lines. They concluded that in cases of functional visual field loss where the pattern is not consistent with retro-chiasmal disease, pupil perimetry can provide objective evidence for normal visual fields. Kardon et al. [4] tested pupil perimetry in normal subjects and patients with various visual field defects. One patient in their study group with functional hemifield loss demonstrated a completaly normal pupil field.

Pupil perimetry has its limitations too. First, only the central 30° of the visual field can be tested. Pupil light reaction elicited by light stimuli further in the periphery is only subtle and variable and can be hardly registered by

Fig. 3 Pupillomotor fields of 2 patients with feigned concentric visual field loss. During standard visual field test, patient 1 could identify only a few stimuli close to the centre of the visual field, patient 2 gave a visual field of 10°. However, their pupillograms at all tested locations are normal, giving no evidence of any concentric visual field loss. For further explanation of the graphs, see Fig. 1

current techniques. Second, it is accompanied by a greater variability in the measurements than the standard perimetry [11] and cannot be performed in patients with marked efferent pupillary disorders. Reduced pupil contraction can also be due to supranuclear inhibition (fear, stress), small pupil size, autonomic neuropathy or systemic drugs with anticholinergic effects. Such a pupil field might appear constricted, however, all responses are reduced, the central and the peripheral. According to our results, the appearance of a pupil field in retinitis pigmentosa patients is typical and should not be mistaken. Third, there is the unavoidable problem of straylight which might pretend a pupil light response in a blind area of the visual field. Fortunately, this played a minor role in our retinitis pigmentosa cases as demonstrated in Fig. 2. The responses outside the functional visual field area are absent or very small. However, when trying to map small defects, straylight may frustrate such an attempt.

Table 2 Mean pupil light reaction [mm] in the centre of the visual field and at the eccentricity of 10, 20 and 30 degrees in two patients with feigned visual field loss

	0°	10°	20°	30°
Patient 1	1.59	1.27	0.83	0.80
Patient 2	1.28	0.85	0.66	0.71

Again, these values were calculated from the mean values at a particular eccentricity in the visual field

Pupillary function in patients with retinitis pigmentosa needs also to be discussed in the context of new knowledge on retinal anatomy. Recent studies in mammals [12] have provided overwhelming evidence that ocular photoreception is not limited to rods and cones. A small subset of retinal ganglion cells expressing melanopsin has been shown to be directly photosensitive. These retinal ganglion cells project to the olivary pretectal nuclei, the retino-recipient area responsible for the pupillary light reflex, and the suprachiasmatic nuclei, the circadian pacemaker in the brain [13, 14]. They do not serve vision and might be spared in retinal cone-rod-dystrophies.

Experiments on rodless and coneless mice have shown that pupillary light response persists in the absence of rods and cones. It could be argued that those ganglion cells might provide light responses even in the blind visual field of retinitis pigmentosa patients. However, melanopsin exerts influence only at high irradiances and does not respond to short stimuli but rather to sustained stimuli. Probably, the rod/cone and melanopsin system together provide the full dynamic range of the normal pupillary reflex [15]. Thus, light stimuli used in our experiments were below the threshold of the photosensitive ganglion cells in the affected regions of the retina.

In conclusion, this study provides sufficient evidence that pupil campimetry is applicable in differential diagnosis of retinal dystrophy and functional concentric visual field loss. To determine specificity and sensitivity further studies with more patients are necessary.

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