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Different effect of dioptric defocus vs. light scatter on the Pattern Electroretinogram (PERG)

Michael Bach & Marcel Mathieu
Universitäts-Augenklinik, Killianstr. 5, 79106 Freiburg, Germany

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Abstract

To assess the quantitative effect of optical deficiencies on the Pattern Electroretinogram (PERG), we degraded the optical imaging onto the retina by dioptric defocus (+1.75–5 D), and by scatter transparencies. With optimal and degraded optics we measured the visual acuity and the steady-state PERG, evoked by checkerboards (check size 0.2–16°), and flash stimuli. When the two optical degradation methods were equated for acuity, scatter transparencies reduced the PERG amplitude more than defocus. For scatter transparencies, there was a significant ($p < 0.001$) effect at 16°, escalating for smaller checks. For defocus, significant effects were only observed for check sizes of 1.6° and smaller. We explain the differences between the two blur techniques by their differing angular scattering functions. Dioptrical defocus leads to an underestimation of the effect of media opacities on the PERG. For the clinically relevant check size of 0.8°, halving acuity reduces the amplitude by 15% with defocus and by 30% with scatter. With an acuity of 0.8 or higher, no clinically relevant effect of suboptimal refraction is seen.

Abbreviations: PERG – Pattern Electroretinogram; VA – visual acuity.

Introduction

The Pattern Electroretinogram (PERG) predominantly reflects activity of the retinal ganglion cells [1–6]. As such, it serves as a sensitive indicator of a variety of pathophysiological conditions, e.g., glaucoma [7–18], possibly before glaucomatous field defects can be detected [19–22]. Because its spatial limitation to the retinal area being imaged on, it is also a sensitive indicator of macular function [23, 24]. Possible limitations include optical problems, such as cataract, leading to degradation of the retinal image, and age dependency, which may also reflect incipient media opacities. It has been shown that –even in normal eyes– optical factors play a significant role for the normal PERG [25, 26]. In routine PERG recording, the visual acuity (VA) could be used as a simple indicator of the retinal image quality, at least if the pathology under study leaves central vision unaffected. A number of studies have looked at the effect of defocus on PERG [26–32]. In all cases the latency was found to be unaffected, but the amplitude to be reduced. However no quantitative relationship between VA and PERG amplitude has been established, which prompted the present study. To this means, of the many factors reducing VA we studied the two most important ones: (1) Dioptric defocus, simulated by plus lenses and (2) scattering, simulated by partial occluder transparencies. The latter blur method may better model media opacities [33]. We found marked differences between the blur techniques in their PERG alteration, even when these two methods were equated for VA.

Preliminary results were reported at the Satellite-ISCEV in Oxford 1991 and the ARVO meeting 1997 [34].

Methods

Subjects

We recorded from 10 eyes of 5 visually normal subjects. With appropriate refraction all had visual acuities ⩾1.2 and gave their written informed consent to participate in the study. Experiments followed the tenets of the Helsinki declaration [35].

Acuity measurement and reduction

Visual acuity (VA) was measured using a fully automated test, freely available from this laboratory [36, 37] and found to be highly reliable [38]. Briefly, Landolt-Cs were displayed on a very high resolution monitor (VM 2440, Lucius & Baer, Geretsried, Germany). In an 8-alternative forced-choice paradigm the subjects indicated the position of the gap by pressing one of the appropriate keys, which were topographically arranged according to gap position. The PEST procedure [39] was used to estimate the threshold over 24 trials. The results were not rounded to the ISO values (European Norm EN ISO 8596) [40, 41]), thus retaining their precision. The special properties of the CRT (pixel size 0.5 minutes of arc) allowed full VA assessment at the relatively low distance of 57 cm, identical to the distance of the PERG stimulation.

Optical imaging quality, and consequently VA was reduced in two ways: Firstly through dioptric defocus by adding plus lenses to simulate poor refraction (0-5 D in steps of 0.5 D). Secondly we used partial occluder transparencies to more closely simulate light scattering in incipient cataract. Partial occluder transparencies are commercially available ('Bangerter Folien') in various grades. The amount of VA reduction by either means varied from subject to subject. With dioptric defocus, the optical transfer function depends on pupil size [42, 43], so care was taken that the retinal illuminance did not change between VA testing and PERG recording. Applying various transparencies and plus lenses, we aimed for 5 VA levels from 0.1 to the full acuity, evenly spaced on a log acuity scale ($\log \text{VA} = -\log \text{MAR}$). When VA was near the desired value, the electrophysiological test was performed. It was not necessary to aim exactly for any specific VA, since the VA scale was sufficiently densely sampled across all subjects. VA is always given in decimal values, 1.0 referring to a threshold Landolt-C gap of 1 minute of arc.

Stimulation

Subjects viewed the stimuli binocularly with natural pupils on a video monitor with a resolution of 480 × 391 pixels. The screen subtended 27 × 31° of visual angle at a distance of 57 cm. Checkerboards with a mean luminance of 45 cd/m^2, a contrast of 98% and check sizes of 0.2, 0.8, 3.2 and 16° were counterphased at 16 reversals/s. For flash stimuli, the entire screen was switched between the values of the dark and white checkerboard squares at a frequency of 8 Hz. We presented the stimuli in an interleaved block design: A stimulus appeared for 6 s during which interval 16 sweeps of 512 ms duration were averaged, then the next stimulus followed. This sequence, comprising the 6 stimuli, recycled 10 times, resulting in a total of 160 sweeps for each condition. This interleaving of stimulus conditions reduced the effects of any trends (e.g., fatigue) on the recordings. A small cross in the center of the screen served as a fixation point. To control for fixation and attention, subjects reported random digits that appeared every 5–10 s for 300 ms in place of the fixation point.

Recording and analysis

PERG responses were recorded with DTL electrodes [44–46] placed in the lower limbus. A gold cup electrode at the outer ipsilateral canthus served as reference. The signal was amplified and filtered with a bandpass of 1.6–70 Hz and digitized to a resolution of 12 bits at a sample rate of 500 Hz by a small laboratory computer which simultaneously generated the stimuli (and early version of [47]). Sweeps were averaged and displayed on-line, traces exceeding $\pm 100\,\mu V$ were rejected as artifacts. Evoked potential amplitude was measured in the frequency domain as the magnitude at the reversal frequency, using Fourier analysis [48, 49].

Results

Representative for all subjects, Figure 1 displays recordings from a single subject at a check size of 0.8° under 3 conditions: free viewing with a VA of 1.5, the specific dioptrical defocus here reducing VA down to 0.32 and the scattering transparency reducing the VA down to 0.39. In all conditions, 8 peaks are seen, as expected with 16 rev/s and 0.5 s sweep time. While the PERG amplitude is reduced to about $\frac{1}{2}$ in

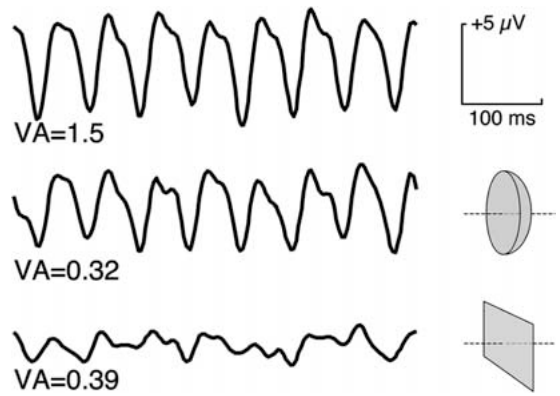

Figure 1. Steady-state recordings from a single subject at a check size of 0.8° under 3 conditions: free viewing with a visual acuity of 1.5, top; with dioptrical defocus reducing acuity down to 0.32 (center); and with light scattering through transparencies reducing the acuity down to 0.39 (bottom). While the amplitude is reduced to about $\frac{1}{2}$ in dioptrical defocus, the scattering transparency nearly abolishes the PERG, even though acuity reduced was comparable to the dioptric defocus condition.

dioptrical defocus, the scattering transparency nearly abolished the PERG, even though VA was slightly higher than in the dioptric defocus condition.

Figure 2 displays amplitudes from all subjects across all check sizes, including flash stimulation (bottom). To factor out interindividual variability, the amplitudes were normalized to each subject's value at full VA. The continuous lines represent a linear regression of PERG amplitude vs. logVA. In the left of each graph, the regression slope b and its significance level p are given. Clearly, from flash (bottom) over large to small check sizes (top), VA reduction attenuates PERG amplitude more and more; the slopes vary from horizontal (bottom) to steep (top). It is further evident that there is less effect for dioptrical defocus (left column), where at 3.2° check size there is no significant effect of VA reduction, while for the scatter transparencies (right column) there is already a sizable and highly significant ($p < 0.001$) effect at 16°. The slope parameter quantitatively links VA and PERG amplitude. For instance, at the clinically relevant check size of 0.8° [50], halving VA reduces the amplitude by 15% with defocus and by 30% with scatter. Flash responses are not affected by either way of VA reduction.

Discussion

We would first like to comment on the VA values with best correction: As can be seen from Figure 2, VA values above 1.6 were regular obtained. It is commonly assumed that the 'normal' acuity is 20/20, equaling decimal 1.0. However, several factors should be taken into account when measuring acuity rigorously: (1) 'forced choice' testing should be used throughout, to avoid influences of the subjects' criterion, and no 'don't know' option should be allowed. (2) The threshold should be defined at the point of steepest slope of the psychometric function which links discrimination success and optotype size. With 8 possibilities of gap orientation of the test figure, there is a 12.5% chance rate, and thus the threshold should be set at $(100\text{–}12.5\%)/2 + 12.5 = 56.75\%$ (European Norm EN ISO 8596) [40, 41]. At this threshold nearly half of the optotypes are not correctly identified; while this is an optimal choice from a psychometric point of view, it is clinically not yet widely used. (3) A sizable number of clinical testing charts or projectors simply stop at 1.26 (at least in Germany) and do not provide the option to test at higher resolutions. All in all, the factors above explain the possibly surprising high VA values obtained.

When the optical quality of the retinal image is reduced, all pattern-based electrophysiological responses diminish, as well known (VEP [51], PERG [50]). It is further immediately obvious that this effect should depend on check size: The extreme case, flash stimulation, evoking the flash ERG, should not be affected, as found (Figure 2, bottom). That the two different optical degradation techniques, dioptrical defocus and scatter transparencies, should have so widely differing effects on PERG amplitude was unexpected for us, even if now clear as detailed below.

To better understand why the PERG would be so different for these two blurring methods, even when equated for VA, we placed a camera where the eye would be and captured images of the screen, with various chequerboards, in their natural condition, and degraded either by defocus or scatter. The camera was selected to be similar to an eye with regard to entrance pupil and focal length. Cross sections through its images are shown in Figure 3. The top row of Figure 3 shows the image profile of a 0.2° checkerboard which –even without optical degradation– already taxed the optical setup and image resolution (the somewhat uneven check sizes are due to aliasing by the low pixel resolution). Still, the massive reduction of luminance modulation after optical degradation is obvious (dotted and dashed lines). It is further seen that the two types of simple optical degradation lead to similar

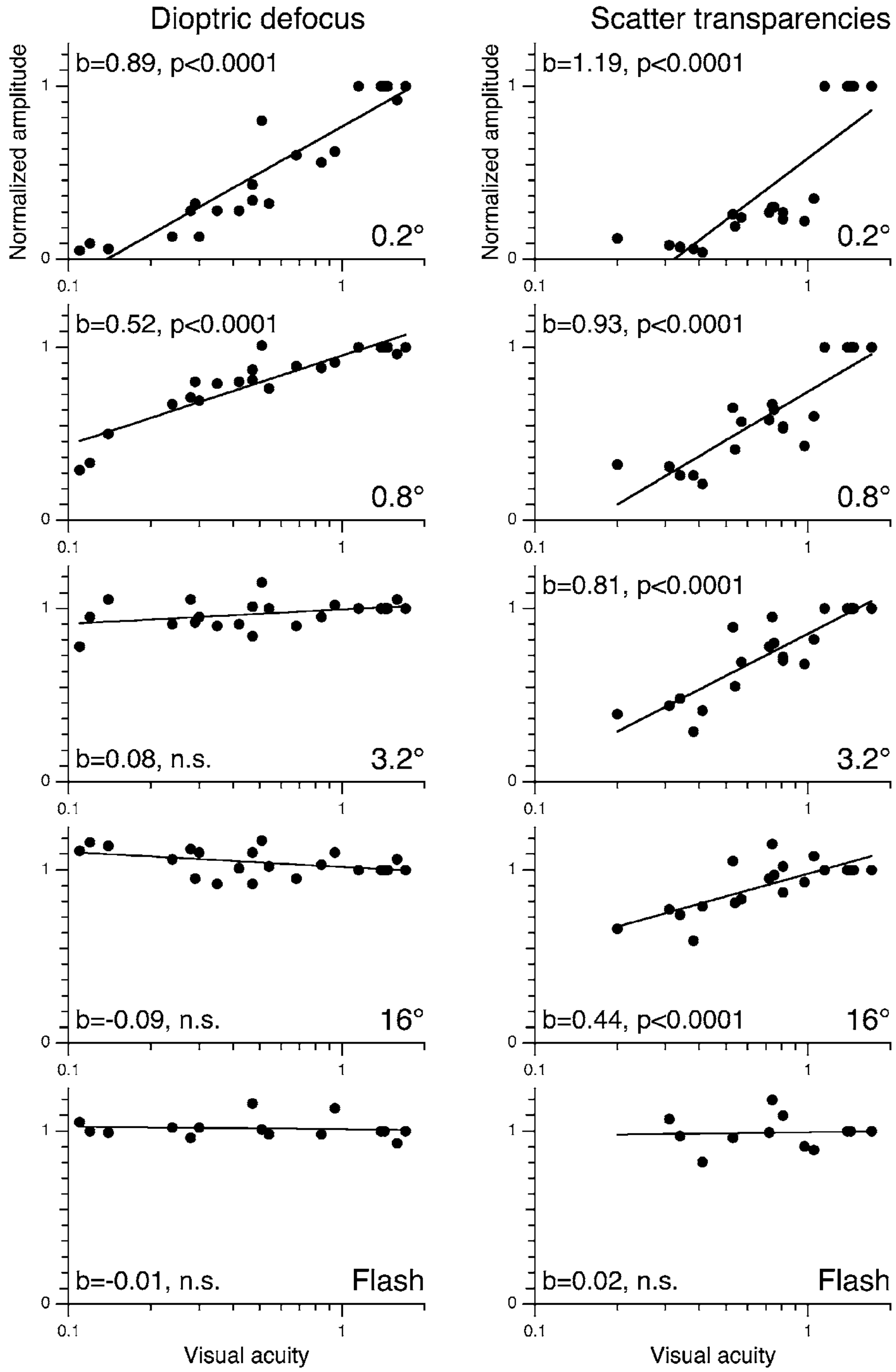

Figure 2. Normalized PERG amplitudes from all subjects at check sizes 0.2° (top) to 16°, and flash stimulation (bottom). Each subdiagram shows amplitude as a function of (artificially reduced) acuity. With decreasing check size there is progressively reduction of PERG amplitude with lower acuity as effected optical degradation. At intermediate check sizes (e.g. 0.8°), the effects on PERG amplitude differ markedly between dioptric defocus (left, little effect) and scattering (right, strong effect).

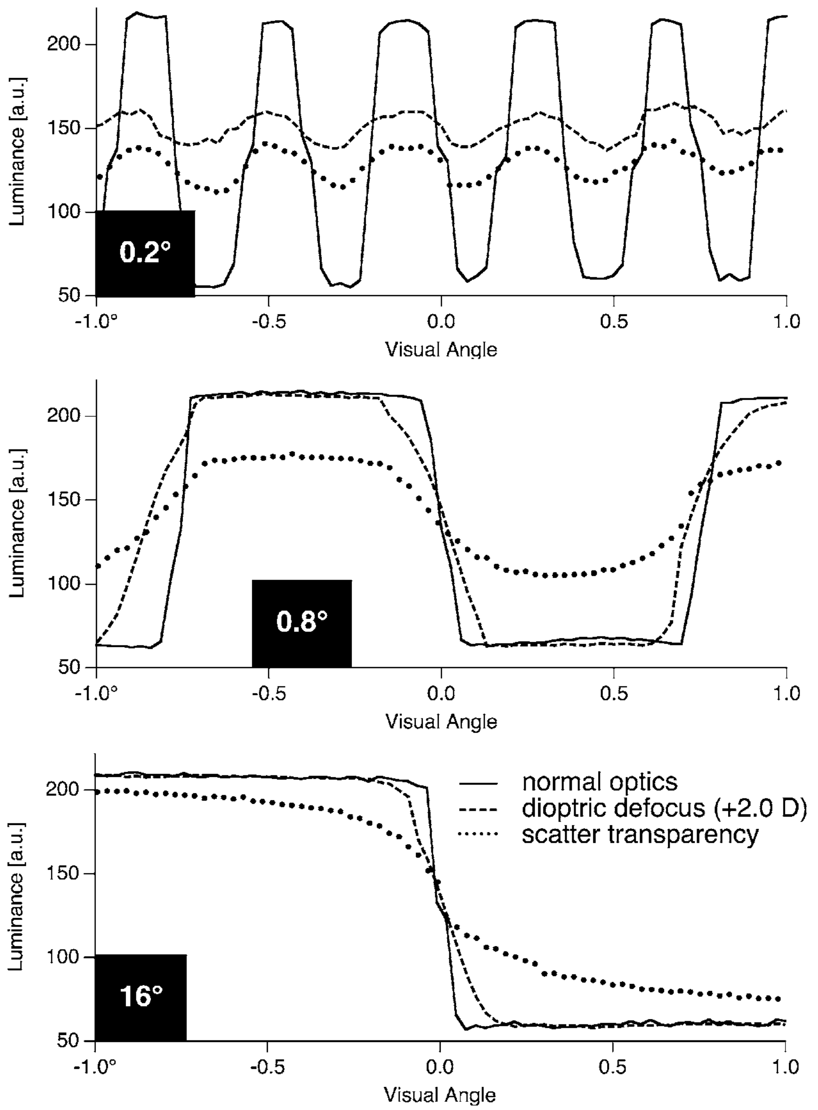

Figure 3. Optical effects of image degradation: Profiles of camera images obtained under conditions similar to the experiments. The ordinate represents luminance in arbitrary units on a scale from 0 to 255, the abscissa the corresponding visual angle. Check size was 0.2° (top, here the finite pixel resolution causes the seemingly uneven check width), 0.8° (center) and 16° (bottom). The luminance profile with optimal optics (full line) has similar amplitude at all check sizes. Degrading optics with defocus (dashed) or scattering (dotted), when equated for acuity, has similar effects on the profile for the small check size (top). At larger check sizes the luminance profile is less modulated after defocus than after scattering (see text for explanation).

effects. This follows from the fact that we chose a blur strength to fit the VA reduction by the scatter transparencies, and 0.2° check size is relatively close to the test figures when measuring VA. At larger check sizes, marked differences appear between the retinal images after blur as compared to scattering. Let us consider the 0.8° condition (Figure 3, center): defocus (dashed) reduces the slope of the luminance step. However, since defocus has only local effects (related to the size of the blur disc), the luminance reaches its full excursion in the major part of the check. Scattering (dotted line) by the type of transparencies used here not only blurs the image (as seen by a reduced slope) but also contains wide-angle scatter effects. Consequently, even far away (>0.3°) from the luminance step there occurs marked contrast reduction, which covers several degrees of visual angle as seen at the bottom.

We have to consider a possibly confounding factor, namely changes in retinal image size that occur with dioptrical defocus [52], but not with scatter transparencies. This effect was counteracted by equating the optical degradation techniques for equal effect on VA. Consequently, any increase in retinal image size, which would lead to less VA reduction than based on the blur alone is counteracted by higher defocus, ultimately ending in the same VA.

The main difference between dioptric defocus and inserting scatter transparencies is thus the differential scattering cross section: Defocus has a narrow scatter width, and the frosted transparencies have a wide scatter angle. When equated for VA, at standard PERG check sizes the optical effects, mediated through the largely linear PERG contrast function [53, 54] on the PERG are quite different. This was already pointed out by van den Berg & Boltjes [26]: ‘Because of the considerable differences in straylight in an older population one has to take into account that loss of pattern electroretinogram can be suffered in patients with otherwise good visual acuity.’ Much in line with this interpretation are findings by Marmor & Gawande [33]. Comparing defocus and optical scattering by ‘cloudy plastic’ (=‘haze filter’), they found that defocus had an effect also at spatial frequencies markedly lower than would be calculated from size of the test letters at acuity threshold (which is expected given the Bessel-function shape of a defocus function). At very low spatial frequencies, however, defocus had no effect (their Figure 3), but scattering did markedly reduce contrast sensitivity (their Figure 2).

Before considering clinical applications, the validity of the two optical degradation needs to be questioned. Clearly, dioptrical defocus is relevant in everyday clinical situations, even if not done on purpose. But do scattering transparencies really mimic media opacities? Hess & Woo [55] assessed the effect of cataracts on the contrast sensitivity function. The results differed widely, even when classified into cortical or nuclear cataracts. But in 6 of their 10 cases the contrast sensitivity function was significantly reduced also for low spatial frequencies (0.1–1 cpd), which corresponds to the wide-angle scatter caused by the scattering transparencies used here (Figure 3).

The present results have shown that there is no trivial relationship between acuity reduction, be it by defocus or scattering. E.g., when a check size of 0.8° is chosen (as suggested in the PERG standard [50]), halving acuity reduces the amplitude by 15% with defocus but by 30% with scatter. Clearly, acuity does not tell the whole story. However, for clinical applications the following rule of thumb will be helpful: For 0.8° check size no clinically relevant effect of suboptimal refraction is expected as long as visual acuity remains at 0.8 or better.

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Address for correspondence: M. Bach, Universitäts-Augenklinik, Killianstr. 5, 79106 Freiburg, Germany
Phone: +49-(761) 270-4060; Fax: +49-(761) 270-4052;
E-mail: michael.bach@uni-freiburg.de