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Differential effects of optic media opacities on simultaneous multifocal pattern electroretinograms and visual evoked potentials

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HIGHLIGHTS

- Simultaneous multifocal pattern-electroretinogram (mfPERG) and multifocal visual evoked potential (mfVEP) recordings are expected to guarantee the highest degree of comparability.
- Simulated optic media opacities, i.e. image blur and reduced stimulus luminance, reduce mfPERGs more strongly than mfVEPs.
- Differential mfPERG- and mfVEP-reductions are not necessarily linked to differential neuronal damage or post-retinal plasticity, as they can be due to optic media opacities.

ABSTRACT

Objective: To identify potential confounds in the comparison of simultaneously acquired multifocal electroretinograms (mfPERGs) and visual evoked potentials (mfVEPs) to pattern reversal stimulation.
Methods: With VERIS Science 5.1.10X monocular mfPERGs and mfVEPs were recorded simultaneously to optimised pattern-reversal stimulation for a reference condition and two filter conditions, i.e. blur and 8% luminance transmission, in two separate experiments in participants with normal vision. The impact of the filter conditions on mfPERG amplitude (P50 and N95 peaks), mfVEP-magnitude (root-mean-squares and signal-to-noise-ratios), and on the response timing was assessed.
Results: Blur reduced mfPERG P50 and N95 amplitudes to 16%, 21%, and mfVEP magnitude to 82%. Decreasing stimulus luminance to 8% reduced only the mfPERG (P50 to 72% and N95 to 74%), but delayed both mfPERG and mfVEP responses by 5.3 and 4.6 ms, respectively.
Conclusions: Comparatively minor stimulus manipulations, mimicking optic media opacities, had a differential effect on mfPERGs and mfVEPs magnitudes.
Significance: Simultaneous mfPERG/mfVEP recordings are a promising approach to compare retinal and cortical function, but caution must be exerted in the interpretation of response differences due to incongruent response characteristics.

1. Introduction

Non-invasive electrophysiology allows for an objective assessment of visual function in humans. There are several methods to explore different stages of the visual pathways (Bach and Kellner, 2000; Heckenlively and Arden, 1991). The electroretinogram (ERG) reflects mainly retinal photoreceptor and bipolar cell function, the pattern-electroretinogram (PERG) reflects retinal ganglion cell function, and visual evoked potentials (VEPs) are recorded from the visual cortex. The multifocal technique allows one to record responses from multiple individual visual field locations within a short time frame (Sutter, 1985, 1991, 2001). The combination of this approach with the above electrophysiological methods provides a topographical account of neuronal function at various stages of the visual system.

Combining the results of multifocal ERG (mfERG) and pattern-reversal VEP recordings (mfVEP) promises a strong potential to localise pathologies along the visual pathways and to uncover the impact of retinal damage on subsequent processing stages. As

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a consequence this would assist to identify compensatory mechanisms in processing stages succeeding the damaged sites. Remarkably, however, severe discrepancies between the most common multifocal electrophysiological recording techniques, i.e. mfERGs to flash and mfVEPs to pattern-reversal stimulation, do not only arise from pathological changes at the neural level (Chen et al., 2006), but also from simple stimulus manipulations, i.e. changes of stimulus contrast and luminance (Herbik et al., 2013). As a consequence, caution has to be exerted in the interpretation of the differences of mfERGs and mfVEPs. The above discrepancy of the two response types is a likely consequence of the fact that mfERGs and mfVEPs require different stimulation protocols, flash and pattern-reversal stimuli, respectively. Further, both recordings cannot be measured simultaneously. It is therefore hypothesised that simultaneous recordings from retina and cortex to the identical visual stimulus might not lead to the above response discrepancies. This was tested in the present study for simultaneous mfPERG and mfVEP recordings to pattern-reversal stimulation. As they tap the system at the ganglion cell and primary visual cortex level respectively (Bach and Hoffmann, 2006; Hood and Greenstein, 2003; Langrova et al., 2007; Monteiro et al., 2012, 2013; Sliesoraityte et al., 2012; Stiefelmeyer et al., 2004), such recordings are of great promise to uncover adaptive changes in the post-retinal processing in a diseased visual system.

The aim of the present study was to assess whether simultaneously recorded mfPERGs and mfVEPs are similarly affected by simple image degradations, that mimic optical problems associated, for example with cataract. Differences in both recording-types would not only be of practical relevance for the interpretation of patient data, but also indicate that mfVEP-changes cannot be directly predicted from mfPERG-changes. For this purpose mfPERGs and mfVEPs were recorded simultaneously and optic media opacities were artificially induced in participants with normal vision. This allows for within participant comparisons, which increases the sensitivity of the approach compared to the typical inter-subject comparisons.

2. Methods

2.1. Participants

Two separate experiments were conducted as specified below in Procedure. Eight (mean age: 28.3; range: 23–33 years; 8 female) and seven participants (mean age: 28.0 years; range: 23–33 years; 7 female) took part in experiment 1 and 2, respectively. All participants had a best corrected decimal visual acuity of $\geqslant 1$ as tested with FrACT (Bach, 1996, 2002) as detailed in Procedure. The participants gave their written consent prior to the study. The procedures followed the tenets of the declaration of Helsinki (World Medical Association, 2000) and the protocol was approved by the ethics committee of the University of Magdeburg, Germany.

2.2. Procedure

Each of the two experiments conducted comprised simultaneous mfPERG and mfVEP recordings with a total session duration of less than 1.5 h. In Experiment 1 the effect of blurring the retinal image ('blur filter' composed of frosted document foil; contrast decrease in the central stimulus area to 24%; Art Nr. 10916997, Herlitz PBS AG, Berlin, Germany) was compared to a neutral reference condition ('no filter') with the same mean stimulus luminance (102 cd/m^2 and 95.12% stimulus contrast). In Fig. 1 the effect of the blur filter on the stimulus is demonstrated by applying a Gaussian blur to the stimulus pattern that mimicks the subjective effect. As determined in separate measurements, the blur filter decreased the decimal visual acuity in normal observers to 0.25 (median: 0.25; interquartile range: 0.08). Visual acuities were measured using FrACT 3.5.5 (Freiburg Visual Acuity and Contrast Test, Michael Bach, University of Freiburg), which applies an adaptive procedure to determine the visual acuity using Landoldt-C optotype presentations (Bach, 1996). In Experiment 2 the effect of a reduction of the stimulus luminance by 92% ('neutral filter', with 8% transmission; TS Filter No. 96–0.9, TS Optics, Teleskop-Service Ransburg, Putzbrunn–Solalinden, Germany) was compared to a neutral reference condition ('no filter'). The luminance levels were determined with a CS-100A photometer (Konica Minolta Holdings, Inc., Marunouchi, Chiyoda-ku, Tokyo, Japan). A recording block for each condition took 7:17 min. Each condition was presented twice in a counterbalanced design (A-B-B-A or B-A-A-B scheme) resulting in a total session duration, including preparation and breaks, of less than 90 min. In both experiments, the stimuli were viewed monocularly at 36 cm distance with the right eye wearing the optimal refractive correction. In accordance with current PERG and VEP standards (Bach et al., 2012; Odom et al., 2010) the participants' pupils were not dilated to maximise retinal image quality. No extreme pupil sizes or anisocoria were observed. The participants viewed the stimuli with and without filters inserted in trial frames to record mfVEPs and mfPERGs for the different experimental conditions. The same filter sets were used for all participants of the respective experiment.

2.3. Stimulation

VERIS 5.01.12X (EDI: Electro-Diagnostic Imaging, San Mateo, CA, USA) was used for stimulus delivery and electrophysiological recordings. Supported by a chin rest the participants viewed the stimuli presented at a distance of 36 cm on a monochrome monitor (MDG403, Philips; P45 phosphor) driven with a frame rate of 75 Hz. The visual stimulus (mean luminance: 102 cd/m^2; contrast: 95.12%) was presented on a grey background (luminance: 102 cd/m^2), while the participants maintained fixation on a central black cross (5° diameter).

2.4. Stimulus pattern and sequence

The stimulus pattern, a circular dartboard (diameter 45°), was subdivided into 36 individual fields, each comprising a checkerboard of 4×4 checks, such that mfPERGs and mfVEPs were recorded from 36 separate visual field locations with independent pattern-reversal stimuli. The elements were arranged in 4 rings spanning following eccentricity ranges: 0.0–3.6°, 3.6–7.6°, 7.6–14.3° and 14.3–22.7°. An illustration of the stimulus as perceived for the no filter and blur filter conditions is given in Fig. 1. The temporal and spatial independence of the stimulation sequences is essential for the multifocal technique. This is achieved by the use of binary m-sequences ["maximum length sequences" (Cohn and Lempel, 1977)]. They have practical advantages, which are due to the property that a different starting point in an m-sequence cycle results in a mathematically independent, i.e. orthogonal, m-sequence. Therefore, the same m-sequence can be applied for each visual field location, as long as different starting points are guaranteed. Consequently, independent stimulation in the individual patterns followed a binary m-sequence (Sutter, 1991). It consisted of a pseudo-random succession of 0 and 1 states. For the pattern-reversal stimulation applied in the present study these two states were represented by two contrast inverted checkerboard fields. An m-sequence length of 2^{14}-1, i.e. 16383, steps was used. In order to optimise simultaneous mfPERG and mfVEP recordings, slow pattern-reversal stimulation was applied (Hoffmann and Flechner, 2008), i.e. each step lasted 2 frames (27 ms), resulting in an average reversal rate of 18.75 Hz. This