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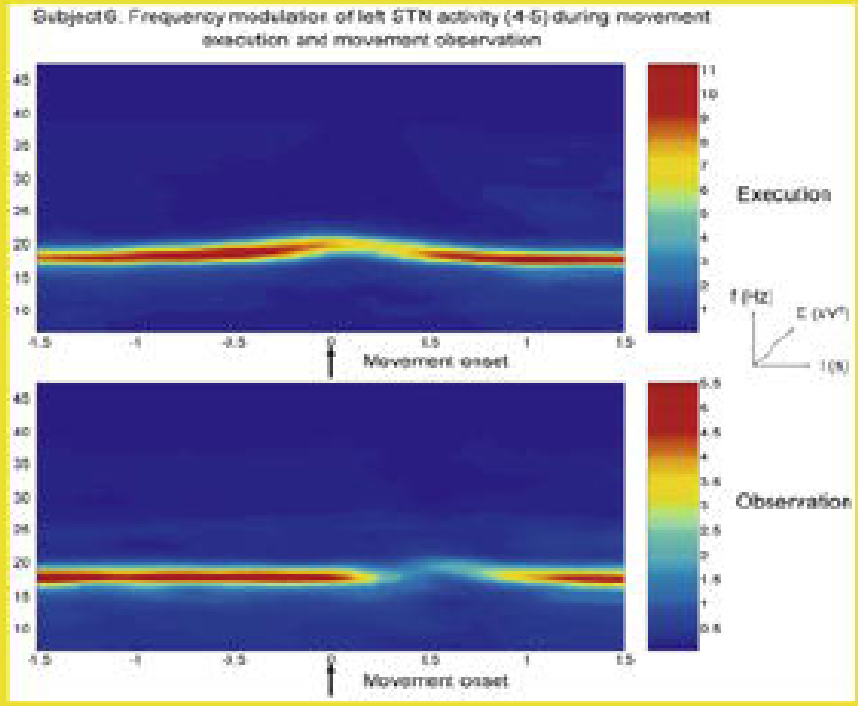

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Impact of regional retinal responses on cortical visually evoked responses: Multifocal ERGs and VEPs in the retinitis pigmentosa model

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ABSTRACT

Objective: To determine the impact of the regional retinal responses on cortical visually evoked responses, by evaluating the relationship between multifocal ERG (mfERG) and multifocal VEP (mfVEP), in the retinitis pigmentosa (RP) model.
Methods: MfERGs and mfVEPs were recorded from 20 typical RP patients. Response amplitude density (RAD, nV/deg^2) and implicit time (ms) of the mfERG 1st order binary kernel (N1-P1) and mfVEP 2nd order binary kernel (P1) components were measured. Ring analysis, matched for mfERG and mfVEP stimuli, was performed between fovea and mid-periphery (0–2.5, 2.5–5, 5–10, 10–15 and 15–20 deg).
Results: At central and pericentral retinal regions (four eccentricities between 0 and 15 deg), mfERG N1 RADs were positively correlated ($r \geqslant 0.68$, $p < 0.01$) with corresponding mfVEP P1 RADs. Similarly, mfERG P1 implicit times were positively correlated ($r \geqslant 0.65$, $p < 0.01$) with corresponding mfVEP N1 implicit times.
Conclusions: There are quantitative correlations between mfERG and mfVEP components in RP.
Significance: The data suggest that regional responses of the photoreceptors and off-bipolar cells, the main generators of mfERG N1, have a major impact on the corresponding cortical activity.
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1. Introduction

The multifocal technique developed from the original work of Sutter and Tran (1992) allows for the simultaneous recording of multiple focal responses from discrete areas of the visual field in a relatively limited time length (Sutter and Tran, 1992; Bearse and Sutter, 1996). Multifocal electroretingram (mfERG) has been widely used to assess regional retinal function in both hereditary and acquired disorders (Hood et al., 1998).

In a number of diseases affecting the outer retina, this signal has shown ability to accurately detect dysfunctional or non-functional retinal areas either in the macula or more peripheral retinal regions. For instance, in retinitis pigmentosa (RP) (Hood et al., 1998, 2002; Nagy et al., 2008) as well as in cone–rod dystrophy (Holopigian et al., 2002), the mfERG P1 component latency and, to a lesser extent, amplitude has been shown to predict psychophysical visual field losses at corresponding retinal locations. Indeed, mfERG parameter changes (i.e. peak latency delays and amplitude losses with respect to normal control values) are quantitatively correlated with corresponding perimetric sensitivity losses, so that maps of ERG delay and loss are in good agreement with corresponding maps of perimetric loss.

The multifocal visually evoked potential technique (mfVEP) is an emerging clinical method which has shown potential clinical utility for detecting pathologies of the visual pathways involving localized field losses. A detailed analysis of mfVEP responses derived from monocular stimulation and the interocular comparison of these responses (Hood et al., 2003) has provided parameters that are good predictors of psychophysical losses, especially in glaucoma (Hood and Greenstein, 2003).

It has been suggested (Hood and Greenstein, 2003) that combined mfERG and mfVEP analysis could help distinguishing disorders involving the outer retina (i.e. photoreceptors and bipolar cells) from diseases of ganglion cells and/or optic pathways, and

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therefore the contribution of different stages of visual processing on the psychophysical visual field. In diseases of the outer retina, it is currently unclear how an abnormality of the mfERG impacts on the corresponding mfVEP response. Given the pathological features common to many sub-types of RP (Milam et al., 1998), and the significant association between mfERG and perimetric losses, this disorder may represent a good human model to investigate the consequences of a regional outer retinal dysfunction, detected by mfERG, on the corresponding cortical mfVEP responses.

The present study aims to determine whether there is an impact of regional retinal function on the visually evoked cortical activity, by evaluating the relationship between mfERG and mfVEP components, using the model of retinitis pigmentosa (RP).

2. Methods

2.1. Patients

Twenty typical RP patients (20 RP eyes), mean age: 35.4 ± 3.2 years (range: 18.3–56.4 years) showing visual acuity >20/30, Goldmann visual field by V/4e target: 30–50 deg, non-recordable Ganzfeld rod-mediated ERGs (Standard ISCEV) (Marmor and Zrenner 1995; Marmor et al., 2004) and severely reduced cone-mediated ERGs were enrolled in the study. The study followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants after the aims and procedures of the study were fully explained.

The clinical characteristic of the RP patients are shown in Table 1.

2.2. mfERG

VERIS Clinic™ 4.9 (Electro-Diagnostic Imaging, San Mateo, California, USA) was used for mfERG assessment using our previously published method (Parisi et al., 2007, 2008).

The multifocal stimulus, consisting of 61 scaled hexagons, was displayed on a high-resolution, black-and-white monitor (size 30 cm width and 30 cm height) with a frame rate of 75 Hz. The array of hexagons subtended 20 deg of visual field. Each hexagon was independently alternated between black (1 cd/m^2) and white (200 cd/m^2) according to a binary m-sequence. This resulted in a contrast of 99%. The luminance of the monitor screen and the central fixation cross (used as target) was 100 cd/m^2. The m-sequence had $2^{13} - 1$ elements and total recording time was approximately 4 min. Total recording time was divided into eight segments. Between segments, the subject was allowed to rest for a few seconds. Focusing lenses were used when necessary. At every mfERG examination, each patient positively reported that he/she could clearly perceive the cross fixation target. The eye's position was monitored by a video system in the screen of the computer.

Table 1
Summary of demographic and clinical characteristics of the study population.

N = 20	
Mean age:	35.4 ± 3.2 years, range: 15–56
Median visual acuity:	20/25, range: 20/30–20/20
Goldmann visual field	(V/4e target): mean field (major diameter): 45 deg, range 30–55
Fundus	Typical RP appearance, with waxy pale disc, attenuated retinal vessels and bone spicule pigmentation in the mid-periphery
Ganzfeld ERG (ISCEV standard)	
Rod-mediated response	Non-recordable
Maximal response	Severely reduced amplitude (<35% of the normal mean)
Single-flash cone-mediated response	Severely reduced amplitude (<40% of the normal mean) and delayed implicit time (3–8 ms slower than the normal mean)
Flicker response	Severely reduced amplitude (<40% of the normal mean)
Inheritance mode (N)	
Dominant	2
Recessive	3
Isolated	12
X-linked	3

In all RP eyes, mfERGs were recorded in the presence of pupils that were maximally pharmacologically dilated with 1% tropicamide to a diameter of 7–8 mm. Pupil diameter was measured by an observer (GG) by means of a ruler and a magnifying lens and stored for each tested eye. The cornea was anesthetized with 1% dicaine. The Dawson Trick Litzkow (DTL) bipolar contact electrode was used to record mfERGs. A small Ag/AgCl skin earth electrode was placed at the center of the forehead. The contralateral eye was occluded to help suppress blinking. Interelectrode resistance was less than 3 kΩ.

The signal was amplified (gain 100.000) and filtered (band pass 1–100 Hz) by BM 6000 (Biomedica Mangoni, Pisa, Italy). After automatic rejection of artifacts (by VERIS Clinic™ 4.9 software), the first order kernel response, K1, was examined. We analyzed the average response amplitude densities (RAD, expressed in nV/deg^2) of N1 peak (from baseline) and between the first negative peak, N1, and the first positive peak, P1, and the N1 and P1 implicit times (in ms) obtained from five concentric annular retinal regions (rings) centered on the fovea. Therefore, we analyzed the N1-P1 RADs derived from 0 to 2.5 deg (ring 1, R1), from 2.5 to 5 deg (ring 2, R2), from 5 to 10 deg (ring 3, R3), from 10 to 15 deg (ring 4, R4) and from 15 to 20 deg (ring 5, R5).

2.3. mfVEP

The mfVEP testing was performed using VERIS Clinic™ 4.9 software (Electro-Diagnostic Imaging, San Mateo, California, USA). The dartboard pattern consisted of 60 sectors, each sector with a checkerboard pattern of 16 checks, eight white (200 cd/m2) and eight black (1 cd/m^2). The sectors were cortically scaled with eccentricity to stimulate approximately equal areas of visual cortex (i.e., central sectors were smaller than peripheral sectors). The entire dartboard subtended a diameter of 20 deg. The stimulus array was displayed on a black-and-white monitor driven at a frame rate of 75 Hz. The 16-element checkerboard of each sector had a probability of 0.5 of reversing on any pair of frame changes and the pattern of reversals for each sector followed a pseudorandom (m-) sequence. The stimulation was monocular, with full occlusion of the fellow eye. In order to maintain a stable fixation, a small red target (0.5 deg) that was perceived by all subjects tested, was placed in the center of stimulation field. Prior to the experiment, each subject was adapted to the ambient room light for 10 min and the pupil diameter was about 5 mm. Mydriatic or miotic drugs were never used.

VEPs were recorded by cup shaped Ag/AgCl electrodes placed 4 cm above the inion (active), at the inion (reference), and on the forehead (ground). The interelectrode resistance was kept below 3 kΩ. VEP signals were amplified (gain 20,000), filtered (bandpass 1-100 Hz, −6 dB/octave), and sampled with 12 bit resolution (BM6000, Biomedica Mangoni, Pisa Italy).

Each recording session was subdivided into 14 recording segments of approximately 60 s duration. The total duration of a recording session was about 14 min. The VERIS Scientific software™ (VERIS software, EDI S. Mateo, CA) was employed for the calculations of the 60 local VEP responses from the measured signal and to analyze the second order kernels. A typical wave form begins with a negative deflection (Nl), followed by a positive deflection (P1), and a second negative deflection (N2). For the analysis of the mfVEP amplitudes, we calculated the amplitude

response density (nV/deg^2) between N1 and Pl peaks. For the analysis of the mfVEP timing, we restricted the analysis to the implicit time (in ms) of the first negative (N1) and first positive (P1) deflections.

2.4. Signal-to-noise ratio

For both mfERGs and mfVEPs recorded from the different rings in each study eye, signal-to-noise ratio (SNR) was estimated following the methodology discussed in Hood and Greenstein (2003). Briefly, a noise window was set as that part of the record which was of equal length to the period within which the response was analyzed, but it was included in a temporal window that was assumed to contain little or no response. Signal temporal window for the mfERG was 0–80 ms. Signal temporal window for the mfVEP was 0–200 ms. SNR was defined as the ratio of root mean square (RMS) signal plus noise (measured in the signal temporal window) of a given record to the mean RMS of all noise windows (61 for the mfERG and 60 for the mfVEP). A SNR of $\geqslant 3$ was accepted for both mfERG and mfVEP measurements. Assuming that either mfERG or mfVEP signal was composed by the linear addition of "noise" plus the "true" signal, a "recordable" response had to have a SNR $\geqslant 3$.

2.5. mfERG and mfVEP ring analysis and correlations

In order to evaluate regional retinal responses as a function of eccentricity from the fovea to the mid-periphery, ring analysis, matched for mfERG and mfVEP stimuli, was performed at five retinal eccentricities: 0–2.5, 2.5–5, 5–10, 10–15, 15–20 deg. For every retinal eccentricity, mfERG N1 and P1 RADs were correlated (Pearson's correlation and linear correlation analysis) with corresponding mfVEP P1 RADs, assuming normal distribution. Similarly, mfERG N1 and P1 implicit times were correlated with corresponding mfVEP N1 and P1 implicit times. In all the analyses, a conservative p value of $\leqslant 0.01$, compensating for multiple correlations, was considered as statistically significant.

3. Results

In Fig. 1, examples of mfERG response density three-dimensional plots and mfVEP trace arrays are reported for one normal and two RP eyes. It can be seen that either the mfERG RAD plots or the distribution of mfVEP traces reflect qualitatively the visual field within the central 30 deg. Recordable mfERG and mfVEP traces can be detected at corresponding sites, suggesting that, in general, visual cortical responses are generated by corresponding functional retinal areas. Similar results were found for the other study eyes.

Fig. 2 shows mfERG and mfVEP recordings obtained from a representative RP patient. Traces represent the spatial average derived from ring analysis, as reported in Section 2. Numbers on the left side of the figure indicate the different retinal eccentricities of the stimuli. It can be seen that, for both responses at each eccentricity, the waveform components are recognizable and measurable. This was the case for most of the study eyes, although for some of them the ring analysis for the most peripheral rings did not yield responses with a S/N $\geqslant 3$ (see also below).

In Table 2, the individual mfERG and mfVEP results, expressed in terms of response detection from the noise level, are reported by retinal eccentricity in all study eyes. Based on the SNR analysis, results have been arranged in four groups: (1) eyes with both mfERG and mfVEP recordable, (2) eyes with mfERG recordable and mfVEP non-recordable, (3) eyes with mfERG non-recordable

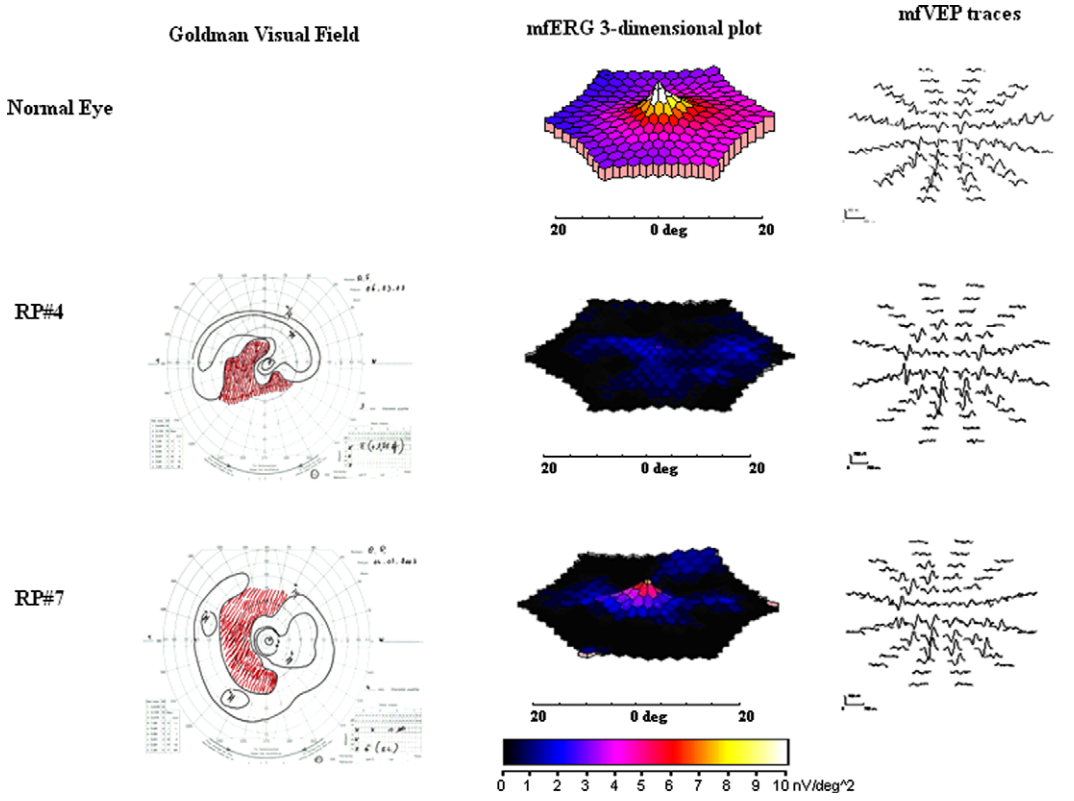

Fig. 1. Examples of multifocal electroretinogram (mfERG) response density three-dimensional plots and multifocal visually evoked potentials (mfVEPs) trace arrays recorded in two representative retinitis pigmentosa study eyes and in one normal eye. In two representative retinitis pigmentosa study eyes it is presented the relative Goldmann visual fields. It can be observed that either the mfERG response density plots or the distribution of mfVEP traces reflect qualitatively the visual field within the central 30 deg. Recordable mfERG and mfVEP traces can be detected at corresponding sites.

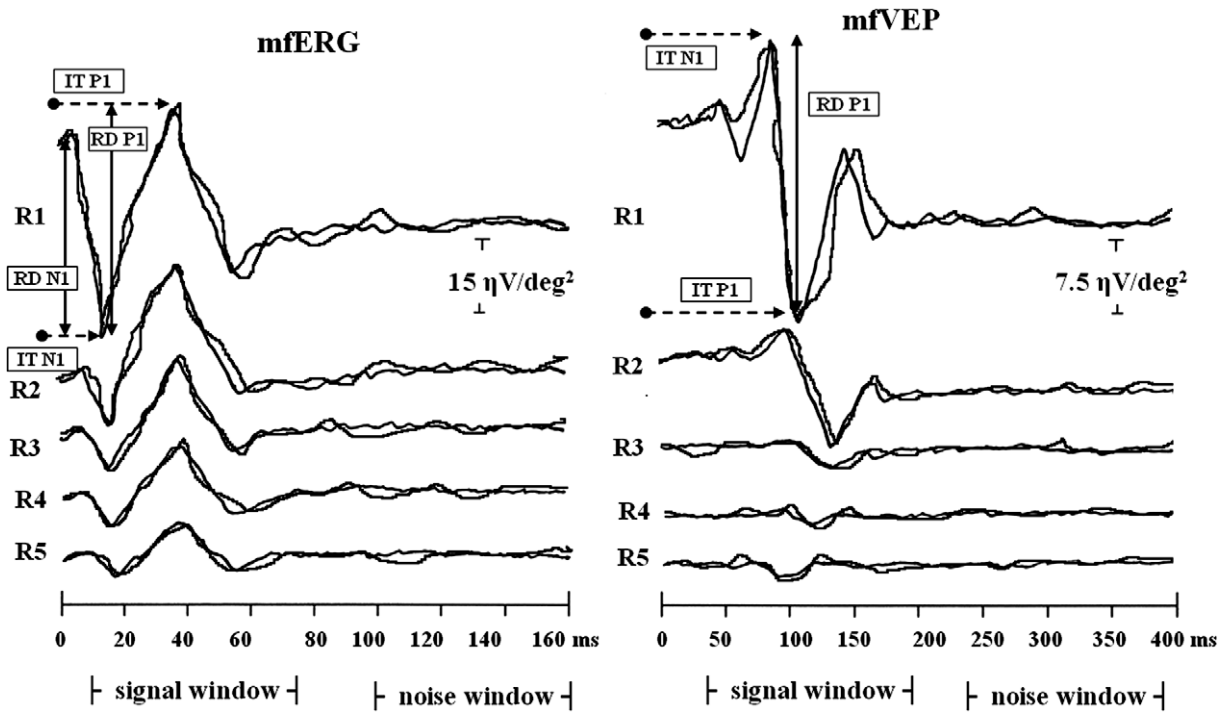

Fig. 2. Examples of multifocal electroretinogram (mfERG) first order response component and multifocal visually evoked potentials (mfVEP) second order response component recorded in one representative retinitis pigmentosa study eye. MfERG and mfVEP local responses were averaged in five retinal areas located at various degrees of eccentricity from the fovea: 0–2.5 (R1), 2.5–5 (R2), 5–10 (R3), 10–15 (R4) and 15–20 (R5) degrees. IT, implicit time; RAD, response amplitude density.

and mfVEP recordable, (4) eyes with both mfERG and mfVEP non-recordable. It can be noted that at each eccentricity, two (0–2.5 deg) to seven (15–20 deg) study eyes had non-recordable mfERGs but recordable (SNR $\geqslant$ 3) mfVEPs. The number of eyes included in group 3 tended to increase with retinal eccentricity. By contrast, at none of the tested eccentricities there were study eyes having recordable mfERG and non-recordable mfVEP.

RADs and implicit times of the different mfERG components recorded from the individual patients for various eccentricity rings were correlated with corresponding measurements of mfVEP response components. The results of linear correlation analysis, shown as scatterplots with linear regression lines fitted to the data points, are reported in Fig. 3a and b. In the figure, *r* and *p* values are also reported for each correlation. Amplitudes of the mfERG N1 response densities were found to be positively correlated with corresponding values of mfVEP P1. The correlations were significant for all but the most eccentric ring (15–20 deg). Implicit times of the mfERG P1 were positively correlated with corresponding values of mfVEP N1. Again, the correlations were significant for all but the most eccentric ring. No other statistically significant correlations (mfERG P1 vs mfVEP P1 RADs; mfERG N1 vs mfVEP N1 implicit time; mfERG P1 vs mfVEP N1 and P1 implicit times) were found between mfERG and mfVEP response measures.

4. Discussion

The purpose of this study was to investigate whether there is an impact of regional retinal function on the visually evoked cortical activity, by evaluating the relationship between mfERG and mfVEP components, using the model of retinitis pigmentosa (RP). It is well established (Milam et al., 1998) that in most RP sub-types an inherited degenerative pathology involves primarily the outer retina, usually leading to a sequential loss of rod and cone photoreceptors. RP can therefore be considered a human neurophysiological model of primary outer retinal disease, in which visual cortical activity, secondary to a peripheral sensory deficit, can be explored.

The main finding of our study was that in patients with typical RP some components of the mfERG responses were quantitatively correlated with mfVEP response components at corresponding retinal locations. Significant correlations were indeed found for the N1 mfERG RAD, which resulted to be positively correlated (for all but the most peripheral ring) with the P1 mfVEP RAD, and for the P1 mfERG implicit time, which was positively correlated with the N1 mfVEP implicit time (for all but the most peripheral ring). Many previous studies have evaluated the mfERG in RP patients (Kondo et al., 1995; Chan and Brown, 1998; Hood et al., 1998;

Table 2
Individual mfERG and mfVEP results, expressed in terms of response detection from the noise level, reported by retinal eccentricity in all study eyes. For both mfERG and mfVEP, a "recordable" response was defined as having a SNR $\geqslant$ 3. A non-recordable response had a SNR < 3.

	RP eyes with mfERG recordable and mfVEP recordable, *N* (%)	RP eyes with mfERG recordable and mfVEP non-recordable, *N* (%)	RP eyes with mfERG non-recordable and mfVEP recordable, *N* (%)	RP eyes with mfERG non-recordable and mfVEP non-recordable, *N* (%)
R1: 0–2.5 deg	18/20 (90%)	0/20 (0%)	2/20 (10%)	0/20 (0%)
R2: 2.5–5 deg	16/20 (80%)	0/20 (0%)	3/20 (15%)	1/20 (5%)
R3: 5–10 deg	15/20 (75%)	0/20 (0%)	5/20 (25%)	0/20 (0%)
R4: 10–15 deg	15/20 (75%)	0/20 (0%)	4/20 (20%)	1/20 (5%)
R5: 15–20 deg	13/20 (65%)	0/20 (0%)	7/20 (35%)	0/20 (0%)

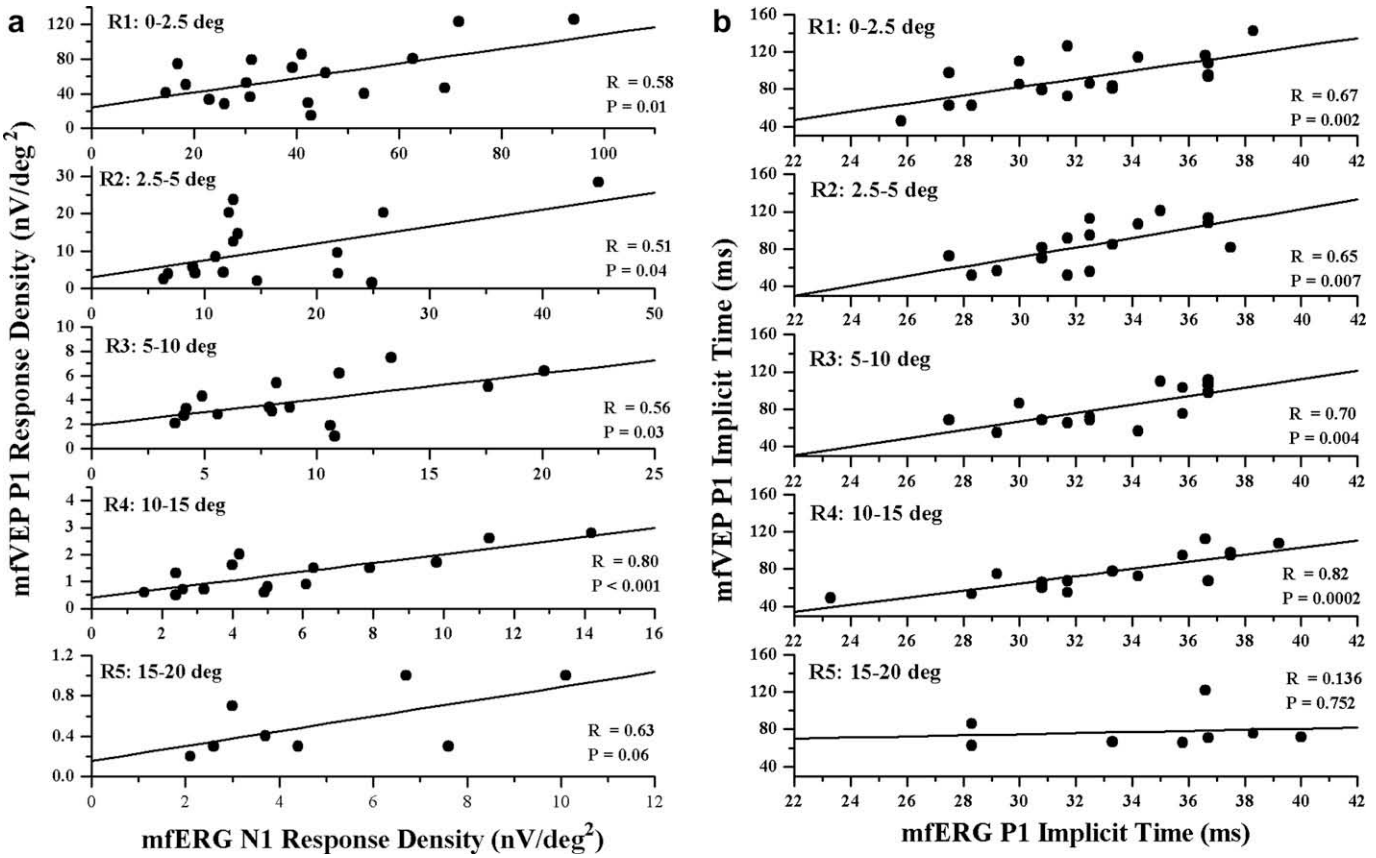

Fig. 3. (A) Individual values of multifocal electroretinogram (mfERG) N1 response amplitude density (RAD) recorded from 0–2.5 central degrees (R1) and from 2.5–5, 5–10, 10.15 and 15.20 paracentral degrees (respectively R2, R3, R4 and R5) plotted against the corresponding values of multifocal visually evoked potentials (mfVEPs) P1 response amplitude density (RAD) recorded in retinitis pigmentosa study eyes. (B) Individual values of mfERG P1 implicit time recorded from 0–2.5 central degrees (R1) and from 2.5–5, 5–10, 10.15 and 15.20 paracentral degrees (respectively R2, R3, R4 and R5) plotted against the corresponding values of mfVEPs N1 implicit time recorded in retinitis pigmentosa study eyes. Pearson's *r* and *p* values are reported in each plot.

Seeliger et al., 1998; Holopigian et al., 2001;) some of these studies have compared the local ERG responses to local psychophysical achromatic thresholds (Hood et al., 1998; Holopigian et al., 2001), but only a few reports have correlated the electrical activity of the retina and the visual cortex at corresponding locations in RP (Gränse et al., 2004; Holopigian et al., 2005). Gränse et al. (2004) evaluated mfERG and mfVEP signals in RP patients with residual small central visual fields. They found a qualitative correlation between ERG and VEP measures, inasmuch as patients with recordable central (1–5 deg) responses also showed residual VEP responses with the central 5 deg of visual field. No quantitative correlations were reported in the study by Gränse et al. (2004). Interestingly, these authors also found that some patients with an undetectable central mfERGs had reliable mfVEPs for the corresponding visual field locations. This was also observed in the present study, indicating that an apparent dissociation between retinal and cortical responses is not uncommon. Holopigian et al. (2005), recorded mfVEP to cone-specific stimuli, evaluating responses driven by L-and M-Cone systems, respectively, and related these responses to mfERG responses. The authors found significant positive correlations between mfERG and both L- and M-Cone mfVEP amplitudes as well as between mfERG and both L- and M-cone mfVEP implicit times. However, exactly which of the mfERG and mfVEP components were correlated was not specified in the Holopigian et al. (2005) study. Also relevant to the present study is the finding by Holopigian et al. (2005) that for the central ring (2–4 deg), relative losses in the mfERG amplitudes were greater than the corresponding mfVEP losses. This is in partial agreement with our results and with those by Gränse et al. (2004), and suggests some mechanism of remodelling or neural reorganization occurring in the post-retinal pathways which may compensate for the losses at retinal level. It cannot be excluded that a newly-formed network of compensatory synapses may develop at the level of primary visual cortex with the finalistic goal of amplification of, and/or compensation for the deficits in the peripheral input. Neural cortical reorganization may account for the presence of recordable mfVEPs associated with non-recordable mfERGs. In support of the present mechanism, MRI data indicate reorganization of human cortical maps caused by inherited photoreceptors abnormalities (Baseler et al., 2002), pointing to a link between a genetic abnormality directly affecting cone photoreceptors and the corresponding cortical activity distribution. However, this interpretation is not the only one possible for our findings. Indeed, mfERG, but not mfVEP responses may have been present but simply below the resolution of our system, yielding a SNR <3.

Clinically, mfERG and mfVEP could provide different but complementary information about the residual vision in RP, the former being more directly related to the function of the retinal cone system, and the latter to the central processing of visual input.

The fact that in our patients the changes in the N1 mfERG component showed a major impact on the mfVEP P1 component has some neurophysiological implications. Indeed, it has been shown by Hood et al. (2002), that mfERG N1 is generated mainly by the activity of hyperpolarizing bipolar cells, with a contribution of cone photoreceptors. Our findings therefore support the hypothesis that the responses of photoreceptors and off-bipolar cells specifically drive cortical responses elicited by multifocal stimuli. Among the various phenotypes of RP and cone–rod dystrophies,

there are some selectively involving the depolarizing or hyperpolarizing outer retinal circuitry (Sieving 1993). Although these phenotypes were not included in the present study, it may be expected that, in these phenotypes, a correlation between mfERGs and mfVEPs, even stronger than that recorded in this study, can be observed.

The present data have characterized the correlation between mfERG and mfVEP components in an inherited disease of the outer retina, and should be considered as specifically applicable only in this family of disorders. This may explain the difference between the results recently reported by Chen et al. (2006) and those of this study. Chen et al. (2006) evaluating the relationship between mfERG and mfVEP in patients with different acquired retinal disorders, including diabetic retinopathy and retinal vascular disease, did not find a significant quantitative correlation between retinal and cortical multifocal responses.

In summary, this study shows the relationship between local retinal responses and the corresponding visual cortical activity in RP, indicating that the hyperpolarization of cone photoreceptors and cone bipolars may play a major role in driving the corresponding central cortical activity. The findings of recordable mfVEP with non-recordable mfERG suggest a cortical reorganization secondary to local retinal dysfunction.

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Editorial

Degeneration/re-organization coupling in retinitis pigmentosa

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The extensive and often conflicting array of hypotheses concerning neuronal representation of objects (sensory, motor or "internally generated" ideas or concepts), reflects an important topic in physiology. At each and every level of observation, physiologists report an ever-increasing range of reaction time scales that are involved in the generation of action potentials and their transformation to post-synaptic signals. Recently, Shahaf et al. (2008) provided evidence "in vitro" for the existence of neuronal stations through which activity is required to pass in order to propagate further into the network. The authors found it convenient to think about these sequences of neuronal stations in terms of chain-like effective structures; thus, even in the face of activity-dependent changes in synaptic efficacies or membrane excitability, activity has nowhere else to go but through ordered stations, reassuring that the rank remains stable. Network architecture, in that sense, serves to protect the representation of stimuli. While activity-dependence of neuronal reactions is a valuable driving force for exploration in a variety of adaptation and learning processes (where representations are modified), it must be balanced mechanisms that allow for stabilization and hence exploitation of existing representations. Since many combinations of latencies to first spikes may realize any given representation by recruitment order, existing representations are invariant to the exploration process, as long as the latter does not degrade the order of neuronal recruitment. Effectively, a separation is formed between the level of absolute time delays, where exploration for new representations occurs, and the level of recruitment order where representations are stable enough to adaptively interact with the environment. But what if one of the stations undergoes major changes including a re-wiring?

It has been recently demonstrated that this is possible at retinal level, where, by rearing animals in complete darkness or blocking glutamate receptors, the receptive field of retinal ganglion cells (RGCs) undergoes profound and permanent morpho-functional re-organization supposedly altering the transfer of information to higher visual centers (Di Marco et al., 2009). The spatial re-organization of synaptic inputs on RGCs is due to malfunction or absence of function in the outer retina (photoreceptors and second order neurons). Accordingly visual cortex appear heavily reorganized in congenital rod monochromats patients, where it was observed how abnormal retinal input alters the development of retinotopic maps in the human brain (Baseler et al., 2002). Something similar it might happen in the dynamic progression of retinitis pigmentosa where photoreceptors progressively die, probably inducing a morpho-functional re-organization of the inner retina. The question is whether the spatial information transferred to higher visual centers deteriorates in parallel with photoreceptor loss or undergoes a functional re-organization leading to a novel, probably distorted, visual perception.

Retinitis pigmentosa is the term given to a set of hereditary retinal diseases that feature degeneration of rod and cone photoreceptors. It is a blinding disease, and its world-wide prevalence is about 1 in 4000 for a total of more than one million affected individuals. The most convenient way to analyze the functional activity of the visual pathways and visual areas in humans is by using visual evoked potentials (VEPs) and this technique has been widely applied for investigating the physiology and pathophysiology of the human visual system and modified according to different requirements (see, for reference, Tobimatsu and Celesia, 2006). Using a dedicated version of this technique (multifocal ERG) lots of information was gained on the time course of retinal visual functional deterioration in RP patients (see Parisi et al., 2010) but until now no studies were available trying to match retinal and cortical functions during degenerative processes.

In the study reported in the present issue, Parisi and coworkers addressed the interesting neurophysiological issue of the potential impact of the retinal photoreceptor functional loss on the primary visual cortical function. The study was conducted in patients with moderate to advanced disease by evaluating both retinal (multifocal ERG, mfERG) and cortical (multifocal VEP, mfVEPs) function tested at different, closely matched locations across the visual field. This groundbreaking approach allowed for the first time the investigators to show the presence of a tight correlation between local retinal function (mfERG response) and its cortical projection as probed with the mfVEPs. Specifically it was shown that a negative component of the mfERG first-order Kernel has a major impact on the mfVEP signal characteristics. The more severe the local retinal functional loss, the more profound the functional re-organization of cortical activity, suggesting that the cortical circuitry may undergo substantial remodelling following primary photoreceptor loss. The results warrant further studies to shed more light on the time course of degeneration/re-organization coupling in retinitis pigmentosa. This aspect may be particularly relevant in developing therapeutic strategies of photoreceptor function replacement by using biotechnological devices.

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