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Impaired visual function in glaucoma

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Abstract

Objective: This work aims to evaluate whether glaucomatous visual field defects could be related to an impaired retinal function, to a delayed neural conduction in postretinal visual pathways, or both.

Methods: Visual field by Humphrey perimeter (central 24-2 threshold test) and simultaneous recordings of visual evoked potential (VEP) and pattern electroretinogram (PERG) were assessed in 21 subjects with open angle glaucoma (POAG) and in 15 age-matched controls (C).

Results: VEP: in POAG eyes we found P100 latency significantly ($P < 0.01$) delayed when compared with controls and correlated with mean deviation (index of global visual field damage, MD) of 24-2 Humphrey perimetry ($P < 0.001$); the P100 amplitudes were significantly ($P < 0.01$) lower in POAG eyes than in control eyes and correlated with MD ($P < 0.001$). PERG: POAG eyes showed P50 latency significantly ($P < 0.01$) delayed when compared with controls and correlated with MD ($P = 0.002$); the P50 and N95 amplitudes were significantly ($P < 0.01$) lower in POAG than in control eyes and correlated with MD (P50: $P = 0.006$; N95: $P = 0.002$). Retinocortical time (RCT: difference between VEP P100 and PERG P50 latencies) and latency window (LW: difference between VEP N75 and PERG P50 latencies) were significantly ($P < 0.01$) longer in POAG eyes than in control eyes and correlated with MD (RCT: $P < 0.001$; LW: $P < 0.001$). No significant correlations ($P > 0.05$) were found between electrophysiological parameters and the corrected pattern standard deviation (index of localized visual field damage) of 24-2 Humphrey perimetry

Conclusion: In patients with open angle glaucoma the reduction of the index of global visual field damage (MD) could be ascribed to two sources of functional impairment: one retinal (impaired PERG) and one postretinal (delayed RCT and LW). In the postretinal impairment, a postsynaptic degeneration at the level of the lateral geniculate nucleus could be suggested.

Keywords: Glaucoma; Pattern electroretinogram; Visual evoked potential; Visual pathway; Static perimetry

1. Introduction

The glaucomatous optic neuropathy provides a rather unique human model of selective and progressive damage to the ganglion cells and their fibers (Quigley et al., 1982, 1987, 1988, 1995). This damage can induce a visual dysfunction that can be revealed by psychophysical and/or by electrophysiological responses.

Psychophysical tests, such as visual field analysis (Krieglstein et al., 1980), color vision (Gunduz et al., 1988), contrast sensitivity (Arden and Jacobson, 1978; Atkin et al., 1979; Hitchings et al., 1981) and recovery of visual acuity after dazzling (Sherman and Henkind, 1988), reveal the presence of a dysfunction in the visual system in patients affected by open angle glaucoma (POAG). In particular, the standard static threshold perimetry, using an automatic system such as the Humphrey field analyzer, gives useful information about the early recognition of visual field damage and its quantification may be used in the assessment of the progression of visual field loss (Graham et al., 1996).

However, psychophysical methods do not selectively reveal which structures contribute to the impairment of the visual system observed in POAG patients. Alternatively, electrophysiological methods allow us to explore and dissect different structures contributing to the visual function.

The function of the different retinal layers can be objectively evaluated by recording electroretinographic signals evoked by flash or patterned stimuli (Flash or Pattern ERG) (Maffei and Fiorentini, 1981, 1982; Morrone et al., 1994) while the function of the whole visual pathway can be assessed by recording cortical potentials evoked by

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patterned stimuli (visual evoked potentials: VEPs) (Celesia et al., 1993) By comparing the VEP and the pattern ERG (PERG) latencies it is possible to construct an index of neural conduction in the postretinal visual pathways. Celesia et al. (1986) suggested the evaluation of the difference between VEP P100 and PERG P50 latencies and called this the 'retinocortical time' (RCT). On the other hand, Marx et al. (1988) proposed the evaluation of the difference between VEP N75 and PERG P50 latencies and termed this the 'latency window' (LW).

A very recent work revealed that glaucomatous changes induce not only a retinal and optic nerve dysfunction, but also a postsynaptic degeneration of the lateral geniculate nucleus (LGN), a primary site of visual integration (Weber et al., 2000). On the basis of this very innovative work about the visual dysfunction in glaucoma, our goal is to evaluate whether the glaucomatous visual field defects could be ascribed to an impaired function of the retinal layers, to impaired neural conduction in the postretinal visual pathways, or both. Preliminary results have been previously published as an abstract (Parisi et al., 1997).

2. Subjects and methods

2.1. Subjects

Visual field analysis and simultaneous recordings of PERGs and VEPs were carried out on 36 subjects: 21 patients with open angle glaucoma (POAG: 21 eyes), compared with 15 age-matched control subjects (C: 15 eyes). When a POAG patient was affected by glaucoma in both eyes, we considered the eye with the greater visual field impairment. Informed consent was received from all subjects enrolled in the study. The research followed the tenets of the Declaration of Helsinki.

The control subjects had intraocular pressure < 21 mmHg, normal visual acuity (10/10), normal visual field (Humphrey 24-2 perimetry: mean deviation $\pm$ 0.5) (Werner and Piltz-Seymour, 1992) and no ocular or neurologic problems. Their mean age ($\pm$SD) was 52.6 $\pm$ 4.4 years.

The patients with open-angle glaucoma were enrolled for the study following these inclusion criteria: intraocular pressure > 21 mmHg without pharmacological treatment; glaucomatous optic nerve head cupping (cup/disc ratio > 0.5); glaucomatous visual field defects (Humphrey 24-2 perimetry with mean deviation between -1.50 and -6 dB); best corrected visual acuity of 10/10 or better; mean refractive error, when present, between -0.50 and $+0.50$ spherical equivalent; no other ocular, neurologic or systemic disease. The mean age was 54.1 $\pm$ 2.7 years.

The observed characteristics of all POAG patients are reported in Table 1.

2.2. Methods

2.2.1. Visual field analysis

Static perimetry (Humphrey field analyzer, model 740,

Table 1
POAG patients: observed characteristics[a]

	Eye	Sex	Age (years)	IOP	VA	C/D	MD	CPSD	VEP P100 latency	VEP P100 amplitude	PERG P50 latency	PERG P50 amplitude	PERG N95 amplitude	RCT	LW
G.I.	LE	M	56	24	10/10	0.6	−3.52	1.49	122	4.8	66	0.45	0.68	56	32
P.A.	RE	F	58	23	10/10	0.4	−1.82	0.69	114	8.2	57	0.76	0.85	57	32
I.D.	LE	F	53	25	10/10	0.5	−3.31	1.57	116	3.3	62	0.63	0.84	54	31
S.C.	RE	M	56	24	10/10	0.4	−2.55	1.06	117	4.7	63	0.44	0.67	54	34
M.M.	LE	M	51	23	10/10	0.4	−2.86	1.24	114	5.5	59	0.55	0.68	55	32
M.T.	LE	F	57	24	10/10	0.6	−2.73	0.70	123	9.3	61	0.64	0.89	62	37
I.D.	LE	M	50	25	10/10	0.7	−3.41	1.36	126	5.6	64	0.73	0.92	62	36
I.S.	RE	M	53	26	10/10	0.7	−2.30	1.81	127	4.2	67	0.45	0.55	60	37
A.P.	LE	F	57	23	10/10	0.5	−1.98	1.40	115	10.4	62	0.72	0.83	53	29
N.V.	LE	M	51	24	10/10	0.6	−3.33	2.60	122	5.6	63	0.45	0.56	59	37
A.D.	LE	M	56	25	10/10	0.6	−3.87	1.89	122	5.4	61	0.53	0.62	61	36
P.A.	RE	F	58	26	10/10	0.4	−3.28	2.69	129	7.8	67	0.36	0.64	62	33
I.D.	LE	F	53	23	10/10	0.5	−4.14	1.76	136	4.1	67	0.25	0.44	69	41
S.C.	RE	M	51	27	10/10	0.4	−5.37	1.21	146	2.7	75	0.34	0.43	71	46
M.B.	LE	M	53	23	10/10	0.4	−2.26	1.07	117	8.2	66	0.57	0.67	51	31
M.A.	LE	F	58	25	10/10	0.6	−1.48	1.57	116	8.4	64	0.62	0.86	52	29
E.S.	LE	M	52	24	10/10	0.7	−3.26	1.42	124	5.9	65	0.35	0.55	59	38
R.T.	RE	M	50	24	10/10	0.7	−3.52	2.41	133	3.0	69	0.34	0.44	64	40
T.F.	LE	F	55	23	10/10	0.5	−4.23	4.04	136	3.7	68	0.55	0.65	68	42
D.G.	LE	M	52	24	10/10	0.6	−2.30	1.57	123	10.6	65	0.47	0.81	58	36
V.B.	LE	M	55	26	10/10	0.6	−4.92	1.14	137	3.7	68	0.36	0.54	69	43

[a] IOP, intraocular pressure in mmHg (mean of different measures) before the medical treatment; VA, best corrected Snellen visual acuity; C/D, cup to disc ratio; MD, mean deviation; CPSD, corrected pattern standard deviation (Humphrey perimeter, central 24-2 program); VEP, visual evoked potentials, P100 latency (ms), P100 amplitude (μV); PERG, pattern electroretinogram, P50 latency (ms), P50 and N95 amplitudes (μV); RCT, retinocortical time: difference between VEP P100 and PERG P50 latencies (ms); LW, latency window: difference between VEP N75 and PERG P50 latencies (ms); LE, left eye; RE, right eye.

24/2 achromatic full threshold strategy, StatPac-2, showing fixation losses, false positive rate and false negative rate each less than 20%; Central 24-2 threshold test) was performed twice in 1 month and the second examination considered for the statistical analysis. The main indices of the Humphrey perimetry are mean deviation (MD) and corrected pattern standard deviation (CPSD). The MD establishes the mean of the defect obtained in all tested points, considers the increasing scatter of sensitivity values with respect to the data obtained in normal subjects according to eccentricity, and therefore may represent an index of the severity of the global damage. CPSD indicates the homogeneity of defect distribution in the visual field and therefore gives information about localized damage (Lachenmayr and Vivell, 1993).

2.2.2. Electrophysiological examination

Simultaneous recordings of VEPs and PERGs were assessed using a previously published method (Parisi, 1997; Parisi et al., 1997, 1998, 1999a,b,c).

The subjects under examination were seated in a semi-dark, acoustically isolated room, in front of the display that was surrounded by a uniform field of luminance of 5 cd/m^2. The subjects were informed on the type of examination and its diagnostic uses.

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.

The visual stimuli were checkerboard patterns (contrast expressed as $L_{max} - L_{min}/L_{min} + L_{max}$ was 80%, mean luminance 110 cd/m^2) generated on a TV monitor and reversed in contrast at the rate of 2 reversals per second. At the viewing distance of 114 cm the check edges subtended 15′ of visual angle (Celesia et al., 1993; Tomoda et al., 1990). The screen of the monitor subtended 12.5°. The refraction of all subjects was corrected for the viewing distance. The stimulation was monocular, after occlusion of the other eye.

2.2.2.1. VEP recordings. Cup-shaped electrodes of silver/silver chloride were fixed with collodion in the following positions: active electrode in Oz, reference electrode in Fpz, ground on left arm. The interelectrode resistance was kept below 3 kΩ. The bioelectric signal was amplified (gain 20 000), filtered (bandpass 1–100 Hz) and averaged (200 events free from artifacts were averaged for every trial) by BM 6000 (Biomedica Mangoni, Pisa, Italy). The analysis time was 250 ms. The transient VEP was characterized by several waves with 3 peaks, which in normal subjects and in our experimental conditions appeared after 75, 100 and 145 ms. These peaks had negative (N75), positive (P100) and negative (N145) polarity, respectively.

2.2.2.2. PERG recordings. The bioelectrical signal was recorded by small Ag/AgCl skin electrodes placed over the lower eyelid. PERGs were derived bipolarly between the stimulated (active electrode) and the patched (reference electrode) eye using a previously described method (Fiorentini et al., 1981) As the recording protocol was extensive, the use of skin electrodes with an interocular recording represented a good compromise between signal-to-noise ratio and signal stability. A discussion on PERG using skin electrodes and its relationship to the responses obtained by corneal electrodes can be found elsewhere (Hawlina and Konec, 1992; Porciatti and Falsini, 1993). The ground electrode was at Fpz (Marmor et al., 1996). The interelectrode resistance was lower than 3 kΩ.

The signal was amplified (gain 50 000), filtered (bandpass 1–30 Hz) and averaged with automatic rejection of artifacts (200 events free from artifacts were averaged for every trial) by BM 6000. The analysis time was 250 ms. The transient PERG was characterized by several waves with 3 peaks, which in normal subjects and in our experimental conditions appeared after 35, 50 and 95 ms. These peaks had negative (N35), positive (P50) and negative (N95) polarity, respectively.

In the recording session simultaneous VEPs and PERGs were recorded at least twice and the resulting waveforms were superimposed to check the repeatability of the results.

For all VEPs and PERGs the latency and the amplitude of each of the averaged waves were measured directly on the displayed records by means of a pair of cursors. Simultaneous recordings of PERGs and VEPs allow us to derive RCT (as the difference between the VEP P100 and the PERG P50 latencies) (Celesia et al., 1986) and the LW (as the difference between the VEP N75 and the PERG P50 latencies) (Marx et al., 1988).

In each subject or patient, the signal-to-noise ratio (SNR) of the PERG and VEP response was assessed by measuring a 'noise' response while the subject fixated at an unmodulated field of the same mean luminance as the stimulus. A noise record of 200 events was obtained. The noise amplitudes were measured in a temporal window corresponding to that at which the response component of interest (i.e. VEP P100, PERG N95) was expected to peak. SNRs for this component were determined by dividing the amplitude of the component by the noise in the corresponding temporal window. A retinal noise < 0.1 μV (mean 0.085 μV) was observed in all subjects tested. In all subjects and patients, we accepted VEP and PERG signals with signals-to-noise ratio >2.

2.3. Statistics

The differences between POAG and Control eyes have been assessed by the unpaired t test for VEP and PERG latencies data and for RCT and LW data, and by the Mann–Whitney U test for VEP and PERG amplitudes data. The correlation between different electrophysiological parameters, and between visual field and electrophysiological parameters was evaluated by Pearson's test. In all statistic tests a P value less than 0.01 was considered significant.

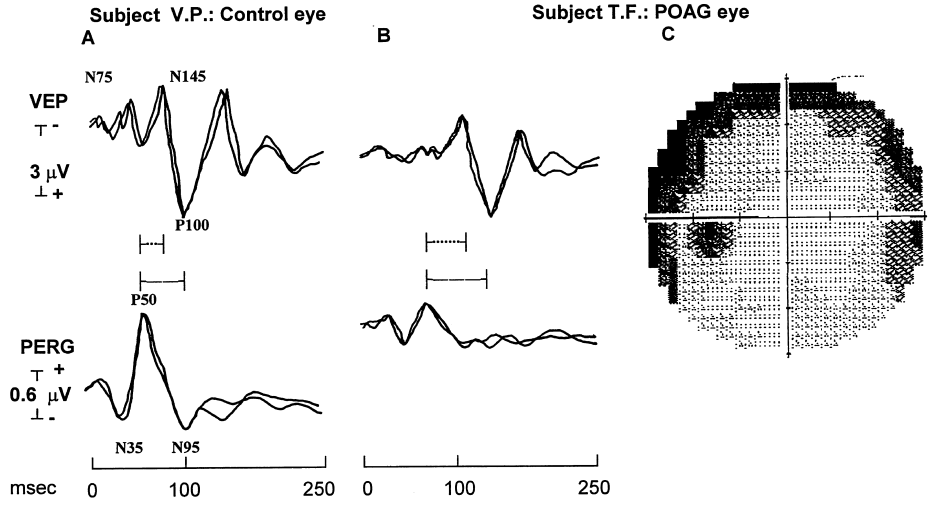

Fig. 1. (A) Layout of simultaneous recordings of VEP and PERG of one control subject (V.P.). (B) Layout of simultaneous recordings of VEP and PERG of one POAG eye (T.F.). (C) Humphrey 24-2 perimetry of the same POAG eye. See Table 1 for electrophysiological, MD and CPSD values. With respect to the control eye, the POAG eye showed a delay in VEP N75, P100, N145 and PERG P50 latencies, a reduction in VEP and PERG amplitudes and longer retinocortical time (difference time between VEP P100 and PERG P50 latencies, solid line) and latency window (difference between VEP N75 and PERG P50 latencies, dashed line).

3. Results

Examples of simultaneous VEP and PERG recordings from a normal subject and a POAG patient are shown in Fig. 1. In Fig. 1, the Humphrey 24-2 visual field examination of the same POAG patient is also reported. The mean data are reported in Table 2.

Regression analysis and correlation between different electrophysiological parameters, and Humphrey static perimetry parameters, observed in POAG patients are presented in Tables 3 and 4.

3.1. VEP

In control eyes, VEP parameters (P100 latency, P100 amplitude) were within the following limits observed in our normal subjects (Parisi et al., 1997): mean value ± 1SD for P100 amplitude, and mean values ± 3SD for P100 latency.

POAG eyes showed P100 latencies significantly ($P < 0.01$) longer and P100 amplitudes significantly ($P < 0.01$) reduced when compared with control eyes. P100 latencies and P100 amplitudes were significantly related to MD ($P < 0.01$), while no correlations with CPSD were found ($P > 0.01$).

3.2. PERG

In control eyes, PERG parameters (P50 latency, and P50 and N95 amplitude) were within the following limits observed in our normal subjects: mean value ± 1SD for P50 and N95 amplitudes and mean value ± 3SD for P50 latency.

In POAG eyes, P50 latencies significantly ($P < 0.01$) delayed and P50 and N95 amplitudes significantly ($P < 0.01$) lower, with respect to those of controls were found.

P50 latencies and N95 amplitudes observed in POAG eyes significantly ($P < 0.01$) correlated with VEP P100 latencies, RCT and LW; N95 amplitudes significantly ($P < 0.01$) correlated with VEP P100 amplitudes; a weak correlation ($P = 0.020$) between P50 latencies or P50 amplitudes and VEP P100 amplitudes was found.

P50 latency, P50 and N95 amplitudes observed in POAG eyes significantly correlated with MD ($P < 0.01$), while no correlation with CPSD was found ($P > 0.01$).

Table 2
Mean data ± one standard deviation of electrophysiological parameters observed in control subjects (C) and in patients affected by glaucoma (POAG)

Group	*n*	VEP P100 latency (ms)	VEP P100 amplitude (μV)	PERG P50 latency (ms)	PERG P50 amplitude (μV)	PERG N95 amplitude (μV)	RCT (ms)	LW (ms)
C	15	106.84 ± 5.42	9.48 ± 2.56	55.28 ± 5.01	1.39 ± 0.41	1.89 ± 0.42	50.93 ± 2.84	25.67 ± 2.63
POAG	21	124.52 ± 8.87[a]	5.95 ± 2.43[a]	64.71 ± 3.91[a]	0.50 ± 0.14[a]	0.67 ± 0.15[a]	59.81 ± 5.90[a]	34.81 ± 4.69[a]

[a] $P < 0.01$ vs. C (unpaired *t* test for VEP and PERG latencies data and for RCT and LW data; Mann–Whitney *U* test for the VEP and PERG amplitude data).

Table 3
Regression analysis and correlation between different electrophysiological parameters observed in POAG patients

Versus	VEP P100 latency	VEP P100 amplitude	RCT	LW
PERG P50 latency	$r = 0.854$, $P < 0.001$	$r = 0.476$, $P = 0.020$	$r = 0.618$, $P < 0.001$	$r = 0.674$, $P < 0.001$
PERG P50 amplitude	$r = 0.651$, $P < 0.001$	$r = 0.500$, $P = 0.020$	$r = 0.534$, $P < 0.001$	$r = 0.611$, $P < 0.001$
PERG P50 amplitude	$r = 0.668$, $P < 0.001$	$r = 0.645$, $P < 0.001$	$r = 0.576$, $P < 0.001$	$r = 0.673$, $P < 0.001$

3.3. Retinocortical time and latency window

In control eyes, the RCT and LW were within the following limits, observed in our normal subjects: mean values ± 3SD.

In POAG eyes, RCT and LW were significantly ($P < 0.01$) longer than in control eyes and significantly correlated with MD ($P < 0.01$), while no correlation with CPSD was found ($P > 0.01$).

4. Discussion

In the present study, a widespread selection of glaucoma patients, with eyes affected by different degrees of glaucomatous optic neuropathy, were tested for PERG, VEP and Humphrey perimetry. Our aim was to evaluate whether the glaucomatous visual field defects could be ascribed to an impaired retinal function, to impaired neural conduction in the postretinal visual pathways, or both.

4.1. Electrophysiological findings

VEPs recorded in our POAG patients showed delayed P100 latencies and reduced P100 amplitudes when compared with those of controls. The abnormal VEP responses observed in glaucomatous patients have been previously ascribed to a retinal dysfunction (Parisi and Bucci, 1992), but recently it has been suggested that delayed neural conduction in the postretinal visual pathways also contributes to VEP impairment (Parisi, 1997).

The retinal function has been assessed by PERG recordings and, in agreement with previous electrophysiological studies (Bobak et al., 1983; Wanger and Persson, 1983; Marx et al., 1986a; Porciatti et al., 1987; Watanabe et al., 1990; O'Donaghue et al., 1992; Bray et al., 1992; Pfeiffer et al., 1993; Arai et al., 1993; Graham et al., 1994, 1996; Komata et al., 1995; Parisi, 1997), our POAG patients presented impaired PERG responses (delayed latencies and reduced amplitudes). Since it is known that the integrity of the innermost retinal layers is essential for the generation of a normal PERG response (Parisi et al., 1999c) and in glaucoma a loss of ganglion cells and their fibers has been documented by histological studies (Quigley et al., 1982, 1987, 1988, 1995) and by morphological evaluation in vivo of the retinal fibers (Orzalesi et al., 1998; Shuman et al., 1995; Yucel et al., 1998), the impaired PERG responses observed in our glaucomatous patients could be ascribed to a dysfunction of ganglion cells and their fibers. This is also supported by experimental studies performed in monkeys, in which monocular glaucoma was induced by laser photocoagulation of the trabecular meshwork (Marx et al., 1986b; Johnson et al., 1989), and the loss of ganglion cells has been directly related to a reduction in amplitude of the PERG signals. Nevertheless, the contribution of preganglionic retinal elements to the impaired PERG responses cannot be entirely excluded. In fact, an affection of the outer retinal layers and even of the photoreceptors, secondary to the pressure damage, has been observed by recordings of Flash ERG in patients with advanced glaucoma (Gur et al., 1987; Veagan et al., 1995) or using focal-ERG (Falsini et al., 1991), 30 Hz flicker VEP (Holopigian et al., 1990) and VEP after photostress (Parisi and Bucci, 1992).

Neural conduction in the visual pathways has been evaluated by the measurement of RCT and LW. According to everything we have suggested in our previous works (Parisi, 1997; Parisi et al., 1998, 1999a,b,c) we believe that RCT and LW do not represent the real transit time of neural conduction between the retina and visual cortex, but they could be considered as an index of the neural conduction in the postretinal visual pathways.

However, both RCT and LW were similarly impaired in our POAG patients and this is in agreement with our previous observations (Parisi, 1997) and with results reported by Marx et al. (1988). An explanation for the abnormal values of RCT and LW observed in our POAG patients could be offered by available data on the effects of

Table 4
Regression analysis and correlation between electrophysiological and Humphrey static perimetry (24-2 program) parameters observed in POAG patients

Versus	VEP P100 latency	VEP P100 amplitude	PERG P50 latency	PERG P50 amplitude	PERG N95 amplitude	RCT	LW
MD	$r = 0.826$, $P < 0.001$	$r = 0.719$, $P < 0.001$	$r = 0.624$, $P = 0.002$	$r = 0.572$, $P = 0.006$	$r = 0.625$, $P = 0.002$	$r = 0.828$, $P < 0.001$	$r = 0.810$, $P < 0.001$
CPSD	$r = 0.367$, $P = 0.101$	$r = -0.293$, $P = 0.196$	$r = 0.329$, $P = 0.144$	$r = 0.264$ $P = 0.245$	$r = -0.318$, $P = 0.159$	$r = 0.338$, $P = 0.139$	$r = 0.270$, $P = 0.235$

glaucoma at the LGN level. Histological studies performed on experimental glaucoma showed a reduced axonal transport to the LGN in monkeys with chronic IOP elevation and damage particularly in the magnocellular layers of LGN (Dandona et al., 1991). A very interesting recent work revealed a morphological involvement of the LGN of monkeys in which experimental glaucoma was induced. In this study it has been observed that an IOP elevation induces a profound degenerative effect on both the magnocellular and the parvocellular regions of the LGN (Weber et al., 2000). A degeneration of the LGN has been observed, by autopsy section, only in 5 patients with a documented history of glaucoma; in these patients there is a greater loss of magnocellular tissue, while there was no statistical difference in the parvocellular layer compared with controls (Chaturvedi et al., 1993).

It is likely that the dysfunction of the innermost retinal layers may be the cause of histological and functional changes at the dLGN level and this involvement could induce an impaired (delayed and/or reduced) bioelectrical activity in those cells in which the visual cortical responses have their source. This hypothesis can also be supported by the fact that in our POAG patients, abnormal PERG responses are significantly correlated with the delay in latency and the reduction in amplitude of the VEP responses and with the longer RCT and LW.

Therefore, as previously observed (Parisi, 1997), both a retinal and postretinal dysfunction may contribute to the VEP impaired responses found in our POAG patients.

4.2. Correlation between electrophysiological and perimetric parameters

Our POAG patients showed different degrees of visual field impairment detected by a reduction in MD and by an increase in CPSD.

As previously expressed, MD may represent a perimetric index of the severity of the global damage, and reflects the average reduction in retinal sensitivity (Lachenmayr and Vivell, 1993). The reduced MD observed in our POAG patients was significantly correlated with the abnormal retinal and cortical electrophysiological responses.

In fact a significant correlation between MD and PERG P50 latencies and P50 and N95 amplitudes was observed, and our results are in agreement with previous studies in which PERG responses were related to visual field defects assessed by Goldmann perimetry (Wanger and Persson, 1983) or by computerized static perimetry (Wanger and Persson, 1987; O'Donaghue et al., 1992; Graham et al., 1994; Watanabe et al., 1990).

A significant correlation between the values of MD and those of VEP parameters has also been found in our POAG patients. This finding is consistent with results reported in others studies in which abnormal VEP responses were related to visual field defects assessed by Goldmann perimetry (Papst et al., 1984; Emers and Van Lith, 1974; Cappin and Nissim, 1975; Galloway and Barber, 1981; Ponte et al., 1984; Nykanen and Raitta, 1989; Bray et al., 1992) or by static perimetry (Nykanen and Raitta, 1989; Bray et al., 1992).

The reduced MD observed in POAG patients significantly correlated with the longer RCT and LW. This is a novel finding, since it has never been assessed whether these electrophysiological parameters could be related to the visual field defects evaluated by Goldmann or static perimetry.

The correlation between all the electrophysiological VEP parameters and the MD of Humphrey static perimetry suggests that the impaired visual cortical responses observed in glaucoma patients can be revealed by both electrophysiological and psychophysical methods. In addition, the severity of the global glaucomatous damage evidenced by the reduction in MD could depend both on the retinal dysfunction and the delay in neural conduction from the retina to the visual cortex, as revealed by the significant correlation between both PERG parameters and RCT or LW and the MD.

In our POAG patients, no correlation was found between the PERG and VEP parameters and the CPSD of the Humphrey perimetry. This perimetrical parameter is considered a more accurate index of localized defects in the visual field (Werner and Piltz-Seymour, 1992). This lack of correlation could be explained by results suggesting that PERG and VEP responses represent respectively the bioelectrical activity of the innermost retinal layers of the entire retina (Bach et al., 1992) and the mass bioelectrical response of the visual cortex, and therefore a localized damage of selectively vulnerable optic nerve fibers cannot be detected by retinal or visual cortical electrophysiological responses.

In conclusion our results indicate that, in patients with open angle glaucoma, the index of global visual field damage (MD) cannot be exclusively related to a retinal dysfunction (impaired PERG), but may also reflect an impairment at the postretinal level (delayed RCT and LW).

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