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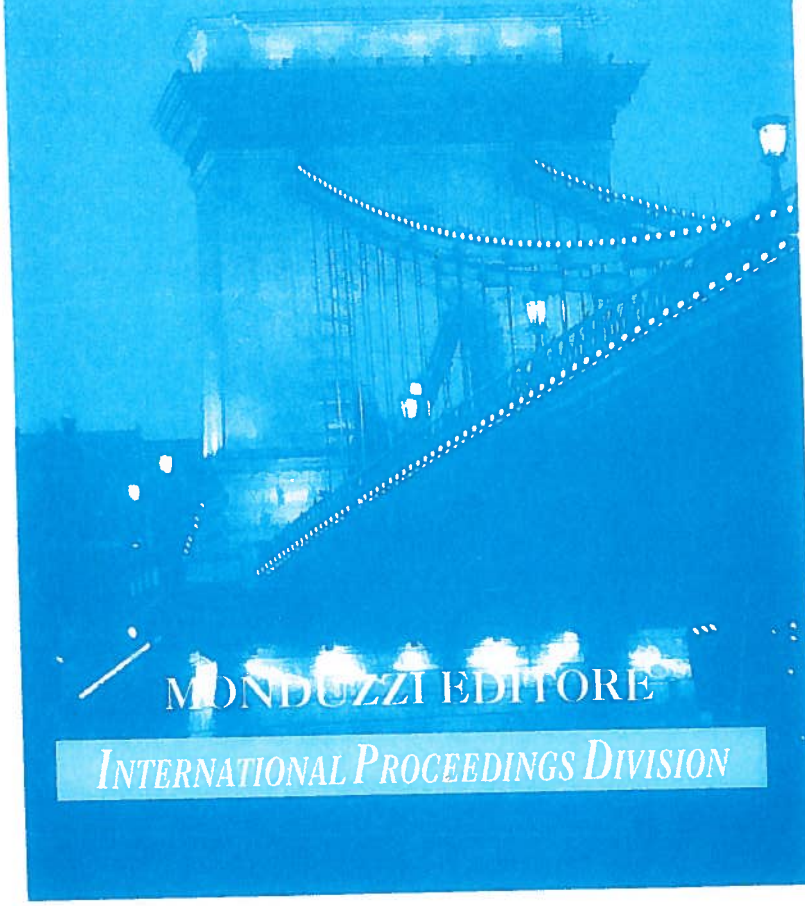

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Delayed nervous conduction in the visual pathways in newly-diagnosed diabetic patients

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SUMMARY

The aim of our work was to evaluate the sources of impaired nervous conduction in visual pathways in newly-diagnosed diabetic patients. We assessed Flash-ERG (ERG), Oscillatory Potentials (OPs) and simultaneous recordings of Pattern-Electroretinograms (PERGs) and Visual Evoked Potentials (VEPs) in 12 insulin-dependent diabetic patients (IDDM: aged 24.8±7.8 yrs, duration of disease 3.0±1.6 months) and in 14 age-matched control subjects. In IDDM patients we found: ERG and OP parameters similar to those in controls (ANOVA $P>0.05$), PERG and VEP latencies significantly ($P<0.01$) higher than in controls, a retino-cortical time (RCT) longer ($P<0.01$) than in controls. In IDDM patients, therefore, there are two sources in the genesis of the functional impairment of VEP: one retinal (delayed PERG) and one postretinal (delayed RCT).

INTRODUCTION

VEPs show delayed latencies in patients with long-standing insulin- dependent diabetes (IDDM) and this has been ascribed to a reduced velocity of neural conduction in the optic pathways (Parisi et al, 1994, Parisi et al, 1997).
In newly-diagnosed IDDM patients we have already shown an impaired VEP P100 latency that suggests an early involvement of neural conduction in the visual pathways (Parisi et al, 1995, Uccioli et al, 1995).
Electrophysiological methods allow us to explore and dissect different structures contributing to the visual function: ERG sources in the outer retinal layres, OPs are originated in the middle retina, while PERG reflects the bioelectrical activity of the innermost retinal layers (Maffei and Fiorentini, 1981). Celesia et al (1984) suggest recording VEP and PERG simultaneously in order to evaluate the RCT (difference between VEP P100 and PERG P50 latencies) and this could be considered an index of neural conduction in the postretinal visual pathways.
The aim of our work was to evaluate if the delay in VEP P100 latency observed in newly-diagnosed IDDM patients is due to impaired function of the outer retinal layers, of the ganglion cell and/or to delayed neural conduction in the postretinal visual pathways.

MATERIALS AND METHODS

Twelve IDDM patients with a duration of disease less than 6 months (mean 3.0±1.6 months) and fourteen age-matched controls (mean age 25.8±7.7 yrs) were included in this study. The following criteria were required for controls and IDDM patients: intraocular pressure < 21mmHg, visual acuity of 10/10, normal visual field and no ocular problems; in IDDM patients we required the absence of any signs of retinopathy evaluated by fluorescein angiography. Informed consent was received from each patient enrolled in the study.

In IDDM patients and control subjects we performed the following evaluation:
Flash-ERG (ERG)
The visual stimulus was a BM 6000 Ganzfield (Biomedica Mangoni, Pisa, Italy) at 0.1 J of intensity. A single flash was presented at the temporal frequency of 1 Hz. The bioelectrical signal was recorded by means of platinum hook electrodes inserted into the external corner of the inferior eyelid (active electrode). Local anaesthesia was provided by application of novesine 0.4%. A silver-silver chloride electrode was positioned and fixed with collodion in Fpz (reference electrode). The ground was in the left arm. The interelectrode resistance was lower than 5 KΩ. The signal was amplified (gain 5000), filtered (band-pass 1-100 Hz) and averaged with automatic rejection of artifacts (40 events for every trial) by BM 6000. The analysis time was 150 msec. The typical ERG is a biphasic signal characterized by a certain number of waves, two of which (a and b waves) have a mean latency of 16 and 40 msec in normal subjects.
Oscillatory Potentials (OPs)
The visual stimulus was BM 6000 Ganzfield at 1 J of intensity. A single flash was presented at the temporal frequency of 0.1 Hz. The signal was amplified (gain 5000), filtered (band-pass 100-5000 Hz) and averaged with automatic rejection of artifacts by BM 6000 (20 events for every trial). The analysis time was 150 msec. OPs are characterized by a certain number of waves: OP1, OP2, OP3, OP4.
Simultaneous recordings of PERG and VEP
The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 11(cd/m^2) generated on a TV monitor and reversed in contrast at the rate of :

reversal/s. At the viewing distance of 114 cm the single check subtended 15' of visual angle and the screen of the monitor subtended 12.5 degrees. The stimulation was monocular after occlusion of the other eye.
PERG recordings: The bioelectrical signal was recorded, by means of platinum hook electrodes inserted into the external corner of the inferior eyelid. PERGs were derived bipolarly between the tested (active electrode) and the patched (reference electrode) eye. Local anaesthesia was provided by application of novesine 0.4%. The ground electrode was in Fpz . The interelectrode resistance was lower than 3 KΩ. The signal was amplified (gain 50000), filtered (band pass 1-30Hz) and averaged with automatic rejection of artifacts (200 events free from artifacts for every trial) by BM 6000. The analysis time was 250 msec. The transient PERG response is characterized by a number of waves with three subsequent peaks of negative, positive, negative polarity. In normal subjects and in the conditions of our experiment, these peaks have the following mean latencies : 35, 50 and 95 msec.
VEP recordings: Cup shaped silver-silver-chloride electrodes 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 3KΩ. The bioelectric signal was amplified (gain 20000), filtered (band-pass 1-100 Hz) and averaged (200 events free from artifacts for every trial) by BM 6000. The analysis time was 250 msec.

The transient VEP response is characterized by a number of waves with three subsequent peaks of negative, positive, negative polarity. In normal subjects and in the conditions of our experiment, these peaks have the following mean latencies : 75, 100 and 145 msec.
In the recording session ERG, OPs, PERGs and VEPs were recorded at least twice and the resulting waveforms were superimposed to check the repeatability of the results.
We accepted PERG and VEP signals with signals-to-noise ratio >2. The noise was measured by recording the bioelectical signals while the monitor was screened by a cardboard and a noise <0.1 microvolt (mean 0.085 microvolt) was observed in all subjects tested.
For all electrophysiological records the peak latency and the peak amplitude of each wave were measured directly from the displayed recordings with a pair of cursors. In the analysis of OP results we considered the addition of the single amplitude of each OP (OP1+OP2+OP3+OP4).

RESULTS

The mean data are presented in Table 1 and 2. In IDDM patients we found ERG and OPs parameters similar to control ones (ANOVA P>0.05), PERGs and VEPs latencies significantly higher than controls (P<0.01); the retino-cortical time (RCT) was longer in IDDM than controls (P<0.01). No correlations were found between PERG P50 latency and PERG P50-N95 amplitude and RCT.

Table 1: Mean ± SEM of ERG and OP parameters;

	ERG: a wave latency, (msec)	b wave latency, (msec)	b wave amplitude. (microvolt)	OPs amplitude (microvolt)
Controls	16.7±0.4	40.7±1.4	74.5±3.2	118.5±1.8
IDDM	16.8±0.7	41.1±1.9	73.7±4.6	116.3±2.2

Table 2: Mean ± SEM of PERG and VEP parameters

	PERG: P50 latency (msec)	P50-N95 amplitude. (microvolt)	VEP: P100 latency (msec)	RCT (msec)
Controls	54.6±1.2	1.85±0.7	102.3±1.4	51.8±1.4
IDDM	60.2±0.7*	0.98±0.9*	112.7±1.1*	59.3±1.3*

ANOVA: * = P<0.01 vs Controls

CONCLUSIONS

In the newly-diagnosed IDDM patients VEPs showed a significantly increased P100 latency suggesting an early involvement of the neural conduction in the visual pathways. To further elucidate this matter we recorded ERG, OPs and simulneously PERG and VEP deriving from the latter an index of postretinal neural conduction (RCT).

ERGs and OPs observed in our IDDM patients are not modified when compared with control ones: this leads us to believe that the outer and the middle retinal layers are not functionally impaired at this time of the disease. An involvement of these retinal structures has been observed after 10 years of disease and is also present without fluorangiographic signs of retinopathy (Parisi et al, 1997). Our IDDM patients show impaired PERG parameters and this may be ascribed to a selective dysfunction of the innermost retinal layers. This impairment was found in patients with a long duration of disease and with or without fluorangiographyc signs of retinopathy (Parisi et al, 1997). RCT is increased in our IDDM patients, suggesting delayed neural conduction in postretinal visual pathways. Our data might appear to contrast with another study (Trick, 1991) in which RCT was evaluated: in fact, an increase in RCT was observed in patients with background retinopathy , while a normal RCT was found in diabetic patients with little or no retinopathy. In conclusion, in newly-diagnosed IDDM patients two factors are involved in the impairment of VEP: one retinal (delayed PERG) and the other postretinal (delayed RCT). The absence of impaired ERG and OPs suggests that the outer and the middle retinal layers do not contribute to the delay of VEP; in addition the absence of correlations between the PERG parameters and RCT leads us to believe that the innermost retinal layers and postretinal stuctures both contribute independently to the VEP P100 delay.

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