·Clinical Research·

Early changes of retinal function in diabetic patients detected by multifocal electroretinogram

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Abstract

• AIM: To investigate the early changes of retinal function in diabetic patients detected by multifocal electroretinogram (mfERG).

• METHODS: The first-order kernel responses of mfERG were recorded from eyes of 33 normal control subjects, 63 diabetic patients without retinopathy and 43 diabetic patients with background retinopathy. The response densities and implicit times of N_1 and P_1 were compared among the control, diabetic patients without retinopathy and diabetic patients with retinopathy.

• RESULTS: The response densities of N_1 and P_1 in central 3 rings were reduced significantly in diabetic eyes with and without retinopathy. And the implicit times of N_1 and P_1 were delayed significantly only in diabetic eyes with retinopathy.

• CONCLUSION: mfERG can detect the early changes of retinal function quantitatively in diabetic patients. Analysis of response densities and implicit times of N_1 and P_1 can reflect the progress of local retinal dysfunction in diabetes.

• KEYWORDS: diabetic retinopathy; multifocal electroretinogram; visual electrophysiology

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INTRODUCTION

Diabetic retinopathy (DR) is a common complication of diabetes mellitus (DM) and a leading cause of vision loss. Up to now, the diagnosis of DR depends on the well-recognized feature of microangiopathy in clinic. Pathology [1-3] reviewed that retinal neurodegeneration is an important change during the early stage of diabetes, thus detection of retinal dysfunction maybe an effective method for early diagnosis of DR. Sutter *et al* [4] has invented a new visual electrophysiological technique since 1990s-Multifocal electroretinogram (mfERG), which allows for the simultaneous recording of many focal retinal responses over the macular region in a relatively short recording period, and has proved to be very useful in identifying areas of decreased retinal responsiveness in diseases affecting the area. Several researchers[5-7] have reported the application of mfERG in diagnosis of DR; however, the early changes of mfERG in DR are still to be studied. In this paper, we investigated the early change of mfERG in DR by checking normal control, diabetic subjects with and without DR.

MATERIALS AND METHODS

Subjects Thirty-three healthy subjects (51.6±10.2 years of age), 63 diabetic patients without retinopathy (52.4 ±8.1 years of age) and 43 diabetic patients with early background retinopathy (54.8±8.3 years of age)were tested monocularly. There were no statistically significant differences among the three groups (F=0.901, P=0.408).

All subjects presented routine screening for DR. An ophthalmic examination consisted of history, refraction, visual acuity (VA), slit-lamp, and fundus. All of diabetic patients were diagnosed as non-insulin independent DM. The duration of DM was 1 month-13 years. The patients with DR had only microaneurysms, dot hemorrhages and hard effusions. All subjects had corrected VA of 1.0. Subjects with blood hypertension or other systemic diseases, which would hurt retina or suspected ocular complications, and those with moderate or high ametropia were not included in the study.

mfERG Recording mfERG were recorded using a visual evoked response imaging system (RETIscan3.15, Rodenstock, Roland, Germany). Following pupil dilation with 10g/L tropicamide and 10g/L epinephrine, the cornea was topically anesthetized, then a bipolar contact lens electrode was placed on the eye, and a ground electrode was

Table 1 Response densities of N_1 in control and diabetes (mean ± SD,nV/deg^2)

	Ring 1	Ring 2	Ring 3	Ring 4	Ring 5
Control	22.24 ± 10.42	13.31 ± 4.07	9.27 ± 2.62	6.34 ± 1.75	5.69 ± 1.48
Without DR	17.99 ± 6.78[a]	10.30 ± 3.49[a]	7.54 ± 2.13[a]	5.77 ± 1.67	4.88 ± 1.43
DM with DR	16.15 ± 9.27[a]	9.66 ± 4.16[a]	7.02 ± 2.47[a]	5.65 ± 1.77	5.07 ± 1.72
F	3.967	7.991	7.826	1.422	2.446
P	0.021	0.001	0.001	0.245	0.091

[a]values were different significantly compared with control

Table 2 Implicit times of N_1 in control and diabetes (mean ± SD,ms)

	Ring 1	Ring 2	Ring 3	Ring 4	Ring 5
Control	20.51 ± 1.65	18.08 ± 1.90	17.22 ± 1.86	17.67 ± 1.68	18.20 ± 1.67
DM without DR	20.20 ± 2.41	19.06 ± 1.95	17.73 ± 1.96	17.80 ± 1.85	18.21 ± 1.56
DM with DR	21.04 ± 3.44	20.52 ± 3.14[a]	18.85 ± 2.35[a]	19.26 ± 2.09[a]	19.10 ± 2.26[a]
F	1.302	10.352	6.506	9.404	3.498
P	0.275	0.000	0.002	0.000	0.03

[a]Values were different significantly compared with control and DM without DR

Table 3 Response densities of P_1 in control and diabetes (mean ± SD,nV/deg^2)

	Ring 1	Ring 2	Ring 3	Ring 4	Ring 5
Control	75.85 ± 25.61	41.47 ± 11.82	28.94 ± 8.97	21.03 ± 6.51	18.11 ± 5.76
DM without DR	59.98 ± 18.87[a]	34.55 ± 11.08[a]	25.47 ± 7.82[a]	19.19 ± 6.72	16.64 ± 7.02
DM with DR	49.93 ± 21.18[b]	29.32 ± 11.14[b]	21.81 ± 7.82[b]	17.29 ± 5.69[a]	15.20 ± 5.36
F	13.617	10.658	7.217	3.208	1.972
P	0.000	0.000	0.001	0.044	0.143

[a]values were different significantly compared with control; [b]values were different significantly compared with control and DM without DR

Table 4 Implicit times of P_1 in control and diabetes (mean ± SD,ms)

	Ring 1	Ring 2	Ring 3	Ring4	Ring 5
Control	39.09 ± 2.68	37.22 ± 2.13	35.64 ± 1.26	34.73 ± 1.25	35.03 ± 1.24
DM without DR	39.55 ± 3.24	36.78 ± 1.99	35.95 ± 1.53	35.31 ± 1.41	35.24 ± 1.37
DM with DR	40.34 ± 4.18	37.88 ± 3.50	37.19 ± 2.04[a]	36.68 ± 1.95[a]	36.79 ± 2.38[a]
F	1.314	2.324	10.239	16.334	13.192
P	0.272	0.102	0.000	0.000	0.000

[a]values were different significantly compared with control and DM without DR

put on the centre of frontal. The stimulus was presented on a 21 inch monitor. The area of the stimulus was 30. A total of 61 elements were used and responses were grouped in 5 rings concentric with fixation. A central X was used for fixation. Data were acquired at a gain of 100 000 over a frequency of 5Hz to 100Hz. Data were acquired in 8 segments each of 47 seconds duration. Responses were sampled at 1 021Hz.

A first order response was calculated and analyzed in 5 concentric rings. The local responses consisted of the first negative trough (N_1) and the first positive peak (P_1). Response densities and implicit times of N_1 and P_1 of each ring were calculated.

Statistical Analysis All data on the subjects clinical characteristics were enrolled into SPSS 11.0. Statistical comparison among groups was performed by ANOVA, and multiple comparisons were performed by S-N-K. A $P< 0.05$ was regarded as statistically significant.

RESULTS

Responses densities of N_1 and P_1 in rings from 1 to 3 in diabetic patients without retinopathy were lower than those in healthy subjects. And response density of P_1 at the same sites in patients with DR was lower than that in diabetic patients without retinopathy (Tables 1-4). There was no statistically significant difference in implicit times of N_1 and P_1 between healthy subjects and diabetic patients without retinopathy. Implicit times of N_1 from ring 2 to ring 5 and P_1 from ring 3 and ring 5 increased significantly in patients with DR.

DISCUSSION

In this study we have shown that there are abnormal local retinal responses in diabetic patients with and without retinopathy, by analyzing the amplitude and implicit time of

complicated indexes in concentric rings. These responses change occurs both in P_1 and in N_1. In diabetic eyes without retinopathy, response densities of P_1 and N_1 decreased from ring 1 to ring 3 around the macula. And in eyes with background DR, besides the more decreased response density of P_1, implicit times of P_1 and N_1 appeared delay in broader retinal. The results indicate that the early change of retinal function can be detected and monitored quantitatively by mfERG.

Several authors had reported the changes of retinal activity in patients of DR detected by mfERG, but the indexes of mfERG and analyzed methods are different, the early changes of mfERG in diabetic eyes are still controversial. Yu *et al* [7] analyzed the local retinal responses by forming regional groups as the same way in our study; they have shown that the change of mfERG lies just in decreased response densities of P_1, but not in implicit times of P_1 or N_1 in background DR. By analyzing the amplitude and implicit time of P_1 in each local ERG responses, Fortunes *et al*[5] found that mfERG reveals local retinal dysfunction in diabetic eye even before retinopathy. Han *et al* [6] have shown that the localized functions abnormalities of the retina reflected by mfERG delays predict the local sites of new retinopathy in later.

The waveforms of mfERG (the first-order kernel) are dominated by the cells of the outer retinal, such as photoreceptors and bipolar cells[8]; the damage of these cells can affect the waveforms of mfERG. In diseases like hereditary cone dystrophy [9] and retinitis pigmentosa [10, 11], which act mainly on bipolar cells and photoreceptors, mfERG appears in decreased response densities and delayed implicit times. Even in eyes with no retinopathy in these diseases, response densities decrease without delayed implicit times. In diabetes, neurodegenerative changes of bipolar cells and photoreceptors have been found in retina occurring before diabetic retinopathy [1-3], indicating that the abnormal response densities of P_1 and N_1 of mfERG in diabetic patients without retinopathy in this study is related to the damage of bipolar cells and photoreceptors in DR.

In summary, in this study we have demonstrated that mfERG allows objective and quantitative assessment of local retinal function in diabetic eyes. Both P_1 and N_1 response densities change to be small in diabetic patients without retinopathy, and are smaller in diabetic patients with retinopathy. Implicit times also appear delay in diabetic patients with retinopathy. The examination of multiple indexes of mfERG can provide effective method to early diagnose and monitor DR.

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