Changes in Focal Macular Electroretinograms and Foveal Thickness after Vitrectomy for Diabetic Macular Edema

Hiroko Terasaki, Takeshi Kojima, Hideyasu Niwa, Chang-Hua Piao, Shinji Ueno, Mineo Kondo, Yasuki Ito, and Yozo Miyake

**Purpose.** To evaluate the changes in the focal macular electroretinogram (FMERG) and foveal retinal thickness after vitrectomy for diabetic macular edema (DME).

**Methods.** FMERGs were elicited from 25 eyes of 21 patients (ages 29–75 years) who underwent vitrectomy for DME by a 15° stimulus. A posterior vitreous detachment (PVD) was created during surgery in 19 eyes (group 1), and 4 eyes had a PVD before surgery (group 2). In the remaining 2 eyes, a PVD could not be created (group 3). FMERGs were recorded before and 3, 6, and 12 months after vitrectomy. The foveal thickness, determined by optical coherence tomography (OCT), and visual acuity were measured on the same day as the FMERG recordings.

**Results.** The postoperative visual acuity (logarithm of the minimum angle of resolution [logMAR]) improved gradually after the surgery and was significantly better at 12 months in eyes in group 1 (P = 0.0395). The postoperative mean foveal thickness was significantly less at 3 months after surgery in group 1 eyes (P = 0.0006), and there was a further decrease thereafter. In the 2 eyes in group 3, the decreased foveal thickness 3 and 6 months after surgery became thicker at 12 months. The mean b-wave amplitude of the FMERGs increased significantly at 12 months in group 1 eyes (P = 0.0297). The mean implicit time of a- and b-waves was more delayed at 3 months, and the change in a-wave was statistically significant in group 1 eyes (P = 0.0474). There was a wide range of changes in the b-wave amplitude at 12 months, however, the increase in the b-wave was correlated with the decrease in foveal thickness (r = .49, P = 0.012).

**Conclusions.** A disparity in the time course and degree of recovery of the foveal thickness and macular retinal function was found in eyes with DME after vitrectomy. Part of the functional recovery could be attributed to decreased retinal thickness and the absorption of the subretinal fluid. (Invest Ophthalmol Vis Sci. 2003;44:4465–4472) DOI:10.1167/iovs.02-1313

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Diabetic macular edema (DME) is the most common cause of decreased visual acuity in diabetic patients. Foveal function in eyes with DME has been assessed by psychophysical tests such as visual acuity, threshold measurements, and color discrimination. ERG has been used to examine the physiological condition of the retina in diabetic patients. In eyes with diabetic retinopathy, abnormalities in various components of the full-field ERG have been reported, e.g., reductions in the amplitude and delayed implicit times of the a- and b-waves, and reduced oscillatory potentials. These changes appear to be correlated with the severity of the retinopathy. To assess the functional status of the macula in diabetic patients’ eyes, the importance of recording focal ERGs from the macula has been reported.

The treatment of DME includes systemic glycemic control, normalizing blood pressure and serum lipids, and weight control. Photocoagulation therapy has also been reported to be beneficial, and the Early Treatment Diabetic Retinopathy Study Group reported that focal macular photocoagulation for clinically significant macular edema leads to only a moderate loss of vision. On the other hand, multifocal ERG studies have shown that the local responses obtained in areas beyond the treated regions have decreased amplitudes and delayed implicit times.

Vitrectomy is an investigational technique for the treatment of DME, however, a randomized clinical trial has not been conducted. Vitrectomy may result in recovery of the anatomic configuration of the macula without photocoagulation or direct surgical manipulation of the retina. Thus, vitrectomy may have the potential to contribute significantly to the recovery of macular retinal function.

Optical coherence tomography (OCT) has been used to evaluate the structure of the macula in patients with DME because an image of the retinal thickness can be obtained objectively and quantitatively. The relationship of the retina to the posterior hyaloid membrane can also be demonstrated by OCT. OCT studies performed before and after vitrectomy for DME have shown good resolution of macular edema.

The purpose of this study was to analyze the relationship between the morphologic structure of the macula and the function of specific retinal layers of the macula. To accomplish this, OCT was performed and focal macular ERGs (FMERGs) were recorded before and after vitrectomy. The visual acuity was also measured, and the relationship between the recovery time of anatomic structure and function was determined.

**Methods**

**Patients and Procedures**

Vitrectomy was performed on 25 eyes of 21 patients (age = 55.0 ± 2.8 years, mean ± SEM; range, 29–75 years) for DME at the Nagoya University Hospital from May 1998 to January 2001. All patients were followed for at least 19 months postoperatively. The visual acuity and
OCT-determined foveal thickness were measured on the same day as the FMERG recordings before, and 3, 6, and 12 months after vitrectomy. In 8 eyes, only the visual acuity was measured and OCT performed at 6 months after surgery because of difficulties in scheduling the FMERG. The mean-glycosylated hemoglobin (HbA1c) and the serum creatinine, measured within 2 weeks of the vitrectomy, were 7.4 ± 1.6 mg/dL and 0.82 ± 0.5 mg/dL (mean ± SD respectively).

The presence of macular edema was determined by contact lens biomicroscopy, fluorescein angiography, and OCT (Humphrey model 2000; Humphrey Instruments, San Leandro, CA). Eyes with a visible epimacular membrane, a partial posterior vitreous detachment (PVD), or evidence of a vitreous traction by OCT were excluded. Eyes that had the internal-limiting membrane removed during surgery were also excluded.

The best-corrected visual acuity (BCVA) was measured with a Japanese standard visual acuity chart and converted to Snellen visual acuity. For statistical analysis, the pre- and postoperative BCVAs were converted to the logarithm of the minimum angle of resolution (logMAR).

All eyes underwent a standard three-port pars plana vitrectomy with endophotocoagulation of the retina beyond the equator. Macular photocoagulation was not applied during or after surgery. A PVD was created during surgery in 19 eyes without a preoperative PVD (group 1) and 4 eyes had a preoperative PVD (group 2). In the 2 remaining eyes, a PVD could not be created and as much of the vitreous gel as possible was removed (group 3).

Six eyes were pseudophakic before vitrectomy, and 11 eyes with mild cataract underwent concurrent phacoemulsification and IOL implantation with vitrectomy to avoid later cataract surgery. The mild cataracts did not affect the visual acuity before surgery. Eyes with significant cataract were excluded. Seventeen eyes were pseudophakic postoperatively.

Seven eyes had preproliferative diabetic retinopathy and 18 eyes had proliferative diabetic retinopathy without fibrous proliferation before surgery. Nineteen eyes had previously received panretinal photocoagulation and had proliferative diabetic retinopathy without fibrous proliferation before surgery. Nineteen eyes had previously received panretinal photocoagulation. One eye had received macular grid photocoagulation, another had received partial peripheral photocoagulation, and one eye had received both.

FMERGs were recorded before, and 3, 6, and 12 months after vitrectomy. The system for eliciting and recording FMERGs under direct fundus observation, and the evaluation of the responses have been described in detail.30,51 Briefly, an infrared televidion fundus camera, equipped with stimulus light, background illumination, and fixation target, was used to monitor the locus of the stimulus on the macula. The size of the stimulus spot was adjustable, and we selected a 15° spot stimulus centered on the fovea. The background light was delivered to the eye from the fundus camera at a visual angle of 45°. Additional background illumination outside the central 45° produced a homogeneous background illumination for nearly the entire visual field.

A Burian-Allen bipolar contact lens electrode was used for the FMERG recordings. This lens not only allowed a very low-electrical noise level but also permitted a clear view of the fundus as seen on a television monitor. The luminances of the white stimulus light and background light were 29.46 cd/m² and 2.89 cd/m², respectively.

After the patients’ pupils were fully dilated with 0.5% tropicamide and 0.5% phenylephrine hydrochloride, FMERGs were elicited with a 5-Hz rectangular stimulus. A time constant of 0.05 second with a 100-Hz high-cutoff filter on one amplifier was used to record the a- and b-waves, and a time constant of 0.003 second and a 300-Hz high-cutoff filter on a second amplifier was used to record the OPs. A total of 512 responses were averaged by a signal processor.

To determine the foveal thickness, OCT scanning was performed horizontally and vertically through the fovea with scan lengths of 2.85 mm and 4.00 mm, respectively. The foveal thickness was determined from the OCT images and was defined as the distance from the internal-limiting membrane to the outer border of sensory retina (foveal retinal thickness) and also to the inner border of the highly reflective retinal pigment epithelium including the serous retinal detachment (total foveal thickness). The measurements were made manually, and the mean thickness for the four scans of the fovea was used for analysis.

The final followup examination ranged from 19 to 51 months (mean ± SD, 32.6 ± 8.1).

Statistical Analyses

The Wilcoxon signed rank test was used to determine whether significant changes in the preoperative and postoperative logMAR visual acuity, foveal thickness, and the amplitude and implicit time of focal macular ERGs had occurred. The correlation between the foveal thickness and the amplitude of FMERGs was calculated by Spearman correlation coefficient.

This research was conducted in accordance with institutional guidelines and conformed to the tenets of the World Medical Association Declaration of Helsinki. After providing sufficient information on other treatment options including observation only, an informed consent for surgery, the FMERG, and OCT examinations was obtained from each patient.

RESULTS

The BCVAs before surgery and at the final postoperative visit were plotted separately for the three groups (Fig. 1). The OCT images and FMERGs obtained before and 6 months after surgery from 7 representative eyes from group 1 are shown in Figure 2A. The 4 eyes in group 2 and the 2 eyes in group 3 are shown in Figure 2B. All of these eyes had markedly thick retina and very reduced FMERGs preoperatively. After surgery, the OCT-determined foveal thickness was reduced, but the FMERGs did not change significantly. However, 3 eyes with negative-type FMERGs (b-wave/a-wave < 1.0; cases 2, 3R, and 5) preoperatively were converted into positive-type FMERGs (b/a > 1.0) postoperatively. Another 2 eyes (cases 1 and 3L) had an increased b/a ratio postoperatively. In the 4 eyes in group 2, 2 had a slight increase in the b-wave amplitude (cases...
8 and 9) although the 6-months recordings were not made for case 8. In the 2 eyes in group 3, 1 had a marked foveal thickness decrease and the other remained increased. The FMERGs of these 2 eyes were unchanged.

**Visual Acuity**

The mean preoperative logMAR visual acuity was $0.63 \pm 0.07$ (mean ± SD; 20/85 Snellen acuity). The mean postoperative visual acuity gradually improved, but the improvement was not significant at 3 and 6 months postoperatively. At 12 months, the BCVA in 10 of 25 eyes improved by $>0.2$ logMAR units, was unchanged (within 0.2 unit) in 13 eyes, and decreased in 2 eyes by $>0.2$ units.

The mean postoperative logMAR visual acuity at 12 months was $0.47 \pm 0.07$ (20/59 Snellen acuity), which was significantly better than that obtained before surgery ($P = 0.0148$, Wilcoxon signed rank test).

One of 25 eyes (4%) had a decrease of visual acuity of 3 lines (0.3 log units) at 12 months. At the final followup, none of the eyes had a decrease of visual acuity of $\geq 3$ lines. A reduction of acuity of $\geq 3$ lines was 5% in eyes with moderate nonproliferative diabetic retinopathy with macular edema (253 eyes) in the Early Treatment Diabetic Retinopathy Study (ETDRS), and was 8% in eyes with severe nonproliferative and early proliferative diabetic retinopathy (68 eyes). Five percent of the eyes with significant macular edema had $\geq 3$ lines of vision reduction at 12 months in the ETDRS.

To compare the gain in visual acuity in eyes with immediate focal photocoagulation in the ETDRS study, 18 of 25 eyes with acuity not worse than 20/200 and $<20/40$ were selected. In 92 eyes in the ETDRS, the gain in BCVA of 1 line (0.1 log unit) was 39%, whereas 11 of 18 eyes (61%) gained visual acuity of $>1$ line in this study. In the ETDRS, a gain of $>3$ lines was uncommon (3%), however, 39% of eyes in our study improved by $>3$ lines.

The logMAR visual acuities for the three groups are shown in Table 1 and plotted in Figure 3A. Only the 19 eyes that had a PVD created during vitrectomy had a significant increase in logMAR acuity at 12 months ($P = 0.0393$, Wilcoxon signed rank test).

**Optical Coherence Tomography**

Before surgery, OCT demonstrated that the fovea was significantly thicker in all eyes. The mean total foveal thickness (including accumulation of subretinal fluid) was $540.1 \pm 35.4 \mu m$ before surgery and decreased significantly to $307.4 \pm 30.2 \mu m$ at 3 months after surgery ($P < 0.0001$, Wilcoxon signed rank test). The mean foveal thickness (internal-limiting membrane to the outer border of sensory retina) was $486.7 \pm 32.5 \mu m$ before surgery and decreased significantly to $288.7 \pm 30.1 \mu m$ at 3 months after surgery ($P < 0.0001$, Wilcoxon signed rank test). A further decrease in thickness was observed at 6 and 12 months. However, the mean foveal thickness was still decreased after surgery, although the parafoveal thickness remained increased in most cases. (A) FMERGs did not change significantly, although 3 eyes with negative-type FMERGs (b-wave/a-wave < 1.0; cases 2, 3R, and 5) preoperatively converted to the positive-type FMERGs (b/a > 1.0) postoperatively. Another 2 eyes (cases 1 and 3L) had increased b/a ratios postoperatively. (B) In the 4 eyes in group 2, although 6-months data was not available in one eye (case 8; PVD), 2 eyes had very slightly increased b-wave amplitudes (case 8 and 9). In 2 eyes without PVD during surgery, 1 eye showed very decreased foveal thickness in OCT, and another retained increased foveal thickness. FMERGs of these 2 eyes were unchanged.
<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>3 Months</th>
<th>6 Months†</th>
<th>12 Months</th>
<th>Normal Eyes</th>
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<tr>
<td><strong>Visual acuity (logMAR, Snellen), mean ± SE</strong></td>
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<tr>
<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>0.57 ± 0.07 (20/74)</td>
<td>0.58 ± 0.08 (20/76)</td>
<td>0.52 ± 0.08 (20/66)</td>
<td>0.42 ± 0.09* (20/53)</td>
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<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>0.77 ± 0.14 (20/118)</td>
<td>0.62 ± 0.11 (20/83)</td>
<td>0.66 ± 0.13 (20/91)</td>
<td>0.60 ± 0.09 (20/80)</td>
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<tr>
<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>0.96 ± 0.44 (20/182)</td>
<td>0.55 ± 0.15 (20/71)</td>
<td>0.55 ± 0.15 (20/71)</td>
<td>0.65 ± 0.05 (20/89)</td>
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<td><strong>Total foveal thickness, mean ± SE (μm)</strong></td>
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<tr>
<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>548.0 ± 45.7</td>
<td>315.9 ± 38.5***</td>
<td>281.6 ± 30.5***</td>
<td>25.4 ± 36.8***</td>
<td>163.6 ± 3.2 (&lt;i&gt;n&lt;/i&gt; = 29)</td>
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<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>497.5 ± 47.4</td>
<td>263.8 ± 47.4</td>
<td>297.3 ± 89.6</td>
<td>208.3 ± 44.8</td>
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<tr>
<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>550.0 ± 10.0</td>
<td>332.0 ± 36.0</td>
<td>315.0 ± 133.0</td>
<td>382.0 ± 81.5</td>
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<td><strong>Amplitude, mean ± SE (μV)</strong></td>
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<tr>
<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>0.64 ± 0.09</td>
<td>0.51 ± 0.07</td>
<td>0.65 ± 0.09</td>
<td>0.53 ± 0.06</td>
<td>2.10 ± 0.64 (&lt;i&gt;n&lt;/i&gt; = 112)</td>
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<tr>
<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>0.51 ± 0.15</td>
<td>0.42 ± 0.19</td>
<td>0.52 ± 0.33</td>
<td>0.59 ± 0.22</td>
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<tr>
<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>0.60 ± 0.08</td>
<td>0.50 ± 0.06</td>
<td>0.61 ± 0.09</td>
<td>0.53 ± 0.06</td>
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<td><strong>b-wave</strong></td>
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<tr>
<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>0.74 ± 0.09</td>
<td>0.87 ± 0.08</td>
<td>0.98 ± 0.14</td>
<td>1.02 ± 0.13*</td>
<td>4.89 ± 0.94</td>
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<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>1.51 ± 0.53</td>
<td>0.95 ± 0.25</td>
<td>0.97 ± 0.63</td>
<td>1.15 ± 0.30</td>
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<tr>
<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>0.60 ± 0.08</td>
<td>0.50 ± 0.06</td>
<td>0.61 ± 0.09</td>
<td>0.55 ± 0.06</td>
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<td><strong>b/a</strong></td>
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<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>1.9 ± 0.5</td>
<td>2.6 ± 0.6</td>
<td>1.8 ± 0.3</td>
<td>2.2 ± 0.3</td>
<td>2.5 ± 0.6</td>
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<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>2.3 ± 0.5</td>
<td>3.2 ± 1.0</td>
<td>1.8 ± 0.3</td>
<td>2.1 ± 0.7</td>
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<tr>
<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>2.5 ± 0.2</td>
<td>1.8 ± 0.9</td>
<td>1.8 ± 0.3</td>
<td>2.9 ± 0.9</td>
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<td><strong>Implicit time, mean ± SE (ms)</strong></td>
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<tr>
<td>a-wave</td>
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<tr>
<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>27.6 ± 1.1</td>
<td>29.6 ± 1.1*</td>
<td>27.4 ± 1.0</td>
<td>27.3 ± 0.7</td>
<td>21.9 ± 1.7</td>
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<tr>
<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>25.0 ± 1.7</td>
<td>26.6 ± 2.7</td>
<td>28.7 ± 2.2</td>
<td>26.4 ± 1.4</td>
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<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>22.8 ± 1.9</td>
<td>27.5 ± 1.2</td>
<td>29.8 ± 3.1</td>
<td>29.4 ± 0.5</td>
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<td>b-wave</td>
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<td>A (&lt;i&gt;n&lt;/i&gt; = 19)</td>
<td>49.2 ± 1.2</td>
<td>51.2 ± 1.1</td>
<td>48.7 ± 1.2</td>
<td>50.6 ± 1.6</td>
<td>42.8 ± 2.1</td>
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<tr>
<td>B (&lt;i&gt;n&lt;/i&gt; = 4)</td>
<td>51.9 ± 3.0</td>
<td>49.8 ± 2.2</td>
<td>50.5 ± 3.7</td>
<td>47.9 ± 1.3</td>
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<td>C (&lt;i&gt;n&lt;/i&gt; = 2)</td>
<td>49.7 ± 1.1</td>
<td>49.5 ± 2.6</td>
<td>52.7 ± 8.0</td>
<td>49.0 ± 4.7</td>
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</table>

A: surgically induced posterior vitreous detachment (PVD); B: pre-operative PVD; C: without postoperative PVD.

*<i>P</i> < 0.05. **<i>P</i> < 0.001, significance between preoperative and postoperative (Wilcoxon signed rank test).

† Data at 6 months was available for 16 eyes.
The mean amplitude of a-wave was $0.60 \pm 0.08 \mu V$ (mean $\pm$ SEM) before surgery and $0.53 \pm 0.06 \mu V$ at 12 months after surgery. This difference was not significant ($P = 0.6475$, Wilcoxon signed rank test). The mean amplitude of the b-wave was $0.88 \pm 0.11 \mu V$ before surgery and $1.06 \pm 0.13 \mu V$ at 12 months after surgery. The increase in the b-wave amplitude after surgery was not significant until 12 months after surgery ($P = 0.1353$, Wilcoxon signed rank test).

The change in the preoperative amplitude relative to that at 3, 6, and 12 months after surgery (Fig. 4A), and the difference in the preoperative implicit times (Fig. 4B) to that at the same postoperative times are plotted in Figure 4 for the three groups. The mean increase in the b-wave in the 19 eyes in group 1 at 12 months was significant ($P = 0.0297$, Wilcoxon signed rank test). The mean b-wave amplitude in the 4 eyes in group 2 and 2 eyes in group 3 was unchanged or slightly decreased after surgery (Table 1).

The mean b-wave to a-wave (b/a) ratio was $2.1 \pm 0.4$ before surgery and increased to $2.3 \pm 0.3$ at 12 months after surgery. This increase was not statistically significant ($P = 0.2641$, Wilcoxon signed rank test). However, the b/a ratio increased significantly ($P = 0.0284$, Wilcoxon signed rank test) except for 3 eyes with severely reduced a-wave amplitude ($<0.15 \mu V$).

Before surgery, 8 of 23 eyes (35%) had a negative-type FMERG form (b/a < 1.0), while only 2 eyes (9%) showed a negative-type after surgery. This difference was significant ($P = 0.0316$, $\chi^2$ test; Fig. 5A).

The percentage increase in the b-wave amplitude was significantly correlated with the percentage decrease in the mean total foveal thickness ($r = -0.49, P = 0.012$; Fig. 5B), and this decrease was correlated to the change in the logMAR visual acuity ($r = 0.44, P = 0.0261$).

The mean implicit time of the a-wave was $26.8 \pm 0.9$ ms (mean $\pm$ SEM) before surgery and $29.0 \pm 0.9$ ms at 3 months after surgery. This difference was significant ($P = 0.0268$, Wilcoxon signed rank test). The mean b-wave implicit time was $49.7 \pm 1.0$ ms (mean $\pm$ SEM) before surgery and $50.8 \pm 0.9$ ms at 3 months after surgery. The implicit times in a-wave and b-wave returned to the preoperative level at 6 months.

Figure 4B and Table 1 show the change in implicit time in three groups. In both a- and b-wave, the delay in implicit time was noted at 3 months in eyes with creation of PVD, and the change in a-wave was statistically significant ($P = 0.0474$, Wilcoxon signed rank test). This pattern was different from the other two categories, however, it should not be considered significant because the numbers of the eyes in other two groups was very small.

**DISCUSSION**

Our results showed that the preoperative amplitudes and implicit times of all components of the FMERGs were markedly abnormal. The decreased macular retinal functions have been found to be partly reversible in different types of macular disease after vitrectomy,33–38 or photocoagulation.43 However, our results on eyes with DME showed that the visual acuity did not improve significantly until 12 months after vitrectomy, and the amplitude of the FMERG did not change for at least 12 months after surgery. There was, on the other hand, a significant reduction in the thickness in the macular region early after surgery.

Twelve months after surgery, the increase in mean amplitude of the b-wave was significant in eyes with a PVD created.
During surgery. In an earlier FMERG and OCT analysis of the macular area in eyes with choroidal neovascularization (CNV) and an epiretinal membrane (ERM), the recovery of the b-wave of the FMERGs elicited by a 15°-stimulus was mainly correlated with the decrease in parafoveal thickness. In this study, the retinal thickness was measured only at the fovea, and thus it is probably not appropriate to compare the changes in the foveal thickness to the FMERGs elicited by a 15°-stimulus, even though the foveal thickness may be related to the overall morphologic condition of macular area in eyes with DME. In fact, the decreased foveal thickness was related to the final recovery of the b-wave as it has been in eyes with CNV and ERM.

**Figure 4.** Closed circles represent data from group 1 eyes (PVD created during vitrectomy; n = 19), open circles represent data from group 2 (PVD present preoperatively, n = 4), and triangles represent data from group 3 (PVD could not be created during surgery, n = 2). (A) The percentage of change in the amplitude before, and 3, 6, and 12 months after surgery are shown. At 12 months after surgery, the mean amplitude of the a-wave in groups 1 and 2 was larger, whereas that in group 3 eyes was smaller. However, these changes were not statistically significant. At 12 months after surgery, the mean b-wave amplitude increased significantly in group 1 eyes (P = 0.0297, Wilcoxon signed rank test), whereas that in group 2 eyes was not different from that obtained before surgery or even slightly decreased, and that in group 3 eyes decreased. These changes in groups 2 and 3 were not statistically significant. (B) The mean implicit times before surgery, and at 3, 6, and 12 months after surgery are shown. The mean implicit time of the a-wave and b-wave was delayed in group 1 eyes at 3 months after surgery and that of the a-wave was significant (P = 0.0474, Wilcoxon signed rank test), but returned to the preoperative level at 6 and 12 months. The implicit times in the other two groups were too variable to analyze statistically.

**Figure 5.** Closed circles represent the eyes in group 1 (n = 19), open circles represent eyes in group 2 (n = 4), and triangles represent eyes in group 3 (n = 2). (A) The mean b-wave to a-wave (b/a) ratio before and 12 months after surgery. Except for the 3 eyes with severely reduced a-wave amplitude (<0.15 μV), the b/a ratio increased significantly (P = 0.0284, Wilcoxon signed rank test). Before surgery, 8 of 25 eyes (35%) showed a negative-type waveform (b/a < 1.0), whereas postoperatively, only 2 eyes (9%) showed negative-type waveforms. Dotted area is the range of 112 normals. (B) The percentage of increase in b-wave amplitude at 12 months after surgery and the percentage of decrease in the mean total foveal thickness. The correlation was significant (r = -0.49, P = 0.012). During surgery. In an earlier FMERG and OCT analysis of the macular area in eyes with choroidal neovascularization (CNV) and an epiretinal membrane (ERM), the recovery of the b-wave of the FMERGs elicited by a 15°-stimulus was mainly correlated with the decrease in parafoveal thickness. In this study, the retinal thickness was measured only at the fovea, and thus it is probably not appropriate to compare the changes in the foveal thickness to the FMERGs elicited by a 15°-stimulus, even though the foveal thickness may be related to the overall morphologic condition of macular area in eyes with DME. In fact, the decreased foveal thickness was related to the final recovery of the b-wave as it has been in eyes with CNV and ERM.
The increase in the mean b/a ratio 12 months after surgery, and the decreased number of eyes with the negative-type FMERG (b/a < 1.0) resulted from an increase in the b-wave with relatively little change in the a-wave amplitude. One explanation for the association of the b-wave and retinal thickness was discussed previously. Because longstanding functional damage and retinal ischemic change are probably present in the diabetic patient retina, the degree of recovery induced by the morphologic improvement may have been limited. Thus, compared with the OCT-determined retinal thickness, a delay or limited recovery of the b-wave amplitude of the FMERG might be expected.

A shortening of the implicit time of the b-wave was demonstrated after macular surgery in eyes with ERM, CNV, and macular holes (MH),35–39 whereas the delay of the a- and b-wave implicit times was found in eyes with DME during the early postoperative period. One of the reasons for the delayed implicit time early after surgery may be the effect of the separation of the posterior hyaloid during the surgery. In eyes with an MH, a prolonged implicit time was found 6 weeks after surgery only when the internal-limiting membrane (ILM) was peeled.38 In most of the OCT images of Stage 2 and 3 MH, the posterior hyaloid was already separated from the retina in the macular area. Thus, the creation of a total posterior vitreous detachment may not significantly affect macular retinal function, and only patients who had the ILM removed would demonstrate the delayed implicit time after surgery. On the other hand, the posterior hyaloid is completely attached at the macular area as the posterior wall of the vitreous pocket in eyes with DME.41 Detachment of the posterior hyaloid from the macula during surgery may induce the delayed implicit time in a similar manner as ILM peeling in MH surgery.38,41

In subhuman primates, the creation of a PVD leads to morphologic damage to the nerve fiber layer as demonstrated by immunofluorescent staining. This suggests that a posterior hyaloid detachment can affect retinal function.42 The delay in implicit time recovered 6 months after vitrectomy for DME and surgery in this study and also after MH surgery with ILM removal in a previous study.48 We cannot compare the three groups of eyes because the number of cases was very small, however, a significant delay in the early postoperative period was noted only in group 1 eyes. Another reason for the prolonged implicit time is likely to be retinal fragility, the result of metabolic and/or osmotic changes from surgery. Analysis of multifocal ERGs after vitrectomy for diabetic macular edema demonstrated delays in the responses which later recovers.43

The good anatomic recovery from the edema probably prevented further deterioration of vision in many of our patients with DME, however, the time course and the extent of recovery in the visual acuity and FMERGs may be further delayed and limited. The limitations of this study include the small number of cases, and the use of 4 eyes from 2 patients as individual cases. In addition, the postoperative period was limited to 12 months and additional functional recovery may be expected if an improved anatomic structure is maintained. Another significant weakness of this study was the lack of controls. A comparison with the ETDRS suggested that the percentage of eyes that had improved vision of ≥3 lines was higher in this study. However, because of the small number of eyes we cannot come to a strong conclusion. The comparison of results from the different methods was not planned, but it was necessary to point out the disparity of anatomic recovery and the delayed and limited improvement of retinal function that takes more than one year.

For future studies, the effect of a longer followup periods should be examined, and the effect of ILM removal on macular function with or without indocyanine green staining should be evaluated. In addition, intravitreal steroid injection for refractory DME has been reported recently and needs further study.44–46

In conclusion, the time course and the degree of recovery of the morphologic and functional characteristics of the macula were different after vitrectomy in eyes with DME, i.e., there was a rapid and significant recovery of foveal thickness, but the visual acuity improved gradually and was significantly better only after 12 months. The increase in the mean b-wave amplitude of the FMERGs in eyes with a surgically created PVD was significant at 12 months. The increase in the b-wave was correlated to the decreased foveal thickness. This may suggest that part of the functional recovery was attributable to the decreased retinal thickness and the absorption of the subretinal fluid. However, the damage to the macular tissue may not recover significantly.

References


