Assessment of factors affecting flicker ERGs recorded with RETeval from data obtained from health checkup screening

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Abstract

The purpose of this study was to determine the ocular, sex- and age-specific, anthropometric, and hematologic factors that affect the implicit times and amplitudes of the flicker ERGs recorded with the RETeval system from individuals 40- to 89-years-of-age. Flicker ERGs were recorded with the RETeval system from 330 individuals who had normal fundus and OCT images. Univariate and multivariate regression analyses were performed to identify factors associated with the implicit times and amplitudes of the RETeval flicker ERGs. Univariate regression analyses showed significant correlations between the implicit times and the BCVA, age, axial length, blood sugar level, and BUN in both eyes. Multivariate regression analyses identified age and axial length as two independent factors that were significantly correlated with the implicit times of the RETeval flicker ERGs. Univariate regression analyses also showed significant correlations between the amplitudes and age, platelet count, HDL level, and creatinine level in both eyes. However, smoking habits, body mass index, and blood pressure were not correlated with the RETeval flicker ERGs. We conclude that age and some ophthalmologic and hematologic findings except for anthropometric findings were suggested to significantly affect the measurements of the RETeval flicker ERGs.

Introduction

Full-field electroretinograms (ERG) is an essential clinical test that is used to evaluate the retinal function in patients with various retinal diseases. Several protocols for the different testing procedures have been recommended by the International Society of Clinical Electrophysiology of Vision (ISCEV)[1]. Among them is the protocol for recording the full-field flicker ERGs that are evoked by 30 Hz stimuli for the assessment of the photopic pathway of the retina. Flicker ERGs represent the response of the cone pathway because rod photoreceptors cannot respond to the frequencies above about 15 Hz[2]. Flicker ERGs are a relatively simple method to assess the photopic pathway and can be completed the recording within 10-20 seconds and does not require dark-adaptation.

A new ERG recording system called the RETeval system (LKC Technologies, Inc., Gaithersburg, MD, USA) was recently introduced, and it has drawn the attention of clinicians because of its ease of use. This system is equipped with a small handheld Ganzfeld dome for eliciting the ERGs, and the ERGs are picked-up by a single-use, skin strip electrodes. This strip contains the active, the reference, and ground electrodes. The RETeval system can record ERGs without mydriasis because the device delivers stimuli with constant retinal luminance (photopic Td-s) by adjusting the luminance (photopic cd-s/m^2) to compensate for changes in the pupillary area (mm^2) in real time. These conditions make the recording of the flicker ERGs easier and more convenient for the patients and clinicians. Therefore, flicker ERGs utilizing RETeval system has been applied not only to evaluate retinal diseases; e.g. central retinal vein occlusion (CRVO)[3,4], blue-cone monochromatism (BCM)[5], and retinopathy of prematurity (ROP)[6], but also for the screening of retinal diseases, e.g., for diabetic retinopathy[7–11].

To use RETeval as a screening tool, it is necessary to determine the factors affecting the amplitudes and implicit times of the RETeval flicker ERGs in normal eyes. The results of earlier studies have shown the influence of the axial length and pupillary area on the different components of the RETeval flicker ERGs[12,13]. However, the correlations of the RETeval flicker ERGs to the results of hematologic tests and anthropometric data of normal individuals have not been determined.

Thus, the purpose of this study was to determine the significance of the correlations between the amplitudes and implicit times of the RETeval flicker ERGs and the results of the hematologic tests and the anthropometric data of the participants. To accomplish this, we recorded RETeval ERGs from a large number of individuals undergoing a health checkup screening. We analyzed the factors affecting the amplitudes and implicit times of the RETeval flicker ERGs.

Results

The main demographic information of the 333 right eyes and 332 left eyes of the subjects is shown in Table 1. The results of the 23 hematologic tests are shown in Table S1 in the supplementary information section. The distributions of the implicit times and amplitudes of the fundamental component of the flicker ERGs are shown in Fig. S1 in the supplementary information. The reference values were calculated by the mean ± 2 SD method, and those for the implicit times were 32.0 ± 3.2 ms for the right eyes and 32.0 ± 3.0 ms for the left eyes. The mean amplitude was 9.75 ± 6.4 μV for the right eyes and 9.75 ± 6.2 μV for the left eyes.

Table 1
Demographic information

	Right eyes	Left eyes
Number of eyes	333	332
Age (years)	62.5 ± 9.5 [40-89]	62.5 ± 9.5 [40-86]
Sex (Male/Female)	142/191	144/188
BCVA (logMAR)	0.048 ± 0.18 [-0.18-1.0]	0.054 ± 0.19 [-0.18-1.0]
IOP (mmHg)	13.7 ± 2.4 [6.3-20.7]	13.7 ± 2.4 [8.0-20.7]
Axial length (mm)	23.8 ± 1.2 [20.72-28.08]	23.8 ± 1.2 [20.82-27.62]
Pupillary area during ERG (mm^2)	5.65 ± 2.03 [1.59-31.8]	5.56 ± 2.68 [1.59-31.8]
Implicit times of flicker ERGs (msec)	32.0 ± 1.6 [27.3-37.5]	32.0 ± 1.5 [27.2-36.4]
Amplitudes of flicker ERGs (µV)	9.75 ± 3.20 [1.8-20.4]	9.75 ± 3.11 [3.5-18.6]
Height (cm)	157.8 ± 8.5 [136.0-181.9]	158.0 ± 8.4 [136.0-181.9]
BMI (kg/m^2)	23.5 ± 3.3 [15.7-34.8]	23.7± 3.4 [15.7-40.9]
sBP (mmHg)	129.7 ± 20.7 [82-190]	129.6 ± 20.6 [86-190]
dBP (mmHg)	75.8 ± 13.9 [43-133]	75.4 ± 13.8 [49-133]
average BP (mmHg)	93.5 ± 15.2 [56.0-149.7]	93.5 ± 15.2 [62.0-149.7]
Brinkman index (cigarettes years/day)	284 ± 414 [0-2400]	280 ± 393 [0-2000]
IMT (mm)	0.9 ± 0.5 [0.4-3.1]	1.0 ± 0.6 [0.4-4.1]
BS (mg/dL)	88 ± 13 [60-156]	89 ± 14 [61-160]
HDL (mg/dL)	59.8 ± 14.5 [34-125]	59.8 ± 14.5 [32-125]
BUN (mg/dL)	14.6 ± 3.7 [5.4-29.2]	14.8 ± 3.9 [5.4-29.2]
Plt ($10^4/\mu L$)	21.9 ± 4.9 [9.3-39.3]	21.9 ± 5.0 [9.3-41.7]
Cre (mg/dL)	0.75 ± 0.16 [0.49-1.55]	0.76 ± 0.17 [0.43-1.55]

BCVA, best-corrected visual acuity; IOP, Intraocular pressure; BMI, Body mass index; sBP, Systolic blood pressure; dBP, Diastolic blood pressure; IMT, Intima Media Thickness; BS, Blood sugar; HDL, High-density lipoprotein; BUN, Blood urea nitrogen; Plt, Platelet; Cre, Creatinine.

Data are expressed as the means ± standard deviations [range].

Correlations between implicit times of flicker ERGs and other health checkup factors

First, we determined the relationship between the implicit times of the flicker ERGs and the 35 health checkup measures including the ophthalmic, anthropometric, and hematologic findings. The results of univariate regression analysis are shown in Table S2 in the supplementary information. The results of the factors that were significantly correlated with the implicit times of the RETeval flicker ERGs at least one eye are summarized in Table 2. The IOP, BMI, HbA1c, IMT, and uric acid levels were significantly correlated with the implicit times of one eye, and the BCVA, axial length, age, blood sugar levels, and BUN were significantly correlated with the implicit times of both eyes (Table 2). The values of the other anthropometric and hematologic factors were not significantly correlated with the implicit times of either eye.

Table 2
Univariate regression analysis between implicit times and explanatory variables

	Right eyes		**Left eyes**	
	Correlation coefficient (r)	***p*-value**	**Correlation coefficient (r)**	***p*-value**
BCVA (logMAR)	0.10	0.049*	0.18	<0.001*
IOP (mmHg)	0.11	0.02*	0.045	0.407
Axial length (mm)	0.20	<0.001*	0.18	0.001*
Age (years)	0.24	<0.001*	0.25	<0.001*
BMI (kg/m^2)	0.077	0.092	0.10	0.039*
IMT (mm)	0	0.319	0.10	0.037*
HbA1c (%)	0.11	0.026*	0.032	0.254
BS (mg/dL)	0.12	0.015*	0.11	0.04*
BUN (mg/dL)	0.12	0.013*	0.15	0.004*
Uric acid (mg/dL)	0.12	0.014*	0.077	0.082

BCVA, best-corrected visual acuity; IOP, intraocular pressure; BMI, Body mass index; IMT, Intima Media Thickness; HbA1c, Hemoglobin A1c; BS, Blood sugar; BUN, Blood urea nitrogen.

*means and *p*-value <0.05

Then we determined the items that were significantly correlated with the implicit times of the flicker ERGs of both eyes. The coefficients of correlation between each explanatory variable and the implicit times were calculated. We confirmed that all of the absolute values of the coefficients of correlation were less than 0.5 ($|r|<0.5$), and we concluded there was no correlation strong enough to require consideration of multicollinearity for each explanatory variable (see Table S3 in supplementary information). These explanatory variables were then tested by multivariate regression analyses. Consecutive multivariate linear regression analyses identified two independent factors, the age (p <0.001) and the axial length (p <0.001), as independent factors that were significantly correlated with the implicit times (Table 3).

Table 3
Multivariate regression analysis between implicit times and explanatory variables

	Right eyes		Left eyes	
	partial regression coefficient (β)	***p*-value**	**partial regression coefficient (β)**	***p*-value**
BCVA (logMAR)	-0.049	0.919	0.67	0.132
Axial length (mm)	0.40	<0.001*	0.35	<0.001*
Age (years)	0.052	<0.001*	0.041	<0.001*
BS (mg/dL)	0.0097	0.114	0.0094	0.097
BUN (mg/dL)	0.0050	0.834	0.018	0.404

BCVA, best-corrected visual acuity; AL, Axial length; BS, Blood sugar; BUN, Blood urea nitrogen.

*means *p*-value <0.05

Correlations between amplitudes of flicker ERG and other health checkup factors

The results of univariate regression analysis for the flicker ERG amplitudes and the 35 items of the health checkup are shown in Table S4 in supplementary information. Of these, the items which were significantly correlated with the amplitudes of the flicker ERGs in at least one eye are summarized in Table 4. Total Chol, γGTP, and BUN were significantly correlated with the amplitudes of only one eye, and the age, Plt count, HDL level, and Cre were significantly correlated with the two eyes. The correlation coefficients between each explanatory variable were calculated, and we confirmed that all of the absolute values of correlation were less than 0.5 ($|r|<0.5$). Thus, we concluded that there was no correlation strong enough to require consideration of multicollinearity for each explanatory variable (see Table S5 in supplementary information). Consecutive multivariate linear regression analyses did not identify any independent factor which can affect the amplitudes of the fundamental components of the RETeval flicker ERGs of both eyes (Table 5).

Table 4
Univariate regression analysis between amplitudes and explanatory variables

	Right eyes		**Left eyes**	
	Correlation coefficient (r)	***p*-value**	**Correlation coefficient (r)**	***p*-value**
Age (years)	-0.16	0.003*	-0.13	0.016*
Plt (10^4/μL)	0.12	0.014*	0.11	0.026*
Total Chol (mg/dL)	0.14	0.012*	0.077	0.087
γGTP (U/L)	0.084	0.062	0.095	0.043*
HDL (mg/dL)	0.11	0.032*	0.095	0.045*
BUN (mg/dL)	-0.071	0.097	-0.11	0.02*
Cre (mg/dL)	-0.15	0.004*	-0.11	0.024*

Plt, Platelet count; Total Chol, Total cholesterol; γGTP, γ- glutamyl transpeptidase; HDL, high density lipoprotein cholesterol; BUN, Blood urea nitrogen; Cre, Creatinine.

*means *p*-value <0.05

Table 5
Multivariate regression analysis between amplitudes and explanatory variables

	Right eyes		**Left eyes**	
	partial regression coefficient (β)	***p*-value**	**partial regression coefficient (β)**	***p*-value**
Age (years)	-0.039	0.040*	-1.5	0.142
Plt (10^4/μL)	0.067	0.069	1.7	0.087
HDL (mg/dL)	0.020	0.118	1.5	0.144
Cre (mg/dL)	-1.8	0.123	-1.0	0.319

Plt, Platelet; HDL, high density lipoprotein cholesterol; Cre, Creatinine.

*means *p-value*<0.05

Discussion

The results of the univariate regression analysis showed that the blood sugar level, BUN, BCVA, age, and axial length were significantly associated with the implicit times of the RETeval flicker ERGs. In addition, multivariate regression analyses identified age and the axial length as independent factors that were significantly correlated with the implicit times of both eyes. The analyses also showed that the age, Plt counts, HDL levels, and Cre were significantly associated with the amplitudes of the RETeval flicker ERGs.

Because other studies have been reported that the smoking habits (Brinkman index), BMI, and blood pressure were correlated with the ocular findings[14–19], we examined whether these items might also be significantly correlated with the different components of the flicker ERGs recorded with the RETeval system. Our analyses showed that these factors were not significantly correlated with the different components of the flicker ERGs.

Our results showed that the mean implicit time of the flicker ERGs was 32.0 ± SD ms which was shorter than the 33.3 ± 1.3 ms or 33.2 ms reported in earlier studies[7,12]. The exact cause for this difference was not determined but a shorter axial length and smaller pupil size might be related to this difference. This is because the earlier study suggested that these factors tended to cause shorter implicit times of the flicker ERGs recorded with a RETeval flicker ERG system[12].

The mean amplitude of the flicker ERGs was about 70% of that of earlier studies recorded under the same stimulus conditions. This lower mean amplitude may be due to the difference in the age of the subjects. In the earlier study, the subjects were between 20- and 29-years-old[12], while our data were obtained from those who were ≥40-years. In support of this, Birch et al. reported that the amplitudes of the conventional flicker ERGs were smaller and the implicit times were prolonged in subjects who were about 70-years compared to those of around 20-years[20]. Our results also suggested that the age affected the amplitudes and implicit times. These data may reflect the decline of the retinal function by the aging process.

The significant correlation between the axial length and the implicit times of the RETeval flicker ERGs has also been reported earlier[12]. The exact cause for the longer implicit times in eyes with longer axial lengths has not been determined, but Kato et al. suggested three possible factors[12]; a decrease in the retinal illuminance in eyes with longer axial lengths, an increase in the distance between the electrical signals in the retina and the electrodes, and a change in the retinal function caused by the stretching and thinning of the retina associated with the axial length elongation[21–26].

Although the multivariate regression analysis did not find a significant correlation between the implicit times and the BCVA, BS, and BUN, this may be related to the implicit times of the flicker ERGs. Basically, we studied participants with normal OCT and fundus findings, and therefore the relations between the BCVA and implicit times of the flicker ERGs suggest two possibilities; one is a subclinical damage of the retina and another is the presence of cataracts which cause a reduction of the BCVA and a delay of the implicit time due to a reduction of the flash intensity as reported[27].

Earlier studies have shown that the prolongation of the implicit times of the flicker ERGs recorded by RETeval was a useful marker of diabetes diabetic retinopathy[7,28,29]. In the current study, we analyzed only 23 participants whose HbA1c was ≥6.5% which is a diagnostic criterion for diabetes[30]. The correlation between HbA1c and the implicit time of the RETeval flicker ERG was found only in one eye possibly because of this small sample size of the participants of diabetes. On the other hand, the significant correlation between the blood sugar level and the implicit times in both eyes in the univariate regression analyses (the blood sugar levels are plotted against the implicit times of the fundamental component of RETeval flicker ERGs in Fig. S2 in supplementary information) suggested that a transient elevation of blood sugar level may lead to a delay in the implicit times even in non-diabetic subject. In this study, the BUN level, which is related to renal function, was correlated with the implicit times of the flicker ERGs recorded with the RETeval system. However, our study did not include participants with severe renal failure (estimated glomerular filtration rate: eGFR <29). Thus, the reason for the significant correlation between implicit times and BUN was not definitive determined, but the correlation between BUN and age (r = 0.39: see Table S3 in supplementary information) might have affected the results.

We did not expect the Plt count, Cre level, and HDL level would be significantly correlated with the amplitudes of the flicker ERGs in the univariate regression analyses. These factors were not highly correlated with age (r = -0.24, r = 0.25, r = -0.1 respectively: see Table S5 in supplementary information), therefore we believe that they are independent factors that affected the flicker ERGs. The variance of the amplitudes was larger than that of the implicit times; the relative standard deviation (RSD) was 1.6/32 =0.05 (right eyes) and 1.5/32 =0.05 (left eyes) for the implicit times, and the RSD was 3.2/9.75 = 0.33 (right eyes) and 3.2/9.75=0.33 (left eyes) for the amplitudes. The reproducibility should be checked by another data set in the future.

There are several limitations in this study. First, the participants were all ≥40 years who lived in a relatively rural area where many people had jobs in agriculture or fishing. The difference of the life style from people in an urban environment, in which myopia is prevalent due to display work or near work[31], would be expected to affect the results. Second, in the current study 36 explanatory variables were analyzed. Considering the possibility of β-errors in both the Bonferroni and Holm methods, these corrections were not used in the present analysis. Instead, we focused on the correlation found in both eyes in univariate regression analysis. Future analyses of a larger number of participants are needed to confirm the correlation detected in this study. However, the explanatory variables of age and axial length were significantly correlated with the implicit times even when the Bonferroni correction was used.

In conclusion, the influence of axial length, age, and possibly the BCVA, BS, and BUN on the implicit times of RETeval flicker ERG should be considered when evaluating the retinal function in the health checkup screenings. In addition, the amplitudes might be affected by the age, Plt count, Cre, and HDL levels, although it is not appropriate to predict the effect of anthropometric findings and lifestyle habits on retinal function.

Methods

Study design

This was a prospective, single center study. All of the procedures conformed to the tenets of the World Medical Association's Declaration of Helsinki and were approved by the Nagoya University Hospital Ethics Review Board. The subjects were volunteers who attended a basic health checkup screening that was supported by the local government of Yakumo town in 2015. All patients signed a written informed consent form after they were provided with information on the procedures to be used. This Yakumo Study was conducted in the town of Yakumo located in a rural area of southern Hokkaido, Japan. All subjects aged ≥40 years underwent assessments of not only the ophthalmic parameters but also anthropometric assessments, and hematologic tests.

Protocols for general examinations related to current study

Fasting blood samples were collected through venipuncture and centrifuged within an hour of the collection. The serums were stored at −80° C until the assay was performed. Routine biochemical analyses were performed in the laboratory of the Yakumo Town Hospital. Anthropometric measurements of the body height and weight were obtained and used to calculate the body mass index (BMI, kg/m^2). Ultrasound examinations were performed to measure the intima-media thickness (IMT) and to determine plaque formation in the carotid arteries as described[32–35]. The mean value of the right and left max IMT was used for the statistical analyses.

Protocols for Ocular Examinations

The best-corrected visual acuity (BCVA) was measured by an automatic vision tester (Nidek, NV-350, Gamagori, Aichi, Japan) with correcting eyeglasses based on the refractive error measured by the auto Ref/Keratometer (Topcon, KR-8900, Tokyo, Japan). Anterior segment examinations were performed by slit-lamp biomicroscopy by ophthalmologists. Color fundus photographs were recorded with a nonmydriatic fundus camera (Topcon TRC-NW8, Tokyo, Japan), and the macular morphology was determined by Optical Coherence Tomography (OCT) (Nidek, RS-3000, Gamagori, Aichi, Japan). All of the data were evaluated by ophthalmolgists. The axial length was measured by partial coherence interferometry (Carl Zeiss Meditec, Inc. IOLMaster, Dublin, CA, USA). The intraocular pressure (IOP) was measured by noncontact tonometry (Nidek, NT-530P Gamagori, Aichi, Japan).

The flicker ERGs were recorded with the RETeval system (LKC Technologies, Gaithersburg, MD, USA) without mydriasis and were elicited by white stimuli of 8 Td-second/m^2. No background illumination was used. The frequency of the flicker stimulus was 28.306 Hz. The diameter of the pupil was measured automatically in real-time by the RETeval system and the diameter at which equilibrium was reached was adopted. The fundamental component of the fliekcer ERGs were automatically measured and displayed by the RETeval system using a special algorithm based on discrete Fourier transformation and cross-correlation analysis (see Fig. 1 for details) [36].

Subjects

A total of 497 individuals took part in the ocular examinations. Of these, the flicker ERGs of 443 right eyes and 446 left eyes were reliably recorded with the RETeval system. Among these subjects, 110 right eyes and 114 left eyes were excluded because of known ocular diseases or abnormal findings in the color fundus photographs or OCT images. The reasons for the exclusion were; glaucoma or glaucoma suspect (46 right eyes, 55 left eyes), drusen (20 right eyes, 17 left eyes), age-related macular degeneration (11 right eyes, 8 left eyes), epiretinal membrane (11 right eyes, 10 left eyes), and others (26 right eyes, 35 left eyes); including duplication of disease. In the end, the findings in 333 right eyes and 332 left eyes were used for the statistical analyses.

Statistical analyses

We analyzed the data of the general condition including the sex, age, height, weight, systolic blood pressure (sBP), diastolic blood pressure (dBP), Brinkman index, and hematologic test of 23 factors. We analyzed the data of the ophthalmic examinations including the BCVA, IOP, AL, radius of the pupil, and the implicit times and amplitudes of the flicker ERGs (see Table S6-8 in supplementary information for details). For the BCVA, the decimal values were converted to the logarithm of the minimum angle of resolution (logMAR) units for the statistical analyses. Categorical variables that were not originally quantitative variables, such as the sex, were analyzed after One-Hot encoding to convert them into dummy variables: the categorical data "Sex" was replaced by two new features, "Sex-male" and "Sex-female" and quantified by giving Sex-male = 1 and Sex-female = 0. The body Mass Index (BMI) was calculated from the weight and height using the equation:

$$\mathrm{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2} = 10000 \times \frac{\text{weight (kg)}}{\text{height (cm)}^2}$$

The average BP was calculated from the systolic and diastolic blood pressures using the equation:
$\text{average BP} = \text{Diastolic BP (mmHg)} +$

$$\frac{\text{(Systolic BP (mmHg) - Diastolic BP (mmHg))}}{3}$$

To assess the effects of the smoking habits, we calculated the Brinkman index as follows:

$$\text{Brinkman index} = \text{Number of cigarettes smoked/day} \times \text{Years of smoking}$$

The pupillary area was calculated from the radius of the pupil using the equation:

$$\text{pupillary area } (\mathrm{mm}^2) = \pi \times (\text{radius of pupil (mm)})^2$$

The coefficients of correlation were used to determine how strong the relationship was between each pair of variables. Univariate and multivariate regression analyses were used to determine the factors which were significantly associated with the implicit times and amplitudes of the fundamental component of the flicker ERGs. The implicit times and amplitudes of the fundamental component of the flicker ERGs were used as the response variables. The explanatory variables included the age, sex, height, BMI, systolic and diastolic BPs, average BP, Brinkman index, IOP, axial length, BCVA, pupillary area, and items of the hematologic test. The coefficients of correlation (r) and *p*-values were calculated for the univariate regression analysis, and standardized partial regression coefficient (β) and *p*- values were calculated for the multivariate linear regression analyses for the independent variables. The results were considered statistically significant when the *p*- values were <0.05. To repeat the linear regression analyses of the 35 items, it was recommended to lower the *p*- values less than 0.05 using the Bonferroni or Holm methods to counteract the problem of multiple comparisons. However, these corrections resulted in the determination of the null hypothesis at a significance level of less than 0.0014, which would eliminate most of the factors affecting the flicker ERGs. Therefore, we did not adjust the results by the Bonferroni or Holm methods, instead the items with *p*- values<0.05 in both eyes were further analyzed (There were 294 eyes in which both eyes were employed, and the correlation coefficient of implicit times in these cases was 0.89, and of amplitudes was 0.85). These analyses were performed with scikit-learn = 0.24.0 (https://scikit-learn.org/stable/install.html) based on python = 3.6.7 (https://www.python.org/downloads/release/python-367/).

Declarations

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Author contributions

S.U. and T.I. wrote the main manuscript. S.U. and T.I. acquired the data. S.U. and T.I. prepared the figures and tables. S.U., T.I., T.K, S.Y., Y.K, J.O., S.O., Y.I., H.T., and K.M.N. worked for the analysis and interpretation of data. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

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Figures

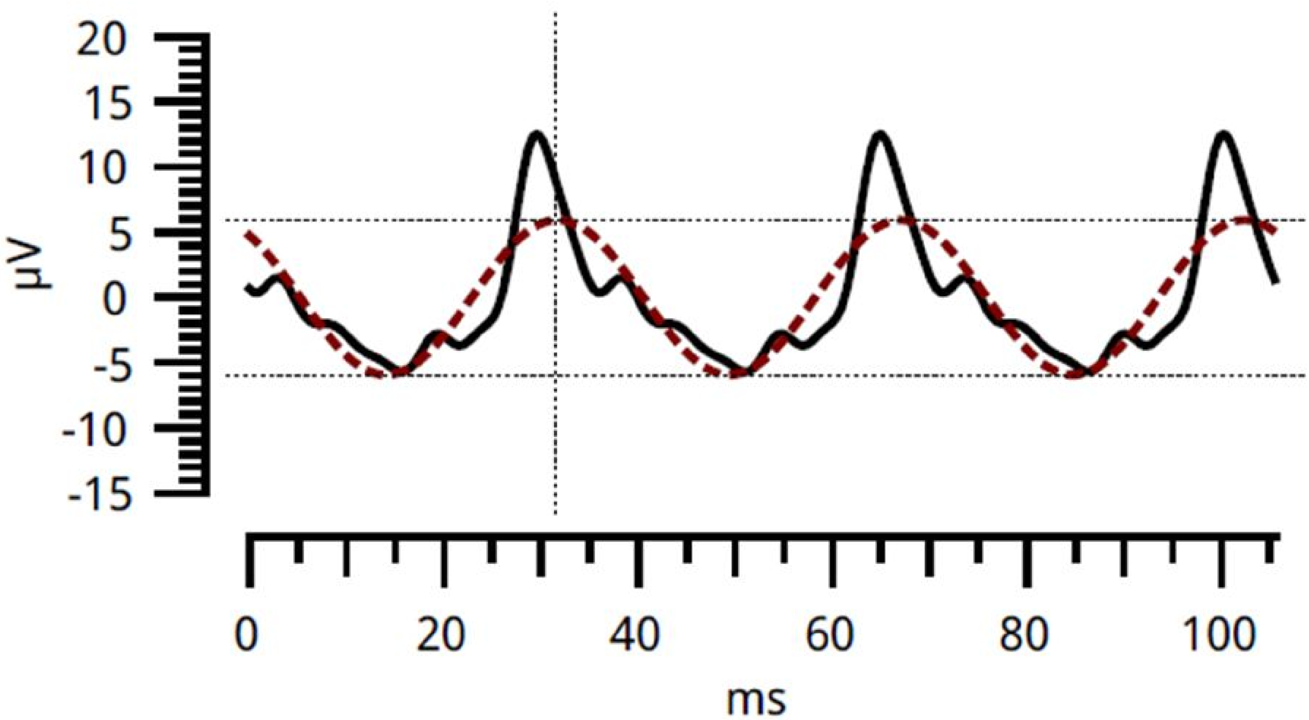

Figure 1

An example of the flicker ERG recorded by the RETeval system. Two flicker ERG waveforms of the fundamental component (colored dotted line) and the reconstructed flicker ERG waveform using the first eight harmonics (solid black line) are presented in this system.

Supplementary Files

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