FOURIER DESCRIPTORS FOR CHARACTERIZING WAVEFORMS OF THE
PUPIL LIGHT RESPONSE TO CHROMATIC STIMULI

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ABSTRACT
The waveform of the Pupil Light Response (PLR) to chromatic stimuli is a key point in non-invasive assessment of the activity of the melanopsin-associated photoreceptive system, which is considered as the basis for proposing new diagnostic procedures in ophthalmology. The article shows a procedure for a quantitative description of the PLR waveform for both eyes across stimuli conditions using Fourier descriptors, and another procedure for emphasizing normal and abnormal pupil responses using Multi Dimensional Scaling. To determine the efficiency of this procedure as a clinical diagnostic, a set of PLR data for healthy subjects and patients with Age-Related Macular Degeneration (ARMD) were analysed. The PLR data were obtained during a classical experiment used to measure melanopsin-associated photoreceptive system activity. The results confirmed the diagnostic utility of the proposed procedures for discriminating between normal and abnormal PLR responses.

KEY WORDS
Pupil Light Reflex, Waveform morphology, Fourier descriptor, Dissimilarity, Multidimensional Scaling

1. Introduction

The pupil light reflex (PLR) to chromatic stimuli has been discussed as a possible clinical diagnostic procedure which allows for differentiation between disorders effecting photoreceptors and those affecting retinal ganglion cells [3]. This is a result of the discovery of a melanopsin-associated photoreceptive system (intrinsically photosensitive retinal ganglion cells – ipRGCs) in the human retina, in addition to the conventional rod-cone system [1, 2]. This system conveys photopic information for ancillary visual functions, such as pupillary light reflex and circadian photo-entrainment. To reveal the sensitivity and activity of these cells the PLR waveform has often been studied [4, 12]. It was found that there are parallels between the behaviour of these retinal ganglion cells and the pupil response to chromatic stimuli (with regulated wavelengths and photopic levels). PLR observations in clinical conditions are based on responses to light pulses. Therefore, to propose PLR as a diagnostic procedure, a simplified metric for single PLR waveforms is required.

The authors have already proposed such a procedure based on Fourier descriptors. The procedure proposed allows for extracting feature vectors of PLR waveforms for four stimuli conditions, and for determining the metrics to compare these waveforms. Additionally, another procedure for emphasizing stimuli and subject differences using Multi Dimensional Scaling (MDS) which uses the descriptors as waveform features was proposed [7]. The usefulness of the proposed procedure was confirmed using PLR data for four stimuli conditions recorded from healthy, young subjects.

In this article, the modification of the extraction procedure is proposed to detect patient subjects. The new procedure allows for a comparison of the pupil responses of the left and right eyes for four types of stimuli conditions because the differences in responses between the two eyes may indicate a degree of abnormality, as most patients have one eye which is healthy. The effectiveness of the procedure for differentiating normal and abnormal pupil responses was presented using data from ARMD patients and healthy subjects.

2. Material and method

The pupil responses were observed and analyzed using the following procedure. The PLRs of a 10 sec. light pulse in healthy subjects and patients are presented in Fig. 1.a. and Fig. 1.b. respectively.
1. a) PLR for a healthy young subject (l-left eye, r-right eye), 1.b) PLR for a classic type of patient (D-diseased eye, N-healthy eye)

2.1 Experimental procedure

A conventional experiment used for the determination of a melanopsin-associated photo-receptive system was conducted. In the experiment, a long wavelength (635 nm bandwidth) red light and a short wavelength (470 nm bandwidth) blue light were used at 2 different light intensities (10 cd/m² and 100 cd/m²). In this paper, the four conditions are defined as follows: r10 (long wavelength – low light intensity), r100 (long–high), b10 (short–low), and b100 (short–high). Subjects were 6 healthy individuals, aged 20-21 years old and 6 patients with ARMD, aged 59-86 years old. PLR was recorded using Hamamatsu Iriscorder Dual equipment at a sampling rate of 30 Hz. All subjects agreed to the experimental procedure before it commenced. The measurements were taken in a darkened room, after a 5 min darkness adaptation period. For each subject, characteristics for both left and right eyes were recorded. In comparing Fig. 1.a. and Fig. 1.b., the constrictions of light pulses for a classic type of patient are smaller than for a healthy, young subject. In particular, both constriction amplitude and duration for the r10 condition are smaller than for the others.

2.2 Analysis method

The feature vectors for PLR waveforms were extracted from the proposed procedure (Nakayama et al. 2010) using the Discrete Fourier Transform (DFT) procedure [9, 14]. PLRs were sampled as discrete signals. Here, the length N of a discrete signal is defined as x(n), which is sampled at time t with spacing Δ. The signal x(n) can be noted as an equation using DFT [6].

\[
x(n) = a_0 + \sum_{k=1}^{N/2} \left( a(k) \cos \left( \frac{2\pi k t(n)}{N\Delta} \right) + b(k) \sin \left( \frac{2\pi k t(n)}{N\Delta} \right) \right)
\]

\[
a_0 = X(1)/N
\]

\[
a(k) = 2re\{X(k + 1)/N
\]

\[
b(k) = 2im\{X(k + 1)/N
\]

The PLR waveforms can be represented using coefficients a0, a(k) and b(k) with periodical cosine and sine functions. To present the features of the waveform, the magnitude of the coefficients is preferred, because coefficient b(k) is the imaginary part of a value. The magnitudes of coefficients, including a0, FDi (i = 0, . . . , N/2 − 1) are used as Fourier descriptors (FD).

In general, the component FDo, a0 in the equation, shows the DC component of the signal, corresponding to the signal amplitude. The remaining frequency components describe the waveform shape of the signal. Also, features are affected by individual factors, so that a standardized feature is preferred in the vector as follows [13]:

\[
f = [FD_0, FD_1, \cdots, FD_{N/2 - 1}]
\]

Additionally, as an appropriate number of components for the feature vector represent the characteristics of most signals only at the low-order values of 4 or 5 FDs [9], 4 components are extracted as FDs in this paper.

3. Results

3.1. Fourier descriptors

According to the analytical procedure in the above section 2.2, the features of PLRs for a patient subject (Left eye: healthy (abbreviation N), Right eye: diseased (abbreviation D)) were extracted. The actual calculations were conducted using MATLAB (Mathworks, Inc.). First, FDs were extracted in order to compare the waveform amplitude as follows:
For $FD_0$ values, the values for both of the b100 conditions are the largest, and the values for both r10 conditions are the smallest. The order of these values coincides with the previous studies [4]. The $FD_0$ values were extracted for all subjects and are illustrated in Fig. 2. The order of these values is maintained across most subjects even for patient subjects, though individual differences are observed. In comparing Fig. 1.a. and Fig. 1.b., the relationships between PLRs for the four conditions are different between healthy subjects and patient subjects, though the orders of $FD_0$ components are almost similar to those in Fig. 2.

Feature vectors are extracted for every waveform using a vector format ($f$). For example, the set of vectors for a patient subject (N-normal eye, D-disease eye) is shown as follows:

- For r10 conditions:
  - $FD_{r10,N} = [0.6526, 0.2313, 0.2302, 0.1418]$
  - $FD_{r10,D} = [0.5444, 0.2211, 0.2142, 0.1731]$

- For b10 conditions:
  - $FD_{b10,N} = [0.2345, 0.5598, 0.2886, 0.2581]$
  - $FD_{b10,D} = [0.5891, 0.3743, 0.2537, 0.1960]$

According to the set of features, the vectors for b100 and r100 (high photopic level) may be similar, but the vectors for r10 and b10 (low photopic level) are relatively different between a normal eye and a disease eye, respectively.
All results for the eight conditions and 6 healthy and 6 patient subjects are mapped in Fig. 4. The stimuli conditions make clusters in response to the configurations of stimuli, as shown in Fig. 3 where all subjects’ data is mapped in a similar style. However, plots for patient subjects are mapped in a different area. In particular, the values for patient subjects deviate from the norm in dimension 3. Even the plots of normal eyes for patient subjects are more widely distributed. The most patient features show the different tendency. All subjects can be configured using their own individual two dimensional information, as shown in Fig. 5. In this figure, the value of dimension 3 clearly indicates the differences between healthy subjects and patient subjects. The healthy subjects produce a cluster in the lower area, and the patient subjects are distributed around the cluster. If the borders of the classes could be defined mathematically, classification by health condition may also be possible.

4. Conclusions

This paper proposes a procedure to detect patient eye responses in order to provide a quantitative description of Pupil Light Reflex (PLR) waveform shapes using the Discrete Fourier Transform (DFT) descriptors (FDs) for both eyes across stimuli conditions, and another procedure for emphasizing stimuli and subject differences using Multi Dimensional Scaling (MDS) and clustering where the dissimilarity between stimuli is defined using the descriptors as waveform features. The demonstrations were conducted using a conventional melanopsin experiment with healthy subjects and patient subjects. As a result, the abnormal responses of eyes by patients are quantitatively configured in a two dimensional space. In particular, the typical responses to a stimuli such as a low intensity long waveform light, are different from the responses of subjects with normal, or healthy eyes. More detailed diagnostic procedures will be the subjects of our further study.

References


