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TECHNICAL NOTE

Improved measurement of intersession latency in mfVEPs

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Abstract
Purpose The purpose of the study is to present a method (Selfcorr) by which to measure intersession latency differences between multifocal VEP (mfVEP) signals.
Methods The authors compared the intersession latency difference obtained using a correlation method (Selfcorr) against that obtained using a Template method. While the Template method cross-correlates the subject's signals with a reference database, the Selfcorr method cross-correlates traces across subsequent recordings taken from the same subject.
Results The variation in latency between intersession signals was 0.8 ± 13.6 and 0.5 ± 5.0 ms for the Template and Selfcorr methods, respectively, with a coefficient of variability $C_{V\_TEMPLATE} = 15.83$ and $C_{V\_SELFCORR} = 5.68$ ($n = 18$, $p = 0.0002$, Wilcoxon). The number of analyzable sectors with the Template and Selfcorr methods was 36.7 ± 8.5 and 45.3 ± 8.7, respectively ($p = 0.0001$, paired t test, two tailed).
Conclusions The Selfcorr method produces smaller intersession mfVEP delays and variability over time than the Template method.

Keywords Multifocal visual-evoked potential · Relative latencies · Cross-correlation · Visual pathway

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Introduction

Multifocal VEP (mfVEP) has been reported as offering high sensitivity, making it particularly suitable for detecting subclinical focal defects and optic nerve damage undetectable by other structural or functional diagnostic techniques [1].

The principal mfVEP signal characteristics analyzed are amplitude and latency. Latency can be measured manually by selecting the highest peak and measuring its absolute timing. This subjective method is very time-consuming, and if the sectors are grouped, spatial resolution is lost.

Few studies propose automated mfVEP signal-latency measurement methods. In [2], latency is measured as the time difference between the first or second major peak and the start of the response. In [3],

the authors define an artificial template with wavelet kernels that model the mfVEP trace profile. Hood et al. [4] perform cross-correlation with a template (the Template method) created for each location, eye and channel obtained from a normative group of 100 individuals: the Portland database [5]. This database was obtained under widely varying conditions that may have had a direct influence on results. By subtracting the value of the absolute latencies calculated in each test (T_1 and T_2), it is possible to calculate the intersession latency difference (the approach most widely used at present).

This technical note proposes a method (Selfcorr) by which to compute variation in latency between mfVEP sessions. This method is an improved version of the one used in [6] to measure interocular latencies. Our proposal is to cross-correlate signals from two sets of recordings of the same eye, sector and channel in the same subject. The hypothesis is that measuring latency changes in a subject will be more accurate if the signals correlated are recorded in subsequent sessions using the same acquisition method.

Materials and methods

The study protocol was approved by the Institutional Review Boards of University of Alcalá-affiliated hospitals and adhered to the tenets of the Declaration of Helsinki. All participants provided written informed consent.

The mfVEP signals have been obtained from 36 eyes in 18 healthy subjects ranging in age from 21 to 43 (31 ± 8.55 years)—8 males and 10 females—with normal neurological and ophthalmologic examination results.

These subjects participated in 2 mfVEP signal-recording sessions on two consecutive days (T_1 and T_2). The sessions took place at similar times of day and the same medical staff, equipment and procedure were employed on each occasion.

Monocular recordings were obtained using VERIS software 5.9 (Electro-Diagnostic Imaging, San Mateo, USA). The authors employed the previously described procedure used to obtain the Portland database [5]: m-sequence visual stimulation (2^{15}-1 steps), signal amplification (Gain:10^5, Bandwidth 3–100 Hz) and a sample frequency of 1,200 Hz.

Three channels were obtained using gold cup electrodes (impedance <2 KΩ). For the midline channel, the electrodes were placed 4 cm above the inion (active), at the inion (reference), and on the forehead (ground). For the other two channels, the active electrodes were placed 1 cm above and 4 cm lateral to the inion on either side.

By taking the difference between pairs of channels, three additional derived channels were obtained, effectively resulting in six channels.

The mfVEP responses were passband filtered using a fast Fourier Transform (3–35 Hz). The signal-to-noise ratio (SNR) was calculated using the same method as in [5]. Root mean square (RMS) amplitudes were calculated over a 45–150 ms interval. Noise was defined as the mean of all 60 RMS amplitudes over an interval of 325–430 ms. The SNR was obtained by dividing the RMS amplitude of the response by the RMS of the noise.

Proposed method: Selfcorr

Two Matlab functions are used: corrcoef (x, y) returns the correlation coefficients between series x and y, while $x$corr(x, y) returns the instant of maximum correlation between x and y (the value considered to represent the shift between x and y).

In every sector, the signals obtained in recordings T_1 and T_2 are denominated, respectively $\mathrm{CH}_i^{T_1}$ and $\mathrm{CH}_i^{T_2}, (i = 1, \ldots, 6)$.

(a) The SNR is calculated for every channel in both T_1 and T_2:

$$\mathrm{SNR}\ (\mathrm{CH}_i^{T_1}); \quad \mathrm{SNR}\ (\mathrm{CH}_i^{T_2}); \quad i = 1, \ldots, 6;$$

(b) If $(\mathrm{SNR}(\mathrm{CH}_i^{T_1}) < 0.23\ \log\ \text{unit})$ OR $(\mathrm{SNR}\ (\mathrm{CH}_i^{T_2}) < 0.23\ \log\ \text{unit})$, then channel i is not analyzed, as signal quality in T_1, T_2, or both, is not high enough to obtain a reliable result.

(c) For signal pairs from the same channel that exceed the minimum SNR value, the correlation coefficient is calculated, eliminating those channels whose signals have a non-positive correlation coefficient:

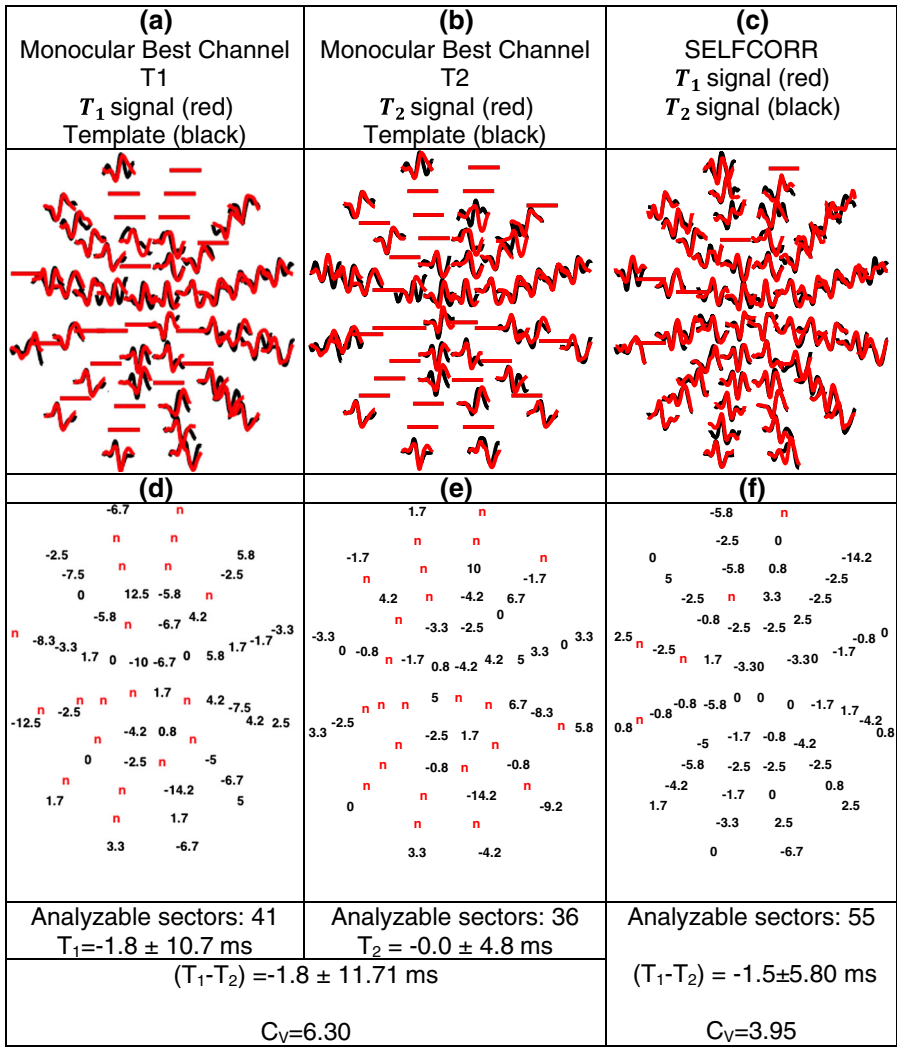

Fig. 1 T_1–T_2 latency changes in a selected subject eye

If corrcoef$\left(\mathrm{CH}_i^{T_1}, \mathrm{CH}_i^{T_2}\right) \leq 0 \rightarrow$ Channel i is excluded.

(d) For those channels not excluded in the preceding steps, the following function is defined:

$$J(i, T_1, T_2) = \mathrm{SNR}(\mathrm{CH}_i^{T_1}) + \mathrm{SNR}(\mathrm{CH}_i^{T_2}); \quad (1)$$

(e) The channel used to calculate the latency is the one that maximizes:

$$\max(J(i, T_1, T_2)) = J(i_{\mathrm{opt}}, T_1, T_2) \quad (2)$$

The intersession latency difference between T_1 and T_2 is:

$$\text{Latency difference} = x\ \mathrm{corr}\left(\mathrm{CH}_{i_{\mathrm{opt}}}^{T_1}, \mathrm{CH}_{i_{\mathrm{opt}}}^{T_2}\right) \quad (3)$$

In [6], the authors first select the channel with the highest SNR and then automatically include its counterpart in the other eye, irrespective of the quality of that channel's signal in that eye. Under the Selfcorr method, the channel selected is the one that maximizes the SNR in T_1 and T_2 (Eq. 1).

Results

Figure 1 shows the results of analysis of the left eye of one of the subjects. Figure 1a, b show the signals that intervene in the correlation for each analyzable sector (SNR >0.23 and correlation coefficient >0). The Template trace corresponds to the signal from the

Portland database, and the T_1 or T_2 trace corresponds to the signal from the subject. A horizontal line indicates the non-analyzable sectors.

Figure 1c shows the signals used to compute correlation under the Selfcorr method. Figures 1d, e shows the relative latency between the Portland database and the signals obtained in T_1 and T_2, respectively. The mean ± SD in T_1 is −1.8 ± 10.7 ms, while in T_2, it is −0.0 ± 4.8 ms. Therefore, the variation in latency between T_1 and T_2 is −1.8 ± 11.7 ms ($\mathrm{SD} = \sqrt{\mathrm{SD}_1^2 + \mathrm{SD}_2^2}$). T_1 has 41 analyzable sectors, while T_2 has 36. The coefficient of variation (C_V) is $C_V = {}^{\mathrm{SD}}/_{|\mathrm{mean}|} = 6.30$. Figure 1f shows the result obtained under the Selfcorr method; the variation in latency is −1.5 ± 5.8 ms, C_V is 3.95, and this eye has 55 analyzable sectors.

When the Template method is applied to 18 subjects, the variation in latency between the signals in T_1 and T_2 is 0.8 ± 13.6 ms. Under the Selfcorr method, the variation is 0.5 ± 5.0 ms. For the first method, the mean value of $C_V = 15.83$, while for the Selfcorr method, $C_V = 5.68$ ($p = 0.0002$, Wilcoxon matched-pairs signed-rank test).

For all subjects' signals, under the Template method, the number of analyzable sectors is 36.7 ± 8.5, while under the Selfcorr method, it is 45.3 ± 8.7. There is a significant difference in the number of sectors analyzable under each method ($p = 0.0001$, paired t test, two tailed).

Discussion

This technical note presents an alternative technique for measuring mfVEP intersession latency differences. Various papers consider that minimum test–retest latency variation is a good indicator of mfVEP reproducibility [2, 3].

With 18 healthy subjects, upon which the signal-recording sessions were carried out 24 h apart, the Selfcorr method obtained latency variations that were closer to 0 (ideal result) than those obtained with the Template method, thereby improving the precision of the measurements (SD = 13.6 ms vs. SD = 5.0 ms). This allows practitioners to detect slight changes in inter-test values more reliably, as variability is lower in the Selfcorr method than in the Template method, thus improving the accuracy of the latency measurements.

The Selfcorr method obtains better results than those reported in other similar papers. In [2], the authors studied the reproducibility of mfVEP latency using 10 control subjects, capturing solely the vertical channel and using an inter-test interval of 1–2 weeks, which obtained a 3.2-ms (mean value) difference in latency values. In [7], the authors obtained a latency change of 2.8 ± 1.9 ms in a sample of 20 healthy subjects with a 3-month inter-test interval.

The number of analyzable sectors is 14.42 % higher under the Selfcorr method (45.3 ± 8.7) than under the Template method (36.7 ± 8.5). In both cases, the quality criterion applied to channel selection is the same (SNR >0.23 log unit). However, when correlating the signals, the Template method compares the signals against a third-party database, making it relatively likely that, due to differences in individual cortex morphology, signal polarity will also differ. In this case, the correlation coefficient is negative, and therefore, that pair of channels is rejected. The Selfcorr method compares signals taken from the same subject, meaning that the probability of the

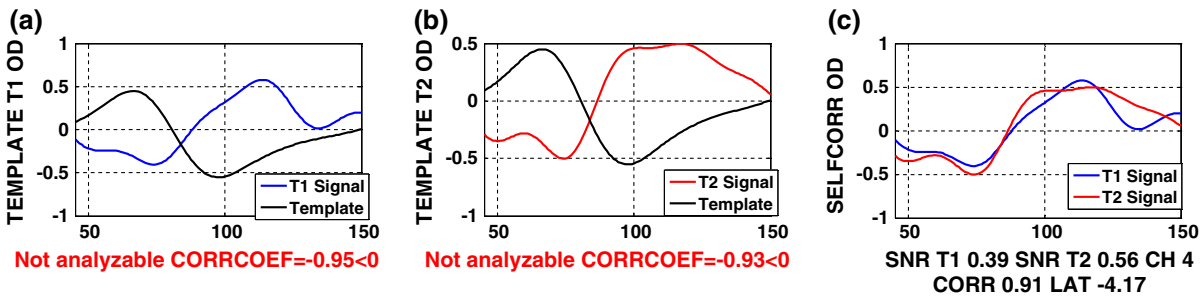

Fig. 2 Examples of correlation coefficient calculation

correlation coefficient being negative is minimal. This may be observed in the examples shown in Fig. 2. In cases (a) and (b), the signals are shown for sessions T_1 (a) and T_2 (b) and are compared against the corresponding signals in the normalized database template. Given that the signals have different polarities to their corresponding values in the template, the pairs are not analyzable for the purposes of latency calculation. Conversely, Fig. 2c shows that the signals are very similar, and their correlation coefficient is positive.

The authors' next step will be to apply this mfVEP latency analysis method to patients with visual pathway pathologies, such as multiple sclerosis.

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Conflict of interest The authors claim no conflicts of interest.

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