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Gaussian wavelet transform and classifier to reliably estimate latency of multifocal visual evoked potentials (mfVEP)

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ABSTRACT

This paper describes a method to reliably estimate latency of multifocal visual evoked potential (mfVEP) and a classifier to automatically separate reliable mfVEP traces from noisy traces. We also investigated which mfVEP peaks have reproducible latency across recording sessions. The proposed method performs cross-correlation between mfVEP traces and second order Gaussian wavelet kernels and measures the timing of the resulting peaks. These peak times offset by the wavelet kernel's peak time represents the mfVEP latency. The classifier algorithm performs an exhaustive series of leave-one-out classifications to find the champion mfVEP features which are most frequently selected to infer reliable traces from noisy traces. Monopolar mfVEP recording was performed on 10 subjects using the Accumap1™ system. Pattern-reversal protocol was used with 24 sectors and eccentricity upto 33°. A bipolar channel was recorded at midline with electrodes placed above and below the inion. The largest mfVEP peak and the immediate peak prior had the smallest latency variability across recording sessions, about ±2 ms. The optimal classifier selected three champion features, namely, signal-to-noise ratio, the signal's peak magnitude response from 5 to 15 Hz and the peak-to-peak amplitude of the trace between 70 and 250 ms. The classifier algorithm can separate reliable and noisy traces with a high success rate, typically 93%.

1. Introduction

The multifocal visual evoked potential (mfVEP) has been investigated as an alternative to subjective perimetry to detect defects in small area of the visual field (Baseler et al., 1994; Graham, Klistorner, & Goldberg, 2005; Hood, Ohri et al., 2004; Klistorner et al., 1998, 2007; Wangsupadilok et al., 2009). Previous works have shown that the amplitude of the mfVEP traces can detect small localised defects with high sensitivity and specificity in diseases such as glaucoma (Baseler et al., 1994; Graham, Klistorner, & Goldberg, 2005; Hood, Thienprasiddhi et al., 2004; Klistorner et al., 1998). This paper describes a method to estimate latency of mfVEP traces with low inter-session variability. A classifier to automatically separate noisy traces from reliable traces is also presented.

Latency has been used in conventional VEP to assess the visual pathway in optic neuritis (Halliday, McDonald, & Mushin, 1972). Ebers (1985) found that optic neuritis patients exhibited delay conduction of conventional full-field VEP and suspected that the delay reflected demyelination of the optic nerve fibres. Latency of multifocal visual evoked potential (mfVEP) traces provides an additional advantage since it can indicate localised severity of demyelination (Grover et al., 2008; Klistorner, Arvind et al., 2008; Klistorner et al., 1998). However measurement of latency of mfVEP traces has been a challenge due to low signal-to-noise (SNR) ratio and variability of the traces' profile. We use the term profile to refer to the overall shape of the mfVEP trace waveform. To our knowledge, only a few studies have proposed methods to quantify latency of mfVEP traces (Hood, Ohri et al., 2004; Klistorner, Arvind et al., 2008).

One method to measure latency is by manual inspection by 1–3 observers and then the mean value is taken. Prior to measuring the latency, observers must first inspect the traces and exclude traces that are deemed too noisy. A typical mfVEP session records traces from at least 24 sectors, 4 channels and 2 eyes per patient, which equates to 192 traces. These manual tasks are laborious. Hence clinical applications of mfVEP latency become impractical.

Klistorner, Fraser et al. (2008) quantified the trace latency by first selecting the mfVEP trace with the largest peak-to-peak amplitude from four channels for each sector and eye. Then timing of the second peak (minimum or maximum) was used as the trace latency. This peak usually has the largest amplitude and occurs between 120 and 180 ms. Traces with low signal-to-noise ratio are excluded from analysis (signal is defined as difference between

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minimum and maximum within interval of 70–210 ms and noise defined as standard deviation of signal between 400 and 1000 ms.

Hood, Ohri et al. (2004) proposed another method to quantify latency which can exclude certain traces whose SNR values are below a specified threshold. The method first formed a template from mfVEP traces collected from 100 subjects and measured the latency of the mfVEP template. Then cross-correlation values between the template and a new mfVEP trace were evaluated. Latency of the new mfVEP trace is equal to the time of the largest cross-correlation plus the latency of the mfVEP template. The authors raised an important challenge on treating traces from the same sector and eye that have reversed polarity. This reversal could be due to noise or real physiological activities resulting from unique folding of the visual cortex. In addition, this method requires users to have a large database of mfVEP traces in the first place. Furthermore, since different visual stimuli would yield mfVEP traces with different characteristics, a new set of database is required when the visual stimulus is changed.

Our investigation arises from the need to estimate mfVEP latency with good reproducibility given a small pool of data. If we only wish to estimate the progression in latency, we could immediately evaluates the cross-correlation of mfVEP traces from two recording sessions. The timing of the maximum cross-correlation then corresponds to the relative latency between the two sessions. Applying this technique to our data produced a relative latency of 0.5 ± 3.2 ms. (Note that the sampling interval was 2.2 ms and so the standard deviation is about 1 sample.) Various methods to estimate the relative latency have been investigated rigorously (e.g. Kong & Thakor, 1996; Rog & Kaufman, 1994). These techniques are useful in following up progression of diseases but they do not provide the actual latency.

We attempted the template-based approach in Hood, Ohri et al. (2004) and could obtain mfVEP latency with reasonable reproducibility. However the latency variability across subjects was quite high since in some traces/subjects, the first peak around 100 ms yielded better reproducibility than the second peak around 150 ms but in other traces/subjects, the opposite was true. This was one of the key motivations to consider adopting pre-determined templates whose largest peak lie between 100 ms and 150 ms. This also allowed us to investigate which peaks would yield good reproducibility. Furthermore, we only had a small pool of data available (seven subjects) for generating the templates for each sector. After filtering out the noisy traces, often we only had five subjects with good traces. But in the peripheral sectors where the signal-to-noise ratio is usually low, only 1–2 subjects provided good traces. Another challenge is that the latency of the template traces have to be manually estimated.

This paper provided three contributions. The first contribution is a method to estimate mfVEP latency by performing cross-correlation with wavelet kernels that model the mfVEP trace profile. (Note that the cross-correlation operation with wavelet kernels is essentially a wavelet transform.) Since we do not create a mfVEP template, we do not have the issue of averaging traces that may have reversed polarity. There are two key advantages. Firstly there is no need for a large database of mfVEP traces. Secondly, there is no need for manually estimating the template latency since the peak of the wavelet kernels are predetermined. The second contribution is to investigate which mfVEP peaks can provide reproducible estimation of latency.

The last contribution is a technique to design a classifier to separate reliable traces from noisy traces in order to estimate overall latency accurately. The technique follows the general framework regularly used in brain computer interface (BCI) (see Wolpaw et al. (2002) for a review). The framework consists of two main stages, namely, feature extraction and classification. In the feature extraction stage, the EEG or event-related responses are converted into a series of variables (features). For example, the features can be peak amplitude, magnitude at predefined frequency bands, etc. In the classification stage, the features are classified to a particular group. In BCI, classification to one group sends a predefined command to the target device while classification to another group sends a different command. The classification stage may employ a linear or non-linear algorithm (e.g. linear discriminant analysis or neural network) (Krauledat et al., 2008; Müller et al., 2008; Pfurtscheller et al., 2000; Wolpaw, McFarland, & Vaughan, 2000). The classifier is usually trained using a set of features that have been associated to a set of groups.

2. Methods

2.1. Latency estimation

Latency of a mfVEP trace is estimated by first cross-correlating the trace with a wavelet kernel. Let R_{xw} denote the cross-correlation values between the mfVEP trace and a wavelet kernel, defined as

$$R_{xw}[m] = \frac{1}{N}\sum_{n=0}^{N-1} x[n]w[n-m], \quad m = -N+1, \ldots, N-1$$

where x and w denote a mfVEP trace and wavelet kernel respectively.

Then the latency is equal to the time at which the cross-correlation magnitude is largest offset by the time at which the wavelet magnitude is largest. That is, let τ denote the latency in unit of samples and is defined as

$$\tau = \arg\max_m |R_{xw}[m]| + \arg\max_n w[n]$$

where "arg max" denotes index that maximizes the function. We use the absolute magnitude of R_{xw} to compensate for traces that may be out-of-phase with the wavelet kernel (i.e. traces with reversed polarity). To convert the latency to time unit, τ must be divided by the sampling rate.

Fig. 1 illustrates an example of the latency estimation. Fig. 1A–C shows a mfVEP trace, a wavelet kernel and the cross-correlation

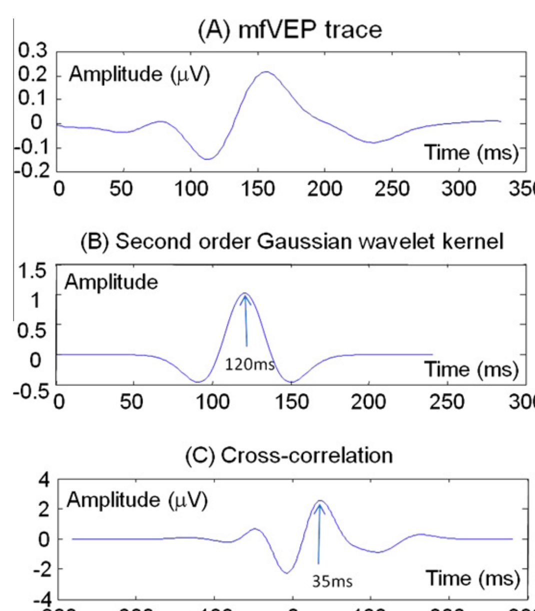

Fig. 1. An example of estimating latency of mfVEP trace using cross-correlation with Gaussian wavelet kernel. (A) mfVEP trace. (B) Second order Gaussian wavelet kernel with peak at 120 ms. (C) Cross-correlation of the mfVEP trace with the Gaussian wavelet kernel. The positive peak indicated occurs at 35 ms.