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Interval Estimate of Physiological Fluctuation of Peak Latency of ERP Waveform Based on a Limited Number of Single Sweep Records

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Abstract

In the single sweep record of event-ralated potential (ERP), the peak latency of P300, which is one of the most prominent positive peaks in the ERP record, might fluctuate according to the recording conditions. The fluctuation of the peak latency (measurement fluctuation) is the summation of the fluctuation caused by physiological factor (physiological fluctuation) and one by noise of background EEG (noise fluctuation). We proposed a method for estimating the interval of the physiological fluctuation of the peak latency of the P300 from the measurement fluctuation based on a limited number of single sweep records. The noise fluctuation was estimated by using the relationship between the signal-to-noise (SN) ratio and the noise fluctuation based on the P300 model and the background EEG model. The interval estimate of the physiological fluctuation were obtained by subtracting the interval estimate of the noise fluctuation from that of the measurement fluctuation. The proposed method was tested by using simulation data of ERP and applied to actual ERP data of normal subjects, and gave satisfactory results.

1. Introduction

Event-related potentials (ERPs) are responses related to recognition of certain stimulation, and recorded from a human scalp. P300 waveform is one of the most prominent positive peaks in the ERP and appears around 300 [msec] after stimulus [1]. The characteristics of P300 for each stimulus, especially the peak latency, might fluctuate according to the recording conditions of a subject. Extraction of the features of the P300 waveform is required for each stimulus. For ERP and evoked potential, the method for extracting the characteristics of waveform, which fluctuated for each stimulus, were proposed [2]- [4]. In our previous work [5] [6], we proposed a method for an automatic detection for P300 waveform of single sweep record, and calculated the fluctuation of the peak latency of the P300 for healthy adults. It is important to investigate whether the fluctuation of the peak latency is caused by the physiological factor or by the noise of background electroencephalogram (EEG). The measurement of the fluctuation, which is the standard deviation of the peak latency of the P300 waveform, is the summation of the physiological fluctuation and the fluctuation cased by the background noise. Previously, we proposed a method for obtaining a point estimate of the physiological fluctuation out of the measurement of the fluctuation based on a large number of single sweeps [7]. However, as a limited number of the single sweeps of the P300 can be used in the actual recording, the physiological fluctuation is required to calculate based on a small number of single sweeps.

In this paper, we proposed a method for obtaining the interval estimate of the physiological fluctuation of the peak latency of the P300 waveform based on a small number of single sweep records. The relationship between the signal-to-noise (SN) ratio of the single sweep P300 and the noise fluctuation was determined by the use of appropriate models for the P300 and the background EEG. The interval estimate of the physiological fluctuation was obtained by subtracting the interval estimate of the noise fluctuation from that of the measurement fluctuation. The proposed method was evaluated based on the simulation data in which the true value of the physiological fluctuation was already known, and proved to have an accurate interval estimate of the physiological fluctuation of the peak latency for the simulated P300 waveforms. The proposed method was applied to actual ERP data of sixteen healthy adults, and the interval estimate of the physiological fluctuation of the peak latency was obtained for a small number of single sweeps of the P300.

2. Estimate Method of Physiological Fluctuation of Peak Latency of P300

2.1 Recording condition of single sweep ERP

Subjects of the present study were sixteen healthy adults (20-30 years old). Two tone stimuli of different frequencies, 1000 [Hz] and 2000 [Hz], were given to the subjects in a pseudorandom order. The 2000 [Hz] tone was given at a low rate (20 %) as the target stimulus, and the 1000 [Hz] tone given at a high rate (80 %) as the non-target stimulus. The subject was asked to push the button quickly as soon as one heard the target stimulus. In the record, the ERP was expected to appear after the target stimulus, because the subject recognized the 2000 [Hz] tone as the target stimulus, while the ERP rarely appeared after the non-target stimulus. The interstimulus interval was 2.5±0.28 [sec]. An exploring electrode was fixed at Pz according to the guidelines of the International 10-20 System [8]. The linked earlobes were used as the reference, and the data was amplified with filter setting of 0.05-60 [Hz] (-3dB).

The positive peak P300, which appears 300 [msec] after the stimulus, is regarded as the most prominent component of the ERP. The P300 waveform is not visible clearly in the raw time series for each stimulus, be-

cause of the contamination with the noise components of background EEG, especially the dominant rhythm. To improve the SN ratio of the single sweep ERP, the raw data were filtered through the discrete Fourier transform (DFT) and inverse discrete Fourier transform (IDFT) filter of 1-8 [Hz]. The processed data were obtained by calculating the Fourier component from the raw data of 1.024 [sec] length after the stimulus, and again implemented the inverse Fourier transform for the Fourier components within the frequency band of 1-8 [Hz]. The sampling interval of the processed data was 2 [msec]. The frequency band of the filter was determined to improve the SN ratio in the healthy adults' data. The fluctuation of the peak latency of the P300 in the processed data was analyzed.

2.2 Characteristics of fluctuation of peak latency of P300

The measured value (y) of the peak latency of the P300 in the single sweep record is the summation of the true value (s) and the noise (n). It is assumed that the components s and n are independent. Then, the measurement fluctuation (σ_y), which is the standard deviation of the peak latency for several single sweeps of the P300, is the summation of the physiological fluctuation (σ_p) caused by the physiological factor and the noise fluctuation (σ_n) caused by the noise of back ground EEG. Then, if the characteristics of the noise fluctuation is known, the physiological fluctuation can be obtained from the following equation

$$\sigma_p = \sqrt{(\sigma_y)^2 - (\sigma_n)^2}. \qquad (1)$$

In order to obtain the characteristics of the noise fluctuation, the simulation data were used. The simulation data were generated by using P300 model and background EEG model. The P300 model was represented by the typical single sweep P300 waveform shown in Figure 1, and its peak latency was fixed at 350 [msec] after stimulus. The peak latency was defined as the time from the stimulus point to the positive peak point of the P300. The background EEG, which consisted of δ wave, dominant rhythm and β wave, was simulated by using the model of sinusoidal waves with Markov process amplitude [9],

$$x(n\Delta t) = \sum_{k=1}^{3} a_k(n\Delta t)\sin(2\pi m_k n\Delta t - \theta_k) \qquad (2)$$

$$a_k((n+1)\Delta t) = \gamma_k a_k(n\Delta t) + \xi_k(n\Delta t)$$

where $x(n\Delta t)$ was an output of the EEG model, $\xi_k(n\Delta t)$ was an independent white noise with zero mean and variance $(\sigma_k)^2$, Δt(=2 msec) denoted the sampling interval. The simulation data of healthy adults' EEG were generated by using the EEG model parameters with mean frequency $m_1 = 1$[Hz], $m_2 = 10$[Hz] and $m_3 = 25$[Hz]. Other model parameters γ_k, σ_k, $k = 1, 2, 3$ were selected appropriately in order to generate the simulation data with various SN ratios.

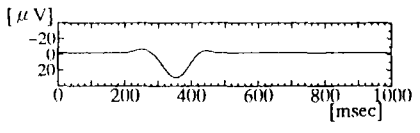

Figure 1 Typical single sweep P300 waveform recorded from Pz of a normal subject in the auditory oddball paradigm.

In order to extract the single sweep P300 waveform, the band-pass filter of 1-8 [Hz] was used. The P300 waveform was detected in the processed data, and its peak latency was measured. The simulation data of 1000 segments were generated under each condition, and the standard deviation (σ_n) of the peak latency was calculated. This standard deviation (fluctuation) was caused only by the noise of the background EEG, since the peak latency of the P300 model was fixed in the simulation data. The relationship between the SN ratio (R) and the fluctuation of the peak latency (σ_n) was investigated based on the simulation data by changing the parameters of the background EEG model. The SN ratio (R) was defined as the ratio of power of the P300 (P_s) to power of the background EEG (P_n) within the frequency band of 1-8 [Hz] ($R = P_s/P_n$). The noise fluctuation was proved to be proportional to the inverse of the square root of the SN ratio [7],

$$\sigma_n = c/\sqrt{R}. \qquad (3)$$

2.3 Estimate of physiological fluctuation of peak latency of P300

2.3.1 Point estimate

The point estimate of the physiological fluctuation of the peak latency of the P300 is obtained according to the following procedure [7].

(i) The several responses for target stimuli are recorded. The processed data for each stimulus are obtained by using the DFT-IDFT filter with 1-8 [Hz].

(ii) The P300 waveforms are detected from the single sweep processed data by using the automatic detection method [5]. The criteria of the automatic detection method are as follows : (a) the peak latency of the positive peak exists within 200-500 [msec] after the stimulus, (b) amplitude (difference between the positive peak value and the prior negative peak value) is 14 [μv] or more, (c) correlation coefficient between the positive peak and the template, which is made for each individual subject and updated, is 0.85 or more, (d) all the other positive peaks after the P300 are smaller than 0.85 of the amplitude of the P300. If the positive peak satisfies all 4 criteria, it is regarded as P300 waveform. The measurement fluctuation (σ_y) is estimated by calculating the standard deviation of the peak latencies of the detected P300 waveforms.

(iii) The SN ratio is estimated. The power of the P300 (P_s^o) is assumed as 15[μV^2], which is the power of the typical P300 waveform within the frequency band 1-8 [Hz]. The power of the noise of the background EEG (P_n) is estimated by subtracting the power of the P300 (P_s^o) from that of the processed

data ($\hat{P}_t$). The power of the processed data ($\hat{P}_t$) is calculated from the power spectrum of the processed data, and include the both powers of the signal and the noise components. Then, the SN ratio (R) is estimated as

$$\hat{R} = \frac{P_s^o}{\hat{P}_t - P_s^o}, \tag{4}$$

where $\hat{R}$ denotes the estimated value of R.

(iv) The estimate of the noise fluctuation ($\hat{\sigma}_n$) is obtained by substituting the estimated SN ratio ($\hat{R}$) into the equation (3) instead of R.

(v) The estimate of the physiological fluctuation ($\hat{\sigma}_p$) is obtained by substituting the estimated values $\hat{\sigma}_y$ and $\hat{\sigma}_n$ into the equation (1) instead of σ_y and σ_n respectively.

2.3.2 Interval estimate

If a limited number of the single sweeps of the P300 can be used in the actual recording, the point estimate of the physiological fluctuation may change according to the samples. In case of few sweeps, the interval estimate of the physiological fluctuation is required for an appropriate estimate of the fluctuation. The procedure for obtaining the interval estimate of the physiological fluctuation is as follows.

(i) The processed data are obtained in the same way as the procedure (i) of the section 2.3.1.

(ii) The P300 waveforms are detected and the standard deviation of the peak latencies is calculated in the same way as the procedure (ii) of the section 2.3.1. It is assumed that the measured peak latency obeys a normal distribution. If the number of samples (the number of single sweeps of the P300) is K, the normalized variance of the peak latencies (square of the measurement fluctuation) ($K(\hat{\sigma}_y/\sigma_y)^2$) obeys a chi-square distribution with degree of freedom $K-1$. Then, the true value of the measurement fluctuation (σ_y) exists in the following interval

$$\hat{\sigma}_y\sqrt{\frac{K}{\chi_2}} \le \sigma_y \le \hat{\sigma}_y\sqrt{\frac{K}{\chi_1}}, \tag{5}$$

where $[\chi_1, \chi_2]$ is the confidence interval with a given confidence level (80%) in the chi-square distribution with degree of freedom $K-1$.

(iii) The SN ratio is estimated. It is assumed that Fourier component of the processed data obeys a normal distribution. Then, the normalized periodogram, which is square of the Fourier component, obeys a chi-square distribution with degree of freedom 2, and the normalized power spectrum ($2K\hat{P}_t/P_t$), which is average of K periodograms, obeys a chi-square distribution with degree of freedom $2K$. Then, the true value of the power spectrum (P_t) exists in the following interval

$$\frac{2K\hat{P}_t}{\chi_4} \le P_t \le \frac{2K\hat{P}_t}{\chi_3}, \tag{6}$$

where $[\chi_3, \chi_4]$ is the confidence interval with a given confidence level (80%) in the chi-square distribution with degree of freedom $2K$. From the equations (4),(6), the interval estimate of the SN ratio is obtained as follows

$$\frac{\chi_3\hat{R}}{2K(1+\hat{R}) - \chi_3\hat{R}} \le R \le \frac{\chi_4\hat{R}}{2K(1+\hat{R}) - \chi_4\hat{R}}. \tag{7}$$

(iv) From the equations (3),(7), the interval estimate of the noise fluctuation is obtained as follows

$$c\sqrt{\frac{2K(1+\hat{R}) - \chi_4\hat{R}}{\chi_4\hat{R}}} \le \sigma_n \le c\sqrt{\frac{2K(1+\hat{R}) - \chi_3\hat{R}}{\chi_3\hat{R}}}. \tag{8}$$

(v) From the equations (1),(5),(8), the interval estimate of the physiological fluctuation is obtained as follows

$$\sqrt{\hat{\sigma}_y^2\frac{K}{\chi_2} - c^2\frac{2K(1+\hat{R}) - \chi_3\hat{R}}{\chi_3\hat{R}}} \le \sigma_p \le \sqrt{\hat{\sigma}_y^2\frac{K}{\chi_1} - c^2\frac{2K(1+\hat{R}) - \chi_4\hat{R}}{\chi_4\hat{R}}}. \tag{9}$$

3. Results

3.1 Relationship between SN ratio and noise fluctuation

The eight cases of the simulations were done for different model parameters. The obtained relationship between the SN ratio and the noise fluctuation is shown in Figure 2. The plots are the results for each simulation, and the straight line of the linear approximation

$$\sigma_n = 10.33/\sqrt{R} \tag{10}$$

was obtained by using the least squares method. The coefficient c in the equation (3) was determined as 10.33.

3.2 Interval estimate of physiological fluctuation for simulation data

In order to evaluate the proposed method, we used the simulation data whose characteristics were known. The physiological fluctuation of the peak latency of the P300

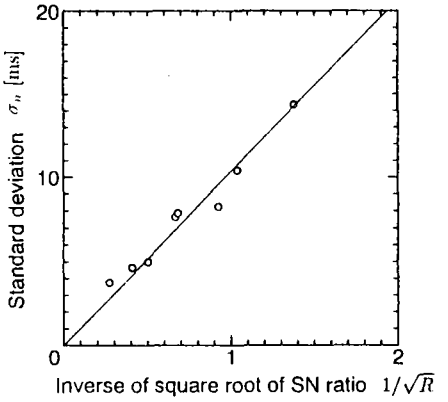

Figure 2 Relationship between $1/\sqrt{R}$ (R, signal-to-noise ratio of the processed data of the single sweep ERP) and the standard deviation (σ_n) caused by noise components. The straight line is the linear approximation for the sample data of the simulation.

was simulated by using the normal random numbers with the mean of 350 [msec] and the variance $(\sigma_p)^2$. The six cases of the simulations were implemented for different variance $(\sigma_p)^2$ and the various parameters of the background EEG model. Figure 3 illustrates the results of the interval estimate of the physiological fluctuation of the P300. In the case 1-4, 5 and 6, the physiological fluctuation (σ_p) was set as 30 [msec], 20 [msec] and 40 [msec], respectively. The number of sweeps of the P300 (K) was 20, and three simulation were done in each case. Figure 3 means that the physiological fluctuation exists in the estimated interval with the confidence level 80%. The points in the Fig. 3 show the results of the point estimate of the physiological fluctuation ($\hat{\sigma}_p$) calculated by using the method mentioned in the section 2.3.1. In all the cases, the estimated interval of the physiological fluctuation always include the true value, although the point estimate value do not always equal to the true value.

3.3 Interval estimate of physiological fluctuation for actual data

Figure 4 illustrates 20 single sweeps of the raw ERP target data from subject 7 and the corresponding processed data by the use of the band-pass filter of 1-8 [Hz]. The positive peaks indicated by arrows were judged to be P300 by the automatic detection method [5]. From Fig. 4, it is seen that the peak latencies of the P300 fluctuate in each single sweep record. The interval of the physiological fluctuation was estimated by subtracting the noise fluctuation from the measurement fluctuation. Figure 5 illustrates the results of the interval estimate of the physiological fluctuation. The ERP data for sixteen subjects were analyzed, however, the results for twelve subjects, for which the number of detected P300 was over 7, were shown. Because, the estimated interval became so wide for a few number of sweeps of the P300, and it was not useful to estimate the interval of the physiological fluctuation. The number of detected P300 was 7-14 for twelve subjects. In all the cases except subject 14, the lower band of the intervals has positive value, then, the physiological fluctuation is proved to exist with the confidence level 80%.

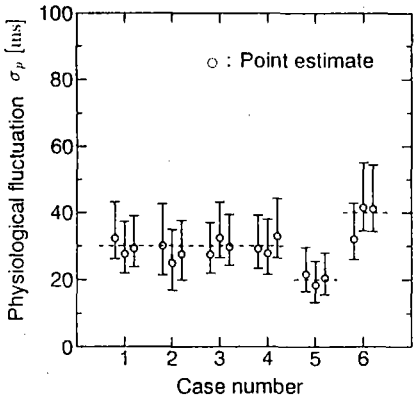

Figure 3 Results of the interval estimates and the point estimates of the physiological fluctuation for the simulation of different conditions. The dotted line shows the true value.

4. Discussion

The method for extracting the physiological fluctuation of the peak latency of the P300 by subtracting the noise fluctuation from the measurement fluctuation was proposed. In the case of a large number of single sweeps of the P300, the plot estimate of the physiological fluctuation of the peak latency is sufficient. However, in the case of a limited number of single sweeps of the P300, the plot estimate changes according to the samples, then, the interval estimate becomes to be an appropriate estimate for analysis of the fluctuation.

The relationship between the SN ratio and the noise fluctuation was obtained by using the P300 model and the background EEG model. By use of the relationship, the noise fluctuation can be estimated from the SN ratio. The P300 model is the typical single sweep P300 waveform generated based on actual data [5], and the background EEG model can appropriately represent the characteristics of the background EEG in the time domain and the frequency domain [9]. Then, it can be declared that the relationship of the equation (10), obtained based on the simulation, represents the characteristics of single sweep ERP data appropriately.

In order to evaluate the proposed method, the physiological fluctuations were estimated for the simulation data. In Fig. 3, the estimated interval of the physiological fluctuation always includes the true value, though the width and the lower band of the estimated interval change according to the condition of the simulation. These simulation results prove that the proposed method is effective. The proposed method was applied to sixteen

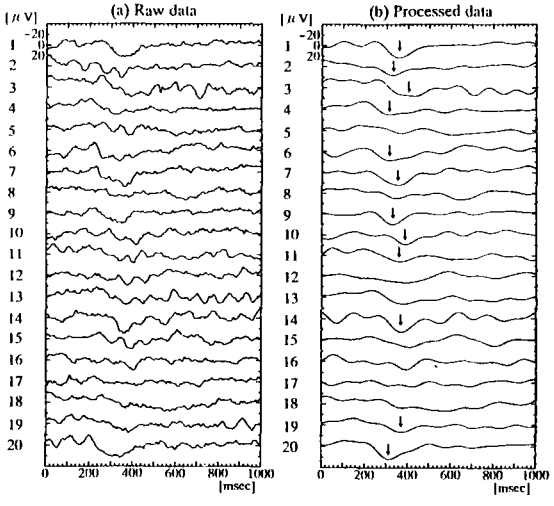

Figure 4 Actual data of the single sweep ERP for the subject 7 (normal mail adult) : (a) raw data and (b)processed data through the band-pass filter of 1-8 [Hz]. The positive peaks indicated by arrows were judged to be P300 by using the automatic detection method.

normal adults' ERP data, and the results were obtained according to the subjects. In almost all the subjects, the physiological fluctuation evidently existed, because the lower band of the intervals had positive value. However, in the subject 14, it was not clear that whether the physiological fluctuation exists or not, since the large noise fluctuation was included in the measurement fluctuation.

The measurement fluctuation was calculated based on the P300 waveforms detected by the automatic detection method [5]. Therefore, accurate detection of the P300 waveform is required. The automatic detection method was developed so that the result of this method agreed with that of visual inspection by investigator [5]. Then, the correct estimate of the measurement fluctuation was obtained. If the SN ratio is extremely low, it is difficult to detect the P300 waveform accurately. In this case, the correct physiological fluctuation can not be estimated. However, the proposed method can be applied to the other biomedical data, if the SN ratio of the processed data is about 1 or more.

In the proposed method, the two-sided interval estimate was done. If the one-sided interval estimate is done in the interval estimate of the SN ratio and the noise fluctuation ($\chi_4 = 2K(1 + \hat{R})/\hat{R}$), the lowest limit of the interval of the physiological fluctuation can be obtained, and it can be indicated that at least how much the physiological fluctuation exists. Furthermore, the requisite number of the single sweeps of the P300 for obtaining the required interval estimate of the physiological fluctuation can be calculated by using the proposed procedure.

5. Conclusion

We proposed a method for extracting the physiological fluctuation of the peak latency of the P300 by subtracting the noise fluctuation from the measurement fluctuation. We clarified the relationship between the SN ratio and the noise fluctuation based on the simulation, and estimated the noise fluctuation by using the relationship. In the case of a large number of samples, the plot estimate of the physiological fluctuation is sufficient, however, in the case of a limited number of samples, the interval estimate of the physiological fluctuation is more useful. In order to evaluate the proposed method, we used the simulation data whose physiological fluctuation was generated by using the normal random numbers, and the physiological fluctuation was estimated accurately. Furthermore, the proposed method was applied to the actual ERP data of sixteen normal adults, and satisfactory results were obtained.

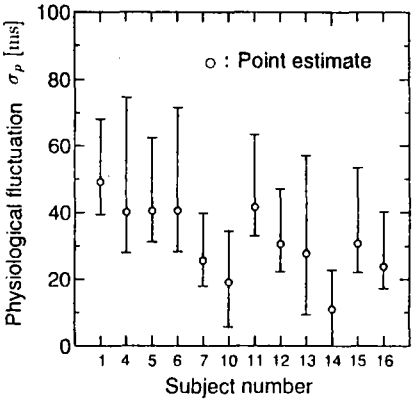

Figure 5 Results of the interval estimates and the point estimates of the physiological fluctuation for the actual data.

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