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Nonlinear Analysis Using Multiple Cutoff Frequencies for Local Cerebral Blood Flow during Biofeedback Training

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Biofeedback (BF) is expected not only as a means for gaining control of bodily processes to increase relaxation, relieve pain and improve health, but also to develop and improve the brain's body control function. The aim of the biofeedback training (BFT) is to promote the recovery and the development of physical dysfunctions under consciousness. A BF instrument has three tasks. First is to monitor (in some way) a physiological process of interest. Second is to measure (quantify) what is monitored. Third is to present what is monitored or measured as meaningful information. One technique for non-invasive measurement of brain activity that has been developed in recent years is brain functional imaging using near-infrared spectroscopy (NIRS). Compared to other techniques of measurement of brain activity, NIRS is a low-restraint and non-invasive measuring technique. In addition, it enables a user to take electrophysiological measurements such as Electromyography and Electrocardiography during training activity or other movements. In recent years, NIRS has a high profile for investigations of the relationship between physical control and brain function.

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Here, we investigated the connection between BFT and local cerebral blood flow, by performing cranial NIRS with simultaneous electromyogram (EMG), recording from the rectus femoris muscle. Our results suggest that We have succeeded in findings of the nonlinearity for hemodynamics in the cerebral blood flow on the frontal lobe during the muscle contraction and the post-rest.

Keywords: Biofeedback training; kicking action; electromyography; cerebral blood flow; near-infrared spectroscopy; mental training; non-linear; low-pass filter; cut-off frequency.

1. INTRODUCTION

The electromyogram (EMG) is frequently used to monitor motion and muscle performance during biofeedback (BF) training (BFT)Pioneered by Jacobson at Harvard University in 1908, the use of BF techniques resulted in the progressive muscle relaxation technique [1].

Indeed, progressive muscle relaxation is used to control anxiety and is thought to encourage self-care and enhance overall health [2]. Jacobsen (1938) worked to develop progressive muscle relaxation as an effective behavioural technique for the alleviation of neurotic tensions and many functional medical disorders. Crude electromyographic equipment was used to monitor the levels of muscle tension in his patients during the course of treatment. The classification of and historical perspective on biofeedback applications can be found in reports by Gatchel and Price (1979), Gaarder and Montgomery (1981), and Basmajian (1989) et al. Comprehensively reviews the applications and historical perspectives of BF, which are beyond the scope of this discussion [3-5]. BFT is not only a technique used for enhancing health, but is predicted to affect the development and maintenance of brain function [6,7]. The connection between BFT and brain function surely will garner further attention in future, as current studies state that BFT involves not only voluntary movement of the extremities and joints, but receives input from high-level integrative functions of the brain.

Recently, it has been shown that hip flexor muscles used to bend the hip joint when walking, rapidly reduce in mass with age. Hip joint flexors include the femoral rectus and abdominal muscles, which have been implicated as being related to falls in elderly people. Brain blood flow in the cerebrum is easy to contain the artifacts such as physical exercise and cardiovascular activity. Therefore, subjects should seat in order to evaluate the effect of local exercise in this study. We herein examined the average rectified sEMG of the femoral rectus muscles performed during the BFT of the dominant leg. BF techniques allow subjects to observe EMG signals or signal-derived outputs in order to encourage self-control of a specific muscle. This technique has been used to develop a technique for the “local exercise” of muscles including the femoral rectus, thus contributing to fall prevention and health enhancement in the elderly. Instruction is frequently provided using a visual or auditory signal.

One technique for non-invasive measurement of brain activity that has been developed in recent years is brain functional imaging using near-infrared spectroscopy (NIRS). With developments such as the miniaturization of diagnostic equipment, brain science is developing rapidly and a variety of brain activities are being defined [8-20].

NIRS requires the subject to be restrained to a lesser degree than with other techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) [21-23].

NIRS measures changes in hemoglobin (Hb) concentration in the blood. There is a limitation to the wavelength range at which near infrared light is absorbed in the body [24], however, near infrared light scattered into brain tissue from above the scalp, can reach the cerebral cortex [25]. The cerebral cortex is located at a depth of 15-20 mm from the scalp and displays a close correlation between neural activity and capillary constriction or dilation. The cerebral cortex is therefore suitable for measuring changes in intracerebral hemoglobin concentration associated with brain activity. Moreover, the cerebral cortex is also critically linked to movement, sensation, language and cognition. During NIRS of the cerebral cortex, activity is measured using multichannel reflection measurements from the scalp. Briefly, light-emitting probes and light-receiving probes are placed on the scalp and then near infrared light (wavelength of 700-900 nm), with high permeability into biotissue, is emitted from these light-emitting probes. The light-receiving probes then detect light that is scattered and reflected by the cerebral cortex.

Blood contains two types of hemoglobin, namely oxygenated hemoglobin (Oxy-Hb) that is bound to oxygen and deoxygenated hemoglobin (Deoxy-Hb) that is not bound to oxygen and the absorption spectra differs for both [24]. The present study uses this characteristic to measure Oxy-Hb concentration (Co) and Deoxy-Hb concentration (Cd) using the continuous wave (CW) method, based on the attenuation of detected light versus the intensity of the near infrared light reflection at two wavelengths, λ_1 and λ_2. The CW method is based on the modified Lambert-Beer (MLB) method and measures the concentration change from the start of recording multiplied by the optical path [24,26]. This method is useful as the human body scatters light strongly, meaning the direct optical path from emission to detection cannot be reliably measured and therefore, obtained values do not represent absolute Hb levels.

Measurements using NIRS assume neurovascular coupling in the same way as other measuring techniques [26]. Neurovascular coupling in the brain refers to blood vessels dilating near active nerves, in order that arterial blood that contains high levels of oxygen and glucose can be supplied, with associated changes in Oxy-Hb and Deoxy-Hb [27]. Additionally, active states in brain regions can be estimated by measuring changes in cerebral blood flow. In fact, it has been demonstrated that localized Hb increase and decrease (Co, Cd) reflect cerebral activity [28,29].

In brain activity measurements using NIRS, the prefrontal cortex (related to working memory, control of attention, cognition and emotion) and the premotor cortex (related to planning and preparing for motion) are activated during low-load “full-body movement” (e.g. walking) [30]. In fact, studies report that cognitive function in elderly people is improved through walking exercise [31]. Furthermore, previous work by the authors demonstrated the possibility that specific“ local movement” (masticatory movement in this case) stimulates activity of the prefrontal cortex [32].

In the present study, measurements were taken from the femoral rectus using EMG and NIRS simultaneously for healthy young subjects, whose physiological properties are not markedly different from those of healthy elderly subjects, to reveal the effect of BFT on the brain and in particular the prefrontal cortex. In addition, the effect of BFT exercise tasks on local cerebral blood flow was investigated.

2. MATERIALS AND METHODS

2.1 Participants

Biometric data were obtained for the femoral rectus muscle in ten healthy young individuals (24.7 ± 4.5 year) with no abnormalities in the extremities and no past medical history of ear or nervous system disease. All subjects were about average size, and their body mass index (BMI) distributed from 18 to 25 kg/m2. The experiment was fully explained to the subjects beforehand, and written consent was obtained. The experiment was approved by the Ethics Committee of Department of human and artificial intelligent systems, Graduate School of Engineering University of Fukui (No.2).

2.2 Materials

Surface EMG tests were performed by connecting an EMG transformation box (AP-U027, TEAC Co., Tokyo) to a commercially available portable multi-purpose bio-signal amplifier-embedded collection device (Polymate AP1532, TEAC Co., Tokyo) and by using dedicated bipolar EMG electrodes with pre-amps(20 dB). Also, AP Monitor is a software to show the teacher signal of the BFT and simultaneously smoothed sequences of the EMG for subjects. Furthermore, an AP Monitor (NoruPro, Tokyo) was used to obtain PC recordings at a 2 kHz sampling frequency to show muscle activity to the subjects in real time. Subjects were given full explanations prior to undergoing the tests and consent was obtained in writing.

2.3 Procedure

The following outline summarizes the experimental process:

Step 1: Subjects were asked to sit back on a chair (with four fixed legs) and to kick with their dominant leg against a belt, attached to the lower part of the chair (Fig. 1).

Step 2: Away from the center of the femoral rectus, AMG electrodes were placed at intervals of a few centimeters and subjects were asked to perform their maximum voluntary contraction. The average integral waveform of the surface

EMG was calculated for this period of muscle contraction and muscular activity corresponding to α=75% (third quartile) of maximum voluntary contraction was then estimated.

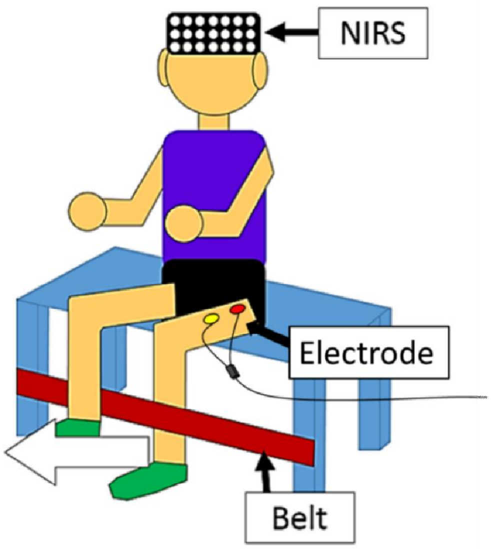

Fig. 1. Biofeedback training experiment for rectus femoris muscle.

Step 3: Muscular activity corresponding to α% of maximum voluntary contraction was shown to the subject as the instruction signal and five cycles of intermittent signals were provided for 40 seconds of contraction (gradual build-up during the first 20 seconds), hereafter referred to as the "transient period (TP)", followed by 20 seconds of constant muscle activity, hereafter referred to as the "muscle contraction period (MCP)" and then 40 seconds of relaxation (the first 20 seconds are referred to as the pre-rest and the last 20 seconds as post-rest) .This series of flows was carried out five times in a row (Fig. 2).

The EMG waveforms obtained over 400 seconds were rectified and smoothed in real time at 0.1 second intervals of integration and these integral waveforms were then shown to subjects (in addition to the instruction signals). Cut-off frequency for the high and low range cutoff filters was set at 1 kHz and 16 kHz, noise was removed from the surface EMG by inserting an AC removal filter and evaluation performed through a "sensor output signal evaluation system".

Step 4: In conjunction with Step 3, the optical brain function imaging device LABNIRS (Shimadzu Corporation, Kyoto) was used to measure Co and Cd at a sampling frequency of 17.5 Hz [26,34]. A holder was placed on the subject's head, with light-emitting/receiving probes arranged based on international 10-20 sensor placement as shown in Fig. 3. Changes in cerebral blood flow concentrations were measured on the frontal lobe, at 54 channels (Fig. 3).

Owing to space limitations, this manuscript focuses on the analysis of Co only.

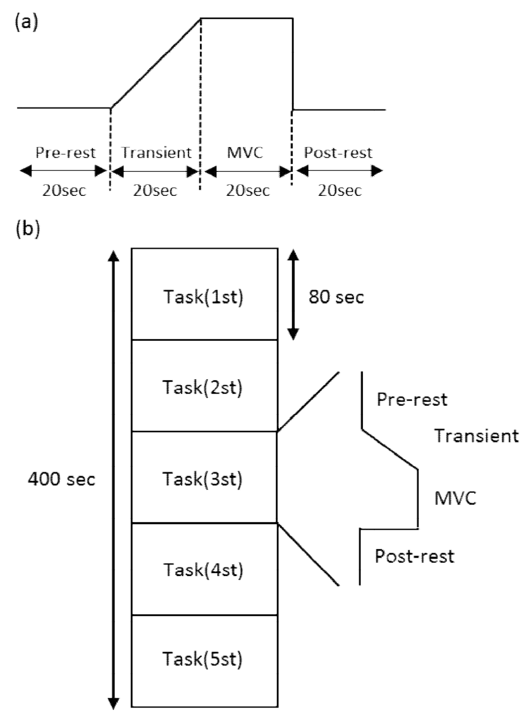

Fig. 2. Experiment protocol: a procedure for single task (a); a series of procedures with repeated tasks (b).

2.4 Data Analysis

For each subject, standardization was performed using average Co in the pre-rest period in each BFT cycle and the standard deviation. Standardized sequences were obtained in each period; the pre-rest, the TP, the MCP and the post-rest.

In this study, we analyzed time sequences of the Co for 8 ch. The time series were smoothed by the low-pass filtering whose cut-off frequency f_0 was set to be 0.1, 0.2, 0.3, 0.5, 1, 1.5, 2 Hz, respectively. We can measure the degree of determinism for the mathematical model of the time series $\{x_t\}$. Translation errors E_{trans} [33] were herein estimated for each time series in addition to sequences of their temporal differences by the Double Wayland algorithm [34, 35]. Also, we compared E_{trans} for the abovementioned time series with their surrogate sequences that were generated by the Fourier shuffle (FS) algorithm [36, 37]. The length of the time series must be 2^n because Fast Fourier Transformation (FFT) is conducted in this algorithm. In this study, the length of the time sequences was set to be 256 (n =8), and time sequences extracted from the onset time (0 s) to 15 s/6 s to 20 s are defined as the first half period/the later half period, respectively. The value of E_{trans} were estimated as an average of those for the first half and the later half period.

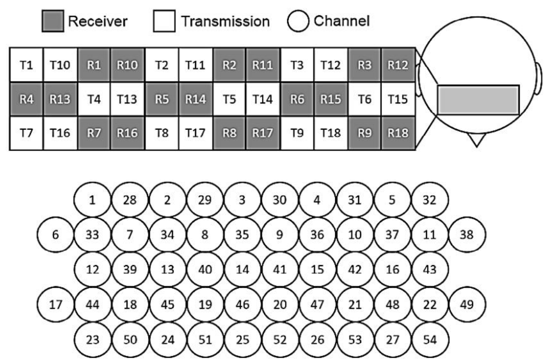

Fig. 3. Array of irradiation and light-receiving probes.

These translation errors were compared with each other by the Welch-Aspin test in order to evaluate the nonlinearity of the mathematical model describing the hemodynamics in the cerebrum. The significant level was set to be 0.05.

3. RESULTS

BFT was carried out for 10 subjects, and we confirmed the records of the muscle performance in the BFT by the sensor output evaluation system. For all subjects, smoothed integral signal of the rectified EMG was fit to the teacher signal well. We also recorded time series data of local cerebral blood flow on the frontal lobe at 54 channels (Fig. 3).

In this study, we focused on a period for the fourth task (Fig. 2b), which is comparatively stable compared to the other periods (Fig. 4). Standardized sequences were extracted for the fourth task as in Fig. 5b. The data analysis was conducted for the time series smoothed by the low-pass filtering whose f_0 was set to be 0.1, 0.2, 0.3, 0.5, 1, 1.5, 2 Hz, respectively. By the Double Wayland algorithm, E_{trans} was estimated for time series data of Co and the sequences of their temporal differences as $\{x_{t+\tau} - x_t\}$ (Fig. 6), where the delay time τ is the time until the autocorrelation function of each time series data becomes less than 1/e (Table 1). The growth of E_{trans} monotonically increased according to the increase of the cut-off frequency f_0 and . Based on this result of the values in E_{trans} for $f_0 \geq 0.2$ Hz, it is a solid argument in the MCP and the post-rest that the hemodynamics in the cerebrum is assumed to be described by a stochastic process. The details of that basis are discussed in the next section.

Setting the following statistical hypothesis, E_{trans} for each time series was compared with their surrogate sequences that were generated by the FS algorithm (Figs. 7).

Null hypothesis H_0: Time series are generated by the linear mathematical model.

Alternative hypothesis H_1: Time series are generated by the non-linear mathematical model.

For the MCP, statistical significances were observed in the comparison of translation errors estimated from standardized time series smoothed by the low-pass filtering (f_0 = 0.1, 0.2) with those from their surrogate sequences, respectively (Fig. 7a). Also, we could find the statistical significances in the comparison of translation errors estimated from the sequences of temporal differences (f_0 = 0.1, 0.2) with those from their surrogate time series, respectively (Fig. 8a).

Table 1. Delay time τ estimated by the auto-correlation functions

Hz / Period	0.1	0.2	0.3	0.5	1	1.5	2	None
Pre-rest	56	46	45	39	29	22	15	1
Transient	57	52	49	35	27	24	19	1
MCV	66	58	53	49	31	26	26	2
Post-rest	51	46	45	46	44	42	36	6

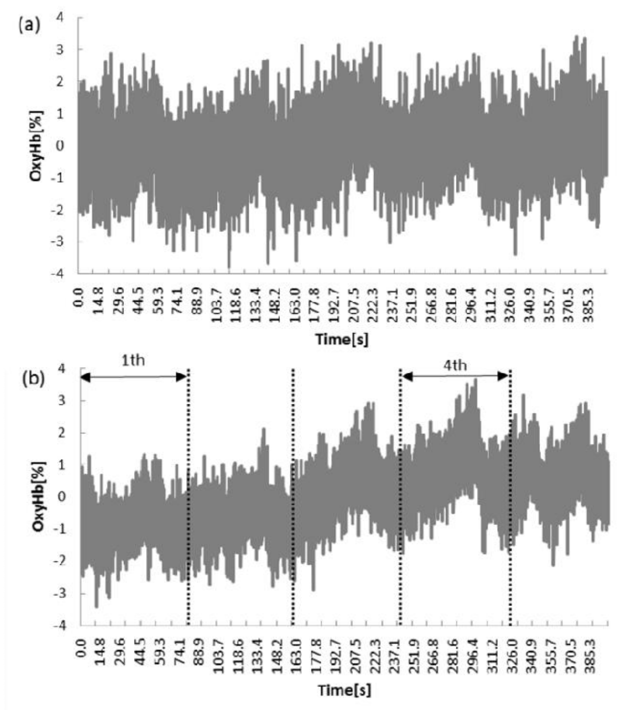

Fig. 4. Standardized variations of the local cerebral blood flow. Typical graph of time series of Co at 36 ch (a); 8 ch (b).

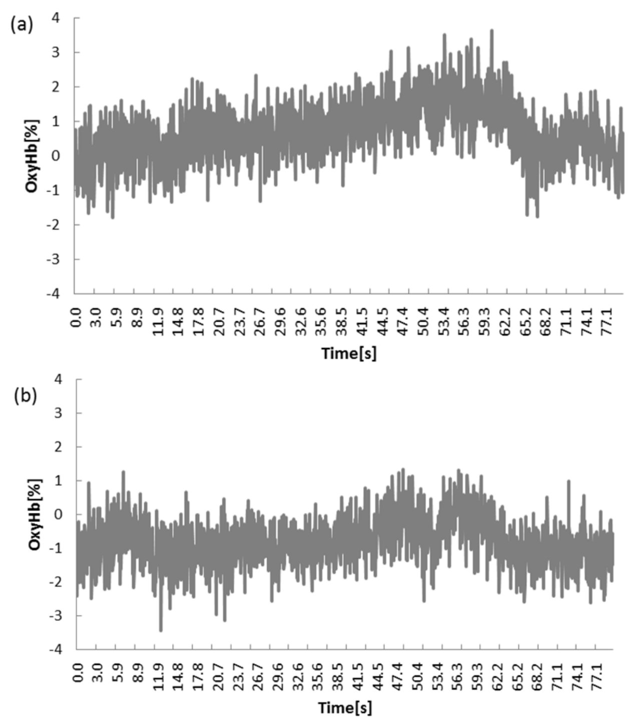

Fig. 5. Typical graph of time series of Co for the following periods. Time sequences extracted from Fig. 4; forth task period (a); the first task period (b).

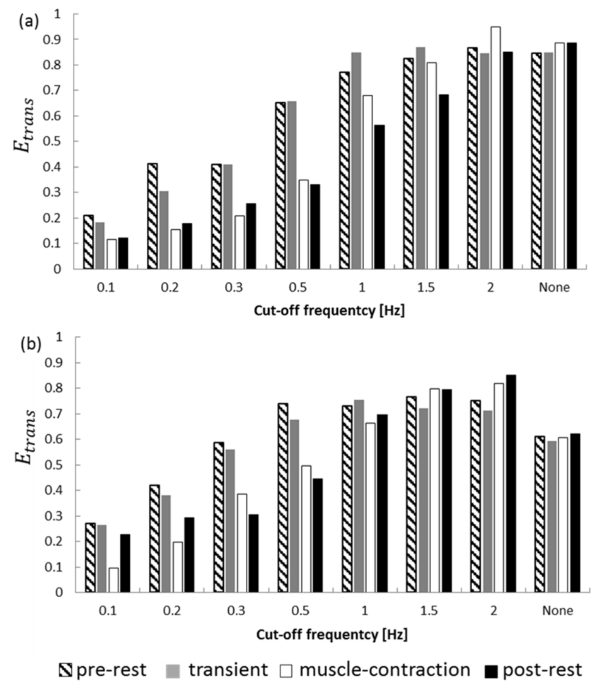

Fig. 6. Translation errors E_{trans} for all experimental periods. We can compare E_{trans} estimated from standardized time series smoothed by the low-pass filtering (a); the sequences of their temporal differences (b).

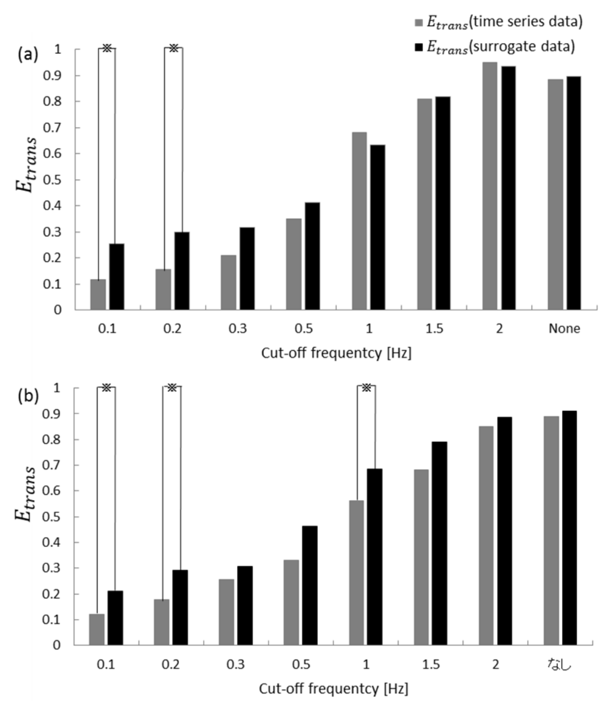

Fig. 7. Statistical comparison of E_{trans} estimated from standardized time series smoothed by the low-pass filtering with their surrogate sequences. Translation errors E_{trans} for MCP (a); post-rest (b).

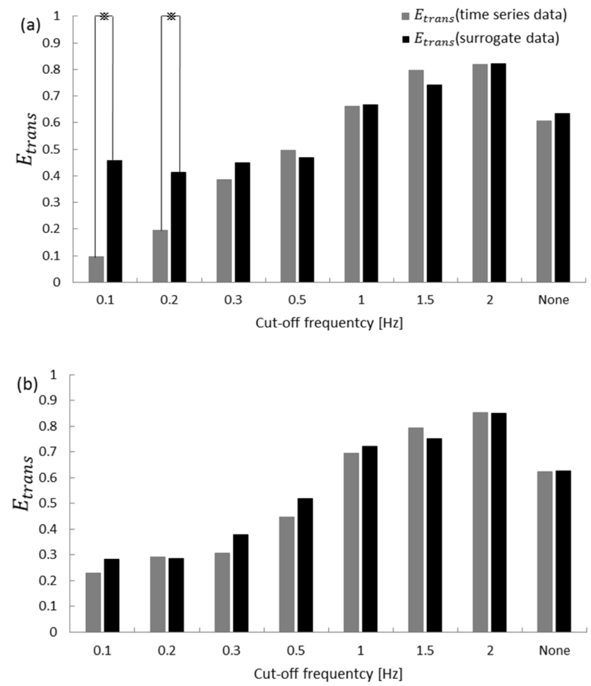

Fig. 8. Statistical comparison of E_{trans} estimated from the sequences of temporal differences with their surrogate sequences. Translation errors E_{trans} for MCP (a); post-rest (b).

In these cases, the null hypothesis was rejected as shown in Fig. 7 (*p<0.05).

For the post-rest, statistical significances were observed in the comparison of translation errors estimated from standardized time series smoothed by the low-pass filtering (f_0 = 0.1, 0.2, 1) with those from their surrogate sequences, respectively (Fig. 7b). However, there was no statistical significance in the comparison of translation errors estimated from the sequences of temporal differences with those from their surrogate time series (Fig. 8b).

4. DISCUSSION

The BFT is also known as a countermeasure for the patients with intractable epilepsy and reduction method for the mental stress [38-47]. However, a method for objectively evaluating does not have been established yet whereas subjective evaluation and findings were stated in the previous study. Also, there is no study to evaluate the cerebral hemodynamics and investigate the cerebral blood flow regulation during the BFT. According to our previous consideration in the bio-signal, it is necessary to evaluate robust bio-system by using the mathematical models because the changes in the system can be hardly found out. Moreover, it is important to set the cut-off frequency to denoise in the bio-signal, especially in the brain function analysis. However, there is no prior research that defined the cut-off frequency, based on the mathematical consideration. Therefore, we herein focused on mathematical design of the cut-off frequency in the low-pass filtering.

In order to evaluate the degree of determinism for the mathematical model of the hemodynamics on the frontal lobe, translation errors were estimated for each time series in addition to sequences of their temporal differences by the Double Wayland algorithm (Fig. 6). Translation errors estimated from the MCP and post-rest were less than those from the other experimental periods. Although it is a relative evaluation, we could confirm the stationarity in the hemodynamics in the cerebrum for the MCP and the post-rest. The BFT might affect the hemodynamics in the cerebrum, especially in the frontal lobe including the prefrontal cortex, in which the degree of determinism is enhanced by the regularity of this exercise protocol. This is why it is important to measure/analyze the hemodynamics in the cerebrum in these experimental periods.

In general, it is a solid argument that the values of E_{trans} is less than 0.1 estimated from the deterministic process as numerical solution to ordinal differential equations for the embedding dimension ≤ 10 dim [48]. In the MCP and the post-rest, the hemodynamics in the cerebrum is regarded as a stochastic process because the values in E_{trans} was not less than 0.1 estimated from standardized time series smoothed by the low-pass filtering for $f_0 \geq 0.2$ Hz. Whereas the values in E_{trans} was saturated for the bounded f_0-value (≥ 0.2 Hz), it decreased without the low-pass filtering as $f_0 \to \infty$. This is because the rhythmic artifacts are contained as cardiovascular bio-signal or body motion with the BFT.

Moreover, the values in E_{trans} estimated from standardized time series smoothed by this low-pass filtering were less than those from the sequences of temporal differences. It is a concept of the Double Wayland algorithm that stochastic generators enhance the degree of complexity in the sequences of temporal differences.

Artifact could be reduced in standardized time series smoothed by the low-pass filtering ($f_0 < 1$ Hz) because the growth of E_{trans} the monotonically increased according to the increase of the cut-off frequency f_0. Setting the cut-off frequency in the low-pass filtering to be less than 0.2 Hz, noise reduction is considered to be more effective than the other cases mentioned above. However, the cerebral blood flow in the frontal lobe is not always generated by the stochastic process as shown in Fig. 6.

Nonlinearity was investigated in the mathematical model of the hemodynamics in the cerebrum; setting the abovementioned null hypothesis H_0, E_{trans} for each time series (including the sequences of temporal differences) was compared with their surrogate sequences that were generated by the FS algorithm (Figs 7-8). For the MCP, statistical significances were observed in the comparison of translation errors estimated from standardized time series (including the sequences of temporal differences) with those from their surrogate sequences (f_0 = 0.1, 0.2) as shown in Figures 7a, 8a. In these cases, the null hypothesis was rejected, and the nonlinearity in the hemodynamics of the cerebrum could be statistically shown for $f_0 < 0.3$. Setting the cut-off frequency to be $f_0 \leq 0.2$ Hz in the low-pass filtering for the time series analysis, the cerebral blood flow is thus considered to be generated by the nonlinear mathematical model. Base on the stochastic theory, a mathematical model could be derived from the set of stochastic differential equations including the nonlinear group only if we set the cut-off frequency to be 0.2 Hz in the low-pass filtering for the analysis of the hemodynamics in the cerebral blood flow.

In the case of the post-rest, however, there was no common significance in the comparison of the sequences of temporal differences with those from their surrogate time series for each cut-off frequency (Fig. 8b). This is because translation errors estimated from the sequences of temporal differences are more sensitive for the evaluation of complexity in the motion process than those from the time series data.

5. CONCLUSION

In this study we investigated the effect of the BFT on the local cerebral blood flow on the frontal lobe. We have succeeded in finding that the effect can be seen in the MCP and the post-rest. Setting the cut-off frequency to be $1 \geq f_0 \geq 0.3$ Hz, We have succeeded in findings that the mathematical model of the cerebral blood flow is regarded as a stochastic differential equation with setting the cut-off frequency to be 0.2 Hz in the low-pass filtering for the time series analysis.

CONSENT

The experiment was fully explained to the subjects beforehand, and written consent was obtained.

ETHICAL APPROVAL

The experiment was approved by the Ethics Committee of Department of human and artificial intelligent systems, Graduate School of Engineering University of Fukui (No.2).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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