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Assessing complexity of skin blood flow oscillations in response to locally applied heating and pressure in rats: implications for pressure ulcer risk

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Abstract

The objective of this study was to investigate the effects of local heating on complexity of skin blood flow oscillations (BFO) under prolonged surface pressure in rats. Eleven Sprague–Dawley rats were studied: 7 rats underwent surface pressure with local heating ($\Delta t = 10^\circ\text{C}$) and 4 rats underwent pressure without heating. A pressure of 700 mmHg was applied to the right trochanter area of rats for 3 h. Skin blood flow was measured using laser Doppler flowmetry. The loading period was divided into nonoverlapping 30 min epochs. For each epoch, multifractal detrended fluctuation analysis (MDFa) was utilized to compute DFA coefficients and complexity of endothelia related metabolic, neurogenic, and myogenic frequencies of BFO. The results showed that under surface pressure, local heating led to a significant decrease in DFA coefficients of myogenic frequency during the initial epoch of loading period, a sustained decrease in complexity of myogenic frequency, and a significantly higher degree of complexity of metabolic frequency during the later phase of loading period. Surrogate tests showed that the reduction in complexity of myogenic frequency was associated with a loss of nonlinearity whereas increased complexity of metabolic frequency was associated with enhanced nonlinearity. Our results indicate that increased metabolic activity and decreased myogenic response due to local heating manifest themselves not only in magnitudes of metabolic and myogenic frequencies but also in their structural complexity. This study demonstrates the feasibility of using complexity analysis of BFO to monitor the ischemic status of weight-bearing skin and risk of pressure ulcers.

Keywords

complexity; loading pressure; local heating; pressure ulcers; skin blood flow

1. Introduction

Pressure ulcers are localized injury to the skin and/or underlying soft tissues that usually occur at bony prominences. Although the etiology of pressure ulcer formation is multifactorial, prolonged pressure-induced soft tissue ischemia is widely accepted as the most important factor [1]. Other factors such as shear, temperature, and moisture also contribute to soft tissue ischemia and subsequent development of pressure ulcers [2]. The influences of surface pressure on soft tissue ischemia have been investigated in the past;

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however, the effect of other factors such as temperature on tissue ischemia has not been well studied [2, 3].

Recent studies conducted on porcine models have provided evidence that under the same loading condition, the severity of soft tissue damage was highly correlated with the skin temperature [4–6]. In these studies, when the skin was cooled to 25°C, no tissue damage occurred, but when the skin was heated to 45°C, full-thickness tissue damage was observed. This evidence indicates that skin temperature affects the rate of tissue damage caused by surface pressure. Patel [7] found that local heating increased perfusion in the rat skin under surface pressures from 3.7 to 18 mmHg, but not for surface pressures greater than 18 mmHg. They also observed increased peak flow after the removal of surface pressure (reactive hyperemia) when local heating was used. A recent study on human subjects showed that local cooling reduced peak hyperemia [3]. The authors therefore suggested that reduced hyperemia may indicate a less severe degree of ischemia. Reactive hyperemia has also been found to be extremely variable, even in the young healthy population [8]. Therefore, evaluation of tissue perfusion under surface pressure may provide additional information of the skin in response to combined surface pressure and temperature stimuli. Such information may improve the understanding of pressure ulcer development.

Spectral analysis of blood flow oscillations has been recently introduced to study the underlying mechanisms of skin blood flow regulation [9, 10]. This technique provides a more sophisticated insight into blood flow responses to loading pressure and/or thermal stress [2, 11]. Using spectral analysis, at least five characteristic frequencies have been found in skin blood flow oscillations (BFO) [9, 10]. The frequencies around 1.0 Hz and 0.3 Hz originate from the heart beats and respirations, respectively, and the frequencies around 0.1 Hz, 0.04 Hz and 0.01 Hz are associated with the myogenic activity of vascular smooth muscles, neurogenic activity and vascular endothelial related metabolic activity, respectively. In anaesthetized rats, five characteristic frequencies have also been identified and are associated with endothelial related metabolic activity (0.01–0.076 Hz), neurogenic activity (0.076–0.2 Hz), myogenic activity (0.2–0.74 Hz), respiration (0.74–2 Hz), and heart beats (2–5 Hz) [2, 12, 13]. Our previous study showed that skin blood flow continually decreased under surface pressure without temperature changes or surface pressure with heating, but maintained relatively stable under surface pressure with cooling [2]. Moreover, wavelet analysis of BFO revealed that stable blood flow under surface pressure with cooling was attributed to smaller changes in amplitudes (powers) of metabolic and myogenic frequencies. However, questions may be immediately raised as to whether amplitudes (powers) of the characteristic frequencies fully quantify the responses and how interactions between the underlying mechanisms are altered during the responses [2].

Skin blood flow has been found to exhibit irregular fluctuations over time [14–16]. Griffith [15] suggested that spontaneous contraction and dilation of the vessel wall and the nonlinear rheological properties of blood may contribute to this phenomenon. Recent studies provide evidence indicating interactions among the underlying physiological mechanisms [17]. Intuitively, a straightforward way to identify and characterize the interactions is to extract instantaneous phases or frequencies of the characteristic frequencies [18]. However, the metabolic, neurogenic, and myogenic frequencies cannot be selectively measured and are not constant but highly time varying [19]. This makes it difficult to directly evaluate the interactions among characteristic frequencies.

The above problem may be addressed by quantifying the complexity of the characteristic frequencies. Goldberger [20] suggested that the complexity of a physiologic system arises from the interaction of structural units and regulatory feedback loops [20]. Lipsitz and Goldberger [21] proposed that a loss of complexity in physiologic function may be due to

the impairment of functional components and/or altered coupling between these components. Our earlier work [16, 22] demonstrates that complexity of BFO can be quantified using the multifractal detrended fluctuation analysis (MDFA) [23]. This method is a generation of the standard detrended fluctuation analysis (DFA) [24]. The advantages of DFA over other commonly used nonlinear measures are that it allows the detection of long-range correlations embedded in seemingly nonstationary time series [25], and also allows the quantification of correlation properties of a specific frequency component [16, 22].

This study investigates the effects of local heating on complexity of BFO under prolonged loading pressure. We assumed that the complexity of a characteristic frequency of BFO is associated with the interactions between the mechanism underlying this frequency and other regulatory mechanisms of skin blood flow. We studied metabolic, neurogenic, and myogenic oscillations under two conditions, including surface pressure with local heating and surface pressure without heating. MDFA was utilized to quantify the DFA coefficients and complexity of BFO. Previous studies have shown that local heating (without simultaneous surface pressure) caused an increased contribution of metabolic component but a decreased contribution of myogenic component to BFO [2, 10, 26]. This is because of increased metabolic demands of local cells and tissues [27] and a direct relaxation of smooth muscle cells within the vessel wall [28]. However, whether such response will be altered when both local heating and surface pressure are applied at the same time largely unclear [2, 29]. We thereby hypothesized that under surface pressure, local heating would reduce dynamics of myogenic response and interactions between myogenic mechanism and other control mechanisms of skin blood flow.

2. Materials and Methods

2.1 Animals

Eleven 8–12 week old male Sprague–Dawley rats weighing between 300 and 400 g were used. These rats were fed with a standard nutrient diet, without supplement of any extra vitamins. All rats had skin temperature around 37°C. The rats were assigned to two protocols: 7 rats underwent pressure with heating and 4 rats underwent pressure without heating. The protocols were approved by an institutional animal care and use committee.

2.2 Data Collection

Room temperature was maintained at 24 ± 2 °C. Each rat was anesthetized with ketamine (67 mg ml⁻¹) and xylazine (33 mg ml⁻¹) injected intraperitoneally. The depth of anesthesia was determined by moustache dithering tests. When the rat was unconscious, the hairs on the left and right trochanter areas were carefully shaved without damage to the skin. Then the rat was positioned prone on a soft air temperature mat. Laser Doppler flowmetry (PF 5001, Perimed, Sweden) was used to measure skin blood flow and temperature and to heat the skin. A heating probe (Probe 415-242, Perimed, Sweden) was placed on the shaved skin of the right trochanter area. Skin blood flow and temperature were recorded at a sampling rate of 32 Hz. A surface pressure of 700 mmHg was applied to the heating probe using a custom designed indenter [2]. The protocol included a 20 min baseline, a 180 min loading period, and a 20 min recovery period. During the loading period, temperature was set to increase 10°C in 7 rats and without temperature changes in 4 rats. The rationales for determining the parameters of the protocols have been described in our previous study [2]. Fig. 1 shows examples of skin blood flow in response to pressure and pressure with heating.

The selection of the parameters of the protocols was based on the protocols used in previous studies [4, 5, 30, 31]. In a study by Kwan et al. [31], a pressure of 100 mmHg was applied to the trochanter and tibialis areas of rats for 6 h each day for four consecutive days. After two

days, cutaneous tissue damage was observed at the trochanter area but not at the tibialis area. Linder-Ganz and Gefen [30] applied pressures of 86, 262 and 525 mmHg to gracilis muscles of rats for 2, 4 and 6 h. They found that muscles exposed to 262 and 525 mmHg became stiffer and the stiffening was accompanied by extensive necrotic damage. To ensure the development of a pressure ulcer, we chose a larger pressure of 700 mmHg for 3 h. As for skin temperature, previous studies showed that a series of skin temperatures of 25, 35, 40 and 45 °C had distinguishable effects on the severity of tissue damage [4–6]. We therefore chose an increase in skin temperature by 10 °C, which would allow us to study the influences of temperature changes on skin blood flow response to prolonged surface pressure in rats.

2.3 Multifractal detrended fluctuation analysis (MDFA)

The MDFA is a generalization of the standard DFA [23]. DFA was introduced by Peng [24] to estimate long-range power-law correlations along DNA sequences. The root-mean-square fluctuation of an integrated and detrended time series is measured at different observation windows and plotted against the size of the observation window on a log–log scale [24]. A power-law relation between the fluctuation and the observation size indicates the presence of scaling. The slope of the log-log graph gives an estimation of the scaling exponent α , which represents the correlation properties of the signal. An uncorrelated signal (white noise) yields $\alpha=0.5$; a scaling exponent $\alpha>0.5$ indicates the presence of positive correlations in the signal; and $0<\alpha<0.5$ indicates anti-correlations in the signal.

The procedure of MDFA consists of five steps, with the first three steps being identical to the DFA procedure. Given a time series $x(k)$ of length N on a compact support, the first step is to integrate the time series

$$Y(i) = \sum_{k=1}^i (x(k) - \langle x \rangle), i=1, \dots, N, \quad (1)$$

where $\langle x \rangle$ is the mean of the time series. Then integrated time series is divided into N_s nonoverlapping segments of length s and the same procedure is repeated starting from the opposite end ($2N_s$ segments totally). For each segment ν , the local trend is estimated by fitting a m th-order polynomial $P_\nu^{(m)}$ and subtracted from the segment. Next, one calculates the variance

$$F^2(\nu, s) = \frac{1}{s} \sum_{i=1}^s \{Y_q[(\nu-1)s+i] - P_\nu^{(m)}(i)\}^2 \quad (2)$$

for each segment ν , $\nu = 1, \dots, N_s$ and

$$F^2(\nu, s) = \frac{1}{s} \sum_{i=1}^s \{Y[N - (\nu - N_s)s+i] - P_\nu^{(m)}(i)\}^2 \quad (3)$$

for $\nu = N_s + 1, \dots, 2N_s$. Finally, a q th order fluctuation function is defined as

$$F_q(s) = \left\{ \frac{1}{2N_s} \sum_{\nu=1}^{2N_s} [F^2(\nu, s)]^{q/2} \right\}^{1/q} \quad (4)$$

for $q \neq 0$ and $F_0(s)$ is defined as

$$F_0(s) = \exp \left\{ \frac{1}{4N_s} \sum_{\nu=1}^{2N_s} \ln [F^2(\nu, s)] \right\}. \quad (5)$$

For a long-range power-law correlated time series, $F_q(s)$ increases with s in a certain range as

$$F_q(s) \sim s^{\alpha(q)}. \quad (6)$$

For $q = 2$, $\alpha(q)$ is the DFA coefficient.

The above procedure yields a family of scaling exponents $\alpha(q)$. For a homogeneous signal, because all segments v have the same variance $F^2(v, s)$, and thus the average $F_q(s)$ is identical for all values of q , Eq. (6) gives a unique value of α that is independent of q . In contrast, for an inhomogeneous signal, different segments v usually have different variances $F^2(v, s)$. For $q > 0$, large values of $F^2(v, s)$ dominate the average $F_q(s)$, whereas for $q < 0$, small values of $F^2(v, s)$ dominate the average. In this case, Eq. (6) gives different values of α for different values of q . For $q > 0$, $\alpha(q)$ mainly reflects the correlation properties of the segments with large fluctuations, whereas for $q < 0$, $\alpha(q)$ mainly reflects the correlation properties of the segments with small fluctuations. The range of $\alpha(q)$, $\Delta\alpha = \max \{\alpha(q)\} - \min \{\alpha(q)\}$, reflects the differences of the scaling behavior between large fluctuations and small fluctuations. Therefore, it can be used as a measure of the complexity of the time series [16, 22].

2.4 Scale intervals corresponding to the characteristic frequencies of BFO

DFA is closely related to power spectral density (PSD) analysis [32, 33]. Let the PSD of the integrated time series, Y (Eq. 1), be $P_Y(f)$. If Y is divided into non-overlapping boxes with a length of s seconds and detrended, the PSD of the detrended series, P_{Y_d} , obeys the following relation [32, 33]

$$P_{Y_d}(f) \approx \begin{cases} 0, & 0 \leq f \leq 1/s \\ P_Y(f), & \text{otherwise} \end{cases} \quad (7)$$

Fig. 2 compares PSD between the integrated time series Y and the detrended series Y_d . It is evident that detrending in boxes with a length of s seconds is equivalent to applying a high-pass filter with a cut-off frequency of $1/s$ Hz. Thus, for a characteristic frequency of BFO with the frequency band f_1 – f_2 Hz, the corresponded scale (box size) interval is $1/f_2$ – $1/f_1$ seconds. As illustrated in Fig. 3, after filtering out the neurogenic component from the original signal, the scaling exponents in the corresponded scale interval are close to zero, while the scaling exponents in other scaling regions are nearly identical to that of the original signal. This is also the case for metabolic and myogenic frequencies. Therefore, assuming that the frequency bands of metabolic, neurogenic, and myogenic BFO are 0.01–0.076 Hz, 0.076–0.2 Hz, and 0.2–0.74 Hz, respectively [13], the corresponded scale intervals are 1/0.076–1/0.01 seconds, 1/0.2–1/0.076 seconds, and 1/0.74–1/0.2 seconds, respectively.

2.5 Application to experimental data

To study the evolutionary changes in the DFA coefficients and complexity of BFO, the 3 h loading period was divided into non-overlapping 30 min epochs [2]. For each epoch of blood flow data, MDFA was performed using the parameter $q \in [-5, 5]$ with a step of 0.1 [16, 22]. In the fitting procedure (Eq. 2), quadratic polynomials were used. These parameters have been validated to be suitable for analyzing skin blood flow data [16, 22]. The range of scaling exponents, $\Delta\alpha = \max \{\alpha(q)\} - \min \{\alpha(q)\}$, was used as a measure of the complexity of BFO. We found that for most of our data sets, $\Delta\alpha$ is more robust than the width of spectrum of Hölder exponents, which has been used as a measure of the multifractality of a signal.

2.6 Surrogate test

To further study whether changes in complexity of BFO $\Delta\alpha$ are related to changes in nonlinearity of BFO, we performed tests using surrogate time series. For each epoch of the original signal, 50 surrogate time series were generated by performing a Fourier transform on the original signal, preserving the amplitudes of the Fourier transform, but randomizing the phases, and then performing an inverse Fourier transform. This procedure destroys the nonlinearity, preserving only linear features of the original signal [34]. Then, complexity of BFO $\Delta\alpha$ was computed for all surrogate time series. A significant difference in complexity of BFO $\Delta\alpha$ between original data and surrogate data indicates that the original data possess nonlinearity.

2.7 Statistical analysis

The rank-sum test was used to examine the difference in α and $\Delta\alpha$ of metabolic, neurogenic, and myogenic components between two experimental conditions. Descriptive statistics were used to describe the evolutionary changes in α and $\Delta\alpha$ of three frequency components. One-sample t-test was used to examine the difference in $\Delta\alpha$ between the original data and surrogate time series. The normality of $\Delta\alpha$ values of surrogate time series was tested using the one-sample Kolmogorov-Smirnov test. All statistical tests were performed using SPSS 16 (SPSS, Chicago, IL) and the significant level was set at 0.05.

3. Results

Fig. 4 shows the DFA coefficients, α , of metabolic, neurogenic, and myogenic frequencies during the baseline and loading periods. α of metabolic frequency showed a sustained increase under both conditions, whereas α of neurogenic and myogenic frequencies underwent distinctly different changes. Surface pressure caused a dramatic decrease in α of neurogenic frequency during the first two epochs of the loading period, but did not have a significant effect on α of myogenic frequency. In contrast, pressure with heating resulted in a sharp decrease in α of myogenic frequency during the first two epochs of loading period, but had only a minor effect on α of neurogenic frequency. Obviously, under pressure with heating α of neurogenic frequency was significantly higher ($p < 0.05$) whereas α of myogenic frequency was significantly lower ($p < 0.05$) during most epochs of the loading period compared to pressure without heating.

Fig. 5 shows the complexity, $\Delta\alpha$, of the three characteristic frequencies. Under pressure without heating, $\Delta\alpha$ of metabolic frequency showed a decreasing trend, while $\Delta\alpha$ of neurogenic and myogenic frequencies showed smaller changes. Under pressure with heating, $\Delta\alpha$ of myogenic frequency underwent a sustained decrease, while $\Delta\alpha$ of metabolic frequency showed an increasing trend, and $\Delta\alpha$ of neurogenic frequency exhibited larger values during the middle phase of loading period. Comparing the two conditions, it is clear that local heating led to significantly higher degrees of complexity of metabolic frequency during the later phase ($p < 0.05$) and a significantly lower degree of complexity of myogenic frequency throughout the entire loading period ($p < 0.05$).

Fig. 6 shows typical examples of surrogate tests. Under pressure with heating, complexity $\Delta\alpha$ of metabolic frequency was significantly higher than that of surrogate data during the later epochs ($p < 0.05$) (Fig. 6b). Strikingly, complexity $\Delta\alpha$ of myogenic frequency gradually approached that of surrogate data for the condition of pressure with heating (Fig. 6f) but not for the condition of pressure without heating (Fig. 6e). This means that heating led to a gradual loss of nonlinearity of myogenic component.

4. Discussion

The major findings of the present study are that under prolonged surface pressure, local heating led to a significantly higher degree of complexity of metabolic frequency during the later phase of loading period and a significantly lower degree of complexity of myogenic frequency throughout the entire loading period. As discussed below, our results suggest that DFA coefficients of BFO give similar but different outcomes as compared to spectral analysis. Particularly, complexity analysis can reveal new features of BFO in response to surface pressure with thermal stress. To our knowledge, this is the first study investigating the combined effect of loading pressure and thermal stress on nonlinear dynamics of skin BFO.

In this study, the complexity measure $\Delta\alpha$ reflects the differences of the scaling behavior between large fluctuations and small fluctuations of BFO, which cannot be reflected by a single DFA coefficient ($q=2$).

Our result showed that under both conditions, DFA coefficients α of metabolic frequency underwent a sustained increase (Fig. 4a) throughout the loading period. A larger value of α means a higher rate at which the fluctuation $F_q(s)$ (Eq. 6, $q=2$) increases with increasing scale s . Because a larger scale corresponds to a lower frequency, our results implied that metabolic oscillations exhibited larger fluctuations at lower frequencies under both conditions. In another point of view, a larger value of α means that correlations decay more slowly and extend over larger distances in time and space. Thus, the sustained increase in α of metabolic frequency indicated that metabolic activity was relatively augmented compared to other control mechanisms of skin blood flow. This observation was somewhat consistent with our previous study [2], in which a significant increase in relative amplitude of metabolic component was observed during the middle phase of loading period. An explanation for the subtle differences is that DFA coefficients can be derived from weighted power spectra favoring the center frequency and de-emphasizing other frequencies in proportion to frequency-squared in both directions. It has been well established that an increase in skin temperature raises the metabolic demands of local cells and tissues [10]. In human subjects, when skin temperature is rapidly increased to 42°C and maintained thereafter, skin blood flow shows a response characterized by an early transient peak followed by a prolonged plateau phase and eventually by a return toward baseline [35]. Findings from a series of studies suggest that each of the nitric oxide (NO) system, adrenergic nerves, and sensory nerves has a role in achieving this response pattern [35]. Particularly, NO is thought to be importantly involved in the prolonged plateau phase [28, 35]. In this study, we applied a loading pressure of 700 mmHg to the rat skin and rapidly heated the skin to around 47°C and maintained that level for 3 h (Fig. 1d). As we expected, we did not observe a typical biphasic blood flow response but observed a sustained decrease in blood flow [2]. This means that vasodilation did not actually occur due to the compression of the vasculature under surface pressure. However, it is likely that under both conditions, local heating and/or deformation of endothelial cells elicited a release of NO [17, 36], which in turn reduced the myogenic response by relaxing vascular smooth muscles [17]. Hence, we speculate that under both conditions, there was an unbalance between relatively raised metabolic demands of local cells and tissues and decreased blood flow supply.

It is clear that under pressure with heating, α of myogenic component showed a sharp decrease during the first two 30 min epochs of loading period (Fig. 4c), indicating that myogenic oscillations became more random. The myogenic response is thought to reflect an increase in the activation state of vascular smooth muscles [17]. Although blood flow regulation is expected to be correlated to the metabolic demands of the tissues, the myogenic mechanism is a determinant of blood flow [37]. It has been demonstrated that a level of local

heating of 42°C is sufficient to cause maximal vasodilation in human skin, implying that the vascular smooth muscles are fully relaxed [35]. Local heating leads to a release of NO from the endothelium [35], and NO relaxes smooth muscle by activating soluble guanylyl cyclase and other intracellular targets in smooth muscle [17]. We deduce that in this study, the skin temperature around 47°C also relaxed vascular smooth muscle. The relaxation of the smooth muscles was likely responsible for the observed reduction in α of myogenic component.

A striking phenomenon is that under pressure with heating, the myogenic component exhibited a significantly lower degree of complexity throughout the entire loading period (Fig. 5c). According to the previous work by Goldberger [20] and Lipsitz and Goldberger [21], it is reasonable to assume that the complexity of myogenic component reflects the richness of its sub-components (if existed), the coupling between the corresponding sub-systems, and the interactions between myogenic mechanism and other control mechanisms of skin blood flow [22]. Indeed, growing evidence indicates that the existence of interactions among the control mechanisms of skin blood flow [17]. For example, NO released from vascular endothelium induces vascular smooth muscle relaxation [35]; changes in blood flow elicit vasomotor responses, which may compete with intraluminal pressure-induced myogenic response [17]. Accordingly, a possible explanation for our results is as follows. NO released from the endothelium in response to heat stress [35] and probably to deformation of endothelial cells [36]. NO relaxed vascular smooth muscle and probably inhibited neural control of the vessels [35]. On the other hand, surface pressure resulted in decreased blood flow and decreased intraluminal pressure. Decreased flow would lead to a reduction in shear stress and therefore a reduction in the amount of released NO, while decreased pressure could potentially evoke myogenic relaxation. Because blood flow underwent small changes [2], we deduce that intraluminal pressure also underwent small changes. These two mechanisms would exert little influence on BFO. Collectively, local heating-induced relaxation of vascular smooth muscles likely led to attenuated interactions between myogenic mechanism and other control mechanisms of blood flow, which might be reflected by reduced complexity of myogenic component.

Another finding is that under pressure with heating, the metabolic component exhibiting a higher degree of complexity during the later phase of loading period (Fig. 5a) is probably due to the accumulation of vasoactive metabolites. Studies of reactive hyperemia suggest that the endothelium can produce multiple vasoactive metabolites, including prostaglandins, adenosine, NO, and reactive oxygen species [17]. These metabolic factors may interact with each other in the later phase of reactive hyperemia [17]. In our case, released metabolites likely accumulated during the later phase of loading period due to heat stress and vascular compression. It is possible that interactions existed between the metabolic factors, which might contribute to the observed higher degree of complexity of metabolic component. Note this distinct difference cannot be detected by a single DFA coefficient (Fig. 4a).

The results of surrogate tests indicate that the measure, $\Delta\alpha$, can reflect the nonlinear properties of BFO, which are eliminated by the randomization of the Fourier phases. It is clear that during baseline, all the three characteristic frequencies possess nonlinearities (Fig. 6). By comparing $\Delta\alpha$ between the two conditions, it can be deduced that local heating led to higher nonlinearity of metabolic component during the later phase of loading period, but a gradual loss of nonlinearity of myogenic component. However, the mechanisms underlying these observations remain largely unknown.

It is worth to note that under pressure without heating, skin temperature showed a slightly decrease (Fig. 1b). A similar phenomenon was reported by Linder-Ganz and Gefen [38] who observed a decrease in temperature of gracilis muscle of rats after 2 h surface pressure. They suggested that such decrease was likely due to the combined effect of skin reflection and

altered thermoregulatory vasoconstriction under anesthesia. However, these observations do not necessarily mean that similar phenomena would occur in human subjects. Previous studies on temperature at the interface between the human buttock skin and support surfaces showed an increase in skin temperature when some types of cushions were used [39]. In this study, a decrease in skin temperature potentially amplified the difference in DFA coefficients and complexity between the conditions of pressure with heating and pressure without temperature changes.

Limitations

A limitation of this study is a small sample size. However, the purpose of this preliminary study was to examine whether complexity analysis could reveal new features of BFO in response to prolonged surface pressure with thermal stress. The 3h loading period was divided into nonoverlapping 30 min epochs. This strategy allows us to compare BFO dynamics between the baseline and each epoch and between successive epochs. In this case, each epoch may serve as a control of the other epochs. Hence, the influence of the small sample size on our findings should be kept minimal. However, future research needs to confirm our findings in a larger sample size.

5. Conclusions

This study demonstrates that the complexity measure $\Delta\alpha$ derived from the MDFA is capable to reflect local heating-induced structural changes in BFO during prolonged surface pressure. Particularly, this measure can reveal new features of BFO that cannot be detected by a single DFA coefficient. Our method provides a basis for monitoring and assessing the ischemic status of weight-bearing skin and risk of pressure ulcers.

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Abbreviations

BFO	Blood flow oscillations
LDF	Laser Doppler flowmetry
MDFA	Multifractal detrended fluctuation analysis

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Fig. 1.

Examples of skin blood flow and temperature in response to locally applied surface pressure and thermal stress in rats. (a) Skin blood flow response to surface pressure at 700 mmHg. (b) Skin temperature under surface pressure at 700 mmHg. It shows a slightly decrease. (c) Skin blood flow response under pressure with heating. (d) Skin temperature under pressure with heating.

Fig. 2.

Comparison of power spectral density (PSD) between the integrated time series Y and the detrended series Y_d . It is evident that detrending in boxes with a length of s seconds is equivalent to applying a high-pass filter with a cut-off frequency of $1/s$ Hz. The data series is the blood flow signal shown in Fig. 1a during 1–20 min. Quadratic polynomials were used in the fitting procedure. (a) $s = 1/0.01$ seconds, (b) $s = 1/0.076$ seconds, (c) $s = 1/0.2$ seconds, (d) $s = 1/0.74$ seconds, (e) $s = 1/2$ second, and (f) $s = 1/5$ second.

Fig. 3.

Illustration of the scale interval corresponding to the neurogenic component of BFO. The data series are the blood flow signal shown in Fig. 1a during 1–20 min. (a) PSD of the original data and filtered data (after filtering out the frequency components between 0.076–0.2 Hz). (b) Scaling exponents of the original data and filtered data. For the filtered data, the scaling exponents in the scale interval 1/0.2–1/0.076 seconds are close to zero, while the scaling exponents in other scaling regions are nearly identical to that of the original data. Because the frequency components between 0.076–0.2 Hz cannot be completely removed and the removed components are not perfectly between 0.076–0.2 Hz, the scaling exponents in the scale interval 1/0.2–1/0.076 seconds are nonzero and in other scale intervals are not exactly identical to that of the original data, especially for $q < 0$.

Fig. 4. DFA coefficients α of the (a) metabolic, (b) neurogenic, and (c) myogenic components during the baseline (epoch 1) and loading period (epochs 2–7). Values are represented as means $\pm$ standard errors. *indicates a significant difference between two conditions ($p < 0.05$).

Fig. 5. Complexity, $\Delta\alpha$, of the (a) metabolic, (b) neurogenic, and (c) myogenic components during the baseline (epoch 1) and loading period (epochs 2–7). Values are represented as means $\pm$ standard errors. *indicates a significant difference between two conditions ($p < 0.05$).

Fig. 6.

Examples of surrogate tests. The original data are the signals shown in Fig. 1. For each epoch (epoch 1 is the baseline) of the original data, 50 surrogate time series were generated. Values of $\Delta\alpha$ for surrogate series are represented as means $\pm$ standard errors. (a), (c), and (e) Characteristic frequencies under pressure without temperature changes. (b), (d), and (f) Characteristic frequencies under pressure with heating. + indicates a significant difference between $\Delta\alpha$ of the original data and those of surrogate time series ($p < 0.05$).