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ORIGINAL ARTICLE

Effects of acupuncture at the Hoku acupoint on the pulsatile laser Doppler signal at the heartbeat frequency

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Abstract We aimed to assess the effects of acupuncture by analyzing the alternating current (AC) component of skin blood-flow signals (around the heartbeat frequency) simultaneously recorded at the Hoku acupoint, which is an important acupoint in oriental medicine, and two nearby non-acupoints following acupuncture stimulation (AS). Laser Doppler flowmetry signals were measured in 28 experiments on nine volunteers. Each experiment involved the recording of a 20-min control-data sequence and two sets of effects data recorded 0–20 min and 50–70 min after the AS had been stopped. The direct current (DC) and AC components (DCflux and ACflux, respectively), pulse width (PW), and foot delay time (FDT) of the flux signal were calculated. The DCflux, ACflux, PW, and FDT were all significantly increased only at Hoku following AS. Regression analysis between the DCflux and ACflux revealed that the slope was largest (>1) at Hoku among the measurement sites. Our results indicated that both the DCflux and ACflux in the microcirculatory perfusion were increased by stimulation at the Hoku acupoint, with the change being greatest for the latter. Parameters calculated from the pulsatile flux waveform, such as the PW and FDT, could contribute to noninvasive evaluations of the sympathetic neural activities and of the improvement in perfusion following AS.

Keywords Acupuncture · Pulse · Laser Doppler · Microcirculation

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Introduction

There is accumulating evidence of the therapeutic effects of acupuncture. It has been suggested that acupuncture can prevent or treat illness by adjusting autonomic functions or microcirculatory perfusion [1–3]. The application of acupuncture stimulation (AS) can change microcirculatory perfusion at the stimulated acupoint as well as at other acupoints [2, 3].

Laser Doppler flowmetry (LDF) has increasingly been used for noninvasive monitoring of the microcirculation. Its fast sampling rate allows the acquisition of detailed pulsatile LDF flux contours, making it very suitable for investigations of the microvascular response following the application of acupuncture. Many studies have focused on the average value [4, 5] or the low-frequency oscillation [6–8] of the microcirculatory flux response elicited by various types of stimulation. For example, spectral analysis of LDF signals reveals blood flow oscillations at frequencies of 0.01–1.6 Hz, which might reflect various physiological rhythms such as respiration, the intrinsic myogenic activity of vascular smooth muscle, and the neurogenic activities of the vessel wall and the vascular endothelium [7, 8].

Among these frequency bands, the band from 0.6 Hz to 1.6 Hz has been suggested as being affected by the propelling force of the heartbeat [6–8]. It has been demonstrated that pulsatility exists in the arterioles, capillaries, and even postcapillary venules [9, 10]. It has also been noted that the pulse pressure (PP) and microcirculatory flux fluctuations occur at the same frequency as that of the heartbeat in the microcirculation, with a small phase difference between them [11, 12]. The arterial wall has a large compliance, and an artery behaves analogously to a combination of resistors and capacitors in an electric circuit, whereas the capillary is generally analogous to a pure resistance, since its pressure–flow relationship can be described by Poiseuille's equation [13]. On the basis of these observations, it has been suggested that the microcirculatory flow can be driven into the capillaries through precapillary openings on the arteriole walls by the propelling force of the PP generated by the heartbeat and transmitted along the artery [11, 14].

In this study, we aimed to assess the effects of acupuncture by analyzing the alternating current (AC) component (around the heartbeat frequency) of skin blood-flow (SBF) signals simultaneously recorded at the Hoku acupoint (which is an important acupoint in oriental medicine) and two nearby nonacupoints following AS. The results could aid the development of an index for monitoring microcirculatory responses following AS and also improve the understanding of the underlying mechanisms.

Materials and methods

Experimental setup and data acquisition

The abbreviations used in this study are summarized in Table 1.

Twenty-eight experiments were performed on nine healthy male volunteers aged 20–28 years (2–4 experiments for each volunteer) and with no signs or symptoms of cardiovascular or neurological diseases. The subjects were lightly clothed, supine, and were allowed to stabilize for at least 20 min before commencing recording. The environmental temperature was within the thermoneutral range (23–25°C) throughout the measuring period. The institutional ethics committee of Taipei City Hospital approved the study protocol; each volunteer gave informed consent before entering the study. Tea, coffee, alcohol, and smoking were forbidden on the previous day. All subjects were asked not to take any medication for 3 days before experiments, and they did not consume food or take exercise during or at least 1 h before each experiment [15, 16].

Electrocardiogram (ECG) and LDF signals were measured simultaneously and noninvasively. ECG signals were measured by surface electrodes and acquired by a preamplifier (lead II, RA-LL; 6600-series, Gould, USA). LDF (MBF3, Moor Instruments, UK) was used for measuring the microcirculatory flux, with a time constant of 0.001 s, a cut-off frequency of 14.9 kHz, and a sampling frequency of 40 Hz at measurement sites between the thumb and the index finger on the back of the left hand. The laser operating wavelength and output power were 780 nm and less than 1.6 mW, respectively. The measuring sites of the LDF probe were at Hoku (Li4, site 1), and two nonacupoints (for comparison) that were halfway between Hoku and Yang-Tsih (Li5, site 2) and halfway between Hoku and San-Chien (Li3, site 3). Figure 1 shows that the chosen measurement sites were all located near the border between the palm and the back of the hand or the foot. The greater number of capillary than arteriovenous (AV) shunt vessels at these measurement sites allows the effects of the latter to be minimized. Moreover, the measurement sites were selected to minimize differences in the basal microcirculatory condition and in the possible depths of the peripheral vascular beds (PVBs) between the groups [15].

Table 1 Summary of abbreviations used in this study

Abbreviation used	Definition
AM	Acupoint microcirculation
AS	Acupuncture stimulation
HR	Heart rate
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
LDF	Laser Doppler flowmetry
Dcflux	DC component of flux
Acflux	AC component of flux
PW	Pulse width: time interval between the 80% rising and falling points
FDT	Foot delay time: time delay between the ECG R peak and the adjacent rising point of LDF pulse
PP	Pulse pressure
PVBs	Peripheral vascular beds
SNAs	Sympathetic neural activities

Fig. 1 Locations of the measurement sites. Measurement sites: *O* Hoku acupoint (site 1), *X* two nearby nonacupoints (sites 2 and 3), and *triangle* location of the thermistor

The subjects were asked to relax and breathe naturally throughout the measurement period so as to prevent motion artifacts. Both signals were connected to an analog-to-digital converter card (PCI-9111DG, Adlink Technology, Taiwan) operating at a sampling rate of 1,024 Hz. A high sampling rate was used to ensure that sufficient data were obtained to determine the profile of each pulse and to determine accurately the locations of the ECG R peaks [16, 17].

During measurement, the subject was supine on a measurement couch. Each assessment established the acupoint microcirculation (AM) recordings as follows: a 20-min baseline AM (control period) was recorded prior to AS, after which the acupuncture needle (stainless steel needle, gauge #30, 7.5 cm in length; Chianhuei) was inserted into the left Hoku acupoint at a depth of around 6 mm for 20 min, and the AM LDF signal was recorded during AS of De-Qi (a special feeling as described mutually by the subjects and the acupuncturist). The needle was then withdrawn to stop AS, with AM being recorded from 0 min to 20 min (first effect) and from 50 min to 70 min (second effect) after AS had been stopped. The measurement time of 20 min was chosen so that we could ensure that all the frequencies of interest could be evaluated accurately. Before the control and after the second-effect period, we measured fundamental physiological parameters of the subject, including heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) using a sphygmomanometer (MediGuard 150i, Rossmax). The two assessments of each subject were separated by at least 3 days to prevent the influence of acupuncture residual effects.

A thermistor was attached to the skin surface to monitor the skin surface temperature near the LDF measurement site (the location is indicated in Fig. 1). The resistance of the thermistor was transformed into voltage (by a custom-made circuit) that was also sampled by the analog-to-digital converter card. The baseline temperature was 32.3±1.0°C [mean ± standard deviation (SD)]. The acceptable temperature stability during the control period was a variation of less than 1.0°C.

Signal analysis

Data files containing spikes that were too large relative to the mean flux value were discarded, since this implied the presence of motion artifacts. The mean, SD, and coefficient of variation (CV; SD/mean) of the HR were calculated in each sequence. In order to ensure that subjects were physiologically stable (to avoid interference from microcirculatory autoregulation), the chosen control-data sequences had to satisfy the following criteria: (1) CV of the HR less than 10%, (2) DBP more than 60 mmHg, (3) SBP less than 130 mmHg, and (4) variations in LDF flux signals less than 30%.

We calculated several parameters of the LDF signal to elucidate the microcirculatory effects induced by AS. The DCflux (DC component of the flux) was defined as the mean value of the laser Doppler flux signals during each 20-min measurement period. In determining parameters of the pulsatile LDF waveform, including the ACflux (AC component of the flux), PW (pulse width of the LDF pulse), and FDT (foot delay time, equal to the time delay between the ECG R peak and the rising point of the LDF pulse), we filtered the LDF flux signal with a digital high-pass filter (11th-order Chebyshev filter) with a cut-off frequency of 0.01 Hz to eliminate the baseline drift. The two neighboring R peaks of the ECG signal were used to help to identify the cut points of each pulse for LDF signals to define each 'pulse' of the microcirculatory flux. We then applied time-domain synchronized averaging analysis of the pulsatile component of the LDF flux—similar to that reported previously [14]—to obtain the averaged segment, from which the ACflux, PW, and FDT (see Fig. 2 for precise definitions) could be calculated [16, 17]. The variations in the four parameters when AS was performed to each volunteer are listed in Table 2.

Since LDF provides only qualitative measurements, we calculated changes relative to the control value for each parameter, to elucidate the effects following AS. All signal processing was performed with MATLAB (MathWorks, Natick, MA). Differences were considered as significant when $P<0.05$.

Results

Typical measured ECG and LDF waveforms are shown in Fig. 3. The basic physiological parameters (HR, SBP, and DBP) are shown in Fig. 4. Only the HR was significantly decreased after AS ($P<0.05$ by two-tailed paired *t*-test).

Typical time-domain changes in the DCflux and ACflux are shown in Fig. 5. The DCflux, ACflux, PW, and FDT are compared between acupoints and nonacupoints in Figs. 6, 7, 8 and 9, respectively. Compared with the control values, the DCflux, ACflux, PW, and FDT values were all significantly increased after AS only at Hoku (all $P<0.01$ by two-tailed paired *t*-test). There were no significant changes in the DCflux and ACflux at the nonacupoints, except for a significantly decreased second effect of the DCflux and first effect of the ACflux at site 3.

We performed linear regression analysis to assess the correlation between changes in the DCflux and ACflux. Figure 10 reveals that the regression line had a coefficient of determination (R^2) of 0.78 at Hoku ($P<0.01$ by *F*-test), whereas R^2 was smaller than 0.43 at the nonacupoints. Moreover, the slope was larger at Hoku (>1) than at the nonacupoints (both <1).

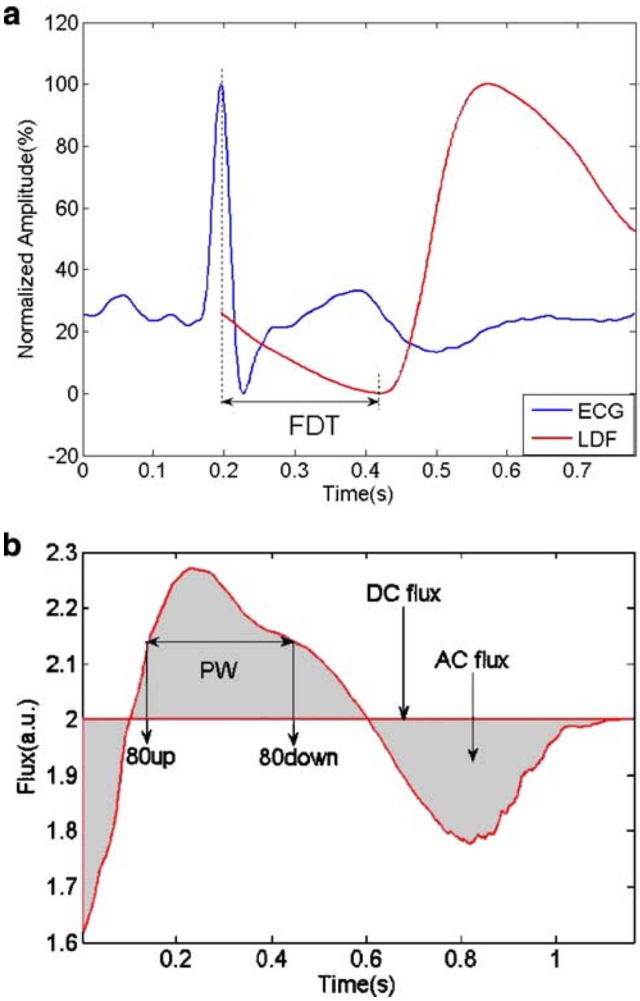

Fig. 2 Definitions of pulse parameters. **a** The FDT was defined as the time delay between the ECG R peak and the adjacent rising point of the LDF pulse. **b** The ACflux was defined as the mean of absolute values of all data points in the DC-filtered LDF waveform (that is, the average value of the *shaded area*). The PW was defined as the time interval between the 80% rising and falling points (*80 up and 80 down*, defined as the points at which the flux is 80% of the pulse peak on the rising and falling edges, respectively). *a.u.* arbitrary units

Table 2 Variations of the four parameters at site 1

Parameter	Measurement period	Average intra-CV	Inter-CV
DCflux	First effect	0.35	0.32
	Second effect	0.27	0.25
ACflux	First effect	0.11	0.10
	Second effect	0.20	0.18
PW	First effect	0.13	0.06
	Second effect	0.13	0.19
FDT	First effect	0.03	0.01
	Second effect	0.05	0.03

In determining the intra-CV, we first calculated parameter CV [defined as (standard deviation)/(average value) of the relative changes of the four parameters to their control values] for each volunteer. The ‘average intra-CV’ presented here was then defined by the average values of parameter CV amongst the nine volunteers. Moreover, the presented ‘inter-CV’ for the four parameters was defined as the CVs of the average relative parameter changes for all volunteers

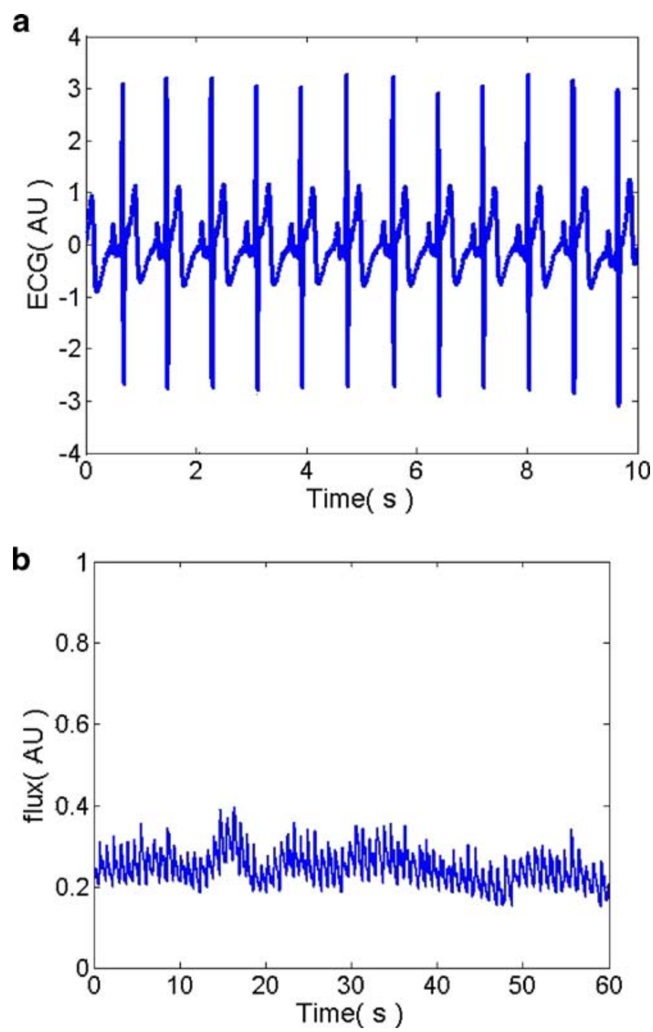

Fig. 3 Typical control time-domain waveforms measured at site 1. Ten seconds of ECG data (**a**) and 1 min of the recorded LDF flux (**b**) in the control period. There were no obvious baseline fluctuations in these waveforms. *AU* arbitrary units

Discussion

DCflux and ACflux responses following AS

In this study we analyzed the effects of AS on SBF. Figures 6 and 7 show that the microcirculatory flux (both the DCflux and ACflux) was significantly increased at the Hoku acupoint. The DCflux response at the acupoint was similar to findings of several previous studies [1–3, 18]; however, the ACflux response has rarely been discussed. Figures 6 and 7 also reveal that the increment during the first effect was much larger for the ACflux than for the DCflux. Moreover, Fig. 10 reveals that the slope of their interrelation was larger at Hoku than at the nonacupoints.

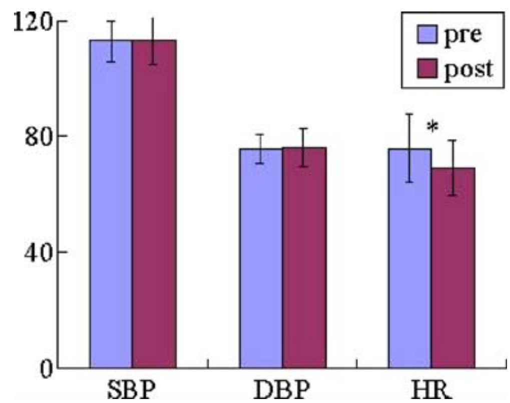

Fig. 4 HR, SBP, and DBP values. Data are mean and SD values. *pre* the values taken before LDF measurement, *post* the values taken after LDF measurement. HR is in beats/min, and SBP and DBP are in mmHg. *The asterisk* indicates $P<0.05$ by two-tailed paired *t*-test between pre and post values. The only significant change before and after the LDF measurement was in HR

The larger slope at Hoku can be explained by the precapillary-opening conjecture mentioned in the Introduction, whereby the microcirculatory flux is driven by the PP at the PVBs, and the pulsatile pressure peak can drive the flux more efficiently than the lower portion of the pulse. The improved perfusion efficiency might be attributable to reduced resistance due to an increased opening diameter or to lowered viscosity due to breaking of the plasma bridges between blood cells induced by the larger force of the pulse peak necessary to distend the precapillary openings [11]. We found that the increases in the DCflux and ACflux—which implied a larger PP propelling force—were largest at the Hoku acupoint. The larger PP led to an increased opening diameter and a much larger reduction in the vascular resistance due to the fourth-order inversely proportional diameter–resistance relationship described by Poiseuille's equation [13]. As a consequence, as the radius became distended by the PP at site 1, AS induced a better distribution efficiency for the ACflux than for the DCflux and a corresponding larger increase in the ACflux than in the DCflux, and, hence, the ACflux-versus-DCflux slope at Hoku was both larger than 1 and larger than those at the other two measurement sites (as shown in Fig. 10).

Figure 6 reveals that, during the second effect at Hoku, the increase in the ACflux was still significantly larger than its control value, whereas this was not the case for the DCflux. Moreover, the increase in the ACflux was also larger than that in the DCflux during the second effect. This illustrates that the enhancement had lasted longer for the ACflux than for the DCflux. This suggests that the increase in the ACflux is an important component of the physiological response to AS.

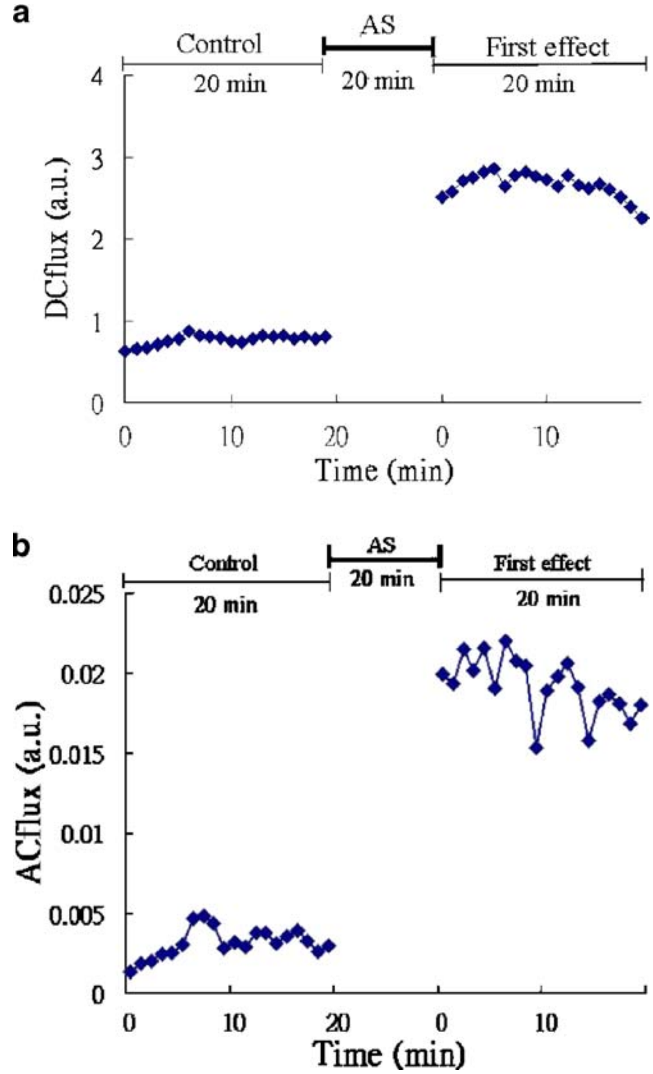

Fig. 5 Time-domain changes in laser Doppler flux signals during the first effect. After AS, the DCflux (**a**) and ACflux (**b**) increased prominently at the Hoku acupoint. *a.u.* arbitrary units

Pulsatile LDF index

As in the findings of Chao et al. [14], indexes calculated in our study from the pulsatile LDF waveform might allow measurement of the PVB resistance and, hence, contribute to the evaluation for the microcirculatory response induced by AS. Figure 8 reveals that AS significantly increased the PW at Hoku. Since a larger PW will increase the proportion of time for which the precapillary openings on the vessel wall are open, Fig. 8 indicates that the injection period through precapillary openings of the PVB was longer at Hoku than at the nearby nonacupoints. Such a longer injection period will result in the ACflux in each pulse passing through the precapillary opening for a longer time, and hence improve the perfusion for both the ACflux and DCflux.

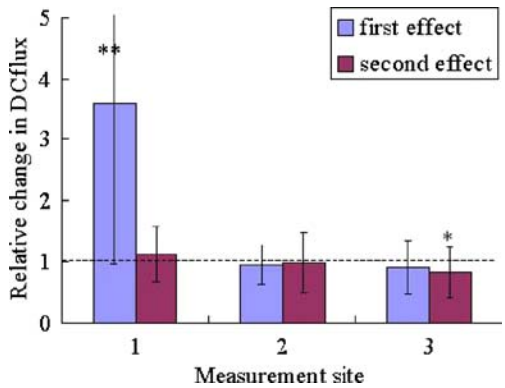

Fig. 6 Comparison of the DCflux between Hoku and the nonacupoints. The relative changes in the first and second effects were divided by the mean DCflux value during the 20-min control sequence. The overall data are mean and SD values at each site. * $P<0.05$, ** $P<0.01$, compared with the control value, by two-tailed paired *t*-test. At Hoku, the first effect was significantly larger than the control value, while the second effect tended to return to the control value. The only significant effect at the nonacupoints was a significant decrease in the second effect at site 3

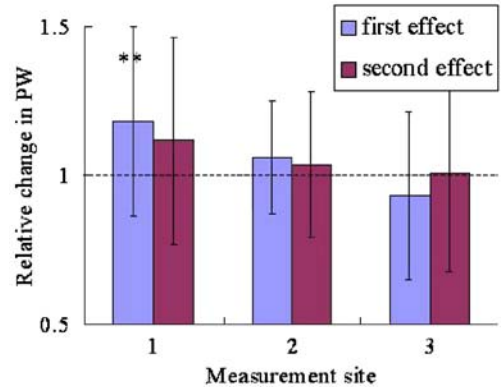

Fig. 8 Comparison of the PW between Hoku and nonacupoints. The relative changes in the first and second effects were divided by the mean PW value during the 20-min control period. The overall data are mean and SD values at each site. ** $P<0.01$ compared with the control value by two-tailed paired *t*-test. At Hoku, the PW was significantly increased during the first effect, and then it tended to return to the control value during the second effect. There were no significant changes at the nonacupoints

Differences in the injection period between the acupoint and nonacupoints following AS might be due to vessel dilation caused by changes in the sympathetic neural activities (SNAs) induced by the needle at Hoku. Reduced SNAs at the acupoint following AS, which have been found in several previous studies [19–23], decrease the elastic modulus of the arterial wall, make it easier for the precapillary openings to distend radially, and lengthen the injection period, which thus leads to an increased PW.

The reduced HR in this study following AS can also be attributed to the reduced SNA, which is consistent with a previous finding [24]. Further support for the notion that SNA after AS differs between Hoku and the nearby nonacupoints can be found in Fig. 9, which shows that changes in another pulsatile LDF index, the FDT, also obviously differed between Hoku and the nearby nonacupoints, significantly increasing only at Hoku. Since the FDT is the time delay between the heartbeat and the rising point of the microcirculatory pulse, it comprises the time delay of arterial wave transmission and the injection time delay between the PP and the microcirculatory flux pulse to pass through precapillary openings. Reduced SNA could lead to decreases in the elastic modulus of the vessel wall, increases in both arterial and microcirculatory time delays, and thus the increased FDT at Hoku. The absence of such prominent

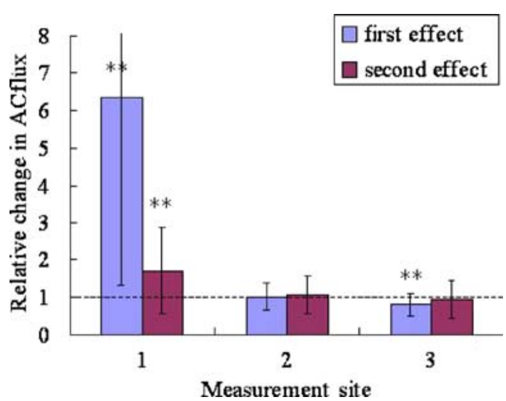

Fig. 7 Comparison of the ACflux between Hoku and nonacupoints. The relative changes in the first and second effects were divided by the mean ACflux value during the 20-min control sequence. The overall data are mean and SD values at each site. ** $P<0.01$ compared with the control value by two-tailed paired *t*-test. Both effects at Hoku were significantly larger than the control value. At the nonacupoints, effects were all nonsignificant except for a significant decrease in the first effect at site 3

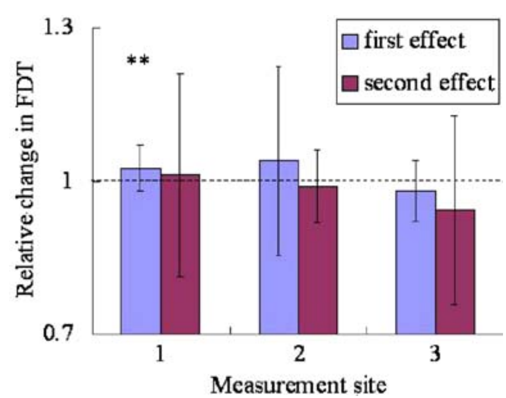

Fig. 9 Comparison of the FDT between Hoku and nonacupoints. The relative changes in the first and second effects were divided by the mean FDT value during the 20-min control period. The overall data are mean and SD values at each site. ** $P<0.01$ compared with the control value by two-tailed paired *t*-test. At Hoku, the FDT was significantly increased during the first effect. There were no significant changes at the nonacupoints

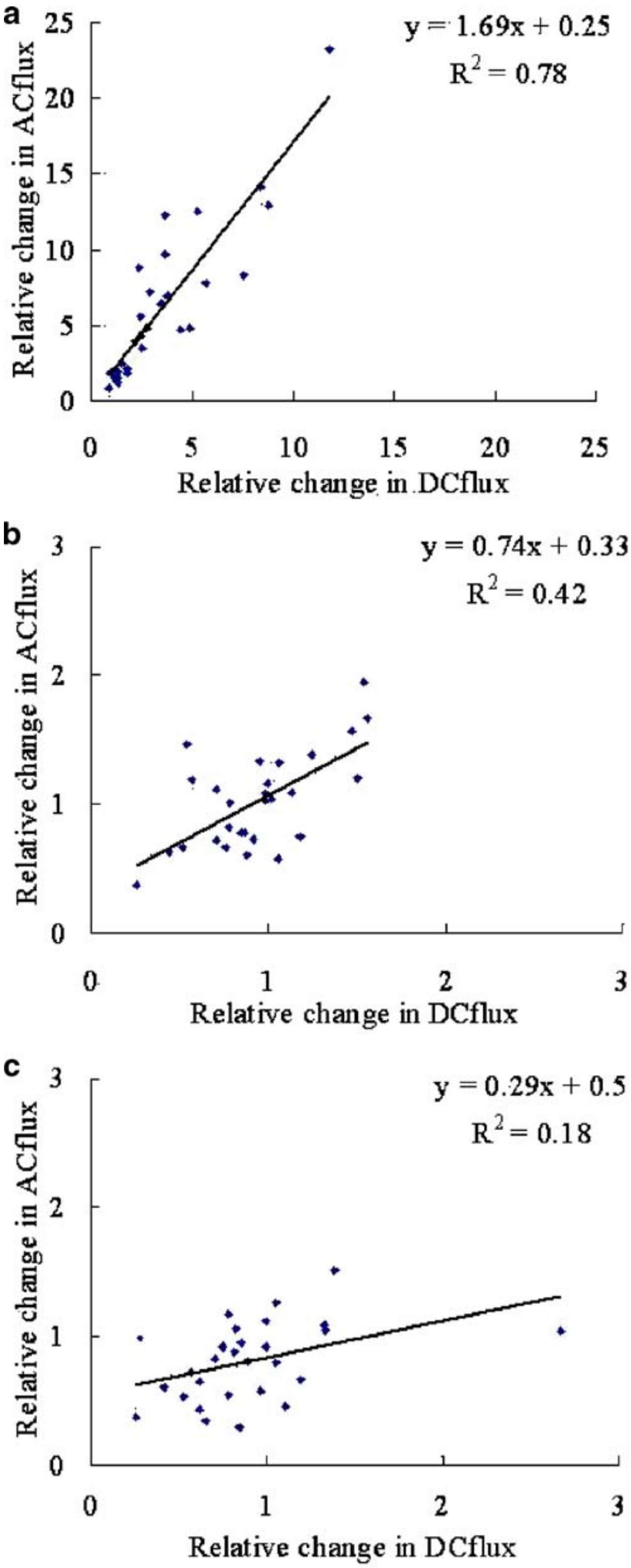

Fig. 10 Relationship between relative changes in the DCflux and the ACflux during the first effect at the three measurement sites. Measurement sites: **a** Hoku (site 1), **b** site 2, and **c** site 3. Relative changes were defined as the changes divided by the control values. R^2 was 0.78 at Hoku ($P<0.01$ by F-test) but smaller than 0.45 at both of the nonacupoints. Moreover, the slope was larger at Hoku (>1.6) than at the nonacupoints (both <0.8)

decreases in SNA at the nonacupoints (where no needle had been applied) would hence result in no significant changes in their FDTs. Indexes calculated from the pulsatile LDF waveform, including the PW and FDT, might, therefore, be useful in evaluating the microcirculatory and SNA responses following AS.

As conjectured above, it is possible that the elasticity changes of the arterial wall following AS can be attributed to the different activities of the smooth muscle in the arterial wall, which can be controlled by the different neural activities or different accumulated amounts of vasodilators. Another possible reason might be that the microcirculatory perfusion can be hindered by the inserted needle. After the needle has been withdrawn, it takes a little time for the microcirculatory perfusion to be restored. The relatively less blood within the vessels at local PVBs may cause slight collapse of the vessel and, hence, lead to a softer arterial wall. The transient response and detailed mechanism can be an important issue in our future studies.

Conclusion

This study has shown that needle insertion at the Hoku acupoint significantly increases the perfusion at Hoku but not at nearby nonacupoints. We also found that changes in flux and certain indexes calculated from the pulsatile LDF waveform induced by AS differed between Hoku and the nearby nonacupoints. Parameters calculated from the pulsatile LDF waveform, such as the PW and FDT, might be useful for noninvasive evaluations of the microcirculatory-resistance-improving effects of AS. Future studies should assess whether the findings of this study represent general characteristics of acupoints.

Microcirculatory flux plays important roles in circulatory transportation, such as supplying nutrients and removing harmful molecules. This study found that AS improved the efficiency of both the DC and AC components of the microcirculatory perfusion at the stimulated Hoku acupoint. The ACflux increased more than the DCflux did at Hoku, perhaps due to the nonlinear diameter–resistance relationship of the precapillary openings on the vessel wall. Improving the transmission of the pulse flux might be an important physiological response to the application of AS. The main driving force for the blood flow to pass through the precapillary openings is suggested to be the local PP at the PVBs. It has previously been demonstrated that AS can affect the transmission of the PP along the artery [25]. Changes in the PP and pulse flux can, thus, be linked by the microvascular precapillary-opening model, and, therefore, pulse analysis of the blood-pressure waveform and the microcirculatory flux could improve the understanding of the physiological effects induced by AS. In the future, comparison of the effects of needle insertion at the acupoint and those at the non-acupoints should be performed to verify further the conjecture presented here.

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