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*AJP - Heart* 289:385-391, 2005. First published Mar 4, 2005; doi:10.1152/ajpheart.00622.2004

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## Dynamic autoregulation of cutaneous circulation: differential control in glabrous versus nonglabrous skin

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Submitted 23 June 2004; accepted in final form 25 February 2005

**Wilson, Thad E., Rong Zhang, Benjamin D. Levine, and Craig G. Crandall.** Dynamic autoregulation of cutaneous circulation: differential control in glabrous versus nonglabrous skin. *Am J Physiol Heart Circ Physiol* 289: H385–H391, 2005. First published March 4, 2005; doi:10.1152/ajpheart.00622.2004.—The purpose of this project was to test the hypothesis that, independent of neural control, glabrous and nonglabrous cutaneous vasculature is capable of autoregulating blood flow. In 10 subjects, spectral and transfer function analyses of arterial pressure and skin blood flow (laser-Doppler flowmetry) from glabrous (palm) and nonglabrous (forearm) regions were performed under three conditions: baseline, ganglionic blockade via intravenous trimethaphan administration, and trimethaphan plus oscillatory lower body negative pressure (LBNP;  $-5$  to  $-10$  mmHg) from 0.05 to 0.07 Hz. Oscillatory LBNP was applied to regenerate mean arterial pressure variability that was abolished by ganglionic blockade. Ganglionic blockade was verified by an absence of a heart rate response to a Valsalva maneuver. Spectral power and transfer function gain between blood pressure and skin blood flow were calculated in this oscillatory frequency range (0.05–0.07 Hz). Within this frequency range, ganglionic blockade significantly decreased spectral power of blood flow in both the forearm and palm, whereas regeneration of arterial blood pressure oscillations significantly increased spectral power of forearm blood flow but not palm blood flow. During oscillatory LBNP, transfer function gain between blood pressure and skin blood flow was significantly elevated at the forearm ( $0.28 \pm 0.03$  to  $0.53 \pm 0.02$  flux units/mmHg;  $P < 0.05$ ) but was reduced at the palm ( $4.7 \pm 0.5$  to  $1.2 \pm 0.1$  flux units/mmHg;  $P < 0.05$ ). These data show that independent of neural control of blood flow, glabrous skin has the ability to buffer blood pressure oscillations and demonstrates a degree of dynamic autoregulation. Conversely, these data suggest that nonglabrous skin has diminished dynamic autoregulatory capabilities.

spectral analysis; laser-Doppler flowmetry; ganglionic blockade

SKIN BLOOD FLOW from nonglabrous regions is controlled by a vasoconstrictor and an active vasodilator system. These systems allow for a large range of cutaneous perfusion from nearly 0 to 8 l/min (11, 12, 16). In addition to neural control, a number of local factors are capable of modulating skin blood flow. For example, local alterations in temperature can cause maximal vasodilation or pronounced vasoconstriction independent of central neural control (15, 27, 30). Moreover, other local factors such as venous congestion or increased transmural pressure can cause vasoconstriction by means of the cutaneous venoarteriolar response (4, 13, 31), which is also independent of central neural control (8). Hence, Henriksen et al. (9) put

forth the notion that the skin might have intrinsic autoregulatory capabilities.

Autoregulation of blood flow is common in tissues such as the brain and kidney (7). In these tissues, throughout a specific range of arterial blood pressure, steady-state blood flow is maintained at a fairly constant level. It is questionable whether the cutaneous vasculature is capable of autoregulation given a number of observations indicating that changes in perfusion pressure result in parallel changes in skin blood flow (10). Relatively recent techniques to assess dynamic autoregulation, in which changes in flow are compared with transient changes in pressure, may provide insight regarding dynamic cutaneous autoregulatory capabilities.

Skin blood flow has long been known to oscillate (3). Maneuvers that increase sympathetic activity (e.g., exercise, inspiratory gasp, and tilt) have the capability to alter skin blood flow oscillations (18, 24). In a novel experimental paradigm, Stauss et al. (25) identified functional changes in glabrous skin blood flow with intraneural stimulation of sympathetic fibers with frequencies of 0.025–0.1 Hz. Intraneural stimulation has also identified similar blood flow oscillations in cutaneous tissue of the rat paw (26). These observations identify the importance of the sympathetic nervous system in the modulation and generation of skin blood flow oscillations.

Skin blood flow oscillations correlate to arterial blood pressure, sympathetic nerve activity, and heart rate (1, 2). Regional sympathectomy and local sympathetic blockade uncouple these correlational relationships and reduce oscillations in skin blood flow (1, 21). However, most sympathetic blockades to date have affected only a small area of skin or focused on a specific ganglion, whereas assessment of skin blood flow upon complete ganglionic blockade has yet to be undertaken. Whole body ganglionic blockade allows for the independent manipulation of arterial blood pressure (32); thus the relationship between blood flow and arterial blood pressure in the cutaneous vasculature can more effectively be elucidated. Importantly, with the use of the techniques of transfer function and power spectral analysis, dynamic pressure-flow relationships in an intact in vivo system can be addressed in the human cutaneous vasculature.

No study has addressed the effects of ganglionic blockade, followed by induction of blood pressure fluctuations, to assess dynamic autoregulatory capabilities of the cutaneous vasculature. Such a study may further an understanding of intrinsic pressure-flow relationships of the cutaneous vasculature. Given

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this background, the purpose of this project was to test the hypothesis that, independent of sympathetic input, glabrous and nonglabrous skin are capable of dynamic autoregulation during changes in perfusion pressure.

## METHODS

**Subjects.** Ten healthy subjects (7 men and 3 women) participated in the study. The participants' mean age was  $29 \pm 6$  yr, and all were of typical height ( $174 \pm 10$  cm) and weight ( $71 \pm 10$  kg). Health of subjects was carefully screened with a medical history and physical examination, including a 12-lead ECG. The protocol and informed consent were approved by the University of Texas Southwestern Medical Center and the Presbyterian Hospital of Dallas. Written informed consent was obtained from all participants before they enrolled in this study.

**Measurements.** Local skin blood flow was indexed via laser-Doppler flowmetry using integrative flow probes (Perimed, North Rayalton, OH) attached to palm and dorsal forearm skin. Integrative flow probes were chosen over single fiber probes because of the larger sampling area. The flux signal from the laser-Doppler device was used for all subsequent power spectral and transfer function analyses. Cutaneous vascular conductance (CVC) was calculated [(laser-Doppler flux  $\cdot$  100)/mean arterial pressure] and expressed in arbitrary units for baseline and ganglionic blockade conditions.

Heart rate was monitored continuously via an ECG (Hewlett-Packard, Palo Alto, CA). A respiratory transducer (UFI, Morro Bay, CA) was attached to the torso to record respiratory rate. Finger arterial blood pressure was monitored continuously and noninvasively on a beat-by-beat basis by a photoplethysmography system (Finapres, Ohmeda, Englewood, CO). Additionally, in four subjects, arterial pressure was measured with a radial arterial catheter connected to a pressure transducer (Abbott Critical Care System, Abbott Park, IL) calibrated and zeroed to the subject's midaxillary line to verify photoplethysmography measures.

**Experimental protocols.** Experiments were performed in the morning, at least 2 h after a light breakfast in a quiet environmentally controlled laboratory with an ambient temperature of  $\sim 25^\circ\text{C}$ . Subjects refrained from heavy exercise and caffeinated or alcoholic beverages for at least 24 h before being tested. All data were collected for 6 min under spontaneous breathing conditions. After a minimum of 30 min resting in the supine position, baseline data collection and the ganglionic blockade agent trimethaphan camsylate (Cambridge Laboratories) was infused initially at 3 mg/min and then increased incrementally 1 mg/min until the heart rate response during a Valsalva maneuver was diminished. The absence of a heart rate response throughout the Valsalva maneuver and continuous decreases in arterial pressure during phase II of the Valsalva maneuver demonstrated the efficacy of ganglionic blockade (20). The dose necessary to achieve this level of blockade typically ranged between 6 and 7 mg/min and was continuously administered throughout the protocol. While continuing to receive trimethaphan, each subject was exposed to low levels of oscillatory lower body negative pressure (LBNP) (from 0 to  $-5$  to  $-10$  mmHg) at a frequency range of 0.05–0.07 Hz. This perturbation was selected to regenerate arterial pressure variability after ganglionic blockade in the low-frequency (LF) range and to provide perfusion pressure oscillations within the frequency range of myogenic modulation.

**Data analysis.** Data are reported from nine subjects because arterial blood pressure was unstable in one subject during trimethaphan administration, resulting in the protocol being discontinued. Data were acquired at a sampling rate of 100 Hz using a data collection system (Biopac, Santa Barbara, CA). Mean arterial pressure and mean skin blood flows were obtained on a beat-by-beat basis with offline analysis software (AcqKnowledge, Biopac Systems). Data were then linearly interpolated and resampled at 2 Hz for further analysis. For spectral analysis, time series of mean arterial pressure and mean skin

blood flow were first detrended with third-order polynomial fitting and then subdivided into 256-point segments with 50% overlap for conducting Fourier transform. This process resulted in five data segments over the 6-min period recordings with a spectral resolution of  $\sim 0.0078$  Hz. Fast Fourier transform was implemented with each Hanning-windowed data segment and then averaged to obtain the spectrum.

For transfer function analysis, the cross-spectrum between mean arterial pressure and mean skin blood flow was obtained and divided by the autospectrum of arterial pressure. Transfer function gain and phase were calculated according to standard techniques (33). Furthermore, coherence function between changes in arterial pressure and skin blood flow was also calculated to assess the linear correlation between these two variables by using the Welch method. All transfer function and spectral analyses were performed with a commercially available software package (DADiSP, DSP Development).

Frequency ranges were divided into LF (0.0078–0.15 Hz) and high-frequency (HF; 0.15–0.35 Hz) regions. These regions were selected based on observations that sympathetic neural control of dynamic changes in skin blood flow likely predominates in the LF region, whereas sympathetic neural control in the HF range may contribute to basal cutaneous vascular tone (1, 2, 23, 25). The key component for this study is the analysis of skin blood flow responses within the portion of the LF range that occurs during regeneration of blood pressure oscillations via superimposition of LBNP swings with ganglionic blockade. This oscillatory frequency range (OSF; 0.05–0.07 Hz), although encompassed within the LF range, is presented and discussed as the primary region of interest in the spectral power and transfer function analyses during the LBNP perturbation. Steady-state hemodynamic parameters before and after ganglionic blockade were compared using paired *t*-tests. Comparisons among baseline, ganglionic blockade, and oscillatory LBNP were performed by using one-way repeated ANOVA with Student-Newman-Keuls post hoc tests if significant main effects were observed (Sigmastat, Jandel Scientific). Data are expressed as means  $\pm$  SE. The significance level was set at  $P < 0.05$ .

## RESULTS

**Steady-state hemodynamics with and without ganglionic blockade.** Steady-state values for blood pressure, heart rate, and skin blood flow are shown in Table 1. Ganglionic blockade did not statistically alter mean arterial pressure, although there was a tendency for a reduction in blood pressure in these subjects. Heart rate increased  $\sim 20$  beats/min following ganglionic blockade. Ganglionic blockade also increased baseline CVC in both the palm and forearm by  $\sim 94\%$  and  $42\%$ , respectively. This increase in CVC is presumably via the release of vasoconstrictor tone in both types of cutaneous tissue during ganglionic blockade.

Table 1. Effects of ganglion blockade on systemic and cutaneous hemodynamic responses

Variable	Baseline	After Ganglion Blockade	<i>P</i> Value
MAP, mmHg	$89 \pm 2$	$82 \pm 4$	0.134
HR, beats/min	$66 \pm 5$	$89 \pm 6$	<0.001
Forearm SkBF, flux units	$13 \pm 2$	$17 \pm 3$	0.021
Forearm CVC, arbitrary units	$14 \pm 2$	$20 \pm 3$	0.004
Palm SkBF, flux units	$98 \pm 20$	$174 \pm 34$	0.018
Palm CVC, arbitrary units	$108 \pm 20$	$210 \pm 36$	0.006

Values are means  $\pm$  SE. MAP, mean arterial pressure; HR, heart rate; SkBF, skin blood flow; CVC, cutaneous vascular conductance.

*Skin blood flow during ganglionic blockade and oscillating LBNP.* Ganglionic blockade reduced the LF spectral power of blood pressure and palm and forearm skin blood flow (see Fig. 1, Tables 2 and 3). These reductions in spectral power were dramatic yet similar between skin types, resulting in 78% and 84% decrease in the LF spectral power for the palm and forearm, respectively. Regeneration of blood pressure oscillations via LBNP during ganglionic blockade caused pronounced increases in spectral power of blood pressure within the OSF range (Fig. 1). Interestingly, oscillating LBNP also caused pronounced increases in the spectral power of forearm skin blood flow without appreciably changing spectral power of palm skin blood flow within the OSF range (see Fig. 1, Tables 2 and 3).

For both baseline and ganglionic-blocked conditions, coherence between blood pressure and skin blood flow was relatively low, with the exception of forearm ( $0.49 \pm 0.01$ ) and palm ( $0.57 \pm 0.04$ ) skin blood flows within the OSF range (Tables 2 and 3). During LBNP, coherence between blood pressure and forearm skin blood flow was very high ( $0.83 \pm 0.01$ ) and transfer function gain significantly increased (from

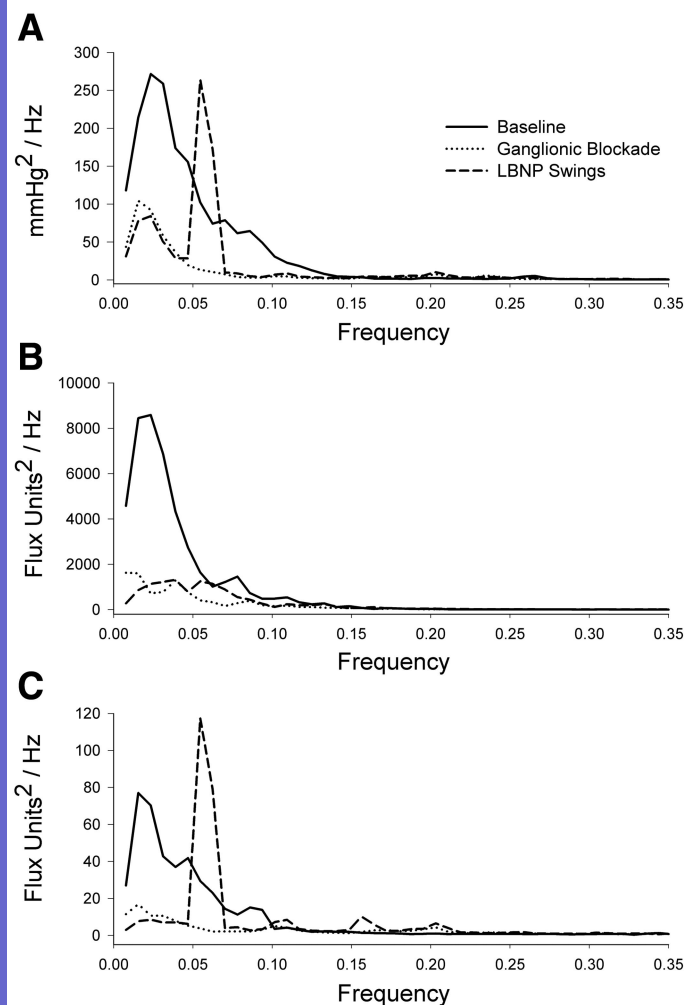


Fig. 1. Group-averaged power spectra of mean blood pressure (A), palm skin blood flow (B), and forearm skin blood flow (C) during baseline, ganglionic blockade, and lower body negative pressure (LBNP) with ganglionic blockade.

Table 2. Forearm skin blood flow spectral and transfer function analysis across LF and HF ranges

	Frequency Range	Baseline	Ganglionic Blockade	Regeneration of Blood Pressure Oscillations
Spectral power, Flux Units <sup>2</sup>	LF	22.2±5.2	5.0±1.0*	14.7±6.9†
	HF	0.2±0.05	1.5±0.19*	2.3±0.45*†
	OSF	26.2±4.8	2.9±0.9*	98.3±19.1*†
Transfer function gain, Flux Units/mmHg	LF	0.23±0.01	0.45±0.04*	0.45±0.03*
	HF	0.42±0.09	0.59±0.10*	0.55±0.16*
	OSF	0.28±0.03	0.29±0.02	0.53±0.02*†
Phase, radians	LF	0.57±0.16	0.38±0.07	0.26±0.10
	HF	-0.45±0.09	0.50±0.09*	0.41±0.08*
	OSF	1.18±0.2	0.39±0.17*	-0.20±0.08*†
Coherence	LF	0.41±0.02	0.43±0.02	0.52±0.04*†
	HF	0.40±0.01	0.42±0.02	0.38±0.02
	OSF	0.49±0.01	0.43±0.04	0.83±0.01*†

Data are means ± SE. Low-frequency (LF) range is 0.0078–0.15 Hz; high-frequency (HF) range is 0.15–0.35 Hz; oscillatory-frequency (OSF) range is 0.05–0.07 Hz. The portion of the LF range that is associated with the regeneration of blood pressure oscillations, via superimposition of lower body negative pressure (LBNP) swings during ganglionic blockade, is presented as the OSF range. Conditions are as follows: baseline, during ganglionic blockade, and regeneration of blood pressure oscillations (0.05 to 0.07 Hz) via superimposition of LBNP swings with ganglionic blockade. \*Significant difference from baseline; †significant difference from ganglionic blockade.

0.29 ± 0.02 to 0.53 ± 0.02 flux units/mmHg; Fig. 2). In contrast, during oscillatory LBNP, coherence between blood pressure and palm skin blood flow was not different relative to baseline ( $0.56 \pm 0.04$ ). Additionally, the transfer function gain was significantly reduced at the palm (from  $3.6 \pm 0.3$  to  $1.2 \pm 0.1$  flux units/mmHg) during combined LBNP and ganglionic blockade compared with the ganglionic blockade condition (Fig. 3).

## DISCUSSION

The primary findings of the present study are as follows: 1) autonomic blockade dramatically reduces the spectral power of both palm and forearm skin in the LF range, and 2) regenera-

difference from ganglionic blockade.

Table 3. Palm skin blood flow spectral and transfer function analysis across LF and HF ranges

	Frequency Range	Baseline	Ganglionic Blockade	Regeneration of Blood Pressure Oscillations
Spectral power, Flux Units <sup>2</sup>	LF	5,520±1,452	903±220*	593±103*
	HF	50±11	32±6*	25±5*†
	OSF	4,568±1,278	668±128*	1,192±291*
Transfer function gain, Flux Units/mmHg	LF	4.4±0.2	4.0±0.3	2.5±0.2*†
	HF	3.2±0.2	2.5±0.2*	1.7±0.1*†
	OSF	4.7±0.5	3.6±1.3	1.2±0.4*†
Phase, radians	LF	1.50±0.09	0.58±0.14*	0.43±0.14*
	HF	0.34±0.10	-0.43±0.07*	-0.49±0.08*
	OSF	1.63±0.25	-0.12±0.31*	-0.17±0.06*
Coherence	LF	0.48±0.03	0.31±0.01*	0.38±0.02*†
	HF	0.32±0.01	0.35±0.02	0.35±0.02
	OSF	0.57±0.04	0.33±0.05*	0.56±0.04†

Data are means ± SE. LF range is 0.0078–0.15 Hz; HF range is 0.15–0.35 Hz; OSF range is 0.05–0.07 Hz. See Table 2 for additional information and clarification. \*Significant difference from baseline; †significant difference from ganglionic blockade.

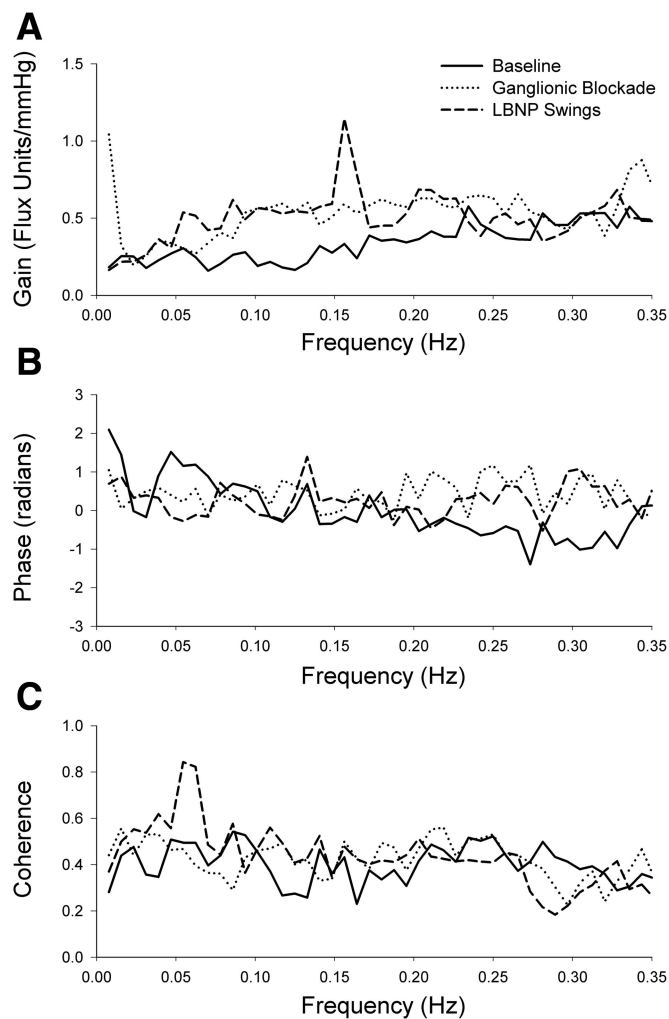


Fig. 2. Group-averaged transfer function gain (A), phase (B), and coherence (C) for nonglabrous forearm skin.

tion of pressure fluctuations via LBNP swings after autonomic blockade were transferred to skin blood flow oscillations in the forearm but not palm skin. These data confirm prior findings (23) that oscillations in skin blood flow within the LF region are dramatically influenced, but not solely caused, by the sympathetic nervous system. The apparent absence of the transfer of blood pressure oscillations to palm skin blood flow during combined ganglionic blockade and LBNP, as indicated by the lack of a change in palm skin blood flow spectral power despite increases in blood pressure spectral power resulting in a reduction in the transfer function gain, suggests that glabrous skin of the palm has the capability to autoregulate blood flow within the OSF range in response to dynamic changes in blood pressure. In contrast, increases in forearm skin spectral power and the transfer function gain during combined ganglionic blockade and LBNP suggest less intrinsic autoregulatory capabilities in nonglabrous skin of the forearm. An increase in the transfer function gain of forearm skin between baseline and ganglionic blocked plus LBNP conditions suggests this region has an important neurally mediated capability to buffer intrinsic blood pressure oscillations.

Oscillations in skin blood flow have been observed in glabrous skin of the ear (2, 21), volar finger (1, 2), and sole and

palm (29) as well as in nonglabrous skin of the forearm (19, 24, 28) and forehead (19, 22, 28). These skin blood flow oscillations occur at various frequencies thought to be associated with local tissue and vessel factors (~0.025 Hz), “Mayer wave” (~0.1 Hz), respiration (~0.25 Hz), and cardiac cycles (~1.0 Hz). However, some controversy exists as to the origin of the oscillations in skin blood flow occurring at frequencies <0.1 Hz, and the role of the sympathetic nervous system in these oscillations remains unclear. For example, recently, it has been suggested that oscillations in glabrous skin blood flow around a very LF range (~0.025 Hz), previously associated with local tissue and vessel factors, may be influenced by the sympathetic nervous system (23). Our data support this assertion because ganglionic blockade resulted in pronounced reductions in skin blood flow spectral power for both the palm and forearm around this very LF range (see Fig. 1). However, because the spectral power of blood pressure is also decreased within these very LF ranges, it is possible that the reduction in skin blood flow spectral power in this range is a factor of reduced oscillations in perfusion pressure. Regardless of the mechanism, it is clear that the majority of the oscillations in palm and forearm skin blood flow within this very LF range are unlikely to be due solely to local factors.

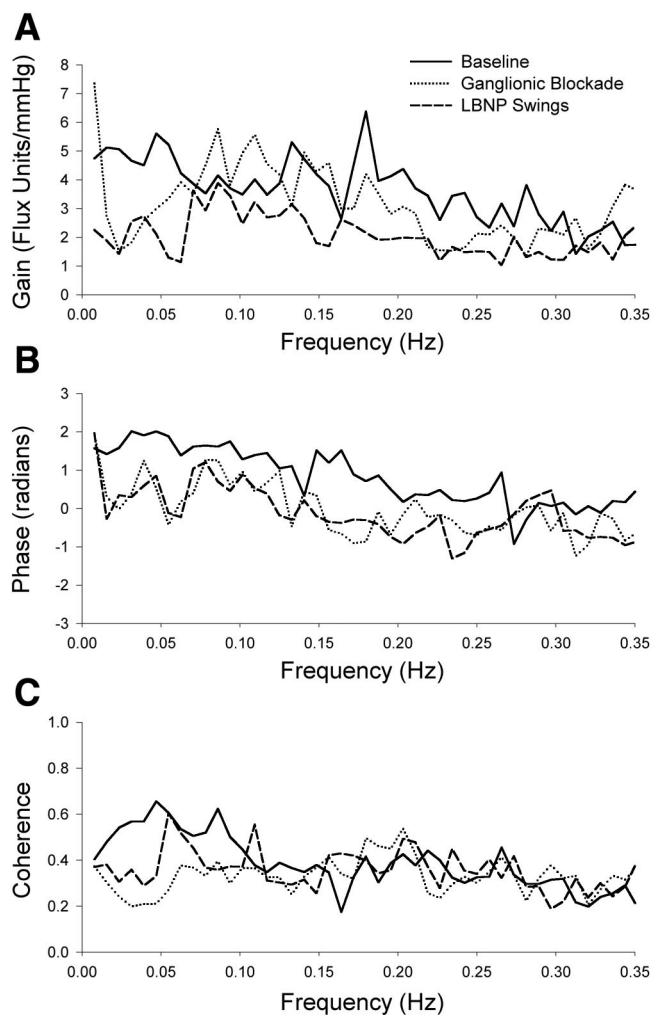


Fig. 3. Group-averaged transfer function gain (A), phase (B), and coherence (C) for glabrous palm skin

The reintroduction of LF blood pressure fluctuations to the systemic vasculature by means of LBNP swings during ganglionic blockade returned mean arterial blood pressure variability to baseline levels (34). However, this return of blood pressure spectral power was not translated to the palm. In fact, there was no significant difference in the spectral power of palm skin blood flow between ganglionic blockade and ganglionic blockade with LBNP, whereas transfer function gain was significantly reduced from  $3.6 \pm 0.3$  to  $1.2 \pm 0.1$  flux units/mmHg (Table 3). In contrast to the palm, the forearm showed a pronounced translation of blood pressure fluctuations in the OSF range (see Fig. 1), as indicated by a significant elevation in the transfer function gain from  $0.29 \pm 0.02$  to  $0.53 \pm 0.02$  flux units/mmHg after ganglionic blockade (Table 2). These data show that upon removal of autonomic neural control, the magnitude of change in skin blood flow per change in blood pressure increased in the forearm and decreased in the palm compared with baseline values. This observation suggests that oscillations in skin blood flow in response to blood pressure fluctuations can be intrinsically buffered in palm skin, but less so in forearm skin. Hence, glabrous skin of the palm demonstrates dynamic autoregulatory abilities around 0.05 Hz that are either not manifested or are manifested in a much lower degree in nonglabrous skin of the forearm.

In further support of the concept that intrinsic dynamic autoregulation is present in palm skin but less so in forearm skin, coherence between blood pressure and forearm skin blood flow significantly increased from 0.49 in baseline conditions to 0.83 with LBNP swings (Table 2). In contrast, coherence between blood pressure and skin blood flow in the palm was unchanged from baseline conditions by LBNP swings (from 0.57 to 0.56; Table 3). These data indicate that during autonomic blockade, forearm skin blood flow more closely followed or tracked blood pressure changes associated with LBNP swings, whereas palm skin blood flow did so to a lesser degree. Such a finding demonstrates the ability of palm skin to autoregulate blood flow in response to changes in arterial blood pressure.

Phase lead of skin blood flow to arterial blood pressure was reduced after ganglionic blockade in both the palm and forearm within the OSF (see Tables 2 and 3). LBNP swings further reduced phase lead in the palm but not the forearm. A reduction in phase coupled with an increase in gain is often linked to an impaired dynamic autoregulation. This pattern was observed in the forearm. In the palm, despite decreases in phase, no significant changes in gain occurred during ganglionic blockade.

Anatomic and associated flow-related differences of glabrous skin may explain the ability of this type of skin to buffer changes in perfusion pressure. Glabrous skin contains both surface capillary loops and deeper arteriovenous anastomoses (AVA), whereas nonglabrous skin contains capillary loops but lacks AVA (6, 16). AVA shunts blood directly from the arterial to venous beds, bypassing the capillary loops. These AVA are innervated predominantly via noradrenergic nerves. Thus on ganglionic blockade and subsequent removal of sympathetic control of AVA, these shunts are relaxed, resulting in the observed large increase in palm skin blood flow (Table 1). With AVA no longer modulating skin blood flow during ganglionic blockade, blood pressure oscillations should transmit blood flow oscillations to the skin through these large

diameter vessels; however, this was not the case. This indicates that in the absence of neural control of skin blood flow, the palm retains its ability to buffer oscillations in blood pressure. This is in stark contrast to the forearm in which pressure oscillations are transmitted to skin blood flow oscillations, as demonstrated by the elevation in transfer function gain during LBNP. An alternate explanation for the differences in spectral power and transfer function gain between palm and forearm skin blood flows during LBNP with ganglionic blockade may be related to differences in neural control of these vascular beds. Glabrous skin blood flow is controlled solely by a tonic vasoconstrictor system. Thus maximum glabrous CVC can be achieved via inhibition of this tonic vasoconstrictor system (17), which occurs during the ganglionic blockade condition in this study. In contrast, nonglabrous skin blood flow is governed by both a sympathetic vasoconstrictor system and a separate sympathetic active vasodilator system (11, 12), and both systems would be blocked upon ganglionic blockade. Thus on inhibition of sympathetic activity via ganglionic blockade, increases in skin blood flow in the palm were greater compared with the forearm (Table 1). It is possible that this difference in baseline skin blood flow between the palm and forearm after ganglionic blockade may influence dynamic modulation of skin blood flow during oscillatory LBNP. However, because LBNP with ganglionic blockade reduced skin blood flow, it is unlikely that the reduction in transfer function gain for the palm during oscillatory LBNP was due to a ceiling effect limiting pressure-induced increases in skin blood flow.

Blood flow autoregulation can be assessed via static and dynamic methods, each providing insight into the multifaceted concept of autoregulation. A recent experiment suggests that both glabrous and nonglabrous skin have static autoregulatory capabilities if perfusion pressure is sufficiently low (5). In that study, we observed increases in cutaneous vascular conductance in both types of skin during substantial reductions in perfusion pressure induced via a 15-s Valsalva maneuver plus ganglionic blockade, thus inferring myogenic vasodilator capabilities. In the current study assessing dynamic autoregulation, we observed blood pressure buffering capabilities in the palm but not the forearm during relatively moderate changes in perfusion pressure. Combining interpretations from these two studies indicate that without sympathetic input, glabrous skin is capable of both static and dynamic autoregulation, whereas nonglabrous skin retains static but not dynamic autoregulatory capabilities.

*Limitations to the interpretation of the results.* Transfer function analysis of the dynamic pressure-flow relationship of cutaneous vascular beds was employed in this study. Implementation of this method assumes that oscillations in skin blood flow are induced linearly by dynamic changes in arterial pressure. Although the underlying mechanisms responsible for spontaneous changes in skin blood flow are not completely clear, the findings of simultaneous reductions in arterial pressure and skin blood flow oscillations within the LF range after autonomic blockade, as well as enhanced oscillations in arterial pressure and skin blood flow during LBNP, provide evidence that oscillations in skin blood flow are mediated at least in part by dynamic changes in arterial pressure. However, interpretation of the estimates of transfer function gain as representing dynamic vascular autoregulation must be viewed with caution because changes in transfer function gain may reflect not only



changes in vascular resistance (traditional concept of autoregulation) but also alterations in vascular compliance under the present study conditions (14). The specific vascular control mechanism(s) of whether, how, and to what extent changes in vascular resistance and/or compliance in response to dynamic changes in arterial pressure buffer the oscillations in cutaneous blood flow (dynamic autoregulation) cannot be delineated in this study.

Coherence was low during a number of study conditions, especially in the HF range. Low coherence values might suggest a nonlinear relationship or an uncoupling of the relationship between skin blood flow and arterial blood pressure. However, within the OSF range, coherence was close to (i.e., 0.49) or >0.5 for baseline and LBNP conditions for both the palm and forearm. Moreover, during LBNP there were dramatic increases in coherence and transfer function gain in the forearm but no change in coherence and decreases in transfer function gain in the palm. These findings indicate a tighter linear relationship between pressure and skin blood flow in the forearm compared with the palm during LBNP.

In conclusion, autonomic blockade dramatically reduced spectral power of both glabrous and nonglabrous skin blood flow oscillations within the LF range. Blood pressure fluctuations via LBNP swings after autonomic blockade were transferred to nonglabrous skin of the forearm but less so to glabrous skin of the palm. Thus glabrous skin of the palm buffered blood flow oscillations induced by changes in arterial blood pressure, thereby demonstrating dynamic autoregulatory capabilities that appear to be absent or attenuated in nonglabrous skin of the forearm.

ACKNOWLEDGMENTS

The authors express appreciation to Dr. Jian Cui for valuable insight regarding data analysis, to Cyrus Oufi and Julie Zuckerman for technical assistance, and to the subjects for willing participation in this project.

This project was a component of a larger project in which blood pressure data have previously been reported (5, 32, 34). In the present publication, we only make reference to data contained in those studies to explain findings regarding blood flow responses in the skin.

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GRANTS

This study was funded in part by National Aeronautics and Space Administration Grant NAG9-1033; American Heart Association Texas Affiliate Grant 98BG058; and National Institutes of Health Grants HL-61388, HL-10488, HL-67422, and GM-68865.

REFERENCES

1. Bernardi L, Hayoz D, Wenzel R, Passino C, Calciati A, Weber R, and Noll G. Synchronous and baroreceptor-sensitive oscillations in skin microcirculation: evidence for central autonomic control. *Am J Physiol Heart Circ Physiol* 273: H1867–H1878, 1997.
2. Bernardi L, Radaelli A, Solda PL, Coats AJ, Reeder M, Calciati A, Garrard CS, and Sleight P. Autonomic control of skin microvessels: assessment by power spectrum of photoplethysmographic waves. *Clin Sci (Lond)* 90: 345–355, 1996.
3. Burton AC. The range and variability of the blood flow in the human fingers and the vasomotor regulation of body temperature. *Am J Physiol* 127: 437–453, 1939.
4. Crandall CG, Shibasaki M, and Yen TC. Evidence that the human cutaneous venoarteriolar response is not mediated by adrenergic mechanisms. *J Physiol (Lond)* 538: 599–605, 2002.
5. Durand S, Zhang R, Cui J, Wilson TE, and Crandall CG. Evidence of a myogenic response in vasomotor control of forearm and palm cutaneous microcirculations. *J Appl Physiol* 97: 535–539, 2004.

6. Eady RAJ, Leigh IM, and Pope FM. Anatomy and organization of human skin. In: *Textbook of Dermatology* (6th ed.), edited by Champion RH, Burton JL, Burns DA and Breathnach SM. Oxford: Blackwell, 1998.
7. Guyton AC and Hall JE. *Textbook of Medical Physiology*. Philadelphia, PA: Saunders, 2000.
8. Henriksen O. Sympathetic reflex control of blood flow in human peripheral tissues. *Acta Physiol Scand Suppl* 603: 33–39, 1991.
9. Henriksen O, Nielsen SL, Paaske WP, and Sejrsen P. Autoregulation of blood flow in human cutaneous tissue. *Acta Physiol Scand* 89: 538–543, 1973.
10. Johnson JM. The cutaneous circulation. In: *Laser-Doppler Blood Flowmetry*, edited by Shepherd AP and Oberg PA. Boston, MA: Kluwer Academic, 1990.
11. Johnson JM, Brengelmann GL, Hales JR, Vanhoutte PM, and Wenger CB. Regulation of the cutaneous circulation. *Fed Proc* 45: 2841–2850, 1986.
12. Johnson JM and Proppe DW. Cardiovascular adjustments to heat stress. In: *Handbook of Physiology. Environmental Physiology*. Bethesda, MD: Am. Physiol. Soc., 1996, sect. 4, vol II, chapt. 11, p. 215–244.
13. Malanin K and Kolari PJ. The venoarteriolar response of the skin in healthy legs measured at different depths. *Clin Physiol* 18: 441–446, 1998.
14. Nichols WW and O'Rourke MF. *McDonald's Blood Flow in Arteries: Theoretical, Experimental, and Clinical Problems*. Philadelphia, PA: Lea & Febiger, 1990.
15. Pergola PE, Kellogg DL, Johnson JM, Kosiba WA, and Solomon DE. Role of sympathetic nerves in the vascular effects of local temperature in human forearm skin. *Am J Physiol Heart Circ Physiol* 265: H785–H792, 1993.
16. Roddie IC. Circulation to skin and adipose tissue. In: *Handbook of Physiology. The Cardiovascular System. Peripheral Circulation and Organ Blood Flow*. Bethesda, MD: Am. Physiol. Soc., 1983, sect. 2, vol. III, pt. 1, chapt. 10, p. 285.
17. Rowell LB. *Human Circulation: Regulation During Physical Stress*. Oxford, UK: Oxford University Press, 1986.
18. Saad AR, Stephens DP, Bennett LA, Charkoudian N, Kosiba WA, and Johnson JM. Influence of isometric exercise on blood flow and sweating in glabrous and nonglabrous human skin. *J Appl Physiol* 91: 2487–2492, 2001.
19. Salerud EG, Tenland T, Nilsson GE, and Oberg PA. Rhythmical variations in human skin blood flow. *Int J Microcirc Clin Exp* 2: 91–102, 1983.
20. Sandroni P, Benarroch EE, and Low PA. Pharmacological dissection of components of the Valsalva maneuver in adrenergic failure. *J Appl Physiol* 71: 1563–1567, 1991.
21. Sasano H, Hayano J, Tsuda T, and Katsuya H. Effects of sympathetic nerve blockades on low-frequency oscillations of human earlobe skin blood flow. *J Auton Nerv Syst* 77: 60–67, 1999.
22. Smits TM, Aarnoudse JG, Geerdink JJ, and Zijlstra WG. Hyperventilation-induced changes in periodic oscillations in forehead skin blood flow measured by laser Doppler flowmetry. *Int J Microcirc Clin Exp* 6: 149–159, 1987.
23. Soderstrom T, Stefanovska A, Veber M, and Svensson H. Involvement of sympathetic nerve activity in skin blood flow oscillations in humans. *Am J Physiol Heart Circ Physiol* 284: H1638–H1646, 2003.
24. Stanton AW, Levick JR, and Mortimer PS. Assessment of noninvasive tests of cutaneous vascular control in the forearm using a laser Doppler meter and a Finapres blood pressure monitor. *Clin Auton Res* 5: 37–47, 1995.
25. Stauss HM, Anderson EA, Haynes WG, and Kregel KC. Frequency response characteristics of sympathetically mediated vasomotor waves in humans. *Am J Physiol Heart Circ Physiol* 274: H1277–H1283, 1998.
26. Stauss HM, Stegmann JU, Persson PB, and Habler HJ. Frequency response characteristics of sympathetic transmission to skin vascular smooth muscles in rats. *Am J Physiol Regul Integr Comp Physiol* 277: R591–R600, 1999.
27. Taylor WF, Johnson JM, O'Leary D, and Park MK. Effect of high local temperature on reflex cutaneous vasodilation. *J Appl Physiol* 57: 191–196, 1984.
28. Tenland T, Salerud EG, Nilsson GE, and Oberg PA. Spatial and temporal variations in human skin blood flow. *Int J Microcirc Clin Exp* 2: 81–90, 1983.

29. **Thomsen MB, Lassvik C, and Bengtsson M.** Changes in skin perfusion after sympathetic block with guanethidine. Laser Doppler flowmetry in human volunteers. *Int J Microcirc Clin Exp* 7: 123–130, 1988.
30. **Wenger CB, Stephenson LA, and Durkin MA.** Effect of nerve block on response of forearm blood flow to local temperature. *J Appl Physiol* 61: 227–232, 1986.
31. **Wilson TE, Shibasaki M, Cui J, Levine BD, and Crandall CG.** Effects of 14 days of head-down tilt bed rest on cutaneous vasoconstrictor responses in humans. *J Appl Physiol* 94: 2113–2118, 2003.
32. **Zhang R, Iwasaki K, Zuckerman JH, Behbehani K, Crandall CG, and Levine BD.** Mechanism of blood pressure and R-R variability: insights from ganglionic blockade in humans. *J Physiol (Lond)* 543: 337–348, 2002.
33. **Zhang R, Zuckerman JH, Giller CA, and Levine BD.** Transfer function analysis of dynamic cerebral autoregulation in humans. *Am J Physiol Heart Circ Physiol* 274: H233–H241, 1998.
34. **Zhang R, Zuckerman JH, Iwasaki K, Wilson TE, Crandall CG, and Levine BD.** Autonomic neural control of dynamic cerebral autoregulation in humans. *Circulation* 106: 1814–1820, 2002.

