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Effects of Repeated Local Ischemia on the Temperature and Microcirculation in the Skin of the Human Hand

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Abstract—Thermal imaging and laser Doppler flowmetry were used to study vascular response–associated infrared (IR) radiation effects in healthy volunteers subjected to regular unilateral arteriovenous occlusion of one of the fingers (four times a day for seven months with a gradual increase in exposure from 10 to 30 min). After repeated unilateral exposures, consistent changes in the temperature and thermoregulation modes were observed on the corresponding skin areas of both hands. There was a high positive correlation between the dynamics of IR emission from the experimental and control skin areas in the recovery phase after clamping, suggesting that the systemic vascular response was involved. The possible mechanisms of postocclusive changes in the skin of the distal phalanges are discussed. Our data suggest that multiple regular unilateral arteriovenous occlusions enhance the intradermal blood flow and can be used to prevent peripheral microcirculation disorders in various pathological conditions.

Keywords: thermography, arteriovenous occlusion, local ischemia, skin microcirculation, regulation of peripheral blood flow, postocclusive reactive hyperemia, laser Doppler flowmetry

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Numerous recent studies have shown that thermal imaging (TI) techniques can be efficiently applied to noninvasive recording of spatiotemporal patterns of microcirculatory reactions in the skin based on the temperature distribution over the skin surface [1]. By analyzing the dynamics of local skin temperature in response to various stimuli, it is possible to conduct a differential diagnosis of microcirculation disorders and to assess quantitatively the contributions of vascular and nervous controls in different functional contexts [2, 3]. Blood flow parameters nonspecifically involved in the response to a broad range of endogenous and exogenous stimuli can be studied using a number of instrumental techniques and are often used as diagnostic markers of impaired vascular control. Using controlled stimulation of microcirculation, it is possible to activate or suppress individual regulatory circuits [4]. Information on the dynamics of microvascular regulation can be obtained using laser Doppler flowmetry (LDF) [5].

Here, in order to study the circuits that regulate the peripheral blood flow and to analyze whether recurrent episodes of local ischemia can serve for directed triggering of vascular reactions, we investigated infrared emission and microcirculatory effects induced by repeated unilateral arteriovenous occlusion of one finger.

EXPERIMENTAL

The study was performed in six healthy male volunteers (mean age, 29 years) and comprised 54 experiments where the dynamics of temperature on the dorsal surface of both hands was recorded using a Thermo Tracer TH-9100 matrix thermal imager (NEC, Japan) at a constant ambient temperature of 20–22°C. During the tests, a volunteer was seated in a chair with his hands positioned on a heat-insulating mesh; a soft cushion under the forearms was used to prevent the compression of blood vessels and nerves. Following a 5-min adaptation in the experimental position, thermal images were recorded with a frequency of 0.125 to 1 Hz during the three stages of the experiment: (1) 20 min at rest without any external influence (background); (2) 10 to 30 min of occlusion of the second finger on the left hand using an arteriovenous tourniquet, and (3) 30 min following tourniquet removal.

In 20 experiments, the microcirculation index (MI) was measured on the distal phalanx of the test finger using a LAKK-M laser Doppler flowmeter

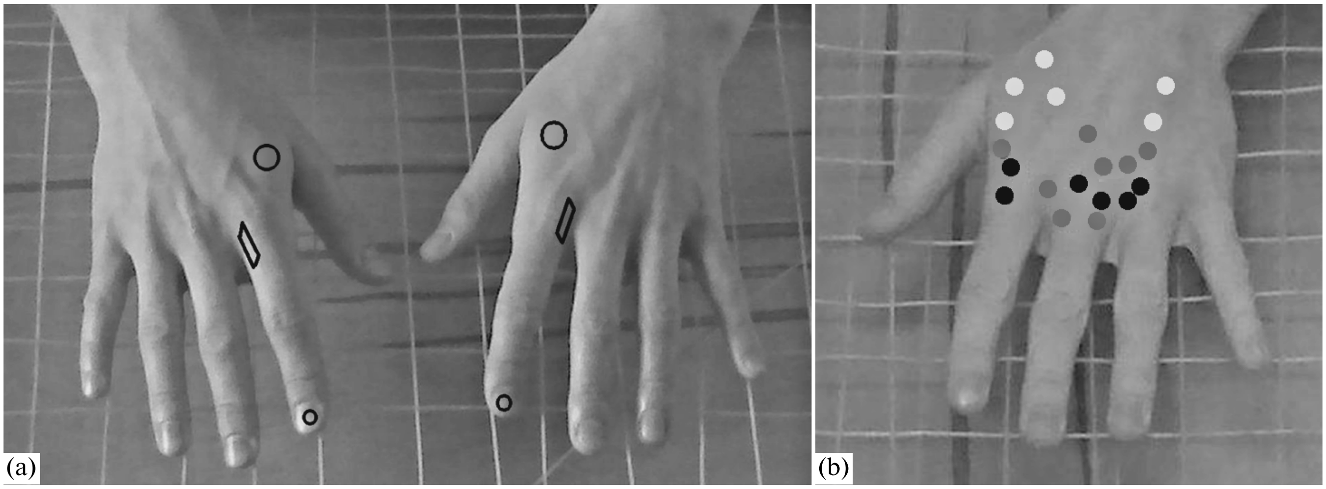

Fig. 1. Sites of temperature measurements on subjects' hands. (a) The ungual phalanx of the second finger; projection of the digital artery in the second interdigital space; first intermetacarpal space (snuffbox). Arrows indicate the level of tourniquet application. The left hand was the experimental one, and the right hand was the control one. (b) Twenty sites of dynamic temperature measurements along the dorsal veins of the hand. Color shows clusters characterized with similar temperature dynamics following a 10-min arteriovenous occlusion of the second finger: gray, cluster I; black, cluster II; white, cluster III.

(Lazma, Russia) at all stages simultaneously to TI analysis. Wavelet transformation was used to analyze the amplitudes of oscillations in the ranges corresponding to active and passive factors of microvascular blood flow regulation [6]. Active tone-forming influences were assessed in the frequency ranges corresponding to endothelial (0.0095–0.02 Hz), neurogenic (0.02–0.046 Hz), and myogenic (0.047–0.145 Hz) modes of blood flow regulation, while passive influences were analyzed in the ranges corresponding to the respiratory (0.2–0.4 Hz) and heart (0.8–1.6 Hz) rhythms. To evaluate the proportion between the capillary and bypass blood flow pathways in the target skin areas of the hand dorsum, which contain a hemodynamically insignificant number of true arteriolovenular anastomoses, changes in the bypass index were calculated as A_{dom}/A_m, where A_{dom} was the dominating maximum amplitude within active ranges (below respiratory rhythms), and A_m was the amplitude of the myogenic range oscillations.

After signing an informed written consent, all subjects exposed themselves to periodic local ischemia by applying, four times a day, an arteriovenous tourniquet on the second finger of the left hand using tight distal–proximal exsanguination-type bandaging and leaving the distal phalanx free. Altogether, subject I was exposed to 760 occlusions (288 episodes of 10 min, 236 episodes of 15 min, 116 episodes of 20 min, and 120 episodes of 30 min); subject II was exposed to 356 occlusions (284 episodes of 10 min and 72 episodes of 15 min); the other subjects were exposed to 22 to 67 occlusions, the first 7–24 of which were 10 min long, and the rest were 15 min long.

Control TI and LDF measurements were performed prior to the first occlusion and regularly throughout the experimental series: 27 measurements in subject I, 24 measurements in subject II, and 5 to 9 measurements in the other subjects. To avoid the potential effect of the bandaging procedure on the blood flow in the control hand during TI and LDF measurements, the tourniquet was applied by the experimenter. The periodical occlusions where no data were recorded were performed by the subjects themselves. In the beginning of the study and prior to every change in the course of the occlusion test, a standard regional cold test was performed and IR radiation from both hands was recorded.

Temperature parameters were recorded on the backs of both hands at three sites: the distal phalanx of the second finger; the projection of the digital artery in the second interdigital space; the first intermetacarpal space (the anatomical snuffbox). The temperature dynamics in 20 areas of 5 pixels each situated along the dorsal hand veins was studied using cluster analysis (Fig. 1).

Four additional experiments were performed in two subjects using the same procedure except that the temperature dynamics was recorded simultaneously on the dorsal and the palmar surface of the test hand using two thermal imagers. The second thermal imager, a G100 matrix device (NEC, Japan), was operated in the same range (8–14 μm) and had a similar accuracy (±1%) and temperature resolution (0.03°C) as the first one.

The obtained TI data were analyzed using the professional Radiometric Complete Online D 5.1.1.011–23.01.2012 software, and analysis of variance (ANOVA) was performed using Statistica 6.1. Using repeated-measures ANOVA for each thermogram (the time–temperature curve) obtained during the postocclusion recovery period, the significance of differences was evaluated with Fisher's post-hoc LSD test for the following variables: the number of the occlusion event, its duration, the sensor position (left/right hand, area of measurement), time after tourniquet removal, average temperature reaction parameters (*min*, *max*, *mean*). Correlation analysis was performed; highly significant correlations ($p < 0.01$) are described in the Results section. Distortions caused by occasional changes in hand or finger positions were compensated for using an automated search for critical points of scale-invariant feature transform (SIFT) to locate the area of interest within images. The obtained thermal image films were analyzed by dividing them into fragments with different temperature growth rates [7].

RESULTS

During the background and finger II occlusion stages, the temperature changed synchronously and symmetrically in the skin of dorsum of the distal phalanges and the snuffbox area. The correlation coefficient for these oscillations was close to unity both for the mean and the extreme temperature values.

During the recovery stage, the temperature reactions observed in the snuffbox and the digital artery projection areas were characteristically delayed relative to the distal phalanx, which suggests that the late response in this area is of predominantly venous nature.

Thermograms of the left and right snuffbox areas diverged starting from 15–20 s after tourniquet removal: the temperature began to increase on the experimental hand (e), but not on the control hand (c), where it remained constant. The patterns of temperature dynamics in the symmetrical digital artery projection areas were also highly synchronous. This area could not be observed on the experimental hand during the occlusion stage, and the temperature dynamics after tourniquet removal was similar to the pattern observed for the distal phalanx and strongly different from that of the snuffbox area. The sequential stages of the experiment are illustrated by thermal maps shown in Fig. 2.

The sequence of events is also reflected in the MI dynamics in the distal phalanx, as assessed using LDF data (Fig. 3). An increase in MI and its subsequent drop below the initial level during the recovery stage (the upper curve) preceded the more inertial changes in temperature (the lower curve).

The same temporal relationship between the dynamics of TI and LDF characteristics was also observed with longer occlusion periods.

Following tourniquet application, MI decreased 6.5-fold, while its standard deviation decreased 1.75-fold, and the neurogenic component increased 1.38-fold.

The reaction of factors regulating microcirculation immediately after tourniquet removal varied between experiments, while MI exhibited a consistent increase. In early experiments, an important role belonged to the bypass blood flow (the bypass index increased twofold). Following a two-month series of occlusions, we observed an enhanced arterial flow (2.4-fold increase in the pulse wave amplitude) and enhanced venous drainage (the respiratory undulation decreased 0.4-fold). Within 15 min after tourniquet removal, the bypass index decreased and the venular blood flow was restored nearly to the baseline level.

In the first occlusion events, the temperatures observed at the end of the occlusion period on the distal phalanges of the experimental finger ($T_{\text{oc-e}}$) and the symmetrical control finger ($T_{\text{oc-c}}$) differed nonsignificantly; until occlusion no. 44 (day 11), the temperature drop by the moment of tourniquet removal was 0.5–1.0°C. However, continuation of the occlusion series was associated with a growing divergence between $T_{\text{oc-e}}$ and $T_{\text{oc-c}}$; that is, IR emission of the test finger (both in the distal phalanx and in the area of the digital artery projection) was restored starting from ever higher values of $\Delta T = T_{\text{oc-c}} - T_{\text{oc-e}}$. By occlusion no. 60, this difference reached 4°C and was maintained (with ±2°C fluctuation) during 224 events of 10-min occlusion; when the occlusion duration was increased to 15 min, it continued to grow slowly, reached 7.4°C by occlusion no. 440, and remained in the range of 7–8°C during 20- and 30-min-long occlusions.

The most interesting were the data on temperature reactions in the distal phalanges. During the first 11 days of the experiment (44 occlusions), there were no significant changes in the recovery reaction in the distal phalanx of the bandaged finger after occlusion. However, at later stages, a significant correlation appeared between the characteristics of IR emission of the left (experimental) and the right (control) hand.

Following tourniquet removal after a 10-min occlusion, the temperature of the distal phalanx of the bandaged finger grew by 2.1 to 10.0°C (6.68 ± 1.98°C) in the first 2 min of recovery. Subsequently, the temperature continued to increase and reached its maximum at different moments after tourniquet removal. At the symmetrical site, the temperature changed by −1 to +1.2°C.

Figures 4a and 4b show ANOVA charts of thermal reactions in distal phalanges that illustrate the spatiotemporal temperature dynamics observed in two experiments with 10-min occlusions (experiment no. 4, occlusion 34 and experiment no. 6, occlusion 50). The chart in Fig. 4c summarizes the spatiotemporal temperature dynamics at three sites on the left and the right hand ((*1*) distal phalanx; (*2*) digital artery; (*3*) snuffbox) in 12 experiments with 10-min occlusions, including tests nos. 4 and 6.

Analysis of temperature growth patterns on the test and the control hand during the recovery stage follow-

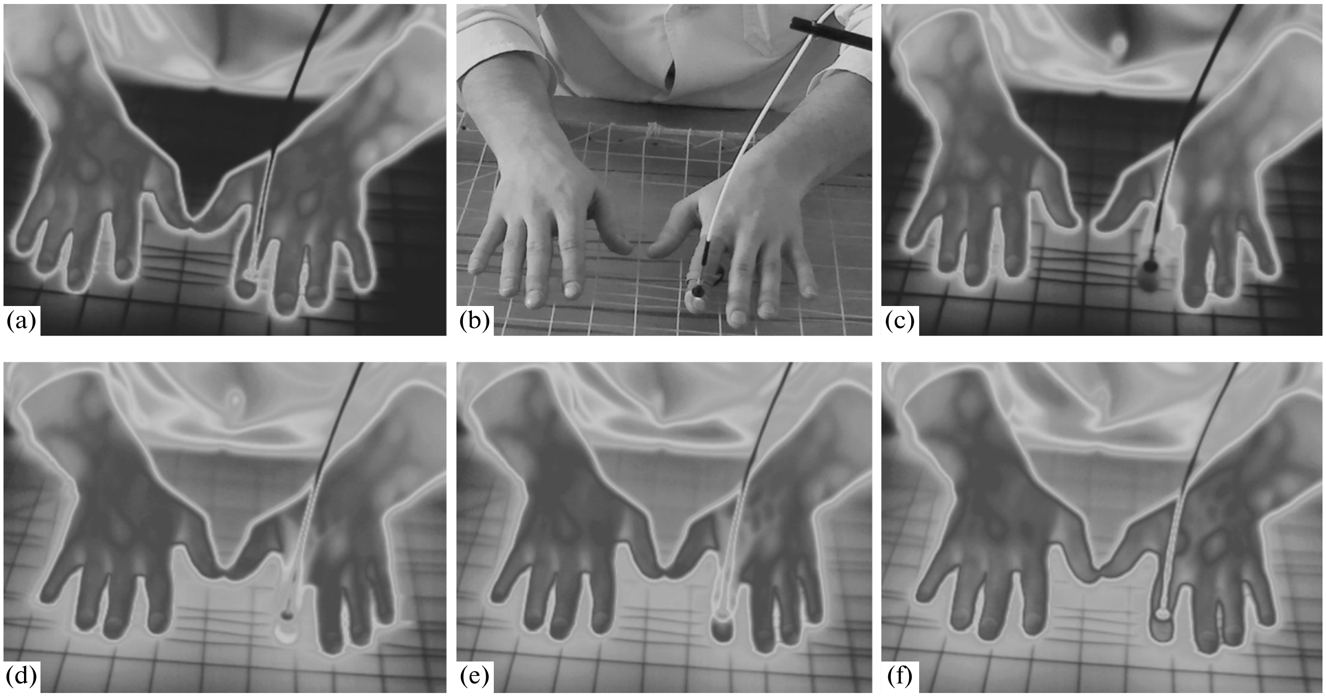

Fig. 2. Design of the experiment: occlusion no. 360 in subject I, 15-min exposure. (a) Background thermal map prior to occlusion; (b) photograph taken at the occlusion step; (c) thermal map at the end of the occlusion; (d–f) dynamics of recovery 10 s, 30 s, and 3 min after tourniquet removal.

ing tourniquet removal after 10-min occlusions showed that both the mean and the maximal or the minimal values followed the same behavior including an initial decrease and growth and a repeated decrease and growth. Therefore, it was considered unnecessary to perform calculations for all three parameters (*min*, *max*, *mean*).

It was found that the changes occurred synchronously in the symmetric areas of the left and the right hand; at the same time, the first and the subsequent experiments with 10-min occlusions showed a high level of correlation in the context of associated events (an occlusion and a change in temperature). The same phenomenon was also observed for 15-, 20-, and 30-min-long occlusions of the test hand, whereas the "mirror effect" on the control hand was the most pronounced following the transition from 15-min to 20-min-long occlusions.

An increase in the duration of occlusions above the 10-min level resulted in further changes in the dynamic patterns of thermal reactions in all areas studied. Since these patterns were similar to each other, we will discuss only the observations concerning the distal phalanx area. Interestingly, the high peak temperatures observed in 10-min occlusion experiments were not reproduced in subsequent experimental contexts, and the mean temperatures, which lied in the range of 32–33°C for 10-min occlusions, shifted to 28–31°C for 15-min events, to 26–29°C for 20-min events, and finally to 24–27°C for 30-min events. The shape of thermograms changed accordingly, with the initial segment showing in most cases a more steep growth of temperature. Mirrored thermal reactions were also observed in several cases.

When the bandaging period was increased from 15 to 20 min, characteristics of the recovery period in the distal phalanx changed: a three-stage thermal reaction included a return to the baseline level, transition above the baseline (reactive hyperthermia), and subsequent gradual decrease in temperature, which, however, still did not reach the baseline within the 30 min of observation. Interestingly, in an uninterrupted series of occlusions, the temperature reached the baseline level at the 51st second on average and continued to grow, while, if the series of periodic exposures failed, the temperature on the recovery stage following 15- and 20-min occlusions returned reliably to the baseline on the 71st second on average but did not exceed this level ($p < 0.05$). This observation could be used as a "lie detector" serving to recognize the potential subjects' negligence.

After a long series of bandaging (200 occlusions in subject I; 232 occlusions in subject II), in 7 of 27 experiments, an unilateral temperature increase was observed on the test finger as early as in the beginning of the background measurement; in one case, it was observed on the control finger, and in two cases, symmetrically on both fingers. In 4 out of 27 cases, the temperature pattern observed at the recovery stage showed a symmetrical increase in temperature of both

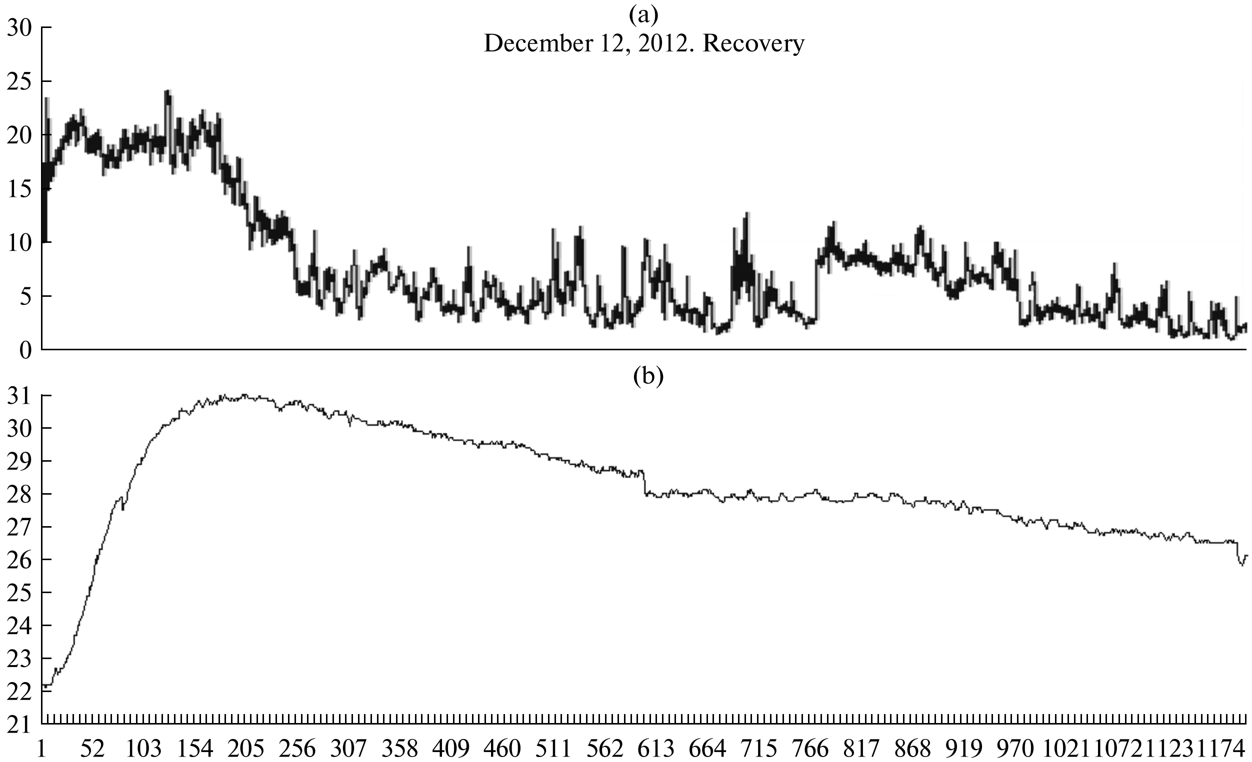

Fig. 3. Dynamics of the (a) microcirculation index (MI) and (b) temperature in the distal phalanx of the experimental finger during recovery after a 15-min occlusion no. 360 in subject I. *X* axis, time, s. *Y* axis, (a) MI (arbitrary units); (b) temperature, °C.

second fingers; at the same time, the temperature of fingers III–V of the test hand characteristically decreased. An increase in the duration of arteriovenous occlusion was associated with an increase in baseline temperatures of the more proximal segments of both hands (the digital artery and the snuffbox). Importantly, this increase was observed in both hands and was stronger in the control hand.

Late into the occlusion series, strong heterogeneity was observed on the test hand, which was most pronounced in the distal phalanx and the digital artery area, whereas on the control hand, a stationary presentation was changing and becoming less homogeneous in the course of the occlusion series; however, no consistent pattern could be identified.

Another phenomenon observed at this stage of the experiment was the development of a characteristic proximal–distal temperature gradient: on the control hand, the distal phalanx area was always colder than the more proximal zones of the digital artery and the snuffbox. On the test hand, this relationship could be disrupted in certain periods after tourniquet removal due different rates of temperature growth in these areas.

According to LDF data, MI dynamics also exhibited postocclusional changes, which were most pronounced at the early stages of the experiment.

To detect the deviations of thermal reactions observed during the occlusion test from the theoretical curves, cluster analysis was performed for 20 sites located along the dorsal hand veins, each one 5 pixels in size, and identified three clusters of zones characterized with different thermal pattern dynamics (Fig. 1).

DISCUSSION

The post-stimulatory hyperthermia observed on the dorsal surface of the distal phalanx, which followed a rapid increase in MI (according to LDF results), apparently reflects the phenomenon of postocclusive reactive hyperemia. It is known that reactive hyperemia following an occlusion of a threshold duration involves a 1.5- to 4-fold increase in blood flow relative to the baseline level and develops in 0.5–6 min [8]. Presumably, the dynamics of oscillation amplitudes within the respiratory rhythm range reflects the postocclusive exhaustion of the venular segment, while the hyperemic response to a short-term ischemia involves primarily the arterio-arteriolar segment [9]. Microcirculatory patterns in skin dermatomes depend also on somatosympathetic connections on the segment level [5]. Presumably, arteriolovenular anastomoses (shunts) in the skin of extremities are not subject to metabolic control and are incapable of reactive hyperemia, but are regulated exclusively via sympa-

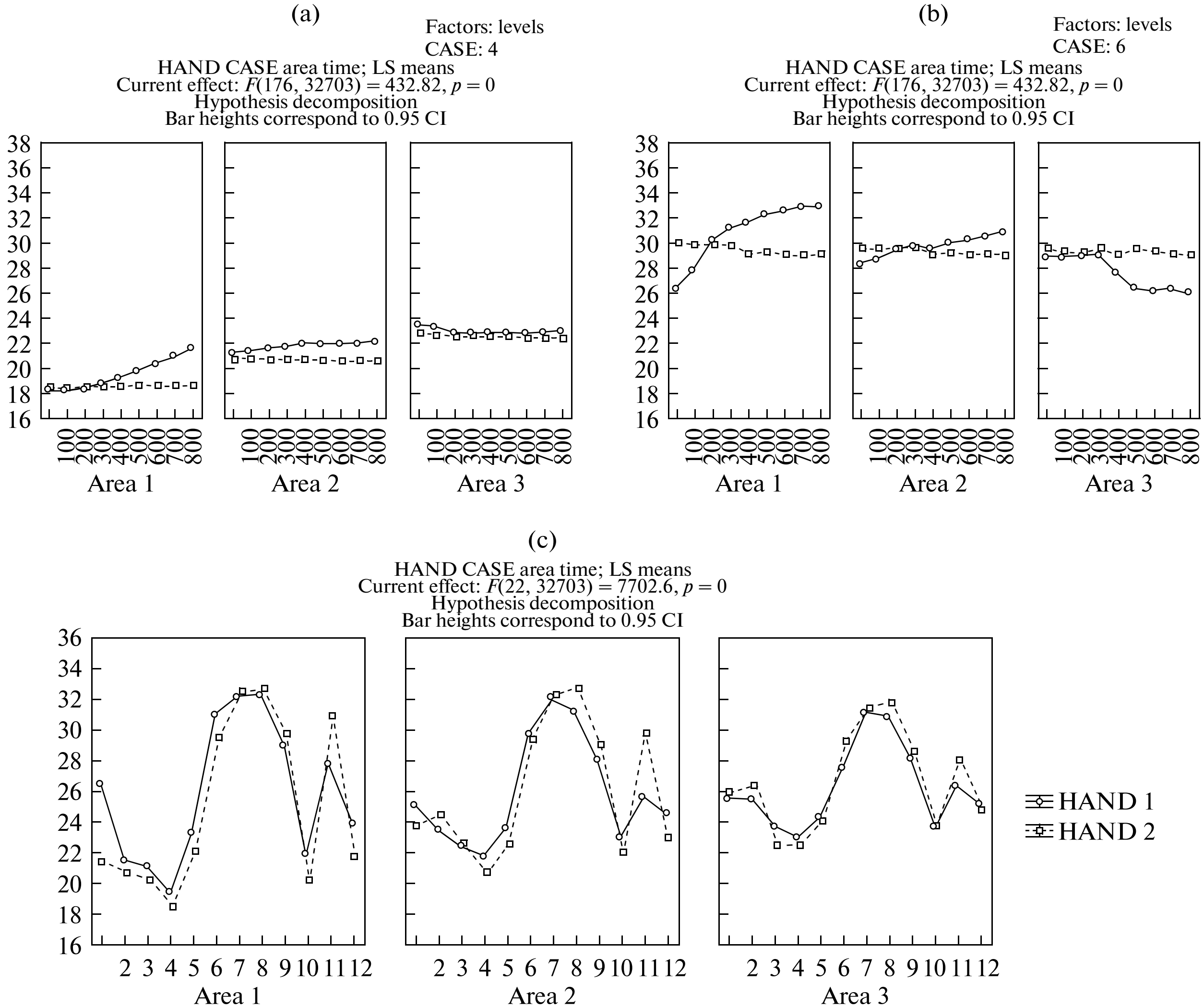

Fig. 4. Temperature dynamics in three skin areas of the hand ((1) distal phalanx; (2) digital artery; (3) snuffbox) on either hand in two experiments: (a) test 4 (occlusion 34); (b) test 6 (occlusion 50). (c) Spatiotemporal temperature dynamics across three areas on the left and on the right hand in 12 experiments with 10-min occlusions. Solid line, experimental hand; dashed line, control hand. *X* axis, time, s; *Y* axis, temperature, °C.

thetic innervation and activated by thermoreceptor or higher central nervous system reflexes [8]. Taking into consideration the data by Mayrovitz and Groseclose, who suggested that the dorsal surface of the distal phalanx provided a good option for investigation of sympathetically associated vasomotor (neurovascular) reactions [10], the observed poststimulatory thermal reactions and MI dynamics on the dorsal surface of the distal phalanx were, most probably, associated with the reactivity of arteries and arterioles. In contrast to true arteriolovenulos anastomoses, whose hemodynamic significance in this skin area is low, arterioles respond well to reactive hyperemia. The changes in the bypass index may thus depend on thoroughfare channels (metarterioles).

Interestingly, bandaging of other fingers of the same subject (subject I, fingers III and IV) caused changes in MI dynamics and temperature that were slightly different from the reactions observed for the second finger, which suggests that there is a variation in the reactivity of resistive arteries and arterioles in the microvascular bed of different fingers of the same individual.

Experiments that analyzed simultaneously the thermal responses on the dorsal and the palmar sides of the distal phalanx to the same occlusion test showed that the blood flow was regulated in a basically the same manner (Fig. 5). The similarity of temperature reactions on the dorsal and the palmar side of the hand was probably related to the fact that arteries and arterioles in these skin regions show similar reactivity to known regulatory factors [6].

It was found that the baseline temperature affected the degree of temperature decrease by the end of the

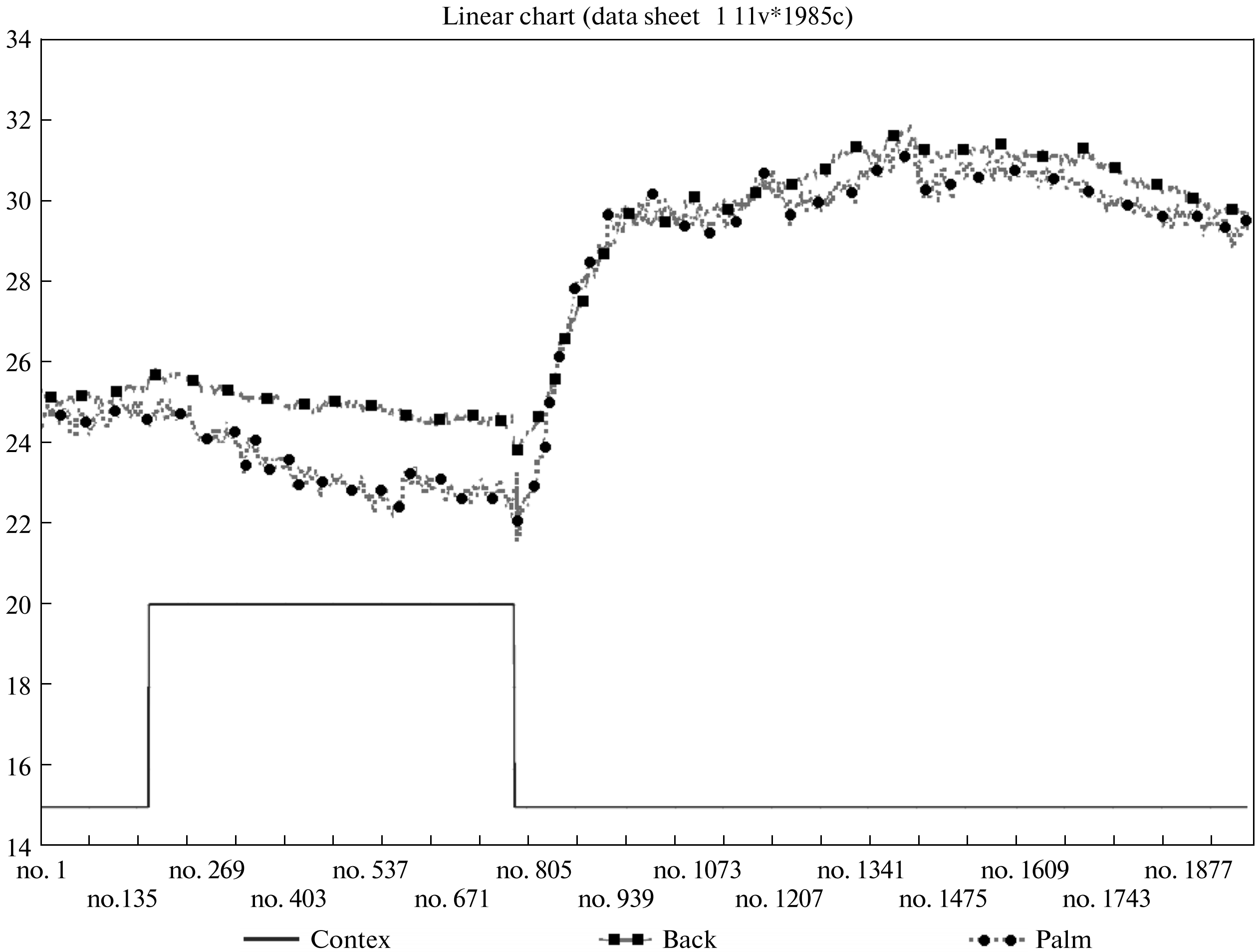

Fig. 5. Temperature dynamics on the dorsal (squares) and palmar (circles) sides of the distal phalanx of the second finger during the three stages of an experiment involving a 10-min-long arteriovenous occlusion (background, occlusion, recovery). *X* axis, image numbers (data recorded with a frequency of 1 Hz); *Y* axis, temperature, °C. Stages of the experiment are marked below.

test: the higher the initial temperature, the stronger its decrease in absolute numbers. This result agrees with the microcirculation data obtained by LDF using a basic heating model that analyzed the changes in the fingertip temperature in the course of arterial occlusion and subsequent reperfusion (hyperemia) [11].

The fact that the degree of temperature drop in the distal phalanx of the stimulated finger depended on its initial temperature is worth a more detailed analysis. For instance, in the experiments where the temperature was recorded simultaneously on both finger surfaces, low initial temperatures (19–20°C) were associated with a delayed recovery reaction. A possible explanation is that the active recovery mechanisms are affected by the current functional condition of the system regulating the peripheral circulation in each particular experiment. It can also play a role whether a particular occlusion event was the first on the given day or a later one.

The high level of correlation between the IR emission characteristics of the test and the control hand during the recovery stage suggests that systemic response was involved. This symmetry or mirror effect [3] was not a systematic finding and was observed only in some experiments, apparently depending not only on the stimulation as such, but also on some other context factors that still have to be determined. For instance, it has long been known that a thermal stimulation of an extremity (with heat or cold) can induce circulatory changes not only in the symmetrical area, but also in other extremities [12].

The dynamics of thermal reactions changed dramatically between experiments no. 4 and no. 6: the recovery curves were now intersecting; that is, the response dynamics altered, and there were no local correlations (Figs. 4a, 4b), although on the global scale, apparently due to the involvement of systemic regulation, we observed a rapid temperature growth to the maximum in experiments nos. 6–8, which corresponded to occlusions 50, 62, and 86 (Fig. 4c).

The curves shown reflect the absence of significant changes in spatiotemporal characteristics of the temperature response to occlusion from one test to another in early experiments; however, following repeated events, the temperature dynamics on the left hand (the test finger) and the right hand (the control finger) became coordinated. It showed be noted that the occlusion factor was observed to have a significant effect on the temperature as early as in the beginning of the test on the left but not on the right hand.

Analysis of temperature dynamics of different occlusion periods showed that its stages were well reproduced and confirmed the significance of the changes in its spatial and temporal characteristics by post-hoc Fisher's LSD test. The duration of occlusion had a nonsignificant effect on the control hand.

Obviously, clamping induces blood redistribution in hand vessels and thus disrupts the normal proximal–distal temperature gradient. Therefore, it is probably unnecessary to perform a long series of arteriovenous occlusions, as it was done in our experiments, to achieve the desired effect of altering the mode of intradermal blood flow regulation in the functionally loaded extremity segment. Based on these considerations, we expect that the method could be adapted for clinical purposes implying a sufficiently rapid response.

Thus, all occlusion experiments induced uniform reactions involving an increase in the baseline temperature, which suggests consistent triggering of the same regulatory mechanisms. The fact that the same pattern was reproduced after 15-, 20-, and 30-min-long occlusions further supports this notion.

Subsequent tests performed after 1–3 weeks to 1.5 months after the series of periodic bandaging was terminated showed that, although the stimulation was discontinued, the mechanisms that it had triggered were still functioning; at the same time, the characteristics of the temperature curve gradually reversed to the pre-experimental pattern. Apart from that, it was found that the thermal map characterizing the recovery stage altered between the beginning and the end of the occlusion series: in particular, the venous pattern on the dorsal surface of the experimental hand became more contrasting. This may indicate either potential morphoanatomical changes (e.g., formation of new bypasses or induction of reserve drainage pathways), or faster venous drainage. This phenomenon requires further investigation by methods directly assessing the blood flow characteristics, such as photoplethysmography and, probably, angiography before the beginning and at the end of an occlusion series. Analysis of thermal maps by mean of techniques conventionally used for video images [13] did not identify any significant alterations in the pattern of dorsal hand veins that could be indicative of underlying anatomical rather than functional changes.

In spite of the complexity of the spatiotemporal structure of the thermal response, the behavior of these areas at the stage of recovery after tourniquet removal suggests that the spatiotemporal characteristics of temperature maps can be an efficient means of monitoring changes in the vascular bed that serve for the blood flow and drainage in the functionally loaded segment.

The repeated occlusion test with varying exposure periods used as a model of provocative stimulation of the distal segment of extremity microcirculation can be compared to other models, e.g., the one proposed in [14], where cold adaptation was studied using repeated unilateral cold applications. Apparently, a long series of repeated arteriovenous occlusions can induce systematic changes in the modes of regulation of both the microcirculation, and the arterial and venous flow, which is reflected in the temperature dynamics and thermal reactions of the involved skin regions. The triggering of a regulatory circuit modulating the intradermal blood flow naturally broadens the adaptive response repertoire of the system.

CONCLUSIONS

The dynamics of local skin temperature following repeated local arteriovenous occlusions reflects the adaptive and compensatory response of the system regulating the peripheral circulation. Using the techniques of thermal imaging and laser Doppler flowmetry, it was possible to investigate the relationship between the structure of temperature patterns and the microcirculation dynamics with high spatial, temporal, and amplitude resolutions. It was demonstrated that multiple periodic unilateral arteriovenous occlusions induced an increase in the intradermal blood flow, and thus can be applied in clinical practice along with other methods used to prevent peripheral microcirculation disorders associated with different pathological conditions. Obviously, further research in this direction should involve a broader range of contexts, including variation of stimulation characteristics (the frequency and duration of occlusion events) and stimulated sites (different fingers and toes, as well as distant limb segments and their combinations), and extending the list of functional and morphoanatomical parameters analyzed for potential effects of the stimulus.

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