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Effects of local forearm skin heating on skin properties

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Abstract

This study investigated impacts of local skin heating on skin properties and tested whether skin changes depended on heat-induced hyperaemia. It was reasoned that heat-induced vasodilation impacts accompanying interstitial fluid changes. Forearm skin was locally heated from a baseline of 35°C to 40–42°C in 30 young adults (15 females, 15 males, 24.9 ± 2.1 years) and non-heated in 10 others (5 females, 5 males, 25.2 ± 1.3 years. Skin blood flow (SBF) was continuously measured using a laser Doppler method and skin tissue dielectric constant (TDC), stratum corneum capacitance (SCC) and transepidermal water loss (TEWL) were measured before and after maintained heat for 12 min. TDC values were determined to effective measurement depths of 1.5 mm (TDC15) and 2.5 mm (TDC25). Results showed a large heat-induced hyperaemia, with SBF increasing on average 8.8-fold from its baseline of 35°C. Heating also caused significant increases in TDC, SCC and TEWL that, compared to preheating, increased approximately 1.1-fold, 3.1-fold and 4.5-fold. None of these skin changes correlated with the magnitude of the SBF hyperaemic response. Absence of this correlation may indicate that in young healthy adults, increased capillary filtration due to heat-induced arteriolar vasodilation is rapidly accommodated by postcapillary reabsorption, enhanced lymphatic activity and TEWL processes. An alternate explanation is that heating caused increased red cell oscillations that were detected as part of the laser Doppler increase without representing increased capillary flux. The major determinant of the Increases in TDC, SCC and TEWL is likely a consequence of heat-induced eccrine gland activation. Studies of older persons or those with depressed function are warranted.

KEYWORDS

eccrine glands, skin heating, skin water, stratum corneum water, sweat, TDC, TEWL, tissue dielectric constant

1 | INTRODUCTION

Skin water content and distribution are determinants of skin physiology with increased values potentially heralding oedema and low values contributing to skin integrity reductions. Skin interstitial water depends on capillary-to-tissue filtration versus lymphatic function. Filtration depends on the precapillary vasodilatory state in which increased vasodilation is expected to increase filtration due to greater intravascular capillary pressure. Local skin heating impacts skin's precapillary vasculature causing a temperature-dependent increase in arteriolar diameter, capillary blood pressure and blood flow. Such heat-induced changes are expected to increase capillary-to-tissue filtration causing at least a transient increase in skin tissue water content. If reabsorption or lymphatic function is impaired, the duration of skin water changes may increase. In addition to capillary pressure-related changes, there is also evidence that heat-induced

hyperaemia has a nitric oxide (NO) component that impacts vascular permeability to water (Kellogg 2006). Although many studies have examined the impact of local skin heating on local skin blood flow (Alekseev, et al. 2005; Freccero, et al. 2003; Kurvers, et al. 1995; Mayrovitz & Leedham 2001; Mayrovitz & Regan 1993; Nagasaka, et al. 1987), none have investigated local skin heating impacts on skin tissue properties directly. The research goal was to study the impact of local skin heating on non-invasive measures of skin properties and to test the hypothesis that skin properties that are sensitive to tissue water depend on the heat-induced hyperaemia magnitude. To accomplish this, local forearm skin was heated for 12 min with measurements made before and after heating. These measurements were skin temperature (TSK), skin tissue dielectric constant (TDC) as an index of skin water, stratum corneum (SC) capacitance (SCC) as an index of SC water and transepidermal water loss (TEWL) as a measure of skin water loss and skin blood flow (SBF) assessed using laser Doppler flow monitoring.

2 | METHODS

2.1 | Subjects

Forty young and self-described healthy adults participated after signing an informed consent. Ages (mean ± *SD*) were 24.9 ± 1.6 years (22–29 years) with 20 males (24.8 ± 1.5 years) and 20 females (24.9 ± 1.8 years). Thirty subjects with age of 24.9 ± 2.1 years (15 male and 15 female) experienced the heating protocol (described subsequently) and 10 other subjects with age of 25.2 ± 1.3 years (5 male and 5 female) experienced a sham no-heat control procedure. Participation required that they (a) be ≥21 years, (b) not have any vascular condition, (c) not have a skin condition or open wound on their arm, (d) were not taking medication or substance that could affect skin water or vascular responses and (e) stated that they could lie still for 45 min.

2.2 | Experimental protocol

The measurement site was the dominant anterior forearm, five cm distal to the antecubital fossa (target site), with the subject supine with arms resting comfortably at their sides. The target site was marked with a surgical pen. Skin water-related measurements consisted of the following: skin temperature (TSK) measured with an infrared thermometer (Figure 1a); stratum corneum capacitance (SCC) measured with a Moisture Meter SC-2 (Delfin, Kuopio, Finland, Figure 1b); tissue dielectric constant (TDC) measured to depths of 1.5 mm (TDC15) and 2.5 mm (TDC25) with the Moisture Meter-D system, (Delfin, Figure 1c) and transepidermal water loss (TEWL) measured with the Vapometer closed chamber device (Delfin, Figure 1d). Measurements were made by

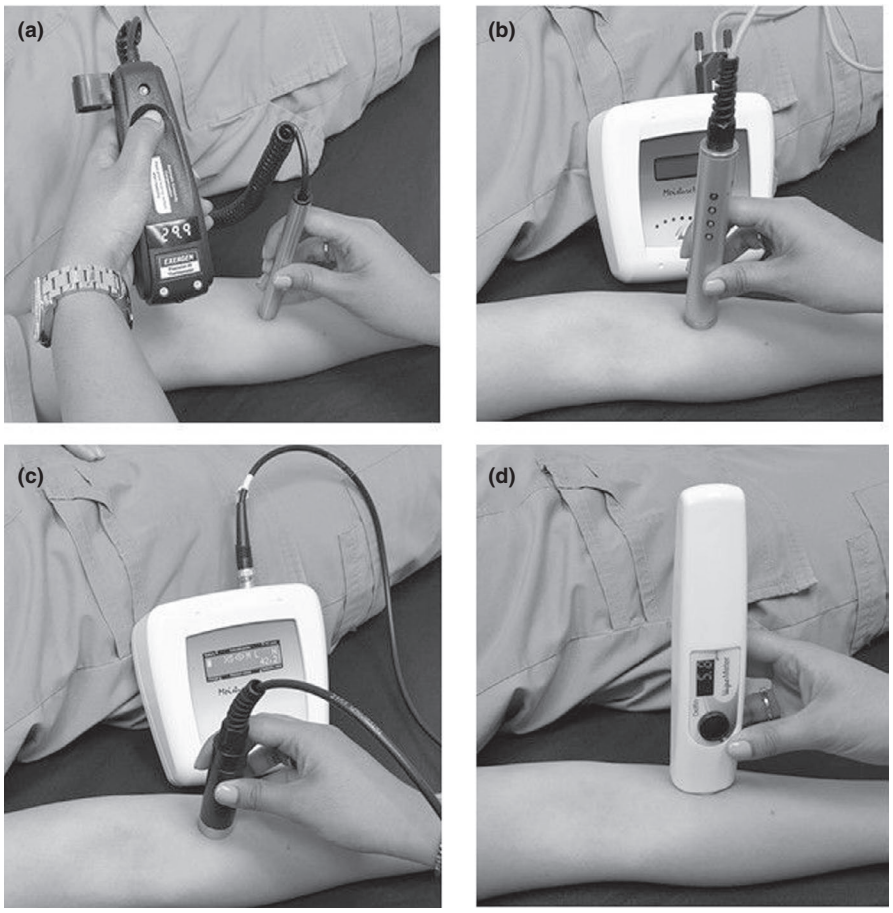

FIGURE 1 Forearm Skin Property Measurements. (a) Skin temperature measured with an infrared thermometer, (b) stratum corneum capacitance measured with a Moisture Meter SC-2 device, (c) tissue dielectric constant measured with the Moisture Meter-D system, (d) transepidermal water loss measured with the Vapometer closed chamber device

placing a probe on the skin with gentle pressure for 10 s or less. Before local heating, six sets of measurements were made in the sequential order TSK, SCC, TDC15, TDC25 and TEWL with 2 min between data sets yielding a baseline skin data set of 12 min. After these baseline measurements, a 2 mm diameter thin laser Doppler probe was passed through a concentric hole in a 20 mm diameter aluminium heater and the combination affixed to the forearm with tape at the target site (Figure 2a). The other end of the laser probe was connected to a blood perfusion monitor to record SBF in arbitrary units. While recording SBF, the heater temperature was gradually raised to 35°C and held at this temperature for 4 min. The average SBF recorded during this interval was taken as the starting SBF $[SBF_{AVG}]_{START}$. Heater temperature was then raised in one degree steps over an interval of 90–120 s until a heater surface target temperature of 42°C was recorded (Figure 2b). This temperature was maintained for 12 min in the heated group ($n = 30$). For the control group ($n = 10$), a sham heating procedure was used that was the same as the heated group except no heating. Average SBF during the last 4-min of heating was determined and denoted as $[SBF_{AVG}]_{END.}$ After the 12-min heating interval, the laser Doppler probe and heater assembly were rapidly removed and the prior measurement sequence set was done in the same order as before. A total of 10 measurement sets were obtained for a postheating interval of 20 min.

2.3 | Measurement device details and principles

2.3.1 | Tissue dielectric constant (TDC)

Tissue dielectric constant was measured at 300 MHz using the open-ended coaxial line method (Aimoto & Matsumoto 1996; Alanen et al., 1998a; Athey, et al. 1982). The TDC value is the ratio of tissue permittivity to that of a vacuum and is dimensionless. A cylindrical coaxial probe contacts the skin (Figure 1c) and is connected to a control unit that displays the TDC value. The physics and validity of this method are well described (Alanen, et al. 1998b Nuutinen, et al. 2004; Stuchly, et al. 1981). A 300 MHz signal generated within the control unit is transmitted to tissue via the probe. The portion of the incident signal reflected depends on tissue dielectric constant that depends on the amount of free and bound water in the tissue volume through which the signal passes. Reflected information is processed in the control unit and the TDC value displayed. For reference, pure water has a dielectric constant value of 76 at 32°C (Gabriel, et al. 1996). Measurement depth depends on probe dimensions with larger diameter probes having greater penetration depths. Probes can measure to effective depths of 0.5, 1.5, 2.5 and 5.0 mm and have been used extensively to assess skin tissue water (1955; Mayrovitz, et al. 2008; Mayrovitz, et al. 2009; Mayrovitz, et al. 2013). In this study, only the 1.5 mm and 2.5 mm depth probes were used so as to include epidermis and dermis with the 1.5 mm probe and epidermis to hypodermis with the 2.5 mm depth probe.

2.3.2 | Stratum corneum capacitance (SCC)

Stratum corneum capacitance measurements (Alanen, et al. 2004) determine stratum corneum capacitance as a stratum corneum hydration index in arbitrary units (au). Effective capacitor plates are formed by the conducting probe in contact with skin (Figure 1b) and well-conducting epidermal–dermal skin layers. The relatively dry and low-conducting SC tissue forms the dielectric constant of the capacitor, the capacitance of which is measured at a frequency of

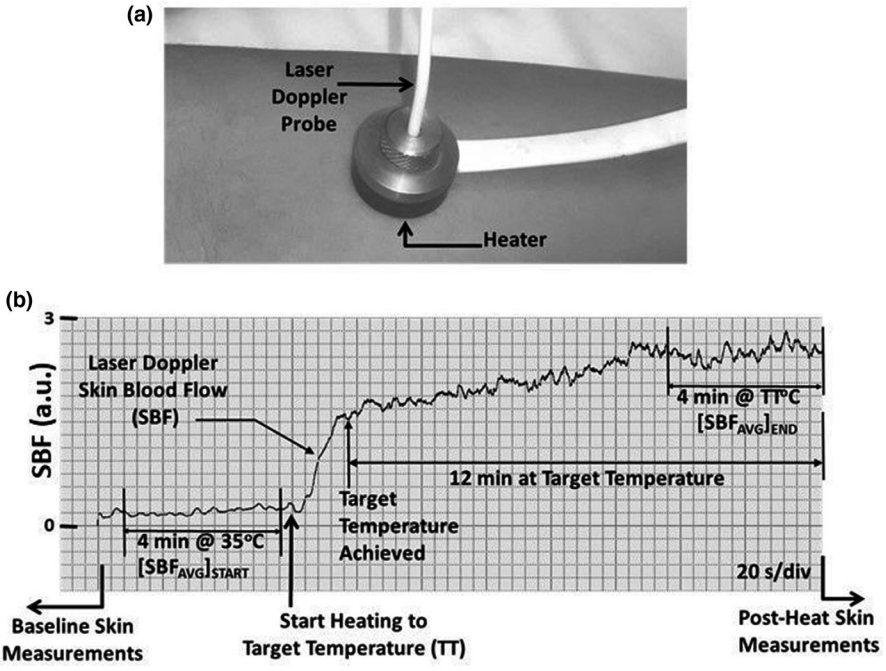

FIGURE 2 Laser Doppler Positioning and Skin Blood Flow Response. In (a) a laser Doppler probe is inserted through a hole in the skin heater and affixed to the forearm target site. In (b) is shown a typical skin blood flow (SBF) response in arbitrary units (a.u.) TT is the target temperature for the heater (42°C)

1.25 MHz. Capacitance measurements for this device provide SC information to a depth up to 45 μm (Clarys, et al. 2012).

2.3.3 | Transepidermal water loss (TEWL)

Transepidermal water loss measurements (Nuutinen, et al. 2003) determine water loss rate by collecting water efflux during a 10-s interval with a closed chamber method. Placing the device against skin (Figure 1d) seals the chamber, so measurements are refractory to ambient airflow. The chamber houses a sensitive humidity sensor that monitors the increase of relative humidity (RH) inside the chamber during the measurement. Water efflux rate (g/m^2 h) is automatically calculated from the RH increase. The chamber is passively ventilated between measurements. Repeated measurements show no significant menstrual cycle effect on TEWL measured on the volar forearm (Berardesca, et al. 1996) using an occlusion test (Berardesca, et al. 1993). It is unknown whether the phase of the menstrual cycle has an impact on heat-induced changes in TEWL.

2.3.4 | Skin blood flow (SBF)

Skin blood flow was measured via laser Doppler using the Vasamedics BPM^2 Blood Perfusion monitor. Output was captured via an analog to digital converter at a sampling rate of 100 samples/sec. Skin heating was via the Vasamedics TCM420 Skin-Heating element (Figure 2a). To get simultaneous heating and SBF monitoring, a 2 mm diameter laser Doppler probe (pencil probe) was passed through a concentric hole in the heater to contact skin. SBF was measured prior to and during a 12-min heating interval. The heater–laser Doppler probe assembly was secured to skin via a masking tape cover that helped minimize generated heat escape into the environment.

2.4 | Analysis

Tests for differences between preheat and postheat parameter values were done using the non-parametric Wilcoxon test, and tests for possible differences in parameter values between genders were done based on the non-parametric Mann–Whitney test. In both, a p-value of 0.05 was assumed to represent statistical significance. Statistical analyses were done using SPSS V16. The hyperaemic response of SBF to local skin heating was calculated as the ratio $[SBF_{AVG}]_{END}/\ [SBF_{AVG}]_{START}$ and referred to as SBF_R. Changes in skin properties as measured by TDC, SCC and TEWL were calculated as ratios of their peak values as measured immediately after heat removal to their preheating value. These ratios are expressed as TDC_{R15}, $TDCR_{25}$ SCC_R and $TEWL_R$. A correlational analysis was done to determine whether any skin property parameter change was related to the SBF hyperaemia magnitude (SBF_R).

3 | RESULTS

3.1 | Skin temperatures

Preheat skin temperatures (mean ± *SD*) were 29.4 ± 1.1 and 29.4 ± 1.4°C for heat and sham groups, respectively. For shams, simple covering of skin for the simulated heating duration caused a temperature increase measured immediately after uncovering (31.5 ± 0.65°C) with an average temperature rise of near 2°C. Contrastingly, the immediate uncovered skin temperature after heating was 39.5 ± 1.9°C with a temporal pattern shown in Figure 3. Postheating skin temperature measurements made every two minutes showed that for the heated group the temperature remained elevated as compared to the preheat level throughout the follow-up postheat 20-min interval ($p < .05$). For shams, the small temperature rise measured immediately after uncovering was followed by a fall in skin temperature to a level slightly below baseline for about 5 min and then became statistically insignificantly different from baseline.

3.2 | Skin blood flow (SBF)

The pattern of SBF responses to local heating was as indicated in Figure 2b. For subjects heated, the 4-min average SBF ($SBF_{AVG}]_{START}$) was 0.338 ± 0.139 for those heated. SBF of males tended to be greater than females (0.383 ± 0.132 versus. 0.294 ± 0.136, $p = .049$). The 4-min average SBF at the end of heating ($[SBF_{AVG}]_{END}$) was similar for males and females (2.59 ± 0.91 versus 2.69 ± 0.67, $p = .439$). SBF hyperaemia: $SBF_R = [SBF_{AVG}]_{END}/\ [SBF_{AVG}]_{START}$, was greater for males than females (7.2 ± 26 versus. 10.4 ± 3.8, $p = .01$) due mainly to a lower $[SBF_{AVG}]_{START}$.

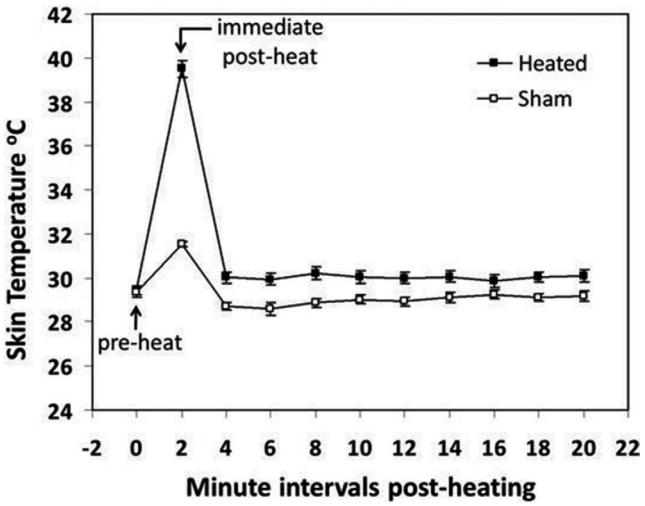

FIGURE 3 Skin temperatures postheating. Data points are mean ± *SD*. Preheat value shown at 0-min. Other values are minutes postheat. The sham group was covered by the heater assembly but the heater was kept off. Preheat skin temperature values did not differ between heated versus. sham. After heater removal, the immediate postheat skin temperature was 39.5 ± 1.9°C with temperatures remaining greater than preheat during the entire postheat duration ($p < .05$)

SBF_R values ranged from 3.4 to 18.2 with a mean of 8.8 ± 3.6. Correlation analysis among SBF_R and the skin related parameters (TDC_R, SCC_R and $TEWL_R$) revealed no significant SBF_R dependency. Associated Pearson correlation coefficients between TDC_{R15}, $TDCR_{25}$, SCC_R and $TEWL_R$ were very low and were, respectively, −0.06, −0.23, 0.01 and 0.07.

3.3 | Tissue dielectric constant (TDC) values

Preheat TDC values (mean ± *SD*) at 1.5 mm depth (TDC15) did not differ between heated and sham (30.5 ± 3.1 versus. 29.2 ± 2.7, $p = .240$) nor did TDC preheat values at 2.5 mm (TDC25) differ between heated and sham groups (27.7 ± 3.4 versus. 27.4 ± 3.9, $p = .842$). Immediately postheating, TDC15 increased compared to baseline ($p < .001$). Its maximum value was 33.2 ± 3.9 (Figure 4a) representing a 1.09-fold increase from preheat. TDC15 remained greater than baseline for the duration of postheating follow-up ($p < .001$). Sham TDC15 values were insignificantly different than baseline for all measurements. Postheated TDC15 was greater than sham until 18 min postheating ($p < .05$). TDC25 increased to 30.3 ± 3.5 (a 1.09-fold increase from preheat) and remained above baseline for the 20-min follow-up (Figure 4b). Contrastingly, TDC25 values measured after sham removal were insignificantly different from baseline for all follow-up measurements.

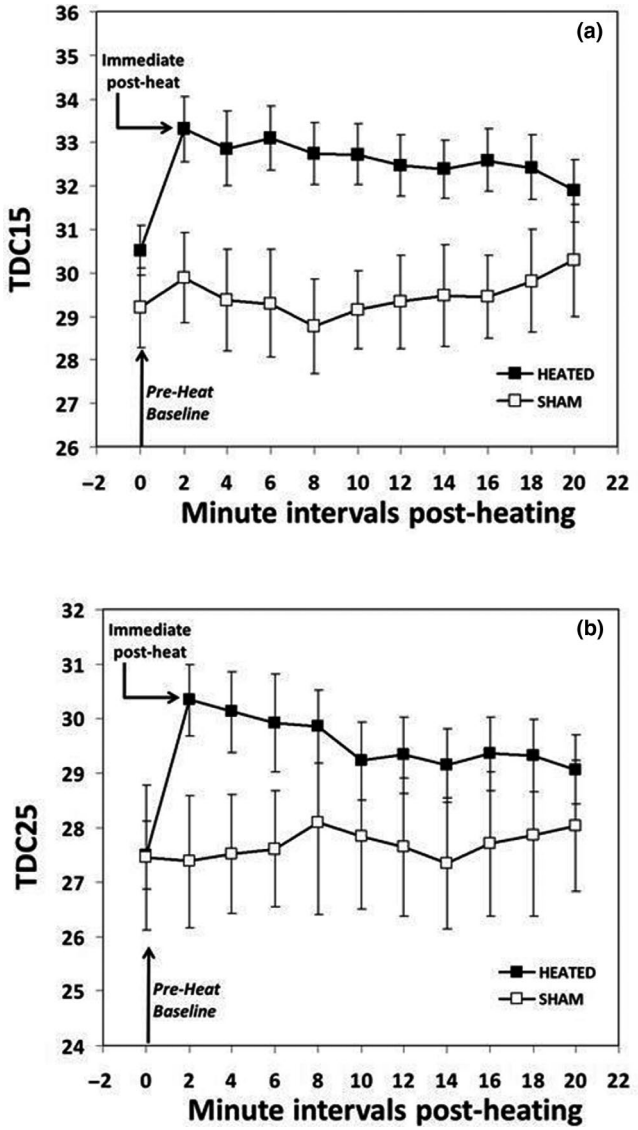

FIGURE 4 Tissue Dielectric Constant (TDC) Pre- and Postheating. Data points are mean ± *SD*. Preheat value shown at 0 min. Other values are minutes postheat. TDC15 (a) and TDC25 (b) show and immediate postheat value greater than preheat ($p < .001$) that remained greater for the duration of the postheat follow-up. Contrastingly, sham TDC values were insignificantly different than preheat for all follow-up measurements. Postheat TDC15 values were greater than sham for 18 min postheating ($p < .05$). Postheat TDC25 values were greater than sham for 6 min postheating

3.4 | Stratum corneum capacitance (SCC)

Preheat SCC values did not differ between heated versus. sham groups (20.6 ± 5.5 versus. 20.1 ± 7.1, $p = .800$). Immediately postheating, SCC was increased compared to preheat ($p < .001$) achieving a maximum value of 63.6 ± 17.7 (a 3.09-fold increase from preheat). As shown in Figure 5a, SCC remained greater than baseline for the duration of postheating follow-up ($p < .001$). Sham SCC values were also greater than preheat for all postheat ($p < .05$), but all postheat SCC values were significantly greater than corresponding sham values ($p < .01$).

3.5 | Transepidermal water loss (TEWL)

Preheat TEWL values did not differ between heated versus. sham (8.8 ± 1.8 versus. 9.2 ± 3.4, $p = .620$). Immediately postheating, TEWL was increased versus preheat ($p < .001$) with a maximum value of 39.6 ± 23.4 g/m^{2}h (a 4.5-fold increase, Figure 5b). TEWL remained greater than preheat during postheating ($p < .001$). Sham TEWL was statistically greater than preheat after uncovering ($p < .05$) with a peak value of 10.8 ± 5.5 g/m^{2}h. Postheat TEWL was greater than corresponding sham values up until 18 min postheating ($p < .05$).

4 | DISCUSSION

4.1 | Skin heating

The target temperature as measured on the heater in contact with the skin was set at 42°C. This target temperature was chosen for several reasons: it has been a widely used heat provocation target temperature (Pergola, et al. 1993); some data suggest that even short-term elevations of skin temperature to this level promotes enhanced transdermal drug delivery (Oliveira, et al. 2014) and it is the threshold for activation of transient receptor potential TRPV1 that affect epidermal permeability (Denda, et al. 2007). Although the temperature of the heating element is maintained at a given

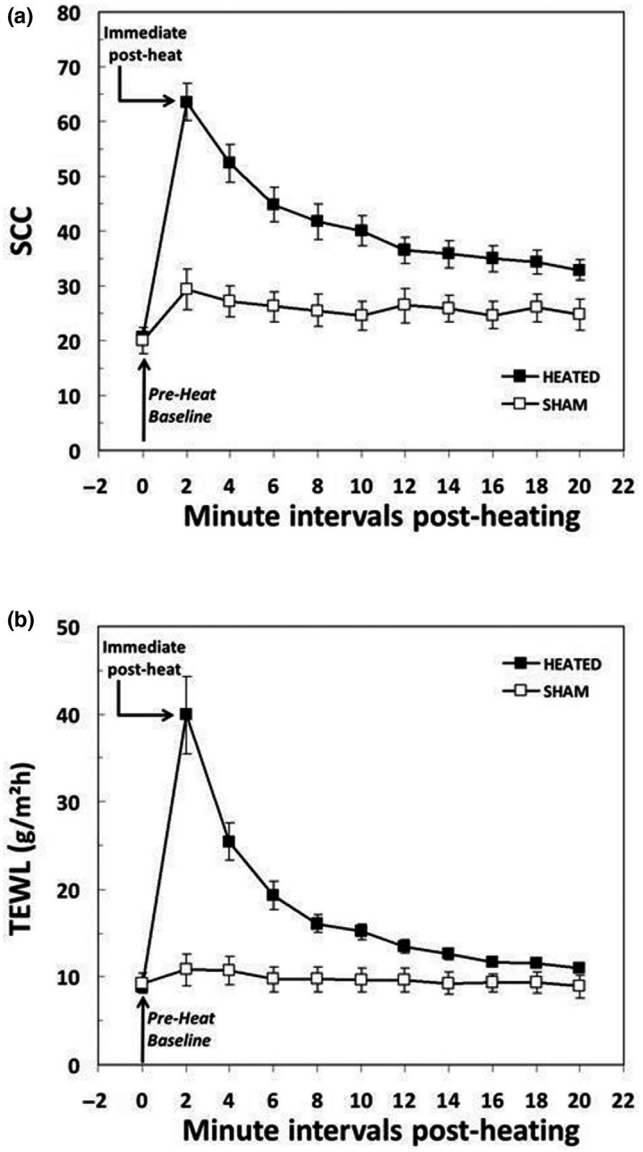

FIGURE 5 SCC and TEWL pre- and postheating. Data points are mean ± *SD*. Preheat value shown at 0 min. Other values are minutes postheat. Stratum corneum capacitance, SCC (a) and transepidermal water loss, TEWL (b) show an immediate postheat value greater than preheat ($p < .001$) that remained greater for the duration of the postheat follow-up ($p < .001$). Sham SCC values were also greater than baseline for all follow-up measurements ($p < .05$) but all postheated SCC values were significantly greater than corresponding sham values ($p < .01$). Sham TEWL values were statistically greater than baseline only immediately after uncovering ($p < .05$) but were otherwise statistically insignificantly different from baseline. Postheated TEWL values were significantly greater than corresponding sham values up until 18 min postheating ($p < .05$)

temperature, the temperature of the underlying skin may differ as a consequence of heat conduction to tissue (Cetingul & Herman 2010) and heat changes associated with skin blood flow changes (Petrofsky, et al. 2011). In the present case, immediately after removal of the heater the average skin temperature recorded was 39.5°C. This is the approximate skin temperature at which axon reflex vasodilation has been elicited (Magerl & Treede 1996). This measured value is less than the heater setting partly due to the fact that even though skin temperature was taken immediately after covering removal, there was an exposure to room environmental conditions that tends to affect skin temperature based on room temperature and relative moisture content (Igaki, et al. 2014). Based on the present postheat measurement, we would judge that average skin temperature during the 12-min heating interval was between 40°C and 42°C.

4.2 | Skin blood flow (SBF) changes

Average SBF hyperaemic changes (SBF_R) in response to local skin heating were 7.2 and 10.4 depending on gender with an overall average of 8.8 ± 3.6. These values are similar to those reported by others. For example, hand skin heating resulted in SBF increases of 6.6–8.0 times that were increases similar to those obtained by sodium nitroprusside iontophoresis (Saumet, et al. 1998). Some workers have reported an initial peak in SBF followed by a transient decline with a subsequent gentle rise in SBF with continued heating (Kellogg 2006; Tew, et al. 2011; Wong, et al. 2006). This bimodal response was not observed in the present study perhaps due to the slow rate of heating herein used. Rather, as shown in Figure 2b the SBF response had a rapid rise followed by a gradual increase with no clearly observable significant dip in SBF. Despite the substantial elevation in SBF measured at the end of the heating interval, correlational analyses found no significant relationship between SBF_R and any of the skin property-related parameters. This indicates that the initial hypothesis, based on the suspected impact of heat-induced arteriolar vasodilation causing added interstitial fluid, is not supported by the current findings and that the observed changes in TDC, SCC and TEWL are not importantly dependent on the SBF hyperaemia over the range of values herein induced. The lack of correlation is unlikely due to a narrow SBF_R range as the overall variation was quite wide (3.4–18.2). A possible explanation is that in these young healthy persons, added interstitial fluid caused by heat-induced arteriolar vasodilation and increased capillary pressure, is rapidly accommodated by well-functioning postcapillary absorption and lymphatic processes. It is unclear whether a similar result would be obtained in more mature persons in whom age-related declines in lymphatic function may be present.

4.3 | Stratum corneum (SC) moisture changes via SC capacitance (SCC) changes

Under the present protocol, one major SC change associated with local skin heating was a slightly greater than a 3-fold increase in SC moisturization as evidenced by Figure 5a. This finding differs from the reported absence of an SCC increase when arm skin was dry-heated to 40°C for 15 min via infrared lamps (Petrofsky, et al. 2009). However, when moist heating was employed using water saturated towels heated to 40°C, the SC moisture changes were found to increase by

about 44% above preheated values. This is considerably less than the approximate 300% change than was herein observed. The difference could be due to the previous authors' use of overlying towels compared with present experimental procedure in which no absorption material was in contact with the skin during heating. The large increase in postheating SCC is consistent with temperature-dependent increase in sweat gland activity (DiPasquale, et al. 2003). This concept is consistent with recent work in which subjects underwent whole body heating during which TDC measurements were sequentially made on forearm skin (Mayrovitz, et al. 2019). Although the heating protocols used herein and previously were associated with increased SCC values, prior field work measurements done on workers in the fish processing industry reported SCC values to be negatively correlated to naturally occurring work-related skin temperatures (Halkier-Sorensen & Thestrup-Pedersen 1991). The immediate postheat increase in SCC herein found is similar to responses after application of distilled water to forearm skin in sorption–desorption tests (Agache, et al. 2001). In these studies, there was a near 2-fold immediate increase in SCC. Although that response was somewhat less in magnitude and more rapidly normalized, its general temporal similarity to the present result may indicate that part of the observed heating response can be attributed to sweat accumulation during the heating process.

4.4 | Transepidermal water loss (TEWL) changes

Similar to the immediate changes in SCC, the major TEWL change associated with local skin heating was an approximate 4-fold increase in TEWL reflecting an immediate peaking and subsequent maintained increase of outward water flux starting with uncovering the target skin. A similar change pattern in TEWL was reported immediately after removal of 100 µl of water that had been on anterior forearm skin for 60 s (Agache, et al. 2001). This similarity in responses may again suggest that part of the observed heating response can be attributed to sweat accumulation during the heating process.

5 | CONCLUSION

Local skin heating for 12 min induced large increases in skin blood flow (8.8-fold) and in skin properties as indexed by changes in TDC, SCC and TEWL but no skin property change correlated with skin blood flow changes. The absence of this correlation may indicate that in young healthy adults as herein studied, increased capillary filtration due to heat-induced arteriolar vasodilation is rapidly accommodated by postcapillary reabsorption, enhanced lymphatic activity and TEWL processes. An alternate explanation is that heating caused increased red cell oscillations that were detected as part of the laser Doppler increase without representing increased capillary flux. The major determinant of the Increases in TDC, SCC and TEWL is likely a consequence of heat-induced activation of eccrine glands. It is unknown whether similar findings would be present in more mature or elderly persons or in persons in whom such functions were depressed. Research incorporating such persons represents a natural continuation of the present investigation.

CONFLICT OF INTEREST

The author has no conflict of interest.

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