Experimental Dermatology

Research Articles

Role of basal sweating in maintaining skin hydration in the finger: a long-standing paradox in dry skin resolved

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Short title: The role of basal sweating in the finger
Abstract word count:233/250
Manuscript word count: 4354/5000

References: 28/120
Figures: 4/4
Tables: 0/2
E-supplements: 5

ACKNOWLEDGEMENTS

We are grateful to Ms. Nana Kojima and Ms. Riko Kondo, a medical student in Kawasaki Medical School for supporting the experiments.

This study was funded by a research grant from Kawasaki Medical School. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest Disclosures: The authors have no conflicts of interest to declare.

IRB approval status: The study was approved by the Institutional Review Board of Kawasaki Medical School, and all participants provided written informed consent (3834, 5468, 5706).

AUTHOR CONTRIBUTIONS

T.Sato, Y. Hayashida, C. Katayama and Y.Asanuma carried out the experiments and collected the data. T.Sato and Y.Aoyama performed the statistical analysis and drafted the manuscript. Y.Aoyama contributed to the conception and design of the work. All authors have read and approved the final manuscript.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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ABSTRACT

A long-standing paradox in dermatology is why skin dehydration in the fingers can be triggered by repeated water exposure despite the action of water to hydrate skin tissue. Potential clues might be provided by identifying a mechanism through which water is held in the skin of the fingers. We speculated that this mechanism would be impaired after repeated water exposure. Here, we investigated whether there might be glabrous skin-specific water-holding machinery and whether this machinery might be impaired in dry skin/hand eczema. We examined this by using an impression-mold technique, allowing for an accurate quantification of sweat gland/duct activity and optical coherence tomography. Unlike in hairy skin, sweat pores were rarely detected at the folds of the finger at baseline. Surprisingly, after water exposure, sweat pores at the folds opened and those at the ridges closed in healthy controls (HCs). Sweating in the dermal folds of the hands correlated with skin hydration, and decreased in dry skin/hand eczema, suggesting that its impairment may be one of the causes of dry skin. After repeated water exposure, basal sweating response at the folds was exhausted in patients with dry skin/hand eczema as well as HCs. This exhaustion was rescued by exposing individuals to high humidity. Basal sweating defects would be a target for dry skin/hand eczema. Maintaining basal sweating responses in the finger is the best preventive measures in achieving prevention of dry skin/hand eczema.

Key words: sweat, sweating, skin aging

1. INTRODUCTION

Conventional thinking in the field of dermatology emphasizes the importance of genetic defects in the barrier function of the stratum corneum (SC),[1] while ignoring the great capacity of sweat to increase skin surface hydration (SSH). Even among dermatologists, the importance of preserving sweating function remains an under-recognized topic.[2] Although sweat allows the outermost layers of the SC to retain moisture, thereby protecting it against the desiccating action of the environment, research on the role of sweat in hydration of the SC and testing of potential therapeutic agents have been hampered by the paucity of measurement tools for accurately quantifying sweating responses. To address this issue, Shimoda-Komatsu et al. have established a novel impression-mold technique (IMT), which allows for an accurate quantification of individual sweat gland/duct activity in terms of sweat secreted in a well-defined location and the volume of sweat.[3,4] Using IMT, we demonstrated that a minute amount of sweat is secreted from the sweat pores in the skin folds under resting conditions (basal or insensible sweating), whereas increased levels of sweat can be secreted from the pores at the dermal ridges upon thermal stimulus (inducible or sensible sweating) in hairy skin such as that of the forearm.[5] In contrast, in glabrous skin such as that of the finger, palm, and sole, the sweat pores open at the dermal ridges but not at the folds.[6] Based on these results, the literature suggests that localization of sweat pores relative to skin folds and ridges differs depending on the anatomical site.[6] These suggestions have been frequently misinterpreted as a total absence of eccrine glands/ducts at the folds of the palm and sole; however, no information is available about whether sweat pores exist at the folds in glabrous skin. Thus, the critical, unresolved question is why sweat pores are not detected at the folds in glabrous skin but are abundantly detected at the folds under quiescent resting conditions in hairy skin. We consider that the major function of sweat glands/ducts at the folds is to maintain SSH, whereas that at the ridges is to regulate skin temperature.[3,5] Thus, the inability to detect sweat pores at the folds in glabrous skin is difficult to reconcile unless glabrous skin uses alternative mechanisms to maintain hydration in the SC independent of basal sweating at sweat pores in the folds.

A high level of water exposure has been suggested to predispose individuals to develop hand eczema through a higher risk of skin barrier damage,[7] suggesting that water exposure triggers skin dehydration. There have been clear inverse dose-response relationships for the association between wet work exposure and healing and improvement of hand eczema in the literature.[8] Thus, water exposure appears to represent a paradoxical effect on skin hydration in view of the action of water to help hydrate skin tissue. This paradox could be reconciled only by assuming that glabrous skin-specific water-holding machinery, although not detected before our experiment yet, would exist and be gradually disturbed after water exposure. Keeping these considerations in mind and building on our previous observations, we hypothesized that basal sweating from sweat pores at the folds of glabrous skin is induced upon contact with exogenous water and that this basal sweating plays a major role in retaining water in the SC under conditions of excessive water exposure. To test this hypothesis, we investigated basal sweating responses after water exposure in healthy volunteers and in patients with dry skin/hand eczema. Our results revealed that basal sweating from sweat pores at the folds was triggered by water exposure and that this activity decreased gradually with age and decreased profoundly in those with dry skin/hand eczema. Given that hydration from water exposure evaporates quickly and dries the skin, our observation suggests that sweating responses from the fold after water exposure restores the dryness of stratum corneum.

2. METHODS/MATERIALS

2.1 Participants

Participants were 55 healthy volunteers (6 males, 49 females; mean ± SD age, 36.9 ± 15.5 years; range, 1–57 years) and 12 patients with dry skin/hand eczema (5 males, 7 females; mean age ± SD, 30.6 ± 6.5 years; range, 21–42 years). The mean ± SD Hand Eczema Severity Index (HECSI) score of patients with dry skin / hand eczema in this study was 9.1 ±7.9 (Supplemental Figure S1b,c); because previous study presented cutoff values for mild (0-11poinnts), moderate (12-27) and severe (≥ 28 points) disease in HECSI score,[9] patients enrolled in this study were considered to have a mild disease. They were asked to minimize the use of moisturizers and topical corticosteroids. The investigators excluded individuals with serious medical conditions or with hyperhidrosis due to mental stress. The study was approved by the Institutional Review Board of Kawasaki Medical School, and all participants provided written informed consent (3834, 5468, 5706).

2.2 Measurement of sweating responses by IMT

Participants were tested in an air-conditioned room maintained at 20.0°C–24.0˚C and 40%–70% relative humidity (RH) and were allowed to acclimatize to these conditions for at least 20 min before the test. Participants were asked to remain quiet during the test.

Basal sweating responses were evaluated by measuring the IMT.[3] To evaluate basal sweating responses under baseline resting conditions, we used the IMT, which allows for an accurate quantification of sweat gland/duct activity and the volume of sweat secreted. In this method, sweat droplets are visualized as small holes corresponding to the sweat pores (Figure S1a). Silasoft, a silicone material used for IMT, was applied to the skin. As the silicone hardened, it retained the impression of sweat droplets as they emerged from the sweat ducts and pushed up into the mold. IMT measurements were performed simultaneously on two or three different sites, including the ventral forearm, palm, and index finger (Figure S1b).

2.3 Measurement of SSH and frictional force

SSH was determined by using an impedance meter (Skicon-200EX; IBS, Hamamatsu, Japan) to measure the high-frequency conductance of the SC, as previously described.[10] Skin surface frictional force of per unit area was determined by using an frictiometer (FR700MP, Courage+Khazaka, Köln,Germany) , as previously described.[10,11]

2.4 Water exposure

Water exposure was performed by immersing the dominant hand for 10 min in water or a NaCl solution maintained at 22°C or 42°C, respectively (Figure S2a). The hands were dried for up for 10 min in an air-conditioned room maintained at 20.0°C–24.0°C and 40%–70% RH, and the basal sweating response was evaluated by IMT. In the repeated-water exposure experiments, 5-min water exposure was repeated up to 12 times (Figure S2b). In other experiments, participants were tested in an air-conditioned room maintained at 22.0°C–24.0°C and > 80% RH to examine the effect of exposure to high humidity.

2.5 Definition of dry skin/ hand eczema

Patients with dry skin/hand eczema were defined as those having dry skin on both hands. Patients with hand eczema were defined as those having dry skin and an itchy rash on both hands.

2.6 Iodine-starch method

Iodine solution was evenly applied to the skin, and mixture of starch powder and oil was spread after it dried.[12] This method is useful for visualizing sweat pores but has obvious disadvantages, including inadequate sensitivity and consistency as well as spotty definition of separate sweat pores.

2.7 Optical coherent tomography (OCT)

OCT is a recently developed image analysis method involving optical coherence. Although this method is useful for observing the movement of sweat inside the SC and epidermis up to a depth of 1000 μm, the range of vision is very limited. OCT helps to illustrate the sweat duct orthogonally.[13]

2.8 Statistical analysis

All data are expressed as the mean± standard error of the mean (SEM). The statistical analysis determined the significance of the measurement variations obtained under the effect of the tested product. Significance was defined as a p-value of <0.05 for all tests.

3. RESULTS

3.1 Basal sweating before and after water exposure in healthy controls (HCs)

Of the various methods currently used to identify the distribution and number of actively secreting sweat glands/ducts [3,4,12,14,15] this study used three. The degree of sweating was initially determined using the IMT. Sweat pores detected by IMT under quiescent baseline conditions without any stimuli (basal sweating or insensible sweating) were largely distributed in the dermal ridges in glabrous skin (e.g., the fingers and palms), unlike in hairy skin (e.g., the forearms) (Figure 1 a,b, baseline). Only a few sweat pores were detected at the folds in the fingers and palms at baseline, so we wondered whether water exposure might alter the basal sweating response in glabrous skin. Surprisingly, sweat pores at the folds opened and those at the ridges closed immediately after immersion of one hand in 22°C water for 10 min (Figure 1 a,b,d, water exposure; Figure S3). Using the iodine–starch method, the appearance of sweat pores at the folds was also confirmed after emotional stress and water exposure, as shown in Figure 1c and d. Black dots were distributed along the folds in the fingers and palms, a finding never observed before water exposure. However, because visible sweating responses at the folds after water exposure were in part detected using the iodine-starch method but not sensitive enough to detect all of this response, this sweating pattern at the folds detectable using the iodine-starch method was only sufficiently induced by emotional stress. We found that the iodine-starch method has obvious disadvantages, such as inadequate sensitivity and spotty definition of separate sweat gland openings. Thus, individual droplets were only traced for quantification by IMT.

Sweating at the folds after water exposure was also confirmed by 3-dimensional image analysis involving optical coherence tomography (OCT) (Figure 1e). Sweat pores and ducts were histologically confirmed to open at the folds in HE staining (Figure 1f). The appearance of sweat pores at the folds was short-lived and not detected 10 min after drying at room temperature (26°C) at 40%–50% RH.

3.2 Age-related basal sweating responses in HCs

Next, we wondered whether the appearance of sweat pores at the folds after water exposure was dependent on age, given that reduced skin hydration has been documented in aged skin [16]. To test this, we investigated whether sweating from sweat pores at the folds or ridges in the fingers and palm after water exposure decreased with age. As shown in Figure 2a,c, the number of sweat pores at the folds, as determined by the number of sweat droplets after water exposure in the finger, was highest in the age range of 20–30 years, whereas that at the ridge before water exposure was highest in the same age range (Figure 2 b, d). The number of sweat pores at the folds in the finger after water exposure steadily increased until the age of 20 and remained constant thereafter. In contrast, the numbers of sweat pores at the ridges at baseline was highest in full-term neonates and gradually decreased in the palm with age (data not shown). The impaired response from sweat pores at the folds after water exposure combined with a decreased sweating response from sweat pores at the ridges at baseline might be involved in the decreased barrier function of finger skin in older adults. The age-related decrease in the basal sweating response at the folds might also explain the paradoxical dehydration induced by water exposure, which is commonly seen in aged skin. As shown in Figure 2e, a positive correlation was found in HCs between SSH at baseline and the numbers of sweat droplets detected at the folds after water exposure, in contrast with those detected at the ridge at baseline Figure 2f. These results indicated that even under resting conditions, SSH might be largely dependent on the sweating responses at the folds after water exposure. Furthermore, we observed whether the SSH could serve to increase the friction force. As shown in Supplemental Figure S4, the friction force of fingers was moderately associated to the SSH (R=0.52, *P*=0.0076), although the correlation coefficient was not high.

We hypothesized that the decrease in osmolarity (hypoosmolality) at the skin surface occurring after water exposure would induce secretion of sweat from the sweat pores at the folds while the increase in osmolarity (hyperosmolality) does not induce secretion of sweat from those at the folds. To this end, we used hypo- or hypertonic NaCl solution instead of isotonic NaCl solution for inducing sweating responses from pores at the folds. Exposure to isotonic NaCl solution most efficiently induced the appearance of sweat pores at the folds of the fingers and palm, as compared with exposure to hyper- or hypotonic NaCl solution, although the difference was not statistically significant (Figure S5). Exposure to 42°C water induced the appearance of sweat pores at the folds with the same efficiency as did 22°C water, but the number of sweat pores appearing at the folds of the finger after water exposure was slightly lower for water at 42°C than at 22°C, indicating that part of the sweating response at the folds of the finger might be attenuated by thermal stimulus.

3.3 Basal sweating under pathological conditions

Hand eczema is more common in adult women. This phenomenon might be dependent on the appearance of sweat pores at the folds after water exposure, which itself might be a major contributor of the water content in the SC. Although a strong association between hand eczema and skin dryness has been suggested,[17] it remains to be determined which is the cause and which is the result. Therefore, we investigated the basal sweating response at the folds after water exposure in patients with dry skin/hand eczema.

As shown in Figure 3, there were few visible sweat pores at the folds in the fingers and palm of patients with dry skin/hand eczema after water exposure, and there was a significant reduction in the number of sweat pores at the folds after water exposure compared with baseline in HCs (Figure 3a). Sweat droplets at the ridge in hand eczema patients was fewer in number than healthy control at baseline and decreased after single and repeated water exposure significantly (Figure 3b). These results suggest that a profound decrease in basal sweating responses from sweat pores at the folds after water exposure in addition to those at the ridges at baseline might be a predisposing factor in the development of dry skin/hand eczema through the disruption of the skin barrier.

3.4 Basal sweating after repeated exposure to water in HCs and in patients with dry skin/hand eczema

Several occupations with high exposure to water are considered high-risk for developing hand eczema.[18] Therefore, we investigated whether the basal sweating response from sweat pores at the folds is exhausted after repeated water exposure. Water exposure cycles were repeated and sweating responses after each cycle were examined (Figure 3). Being exposed to water for a period of 5 min more than 10 times was found to result in a decrease in the number of sweat pores at the folds after exposure to water in patients with dry skin/hand eczema; this basal sweating response in

HCs was also decreased after repeated water exposure. Such artificially induced reduction in the basal sweating response after water exposure might lead to a reduced perception of finger skin moisture. This decrease was most evident in the fingers but not in the palm and forearm, indicating that the basal sweating response at the folds of the finger is most vulnerable to exhaustion after repeated water exposure.

Finally, we investigated whether increased environmental humidity might preserve the basal sweating response after repeated water exposure. As shown in Figure 4, the significant decrease in the number of sweat pores at the folds after repeated water exposure became obscured at 80% RH.

4. DISCUSSION

In this study, we demonstrated for the first time that sweat pores open at the folds of the finger after water exposure and that few or no visible sweat pores are detectable at baseline. In contrast, sweat pores at the ridges close after water exposure and abundant sweat pores are detectable at the ridges in glabrous skin at baseline. Because previous studies exclusively investigated the response from sweat pores at the ridges of the finger at baseline or after thermal or psychological stimuli,[6] the sweating response at the folds of glabrous skin after water exposure is likely to be overlooked as a contributor to skin hydration. Shimoda-Komatsu et al. and we consider that the major function of sweat glands/ducts at the folds is to maintain skin hydration, whereas that of sweat glands/ducts at the ridges might function as a key thermoregulator.[3] Thus, the critical question is why the fingers do not have a mechanism for maintaining water in the skin, such as the sweat pores at the folds of hairy skin. If it is true that the sweating response from sweat pores at the folds maintains hydration in hairy skin, the sweat pores at the folds in fingers might also play a role in retaining water in the SC after water exposure. Therefore, we consider the basal sweating response at the folds of fingers after water exposure the likely mechanism for preventing rapid evaporation of water from the finger skin; a defect in this response might cause dry skin. Accordingly, an age-related decrease in the basal sweating response at the folds after water exposure would be responsible for the age-related higher prevalence of hand eczema.[19,20]

Hand eczema is more common in the fingers than the palms in adults. Because the number of sweat pores appearing at the folds after water exposure was lowest in the fingers compared with the palms, especially after repeated water exposure, hand eczema is likely to arise in areas with lower basal sweating, although other confounding factors such as frequent washing might also be involved. Decreased basal sweating at the folds after water exposure and that at the ridges at baseline, both of which were demonstrated in this study, might be involved in decreased skin barrier function. Recently, Doi et.al. used an atopic mouse model to demonstrate that maintenance of high water content in the SC via exposure to a high-humidity environment prevented development of hapten-induced chronic contact hypersensitivity [21](unpublished data). Increasing the water content in the SC of these mice also reduced the inflammatory response. Accordingly, we speculated that sweat from sweat pores at the folds is an efficient natural moisturizer that provides protective immunity against various allergens at points of allergen entry.[5] These findings suggest intriguing implications about the use of moisturizers in altering the course of inflammatory dermatoses in the fingers, considering that application of moisturizers has been shown to improve barrier function in human skin.[22]

A surprising finding of the present study was that the sweating response that occurred at the folds only after water exposure was a major contributor to skin hydration in the finger at baseline compared with those occurring at the ridge at baseline. Given the fact that skin hydration prevents allergen entry, sweating responses occurring at the folds of the fingers after water exposure may play an important role in protection against primary allergic sensitization to environmental allergens by providing water in the SC. This suggests that a higher severity of dry skin/hand eczema might be associated with a more seriously impaired basal sweating responses at the folds in the finger. As suggested by Sheehan et al.,[23] cutaneous exposure to environmental allergens through finger skin with basal sweating defects may be associated with the sensitization and development of allergies. This could have major implications for how dry skin/hand eczema should be targeted early in the disease course.

Several questions on hand eczema remain to be resolved, including why the prevalence of hand eczema is particularly high in people who wash their hands frequently as well as why dry skin has been associated with allergies to metals, foods, or drugs. Assuming that the basal sweating response that occurs at the folds after water exposure is essential for maintaining water in the SC after water exposure and that this ability decreases gradually with age, this age-related change might lead to severe dehydration and compromised skin barrier function, thereby enhancing the penetration of allergens. A long-standing paradox is why skin dehydration can be triggered by repeated water exposure in fingers despite the action of water to hydrate skin tissue. We consider that repeated exposure to water exhausts the sweating response at the folds, possibly because sweat from the sweat pores at the folds functions as water-holding machinery in the fingers as well as in hairy skin; when this response is exhausted, water cannot be retained in the SC and the barrier function becomes damaged. A plausible explanation is that when the air becomes drier, water from the skin ridges evaporates more quickly than that in the folds, thereby maintaining water content in the folds rather than that in the ridges. Even when the skin gets hydrated after water exposure and then dried, skin hydration would be maintained mainly by water content in the folds, which is dependent on sweat from sweat pores at the fold after water exposure. Thus, a positive correlation between SSH and sweating responses from the sweat pores at the folds after water exposure was observed (Figure 2e).

Interestingly, in the fingers a decreased basal response from sweat pores at the folds was associated with disruption of the skin surface structure (Figure S1b), a finding frequently observed in the early phase of hand eczema. Decreased basal sweating response at the folds leading to loss of water in the SC would in turn cause the otherwise refractory finger skin to become more fragile and more permissive of allergen entry. Given the central role of the sweat in maintaining skin hydration at points of allergen entry, the preservation of basal sweating at the folds of fingers would be a logical target for clinical situations that disturb such basal sweating, including repeated liquid exposure. Although it was concluded that fingerprints can help to grasp by changing the contact area between objectives and fingers,[24] the friction would greatly change depending on the amount of sweat excreted into the folds. We therefore investigated whether the amount of basal sweating responses from sweat pores at the fold could serve to increase the friction force. As shown in Figure S4, the friction of fingers was proportional to the SSH either at rest or after water exposure, which was dependent on the basal sweating responses from at the ridge and folds, respectively, although the correlation coefficient was not high (Figure S4). These results indicate that basal sweating responses at the folds can provide an optimal amount of moisture in the fold, thereby allowing the fingers to hold objectives, unless the hydration does not exceed a certain value. Thus, humans can regulate their ability to grip objectives by controlling basal sweating responses.

A higher prevalence of hand eczema has been reported in northern parts of Norway than in southern parts of Sweden,[25] and contact dermatitis has been shown to be more prevalent during winter. These findings might indicate an association of low temperature or dry air with hand eczema. The available evidence suggests a detrimental effect of cold and dry environments on the skin, but similar evidence for the role of sweat is lacking. We found that the decrease in basal sweating response at the folds after repeated water exposure was obscured when tests were performed in a high-humidity environment (Figure 4). Risk of flare-ups in patients with dry skin/hand eczema might be reduced by maintaining the basal sweating response at the folds after repeated water exposure in ordinary and humid climates. We consider that the barrier of finger skin might become damaged after repeated water exposure, resulting in loss of the basal sweating response at the folds. This is less likely to be related to disturbances within the SC because the basal sweating response was restored at hairy skin by the repeated application of moisturizers, namely, heparinoids.[10,26]

This study has several limitations. First, for practical and ethical reasons, we recruited only a small number of health care workers as HCs and patients with dry skin/hand eczema, which may not be generalizable to other individuals in high-risk occupations. Second, our subjects were Japanese and there is some evidence of physiological differences in skin by race or pigmentation, including that more darkly pigmented skin has greater barrier resistance, but the evidence is inconclusive.[27,28] Although our study focused on simulating a level of handwashing typical at the community level, more frequent handwashing is likely to lead to greater irritation or dry skin. Future studies focusing on the long-term effectiveness of exposure to high humidity might lead to the development of treatments for dry skin/hand eczema and address the chronic nature of dry skin.

A combination of basal sweating responses at the folds after water exposure and at the ridges at baseline might also explain why the fingers tend to be more sensitive to water exposure compared with the forearm. Clinicians involved in the care of inflammatory skin diseases such as atopic dermatitis and hand eczema, which are characterized by various degrees of skin dryness, need to be aware of the great potential of sweat, especially that secreted by sweat glands/ducts at the folds in glabrous skin, to increase and maintain skin hydration.[3,29] Our results suggest the use of topical agents to preserve or restore the basal sweating response. Successful management might require biological agents that target the dysregulation of several pathways resulting in basal sweating defects. Based on our findings, we speculate that basal sweating defects might be a potential target for the development of a new class of topical agents for dry skin/hand eczema in patients frequently exposed to water.

In conclusion, we demonstrate that basal sweating responses at the folds of fingers play a decisive physiological role in preventing further progression to dry skin/hand eczema. Hence, reduction of basal sweating responses in the fingers would represent a crucial initiating event in the progression to dry skin/ hand eczema. Maintaining basal sweating responses in the finger is the best preventive measures in achieving prevention of dry skin/hand eczema.

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FIGURE LEGENDS

Figure 1. Representative sweating responses from the finger, palm, and forearm showing basal sweating at baseline and after water exposure.

(a) Sweat pores at the folds (arrow) opened and those at the ridges closed immediately after immersion of both the fingers and palm in 22°C water. Observed by impression mold technique (bar, 500 μm). (b) The mean numbers of sweat droplets (per centimeter squared) at the skin fold and skin ridge of the finger (N=6), palm (N=6), and forearm (N=5) at baseline and after water exposure from six healthy controls. Error bars represent mean ± SEM. A paired-sample *t*-test was performed. *p < 0.05, **p < 0.01, ***p < 0.001. (c) Representative image showing the appearance of sweat pores at the folds (white arrows) was also confirmed using the iodine–starch method under emotional stress, such as subtracting by mental calculation. Bar,500 μm. (d) Representative image showing the appearance of sweat pores at the folds (white arrows) was also partly detected using the iodine–starch method after water exposure, but less sensitive to detect all of sweating responses at the folds than IMT. Bar,500 μm. (e)Representative image showing the appearance of sweat pores at the folds after water exposure by optical coherence tomography (sweat duct opened at the fold, arrow). Bar,500 μm. (f) Representative histopathological image shows sweat ducts open at the dermal folds of the palm (arrow). Bar, 200 μm.

Figure 2. Mean numbers of sweat pores at the folds of the finger and palm at baseline and after water exposure in relation to age. Relationship between skin surface hydration and numbers of sweat droplets at the folds and ridges.

(a) Number of sweat droplets at the skin fold of the finger. (b) Number of sweat droplets at the skin ridge of the finger. (c) Number of sweat droplets at the skin fold of the palm. (d) Number of sweat droplets at the skin ridge of the palm. They tend to decrease steeply after the menopause (age >50 years). Age 1–5 years, n = 5; age 20–39 years, n = 6; age >50 years, n = 5. Error bars represent mean ± SEM. A paired-sample *t*-test was performed. *p < 0.05, **p < 0.01, ***p < 0.001.

(e) Relationship between skin surface hydration at baseline and numbers of sweat droplets at the folds after water exposure. (f) Relationship between skin surface hydration at baseline and numbers of sweat droplets at the ridges at baseline. Thirty-one female volunteers without hand eczema were enrolled (mean age ± SD, range, 44.9 ± 7.5; range, 35–57 years). A simple linear regression analysis was performed.

Figure 3. Mean numbers of sweat pores at the folds and ridge after repeated water exposure compared between healthy controls and patients with dry skin/hand eczema

Number of sweat droplets at the skin fold (a) and ridge (b) of the finger.

Number of sweat droplets at the skin fold (c) and ridge (d) of the palm.

Number of sweat droplets at the skin fold (e) and ridge (f) of the forearm.

Healthy controls (n = 5) and patients with dry skin/hand eczema (n = 5) were subjected to single water exposure. Healthy controls (n = 3) and patients with dry skin/hand eczema (n = 3) were subjected to repeated water exposure. Error bars represent mean ± SEM. One-way ANOVA was performed. *p < 0.05, **p < 0.01, ***p < 0.001.

Figure 4. Mean numbers of sweat pores at the folds of the finger and palm of healthy controls and patients with dry skin/hand eczema after repeated water exposure under 40%–50% and 80%–90% relative humidity

(a) Number of sweat droplets at the skin fold of the finger. (b) Number of sweat droplets at the skin fold of the palm. (c) Number of sweat droplets at the skin fold of the forearm. Healthy controls, normal humidity n = 3, high humidity n=3; patients with dry skin/hand eczema, normal humidity n = 4, high humidity n=3. Error bars represent mean ± SEM. Student's *t*-test was performed. *$p < 0.05$.

Figure S1. Impression mold technique and representative images of finger skin. (a) Silicon is applied to the surface of the skin, and the impression of the skin surface was observed under a microscope. (b) Representative images of healthy finger skin and dry finger skin. (c) Representative clinical images of patient with dry skin and hand eczema.

Figure S2. Procedure of water exposure

(a) Schematic diagram of water exposure.

(b) Time course of single and repeated water exposure.

Figure S3. Schematic model showing the opening site of the sweat duct at the folds and ridges of the finger. Sweat ducts open at the ridges under resting conditions (baseline). Sweat ducts open at the folds after water exposure.

Figure S4. Relationship between skin surface hydration and friction force of finger skin.

Skin surface hydration and friction force of finger skin were moderately correlated (R=0.52, P=0.0076).

Figure S5. Mean numbers of sweat pores at the folds and ridges of the finger and palm at baseline and after water exposure in relation to temperature and salinity. (a) Number of sweat droplets at the skin fold of the finger. (b) Number of sweat droplets at the skin ridge of the finger. (c) Number of sweat droplets at the skin fold of the palm. (d) Number of sweat droplets at the skin ridge of the palm. Water (22℃), n = 6; water (42℃), n = 4; 0.9% NaCl (22℃), n = 5; 5% NaCl (22℃), n = 5. Error bars represent mean ± SEM. Student's *t*-test performed. *p < 0.05, **p < 0.01, ***p < 0.001.

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Figure 1

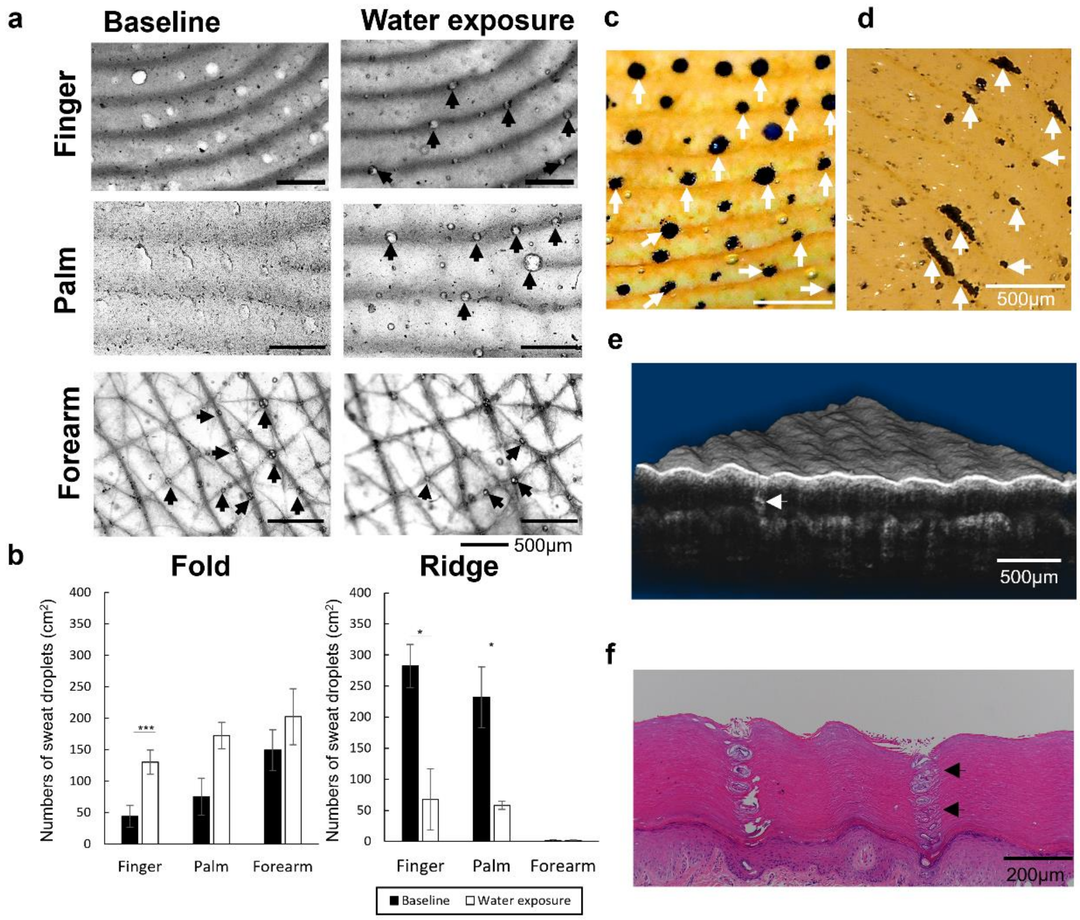
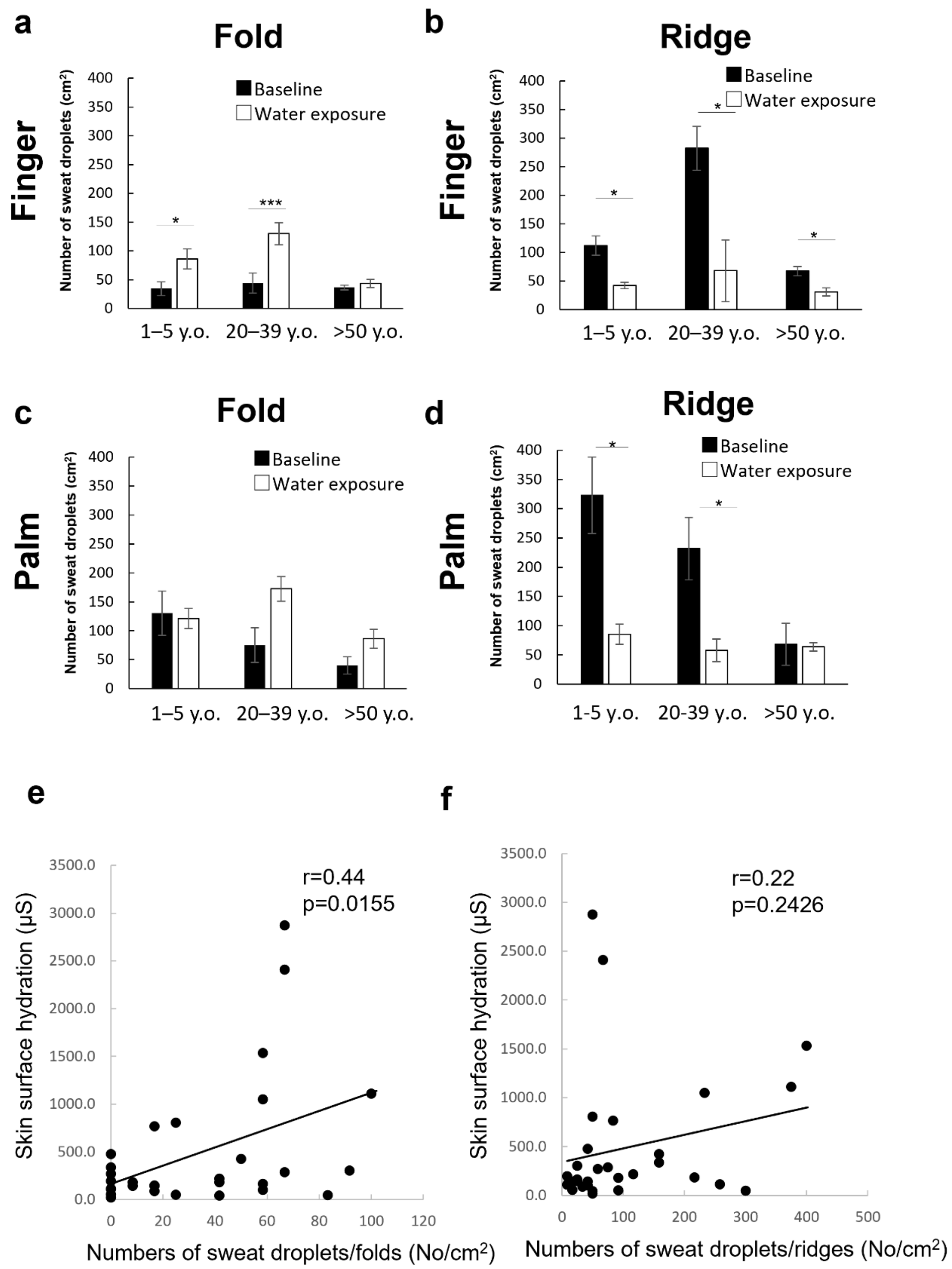

a
Baseline
Water exposure
Finger
Palm
Forearm
500μm
b
Fold
Ridge
Numbers of sweat droplets (cm²)
400
350
300
250
200
150
100
50
0
***
*
*
Finger
Palm
Forearm
Baseline
Water exposure
c
d
500μm
e
500μm
f
200μm

Figure 2



a
Fold
Finger
Number of sweat droplets (cm²)
Baseline
Water exposure
1–5 y.o.
20–39 y.o.
>50 y.o.
b
Ridge
Finger
c
Fold
Palm
d
Ridge
Palm
1-5 y.o.
20-39 y.o.
e
r=0.44
p=0.0155
Skin surface hydration (µS)
Numbers of sweat droplets/folds (No/cm²)
f
r=0.22
p=0.2426
Numbers of sweat droplets/ridges (No/cm²)

Figure 3

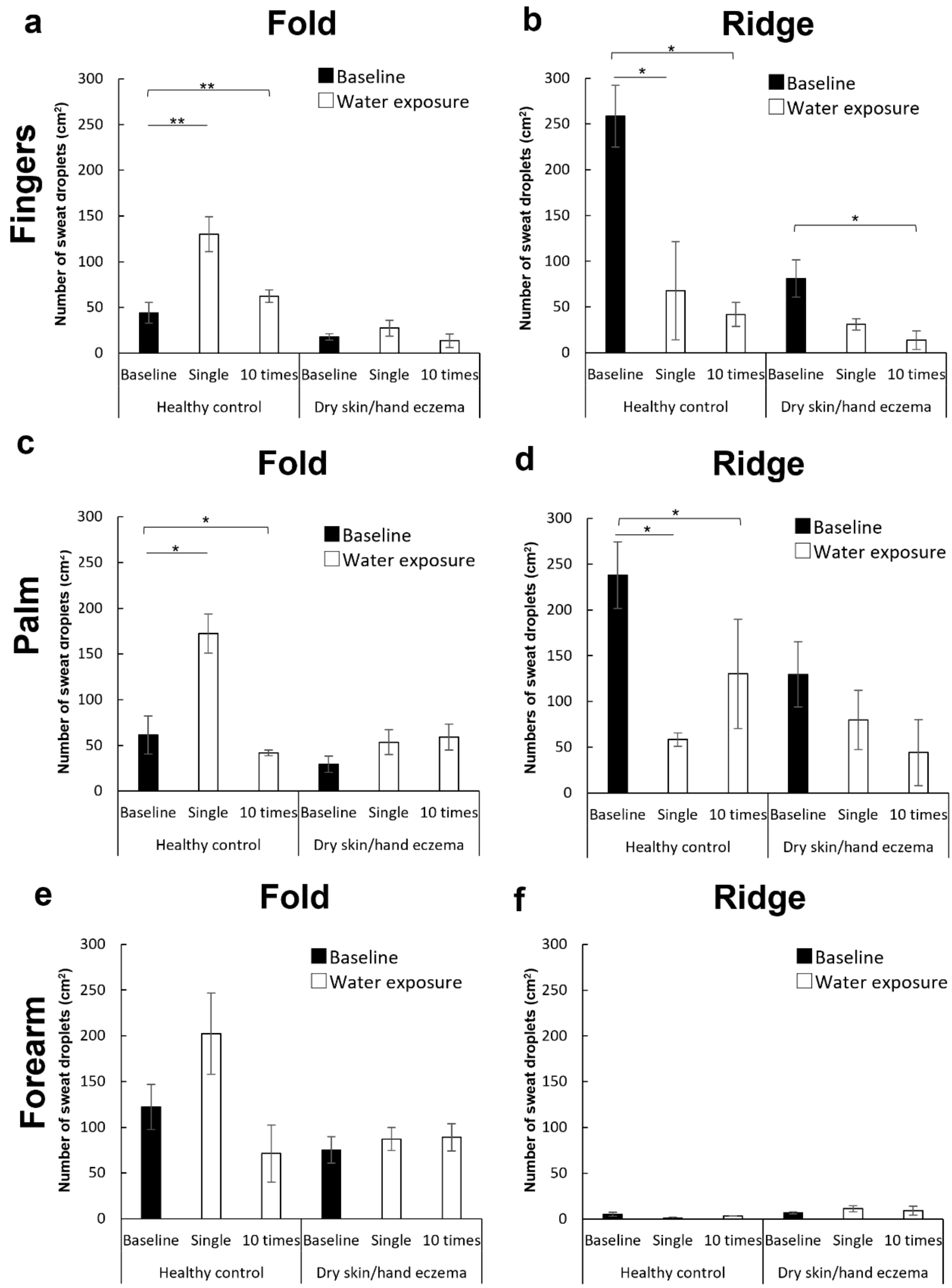
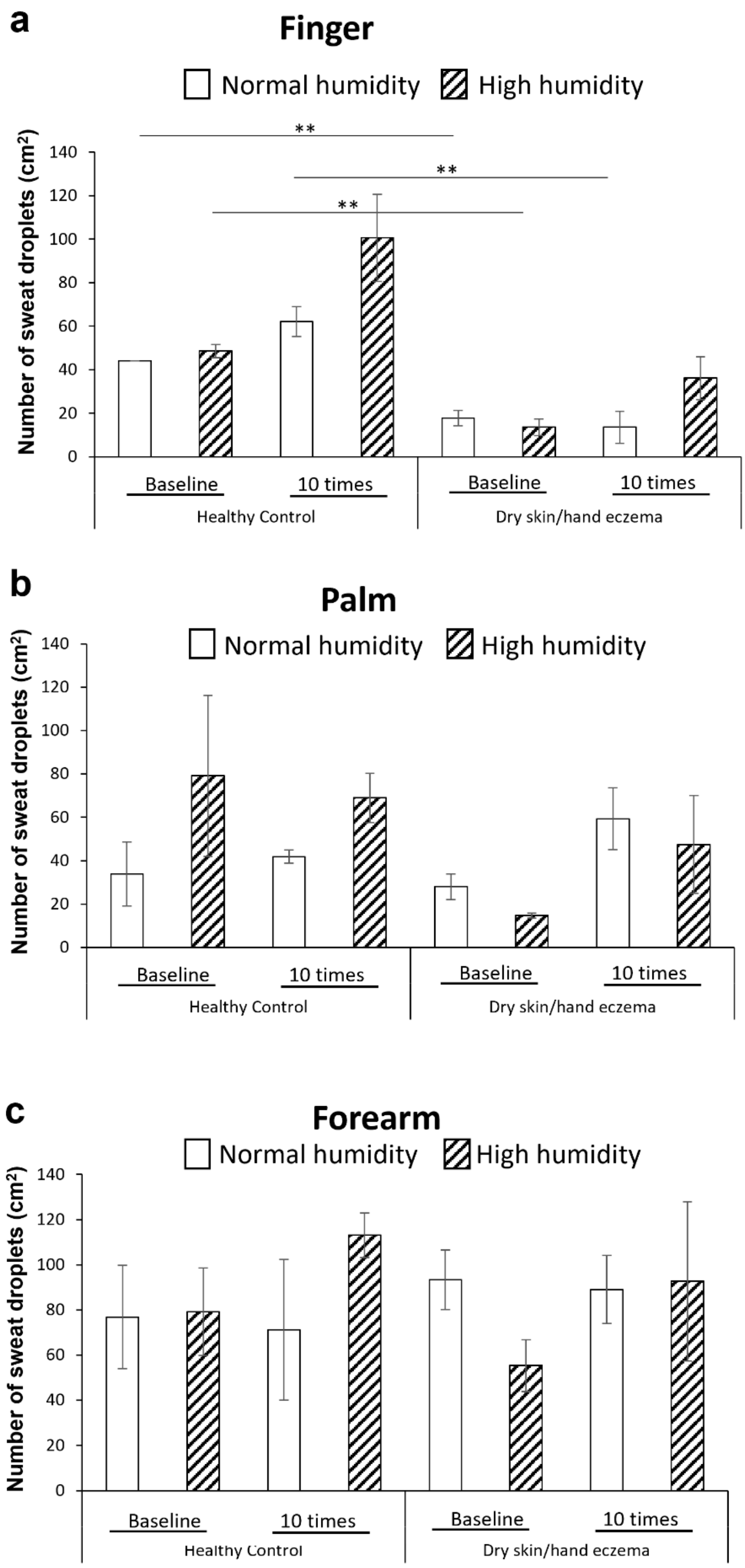

a
Fold
b
Ridge
Fingers
c
Fold
d
Ridge
Palm
e
Fold
f
Ridge
Forearm
Number of sweat droplets (cm²)
Numbers of sweat droplets (cm²)
300
250
200
150
100
50
0
**
*
Baseline
Water exposure
Baseline
Single
10 times
Healthy control
Dry skin/hand eczema

Figure 4



a
Finger
Normal humidity
High humidity
Number of sweat droplets (cm²)
0
20
40
60
80
100
120
140
**
**
**
Baseline
10 times
Healthy Control
Baseline
10 times
Dry skin/hand eczema
b
Palm
Normal humidity
High humidity
Number of sweat droplets (cm²)
0
20
40
60
80
100
120
140
Baseline
10 times
Healthy Control
Baseline
10 times
Dry skin/hand eczema
c
Forearm
Normal humidity
High humidity
Number of sweat droplets (cm²)
0
20
40
60
80
100
120
140
Baseline
10 times
Healthy Control
Baseline
10 times
Dry skin/hand eczema

Figure S1

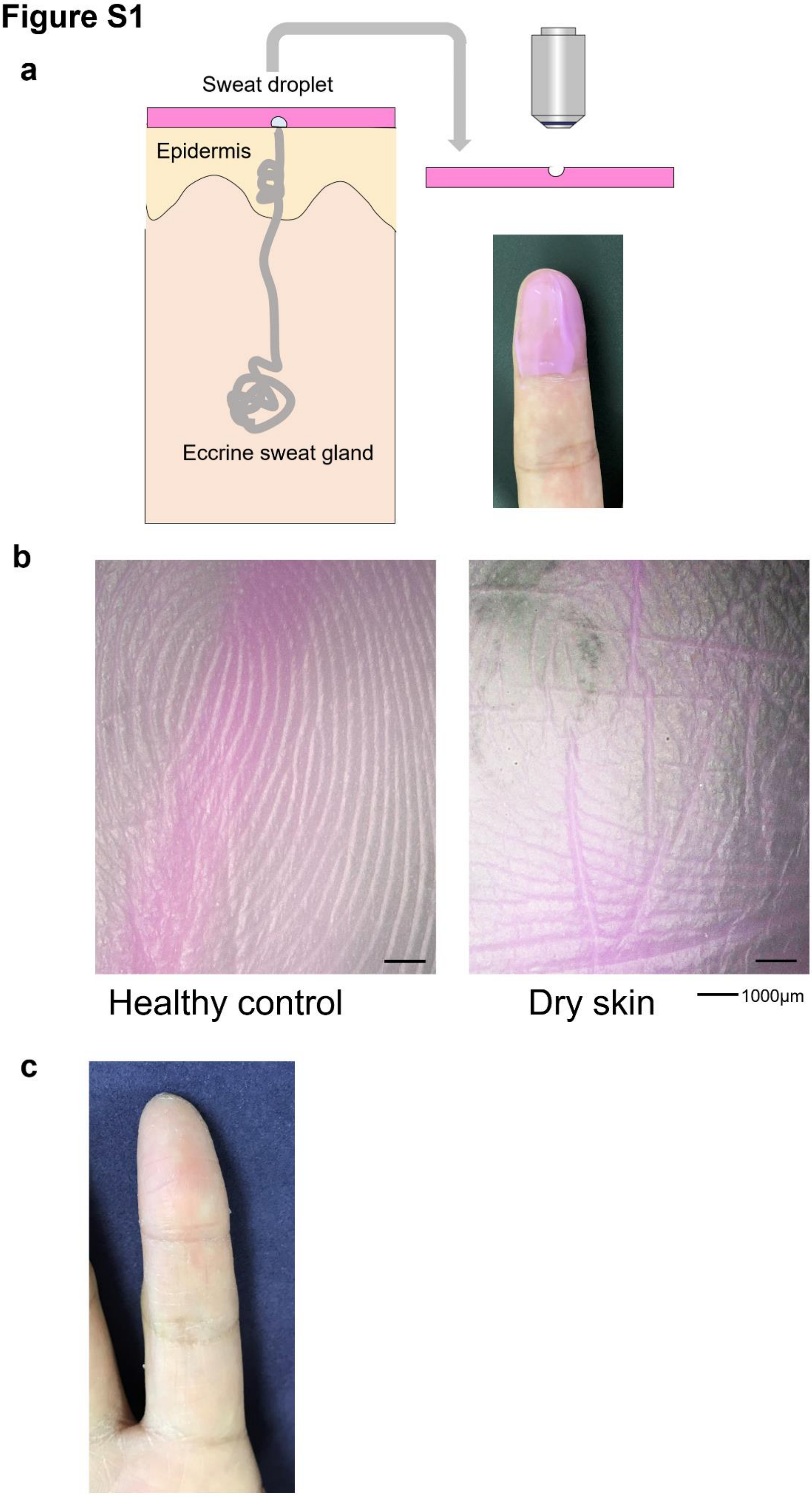

a
Sweat droplet
Epidermis
Eccrine sweat gland
b
Healthy control
Dry skin
1000μm
c

Figure S2

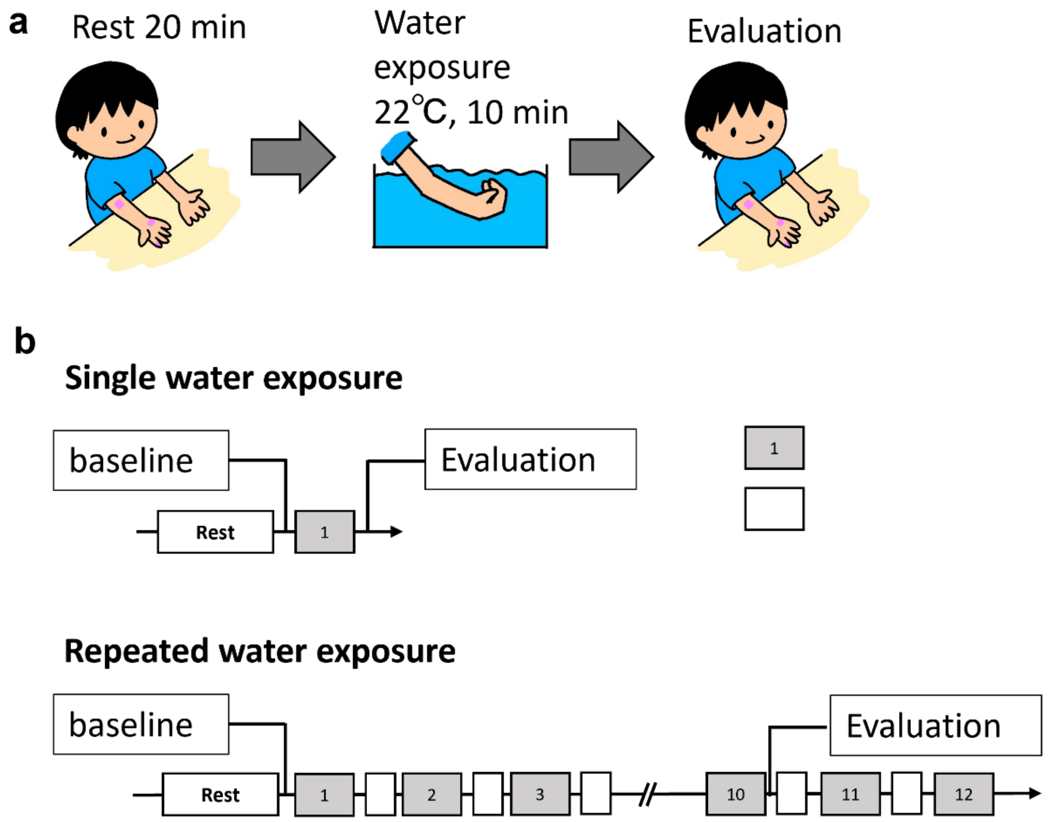


Figure S3

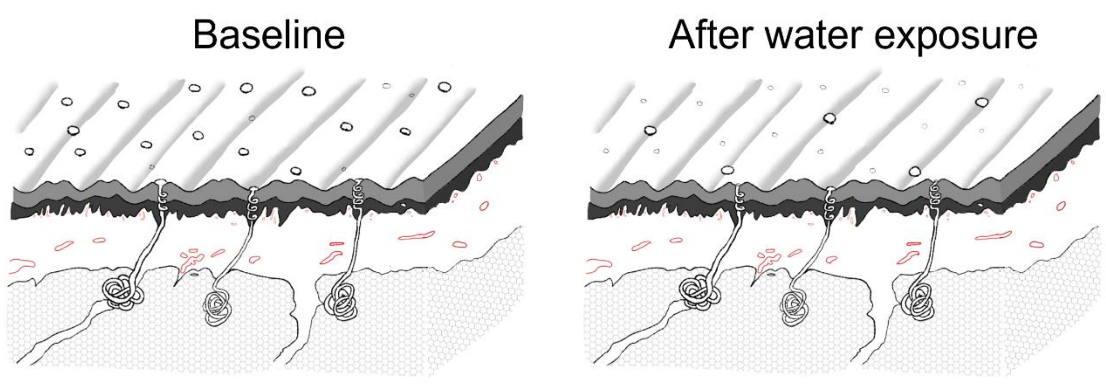


Figure S4

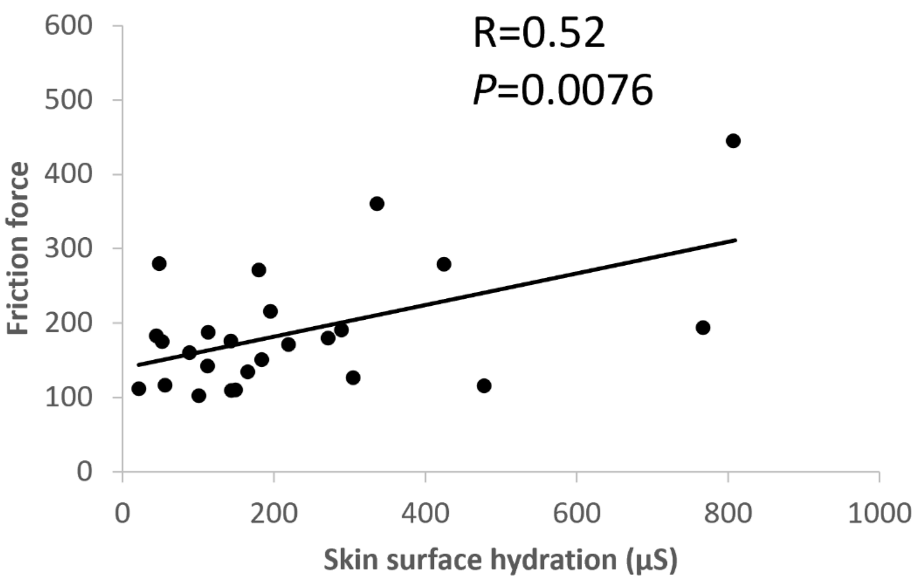


Figure S5