



Association between lactic acid sting test scores, self-assessed sensitive skin scores and biophysical properties in Chinese females

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Abstract

BACKGROUND: Lactic acid sting test (LAST) is a classical method to identify sensitive skin. However, some subjects with self-perceived sensitive skin are negative for LAST.

OBJECTIVE: To determine whether LAST scores are associated with specific phenotype of sensitive skin.

METHODS: A total of 292 subjects with self-perceived sensitive skin were enrolled in this study. The Sensitive Scale was used to evaluate the severity of burning, stinging, itching, tautness, erythema and scaling based on 0–10 scale scores. In addition to the assessment of LAST scores, epidermal biophysical properties were measured using an MPA system.

RESULTS: The Sensitive Scale scores of stinging, itching, tautness and scaling were significantly different between the LAST-positive and -negative groups. However, burning and erythema scores did not differ between the LAST-positive and -negative groups. LAST scores were positively correlated with the Sensitive Scale scores for stinging, itching, tautness and scaling, but not for burning and erythema scores. Moreover, LAST scores negatively correlated with stratum corneum hydration, but positively with transepidermal water loss (TEWL) rates.

CONCLUSIONS: Lactic acid sting test scores positively correlated with TEWL rates. LAST scores could be used to identify subjects with sensitive skin characterized mainly by stinging and itching, but not those mainly by burning and erythema.

Résumé

CONTEXTE: Le test de la piqûre d'acide lactique (LAST) est une méthode classique pour identifier les peaux sensibles. Cependant, certaines personnes s'évaluant ayant une peau sensible sont négatifs au test LAST.

OBJECTIF: Déterminer si le score du LAST est associé à un phénotype spécifique de peau sensible.

MÉTHODES: Au total, 292 personnes s'évaluant ayant une peau sensible ont été inclus dans cette étude. L'échelle de sensibilité a été

utilisée pour évaluer la sévérité de la brûlure, du picotement, de la démangeaison, de la tension, de l'érythème et des desquamations basée sur une échelle de 0-10. En plus de l'évaluation du score LAST, les propriétés biophysiques épidermiques ont été mesurées à l'aide d'un système MPA.

RÉSULTATS: Les scores de l'échelle de sensibilité pour le picotement, les démangeaisons, la tension et la desquamation étaient significativement différents entre la groupe LAST positif et celle du LAST négatif. Cependant, les scores de la brûlure et de l'érythème n'étaient pas différents entre les deux groupes. Le score LAST était positivement corrélé avec les scores de l'échelle de sensibilité du picotement, des démangeaisons, de la tension et des desquamations, mais pas pour la brûlure et l'érythème. En plus, les scores LAST étaient négativement corrélés avec l'hydratation du stratum corneum, mais positivement corrélés avec le taux de perte en eau transépidermique (TEWL).

CONCLUSIONS: Les scores LAST étaient corrélés positivement avec le taux de perte en eau transépidermique. Les scores LAST pourraient être utilisés pour identifier les personnes avec la peau sensible caractérisée principalement le picotement et les démangeaisons, mais pas la brûlure et l'érythème.

Introduction

Sensitive skin is a complex, self-perceived condition of the skin, characterized by hyper-reactivity to various stimuli, including cosmetics, water, temperature, humidity, sun screens, food, menstruation or other physical or chemical factors [1]. Patients with sensitive skin often experience unpleasant sensations, such as burning, stinging, itching and tautness, but without objective signs although transient erythema and scaling could be observed occasionally. These unpleasant sensations cannot be explained by lesions associated with other dermatoses although certain inflammatory dermatoses, such as acne, rosacea, atopic dermatitis, are associated with sensitive skin [2]. The prevalence of sensitive skin varies with geographical region and gender [3]. Because of its high prevalence and negative impact on quality of patients' live, both diagnosis and management of sensitive skin have attracted much attention.

The methods to evaluate sensitive skin include subjective, semi-subjective and objective evaluation. Subjective evaluation mainly relies on self-assessment questionnaire [4, 5]. The severity of sensitive skin is graded according to a four-grade method (non-sensitive,

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Table I Questionnaire for diagnosis of sensitive skin [5]

1	Would you say that your face/neck does not tolerate cold/hot weather or a cold/hot environment?
2	Would you say that your skin face/neck does not tolerate rapid temperature changes?
3	Have you already avoided the use of some cosmetic products that could, according to you, make your skin reactive?
4	Have you already had an adverse reaction on your face/neck to a cosmetic or hygiene product?
5	Would you say that your face/neck is reactive?
6	Have you already felt some itching, burning or tingling on your face/neck skin because of the wind or some cosmetics or hygiene products?
7	Is your face skin reactive to pollution, stress/emotions or menstrual cycle changes?

slightly sensitive, sensitive or very sensitive) [4,6,7]. Various types of self-assessment questionnaire have been used to assess skin sensitivity. The Sensitive Scale is a new method to measure the severity of skin sensitivity and enable the measurement of therapeutic efficacy [8]. The semi-subjective evaluation relies on subjects' report of cutaneous responses to stimuli, such as lactic acid stinging test (LAST), dimethyl sulphoxide, sodium lauryl sulphate, capsaicin and menthol [1,9]. The objective assessment is carried out using respective instruments to measure epidermal biophysical properties, including stratum corneum hydration (SCH), transepidermal water loss (TEWL), sebum content, pH, erythema indices [10–13]. Moreover, reflectance confocal microscopy and mobile-connected dermatoscope are used to facilitate the diagnosis of sensitive skin [14,15].

Although many methods have been used to differentiate sensitive and non-sensitive skin, LAST has been considered as the most typical and suitable method. However, some subjects with sensitive skin diagnosed through self-evaluations and questionnaires were LAST negative, suggesting the limitation of LAST in the diagnosis of sensitive skin. Therefore, this study aimed to elucidate the correlation between the LAST scores and the Sensitive Scale scores of burning, stinging, itching, tautness, erythema and scaling, and epidermal biophysical properties.

Materials and methods

Subjects

Sensitive skin was identified by a self-assessment questionnaire (Table I) [5]. Subjects who answered 'yes' to at least five of the seven questions in the questionnaire were considered as sensitive skin. A total of 292 Chinese females, aged 13–65 years with mean age of 31.52 years, were identified as sensitive skin and were enrolled in this study. The exclusion criteria included subjects with any other facial skin diseases, such as acne, rosacea, glucocorticoid-dependent dermatitis, ulceration and infections. An informed consent was obtained from each participant prior to the study. Human research protocol was approved by human research committee of The First Affiliated Hospital of Kunming Medical University, Kunming, China. This study was conducted from January 2017 to March 2018.

The Sensitive Scale

The severity of sensitive skin was evaluated using the Sensitive Scale, including burning, tingling, itching, tautness, erythema and

scaling as described in previous publication [8]. Participants were asked to grade each symptom from 0 to 10. A global score of skin irritation was scored from 0 to 10 using a visual analogue scale (VAS: 0 = no feeling, 10 = very strong feeling).

Lactic acid sting test

Lactic acid sting test was performed according to the methods described previously [16]. Briefly, lactic acid (purity > 98%, Sigma, USA) was prepared at 10% concentration in distilled water. A quantity of 50 μ L of 10% lactic acid solution was applied to the right nasolabial fold, whereas the equal volume of saline was applied to the contralateral site. The participants were asked to grade the intensity of sting using a 4-point scale (0 = no stinging; 1 = slight stinging; 2 = moderate stinging; and 3 = strong stinging) at 0 s, and 2.5 and 5 min after application of lactic acid. Cumulative scores at 2.5 and 5 min ≥ 3 were considered as the LAST positive group.

Measurement of skin biophysical properties

All subjects stopped using skin care/cosmetic products for at least 24 h prior to the measurement. After cleaning the face with water and drying gently with paper towels, subjects rested for 30 min in a controlled environment (room temperature at 20–25°C, relative humidity of 50–60%). Afterwards, the following parameters were sequentially measured on the right cheek with the respective device: TEWL values (Tewameter TM 300) first, stratum corneum hydration (SCH) (Corneometer CM 825), sebum content (Sebumeter SM 815), erythema index (Mexameter 18) and skin surface pH

Table II LAST scores in 292 subjects with sensitive skin

LAST scores	0	1	2	3	4	5	6
Number of subjects	13	19	47	69	71	52	21

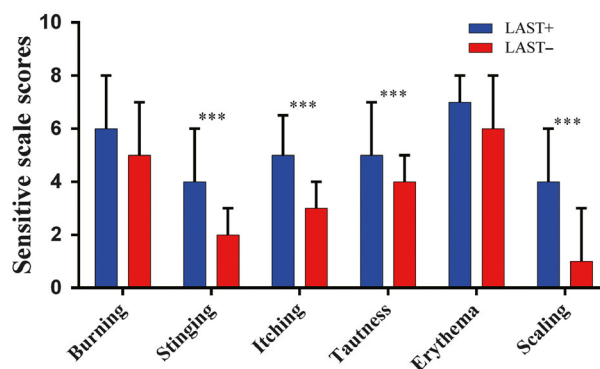


Figure 1 Comparison of Sensitive Scale scores between LAST-positive and -negative groups. A non-parametric two-independent sample test was used to analyse the significance between groups. *** $P < 0.001$.

Table III Correlation between LAST scores and the Sensitive Scale scores of symptoms and signs

		Burning	Stinging	Itching	Tautness	Erythema	Scaling
LAST scores	R_s	0.310	0.469	0.360	0.224	0.045	0.329
	P	0.596	<0.001*	<0.001*	<0.001*	0.455	<0.001*

$R_s > 0$: positive correlation; $R_s < 0$: negative correlation; *: statistically significant.

values (Skin-pH-meter pH 905) [17,18]. Each measurement was repeated three times, and the average of three readings was taken. These measurements were performed prior to the LAST.

Statistical analysis

Statistical analyses were performed with SPSS17.0. The median values and quartiles were calculated for age, the Sensitive Scale

scores of each symptom and LAST scores. Data for SCH, TEWL, sebum content, pH and erythema index were expressed as mean \pm SD. The differences in the Sensitive Scale scores of symptoms between the LAST-positive and -negative groups were compared using non-parametric two-independent samples tests. The correlations between age, the Sensitive Scale scores of sensitive skin symptoms, LAST scores, and skin biophysical properties were determined using the Spearman test.

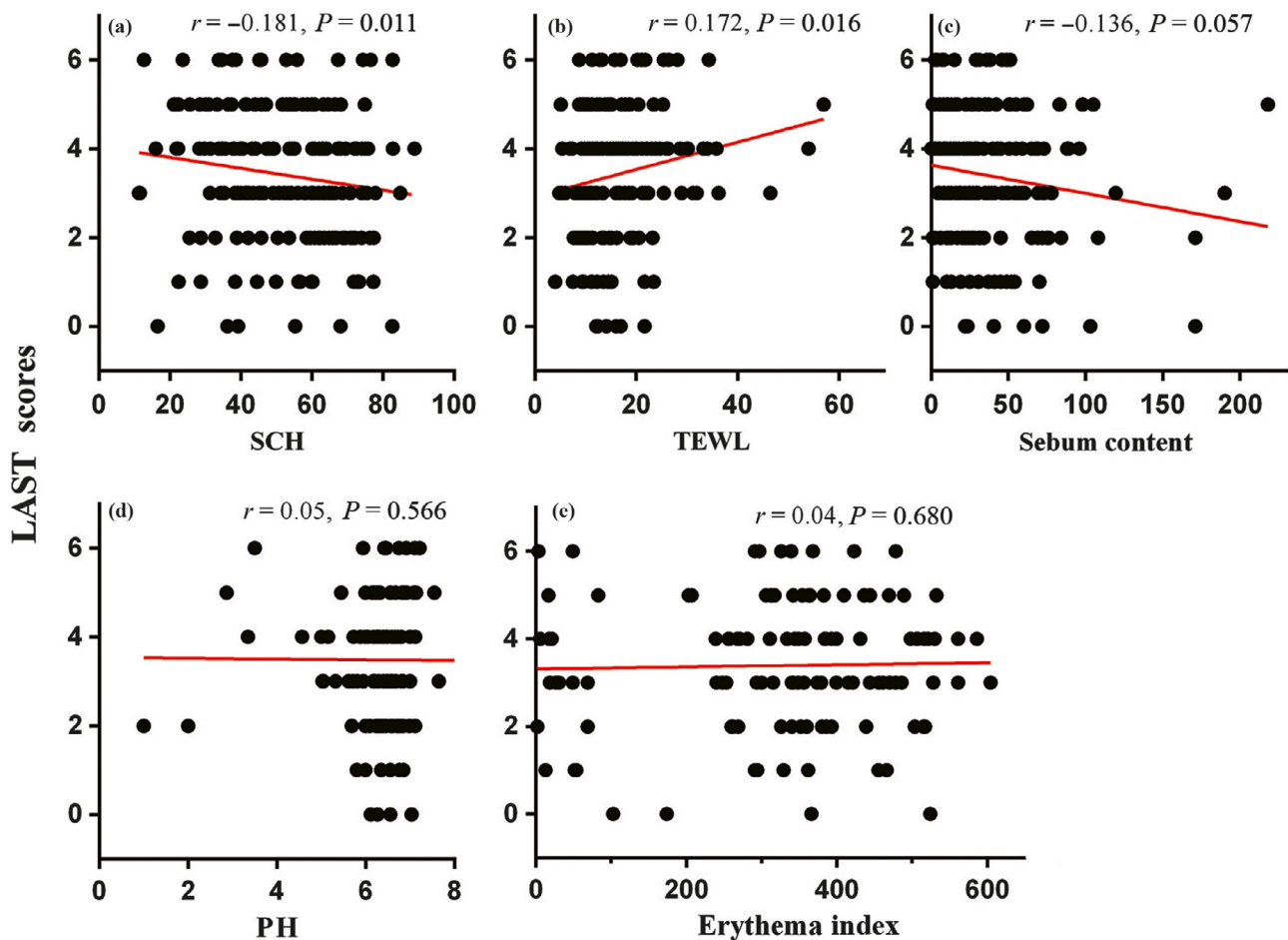


Figure 2 Correlation between LAST scores and skin biophysical properties. Spearman's test was used to determine the significances. r and P values are indicated in the figures.

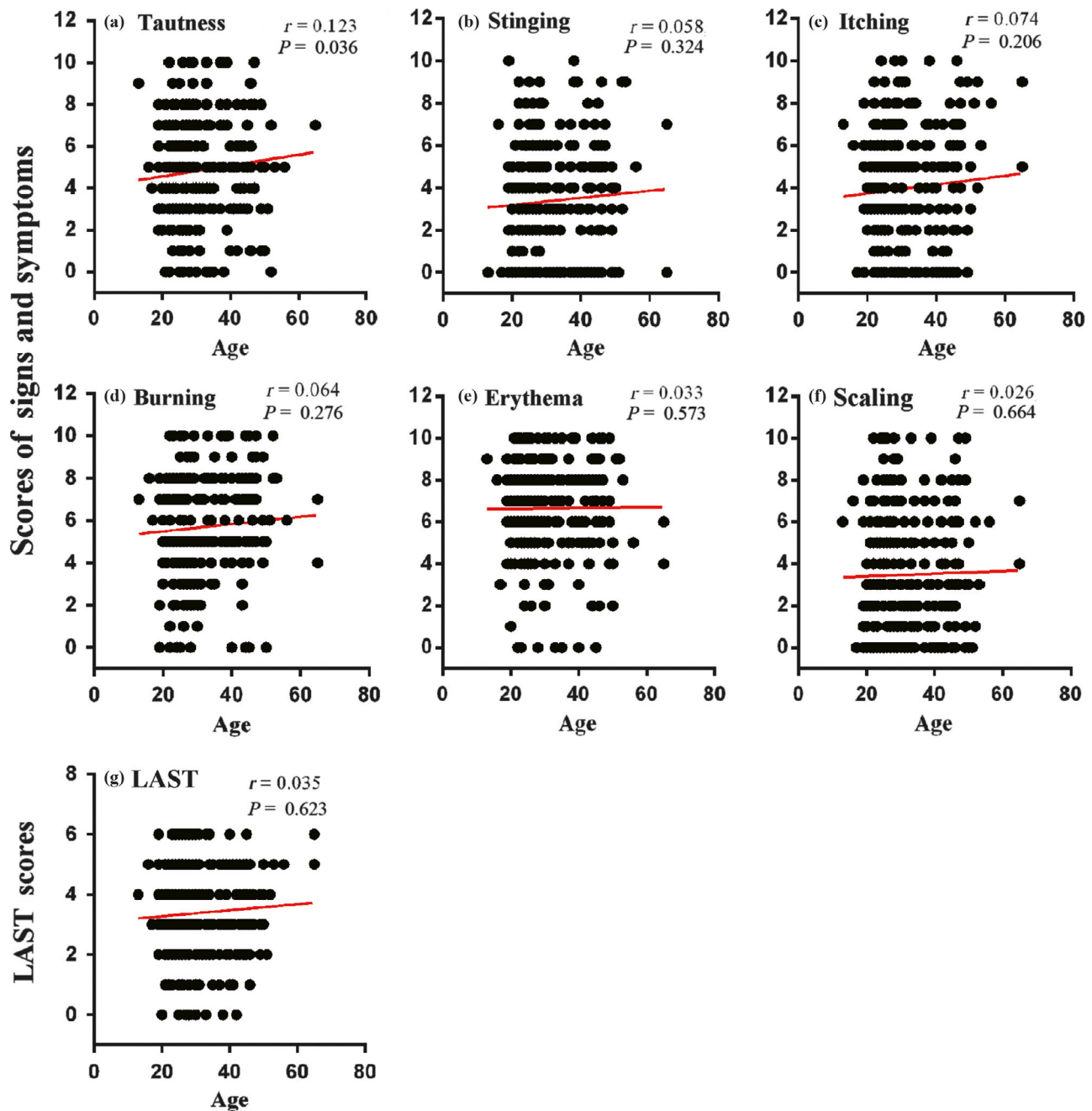


Figure 3 Correlations of age with scores of LAST, and signs and symptoms of sensitive skin. Spearman's test was used to determine the significances. r and P values are indicated in the figures.

Results

Distribution of LAST scores among subjects

Out of the 292 subjects with sensitive skin, 213 subjects were LAST positive, whereas 79 subjects were negative. Distribution of LAST scores among subjects was detailed in Table II.

LAST scores are associated with specific symptoms and signs

We first analysed the differences in the Sensitive Scale scores between LAST-positive and -negative groups. As shown in (Fig. 1), the Sensitive Scale scores of stinging, itching, tautness, scaling differed significantly between LAST-positive and -negative groups ($P < 0.05$). But the Sensitive Scale scores of burning and erythema were no differences between LAST-positive and

Table IV Correlation between age and biophysical properties

		SCH	TEWL	Sebum content	PH	Erythema index
Age	R_s	-0.010*	-0.136	-0.206	0.039	0.072
	P	0.886	0.057	0.004	0.656	0.459

$R_s > 0$: positive correlation; $R_s < 0$: negative correlation; *: statistically significant.

-negative groups. Moreover, LAST scores positively correlated with the Sensitive Scale scores of stinging, itching, tautness and scaling ($P < 0.05$), but not with burning, erythema (Table III). These results indicate that LAST scores are associated with specific symptoms and signs in subjects with sensitive skin.

LAST scores correlate with SCH and TEWL

We next determined whether LAST scores correlated with epidermal biophysical properties. Indeed, LAST scores negatively correlated with SCH (Fig. 2a), and positively with TEWL (Fig. 2b), but did not correlate with either sebum content (Fig. 2c) or skin surface PH (Fig. 2d) or erythema index (Fig. 2e).

Age correlates positively with tautness scores

Because prior studies demonstrated age differences in perception of sensitive skin [19], we next determined correlations of age with LAST scores, specific symptoms and signs, and epidermal biophysical properties. Surprisingly, age only positively correlated with tautness scores (Fig. 3a), but neither other symptoms/signs (Fig. 2b-f) nor LAST scores (Fig. 3g). Moreover, a negative correlation of age with sebum content was also observed (Table IV), consistent with prior report [20]. These results demonstrate a possible link of age to specific symptoms of sensitive skin.

Discussion

LAST has been widely employed as a diagnostic tool of sensitive skin. However, we demonstrate here that over 27% (79/292) of subjects with sensitive skin were LAST negative, suggesting the limitation of the diagnosis of sensitive skin by either LAST or questionnaire alone because criteria for the diagnosis of sensitive skin varies with questionnaire and cutaneous reactions to the same substance vary with subjects. Moreover, some subjects with sensitive skin can display normal permeability barrier function, possibly leading to LAST negative [16,21,22]. Thus, neither LAST nor a questionnaire alone can serve as a gold standard for the diagnosis of sensitive skin in all subjects.

Interestingly, the present study show that LAST scores positively correlated with specific symptoms and signs, such as severity of stinging, itching, tautness and scaling, in subjects with sensitive skin. However, substantial portion of subjects with erythema were LAST negative although 74% of subjects with sensitive skin display erythema [3]. These phenomena could reflect the differences in individual's cutaneous conditions, which can largely determine both symptoms and LAST scores. For example, thinner skin is more prone to flushing because of both defective permeability barrier and

increased vascular reactivity [23]. The latter positively correlates with LAST scores [16]. Subjects with high vascular reaction can display strong stinging sensation [16]. These subjects may display normal barrier, which could result in LAST negative. It has also been postulated that DMSO is suitable for assessing cutaneous vascular reactions [16], whereas LAST is more sensitive to assess cutaneous neurosensitivity [24]. Additionally, some subjects with sensitive skin display positive response only to either capsaicin or lactic acid [25]. Thus, individuals with different skin conditions can respond differently to skin sting test. Nevertheless, the results of the present study suggest that LAST could be only reliable for the diagnosis of sensitive skin with specific symptoms and signs, such as tingling, itching, tautness and scaling.

Clinical studies have shown that subjects with sensitive skin exhibit a defective epidermal permeability barrier and reduced SCH [10,13], whereas improvements in these epidermal functions alleviate both clinical signs and symptoms of sensitive skin, and lower LAST scores [10,26], suggesting, at least in some cases, a link between epidermal functions and LAST scores. A study showed a positive correlation between stinging responses and TEWL [27]. Indeed, we show here that LAST scores negatively correlated with SCH, whereas positively with TEWL, consistent with previous findings [28]. It is no surprise that compromised permeability barrier can enhance penetration of lactic acid, whereas reduced SCH can induce inflammation, which both can result in increased LAST scores. Thus, both SCH levels and TEWL rates could possibly predict LAST scores in subjects with abnormal epidermal function.

Pathomechanisms of sensitive skin are very complicated. It is generally accepted that development of sensitive skin could be attributable to epidermal dysfunction, increased neural and/or vascular reactivity, and inflammation, among which epidermal dysfunction appears particularly important. For example, acetone-induced disruption of epidermal permeability barrier and SC hydration can increase nerve innervation [29,30], leading to an increase in neural sensitivity. Moreover, either elevation in TEWL rates or reduction in SC hydration levels can upregulate expression levels of cutaneous cytokines and vascular endothelial growth factor, and increase mast cell infiltration in the dermis, resulting in the development of symptoms and signs associated with sensitive skin [31–33]. Of course, involvements of transient receptor potential (TRP) vanilloid 1 and TRP melastatin 8 in sensation of sting, pain and itching are also appreciated [34,35]. Sensitive skin with LAST-positive and -negative may represent the involvement of different pathomechanisms.

Although prior study demonstrated the age-related difference in the prevalence of sensitive skin [36], here, we showed an age-related difference in the scores of tautness. In contrast to prior study [20], we did not observe age-associated changes in skin biophysical properties. The discrepant results between the present study and others could be because of the age range of subjects. The majority of subjects were in age 30s (13–65 years old), whereas in other study, subject were 0.5–94 years old [20]. Moreover, declines in sebum content, SCH and skin surface pH occur at around age 50 years [20]. Hence, age-related differences in some biophysical properties and/or symptoms and signs of sensitive skin may not be identified because of such narrow range of age. In order to elucidate the age-associated characteristics of sensitive skin, it would be helpful to enrol subjects in a wide range of age.

Of note, the aims of the present study were to reveal the association of LAST with signs and symptoms of sensitive skin, and skin

biophysical properties although atmospheric conditions can influence both skin biophysical properties and sensitive skin [27]. It is likely that atmospheric conditions can also alter the association of LAST with signs and symptoms of sensitive skin, and skin biophysical properties. However, further studies are required to validate the presumption.

In summary, LAST scores are associated with sensitive skin with symptoms of stinging, itching, tautness and clinical sign of scaling. LAST may not be suitable for identification of sensitive skin mainly characterized by burning and erythema. Multiple approaches of assessments may be required to diagnose sensitive skin.

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Conflict of interest

All authors have no conflicts of interest.

References

- Berardesca, E., Farage, M. and Maibach, H. Sensitive skin: an overview. *Int. J. Cosmet. Sci.* **35**, 2–8 (2013).
- Darlenski, R., Kazandjieva, J., Fluhr, J.W., Maurer, M. and Tsankov, N. Lactic acid sting test does not differentiate between facial and generalized skin functional impairment in sensitive skin in atopic dermatitis and rosacea. *J. Dermatol. Sci.* **76**, 151–153 (2014).
- Misery, L., Myon, E., Martin, N., Consoli, S., Boussetta, S., Nocera, T., Taieb, C. Sensitive skin: psychological effects and seasonal changes. *J. Eur. Acad. Dermatol. Venereol.* **21**, 620–628 (2007).
- Misery, L. Sensitive skin. *Expert. Rev. Dermatol.* **8**, 631–637 (2013).
- Buhé, V., Vié, K., Guéré, C. et al. Pathophysiological study of sensitive skin. *Acta Derm. Venereol.* **96**, 314–318 (2016).
- Misery, L., Boussetta, S., Nocera, T., Perez-Cullell, N. and Taieb, C. Sensitive skin in Europe. *J. Eur. Acad. Dermatol. Venereol.* **23**, 376–381 (2009).
- Misery, L., Sibaud, V., Merial-Kieny, C. and Taieb, C. Sensitive skin in the American population: prevalence, clinical data, and role of the dermatologist. *Int. J. Dermatol.* **50**, 961–967 (2011).
- Misery, L., Jean-Decoster, C., Mery, S., Georgescu, V. and Sibaud, V. A new ten-item questionnaire for assessing sensitive skin: the sensitive scale-10. *Acta Derm. Venereol.* **94**, 635–639 (2014).
- Richters, R.J., Hendriks, J.C., Uzunbajakava, N.E., Janssen, L.D., Falcone, D., van Erp, P.E. and van de Kerkhof, P.C. Responses to sodium dodecyl sulphate as an in vivo human model to study the pathomechanisms underlying sensitive skin. *Exp. Dermatol.* **25**, 407–409 (2016).
- Farage, M.A., Katsarou, A. and Maibach, H.I. Sensory, clinical and physiological factors in sensitive skin: a review. *Contact Dermatitis.* **55**, 1–14 (2006).
- Cui, L., Jia, Y., Cheng, Z.W., Gao, Y., Zhang, G.L., Li, J.Y. and He, G.F. Advancements in the maintenance of skin barrier/skin lipid composition and the involvement of metabolic enzymes. *J. Cosmet. Dermatol.* **15**, 549–558 (2016).
- Li, X., He, C., Chen, Z., Zhou, C., Gan, Y. and Jia, Y. A review of the role of sebum in the mechanism of acne pathogenesis. *J. Cosmet. Dermatol.* **16**, 168–173 (2017).
- Fan, L., He, C., Jiang, L., Bi, Y., Dong, Y. and Jia, Y. Brief analysis of causes of sensitive skin and advances in evaluation of anti-allergic activity of cosmetic products. *Int. J. Cosmet. Sci.* **38**, 120–127 (2016).
- Ma, Y.F., Yuan, C., Jiang, W.C., Wang, X.L. and Humbert, P. Reflectance confocal microscopy for the evaluation of sensitive skin. *Skin Res. Technol.* **23**, 227–234 (2017).
- Zha, W.F., Song, W.M., Ai, J.J. and Xu, A.E. Mobile connected dermatoscope and confocal laser scanning microscope: a useful combination applied in facial simple sensitive skin. *Int. J. Cosmet. Sci.* **34**, 318–321 (2012).
- Chen, S.Y., Yin, J., Wang, X.M., Liu, Y.Q., Gao, Y.R. and Liu, X.P. A new discussion of the cutaneous vascular reactivity in sensitive skin: a sub-group of SS? *Skin. Res. Technol.* **24**, 432–439 (2018).
- Fan, L., Jia, Y., Cui, L., Li, X. and He, C. Analysis of sensitive skin barrier function: basic indicators and sebum composition. *Int. J. Cosmetic. Sci.* **40**, 117–126 (2017).
- Rogiers, V. and EEMCO Group. EEMCO guidance for the assessment of transepidermal water loss in cosmetic sciences. *Skin Pharmacol. Appl. Skin. Physiol.* **14**, 117–128 (2001).
- Farage, M.A. Perceptions of sensitive skin of the genital area. *Curr. Probl. Dermatol.* **40**, 142–154 (2011).
- Man, M.Q., Xin, S.J., Song, S.P. et al. Variation of skin surface pH, sebum content and stratum corneum hydration with age and gender in a large Chinese population. *Skin Pharmacol. Phys.* **22**, 190–199 (2009).
- Yatagai, T., Shimauchi, T., Yamaguchi, H. et al. Sensitive skin is highly frequent in extrinsic atopic dermatitis and correlates with disease severity markers but not necessarily with skin barrier impairment. *J. Dermatol. Sci.* **89**, 33–39 (2018).
- Li, Z., Hu, L., Elias, P.M. and Man, M.Q. Skin care products can aggravate epidermal function: studies in a murine model suggest a pathogenic role in sensitive skin. *Contact Dermat.* **2**, 151–158 (2018).
- Duarte, I., Silveira, J.E.P.S., Hafner, M.F.S., Toyota, R. and Pedrosa, D.M.M. Sensitive skin: review of an ascending concept. *An. Bras. Dermatol.* **92**, 521–525 (2017).
- Li, S., Wang, X., Gao, Y., Chen, S., Liu, X., Wang, H. and Dong, Y. CPT, the main test method of skin neuronal sensitivity. *Cutan. Ocul. Toxicol.* **34**, 208–211 (2014).
- Sun, L., Wang, X., Zhang, Y., Wang, T., Li, X. and Ma, Y. The evaluation of neural and vascular hyper-reactivity for sensitive skin. *Skin Res. Technol.* **22**, 381–387 (2016).
- Jeong, S., Lee, S.H., Park, B.D., Wu, Y., Man, G. and Man, M.Q. Comparison of the efficacy of Atopalm® multi-lamellar emulsion cream and Physiogel® intensive cream in improving epidermal permeability barrier in sensitive skin. *Dermatol. Ther. (Heidelb)*. **6**, 47–56 (2016).
- Tan, Y.M., Wang, X.M., Yuan, C. et al. Skin sensitivity and intolerance in shanghai: cumulative influence of different meteorological parameters. *Cutan. Ocul. Toxicol.* **34**, 132–138 (2015).

28. An, S., Lee, E., Kim, S., Nam, G., Lee, H., Moon, S. and Chang, I. Comparison and correlation between stinging responses to lactic acid and bioengineering parameters. *Contact Dermat.* **57**, 158–162 (2007).
29. Tominaga, M., Ozawa, S., Tengara, S., Ogawa, H. and Takamori, K. Intraepidermal nerve fibers increase in dry skin of acetone-treated mice. *J. Dermatol. Sci.* **48**, 103–111 (2007).
30. Kamo, A., Tominaga, M., Tengara, S., Ogawa, H. and Takamori, K. Inhibitory effects of UV-based therapy on dry skin-inducible nerve growth in acetone-treated mice. *J. Dermatol. Sci.* **62**, 91–97 (2011).
31. Lin, T.K., Man, M.Q., Santiago, L.S. *et al.* Topical antihistamines display potent anti-inflammatory activity linked in part to enhanced permeability barrier function. *J. Invest. Dermatol.* **133**, 469–478 (2013).
32. Ashida, Y. and Denda, M. Dry environment increases mast cell number and histamine content in dermis in hairless mice. *Br. J. Dermatol.* **149**, 240–247 (2015).
33. Elias, P.M., Arbiser, J., Brown, B.E. *et al.* Epidermal vascular endothelial growth factor production is required for permeability barrier homeostasis, dermal angiogenesis, and the development of epidermal hyperplasia: implications for the pathogenesis of psoriasis. *Am. J. Pathol.* **173**, 689–699 (2008).
34. Jain, A., Brönneke, S., Kolbe, L., Stäb, F., Wenck, H. and Neufang, G. TRP-channel-specific cutaneous eicosanoid release patterns. *Pain* **152**, 2765–2772 (2011).
35. Inamadar, A.C. and Palit, A. Sensitive skin: an overview. *Indian J. Dermatol. Venereol. Leprol.* **79**, 9–16 (2013).
36. Misery, L., Jourdan, E., Huet, F. *et al.* Sensitive skin in France: a study on prevalence, relationship with age and skin type and impact. *J. Eur. Acad. Dermatol. Venereol.* **32**, 791–795 (2018).