Lipidomics Profiling of Skin Surface Lipids in Senile Pruritus

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Research

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Abstract

Background: Senile pruritus is common, yet its etiology remains unknown. Aging-associated skin barrier defects and skin surface lipids (SSL) alterations have been postulated to play important roles in its occurrence. In the present study, the lipidomic profiles of SSLs in elderly patients were examined to better understand the potential causes of senile pruritus.

Methods: Transepidermal water loss (TEWL) was evaluated to assess the skin barrier function. The Ameliorated Kawashima Itch Scale score was used to measure the pruritus severity. Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) and multivariate data analysis were employed to investigate SSL alterations.

Results: The results showed that senile pruritus patients had higher TEWL values than control subjects (13.13±4.28 versus 6.71±2.45, $P<0.01$). LC-MS/MS revealed significant differences in the lipidomic profiles and identified 81 species of SSLs that differed between the two groups. Compared with control subjects, senile pruritus patients had increased levels of ceramides (Cers), diacylglycerols, fatty acids, phosphatidylcholines, phosphatidylethanolamines, phytosphingosines, sphingosines, diacylceryl-3-O-carboxyhydroxymethylcholine, diacylglyceryl trimethylhomoserine, and unsaturated free fatty acids, but decreased levels of triacylglycerol. Cer-EOS, Cer-NDS, and Cer-NS were positively correlated with TEWL value ($P<0.05$). Pruritus severity score was positively correlated with sphingomyelin, Cer-NP, Cer-AS, Cer-NDS, and Cer-NS, but negatively correlated with Cer-BS, Cer-EODS, Cer-EOS, and Cer-AP.

Conclusions: The present study indicated that patients with senile pruritus have impaired skin barrier function and altered SSL composition. Certain SSL species identified in this study may be potential targets for future studies on the pathogenesis of senile pruritus.

Trial registration: Peking University International Hospital (Number: YN2018QN04; date: January 2019).

Background

Senile pruritus is defined as chronic itching in elderly people with unknown etiology, and is a diagnosis of exclusion after all other causes of pruritus have been ruled out (1). With the prolonged life expectancy worldwide in the setting of rapid medical advances, ageing-related skin diseases like senile pruritus are becoming increasingly relevant (2). Pruritus is the most frequently reported dermatological complaint in the elderly population (3). This severe itching may not be self-limiting, and can lead to sleep disorders and even psychiatric complications such as depression in certain cases that significantly decrease the quality of life (4). The pathophysiology of senile pruritus remains unclear, although several causes have been hypothesized, including age-related changes in skin, neurological disorders, and abnormal immunological responses (5). Thus, research on pruritus in the elderly population is urgently needed.

Skin surface lipids (SSLs) are a mixture of sebaceous gland lipids and intercellular lipids located in the outer layer of epidermal cells. SSLs play an important role in maintaining the skin barrier function and help to regulate various aspects of the integumentary system, including cell proliferation, cell apoptosis, immunity, and inflammation (6). Abnormalities in SSL composition are involved in the pathogenesis of common skin diseases such as atopic dermatitis(AD), acne, psoriasis, and seborrheic dermatitis (7). Lipidomics is an emerging field of study that involves large-scale comprehensive evaluation of the end-products of lipid metabolism (8). Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) is a new analytical technique employed in lipidomics that allows the identification and quantification of cellular lipid species (9).

Because little is known about the SSL profiles in senile pruritus, the present study employed LC-MS/MS to compare the SSL profiles in senile pruritus patients with those in control subjects without pruritus to investigate the role of SSLs in the pathogenesis of senile pruritus.

Methods

Chemicals and reagents

Methanol, chloroform, ammonium formate, isopropyl alcohol, acetonitrile, formic acid, and distilled water used during sample preparation and LC-MS/MS were purchased from Thermo Fisher Scientific (Waltham, MA, USA). SSL-adsorbent tape (Sebutape) was purchased from CuDerm Corporation (Dallas, TX, USA).

Participants

The study was reviewed and approved by the Ethics Committee of Peking University International Hospital. Informed consent to participate in the study was obtained from all patients (elderly with senile pruritus) and healthy individuals (elderly without pruritus) before enrollment. Individuals aged >60 years were eligible for inclusion. A total of 40 participants from the Beijing area were enrolled in the study, including 20 patients with senile pruritus and 20 healthy controls. All 20 patients had physician-confirmed diagnosis of senile pruritus and were able to complete the study. The patients underwent a complete examination and checkup to exclude diabetes, liver or kidney dysfunction, malignant tumor, HIV infection, thyroid disorder, anxiety or depression disorder, psoriasis, atopic dermatitis, ichthyosis, scabies, eczema, bullous pemphigoid, and other dermatoses that can cause skin pruritus. The participants had not receive any treatments or drugs that could interfere with the study assessment for 6 months, including cardiovascular, antiepileptic, antibiotic, and antipsychotic drugs. The participants did not bathe or apply topical moisturizer for 24 hours before the test. The study protocol ensured that the participants were matched for demographic characteristics of sex and age.

TEWL measurement

Transepidermal water loss (TEWL) measurements were performed at a site 1 cm below the right knee using a portable VapoMeter (TM300; CK, Cologne, Germany). The measurement time was 8–10 s. Briefly, the VapoMeter was maintained under standard ambient conditions in a cool air-conditioned room at temperature 23℃ and humidity 50%. After the detection probe was placed on the target area, three consecutive readings were collected from the same site and averaged for each participant.

SSL sampling

Before sample collection, participants were instructed to remain under standard ambient conditions (room temperature 23℃ and humidity 50%) in a cool air-conditioned room for 30 min. Sebum was collected from an approximately 4-cm^2 area at the same site 1 cm below the right knee using Sebutape. Prior to sebum collection, the collection area was wiped with a 5% saline swab and one Sebutape patch was placed on the target site. The Sebutape patch was left in place for 10 min, and then removed to a sterile centrifuge tube using curved forceps. All samples were immediately stored at −80℃ until further analysis.

Itch intensity scale for assessment of pruritus severity

Pruritus severity in each patient was evaluated by the Ameliorated Kawashima Itch Scale (Supplementary Table 1) (10), which rated itch severity on a five-point scale (0, 1, 2, 3, 4) in separate diurnal and nocturnal assessments. The pruritus score was calculated by adding the diurnal score to the nocturnal score (range, 0–8).

Sample preparation

Samples were retrieved from the −80°C freezer, and 1.5 mL of reagent mixture (chloroform/methanol) was added. The samples were vortexed and allowed to settle for 30 min. An equal volume of chloroform was then added, and the samples were vortexed and allowed to settle for 10 min. The lipid extracts were dried using a low-temperature concentrator (SpeedVac SPD131P; Thermo Fisher Scientific). Finally, the lipids were redissolved in a reagent mixture (methanol/isopropyl alcohol). Before analysis by ultra performance liquid chromatography coupled with quadrupole time-of-flight tandem mass

spectrometry(UPLC-QTOFMS), a mixture of samples was prepared for use as quality control samples for the analytical performance.

LC-MS/MS analysis and identification

LC separation was performed using a Phenomenex Kinetex 1.7u EVO C18 column (2.1 × 50 mm, 100A; Agilent, Santa Clara, CA, USA). The column was maintained at 40°C. The injected sample volume was 3 µL for each run in the full loop injection mode. The flow rate of the mobile phase was 0.5 mL/min. In the reverse-phase LC mode, gradient elution was performed with the following solvent system: (A) 50% acetonitrile (Optima™ LS/MS grade; Fisher) in water and 10 mM ammonium formate; (B) isopropyl alcohol with 10% formic acid and 10 mM ammonium formate. The gradient started with 90% A, decreased to 0% A in 11 min, was held at 100% B for 6 min, immediately returned to 90% A, and was held at 90% A for 3 min. MS was performed using a Triple TOF 5600+ (AB SCIEX, Concord, Ontario, Canada), an orthogonal accelerated time-of-flight mass spectrometer equipped with an electrospray ion source. Data were acquired in the positive and negative V-geometry mode for each chromatography separation in the LC-MS/MS analysis. The capillary voltages were set to 5500 V and −4500 V, cone gas at 50 L/h, desolvation gas at 600 L/h, and source temperature at 550°C. The scan range was *m/z* 50 to *m/z* 1200 in the full scan mode and data were collected in the IDA mode. An independent reference, Lock-mass ion, via the MS-Dial (ver. 3.70, 17 April 2019) was used to ensure mass accuracy during data acquisition.

The assigned modified metabolite ions were identified by database searches in the MS-Dial Lipidomics MSP databases(http://prime.psc.riken.jb/compms/msdial/mail.html). The chromatographic retention behavior was considered to reduce false-positive matches (11).

Statistical analysis

A multivariate analysis, comprising partial least-squares discrimination analysis (PLS-DA), was constructed to determine the distributions and identify metabolic differences between the senile pruritus patients and healthy controls using MetaboAnalyst 4.0 (http://www.metaboanalyst.ca/MetaboAnalyst/). The PLS-DA models were cross-validated using a 10-fold method with unit variance scaling. R^2 was used to evaluate the fitting condition of the PLS-DA models, and Q^2 was used to assess the predictive ability. Negative or very low Q^2 values indicated that the differences between the groups were not statistically significant. The PLS-DA models removed any variation in the X matrix that was not correlated with the Y matrix. Thus, only one predictive component was normally used for discrimination between the two classes.

Comparisons of the two groups related to the intensities of integrated regions were carried out using a two-tailed Welch's *t*-test, which was performed within MetaboAnalyst 4.0. Values of $P<0.05$ were considered statistically significant.

Results

Clinical data of patients and controls

The clinical data of the patients and control subjects enrolled in the study are listed in Table 1. All of the participants were enrolled from January 2019 to March 2019. The 20 patients with senile pruritus comprised 9 males and 11 females, and had a mean age of 69.05±6.38 years. All patients had complained of pruritus for >6 months. Dermatology examinations showed cutaneous xerosis, decrustation, or excoration in the lower limbs. The 20 control subjects comprised 8 males and 12 females, and had a mean age of 67.4±6.35 years. The two groups did not differ significantly in age ($P=0.208$) and sex ($P=0.584$).

Table 1 Clinical data of patients and controls

No. of Patients	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20	Average	SD
Sex	M	M	M	M	F	M	F	M	M	F	F	F	F	F	F	M	M	F	F	F		
Age (y)	60	65	79	71	60	62	76	68	70	70	78	60	64	63	72	69	80	70	69	75	69.05	6.38
TEWL	13.02	10.4	10.29	14.62	11.38	24.66	17.56	9.84	10.55	15.38	7.59	21.46	8.22	10.05	12.76	11.28	13.13	12.89	16.37	11.07	13.13	4.28
Pruritus Score	1	4	6	4	2	3	7	5	2	2	5	3	2	6	3	2	2	8	6	8	4.05	2.19
No. Of controls	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**	**C11**	**C12**	**C13**	**C14**	**C15**	**C16**	**C17**	**C18**	**C19**	**C20**	**Average**	**SD**
Sex	F	M	F	F	F	F	F	M	M	F	F	F	F	M	F	M	F	M	M	M		
Age (y)	75	61	65	77	61	77	72	64	73	65	65	71	63	79	71	62	61	60	66	60	67.40	6.35
TEWL	7.41	4.83	5.11	5.35	4.71	7-93	10.46	7.83	9.12	10.86	5.34	4.55	5.26	4.76	5.35	4.66	10.12	5.38	4.94	11.43	6.71	2.45
Pruritus Score	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

TEWL：Transepidermal water loss； Pruritus Score：Rated by the Ameliorated Kawashima Itch Scale

Skin barrier function

TEWL is commonly used for assessment of human skin barrier function. An increase in TEWL usually represents damage to the skin barrier (9). In this study, senile pruritus patients had significantly higher TEWL values than control subjects (13.13±4.28 versus 6.71±2.45, P<0.01; Table 1). These results suggest that senile pruritus is associated with dysfunction of the skin barrier, consistent with the symptom of xerosis commonly observed in senile pruritus (5).

SSL profiles

To understand whether SSL changes occur in senile pruritus, we analyzed the SSL profiles in the skin of the senile pruritus patients and healthy controls using LC-MS/MS. The abundance of each entity was normalized for all compounds, followed by peak-picking to extract the molecular features of the entities. A PLS-DA, as a supervised multivariate data analysis method, was used to analyze the lipids in the senile pruritis patients versus the healthy controls. Based on the lipid dataset analyses, the SSL profiles in the patient group appeared distinct from those in the control group (R^2=0.9469, Q^2=0.12092; Fig. 1). These results indicate that alterations in SSLs may be related to the development of senile pruritus.

Differences in SSLs

We detected a total of 796 SSLs by LC-MS/MS, which were classified into 25 categories. We also compared the two groups by lipid species. Based on the PLS-DA analysis and Q-value (false discovery rate) evaluation, several parameters were used to identify lipid species with significant differences between the senile pruritis patients and control subjects. These parameters included variable importance for projection >1, fold change >1.2 or <0.83, and Q-value <0.05. Based on these criteria, a volcano plot and heat map were created (Fig. 2a,b). A total of 81 lipids with significant changes were identified based on their differences between the two groups (Supplementary Table 2). These 81 SSLs belonged to 17 categories according to their biochemical features. The relative amount of each lipid class was calculated and compared between the two groups (Fig. 2c). Several main classes of lipids including diacylglycerols(DAGs), fatty acids(FAs), phosphatidylcholines(PCs), phosphatidylethanolaine(PE), phytosphingosine, sphingosines, diacylceryl-3-O-carboxyhydroxymethylcholine(DGCC), and diacylglyceryl trimethylhomoserine(DGTS) were significantly increased among the SSLs in the senile pruritus patients, while triacylglycerol (TAG) was significantly decreased.

Associations between SSL alterations and skin barrier damage

To determine whether certain SSL components are related to the impaired skin barrier function in senile pruritus patients, we analyzed the correlations of TEWL with categories of lipids. Among all lipids compared, only several ceramide (Cer) species had positive correlations with TEWL (Table 2). Specifically, levels of Cer-EOS, Cer-NDS, and Cer-NS had significant positive correlations with TEWL value.

Table 2. Correlation between TEWL and ceramide levels

Species of Cers	Total Cers	Cer-AP	Cer-BDS	Cer-EOS	Cer-NDS	Cer-NP	Cer-NS	Cer-OS
Correlation Coefficients with TEWL*	0.23336	0.061623	0.21673	0.34001	0.48352	0.08259	0.46858	0.27462
P value	0.14	0.7	0.17	0.03	0.002	0.61	0.002	0.08

*Pearson product-moment correlation coefficient was used to show the association between CER profiles and TEWL index. Note that Cer-EOS, Cer-NDS and Cer-NS in the table have significant positive correlations with the corresponding TEWL indexes ($P<0.05$).

Correlations of SSL alterations and itch severity in senile pruritus

Severe itching in senile pruritus can significantly affect the quality of life of patients. Therefore, we evaluated the correlations of itch severity with Cer levels. The correlations of SSL alterations with pruritus severity score rated by the Ameliorated Kawashima Itch Scale were evaluated. The comparative results are summarized in Table 3. Generally, sphingomyelin, Cer-NP, Cer-AS, Cer-NDS, and Cer-NS showed positive correlations with pruritus score, while Cer-BS, Cer-EODS, Cer-EOS, and Cer-AP had negative correlations, although statistical significance was not observed. Because sphingolipids were identified as important pruritogenic substances (12), the present results suggest that the significance of sphingomyelin in senile pruritus warrants further investigation.

Table 3. Correlation between Pruritus Scores and SSL

Species of SSL	sphingomyelin	Cer-BS	Cer-EODS	Cer-NP	Cer-BDS	Cer-OS	Cer-ADS	Cer-AS	Cer-EOS	Cer-NDS	Cer-NS	Cer-AP
Correlation Coefficients with pruritus scores*	0.24624	-0.02536	-0.03254	0.13395	0.037961	0.11059	0.11935	0.16527	-0.06283	0.14215	0.17252	-0.00483
P value	0.13	0.88	0.84	0.41	0.82	0.49	0.46	0.31	0.7	0.38	0.29	0.98

*Pearson product-moment correlation coefficient was used to show the association between SSL and pruritus severity（scaled by pruritus score) in senilepruritus. Note that sphingomyelin, Cer-NP, Cer-AS, Cer-NDS, Cer-NS have positive correlations with pruritus scores, while Cer-BS, Cer-EODS, Cer-EOS, Cer-AP have negative correlations, but *P* value did not reach to statistically significant.

Discussion

The pathophysiology of senile pruritus remains unclear. Cutaneous xerosis is the most common clinical feature in senile pruritus and is considered a consequence of skin aging associated with decreases in sweat and sebum production (3, 13). Dry skin is also thought to be an important factor for triggering pruritus through alterations in the barrier function of the stratum corneum (SC) (14). In humans, SSLs originate from sebum secreted by sebaceous glands and cornified keratinocytes that cover and protect the skin surface and play a role in maintaining skin moisture (15). As a result, variations in SSL composition can damage the skin barrier function. In turn, skin barrier damage may further alter SSL components

and accelerate cutaneous xerosis. Because of the complex interplay among components of the skin barrier, any changes in the skin surface condition, such as SSL composition, may be related to pruritus development. In the present study, LC-MS/MS was used to elucidate the lipid compositions in senile pruritus patients and asymptomatic control subjects.

Epidermal barrier dysfunction is strongly linked to chronic pruritus (16). Increased TEWL leads to activation of serine proteases such as SC chymotryptic enzymes by increasing the pH on the skin surface (17). Increased TEWL is also correlated with xerosis (18). In the present study, senile pruritus patients had higher TEWL values than control subjects, and TEWL value was positively correlated with pruritus severity score (data not shown). Thus, the results indicate an impaired skin barrier function in senile pruritus patients compared with asymptomatic elderly control subjects. Given that AD is an inflammatory skin disease characterized by severe itching and skin barrier damage, it is a good example for understanding the physiological role of the epidermal barrier. When the epidermal barrier function is damaged, external stimulants can enter the skin, cause inflammation, and elicit itch-inducing mediators (19). Although no significant inflammation exists in senile pruritus, it is reasonable to conjecture that the skin barrier damage in senile pruritus plays a crucial role in inducing a similar itch-scratch cycle to that seen in AD.

Alterations in SSLs have previously been reported in several inflammatory diseases, including AD and acne (15, 20, 21). In our comparisons of the lipid profiles between senile pruritus patients and healthy controls, the PLS-DA scores showed distinct SSL compositions in the two groups.

Cers are the most abundant lipid constituents among human SSLs, and comprise approximately 50% of the intercellular lipid content by mass. Changes in skin Cer contents are associated with several diseases, including AD and psoriasis (22). Cer-EOS and Cer-NS are the two main subclasses of Cers. These Cers are related to packing of corneocytes in the SC and play a crucial role in formation of an intact epidermal permeability barrier (23). In the present study, the relationships between Cers and skin barrier function were determined by Pearson’s correlation analysis. Cer-EOS, Cer-NDS, and Cer-NS showed significant positive correlations with TEWL value. These findings may provide insights into the respective roles of Cers for the skin barrier function and warrant further investigation in studies on senile pruritus.

TAG was the only main lipid class that showed a significant decrease in senile pruritus. TAG is a minor component of lamellar bodies and the extracellular matrix of the SC in healthy skin (24, 25). Reduction of TAG synthesis or increased degradation of TAG can lead to severe skin defects in humans and mice, and epidermal TAG metabolism plays a key role in maintenance of a proper permeability barrier in the skin (26, 27). Previous studies showed that certain groups of TAG are correlated with impaired barrier function in AD (28). Thus, TAG deficiency may be another contributing factor to the barrier dysfunction in senile pruritus.

Skin lipids not only play a structural role in maintaining the skin barrier, but also have a variety of biological and pathophysiological functions in the skin (29). Sphingolipids, as one of the important pruritogenic substances, comprise a complex set of lipids including sphingomyelin and Cers. The activity of sphingomyelin deacylase, an enzyme that converts sphingomyelin into sphingosylphosphorylcholine (SPC) and free fatty acid, was elevated in AD patients (30). Intradermal injection of SPC elicited hind-paw scratching in mice (31). Although the pruritus in AD is orchestrated by the complex interplay of numerous different mediators, SPC was one of the contributing factors, suggesting that lipids may be an important pruritogenic substance in chronic pruritus (16). In the present study, we observed that sphingomyelin and some Cers were positively correlated with pruritus score. Therefore, further investigations into the pruritogenic function of certain SSLs may be valuable.

Conclusions

In summary, the study has presented a comprehensive quantitative characterization of SSLs and clearly revealed that senile pruritus patients have distinct SSL profiles in their SC compared with normal healthy controls. Differences in expression of 81 individual lipids were identified between the senile pruritis patients and control subjects. Correlation analyses showed

that some SSL components were correlated with skin barrier damage. Although we cannot conclude that the changes in SSLs cause the skin itching, the results indicate that certain SSLs may be the trigger or consequence of pruritus in elderly people. Therefore, further investigations on the pruritogenic function of certain SSLs may be valuable. Further research on senile pruritus is necessary to help elderly people find appropriate treatments for senile pruritus. Future studies focusing on certain SSL components may lead to novel therapies for senile pruritus.

Study strengths and limitations

Our study has several strengths. First, it is the first analysis of SSLs in senile pruritus to date, and allows characterization of the general lipid profiles as well as subgroup comparisons between patients and control subjects. Second, we were able to improve the sensitivity of the analysis by using a new approach of independent data acquisition in LC-MS/MS, which allows comprehensive untargeted acquisition of molecular data. Third, Pearson product-moment correlation coefficient analysis was used to show the associations between SSLs and pruritus severity as well as between Cer profiles and TEWL value, thus providing a basis to identify the mechanism of lipid involvement in the skin barrier function and itching.

As one of the weaknesses of the study, we acknowledge that the small sample size led to statistically insignificant differences in some measured lipids. We are also aware that other factors, including social economic status, diet preferences, and geographic locations, may be confounders and should thus be taken into account. Therefore, larger studies with more data on patient demographics are needed to provide more definitive evidence for the pathologic changes in lipid composition in senile pruritus. Nevertheless, our study clearly demonstrates that SSLs are changed in senile pruritus. Future studies on certain SSL components toward novel therapies for senile pruritus could bring promising results.

List Of Abbreviations

SSL: skin surface lipids;

TEWL: transepidermal water loss;

LC-MS/MS: liquid chromatography coupled tandem mass spectrometry;

Cers: ceramides: DAGs: diacylglycerols; FA: fatty acids; PCs: phosphatidylcholines; PE: phosphatidylethanolaine;DGCC: diacylceryl-3-O-carboxyhydroxymethylcholine; DGTS: diacylglyceryl trimethylhomoserine; TAG: triacylglycerol

SC□stratum corneum

AD: atopic dermatitis

SPC: sphingosylphosphorylcholin□

PLS-DA: partial least squares discrimination analysis.

Declarations

Ethic approval and consent to participate: The study was reviewed and approved by the ethics committee of Peking University International Hospital. Informed consent to participate in the study was obtained from each patient and healthy person before enrolling in the study. Clearance No for Ethical approval:2018-065(BMR)

Consent for publication: All the participants had signed the consent for publication in the informed consent in our institutional consent form.

Availability of data and materials: All data generated or analysed during this study are available from the correspongding author on reasonable request.

Competing interests: No competing interest

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Authors contribution:

Xiaolei Ma: data collection and analysis

Lulu Lu, Na Gao: Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) and multivariate data analysis

Zheng Zhao: Transepidermal water loss detection

Mingru Cai: Ameliorated Kawashima itch scale detection

Gangwen Han: Clinical cases collection and experimental guidance

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Figures

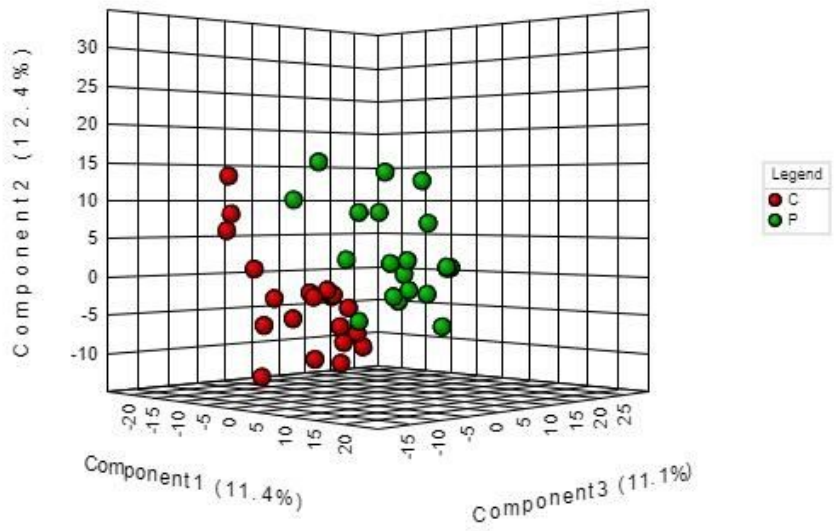

Figure 1

PLS-DA score plot of skin surface lipid (SSL) from senile pruritus patients and healthy person controls. SSL profiles of idiopathic senile pruritus (green dots) and controls (red dots) are obvious separated. R2=0.9469, Q2=0.12092.

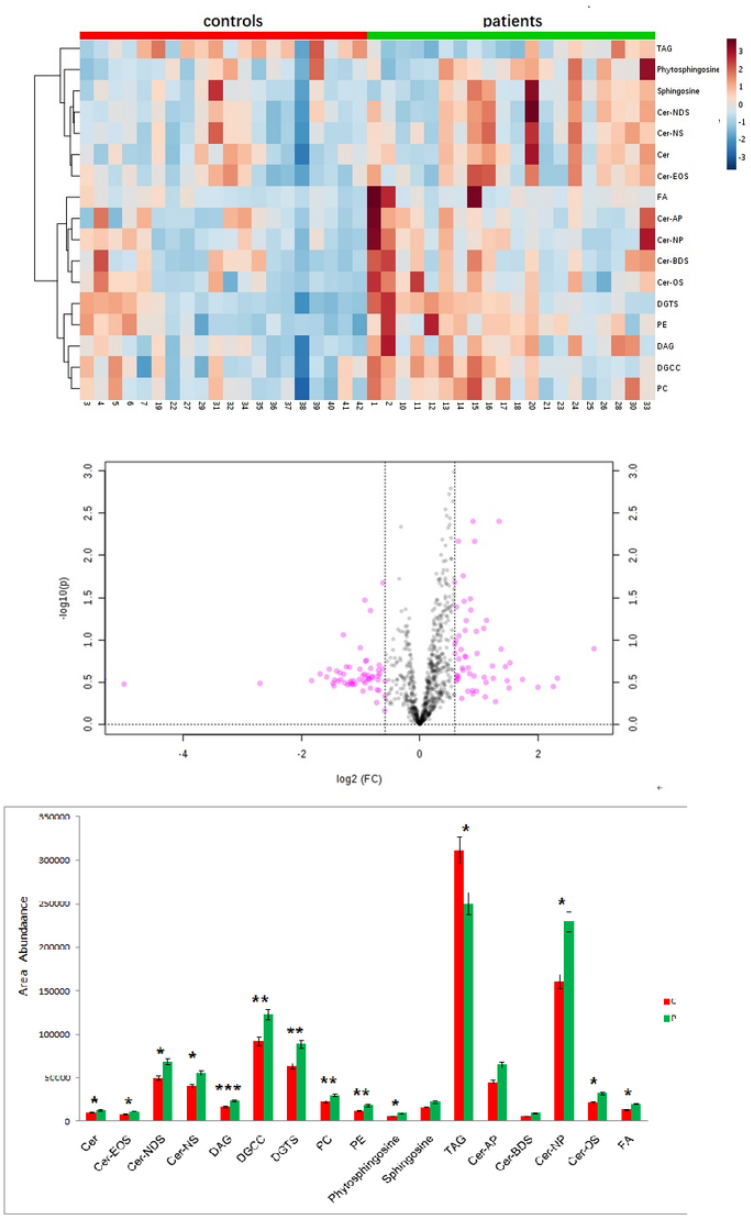

Figure 2

Identification of differential lipids and lipid metabolites between senile pruritus patients and healthy person controls. (a) Heat map of SSL.The color is proportional to the intensity of SSL changes; red color represents upregulation, and blue represents down-regulation. (b)Volcano plot of SSL. The red dot represents 1.2 fold (right) and 0.83 fold (left) of variation and P <0.05. Total 81 lipids with significant change have been identified based on their difference between two groups. (c) The comparison of 17 main class of lipids between idiopathic senile pruritus and controls. Compaired to controls, 16 main class of lipids increased and only TAG decreased in senilepruritus. Results showed that there were significantly increased levels of Cer, Cer-EOS, Cer-NS, DAG, DGCC, DGTS, PC, PE, Cer-NP, Cer-OS, FA phytosphingsines and decreased level of TAG, while there were no significant change of the relative amount of Cer-NP, Cer-BDS and sphingosines. *** P 0.001, ** P <0.01, * P <0.05.

Supplementary Files

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- supplementarytable1.pdf
- SupplentmentTable2.pdf