Evidence of defective fattyacidome and aminoacidome in sebaceous and non sebaceous skin areas in atopic dermatitis

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BACKGROUND

Atopic dermatitis (AD) is a composite disease characterized by derangement of the skin permeability barrier (SPB). The lipids in the stratum corneum (SC), i.e. ceramides (CERs), free fatty acids (FFAs) and cholesterol account for most relevant for the skin barrier function. Little is known about the role played by the sebaceous gland (SG) activity in the SPB integrity in AD.

OBJECTIVES

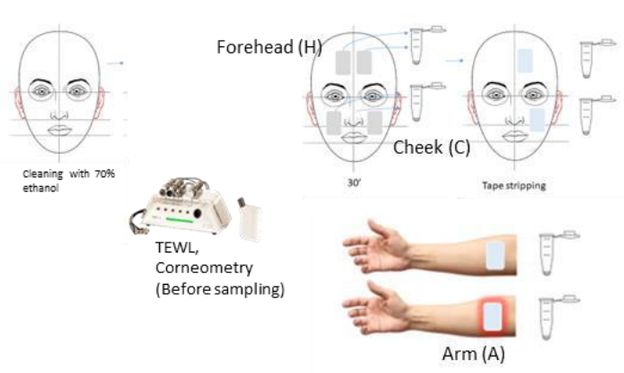
To investigate lipidomics profiles of sebaceous-type and epidermal-type FFAs, together with levels of squalene, cholesterol, triglycerides (TGs), and wax esters (WEs) in sebum and SC. To integrate sebum lipidomics with SC aminoacidome.

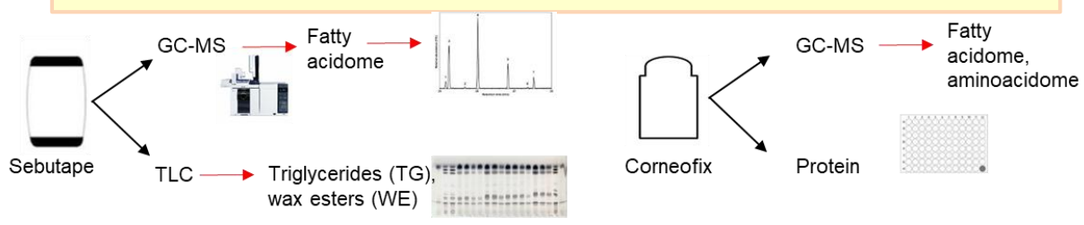
METHODS

Integrity of SPB was verified on the sampling areas by assessing TEWL and skin hydration (corneometry). FFAs, squalene, cholesterol, and vitamin E of sebum and SC, as well as aminoacids in the SC, were quantified by gas chromatography – mass spectrometry (GCMS). Total TGs and WEs in sebum were determined by thin layer chromatography (TLC). Results were expressed as average ± SD. Kruskal-Wallis test followed by Dunn multiple pairwise comparisons (XLSTAT) were used to compare the effects of different cases. Results were significant at $p \leq 0.05$. The Multivariate ANOVA-simultaneous component analysis (ASCA) was used to determine the effect of the investigated factors.

STUDY POPULATION

- **44 Controls (hC)** — F 27 (Age 35,7±16,2); M 17 (Age 35,5±14,1)
- **54 Atopic Dermatitis (AD):**
  - 20 (face not involved, fnAD) — F 11 (Age 30,4±12,9); M 9 (Age 28,4±9,08)
  - 34 (face involved, fyAD) — F 16 (Age 32,1±14,2); M 18 (Age 30,4±12,0)





Units: Sebum lipids (pmol/2*tapes); SC lipids and aminoacids (pmol/µg protein)

RESULTS

The characteristics of the studied groups: Age, Eczema Area and Severity Index (EASI), and sebum excretion rates (SER)

Group	Label	Count	Age	EASI	SER (H)	SER (C)
Healthy controls	**hC**	**44**	**35,6±15,2**	**NA**	**5,04±1,91**	**5,26±2,01**
Atopic dermatitis Face no (fn)	**fnAD**	**20**	**29,5±11,1**	**28,7±10,8**	**4,93±1,64**	**4,65±1,55**
Atopic dermatitis Face yes (fy)	**fyAD**	**34**	**31,2±12,9**	**36,4±10,6** #	**3,52±2,13** °°°#	**3,60±2,87** °°°

Tab.1 °Differences between controls and AD subgroups and #differences between AD subgroups (Bonferroni corrected significance level: 0,0167; [1]p≤0,0167, [2]p≤0,00167; [3]p≤0,000167). The 3 groups had comparable age and F/M balance. EASI was higher in fyAD. SERs were significantly lower in fyAD.

ASCA models of sebum on forehead and cheek

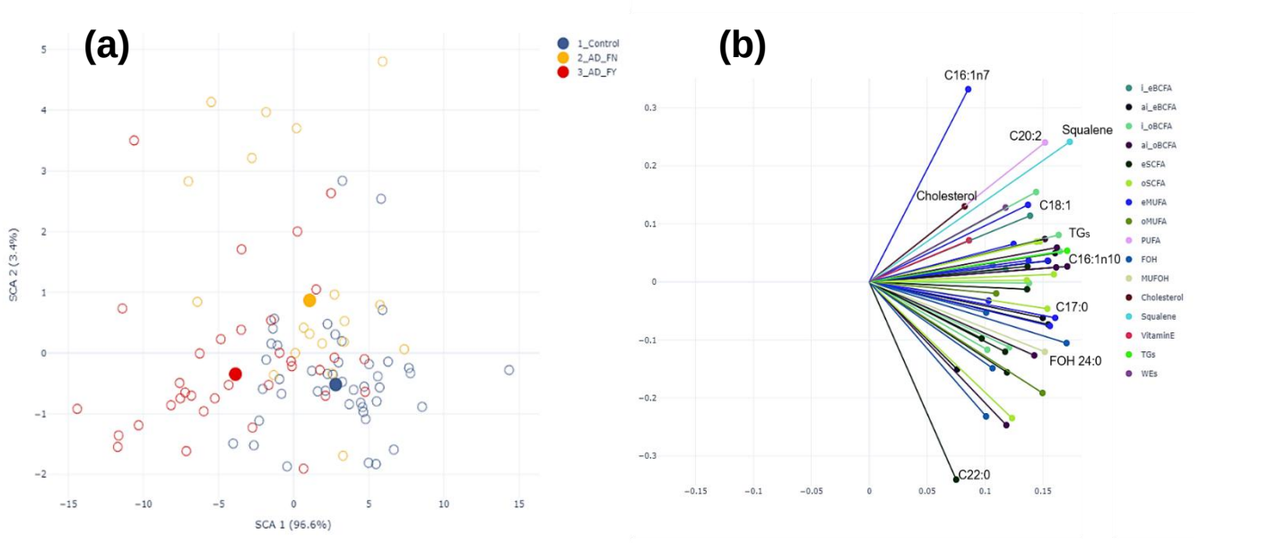


Fig.2 SCA analysis on the effect matrix for pmole/2*tapes of sebum lipids for hC, fnAD and fyAD conditions investigated in sebum from SGR areas. (a) Scores plot after projection of the residuals onto the space spanned by the significant SCA1 and SCA2 when considering hC, fnAD and fyAD conditions. (b) Variables loadings on SC1 and SC2. The significant variables are coloured according to the lipid species/classes described in the legend. The SCA analysis shows that the majority of hC and fnAD subjects have positive values of SCA1. Most fyAD subjects had negative values of SCA2. The latter group was characterized by significantly lower levels of nearly all sebum components.

ASCA models of stratum corneum on forehead, cheek, and arm

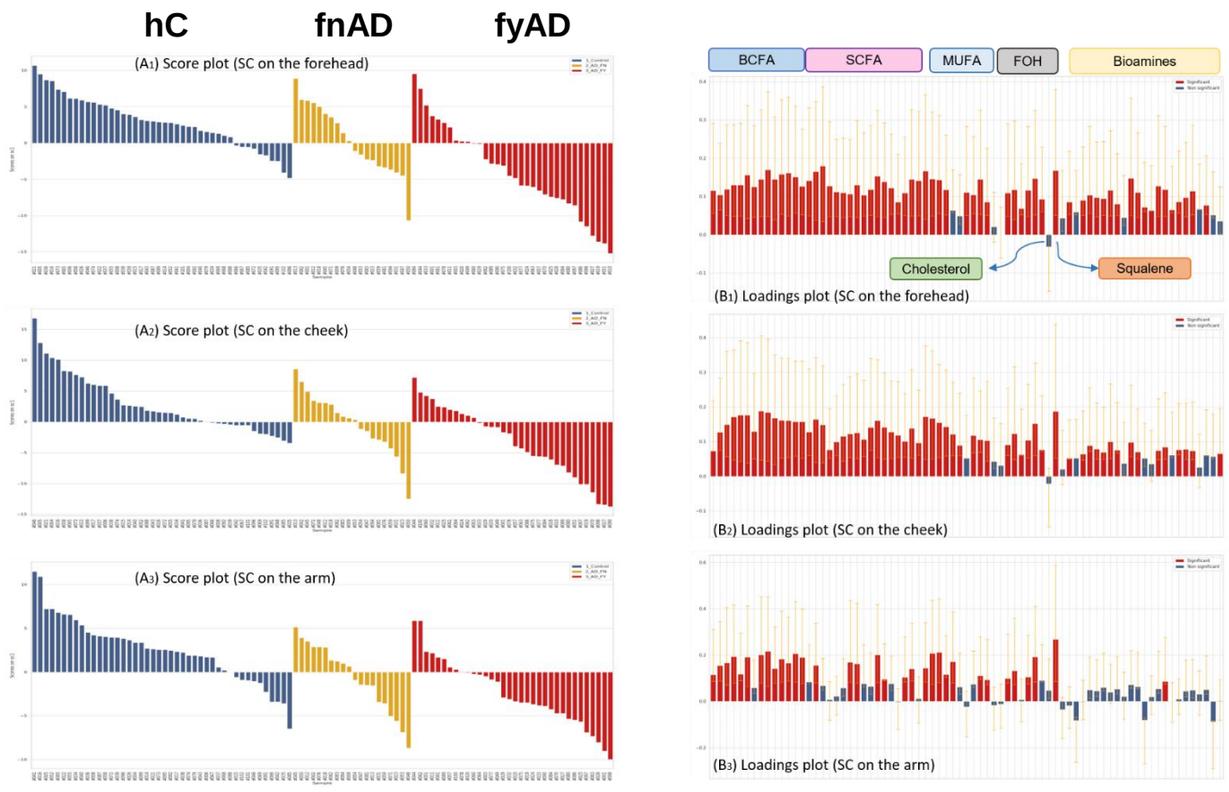


Fig1. SCA analysis on the effect matrix for lipids (pmole/µg protein) investigated in SC from sebaceous gland rich (SGR) areas (foreheads, and cheeks) and SG poor (SGP) area (arm) in hC, fnAD, and fyAD conditions. (A1, A2, A3). Scores plots after projection of the residuals onto the space spanned by the significant SCA1 for forehead, cheek, and arm, respectively. (B1, B2, B3) Variable loadings on SC1, together with their confidence interval, of the respective scores plots (A1, A2, A3); red and blue bars indicate significantly and not significantly contributing descriptors, respectively. The results indicated that the profiles of lipids and bioamines/aminoacids determined in SC from SGR areas discriminated clearly between hC and AD conditions. Both metabolites' domains were depleted in SGR areas of AD. In contrast, the SC sampled from SGP area of AD subjects was deficient in lipids rather than bioamines/aminoacids.

Measurements of SER, and biophysical parameters/protein amount in the SC of hC, and AD patients (fn and fyAD)

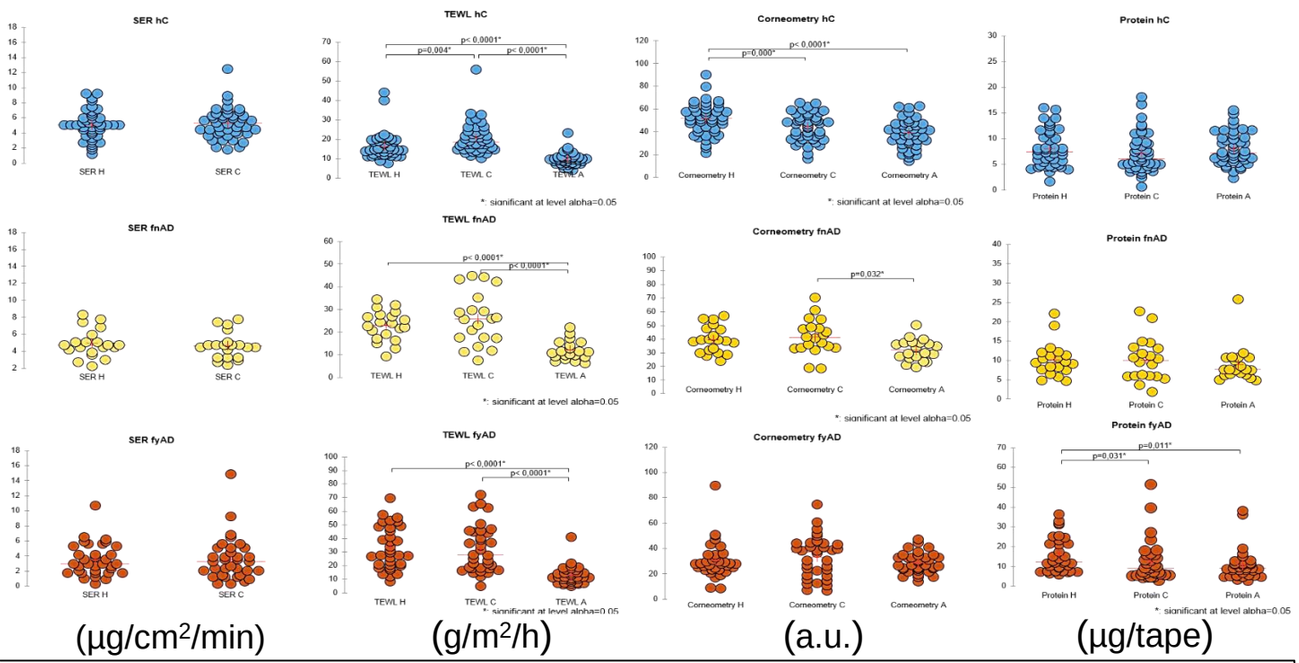


Fig.3 TEWL was significantly lower in the SGR areas the three groups compared to SGP arm surface. In contrast, difference of TEWL between H and C was significant in the hC group only. Similarly, corneometry was significantly different between H and C in the hC group. Differences in corneometry between SGR and SGP in the AD patients was weakened or absent. Protein levels were significantly higher in AD SC (statistics not shown). Protein content in the SC was comparable in the three areas in hC and fnAD groups. In contrast, extent of protein perturbation was different among the 3 areas in fyAD, with forehead associated with higher protein amounts.

DISCUSSION/CONCLUSIONS

The overall results demonstrated deranged sebogenesis in adult AD. Declined sebometry and disruption of the SBP were associated with decreased levels of lipids of both sebaceous type (squalene, MUFAs, BCFAs) and epidermal types (SCFAs, C24:0) In particular, squalene was significantly depleted in both SGR and SGP areas. Bio-signature of sebum in the SC in association with aminoacidome and skin physical properties may serve the better definition of AD phenotypes.

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