

## Article

# Skin Condition and Behavioral Factors in High-Performance Athletes Based on the Example of Professional Dance—An Explorative Pilot Project

Eileen M. Wanke <sup>1,\*</sup>, Olga L. Zimmermann <sup>1</sup>, Mike Schmidt <sup>2</sup>, Alexandra Wallner <sup>3</sup> and Tanja Fischer <sup>1,3</sup>

<sup>1</sup> Institute for Occupational, Social and Environmental Medicine, Johann Wolfgang Goethe University Frankfurt am Main, Theodor-Stern-Kai 7, House 9, 60590 Frankfurt am Main, Germany

<sup>2</sup> Faculty of Human Movement Sciences, Institute of Sport and Exercise Medicine, University of Hamburg, 20146 Hamburg, Germany

<sup>3</sup> Skin and Laser Centre Berlin, Richard-Strauss-Str. 27, Grunewald, 14193 Berlin, Germany

\* Correspondence: wanke@med.uni-frankfurt.de; Tel.: +49-69-6301-6650

**Abstract:** The high work-related loads on the skin of dancers is the result of numerous factors. While initial studies have looked at the consequences of exposure, information on skin condition is still completely lacking. This study includes for the first time an analysis of the skin as well as the relevant skin care behaviour. **Methods:** A total of  $n = 35$  professional dancers (PT) underwent skin analysis (transepidermal water loss, TEWL; moisture content and oil level) as part of a dermatological examination. This was done at different work load periods (phase of increased demands and resting phases, T1 and T0, respectively). **Results:** Acne (17.1%), herpes labialis (8.6%), and allergic rhinitis (14.3%) were among the most common pre-existing conditions. Low moisture contents and oil levels of the skin were found in selected localizations. TEWL index values were normal. There were no significant differences in measured values between T0 and T1. Subjects with skin lesions at rest showered significantly more often than their unaffected counterparts. Inflammation was particularly frequent after hair removal, especially in the intimate area (40.6%). **Conclusions:** Occupational exposures appear to be reflected in the results. However, studies with larger groups are needed to verify these results.

**Keywords:** professional dance; skin condition; skin analysis; skin health care; skin health behaviour



**Citation:** Wanke, E.M.; Zimmermann, O.L.; Schmidt, M.; Wallner, A.; Fischer, T. Skin Condition and Behavioral Factors in High-Performance Athletes Based on the Example of Professional Dance—An Explorative Pilot Project. *Appl. Sci.* **2023**, *13*, 1297. <https://doi.org/10.3390/app13031297>

Academic Editor: Jongsung Lee

Received: 31 December 2022

Revised: 14 January 2023

Accepted: 16 January 2023

Published: 18 January 2023



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## 1. Introduction

Professional dance is a combination of high-performance sport and performing art form [1]. The work tool of dancers is their own body. There are no conventional work tools to ease the strain, as it is common in other professions [1]. The work-related stresses therefore have a direct effect on the dancing body, with protective measures almost lacking. Health problems that occur due to work-related activities are of particular relevance, as they entail measures in behavioural and environmental prevention, which fall under occupational safety, taken care of by the employer [2,3]. In addition to the musculoskeletal and cardiovascular system, the skin is exposed to numerous work-related noxae, which in this combination are specific to the professional dance sector [4–10]. From a dermatological point of view, beautiful skin is only possible in the long term if it is kept healthy. This includes appropriate care on the one hand and the avoidance of skin-damaging noxae on the other. Initial studies from the field of dance point to the consequences of high levels of stress in the context of the work process [4–6]. Zahn et al. [4] were able to show that all examined dancers had work-related dermatological changes on their feet that were characteristic of the dance style. These were observed independently of the stress phase. Furthermore, it could be shown that classical dancers were significantly more frequently affected by dermatoses than dancers of other styles [5,7]. The changes described were partly

gender-specific [4,6]. For example, significantly more females developed perioral dermatitis and xerosis cutis in the extremities compared to their male colleagues. A dependence on the intensity of exercise was also described [5,6].

The first studies described above examined the skin-related effects of work-related stress in the context of working as a professional dancer. However, there has been a lack of evaluations on skin condition and the handling of one's own skin (skin care behaviour, removing make-up, shaving, etc.). These aspects are important, however, because one's own behaviour in dealing with the skin, such as the quality of skin care, can have a potentially favourable or preventive effect on the development of work-related skin changes in professional dance. Here, skin condition analysis represents an increasingly relevant method for the scientific assessment of skin health at the interface between cosmetics and dermatology [11]. Therefore, it can potentially also be considered an important parameter in the assessment of workplace hazards. In particular, transepidermal water loss and the moisture content of the skin should be mentioned here [12]. In order to be able to take preventive measures to improve the skin stressed by the occupational activity, it is initially important to assess the aspects of skin condition and the occupational extent with the skin in addition to other influencing factors (e.g., smoking, alcohol, sleep behaviour). Furthermore, it is important to find out whether work-related influences on the skin can be made measurable with existing options. For this reason, the aim of the present study was to assess skin condition within the framework of a skin analysis with regard to moisture content, oil level, and transepidermal water loss in two different work load periods as well as an analysis and evaluation of skin care behaviour and other influencing factors in professional dance in the sense of a pilot project.

## 2. Materials and Methods

This descriptive study design enabled us to collect data from two parts. Part A comprised a questionnaire and part B a skin analysis, and was conducted at two time points (T0 and T1; see below).

### 2.1. Part A: Questionnaire

A questionnaire was used to collect sociodemographic data and a general and specific dermatological history. The questionnaire used was a modified form of the Nordic Occupational Skin Questionnaire NOSQ-2002 from the National Research Centre for the Working Environment, which was created and modified in co-operation with the Skin and Laser Centre Berlin-Potsdam [13]. Furthermore, supplementary questions were added on the basis of the employee questionnaire of the prevention campaign "Skin" of the Federal Accident Insurance Fund from 2007 [14]. The questionnaire included questions on the following aspects:

- Basic sociodemographic data (height, weight, age, gender);
- Anamnestic information on general and dermatological previous diseases as well as the regular intake of medication;
- Aspects of stimulant consumption (nicotine, alcohol);
- Specific history of the subjects' allergies and atopic diseases;
- Questions on skin and hair care (for example, showering habits and depilation methods).

### 2.2. Part B: Skin Analysis Parameters

The skin analysis was carried out by the Multi Skin Test Center MC 900 and the software Complete Skin Investigation CSI from Courage + Khazaka electronic GmbH (Cologne, Germany). The parameters "moisture", "oil level", and "TEWL" were recorded in the "individual measurement" programme. The classification and evaluation of the results were conducted with the reference values provided by the manufacturer, and had been determined on the basis of scientific studies. These values were conducted under the following room conditions: room temperature of 20 °C and humidity of 40–60% [12]. After

each measurement was taken, the probes were cleaned and disinfected with a soft cloth as recommended by the manufacturer.

### 2.2.1. Measurement of the Moisture Content

The above-mentioned device works according to a capacitive measuring principle, which measures the water content in the stratum corneum on the basis of the electrical conductivity (capacitance) (Corneometer® method). The higher the water content in the stratum corneum, the higher the electrical conductivity and the higher the corresponding measured value. This method is one of the most frequently used methods for measuring skin moisture [15,16]. The probe used for this measurement is the Corneometer® CM 825 from Courage + Khazaka electronic GmbH. The measuring probe was vertically pressed onto the skin and left there for a few seconds as indicated in the instructions for use.

For the interpretation, the reference values given by the manufacturer were used in relative values from 0 to 99. The boundary between dry and sufficiently moist skin has also been stated at a relative value of 40 in the literature [17]. Nevertheless, the values given by the manufacturer and shown in Table 1 were used as a reference in the present study.

**Table 1.** Reference values for skin analysis.

Aspect	Localisation of the Measurement and Values		
<b>Moisture content</b> (in relative values from 0–99 [12].	<b>Forehead, cheek, upper body</b>		
- Very dry	<30		<b>Hand</b> <5
- Dry	30 to 60		5 to 25
- Sufficiently moist	>60		>25
<b>Oil level</b> (in relative values from 0–99) [12].	<b>Forehead</b>	<b>Cheek</b>	<b>Hand</b>
- Dry/Low Fat	<40	<30	<5
- Normal	40 to 70	30 to 65	>5
- Greasy	>70	>65	Not specified
<b>TEWL index values</b> as relative values from 0–20 [12].		<b>Value</b>	
Interpretation aid			
- Very healthy skin condition		0 to 4	
- Healthy skin condition		5 to 9	
- Normal skin condition		10 to 12	
- Stressed skin		13 to 16	
- Critical skin condition		17 to 20	

### 2.2.2. Oil Level Measurement

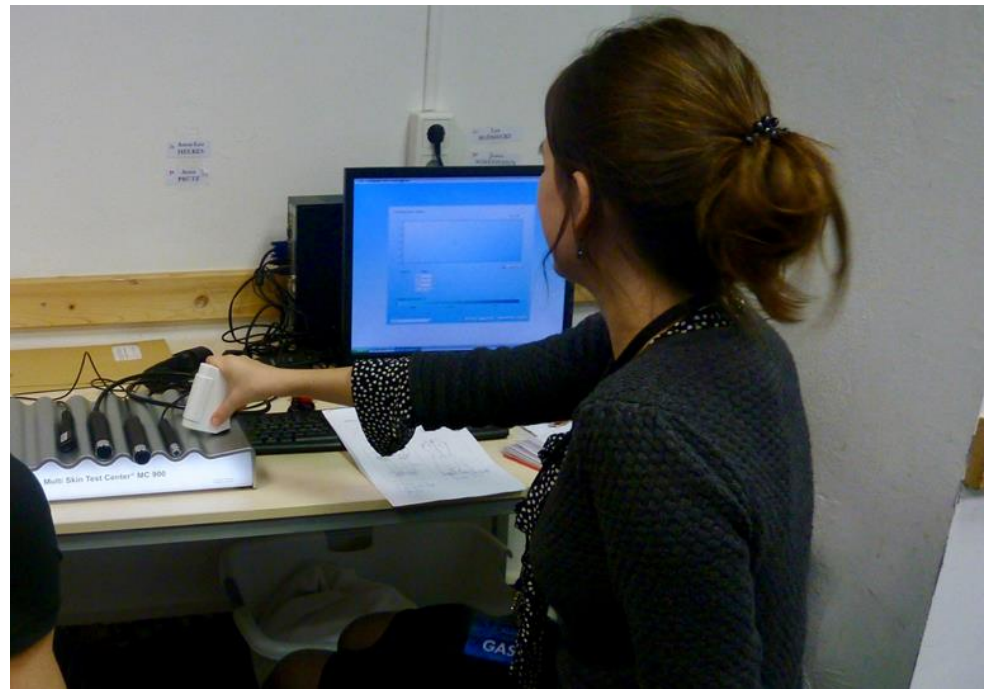
The measuring probe used to measure the oil level (Sebumeter® SM 815 by Courage + Khazaka electronic GmbH) works with the photometric measuring principle, which measures the light transmission of a 0.1 mm-thick matt plastic measuring tape [12]. The photometric principle is a frequently used and recognised principle for measuring the fat content of the skin [18].

First, a zero adjustment was carried out (the measuring cassette was pressed into the measuring shaft for a few seconds until a zero adjustment was reached, cf. Figure 1). For the subsequent measuring phase, the probe was pressed for 10 s onto the skin to be analysed. To keep the pressure constant, the device works with a 4 Newton spring. Finally, the probe was held in the measuring shaft and the changed light transmission of the measuring tape was determined as a measure of the fat content of the skin. For each new measurement, the measuring strip was then transported in the measuring cassette by means of a pusher. The values were interpreted using the manufacturer’s reference values in Table 1.

### 2.2.3. Measurement of Transepidermal Water Loss (TEWL)

To measure the TEWL index value, the measuring probe Tewameter® TM 300 from Courage + Khazaka electronic GmbH was used. A TEWL index value is determined by means of the “open chamber” principle. The water evaporating from the skin surface enters the probe and a density gradient is created, which is measured by two pairs of sensors [12]. This process takes 15 s. The probe is pressed flat and precisely onto the skin surface during the measurement. The reference values of the manufacturing company for

the determined TEWL index values from 0 to 20 shown in Table 1 were used to interpret the measurement results.



**Figure 1.** Carrying out the skin analysis on professional dancers.

### 2.3. Participants

A professional dance ensemble was recruited for voluntary participation ( $n = 35$ ) with the following inclusion criteria applied:

- All dancers signed written declaration of consent;
- All dancers were at least 18 years old;
- All dancers were employed;
- All dancers were without an injury that results in or has resulted in a restriction of the ability to work (last 8 weeks).

### 2.4. Course of the Study

Before starting the present study, a pre-test was conducted with adult ballet teachers ( $n = 8$ ). There were neither comments nor required changes regarding the methods. Subsequently, the recruitment for the present study took place over a total of two study days:

- T0: The first examination round took place immediately after the average 3-week, training-free recovery period (T0).
- T1: Examination during a phase of increased stress with training sessions, rehearsals, and daily performances.

A positive ethics vote was obtained before the start of this study which has been approved by the Ethics committee of the Department of Medicine of the Charité-Universitätsmedizin Berlin (EA4/120/14). Contact was made through the ballet director of the theatre. Participation in this study was on a voluntary basis. The examinations took place during working hours. Before the study began, the participants were informed in detail about the study procedure in an oral presentation for the whole group. Informed consent was obtained from all subjects involved in the study. The first time point (T0) for the skin analysis took place in appropriately prepared rooms in the theatre which were provided for the study phase. The subjects received the questionnaires individually in their preferred language (German or English) and were subsequently examined. The times for the examinations

were chosen during the current working day at the theater so that rehearsals or training sessions were disturbed as little as possible and at the same time the dancers had as much rest as possible. The results were communicated to the dancers after each examination and possible diagnostic or therapeutic measures were pointed out at this point. A paper version of the questionnaire was collected before starting the second examination. The subjects were individually examined. All examinations were carried out by one examiner. At T1, the second dermatological examination was done and the questionnaires distributed at T0 were collected. The first diagnostic and therapeutic consequences of the skin findings were presented and discussed with the participants.

At T0, the oil level and TEWL were determined in the three locations of the right cheek, forehead, and dorsal side of the right hand. At time T1, the moisture content of the skin in the above-mentioned locations was determined in addition to these parameters. For technical reasons, this had not been possible at T0 (defective probe).

After the analysis was completed, another meeting was held with all participants in the study. The general results of the study and the resulting recommendations were presented. Following this, there was an opportunity to receive individual dermatological consultations, which were conducted by experienced dermatologists from the Skin and Laser Center Berlin. The study was concluded with individual written evaluations for each participant, which could be used for further treatment if necessary.

### 2.5. Data Preparation and Evaluation

The data were processed, statistically analysed, and graphically presented using the programme Microsoft Excel for Mac 2011 and IBM SPSS Statistics 21. Frequencies (absolute and relative) were determined for the nominal data and analysed inferentially using the chi-square test and adjusted depending on the application requirements (e.g., Fisher's exact test). The metric data were calculated via mean values and standard deviations. The significance level was set at 5% and all comparisons were made under two-tailed testing. Due to the small number of male participants ( $n = 9$ ), a gender-specific analysis was not carried out.

In this study, a cohort took part that had been examined within the framework of the previously published study. Hence, the sociodemographic data match [5,6].

## 3. Results

### 3.1. Cohort Characteristics

$n = 35$  professional dancers (m:  $n = 9$ ; w:  $n = 26$ , 19–39 years) volunteered for this study. The average age was  $25.5 \pm 4.1$  years. The participants had an average height of  $178.3 \pm 6.1$  cm and an average weight of  $64.3 \pm 10.2$  kg (BMI:  $20.1 \pm 1.9$ ).

### 3.2. Part A: Results of the Survey

The average sleep duration was  $7 \pm 0.9$ . Of the dancers, 25% indicated that they smoke, 71.4% drink alcohol occasionally, 18.5% ( $n = 5$ ) take oral contraceptives, 22.6% take painkillers, and 5.7% take medication for thyroid disorders. Acne and herpes labialis were among the most common skin-related pre-existing conditions.

Among the general pre-existing conditions, allergic rhinitis was the most frequent (Table 2). The following substances were stated as allergenic: pollen/grasses, pome fruits/nuts, animal hair, and house dust. Occasionally, test persons reported allergic reactions to eyelash glue, plasters, nickel, and hair dye.

No correlation was found between consumption behaviour and abnormalities in the area of the skin ( $p = 0.357$ ). The same applies to nicotine consumption ( $p = 0.228$ ).

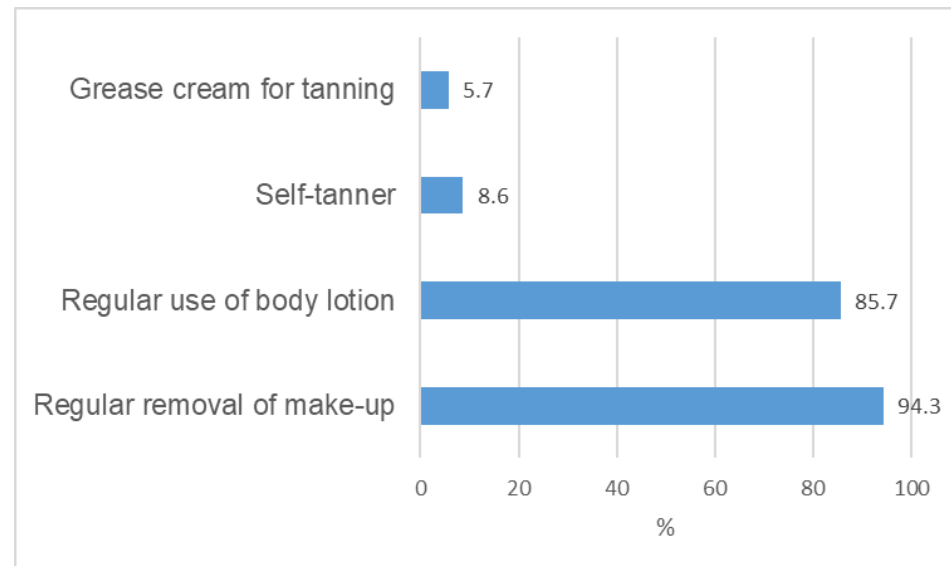
**Table 2.** Skin-related and other pre-existing conditions of the participants as self-assessment.

Skin-Related Condition or Disease ( <i>n</i> = 35)	%
Atopic	8.6 (3)
Acne	17.1 (6)
Eczema	2.9 (1)
Herpes labialis	8.6 (3)
Skin fungi	5.7 (2)
Allergies	2.8 (1)
<b>General Pre-Existing Conditions (<i>n</i> = 35)</b>	<b>% (<i>n</i>)</b>
Sleep disorders	8.6 (3)
Eating disorders	2.9 (1)
Depression	2.9 (1)
Allergic rhinitis	14.3 (5)
Allergic asthma	2.9 (1)

### 3.2.1. Skin Care Behaviour

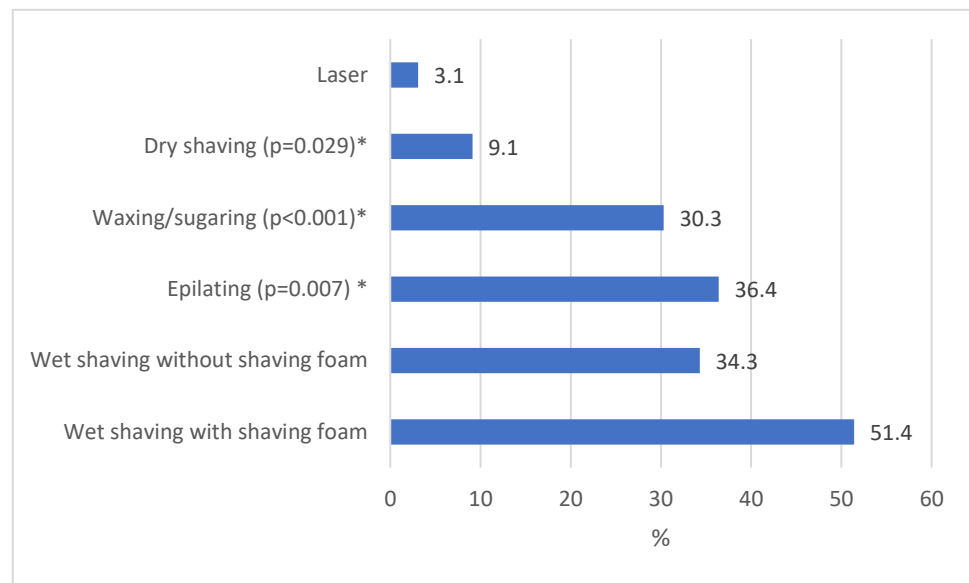
Of the dancers, 66% indicated that they shower “lukewarm to warm”, while 34% indicated “very warm to hot”. The shower duration was reported to be 8 min on average. The interval between the end of the training and the start of the shower was 14.6 min and the interval between the end of the performance and the start of the shower was calculated as 10.7 min.

Figure 2 shows aspects of the skin care behaviour of the dancers examined. While not for all dancers, regular make-up removal was part of the routine, and despite the preference for very warm or hot water temperatures when showering, only 86% stated that they regularly use a nourishing body lotion.

**Figure 2.** Selected aspects regarding skin care behaviour in professional dance (*n* = 35).

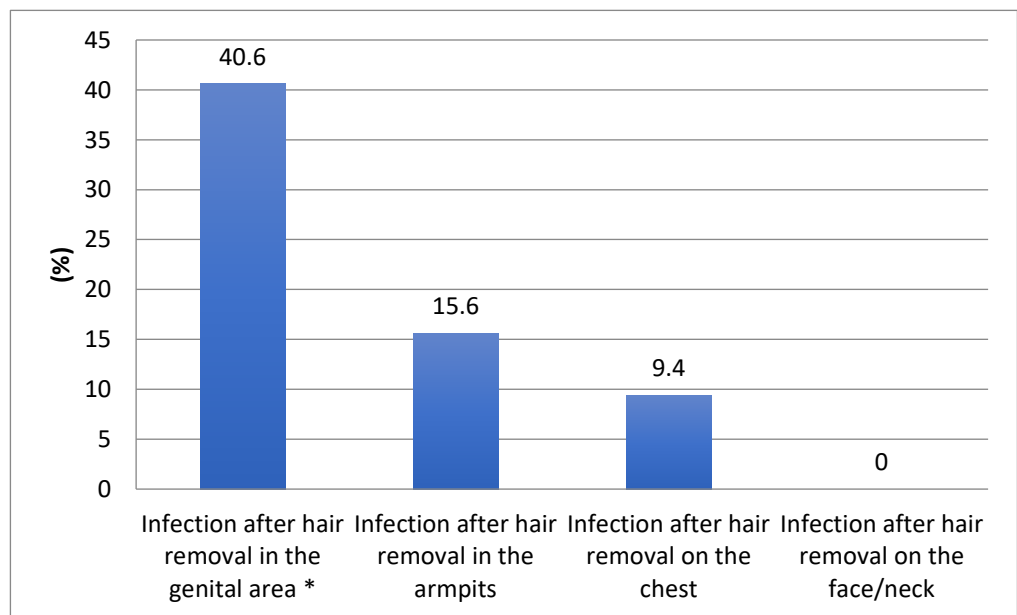
### 3.2.2. Hair Removal

Of the dancers, 91.4% stated that they regularly remove unwanted hair from the armpit area, followed by 82.7% who stated that they remove intimate hair, with 77.1% hair from the legs, 17.1% from the chest, and 5.7% from the back. Figure 3 shows the hair removal method used. The majority of dancers use wet shaving with (51.4%) or without (34.1%) shaving foam.



**Figure 3.** Hair removal methods in professional dancers ( $n = 35$ ). \*:  $p < 0.001$ .

Figure 4 shows the consequences after hair removal by shaving. Infections after hair removal (predominantly shaving) in the intimate area represent the most frequent consequences.



**Figure 4.** Skin-related consequences after hair removal in professional dancers ( $n = 35$ ). \*:  $p < 0.001$ .

### 3.2.3. Use of Wigs

Overall, all professional dancers indicated that they regularly wear wigs in performances for an average of 263.2  $\pm$  49.1 days per year (MW  $\pm$  SD). For this purpose, 58.8% of the professional dancers wear their long hair twisted into small snail-shape hair portions fixed to the scalp with pins on a daily basis. This is a method of fixing long hair under a wig.

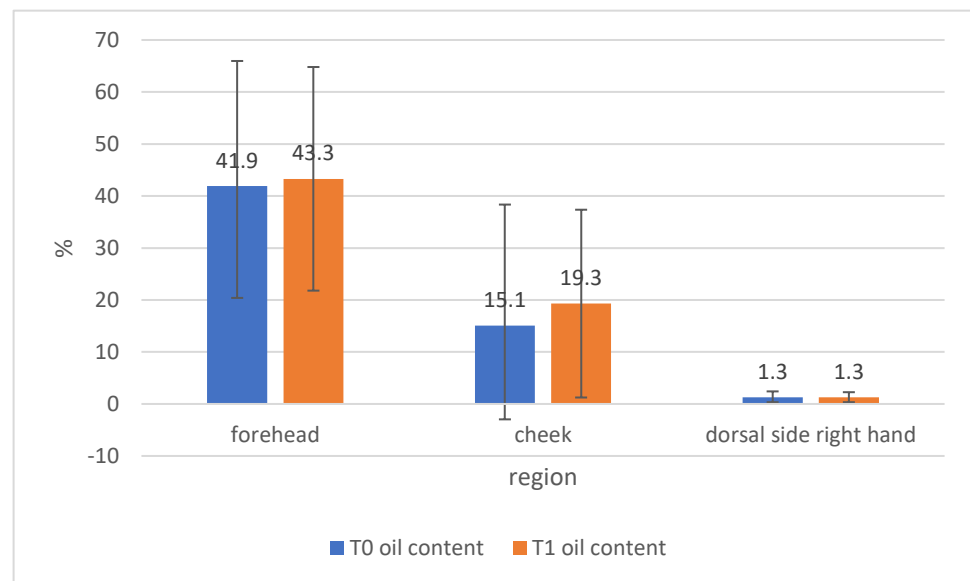
### 3.3. Part B: Skin Analysis

#### 3.3.1. Moisture Content of the Skin

For the moisture content of the skin, values were recorded in the stress test which, in the localisation of the cheek on the right (43.3) and forehead (43.0), were classified in the category “dry”, and, on the dorsal side of the hand (38.4), in the category “sufficiently moist”.

#### 3.3.2. Oil Level of the Skin

The data collected in the skin analysis regarding the oil level of the skin at both time points showed values in the area of the cheek as well as on the dorsal side of the hand that were to be rated as “dry”. In the area of the forehead, the mean value for the fat content was to be classified as “normal”. No significant changes in the values were observed between the two time points T0 and T1 (Figure 5).



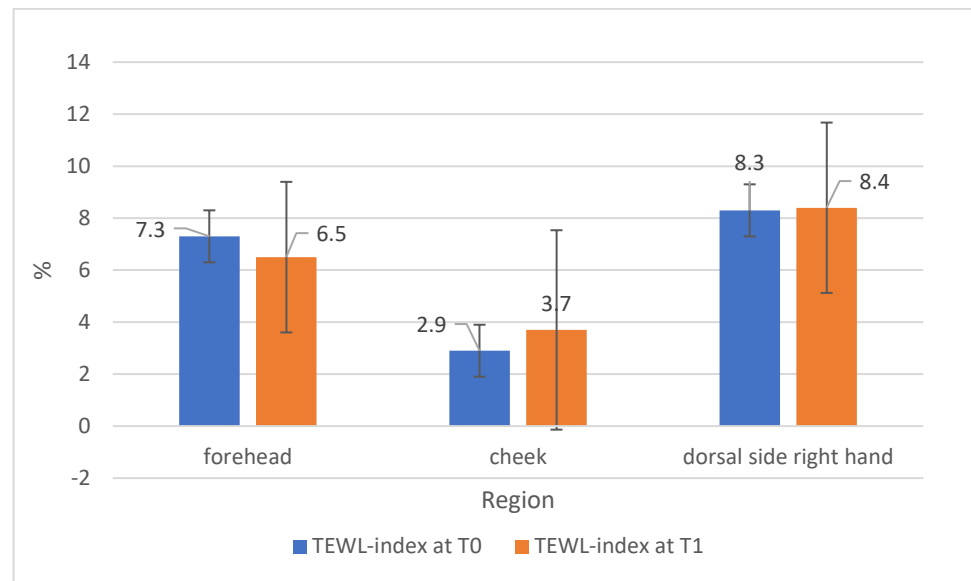
**Figure 5.** Oil content of the skin in professional dancers at T0 and T1;  $n = 35$ .

#### 3.3.3. Transepidermal Water Loss

The analysis of the collected data regarding transepidermal water loss (TEWL indices, Figure 6) showed normal to very healthy values in all localisations and at both time points, which were below the limit of stressed skin of 13. The analysis to compare the data at the respective examination times did not reveal any significant differences.

Correlations between the occurrence of dry skin and showering behaviour could be proven ( $p = 0.037$ ). The test persons with skin problems (Table 1) showered an average of  $9.8 \pm 5.2$  times per week and thus significantly more often than dancers without any information. The water temperature, and time intervals between the end of the training or performance and the start of the shower in relation to the degree of moisture and fat content of the skin were not significant.





**Figure 6.** TEWL index values of the professional dancers at time points T0 and T1;  $n = 29$ .

## 4. Discussion

### 4.1. Skin Analysis

The moisture content of the skin is an indicator of skin health. For example, it is low when observing clinically dry skin in subjects with atopic dermatitis [19]. In addition, by measuring the moisture content of the skin, minimal skin lesions and irritations (for example, caused by surfactants) can also be detected [20]. The dry skin on the cheek and forehead of the dancers may indicate that the skin is considered occupationally stressed. It could thus be impaired in its function. Similar observations were made for the oil level of the skin: in the area of the cheek and the dorsal side of the hand, reduced “dry” values were found in the oil level at T0 and T1, while the oil level on the forehead could be classified as “normal”. As a rule, the oil level of the skin only decreases with age. Reduced values are thus often only found from an age exceeding 70 years [21]. These conspicuous values in the younger dancers are all the more astonishing. One explanation is that sweat and frequent showering dissolve the lipids from the horny layer and thus cause a defect in the skin barrier [22].

The TEWL index values showed normal to very healthy values in all areas examined and at both time points. In preparation for the study, it was assumed that professional dancers perform an activity at least comparable to wet work. As already mentioned many times, this is one of the most important damage factors to the skin in occupational medicine [23,24]. The damage caused by work in a humid environment leads to a skin barrier disorder and can be measured, for example, as an increase in the TEWL index value [25]. Furthermore, TEWL index values can indicate a predisposition to atopic dermatitis [26,27]. Therefore, it is surprising that these values were not elevated in the professional dancers. This may be due to the fact that the studies were conducted during a short break in training and were thus influenced by the professional dancers’ own sweat production. In addition, the feet, which may be exposed to a humid environment for a longer, relevant period of time, were not examined. The inconspicuous result in the professional dancers in this regard is consistent with the data on atopic diathesis.

The skin analysis did not show significant differences between time points T0 and T1, neither in moisture or oil content nor in the measurement of TEWL. These measurement results of the TEWL measurement support the fact that a complete regeneration of the skin of professional dancers may not be measurable during the 3-week training and performance break. As a longer break in the middle of a season is not realistic, other measurement methods may be needed to prove the stress on the skin. Alternatively, this examination

would have to be carried out directly after the summer break in order to completely exclude work influences. Furthermore, it would have been of benefit to complement these measurements with a dermatological evaluation from a professional dermatologist in addition to self-assessment questionnaire.

#### 4.2. Questionnaire

Acne as one of the most common dermatological diseases was mentioned as the most common of the skin-related and other pre-existing conditions of the participants as self-assessment. Already in other studies seborrhoea was found as a predisposing factor in professional dancers [5]. Explanations for these results could be the change in the acid mantle due to work-related sweating. Another possible explanation could be the oil-based body make-up or the hygienic aspects or the combination of all aspects [28,29].

According to Diepgen, a detailed anamnesis regarding atopic diseases of the affected person and his/her family may be necessary in the case of work-related skin exposure [23]. This is supported by the fact that the atopic diathesis plays a decisive role in about 40% of cases of occupational skin diseases [23]. It should also not be disregarded that the exacerbation of atopic diseases (especially atopic dermatitis) is possible in the context of sports activities and has already been described in sports dermatology [30,31]. Atopic diseases have increased in recent decades and have reached prevalences of 10–20% for atopic eczema, 15–20% for allergic rhinitis, and 5–10% for allergic asthma in Germany [32]. Hence, the determined prevalence of allergic rhinitis in professional dancers is comparable to the prevalence in the normal population. In contrast, atopic eczema and allergic asthma are somewhat rarer in dancers than in the normal population. In summary, no allergies could be traced back to dance-specific exposure in the context of the present study.

##### 4.2.1. Sleep Duration

No statistically significant correlations with sleep duration could be observed in subjects with skin lesions in the questionnaire and skin analysis in the study compared to their counterparts not affected by skin lesions. It has been described in the literature that skin diseases are more associated with sleep disturbances and inadequate sleep. This is especially true for pruritic skin diseases such as atopic dermatitis [33,34]. Such a connection could not be found in the context of the study.

##### 4.2.2. Nutritional Aspects

A connection between a low BMI and skin changes can manifest itself, among other things, in diffuse dryness of the skin (84.4% in patients with eating disorders) or in the form of mild to severe acne vulgaris (70.5% in patients with eating disorders), diffuse alopecia with frontal accentuation (67.2% in patients with eating disorders), seborrhoeic eczema (20.5% in patients with eating disorders), or many other skin diseases [35]. Due to the small number of participants and the associated small number of skin lesions, these correlations and others, such as between BMI or alcohol and nicotine consumption and skin lesions, could not be established.

##### 4.2.3. Skin Care Behaviour

It is well known that recurrent exposure to mild substances such as soap or water can lead to skin damage and—in the worst case—to chronic, cumulative toxic skin eczema. This circumstance is referred to in occupational and social medicine as wet work and the criteria for this have been defined by the BAuA [36]. The extent to which the work of dancers meets the criteria for wet work, especially since the work is not done in a watery environment but in a sweaty, electrolyte-rich environment that the body produces itself, still needs to be clarified in the future [37]. Apart from that, however, it is clear that dancers work for several hours a day in a humid environment and show a showering behaviour that is clearly above the recommended norm.

Subjects who regularly removed their make-up had less dry skin. Dry skin is one of the major problems of the dancers examined. It is possible that subjects who regularly remove their make-up also take good care of their skin in other ways. This includes, for example, the use of a regular day care after removing make-up.

#### 4.2.4. Hair Removal

A major problem for professional dancers was the methods of hair removal. Professional dancers complained about inflammations after hair removal. This was especially true for the localisation “intimate area”. Dancers who suffer from inflammation after hair removal could be suggested long-term alternative methods to shaving. While shaving needs to take place almost daily to achieve an optimal, smooth result, some methods only need to take place every four to six weeks (for example, “waxing”, “sugaring”, or epilating). For longer-term hair removal, laser techniques can be chosen. According to Goldberg, Alexandrite laser, diode laser, Nd:YAG laser, and intense pulse light (IPL) are mainly used [38].

#### 4.3. Limitations

Despite its importance for occupational safety and work-related health, only very limited data exist on the skin health of performing artists. This study is a pilot project to obtain initial data through a cross-sectional (questionnaire) and longitudinal (skin analysis) survey. The number of participants is correspondingly small, although it is a complete dance ensemble, which again ensures a certain degree of representativeness. Unfortunately, due to the small number of participants, gender differences could not be calculated. Nevertheless, as a pilot project, these results provide an initial orientation with regard to the aforementioned given information. In order to ensure the participation of a complete group, the investigations were carried out parallel to work. However, it cannot be excluded that the dermatological examination may have been influenced as a result of skin reactions during the physical work. In addition, the examinations took place in winter, which could also have influenced the results. In this case, a control examination in a warmer season would be desirable. For organizational reasons, we also decided not to conduct a control examination, which seemed dispensable due to the device-based diagnostics. In addition, further questions on quality of life in the questionnaire would have been a valuable addition to the present questionnaire. The DLQI (Dermatology Quality of Life Index) [39], which is frequently used in studies, could have been used for this purpose. In addition to that, information on dancers’ care of their skin at home (e.g., what kind of cosmetics used) would have been advisable as the quality of skin care can change skin parameters. Detailed questions on the skin care products used including their ingredients would also have been an important addition. Furthermore, a comparison with an appropriate control group (e.g., a group of subjects practising similar sports without the application of make-up or hair removal procedures) could add important information.

In spite of all the limitations mentioned above, the pilot project is nevertheless able to provide initial results in a field of research that has received little attention to date and which can serve as a basis for further investigations.

## 5. Conclusions

The skin of dancers seems to show measurable consequences of high work-related stress, which could be made visible with the help of the measurement methods. Based on the results, further studies with larger groups are necessary.

**Author Contributions:** Conceptualization, E.M.W. and T.F.; data curation, M.S.; formal analysis, O.L.Z. and M.S.; investigation, O.L.Z. and A.W.; methodology, E.M.W., T.F.; project administration, E.M.W.; resources, T.F.; software, M.S.; supervision, E.M.W., A.W., and T.F.; validation, M.S.; visualization, O.L.Z.; writing—original draft, O.L.Z. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** This study is approved by the Ethics committee of the Department of Medicine of the Charité-Universitätsmedizin Berlin (EA4/120/14).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** All relevant data are within the text.

**Conflicts of Interest:** The authors declare no conflict of interest.

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