

Factors That Affect Skin Aging

A Cohort-Based Survey on Twins

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Objective: To identify environmental factors that correlate with skin photoaging, controlling for genetic susceptibility by using a questionnaire administered to twins.

Design: The survey collected information about each participant's Fitzpatrick type, history of skin cancer, smoking and drinking habits, and weight from a cohort of twins. Clinicians then assigned a clinical photodamage score to each participant.

Setting: The annual Twins Days Festival in Twinsburg, Ohio.

Participants: A voluntary cohort of twins from the general community, mostly from Ohio, Pennsylvania, and the northeastern United States. The survey was completed on a voluntary basis by sets of monozygotic (MZ) and dizygotic (DZ) twins. A total of 130 surveys taken by 65 complete twin pairs were analyzed.

Main Outcome Measure: Skin aging was assessed using a validated photographic scale of photodamage, graded by such characteristics as wrinkling and pigmentation change.

Results: Photodamage scores among twins of a pair, whether MZ or DZ, were highly correlated ($P = .92$). Factors found to predict higher photodamage include history of skin cancer ($P < .001$), zygosity status (MZ vs DZ) ($P = .001$), weight ($P = .02$), and cigarette smoking ($P = .046$). Alcohol consumption was significantly associated with lower photodamage scores ($P = .003$).

Conclusions: The study of twins provides a unique opportunity to control for genetic susceptibility in order to elucidate environmental influences on skin aging. The relationships found between smoking, weight, sunscreen use, skin cancer, and photodamage in these twin pairs may help to motivate the reduction of risky behaviors.

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AGING IS ATTRIBUTED TO BOTH intrinsic and extrinsic processes.¹ Photoaging—the most recognized form of extrinsic aging of the skin—describes changes brought about by long-term sun exposure, resulting in photodamage.² Photodamage, therefore, refers to the physical and morphologic alterations secondary to solar UV exposure and is the main component of photoaging.³ Intrinsic aging of the skin is characterized by finely wrinkled skin, cherry hemangiomas, and seborrheic keratoses.⁴ Photodamage, however, includes other characteristics, such as coarsely wrinkled skin, hyperpigmentation, hypopigmentation, and telangiectasia,^{1,5,6} and has been associated with the development of malignant neoplasms.²

Up to 40% of changes that contribute to the aged appearance are the result of non-genetic factors.^{7,8} Studies have implicated smoking and sun exposure as contributory,⁹⁻¹² whereas avoidance of UV^{2,13} and use of protective clothing and sunscreens¹⁴⁻¹⁶ have been shown to be protective. Some factors remain controversial. For example, some studies show that smoking had little or no contribution to skin wrinkling.¹⁷

The study of twins provides the opportunity to control for genetic susceptibility.¹⁸ Few epidemiological studies of twins have adequately examined associations between environmental factors and aging. The objective of this study is to determine the environmental factors that correlate with photoaging by obtaining a history (questionnaire format) and performing a skin examination on a cohort of monozygotic (MZ) and dizygotic (DZ) twins. Photoaging was assessed using a validated, photographic photodamage scale, examining such characteristics as wrinkling and pigmentation changes.¹⁹ Variables collected from the questionnaire (**Table**) were compared with photodamage scores, and statistical analyses were used to determine correlations.

METHODS

STUDY DESIGN

A questionnaire was administered at the annual Twins Days Festival, August 2-3, 2002, in Twinsburg, Ohio, to 130 adult (ages ≥ 18 years) participants (65 twin pairs). The questions and responses from the survey are included in the Table. Each twin completed the survey separately in the

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Table. Questionnaire Including Responses by 130 Twins

Question and Response ^a	No. (%)
You and your twin are	
Fraternal	104 (80)
Identical	20 (15)
Don't know	6 (5)
Does your skin burn when you are in the sun without sunscreen?	
Always burns, never tans	25 (19)
Always burns, tans a little	63 (48)
Burns some, tans gradually	32 (24)
Burns a little, always tans well	7 (5)
Rarely burns, tans a lot	3 (2)
Never burns	0
Have you ever had any kind of skin cancer?	
No	119 (92)
Yes	11 (8)
Have you ever smoked 100 cigarettes in your life?	
Yes	46 (36)
No	83 (64)
Do you currently smoke every day, on some days, or not at all?	
Everyday	11 (11)
Some days	6 (6)
Not at all	81 (83)
A drink of alcohol is 1 can or bottle of beer, 1 glass of wine, a can or bottle of wine cooler, 1 cocktail, or 1 shot. During the past 30 days, on how many days did you have ≥1 drink of alcohol per day?	
0	38 (30)
1-2	25 (19)
3-5	20 (16)
6-9	25 (19)
10-19	10 (8)
20-29	8 (6)
All 30	1 (0)
How do you describe your weight?	
Very underweight	1 (0)
Slightly underweight	6 (5)
About the right weight	61 (47)
Slightly overweight	54 (42)
Very overweight	7 (5)

^aQuestions that were not answered were excluded from the analysis.

presence of dermatology clinical faculty and residents. Specific questions from the survey are presented in the Table. Each twin also received a Fitzpatrick skin type score and clinical photodamage score (range, 0 to 9, with a score of "0" meaning no damage and "9" indicating severe photodamage). The scale was based on the photoaging classification system developed and validated by Griffiths et al.¹⁹ Scores were completed by 5 clinicians conducting the survey, and each score was overseen by 1 clinician (A.M.P.).

STATISTICAL ANALYSIS

Statistical analyses examined associations between several factors surveyed and the outcome variable, photodamage score, using both univariate and multivariate methods. In the univariate analysis, the association of individual ordinal factors, including age, alcohol consumption, and weight, with photodamage was estimated using the Spearman correlation coefficient. Use of the Kruskal-Wallis test examined the median difference of scores of photodamage between or among the level of other variables such as smoking, type of twins, and skin cancer. In the multivariate analysis, multivariable linear regression with the forward model selection procedure was used. To take into account the possible correlation of photodamage outcome between each pair of twins,

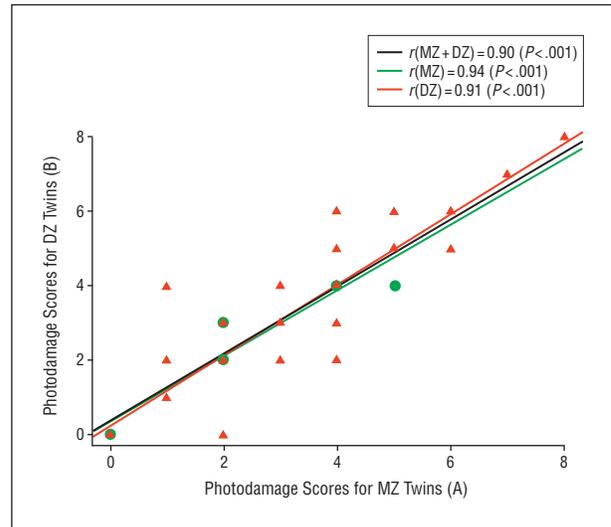


Figure 1. Scatterplot of photodamage scores of twins (where 0 means no damage; 9, severe photodamage). The figure shows a strong relationship of photodamage between twins (overall) and within twin pairs of each type (A, Twin A of the pair and B, twin B of the pair). There was no significant difference of correlation between monozygotic (MZ) and dizygotic (DZ) twins ($P=.60$). The circles represent the photodamage scores from MZ twins, and the triangles represent the scores from DZ twins. The scatterplot is based on data from 65 intact twin pairs.

the generalized estimating equations (GEE) model was used for inference.²⁰ When examining the correlations in photodamage between twins of a pair, Fisher z transformation was used to test for equality of 2 population correlations (the correlation of DZ twin pairs vs the correlation of MZ twin pairs). This method examined correlations in photodamage between twins of a pair. This was compared between MZ and DZ twins. All tests were 2-sided, and $P<.05$ was considered statistically significant.

RESULTS

A total of 130 questionnaires were included in this study. Missing information was excluded from analysis. Participants ranged in age from 18 to 77 years and represented all regions of the United States, although most hailed from Ohio, Pennsylvania, and the northeastern states. Dizygotic twins comprised 52 twin pairs, MZ twins comprised 10, and 3 twin pairs marked "don't know" with regard to their zygosity status. The correlation in photodamage between twins of a pair was tested by using Fisher z transformation, comparing MZ vs DZ cohorts vs the entire cohort. As shown in **Figure 1**, the correlation between MZ twins was higher ($r=0.94$) than that between DZ twins ($r=0.90$), although the difference was not significant ($P=.53$). Overall, the correlation between twins of any pair was high ($r=0.92$).

In the univariate analysis, age, frequency of alcohol consumption, and self-reported weight related significantly to photodamage score. Advanced age was strongly associated with higher photodamage scores, with $r=0.78$ ($P<.001$), as was weight, with $r=0.21$ ($P=.02$). However, more frequent consumption of alcohol was negatively associated with higher photodamage scores, with $r=-0.26$ ($P=.003$). Sunscreen use ($r=-0.06$) and Fitzpatrick type ($r=-0.06$) were also negatively correlated with photodamage. The influence of weight and alcohol con-

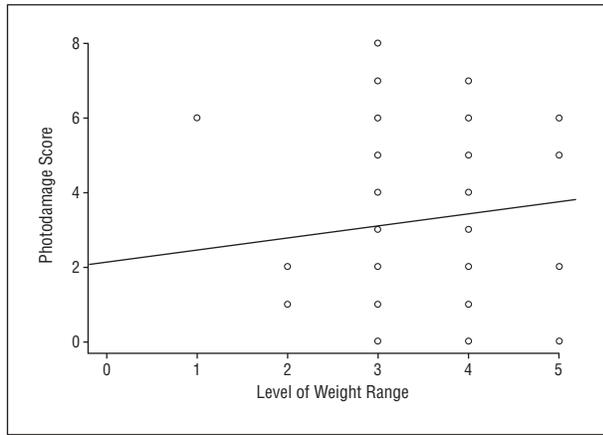


Figure 2. Scatterplot of weight and photodamage. Increased weight significantly correlated with higher photodamage scores (where 0 means no damage; 9, severe photodamage) overall with $r=0.21$ ($P=.02$). On the x-axis, 1 represents "very underweight"; 2, "slightly underweight"; 3, "about the right weight"; 4, "slightly overweight"; and 5, "very overweight." Each open circle represents a data point (ie, the photodamage score for a certain weight).

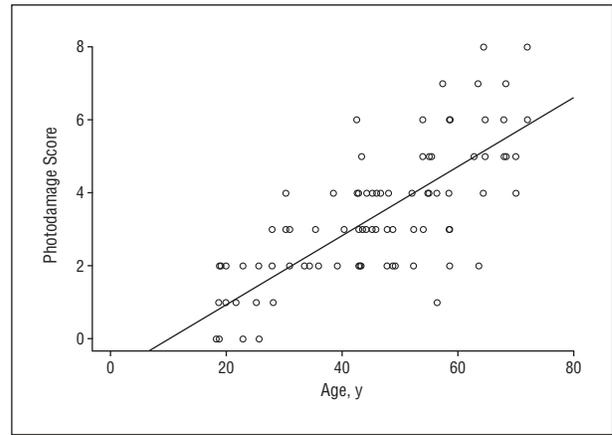


Figure 4. Scatterplot of age and photodamage. Age was strongly linked to increased photodamage score (where 0 means no damage; 9, severe photodamage) with a correlation coefficient of 0.78 ($P<.001$), implicating a strong role for intrinsic aging in photoaging assessment. Age as a covariate in the multivariate analysis was excluded because of the problem of multicollinearity. Each open circle represents a data point (ie, photodamage score for a certain age).

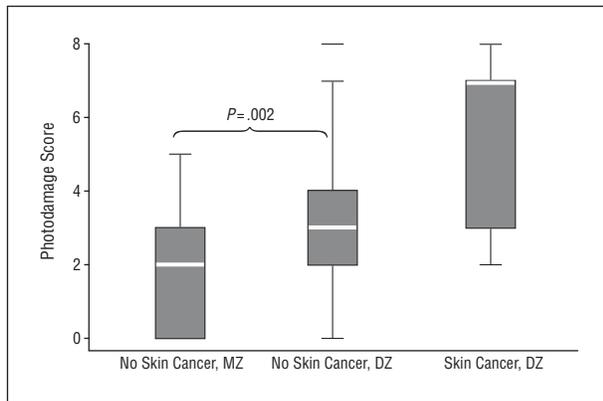


Figure 3. Box plot of photodamage by history of skin cancer as a function of twin type. Participants with a personal history of skin cancer had higher photodamage scores (where 0 means no damage; 9, severe photodamage) than those who had no history of skin cancer. There was a significant difference between monozygotic (MZ) and dizygotic (DZ) twins with no skin cancer ($P=.002$).

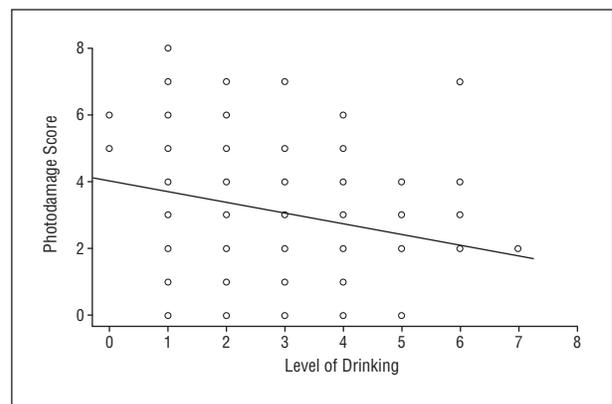


Figure 5. Scatterplot of drinking level and photodamage. Less alcohol consumption significantly correlated with more photodamage with $r=-0.26$ ($P=.003$) (where 0 means no damage; 9, severe photodamage). The level of alcohol consumption ranged from 0 days to all 30 days in the past 30 days. On the x-axis, 0 represents "no drinking"; 1, "drinking 1 day"; 3, "drinking 3 to 5 days"; 4, "drinking 6 to 9 days"; 5, "drinking 10 to 19 days"; 6, "drinking 20 to 29 days"; and 7, "drinking all 30 days." Each open circle represents a data point (ie, the photodamage score for a certain level of drinking alcohol).

sumption on photoaging was examined after stratifying age groups. For participants older than 54 years, higher weight predicted significantly lower photodamage scores than those who weighed less ($r=-0.03$; $P=.08$) (**Figure 2**). The finding for alcohol consumption in participants older than 54 years was consistent with the rest of the data in that more frequent consumption was negatively associated with photodamage. Differences of photodamage between or among the level of other factors using the Kruskal-Wallis test found significant associations of skin cancer and type of twins (MZ vs DZ) with photodamage score, and a significant association for quantity of cigarettes smoked ($P<.12$). A history of skin cancer ($P<.001$) and cigarette smoking ($P=.12$) positively correlated with higher photodamage scores. Dizygotic twins were found to have more photodamage than MZ twins ($P=.001$). Among 11 incidences of skin cancer, all were in DZ twins, and 8 of them were in 4 intact twin pairs. Box plots and scatterplots for factors with significant associations with photodamage are shown in **Figures 2, 3, 4, 5, and 6**.

Factors significantly associated from the univariate analyses were further examined using multivariable linear regression with the forward model selection procedure. Covariates included in the multiple linear regression were skin cancer history, Fitzpatrick type, weight, and alcohol consumption. The type of twins (MZ vs DZ) was also controlled for in the analysis. Factors found to predict photodamage include skin cancer, type of twins, and alcohol consumption. Participants with a history of skin cancer had photodamage scores that were an average of 1.39 points ($P=.08$) higher than scores of those who had never had skin cancer. Dizygotic twins had photodamage scores that were an average of 1.41 higher than those of MZ twins ($P=.005$), and those with more frequent alcohol consumption had scores that were 0.22 points lower than those with less frequent consumption ($P=.06$). Age as a covariate in the multivariate analysis was excluded because of the problem of multicollinear-

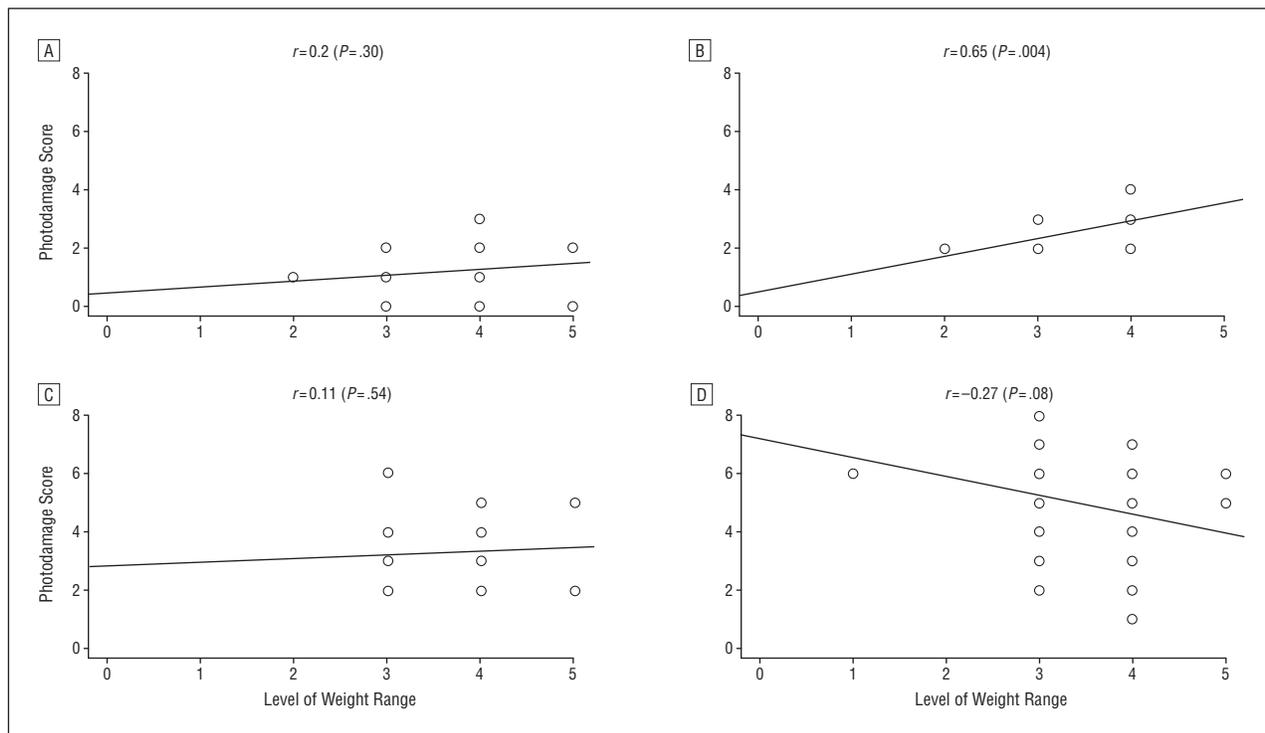


Figure 6. Scatterplots of weight and photodamage, stratified by age group. A, Age older than 18 years but not older than 30 years; B, age older than 30 years but not older than 42 years; C, age older than 42 years but not older than 54 years; and D, age older than 54 years. Increased weight significantly correlated with higher photodamage scores (where 0 means no damage; 9, severe photodamage) for participants aged 30 to 42 years, with $r=0.65$ ($P=.004$). For participants older than 54 years, increased weight was correlated with a decreased photodamage score, with $r=-0.27$ ($P=.08$). On the x-axis, 1 represents “very underweight”; 2, “slightly underweight”; 3, “about the right weight”; 4, “slightly overweight”; and 5, “very overweight.” Each open circle represents a data point (ie, the photodamage score for a certain weight).

ity. However, when age was included in the multivariate regression, age ($P < .001$) and type of twins ($P = .003$) were significantly correlated with photodamage.

COMMENT

We examined environmental factors associated with skin photoaging. The Twins Days Festival provides a rare opportunity to study a large number of twin pairs to control for genetic susceptibility. Among the most important results is that a history of skin cancer and photodamage are highly associated in a population that shares genetic commonalities. The relationship between differences in MZ vs DZ photodamage (as examined by the GEE logistic model), revealed similar correlation between twins of a pair, whether MZ or DZ.

Genetic and environmental factors are considered contributory in the development of melanoma and non-melanoma skin cancer, as investigated by recent studies.^{21,22} However, analyses of the relative contributions of genetic and environmental factors have been limited.²³ Lindström et al²⁴ estimated the genetic components for melanoma and squamous cell cancer to be 18% and 8%, respectively. For melanoma, it has been documented that first-degree relatives of patients have an increased risk of developing melanoma,²⁵ but the degree of genetic contribution remains unclear. The cell cycle regulator *CDKN2A* is implicated in the genetic component to melanoma,^{26,27} while *PTCH*^{28,29} and *p53*^{30,31} are involved in nonmelanoma skin cancers (NMSCs). As for the environmental compo-

nent, UV plays an important role in inducing DNA mutations and suppressing cellular antitumor immune responses.³² Mitochondrial DNA is particularly susceptible to damage by UV owing to its small size and higher exposure to reactive oxygen species.^{33,34} Some studies treat skin cancer as a component of photoaging. However, this study addresses skin cancer as an independent factor. The persistent strength of correlation between the 2 thus confirms this relationship, implicating environmental and genetic factors that affect photoaging as components in the development of skin cancer.

Self-reported weight was found to positively correlate with photoaging score, contrast to the study of Danish twins by Rexbye et al,¹⁸ which reported body mass index to negatively correlate with facial aging. Previous animal experiments have suggested that high fat intake may increase skin sensitivity to UV damage and photocarcinogenesis.³⁵ However, the relationship between fat intake and NMSC is complex, and lipids may potentially have an antioxidant and, thus, protective action.³⁶ For participants 54 years or older, weight correlated negatively with photoaging, implying that although excess fat may increase skin's susceptibility to damage, it may help mask the appearance of wrinkles in older age.

Drinking alcohol was found to be negatively correlated with photodamage. In their study of Danish twins, Rexbye et al¹⁸ found no significant correlation between drinking and photodamage in either direction.¹⁸ Although our survey did not specify what type of alcohol was consumed, it is known that certain alcoholic beverages (eg, red wine) contain polyphenols such as resveratrol, which is an

effective antioxidant.^{37,38} Finally, our finding that cigarette smoking is associated with higher photodamage ($P=.046$) is consistent with most of the data in the literature.^{9-12,18,39} Cigarette smoke induces matrix metalloproteinases in the skin and inhibits procollagen synthesis through alteration of transforming growth factor β .⁴⁰⁻⁴²

This study is one of the few twin studies examining the relationship between environmental factors and photodamage. As with all self-report methods, data may not be accurately reported by participants. The classification of zygosity was also based on self-report, which may have 96.8% accuracy.⁴³ Finally, with clinical photodamage scales, there is room for interobserver discrepancy, which was minimized by having 1 senior resident (A.M.P.) oversee scores given, and by using a standardized, validated, photographic photoaging scale.¹⁹

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Author Contributions: Dr Baron had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Polster and Cooper. *Acquisition of data:* Polster and Cooper. *Analysis and interpretation of data:* Martires, Fu, Cooper, and Baron. *Drafting of the manuscript:* Martires. *Critical revision of the manuscript for important intellectual content:* Fu, Polster, Cooper, and Baron. *Statistical analysis:* Fu. *Obtained funding:* Cooper. *Administrative, technical, and material support:* Martires, Polster, and Cooper. *Study supervision:* Polster, Cooper, and Baron.

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