Int J Clin Exp Med 2019;12(5):5536-5544
www.ijcem.com /ISSN:1940-5901/IJCEM0084644

Original Article

Do dark circles under the eyes predict health status?

Ilkoo Ahn, Siwoo Lee, Hee-Jeong Jin

Future Medicine Division, Korea Institute of Oriental Medicine, Daejeon 34054, Republic of Korea

Received August 27, 2018; Accepted February 11, 2019; Epub May 15, 2019; Published May 30, 2019

Abstract: Mibyeong (sub-health) refers to a condition in which physical, mental, and social abnormalities cause discomfort in daily life or non-pathological abnormalities observed during clinical examinations. The objective of this study was to investigate the association between dark circles under the eyes (DCE) values with Mibyeong scores (MBSs) using a fully automated analysis system. A DCE score (DCES) was determined in 169 participants, which was calculated as the difference between the intensity of the region under the eyes and that of the adjacent region. Self-rated Mibyeong severity was determined using a questionnaire. DCES was positively associated with the Mibyeong score (MBS) (p = 0.175, p = 0.024), and it was significantly correlated with specific Mibyeong symptoms, including depression persistence (p = .168, p = .030), anger degree (p = .223, p = .004), anger discomfort (p = .203, p = .009), anger persistence (p = .235, p = .002), anger degree after rest (p = .195, p = .012), anxiety degree (p = .176, p = .023), anxiety discomfort (p = .163, p = .035), and anxiety degree after rest (p = .192, p = .013). The DCES was further statistically quasi-significant with sleep disturbance persistence, depression discomfort, and anxiety persistence. Darker circles under the eyes were associated with a higher MBS, which indicates that DCE can be used as an indicator of Mibyeong status. DCE was correlated with anger, anxiety, depression, and sleep disturbance.

Keywords: Dark circles, periorbital hyperpigmentation, facial complexion, face analysis

Introduction

Mibyeong (sub-health, China: *Weibing*, Japan: *Mibyou*) refers to a non-pathological condition in which individuals suffer from discomfort due to the physical, mental, or social stresses of daily life. In other words, Mibyeong represents a domain between health and disease. In traditional East Asian Medicine (TEAM), Mibyeong is regarded as a condition that requires medical care and treatment. TEAM's oldest book, *Huangdi Neijing* (*The Yellow Emperor's Classic of Internal Medicine*) [1], indicates the enduring nature of this concept by stating that "a good doctor treats a person who is in Mibyeong state, rather than treating a person who is already afflicted with disease".

The causes of Mibyeong are thought to be very diverse. Aging, an inadequate diet, an unhygienic environment, and stress in daily life can all cause Mibyeong. The most representative cause of Mibyeong from the perspective of TEAM is *deficiency* [2]. According to this perspective, deficiencies or a deficiency pattern in daily life leads to lowered resilience and to Mibyeong symptoms. The exact cause of Mibyeong is often difficult to determine, and further research pertaining to its clinical features is required.

The face is one of the easiest parts of the body to observe, and it can provide important information regarding a person's emotional state or health status. From the perspective of TEAM, the face has been regarded as an important body part that reflects physiological and pathological changes, with facial complexion being used as one of the main diagnostic indicators [3-6]. Changes in the facial color are easily visible given that the face is rich in meridians and the facial skin is soft and thin. The face can provide a variety of critical health-related cues, such as dark circles under the eyes (DCE) or periorbital hyperpigmentation, hanging eyelids, red eyes, swollen eyes, glazed eyes, and pale skin [7]. Many individuals with poor general health experiences DCE [7].

The concept of health being reflected in the eyes is not new or novel. The classical medical textbook *DonguiBogam* was compiled by the royal physician Heo Jun (1539-1615) and was first published in 1613 during the Korean

Table 1. The inclusion and exclusion criteria for participants

Inclusion criteria
1. Healthy men and women aged 35 to 44 years
2. People who complained of persistent or recurrent fatigue during the last 6 months
3. People with a Chalder Fatigue Scale Questionnaire score of ≥ 15
4. People with a Mibyeong questionnaire score of ≥ 14
5. People with a regular job
Exclusion criteria
1. People with primary sleep disorders
2. Those who had been diagnosed with depression within the last 5 years
3. People with fatigue due to physical reasons:
- Organ failure (emphysema, cirrhosis, heart failure, chronic kidney failure, etc.),
- Chronic infectious diseases (AIDS, hepatitis B or C),
- Rheumatic/inflammatory diseases (SLE, rheumatoid arthritis, inflammatory bowel disease, chronic pancreatitis, etc.)
- Major neurological diseases (multiple sclerosis, neuromuscular diseases, epilepsy, etc.)
- Endocrine/metabolic diseases (diabetes, thyroid disease, severe obesity with BMI > 45)
- Other diseases (anemia, tuberculosis, chronic lung disease, hypertension, etc.),
- Malignant tumors
4. Those with fatigue due to a mental or social cause:
- Mental illness (anxiety, neuropathy, bipolar affective disorder, schizophrenia, delusional disorder, dementia, anorexia nervosa, bulimia, etc.)
- Alcoholism and drug abuse within the last 2 years
- Those who have recently been severely stressed
5. Those taking antihypertensive drugs, antidepressants, anxiolytics, hypnotics, and antihistamines within the last 2 weeks
6. Mibyeong questionnaire responses with no complaints of fatigue symptoms
7. Those who have received medical or oriental medical care for fatigue within the past month
8. Pregnant women, women who are breastfeeding, and those who plan to become pregnant within 6 months
9. An overworked person, or those with occupations involving night shifts and shift work
10. Those who believe that they cannot take medications that may affect clinical studies or that they cannot comply with other test compliance

Joseon Dynasty [8]. *DongUiBoGam* was the most recent medical book of the time, and is regarded as the preeminent medical textbook on traditional Korean medicine. The following statement pertaining to DCE was mentioned in the second volume of *Internal Bodily Elements of DongUiBoGam*, "When the person has phlegm, an ash-like black color must appear on the eyelids and under the eyes".

Phlegm is a pathological substance that is produced when bodily fluids stagnate and accumulate in certain regions of the body [9]. Symptoms that are associated with phlegm production include expectoration, chest tightness, gastrectasia, anorexia, nausea, vomiting, dizziness, and greasy stool [9, 10]. An unhealthy individual who experiences phlegm production may experience DCE, and the degree of their illness may be estimated by the severity of their DCE.

We have based the present study on others, which suggest that DCE may serve as an index of overall health, and further hypothesized that the degree of DCE in facial images is associated with an individual's Mibyeong state. Here, we used a fully automated analysis system to detect the face, normalize the intensity of the face image, and then calculate a DCE value. We then investigated the association of DCE values with Mibyeong scores (MBSs) in an effort to demonstrate that this biomedical index is in fact associated with meaningful, health-related outcomes in individuals.

Methods

Participants

This cross-sectional study was conducted between March 2016 and May 2016. Mibyeong questionnaires and all facial images were collected from the Korea Institute of Oriental Medicine's Korean medicine Data Center [11]. A total of 169 subjects participated in this study, and **Table 1** shows the inclusion and exclusion criteria for participants. The age of

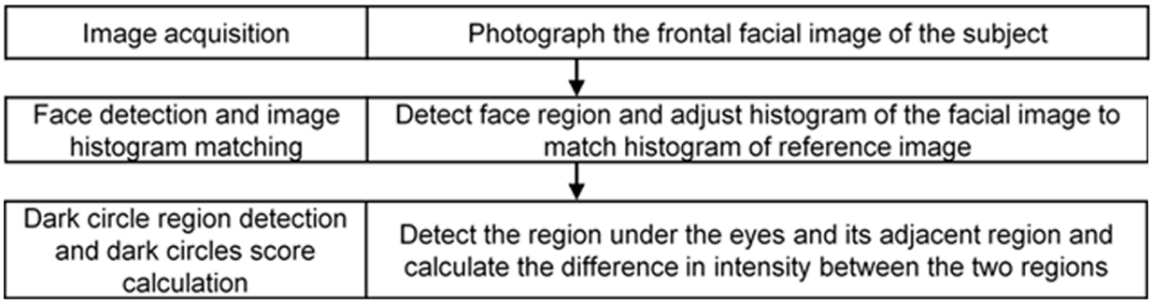

Figure 1. Schematic diagram of the dark circles score calculation.

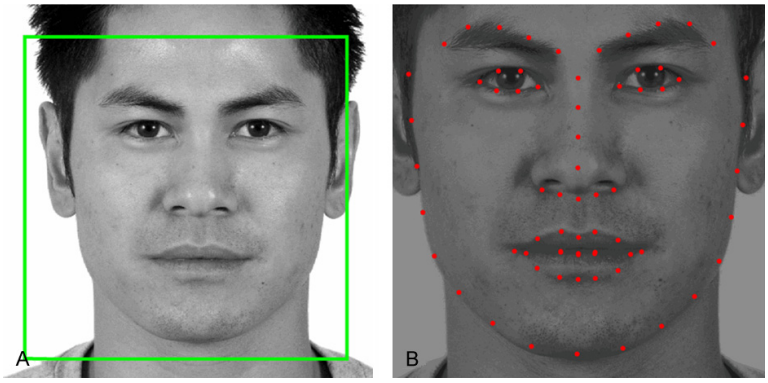

Figure 2. Examples of face detection, image histogram matching, and detection of the facial landmarks. (A) The detected face region was marked with a green line. (B) The intensity distribution of the original image (A) was converted by histogram matching. The red dots denote the facial landmark points. This original image is from the Chicago Face Database [14], which is a publicly available image database.

the participants ranged between 34.3 and 45.9 years, and the BMI ranged from 16.6 to 32.9 kg/m^2. The hospital's institutional review board approved the study protocol (KHNMCIH 2014-09-010), and all participants provided informed, written consent prior to their inclusion.

The DCE score calculation

We assessed the severity of DCE using a dark circles under the eyes score (DCES) derived from facial images. The DCES was determined based on the difference between the intensity of the region under the eyes and that of its adjacent region. The processes for calculating the DCES are depicted in **Figure 1** and are described further in the following subsections.

Image acquisition: The purpose of this study was explained to all participants prior to facial image acquisition. Participants were asked to wear a hair band to prevent their hair from covering the ears and forehead. Participants were instructed to sit comfortably in a chair located about 1.6 m from the camera. A frontal facial image of the participant was then captured using a digital camera (Nikon D5100 with an 85-mm lens; Nikon Co., Ltd., Japan) equipped with a prime lens (a lens with only one focal length). We prepared a strict standard operating procedure for the acquisition of these pictures to reduce inter-rater bias. All face images were taken at the same location with an outer fluorescent light source and saved in jpeg format at a resolution of 3696 × 2448 pixels.

Face detection and image histogram matching: To detect faces, we used a facial landmark detector included in the Dlib library [12], which implements the Kazemi and Sullivan method [13]. The detector calculated a rectangular face region as shown in **Figure 2A** (the original image is from the Chicago Face Database [14]). The face images for all subjects were normalized to have the same intensity distribution to account for differences in skin intensity, which were present despite our use of identical illumination conditions across all subjects. Histogram matching was conducted by adjusting the histogram of the facial image to match the histogram of the average image for all the grayscale face images (**Figure 2B**).

Dark circle region detection and dark circles score calculation: Because facial shape differs from person to person, the dark circle region

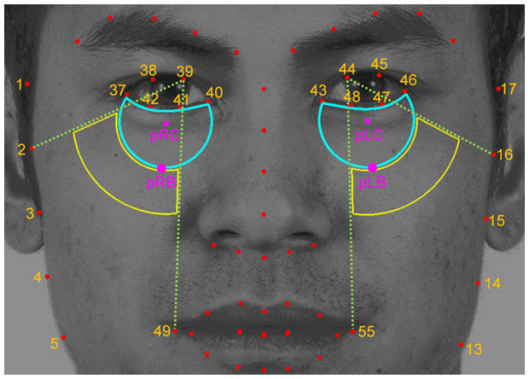

Figure 3. An example of the detection of the dark circles region. The red dots represent the facial landmark points, and the numbers next to the red dots indicate the order of the points. The DCES was calculated as the difference between the intensity of the region under the eyes (the region marked with cyan under the eyes) and the intensity of the adjacent region (the region marked with yellow under the eyes). This original image is from the Chicago Face Database [14], which is a publicly available image database.

also differs. Facial landmarks were used for accurate dark circle region detection across varying facial shapes. To detect facial landmarks, we also used the facial landmark detector included in the Dlib library [12], which provides 68 landmark points (**Figure 2B**).

The DCES was calculated as the difference between the intensity of the region under the eyes (the moon-shaped region outlined in cyan in **Figure 3**) and the intensity of the adjacent region (the fan-shaped region outlined in yellow in **Figure 3**). The region under the eyes is where we expected to find hyperpigmentation.

A prescribed methodology was used for determining the region under the left eye (RULE) and the region adjacent to RULE (RARULE). For example, if points 43 and 46 are both horizontal end points for the subject's left eye, the pLB point is located equidistant between points 43 and 46. That is, the distance between points 43 and 46, points 43 and pLB, and points 46 and pLB are identical. RULE was taken to be the region in the circle passing through the points 43, 46, and pLB-excluding the left eye itself. Point pLC represents the center of this circle, and it is the center point of the points 43, 46, and pLB.

The region adjacent to RULE (RARULE) was an area not expected to have hyperpigmentation; it is depicted in **Figure 3** as a yellow-outlined fan shape. Let r be the distance from pLC to pLB and let LCircularSector be the intersection of the circle with a radius of $2r$ around pLC and the triangle formed by points 44, 55, and 16. Excluding the region of the circle passing through points 43, 46, and pLB from the LCircularSector, the remaining region was considered RARULE. The trimmed averages of pixel intensity values of RULE and RARULE regions were computed, where the trimmed average is the mean after discarding the upper and lower quartiles of each region's distribution. The trimmed mean excludes the effects of outlying intensities and is, therefore, suitable for this study.

The dark circles under the left eye score (DCLES) is the value obtained by subtracting the trimmed average of pixel intensities of RULE from the trimmed average of pixel intensities of RARULE. The region under the right eye (RURE), the region adjacent to RURE (RARURE), and the dark circles under the right eye score (DCRES) were obtained by applying the same method to the right eye. Finally, the DCES was calculated as the average of both the DCLES and DCRES. This assessment system was implemented in Matlab R2016a (MATLAB and Image Processing Toolbox, The MathWorks, Inc., Natick, Massachusetts, United States) in a Win64 environment.

Mibyeong

The Mibyeong (sub-health) questionnaire utilized in the present study covered seven symptoms: fatigue, pain, sleep disturbance, indigestion, depression, anger, and anxiety. The Mibyeong questionnaire evaluated each symptom across four dimensions: degree (the severity of the symptom), discomfort (the discomfort severity caused by the symptom), persistence (the number of days the symptom persisted), and degree after rest (the degree of symptom improvement after rest). The Mibyeong questionnaire consisted of 28 questions in total, each presented on a 7-point scale from "very weak" (score 1) to "very severe" (score 7). The sum of these scores was the Mibyeong score (MBS), which ranged from 28 to 196, with higher values indicating more severe Mibyeong symptoms. The Cronbach's α of the Mibyeong questionnaire was previously reported to be .913 [15].

Table 2. Characteristics of the participants

Number of participants	169	Male	Female	*p*-value
		69 (40.8%)	100 (59.2%)	
Age (yrs)	39.6 ± 3.1	39.0 ± 3.0	40.0 ± 3.1	**0.000**
MBS	57.6 ± 20.3	57.2 ± 20.1	57.9 ± 20.6	**0.000**
BMI	23.6 ± 3.4	25.1 ± 3.2	22.5 ± 3.1	**0.000**

Statistically significant differences between group means as determined by two-sample t-test are in bold. MBS, Mibyeong score; BMI, body mass index.

Table 3. Correlation between the DCES and specific Mibyeong symptoms

Symptoms	Dimensions	*ρ*	*p*-value	Symptoms	Dimensions	*ρ*	*p*-value
Fatigue	Degree	0.071	0.363	Indigestion	Persistence	0.070	0.372
	Discomfort	0.097	0.210		Degree after rest	0.085	0.277
	Persistence	-0.022	0.780	Depression	Degree	0.122	0.115
	Degree after rest	0.079	0.307		Discomfort	**0.136**	**0.079**
Pain	Degree	0.108	0.165		Persistence	**0.168**	**0.030**
	Discomfort	0.076	0.329		Degree after rest	0.106	0.171
	Persistence	0.004	0.959	Anger	Degree	**0.223**	**0.004**
	Degree after rest	0.049	0.531		Discomfort	**0.203**	**0.009**
Sleep disturbance	Degree	0.054	0.486		Persistence	**0.235**	**0.002**
	Discomfort	0.131	0.091		Degree after rest	**0.195**	**0.012**
	Persistence	**0.145**	**0.061**	Anxiety	Degree	**0.176**	**0.023**
	Degree after rest	0.096	0.215		Discomfort	**0.163**	**0.035**
Indigestion	Degree	0.064	0.410		Persistence	**0.134**	**0.084**
	Discomfort	0.012	0.876		Degree after rest	**0.192**	**0.013**

Partial correlation coefficients adjusted for sex and age. Statistically quasi-significant ($p < 0.09$) and significant ($p < 0.05$) results are in bold; DCES: the dark circles under the eyes score.

Statistical analysis

Continuous variables were presented as the mean and standard deviation, and categorical variables were reported as percentages. A correlation analysis (partial correlation coefficients which controls for the effect of potential confounding factors) was conducted to assess the degree of association between the DCES and MBS after adjusting for sex and age. *p*-values less than 0.05 were considered statistically significant, and *p*-values less than 0.09 were considered statistically quasi-significant. All statistical analyses were performed using SPSS 22.0 (IBM, Chicago, IL, USA).

Results

Participant characteristics

This study included 69 male and 100 female participants with a mean age of 39.6 ± 3.1 years (range 34.2-45.9 years). The mean MBS and mean BMI were 57.6 ± 20.3 (range 22-119) and 23.6 ± 3.4 (range 16.6-32.9), respectively (**Table 2**).

Association of DCES with MBS

The DCES was positively associated with the MBS (partial $p = .175$, $p = .024$) after adjusting for sex and age. In other words, darker circles under the eyes were associated with more severe Mibyeong symptoms.

Correlation of DCES with specific Mibyeong symptoms

Table 3 shows the results of the DCES correlation analyses with specific Mibyeong symptoms after adjustment for sex and age. Eight and three of the 28 items were statistically significant ($p < 0.05$) and quasi-significant ($p < 0.09$) with regard to the DCES, respectively (3 items with a *p*-value less than 0.01, 5 with a *p*-value less than 0.05, and 3 with a *p*-value less than 0.09). By symptom, sleep disturbance persistence was statistically quasi-significant with the DCES ($p < 0.09$). Discomfort and persis-

tence of depression were statistically quasi-significant and significant with the DCES, respectively. All four dimensions of anger (degree, discomfort, persistence, degree after rest) had a significant correlation with the DCES. Three dimensions (degree, discomfort, and degree after rest) and one dimension (persistence) of anxiety showed significant and quasi-significant correlations with the DCES, respectively.

Discussion

In the present study, we hypothesized that the DCES was related to Mibyeong (sub-health) severity and assessed this relationship using a fully automated facial image analysis system. Our results indicated that health status can be estimated based on the DCES.

Human faces provide a wealth of information, including an individual's identity, health, age, sex, and attractiveness to the opposite sex [3, 16-18]. Because the face is easily observed during interpersonal interactions, its applicability is even greater. It is already known that the face carries information about health and that humans can easily distinguish healthy from unhealthy faces [19] and are reminiscent of positive features on a healthy face unconsciously [20]. Evaluating facial appearance not only reveals information regarding health, but it can also provide insight into other social aspects, such as a attractiveness [21, 22] and leadership ability [23]. Research findings that support the associations between facial appearance and health are increasing [5, 24-26].

Previous studies have primarily analyzed the whole facial area; however, in this study we focused on a specific area of the face for health status diagnosis-DCE. We conducted this study in an objective way using a fully automated computer-based method to test the hypothesis that sub-health status is associated with DCE. We hypothesized that darker circles under the eyes would be associated with more severe Mibyeong states, and we defined the DCES as the value obtained by subtracting the brightness of the region under the eyes from that of its adjacent region.

We found that the DCES was correlated with the Mibyeong score (MBS) ($p = .175$, $p = .024$), even after adjusting for sex and age. This result confirms our hypothesis that participants with darker under-eye regions would exhibit more severe Mibyeong symptoms.

Because Mibyeong is traditionally diagnosed based on the presence of multiple symptoms or signs (rather than a single symptom), we investigated the association between the DCES and the four dimensions of specific symptoms. The persistence of sleep disturbance was statistically quasi-significant ($p < 0.09$), as were the one dimension (discomfort) of depression symptoms and the one dimension (persistence) of anxiety symptoms. Another dimension (persistence) of depression symptoms was significant ($p < 0.05$), as were all dimensions of anger symptoms and three dimensions of anxiety symptoms.

The biological basis for the correlation between DCE and Mibyeong could be explained by previous studies. Many existing studies have reported that non-pathological symptoms, such as general fatigue [27-29], anxiety [30-32], and sleep disturbances [7, 28, 33-35] cause DCE. The adrenals, which are located on top of the kidneys, produce a variety of hormones, such as cortisol or hydrocortisone, corticosterone, aldosterone, adrenaline or epinephrine, etc. Cortisol controls the autonomic nervous system's fight-or-flight response. If chronic stress symptoms, such as fatigue, anxiety, and depression persist, they can result in adrenal fatigue and diminished cortisol levels [36, 37]. Some studies have also reported that plasma or urinary cortisol hormone levels decrease when individuals experience sleep deprivation lasting 48 hours or more [38, 39]. When cortisol levels are chronically low, the pituitary gland produces adrenocorticotropic hormone (ACTH or corticotropin) to stimulate more cortisol production. However, ACTH also stimulates melanin production, which darkens the under-eye skin tone and causes hyperpigmentation [40, 41]. Similar to the findings of previous studies, our results demonstrate that anxiety and anger were significantly correlated with DCE and that sleep disturbance was weakly correlated with DCE. However, we also found that fatigue and DCE were not correlated, which was an unexpected result [4].

Metabolic disorders are also associated with DCE [42, 43]. According to Boxrud *et al.* [43], systemic conditions, such as metabolic and endocrine disorders, can lead to hyperpigmen-

tation of the periorbital area. Metabolic disorders can also cause excessive accumulation of carbon dioxide and diminished oxygen saturation levels [44, 45]. Decreased blood oxygen can cause the skin to turn blue [46]. Due to its decreased levels of collagen, elastin, and glycosaminoglycans [47], the skin over the lower eyelid is relatively thin, meaning that the blood vessels around the eyes are more visible there than they are elsewhere. Moreover, previous studies have reported that blood stasis or venous congestion and the degree of blood oxygen saturation are associated with the DCES [48, 49]. This is also consistent with the finding in DonguiBogam, in which individuals with phlegm have DCE [8].

While it offers significant strengths, the present study also has some limitations worth mentioning. First, although traditional diagnoses are performed by practitioners after a comprehensive clinical exam involving listening, smelling, questioning, and palpation (i.e., "the four diagnostic methods"), Mibyeong was diagnosed in this study using a subjective self-questionnaire comprising questions regarding typical, self-perceived Mibyeong symptoms. Additionally, although sex and age were used as covariates in our analyses, other external variables that could affect the DCES, such as the participants' level of sun exposure, were not included in the analyses. Finally, the present study was performed on only 169 subjects. A larger sample size is necessary to generalize our findings.

Conclusions

In the present study, we reveal significant correlations between DCE and Mibyeong using a fully automated facial image analyzing system. Participants with high Mibyeong scores (unhealthy) had darker skin under eyes. The results of this study demonstrate that the degree of dark circles under the eyes may be an indicator of health status. To the best of our knowledge, this is the first study to investigate the association between DCE and Mibyeong status and to suggest that dark circle analysis may be helpful in identifying non-pathological patient health status.

Acknowledgements

This work was supported by the Ministry of Science and ICT [NRF-2014M3A9D7034351] and the Korea Institute of Oriental Medicine [K17092].

Disclosure of conflict of interest

None.

Abbreviations

DCE, dark circles under the eyes; DCES, dark circles under the eyes score; MBS, Mibyeong score; TEAM, traditional East Asian Medicine; RULE, the region under the left eye; RARULE, the region adjacent to RULE; DCLES, dark circles under the left eye score; RURE, the region under the right eye; RARURE, the region adjacent to RURE; DCRES, dark circles under the right eye score.

Address correspondence to: Hee-Jeong Jin, Future Medicine Division, #202 2F Dasan-Building 1672 Yuseong-daero, Yuseong-gu, Daejeon 34054, Republic of Korea. Tel: +82-42-868-9305; Fax: +82-42-868-9388; E-mail: jinijeong77@gmail.com

References

[1] Veith I. The yellow emperor's classic of internal medicine. Univ of California Press 2015.

[2] Lee J, Dong SO, Lee Y, Kim SH, Lee S. Recognition of and interventions for Mibyeong (subhealth) in South Korea: a national web-based survey of Korean medicine practitioners. Integr Med Res 2014; 3: 60-66.

[3] Henriquez P, Matuszewski BJ, Andreu-Cabedo Y, Bastiani L, Colantonio S, Coppini G, D'Acunto M, Favilla R, Germanese D and Giorgi D. Mirror mirror on the wall... an unobtrusive intelligent multisensory mirror for well-being status self-assessment and visualization. IEEE Transactions on Multimedia 2017; 19: 1467-1481.

[4] Coppini G, Favilla R, Gastaldelli A, Colantonio S; Marraccini PIJCoBEST. Moving medical semeiotics to the digital realm. 2014; 5: 606-613.

[5] Li XQ, Li F, Wang Y, Qian P, Zheng XY. Computer-aided disease diagnosis system in TCM based on facial image analysis. International Journal of Functional Informatics & Personalised Medicine 2009; 2: 303-314.

[6] Zhang XW, Wang FM, Yu SS, Zhou Q-HJIJOC and Medicine E. The effect of acupuncture on Bell's palsy: an overall and cumulative meta-analysis of randomized controlled trials. 2018; 11: 3309.

[7] Sundelin T, Lekander M, Kecklund G, Van Someren EJ, Olsson A, Axelsson J. Cues of fa-

tigue: effects of sleep deprivation on facial appearance. Sleep 2013; 36: 1355-60.
[8] Heo JJN, Seoul. Donguibogam. 1994; 276.
[9] Zhang Z, Hu J. Recent advances and perspective of studies on phlegm syndrome in chinese medicine. Evid Based Complement Alternat Med 2016; 2016: 6463270.
[10] Cai J, Chao GC, Chen DJ, Chen KJ, Chen XQ and Cheng XZ. Advanced textbook on traditional Chinese medicine and pharmacology vol. 1. 1995.
[11] Jin HJ, Baek Y, Kim HS, Ryu J, Lee S. Constitutional multicenter bank linked to Sasang constitutional phenotypic data. BMC Complement Altern Med 2015; 15: 46.
[12] King DEJJoMLR. Dlib-ml: a machine learning toolkit. Journal of Machine Learning Research 2009; 10: 1755-1758.
[13] Kazemi V and Sullivan JICoCVPR. One millisecond face alignment with an ensemble of regression trees. IEEE 2014; 1867-1874.
[14] Ma DS, Correll J, Wittenbrink B. The Chicago face database: a free stimulus set of faces and norming data. Behav Res Methods 2015; 47: 1122-1135.
[15] Jang E, Yoon J and Lee Y. The evaluation of reliability and validity for mibyeong questionnaire. The Journal of The Korea Institute of Oriental Medical Diagnostics 2017; 21: 13-25.
[16] Henderson AJ, Holzleitner IJ, Talamas SN and Perrett DI. Perception of health from facial cues. Philos Trans R Soc Lond B Biol Sci 2016; 371: 20150380.
[17] Jones AL and Behavior H. The influence of shape and colour cue classes on facial health perception. Evolution and Human Behavior 2018; 39: 19-29.
[18] Zhang B, Wang X, Karray F, Yang Z and Zhang DJ. Computerized facial diagnosis using both color and texture features. Information Sciences 2013; 221: 49-59.
[19] Jones AL, Kramer RS, Ward R. Signals of personality and health: the contributions of facial shape, skin texture, and viewing angle. J Exp Psychol Hum Percept Perform 2012; 38: 1353-61.
[20] Grandfield TA, Thompson AR and Turpin G. An attitudinal study of responses to a range of dermatological conditions using the implicit association test. J Health Psychol 2005; 10: 821-9.
[21] Coetzee V, Re D, Perrett DI, Tiddeman BP and Xiao D. Judging the health and attractiveness of female faces: Is the most attractive level of facial adiposity also considered the healthiest? Body Image 2011; 8: 190-3.
[22] Boothroyd LG, Scott I, Gray AW, Coombes CI and Pound N. Male facial masculinity as a cue to health outcomes. Evol Psychol 2013; 11: 1044-58.
[23] Spisak BR, Blaker NM, Lefevre CE, Moore FR and Krebbers KF. A face for all seasons: Searching for context-specific leadership traits and discovering a general preference for perceived health. Front Hum Neurosci 2014; 8: 792.
[24] Zhao C, Li GZ, Li F, Wang Z and Liu CJ. Qualitative and quantitative analysis for facial complexion in traditional Chinese medicine. Biomed Res Int 2014; 2014:207589.
[25] Zhang B, Vijaya kumar BV, Zhang D. Noninvasive diabetes mellitus detection using facial block color with a sparse representation classifier. IEEE Trans Biomed Eng 2014; 61: 1027-33.
[26] LI FF, ZHENG XY, WANG YQ, LI GG, HE JC, Zhuang YH and Zhao JJCAoTCM. Studies on the relationship between the facial complexion characters and kidney function in TCM clinical syndrome of chronic renal failure. Chinese Archives of Traditional Chinese Medicine 2011; 9: 019.
[27] Hobson EJPB. The positive side of stress. 2017; 84.
[28] Roh MR and Chung KY. Infraorbital dark circles: definition, causes, and treatment options. Dermatol Surg 2009; 35: 1163-71.
[29] Freitag FM and Cestari TF. What causes dark circles under the eyes? J Cosmet Dermatol 2007; 6: 211-5.
[30] Nayak CS, Giri AS and Zambare US. A study of clinicopathological correlation of periorbital hyperpigmentation. Indian Dermatol Online J 2018; 9: 245-249.
[31] Ranu H, Thng S, Goh BK, Burger A and Goh CL. Periorbital hyperpigmentation in Asians: an epidemiologic study and a proposed classification. Dermatol Surg 2011; 37: 1297-303.
[32] Jage M, Mahajan SJ, Dermatology D. Clinical and dermoscopic evaluation of periorbital hyperpigmentation. 2018; 5: 42.
[33] Sheth PB, Shah HA and Dave JN. Periorbital hyperpigmentation: a study of its prevalence, common causative factors and its association with personal habits and other disorders. Indian J Dermatol 2014; 59: 151-7.
[34] Gendler EC. Treatment of periorbital hyperpigmentation. Aesthet Surg J 2005; 25: 618-24.
[35] David BG, Menon R and Shankar R. A clinico-epidemiological study of periorbital melanosis. 2017; 3: 245-250.
[36] Meerlo P, Sgoifo A and Suchecki D. Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity. Sleep Med Rev 2008; 12: 197-210.
[37] Sapolsky R. Stress, the aging brain, and the mechanisms of neuron death. The MIT Press, 1992; 441.

[38] Akerstedt T, Palmblad J, de la Torre B, Marana R, Gillberg M. Adrenocortical and gonadal steroids during sleep deprivation. Sleep 1980; 3: 23-30.
[39] Kant GJ, Genser SG, Thorne DR, Pfalser JL and Mougey EH. Effects of 72 hour sleep deprivation on urinary cortisol and indices of metabolism. Sleep 1984; 7: 142-6.
[40] Hunt G, Todd C, Kyne S and Thody AJ. ACTH stimulates melanogenesis in cultured human melanocytes. J Endocrinol 1994; 140: R1-3.
[41] Inoue K, Hosoi J, Ideta R, Ohta N, Ifuku O and Tsuchiya T. Stress augmented ultraviolet-irradiation-induced pigmentation. J Invest Dermatol 2003; 121: 165-71.
[42] Agrawal SJNJoD, Venereology and Leprology. Periorbital hyperpigmentation: overcoming the challenges in the management. 16: 2-11.
[43] Boxrud CA and Sylvester DAJTiCESACSA. Infraorbital discoloration: dark circles-an anatomic analysis and treatment. 2004; 1: 291-305.
[44] Peate I and Wild K. Nursing practice: knowledge and care. John Wiley & Sons 2018.
[45] Naish J and Revest P. Medical sciences. Elsevier Health Sciences 2009.
[46] Lim EK, Loke YK and Thompson AM. Medicine and surgery e-book: an integrated textbook with student consult online access. Elsevier Health Sciences 2007.
[47] Lee Y, Hwang K. Skin thickness of Korean adults. Surg Radiol Anat 2002; 24: 183-9.
[48] Matsui MS, Schalka S, Vanderover G, Fthenakis CG, Christopher J, Bombarda PC, Bueno JR, Viscomi BL, Bombarda Júnior MS. Physiological and lifestyle factors contributing to risk and severity of peri-orbital dark circles in the Brazilian population. An Bras Dermatol 2015; 90: 494-503.
[49] Lowe NJ, Wieder JM, Shorr N, Boxrud C, Saucer D, Chalet M. Infraorbital pigmented skin. Preliminary observations of laser therapy. Dermatol Surg 1995; 21: 767-70.