# Fluctuating facial asymmetry and visual perceptive background during a tissue diagnostic histopathological

Edward Acero Mondragón, Eduardo Andrés Tuta Quintero

Faculty of Medicine, Universidad de La Sabana, Chía, Colombia

# ABSTRACT

**Background.** Fluctuating facial asymmetry (FFA) is accentuated throughout life and has perceptual psychological implications; tissue diagnosis shows interindividual differences at first glance, for example, in the number of fixations, but no reports are available regarding the visual perceptual background in relation to individuals with less or more FFA during the tissue diagnostic task.

**Materials and methods.** In medical students, including 13 men (SD = 19.4 years) and 8 women (SD = 18.1 years), FFA was determined as follows: n = 9 < FFA and n = 12 > FFA. The entire population performed tissue diagnostic analysis of normal skin and skin with squamous cell carcinoma pathology from digital images to establish the duration and number of fixations and the total time taken for diagnosis.

**Results.** Individuals with > FFA show significant differences in the visual perceptual background during diagnostic analysis of normal and pathological skin, which are magnified by the fixation duration and the number of fixations when the tissue diagnosis is pathological.

**Conclusion.** Compared to those with lower FFA, medical students with greater FFA performing tissue diagnosis of pathological tissue have visual perceptual backgrounds characterized by less time spent in each fixation but with more fixations.

Keywords: facial asymmetry, perception, histological diagnosis

# INTRODUCTION

Fluctuating asymmetry (FA) is the extent to which an average individual deviates from perfect symmetry [1,2]. For human populations, FA refers to random variation in terms of the standard deviation (SD) from a symmetrical trait [3]. In this dimension, the symmetry of the human face exhibits fluctuation in the middle and lower regions, i.e., fluctuating facial asymmetry (FFA) [4], as a manifestation of unstable genomics during embryonic development [1,5], which is postnatally accentuated throughout life, resulting in perceptual psychological implications [6].

The challenge of tissue diagnosis has large interindividual perceptual differences [7]. For example, individuals who make a normal or pathological diagnosis for the first time present greater saccadic movements at first glance [8,9] a phenomenon that can be related to cognitive strategies of initial searching for symmetrical morphological patterns [10]. Principles of continuity and similarity of the observed forms [11], or the perception of contrast relative to the background [12]. All these relationships explain the cognitive optimization of image identification among initial visual stimuli [13]. Recently, studies with tissue diagnostic exercises have demonstrated visual perceptual backgrounds quantifying the number of fixations [14], but the associations with the FFA of those who make the tissue diagnosis have not been documented. Thus, the objective of this research was to evaluate the visual perceptual background of FFA in a group of medical students during histological diagnosis of normal and pathological skin with squamous cell carcinoma under the hypothesis that the visual perceptual background differs among individuals with less (<FFA) and more (>FFA) FFA during this diagnostic challenge.

Corresponding author: Edward Javier Acero-Mondragón E-mail: edward.acero@unisabana.edu.co Article history: Received: 6 September 2022 Accepted: 20 September 2022

# **MATERIALS AND METHODS**

### Population

Sixty third-year medical students of the School of Medicine of Universidad Militar without congenital disease, glasses or contact lenses, a history of aesthetic surgical, pathological, or neurological interventions, or a history of consumption of medications, alcohol, or cigarettes and with nocturnal sleep patterns between 7 and 8 hours who were nonrepeating and active within the 2016 academic cycle were considered for the study. The final selection included 21 students, including 13 men and 8 women, with average ages of 19.4 and 18.1 years, respectively.

### Analysis of FFA

A 2D digital photograph of the face was taken from the participants in the Frankfurt plane with a Nikon Coolpix L120 camera of 14.1 megapixels attached to a tripod at a distance of one meter and at right angles to the ground and perpendicular to the height of the subjects' faces. The digitized photos were printed at a 1:1 scale, and a sagittal line was traced by two independent researchers to calculate FFA, as suggested by Liu et al. [15], that is, with an American Optical micrometer, and to measure the bilateral craniometry points, medial corner of the canthus of the eye, zygomatic arch, ala of the nose, and gonion on the edge of the upper lip and the edge of the lower lip considering the Huang methods for normal young adults [16]. With the measurements obtained, the FFA was calculated using protocol presented by Klingenberg [3] with the following formula:

Asymmetry Index:

- $\Sigma$  right side face  $\Sigma$  Left side face
- $\Sigma$  right side face +  $\Sigma$  Left side face

Asymmetric (or > FFA) individuals were those whose measurements exceeded one SD of the FFA in the total study population, and symmetric (or <FFA) individuals were those whose measurements did not exceed one SD of the FFA of the population.

### Eye tracking

Digitized photographs of 40X histological sections of normal skin from the School of Medicine Universidad de La Sabana HISTOTECA (Virtual Atlas of Histological Preparations, in Spanish) were displayed on a laptop computer along with photographs of squamous cell carcinoma provided by Dr. Ghassan A. Tranesh, MD, MSPath – Skin nonmelanocytic - Chief Resident, Pathology Department, Saint John Hospital and Medical Center – Detroit, Michigan, USA. Subjects performed tissue diagnostic with no time limitations. The visual perceptual background based on the optical path and the number and duration of fixations was measured with a GP3 Eye Tracker Gazepoint device (Vancouver, Canada) at 60 H, which was connected to the monitor at a visual angle of 0.50° to 1° for analysis with the program Gazepoint Pro Version 3.1. (Vancouver, Canada).

### Statistical analysis

The Mann–Whitney U test and inferential statistics with 95% confidence intervals were applied. To establish the correlation between the indices of facial asymmetry with the perceptual background based on the number and duration of fixations and the total time for normal and pathological diagnosis, the Pearson correlation coefficient was calculated, and the interpretation criteria for the correlation were established as follows: <0.1 negligible, 0.1 to 0.3 small, 0.3 to 0.5 moderate, 0.5 to 0.7 large, 0.7 to 0.9 very large, and 0.9 to 1.0 almost perfect. A value of p <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics 23 analysis software.

### **Ethical considerations**

The methods were considered innocuous, and the research was classified as minimal risk – Art. 11 – Resolution 8430 of 1993 of the Ministry of Health of the Republic of Colombia. Once the intervention was explained, all participants signed an informed consent form, and feedback was given regarding each participant's results.

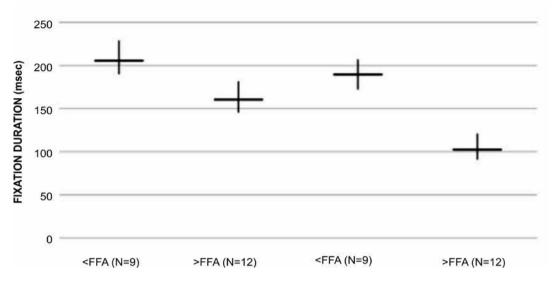
# RESULTS

During the study, a total facial asymmetry index of 9.1 mm (SD +/- 7.8 mm) was found. Visual perceptual backgrounds for <FFA and >FFA individuals showed significant differences in the duration of fixations for tissue diagnosis of both normal skin (p = 0.011) and pathological skin with squamous cell carcinoma (p = 0.088) (see Figure 1).

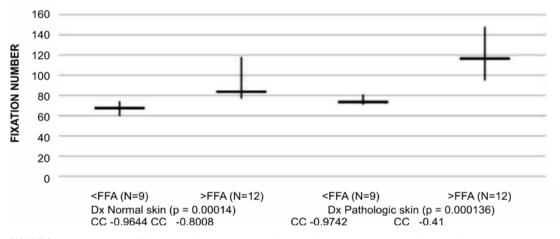
Regarding the number of fixations, <FFA and >FFA individuals differed significantly in their perceptual background in the diagnosis of both normal skin tissues (p = 0.014) and skin with squamous cell carcinoma (p = 0.013) (Figure 2).

The correlation coefficients (see Figure 2) during the diagnostic exercise were always negative for normal skin, with values of 0.09644 and -0.8008 between symmetric individuals (<FFA) and asymmetric individuals (>FFA), respectively, and for pathological skin, with values of -0.9742 and of -0.4177 between symmetrical (<FFA) individuals and asymmetric (>FFA) individuals, respectively.

Regarding the total time required for diagnosis between <FFA and >FFA individuals, no significant



**FIGURE 1.** The duration of fixations for symmetric (<FFA) and asymmetric (>FFA) individuals when diagnosing normal skin (significant (p = 0.00116)) and pathological skin with squamous cell carcinoma (significant (p = 0.088)



**FIGURE 2.** The numbers of fixations for symmetric (or <FFA) and asymmetric (or >FFA) individuals during the scan paths for the diagnosis of both normal skin (p = 0.014) and pathological skin with squamous cell carcinoma were significant (p = 0.013)

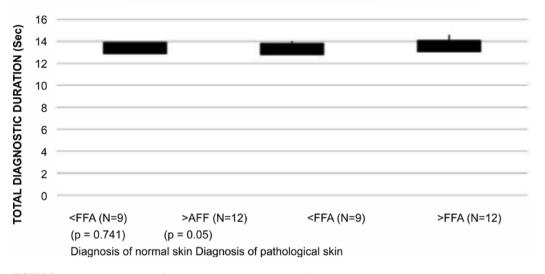
differences were found in the diagnosis of normal skin (p = 0.741) or pathological skin (p = 0.05) (see Figure 3).

# DISCUSSION

During visual exploration of images, a perceptual background of gaze fixation with short-duration patterns has been demonstrated to be cognitively related to context or environmental attention processing, while long-duration patterns are cognitively related to focal attention processing [3,17], the latter of which may be negligible in the absence of cognitively assigned identification tasks.

For this research, the cognitive task involved examining a digital tissue image to diagnose normal skin or skin with squamous cell carcinoma. Differences were found in the duration of fixations at first glance, indicating a mode of environmental attentional cognitive processing and greater compensatory perceptual background with a greater number of fixations for >FFA individuals. Thus, as they are associated with the cognitive effort of identifying digital images, when fixations are longer (Meghanathan et al. 2015; Raptis et al. 2016) [18], this could explain why individuals with >FFA exert less cognitive effort in the tissue diagnosis of normal and pathological skin: with a greater number of fixations, these individuals would extract diagnostic information but would do so from the tissue context, either by contrast or by disorganization of what was observed, and not from the cognitive effort required to identify normal or pathological tissue structures.

Thus, as they are associated with the cognitive effort of identifying digital images, when fixations are longer [18], this could explain why individuals



**FIGURE 3.** The time required for histological diagnosis of normal skin and squamous cell carcinoma by symmetrical (or <FFA) and asymmetrical (or >FFA) individuals during the scan paths did not demonstrate significant differences (p = 0.741 and p = 0.05, respectively)

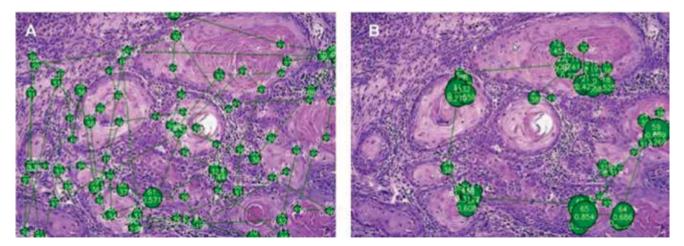
with >FFA exert less cognitive effort in the tissue diagnosis of normal and pathological skin: with a greater number of fixations, these individuals would extract diagnostic information but would do so from the tissue context, either by contrast or by disorganization of what was observed, and not from the cognitive effort required to identify normal or pathological tissue structures.

Interestingly, looking at disorganized images stimulates a greater number of saccadic movements, resulting in increases in the number of fixations [1,2,6]; this fact may explain why in >FFA individuals performing diagnosis of pathological skin, where the disorganization of squamous cell carcinoma is conspicuous, a diagnostic strategy is useful.

However, based on principles of "similarity" with the environment within Gestalt's laws of per-

ceptual organization, another strategy used for image recognition, a specific benefit in assigning the area of interest to identify digital images [20]; It is noted when observing the optical path during the diagnosis of skin with squamous cell carcinoma by >FFA subjects (figure 4A); here, patterns of greater fixation numbers of short durations are observed, which are distributed among the epithelial disorganization represented in the eosinophilic "swirls" of keratinocytes and the stroma surrounding them, without concentrating in any area of interest; in contrast, the diagnostic path of <FFA subjects (figure 4B) reveals how areas of visual interest with patterns of low fixations and long durations are focused on the eosinophilic "swirls" of keratinocytes.

This perceptual strategy outlined here can be validated for phylogenic reasons. For example, the



**FIGURE 4. A.** On the left: an example of an optical path pattern for the diagnosis of pathological skin with squamous cell carcinoma by an asymmetric (>FFA) individual. **B**. On the right: an example of an optical path pattern for the diagnosis of pathological skin with squamous cell carcinoma by a symmetrical (<FFA) individual. Each green circle represents an eye fixation, and a larger size represents a longer dwell time

visual search for subtle hidden targets that predators use to identify prev establishes that this search is initially based on what stands out in the middle of the contrast <sup>21</sup>, representing an evolutionarily successful visual preference for a reasonably rapid processing byproduct of cognitive recognition, illustrated in their work on eye tracking in humans compared to primates [19,20]. Finally, although in this study the speed for achieving tissue diagnosis did not show statistically significant differences between > FFA and <FFA individuals for normal (p = 0.741) and pathological (p = 0.5) tissue (see Figure 3), > FFA subjects were qualitatively faster at the diagnosis of pathological skin.

The results presented here and in a simplified manner demonstrate only an associative relationship between visual perceptual patterns in > FFA individuals and the task of tissue diagnosis, contributing to an understanding of the expertise required for this task, where visual and cognitive skills in the process of continuous integration have been speculated to have a common origin [21]. However, beyond the focus of this study, the results allows us to reasonably conclude that >FFA individuals show

Conflict of interest: none declared Financial support: none declared

### REFERENCES

- 1. Hou M, Fagan MJ. Assessments of bilateral asymmetry with application in human skull analysis. PLoS One. 2021 ;16(10):e0258146. Doi: 10.1371/journal.pone.0258146
- 2. Klingenberg, C.P. Analyzing Fluctuating Asymmetry with Geometric Morphometrics: Concepts, Methods, and Applications. Symmetry. 2015;7:843-934. Doi: 10.3390/sym7020843.
- 3. Thiesen G, Gribel BF, Freitas MP. Facial asymmetry: a current review. Dental Press J Orthod. 2015 ;20(6):110-25. doi: 10.1590/2177-6709.20.6.110-125.sar.
- 4. Salamanca Carreño A, Parés-Casanova PM, Vélez Terranova OM, Monroy Ochoa NI. Shape Directional Asymmetry in Hindlimb Pairs among Calves (Bos Taurus). Animals (Basel). 2022 ;12(5):559. doi: 10.3390/ani12050559.
- 5. Brown JR, van der Zwan R, Brooks A. Eye of the beholder: Symmetry perception in social judgments based on whole body displays. Iperception. 2012;3(7):398-409. doi: 10.1068/i0495sas.
- Appelbaum LG, Cain MS, Schroeder JE, Darling EF, Mitroff SR. 6. Stroboscopic visual training improves information encoding in short-term memory. Atten Percept Psychophys. 2012;74(8):1681-91. doi: 10.3758/s13414-012-0344-6.
- Zormpas-Petridis K, Noguera R, Ivankovic DK, Roxanis I, Jamin Y, Yuan Y. 7. SuperHistopath: A Deep Learning Pipeline for Mapping Tumor Heterogeneity on Low-Resolution Whole-Slide Digital Histopathology Images. Front Oncol. 2021 ;10:586292. doi: 10.3389/ fonc.2020.586292.
- Wen S, Kurc TM, Gao Y, Zhao T, Saltz JH, Zhu W. A Methodology for 8. Texture Feature-based Quality Assessment in Nucleus Segmentation of Histopathology Image. J Pathol Inform. 2017;8:38. Doi: 10.4103/jpi. ipi 43 17.
- 9. Hafed ZM, Yoshida M, Tian X, Buonocore A, Malevich T. Dissociable Cortical and Subcortical Mechanisms for Mediating the Influences of Visual Cues on Microsaccadic Eye Movements. Front Neural Circuits. 2021;15:638429. Doi: 10.3389/fncir.2021.638429.
- 10. Wagemans J, Feldman J, Gepshtein S, Kimchi R, Pomerantz JR, van der Helm PA, et al . A century of Gestalt psychology in visual perception: II.

229

more visual fixations than <FFA individuals during disorganized, cryptic, or hidden visual challenges, which then extend to morphophysiological spectra of visual perceptual performance and can be a product of adaptations to body asymmetries caused by developmental instability [19].

## CONCLUSION

Compared to those with lower FFA, medical students with greater FFA performing tissue diagnosis of pathological tissue have visual perceptual backgrounds characterized by less time spent in each fixation but with more fixations.

### Acknowledgments

We are most thankful for the support of the Universidad de La Sabana.

### Financing

The research did not receive specific funding, but was conducted as part of the authors' semployment at the University of La Sabana.

Conceptual and theoretical foundations. Psychol Bull. 2012;138(6):1218-52. Doi: 10.1037/a0029334.

- 11. Yorzinski JL, Harbourne A, Thompson W. Sclera color in humans facilitates gaze perception during daytime and nighttime. PLoS One. 2021;16(3):e0249137. Doi: 10.1371/journal.pone.0249137
- 12. Eisenberg ML, Zacks JM. Ambient and focal visual processing of naturalistic activity. J Vis. 2016;16(2):5.\_Doi: 10.1167/16.2.5.
- 13. Brunyé TT, Mercan E, Weaver DL, Elmore JG. Accuracy is in the eyes of the pathologist: The visual interpretive process and diagnostic accuracy with digital whole slide images. J Biomed Inform. 2017;66:171-179. Doi: 10.1016/j.jbi.2017.01.004.
- 14. Liu Y, Schmidt KL, Cohn JF, Mitra S. Facial asymmetry quantification for expression invariant human identification. Comput Vision Image Understanding 2003:91(1-2):138-159.
- 15. Huang CS, Liu XQ, Chen YR. Facial asymmetry index in normal young adults. Orthod Craniofac Res. 2013;16(2):97-104. Doi: 10.1111/ ocr.12010.
- 16. Helo A, Pannasch S, Sirri L, Rämä P. The maturation of eye movement behavior: scene viewing characteristics in children and adults. Vision Res. 2014;103:83-91. Doi: 10.1016/j.visres.2014.08.006.
- 17. Meghanathan RN, van Leeuwen C, Nikolaev AR. Fixation duration surpasses pupil size as a measure of memory load in free viewing. Front Hum Neurosci. 2015;8:1063. Doi: 10.3389/fnhum.2014.01063.
- 18. Serrien DJ, O'Regan L. The interactive functional biases of manual, language and attention systems. Cogn Res Princ Implic. 2022;7(1):20. Doi: 10.1186/s41235-022-00365-x.
- 19. Bornstein MH, Mash C, Arterberry ME. Perception of object-context relations: eye-movement analyses in infants and adults. Dev Psychol. 2011;47(2):364-75. Doi: 10.1037/a0021059.
- 20. Mühlenbeck C, Liebal K, Pritsch C, Jacobsen T. Differences in the Visual Perception of Symmetric Patterns in Orangutans (Pongo pygmaeus abelii) and Two Human Cultural Groups: A Comparative Eye-Tracking Study. Front Psychol. 2016;7:408. Doi: 10.3389/fpsyg.2016.00408.