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Sex and gender optometry: From retinal design to stereopsis

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Summary. — Scientific research in optometry aims to increase the ability to predict optical effects induced by lens fitting, allowing us to understand how geometrical concepts and physical phenomena translate into perceptual responses. It is possible, for instance, to investigate how differential perspective affects three-dimensional perception, indeed the ocular parallax error, that occurs as the eyes are separated horizontally by a certain distance (DAV), allows for the depth interval between two object points to be appreciated and transferred to the retina. In a study conducted at the University of Turin, the DAVs measured on a group of students were compared with the students' stereo acuity values, with the aim of highlighting whether female subjects, whose DAVs are smaller than those of men, actually have less sense of depth. The measurement protocol and the results obtained will be explained. The research perspective is the parameterization of optometric tests to take into account differences due to gender, in order to detect any abnormalities more accurately.

1. – Introduction

The aim of this paper is to highlight how even in optometry as well as in medicine, when dealing with personal well-being, it is necessary to treat the various topics by correlating them with sex and gender. Following this principle, didactics, research and clinical practice should renew themselves and consider these aspects of diversification as central. Currently, despite 20 years of history on gender medicine, little is still understood [1]. Indeed, a 2019 study by Gemmati *et al.* highlights all that could have been avoided if gender medicine, pharmacogenetics, and personalized medicine had been applied in the "Gender-omics and sex-omics era" [2], thus underlining how the era of gene, DNA and biological insights have neglected basic clinical applications. Although a number of reviews focusing on current knowledge on the role of hormone regulation in gender medicine and gender peculiarities in major clinical areas are provided in the scientific literature [3], according to studies that have examined the practical issues related to

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the application of gender medicine to preclinical and clinical studies in the biomedical sciences, "the future application of gender medicine may increase the reproducibility of studies, promote discoveries, expand the relevance of studies, and ultimately improve the care of both male and female patients" [4].

2. – Sex and gender

When we talk about sex, we mean the biological marker, while gender refers to psychosocial attributes. Giving an example to clarify the practical difference between sex and gender: a disease may manifest differently due to biological difference between the two sexes and at the same time be easier or more difficult to diagnose due to a different predisposition of the two genders in getting examined. "Sex" and "gender" are therefore often misused as synonyms, generating frequent misunderstandings in those who are not deeply involved in the field [2]. However, in today's society, we refer to gender medicine by including and substituting sex for gender, which is why the expression "sex medicine" or "gender medicine" can be found interchangeably in the scientific literature. Current gender medicine was thus introduced about 20 years ago under the name "sex and gender medicine" and its aim was to analyze pharmacological and prognostic diagnostic aspects by relating them to a person's sex and gender [1]. In recent years, even in optometry some studies have been analyzed differentiating by sex and gender.

When reviewing the relevant literature, the results obtained by the Tear Film and Ocular Surface Society appear interesting. In fact, during the TFOS Dry Eye Workshop II with a meta-analysis of dry eve prevalence, data estimated the impact of age and gender reporting that women have a higher prevalence of DED (dry eye disease) than men, although the differences become significant only with age [5]. On the other hand, regarding the issue of myopic progression, it was found in an observational study that female sex was one of the factors associated with more rapid progression of myopia [6]. Furthermore, in a pilot study conducted on 155 eyes that among other specifications evaluated whether sex influenced the biometric properties of eyes in young adults, male subjects had significantly thicker and flatter corneas than female subjects [7]. Nevertheless, in a retrospective study, in which the medical records of 6687 patients aged 6 to 85 years, including 2168 males and 4519 females, were examined, males were the ones to manifest significantly more myopia and astigmatism, while females were more hypermetropic in all age groups [8]. The female sex is also most likely to be sensitive in reporting early onset of presbyopia (for subjective measures such as prescriptions of near spectacles) while measures of accommodative amplitude show a weak trend to the contrary. As suggested by a meta-analysis that compared the prevalence and magnitude of presbyopia among men and women using nine cross-sectional studies, this would indicate that the greater association of presbyopia in women is not due to a physiological difference in accommodation, but rather to other sex and gender differences, such as the tasks performed and viewing distances [9]. Finally, a review study on the influence of sex and gender on ocular diseases is reported, which clarified how sex and sex hormones by influencing the tear system, eyelids and blinking, anatomy, cornea, aqueous humor dynamics, lens, etc. make gender differences in ocular conditions and diseases need to be considered in the context of the underlying physical and social environment [10].

3. – Retinal design and stereopsis

Given the differences in visual performance due to sex and gender that emerged from research, in a study carried out at the University of Turin, the DAVs (visual axis distances) of 90 subjects were measured and compared with their stereoacuity values, with the aim of highlighting whether female subjects, whose DAVs are of a lower magnitude than those of men, had less sense of depth.

3[•]1. Visual axis distances. – During gaze orientation on a three-dimensional object in the visual field, due to the horizontal anatomical separation of the eyes, the images that are projected onto the retina report the same object but at two different angles. The distance between the two eyes is necessary to perceive as much information as possible about the separation between the two images of the object in the visual field; thus, the three-dimensionality of the object is perceived precisely because the object is viewed from two different angles. From the morphological and anatomical point of view of the human body, sexual dimorphism is the phenomenon whereby individuals of the two sexes present a set of morphologically and functionally different physical characteristics due to what are generically called sexual characters. Among the secondary sexual characters, we find skeletal characters such as the facial set-up that is narrower for the female individual and the smaller female head compared to the morphology of the male individual [11].

Based on what has been said from a geometric point of view, greater parallax is a manifestation of greater interpupillary distance, so it is safe to assume that individuals of different sexes have different visual axis distances. Since stereopsis varies with interpupillary distance, it is useful to compare stereopsis values in female and male subjects.

3[•]2. Stereopsis. – The word "stereoacuity" therefore denotes the minimum angle of binocular disparity, caused by the projection of images onto the retina, for which depth perception is possible. The minimum disparity angle corresponds to the minimum perceivable distance between two stimuli. This value is known as retinal disparity and represents the threshold below which stimuli are not perceived as separate. The retinal disparity depends on the DAV and the distance to the target, so the higher the DAV, the greater the depth perceived. The maximum disparity limit that can lead to stereoscopic vision is 1000' of arc, while the minimum limit (stereoacuity value) considered normal is about 30" of arc but can reach even lower values such as 2" [12]. In the study, both local stereopsis and global stereopsis were tested. The local stereopsis is responsible for depth perception in patterns (stereograms) consisting of even simple lines that exhibit a certain degree of lateral disparity and the global stereopsis is responsible for depth perception in randomized patterns that require greater binocular performance from the subject examined, without the facilitation of monocular cues.

Stereoscopic perception, as an expression of the highest level of binocular cooperation, allows the visual system to estimate the depth of objects located in the surrounding visual field; those who lack fused binocular vision from birth learn to maximize monocular cues and often do not realize their deficiency until they are subjected to specific tests [13]. The choice to conduct a study concerning stereopsis comes from its impact on many aspects of life, so its qualitative and quantitative evaluation at the clinical level is relevant.

4. – Materials and methods

The study included a sample of 90 subjects, ranging in age from 8 to 62 years (with a mean age of 27.3 ± 1.4 years). Each participant was asked to fill out the informed consent

form and provide age and gender information. In addition, the refractive condition in use for both distance and near was noted; if the participant did not report any known visual defect, data were collected without the subject wearing any correction. In the study, the relationship between stereopsis values and variables such as age, gender, interpupillary distance and refractive condition were statistically investigated. Based on the data collected, confidence interval tables were developed for stereopsis values according to the other variables listed above. Several stereopsis tests are available to measure stereopsis and so the choice is relevant because the results obtained using different tests, each with their own advantages and disadvantages, are not necessarily comparable [14]. The choice can be guided by the preference for a local- or global-type stereopsis measurement. Tests for global stereopsis require both systems activated, recognition and localization, while tests for the local one only require activation of the parvo cellular system. The stereopsis tests used for the study are the Random Dot Stereo Acuity Test (RDT) and the Fly Stereo Acuity Test. Both use polarization to achieve the stereoscopic effect, making use of polarized plates and goggles. The plates are the result of superimposing two images having reverse polarization, which, separately, are destined to the eye that has the goggle lens with the same polarization as the plate image. It follows that the image perceived by one eye has a different polarization than that of the contralateral eye, and only through cooperation and integration by both eyes the perception of three-dimensionality is achieved. In the first section of the RDT there are four parts, each divided into four quadrants of randomized points of which three contain one of the LEA symbols (square, circle, house and apple); this section allows detecting global stereopsis through the recognition of the symbols hidden within them. The sensitivity scale for this part of the test ranges from 500 sdc to 63 sdc. The second section of the RDT allows the assessment of local stereopsis through the recognition of one of the three Wirth circles, the one that is prominent compared to the others. The circles are contained in twelve rectangular geometric figures, and the sensitivity reaches 12, 5 sdc. The third section also allows for the assessment of local stereopsis and involves the recognition of the relief of one of the four Lea symbols for each horizontal stripe (A, B, C), but it was not administered as it is mainly suitable for pediatric subjects. Similarly, two of the three sections of the Fly, the first showing a fly with raised wings and the last one, which is equivalent to the third section of the RDT, were not administered because they were suitable for younger subjects. Instead, the second section of the Fly was presented and is equivalent to the second section of the RDT with the difference that there are ten figures, geometrically rhomboidal, each containing four Wirth circles and with a sensitivity reaching 20 sdc. To perform, subjects were asked to sit, wear their usual optical correction at the 40 cm distance (the distance at which the tests were administered), and wear polarized glasses. Measurements were taken while maintaining constant illumination above 300 lux. During the procedure, it was the task of the operator to maintain the correct test position at the examination distance; specifically, it was verified that the subject did not move and did not move the test facilitating the perception of the three-dimensional image. Having performed the stereopsis tests, as a final step, the subject's interpupillary distance was measured using a manual interpupillometer. At the end, statistical analyses were performed with the collected data, during which stereopsis values were divided, based on the tests administered, into three estimates for each subject. Estimate 1 includes the global stereopsis values obtained by administering the first section of the RDT test, estimate 2 and estimate 3 include the local stereopsis values obtained by administering sections number two of the RDT and the Fly test, respectively.

DAV M	$61, 3 \pm 0, 7$	mm
Stereo M Estimate 1	$88,6 \pm 14$	sdc
Stereo M Estimate 2	$47, 1 \pm 11, 7$	sdc
Stereo M Estimate 3	$43,3\pm11,4$	sdc
DAV F	$59, 4 \pm 0, 4$	mm
Stereo F Estimate 1	$79,7\pm8,6$	sdc
Stereo F Estimate 2	$36, 2 \pm 2, 9$	sdc
Stereo F Estimate 3	$41,0\pm7,0$	sdc

TABLE I. – Means of DAV and stereopsis values for each estimate in female (F) and male (M) subjects.

5. – Results and conclusions

The study included a sample of 90 subjects, ranging from 8 to 62 years of age. The age, sex and refractive condition were noted for each participant, and then interpupillary distance and stereopsis were measured with different tests. Statistical analyses were performed with the collected data, during which stereopsis values were divided, based on the tests administered, into three estimates for each subject. Estimate 1 includes the global stereopsis values obtained by administering the first section of the RDT test, estimate 2 and estimate 3 include the local stereopsis values obtained by administering sections number two of the RDT test and the Fly test, respectively. The aim of the study was to analyse the relationships of stereopsis values with gender, age, visual axes distance and refractive condition. The analyses performed in relation to gender showed results compatible with those obtained in a previous study with a different data set [15]. It is therefore not possible now to state the existence of a significant difference between the sexes regarding stereopsis values, while a significant difference was found in the distance value of the visual axes. Although not at a statistically significant level, the female sample showed slightly better stereopsis scores despite significantly lower visual axis distances, as shown in table I. As the opposite would be expected from the point of view of geometric optics, the entire sample was analysed for a more comprehensive evaluation. In this case, the stereopsis values did not show any correlation with the visual axis distance, but unlike in the analysis conducted differentiating by gender, better stereopsis scores corresponded to higher visual axis distance values. This agrees with the theoretical model according to which the greater amplitude of the perspective difference between the two eyes confers higher stereoscopic performance, although in the study the variations were minimal given the correlation coefficients very close to zero. On the other hand, they showed a positive correlation with age; in fact, stereoscopic performance tends to decrease with the physiological deterioration of the visual system.

The reason why the relationships between the variables appeared weak and therefore not significant may be due to the fact that current tests are limited in their assessment of stereoscopic abilities. In particular, the scales of the most popular stereopsis tests allow limited minimum levels of measurement, as well as having reduced accuracy because the deviation between each single value is quite large. In this study, the subjects with optimal stereopsis values were more numerous. There is an extensive discussion in the literature on the limitations of these tests. A recent study cites the situation in which subjects without stereopsis at the time of the clinical measurement instead reported appreciating the three-dimensionality of the surrounding space, this because they exploit monocular cues [16]. The discrepancy between clinical tests and the actual stereoscopic perceptual experience of the subject with inefficient binocular cooperation could be traced back to another characteristic of the most common stereoscopic tests, namely that of only partially assessing depth perception. This limitation can be assimilated to a static presentation of three-dimensionality by the test. It follows that, according to the study, in the presence of dynamically changing depths, a reception of three-dimensionality more congruent with real spatial perception is possible [16]. In conclusion, having analysed several factors that are supposed to significantly influence stereoscopic abilities with results that do not conform to expectations if only slightly, this study has been able to highlight both the limitations of the tests already discussed in the literature and the need to investigate the correlation between visual performance, sex and gender through clinical measures. Thus, although in the field of medicine they show the variability of a diagnostic approach in relation to gender [17] and the role of gender medicine in public health [18] with regard to optometry the expansion of clinical research on the topic would allow the implementation of guidelines that take into account sex and gender. Given their leading role, clinical care algorithms should include gender-based assessment [19]. Several studies also suggest that teaching should be integrated with these aspects [20-23].

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