Effects of Environmental Exposure to Tobacco on Modulation of Color Vision

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Abstract

The chronic use of cigarettes causes toxic and oxidative effects on the visual system, which can cause changes in color vision. Although there are studies on the harmful effects of tobacco in active smokers, the literature on secondhand/passive smokers (or environmental tobacco smoke) is still scarce. Therefore, the aim of this study was to investigate the ability of color vision in active and passive smokers. This is a cross-sectional observational study in which 103 individuals were divided pseudorandomly into 3 groups: control group (CG) n = 44 individuals (72 eyes), with a mean age of 28.65 ± 7.90; group of passive smokers (GPS) n = 28 (56 eyes), mean age 28.74 ± 9.42; group of active smokers (GAS) n = 31 (60 eyes), mean age 34.91 ± 11.30. The psychophysical evaluation of color vision was performed using the Ishihara pseudoisochromatic plates, the computer program of the Freiburg Visual Acuity & Contrast Test, version 3.7, and the desaturated Lanthony D15 ordering test. The results indicate that there was no correlation in GAS and GPS with age, time of exposure to tobacco and daily consumption. It was observed that both GAS and GPS showed changes in visual acuity (P <0.05), and only GPS showed changes in color vision (P <0.05); GFP showed a deficit in visual acuity and worse color vision when compared to GAS (P <0.05). These results are discussed in relation to the biochemical and pathophysiological effects that exposure to cigarettes may have on the visual system, which would explain the functional changes observed. We conclude that passive and active smokers have impaired color vision and that the psychophysical methods used in this study are effective for the subclinical tracking of changes in color vision.

Keywords: smoking; color vision; environment; active and passive smokers.

1. Introduction

The World Health Organization estimates that approximately 6 million people die each year as a result of the harmful effects of tobacco consumption, however, only 5 million are active users, the rest are passive

smokers (or environmental tobacco smoke), which makes tobacco one of the largest threats to public health [1,2].

Cigarettes have about four thousand types of substances, including benzene, polonium 210, hydrogen cyanide, formaldehyde, xylene, dichloro-diphenyl-trichloroethane (DDT), phosphorus P4 and P6, phenol and nicotine. [2, 3, 4]. Among the top five risk factors for mortality, smoking is one of the preventable causes of death. It is estimated that approximately 10 million deaths will occur in the year 2030 if global control measures are not adopted [5, 6, 7].

In Brazil, 23 people die every hour due to problems related to smoking, which affects 17.2% of the population over 15 years of age [8, 9].

The age range for starting smoking and becoming a smoker is estimated to be between 18 and 24 years, which makes smoking an important socioeconomic problem and is a serious health warning [10, 11].

Cigarette smoking is a risk factor for several diseases including cardiovascular and respiratory diseases [10, 11]. In addition to smoking affecting the entire organism, its consumption is also associated with neuro-ophthalmological changes such as age-related macular degeneration, cataracts, shortening of the time to break the tear film, itching, burning in the eyes and dryness suggestive of dry eye syndrome [7, 10]. Some authors also suggest that chronic cigarette use is related to toxic neuropathy linked to smoking that affects color vision both on the green-red axis [12, 13, 14] and on the blue-yellow axis [15, 16].

Many of the changes in visual functions resulting from intoxication can happen before other more serious neurological disorders. These manifestations can occur subclinically, making the assessment of visual function to be used as a signal that the intoxication process is happening [17, 18]. To investigate visual functions, there are several methods, including psychophysics, which has tests and non-invasive instruments capable of detecting early changes, indicating losses before the appearance of more harmful signs and symptoms [19].

Given the above, the general objective of this study was to investigate the effects of environmental exposure to tobacco on color vision. More specifically, the experiments carried out investigated (1) possible differences in color vision performance in active and passive smokers and; (2) possible relationships between the performance in color perception with time and the intensity of cigarette consumption.

2. Material and Methods

This is an observational, analytical cross-sectional study carried out in the city of São Luís-MA, whose research protocol was approved by the Ethics Committee for Research with Humans at the CEUMA University (registration # 3.115.352). All volunteers signed an informed consent form to participate in the research.

2.1 Sample

171 subjects were recruited, of these 68 were excluded due to the exclusion criteria, thus leaving 103 subjects who remained in the study and were divided into three groups: group of active smokers, group of passive smokers and control group (Figure 1).

The group of active smokers (GAS) consisted of 31 subjects who were smokers on average for 16 years and smoked on average 7 cigarettes per day. The average age of this group was 34 years.

The group of passive smokers (GPS) was composed of 28 subjects who had been cohabiting with active smokers for at least 1 year (mean of 17 years and standard deviation of 11 years). The average age of this group was 29 years.

The control group (CG) consisted of 44 subjects who were neither exposed to active nor passive smoking. The average age of this group was 29 years.

The recruitment of volunteers took place through an invitation to participate in the research published on social networks, posters posted in schools and health centers. Inclusion criteria were health and age over 18 years, with smoking being the criterion for the experimental group. The exclusion criteria were chronic diseases, such as diabetes and systemic arterial hypertension, psychiatric and neurological diseases, such as depression, anxiety, schizophrenia and epilepsy, eye diseases such as cataracts and glaucoma, infections such as toxoplasmosis and malaria and a history of exposure to chemical agents such as such as heavy metals, organic solvents and agrochemicals.

All study participants underwent rigorous medical history and medical evaluation. Then they performed a battery of psychophysical tests evaluating visual acuity and color vision. The flowchart below illustrates the sample selection and the composition of the groups.

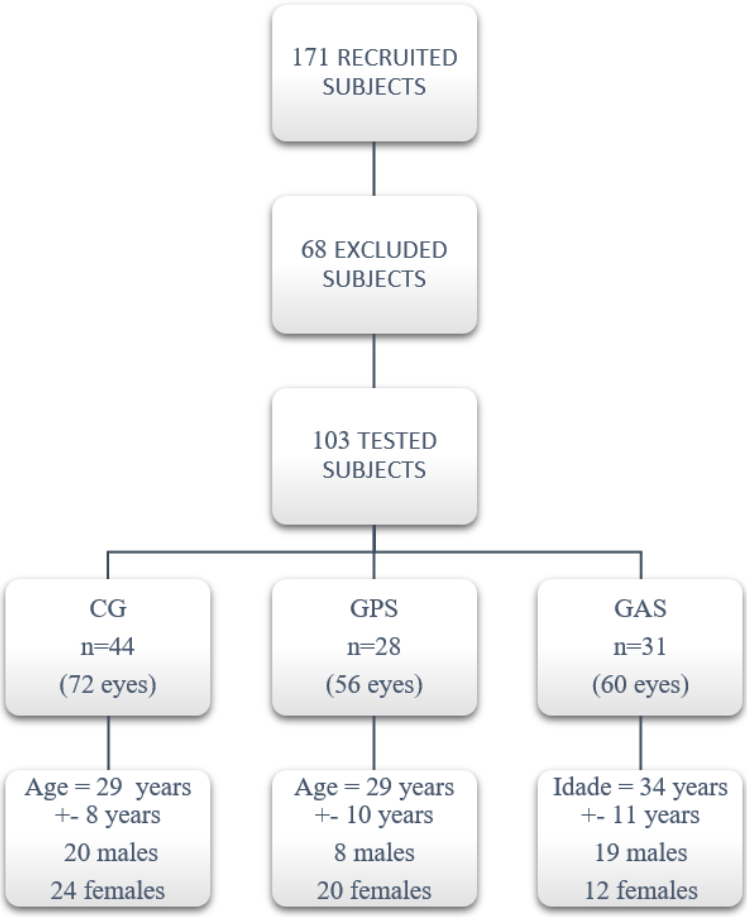

Figure 1. Flowchart of the studied sample.

2.2 Tests and instruments for visual assessment

2.2.1 Ishihara Pseudoisochromatic Plates

The assessment of color vision was performed using the Ishihara pseudoisochromatic plates widely used in studies of visual psychophysics because they have high sensitivity and specificity [20, 21]. In addition, studies show that this test is effective for the rapid identification of congenital and acquired deficiencies. The Ishihara test contains boards that differentiate protanomalias from deuteranomalias [21]. The test was carried out with a book containing the pseudoisochromatic plates - Ishihara's Test for Color Deficiency, edition of 24 plates (2009, Kanehara Trading Inc., Japan), under lighting of approximately 67000 Kelvin to 25 candles of the Illuminant, which is a Richmond Illuminator Flat Tray Tru-Daylight.

In the test the target is composed of a group of circles that form numbers and that differ from the background only by the difference in chromaticity. For this study, 17 plates were used; the first stimulus presented to the subject was a control stimulus that can be viewed by healthy subjects with dyschromatopsies. It does not have a pseudoisochromatic configuration and serves to verify if the subject understood the command. Another 14 plates contain stimuli for evaluating protans and deutans dysromatopsies; and 2 plates are for making a differential diagnosis between protan-type dyschromatopsia and deutan-type dyschromatopsia.

These plates were presented (for 3 seconds each) at a distance of 75 cm from the subject's eye, and the subject was instructed to answer which number he could see. The test was performed on both eyes in a monocular form.

As a result, the number of errors and the plates on which the confusions took place were considered. Thus, the results of each tested subject could be compared with the reference values indicated in the test manual. For the screening of altered color vision, the tested subject was considered normal if there was a maximum of 6 errors in the response.

2.2.2 Freiburg Visual & Contrast Test (FrACT)

This test consists of the computer program Freiburg Visual Acuity & Contrast Test, version 3.7, which aims to assess visual acuity. The test was performed in a photopic environment with the computer monitor light used to present the stimuli.

The test stimulus consists of the shape of the letter “C” by Landolt in high contrast of luminance in relation to the background. The opening of the “C” was presented to the subject in 4 different orientations (above, below, right and left) and the individual should inform the direction in which the stimulus is being presented. With each presentation, the program automatically increases or decreases the size of the letter “C” according to the responses obtained, totaling 30 presentations of the stimulus.

The stimulus presentation follows a random sequence and the computer program records the minimum stimulus size that the subject can detect (inform). To perform the test, the subject was positioned at a distance of four meters from the screen of a 15 ”computer monitor, according to the Freiburg Visual Acuity & Contrast Test manual (version 3.7). The test was performed in both eyes of each subject in a monocular form. The test result was plotted from data made available by the evaluation program itself considering decimal values.

2.2.3 Desaturated Lanthony D15 hue ordering test

The Lanthony D15 desaturated tint ordering test (number 4428, Richmond Products Inc., USA) was performed under lighting of approximately 67000 Kelvin at 25 foot-candels of the Illuminant, which is a Richmond Flat Tray Tru-Daylight Illuminator.

The test consists of 16 pieces that have 2 degrees of visual angle with constant saturation of 2 and varied hue. The stimulus (piece) was presented at a distance of 75 cm from the subject's eye.

At first, the tested person had a minute to view the pieces correctly arranged on a table according to the color gradation. Then, the experimenter dispersed the pieces leaving only the first piece of the fixed organization (piece number 0) to serve as a reference for the ordering.

The subject was instructed to reorder (position) the pieces as presented in the first moment, taking into account pieces with a similar hue next to each other. Each piece is internally numbered from 0 to 15 so that only the experimenter has control of the correct order to be followed.

At the end of the reorganization of the pieces, the subject was able to make the adjustments he deemed necessary for the best ordering. The test was performed in both eyes of the tested subject, monocularly, twice in each eye, with the first attempt in each eye being used only for training and discarded afterwards.

For the analysis of the results, the Color Confusion Index (CCI) was calculated, which takes into account the number of pieces placed in the wrong position and the distance it was from its proper position. The results were quantitatively evaluated using the CCI, which indicates that the worse the vision, the greater the number of pieces placed in the wrong position [22]. Also analyzed were the parameters of the C-Index, which takes into account the magnitude of the error made, the S-Index, which takes into account how far the error was made, and the Angle, which takes into account the location where the error it was more persistent [3].

2.3 Statistical design

Initially, the data were analyzed for normality using the D'Agostino Pearson test. For all the visual parameters studied, a comparison was made between active and passive smokers with control subjects and between them using ANOVA one way with Tukey post test.

To analyze the relationship between variables raised (age, consumption time in years, number of cigarettes per day) in the interviews with subjects and the results observed in the visual tests, the linear correlation coefficient in a correlation matrix was used. In all cases, an $\alpha = 0.05$ value was considered.

3. Results

The CG showed better visual acuity when compared to the GAS and GPS groups ($p < 0.05$ and $p < 0.01$, respectively). Interestingly, the GPS group showed lower results when compared to the GAS ($p < 0.05$) (Figure 2).

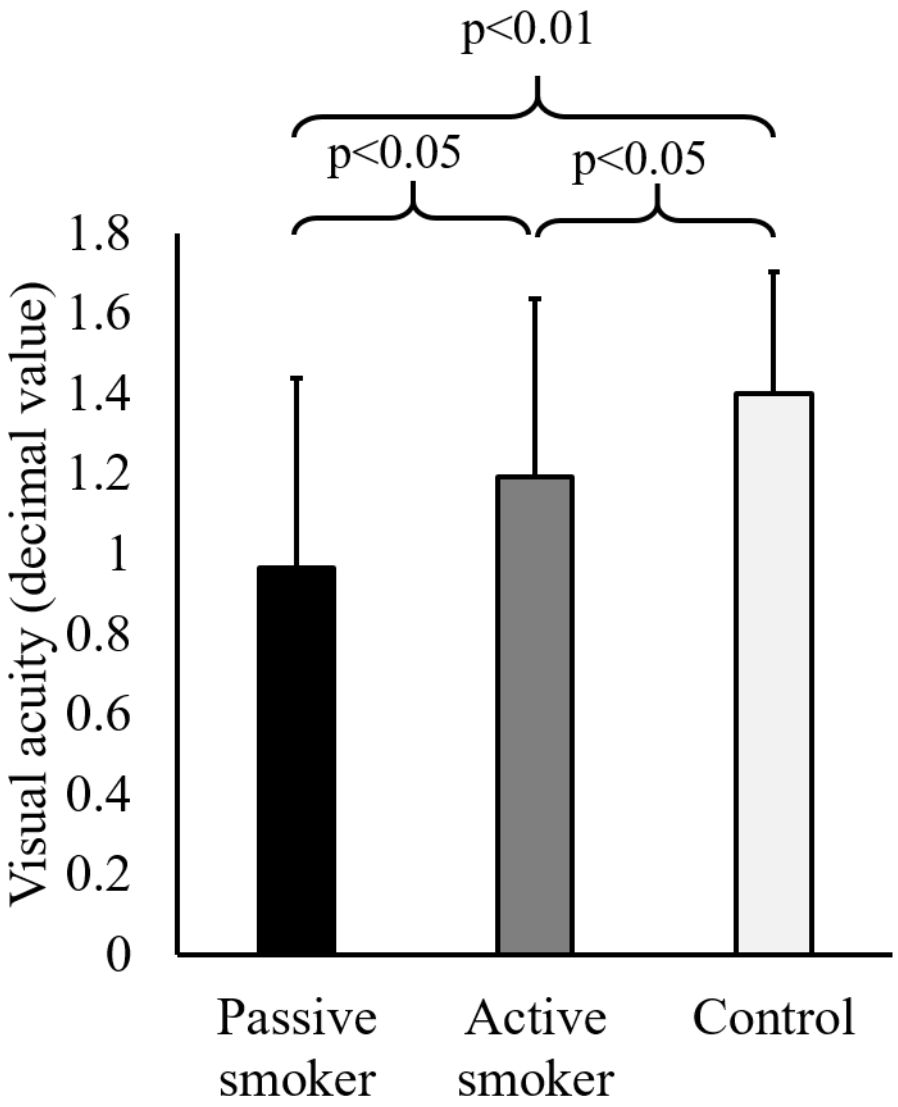

Figure 2. Visual acuity of the three studied groups: passive smokers, active smokers and control group. The vertical columns indicate the average visual acuity in decimal value and the bars indicate the standard deviation. The horizontal bracket indicates statistical difference between the groups with the significance value of $p < 0.05$ for the one-way ANOVA.

GPS subjects showed, on average, lower values for CCI when compared to CG ($p < 0.01$) and C index ($p < 0.05$). There was no difference between GAS and GC. For all other color vision assessment parameters, there was no difference between groups (Figure 3).

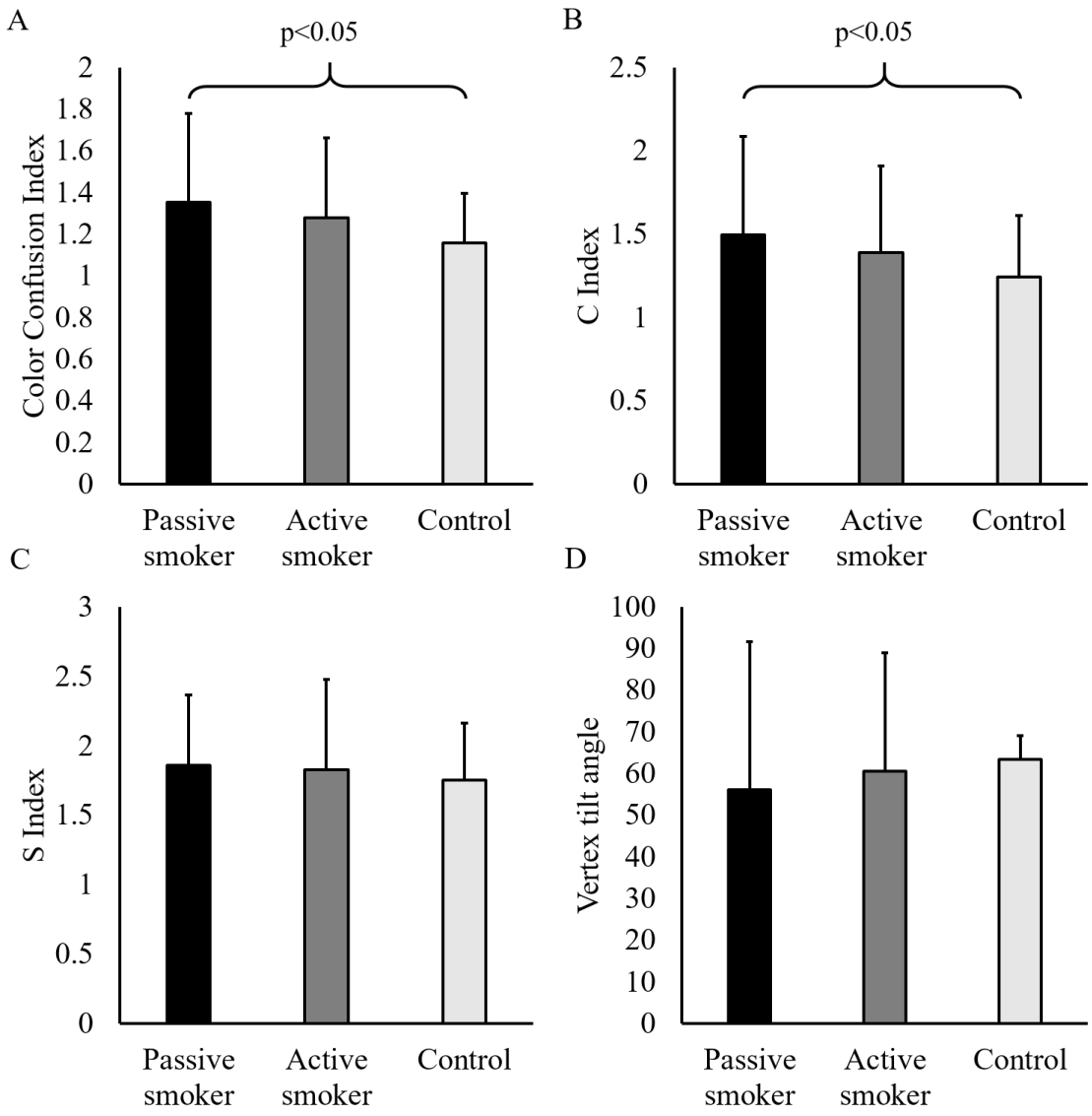

Figure 3. Color vision analysis performed by the Lanthony D15 test desaturated for the three groups studied. (A) Analysis of the Color Confusion Index with p <0.01. (B) Analysis of the C index with a value of p <0.05. (C) Analysis of the S. (D) index of the Tilt angle analysis of the color vector. The vertical columns indicate the average of each studied parameter and the bars indicate the standard deviation. The horizontal bracket indicates statistical difference between the groups with the p significance value for one-way ANOVA.

There was no significant correlation between age and visual performance of active and passive smokers in the tests used (Table 1). In addition, there was no correlation between the time of exposure to tobacco and the visual performance of active smokers in the tests used (Table 2) and there was no correlation between exposure time and visual performance of passive smokers (Table 3).

Table 1. Correlation between groups of active, passive smokers and age.

Age *vs* GAS and GPS						
GAS	Erros Ishihara	Visual Acuity	CCI	C-Index	S-Index	Tilt Angle
n (pairs)	53	53	53	53	53	53
r(Pearson)	-0,0703	-0,0103	0,1905	0,1907	0,1643	0,1689
R2	0,0049	0,0001	0,0363	0,0364	0,027	0,0285
t	-0,503	-0,0732	1,3859	1,3873	1,1892	1,224
(p)	0,6171	0,9419	0,1717	0,1713	0,2398	0,2265
GPS						
n (pairs)	49	49	49	49	49	49
r(Pearson)	-0,0371	-0,2785	0,0376	0,0461	0,1224	0,0234
R2	0,0014	0,0776	0,0014	0,0021	0,015	0,0005
t	-0,2543	-1,9882	0,258	0,3161	0,8452	0,1603
(p)	0,8004	0,0525	0,7975	0,7533	0,4023	0,8734

CCI= Color Confusion Index.

Table2. Correlation between the group of active smokers and time of exposure to tobacco.

Time of exposure *vs*						
	Erros Ishihara	Visual Acuity	CCI	C-Index	S-Index	Tilt Angle
n (pairs)	53	53	53	53	53	53
r(Pearson)	-0,0708	-0,0516	0,1737	0,1631	0,1645	0,1856
R2	0,005	0,0027	0,0302	0,0266	0,0271	0,0344
t	-0,5072	-0,3693	1,2598	1,1806	1,1909	1,3488
(p)	0,6142	0,7134	0,2134	0,2432	0,2391	0,1833

CCI= Color Confusion Index.

Table 3. Correlation between the group of passive smokers and time of exposure to tobacco.

Time of exposure *vs*						
	Erros Ishihara	Visual Acuity	CCI	C-Index	S-Index	Tilt Angle
n (pairs)	49	49	49	49	49	49
r(Pearson)	-0,1466	-0,0866	-0,013	-0,0528	-0,1456	-0,0599
R2	0,0215	0,0075	0,0002	0,0028	0,0212	0,0036
t	-1,0159	-0,5959	-0,0889	-0,3624	-1,0093	-0,4114
(p)	0,3148	0,5541	0,9295	0,7187	0,318	0,6827

CCI= Color Confusion Index.

4. Discussion

This study demonstrated that there are statistical differences between the visual performance of active, passive smokers and the control group. Visual changes were observed for visual acuity and color vision. According to the experimental design that excluded from the sample all subjects with suspected eye changes or visual changes resulting from health conditions and changes due to pre-established diseases, we consider that the visual changes found may be due to changes in the neuro-ophthalmological functions involved in the visual processing.

Since the worsening of visual performance with age represents a physiological condition of the visual system, the age of the volunteers could be an important bias for the subjects' visual performance, however our analysis showed that it did not show a correlation with the results, demonstrating no interfere with the results of present sample.

Thus, our results corroborate the literature that reports harmful effects of tobacco on the visual system. Even if the retinal tissue is not directly and morphologically affected [23], from a chemical and molecular point of view, chronic smoking reduces the production of oxygen and collagen in the tissues during healing, which would be related to ocular hypoxia caused by ocular hypertension and consequent decrease in corneal thickness [1].

The literature suggests that cigarette users are at an increased risk of developing diabetic retinopathy, glaucoma, severe ophthalmopathy and optic neuritis, in addition to nuclear cataracts [7, 11, 24, 25, 26], hyperopia and dry eye [27]. As any of these findings was the reason for exclusion from the sample, we suggest that the changes observed in this study could be caused by less severe subclinical conditions of affections such as those mentioned above.

Cigarette consumption is also related to the decrease in color vision involving both the green-red axis and the blue-yellow axis [15, 16]. As in our results, smokers who had their color vision assessed by a method similar to the desaturated Lanthony D15 test, the Farnsworth-Munsell 100 test, showed a lower Color Confusion Index, compared to those who did not smoke [15, 28, 29]. Additionally, these studies did not find statistical differences between smokers and non-smokers in relation to the red-green and blue-yellow sectors, which corroborates our findings in the S Index and tilt angle, suggesting a diffuse loss of color vision in chronic smokers [15]. That is, a diffuse impairment in processing that includes the magnum and parvocellular pathways in the subjects of the groups of active and passive smokers studied.

Toxic neuropathy related to smoking, especially affecting red-green color vision and carbon monoxide in cigarette consumption, may be the cause of this dyschromatopsia [12, 13]. It is also suggested that the saturation of the cones, alter the amplification of signals that reach the visual cortex or toxic action in the parvocellular pathway, resulting in changes in color discrimination [28]. These toxic and oxidative effects are believed to play an important role in eye changes and are considered one of the risk factors for many disorders [27, 28, 30].

The toxins in cigarettes cause a decrease in blood flow, helping to form clots within the eye capillaries, preventing the arrival of essential nutrients for eye health, increasing free radicals and promoting macular degeneration and ischemia, as well as decreased flow retinal blood pressure and reduced retinal vessel self-regulation ability after smoking [7, 11, 27, 28, 31].

The toxins and irritants present in cigarette smoke cause a reaction of the conjunctiva and redness of the eye, increasing the vulnerability of the optic nerve and modifying its blood supply; this can alter the histological structure of the conjunctiva and the characteristics of tears, indirectly exposing the corneal endothelial cells to ischemia [6, 7, 23, 32, 33].

Cigarette smoke contains approximately 1017 molecular oxidants. Free radicals cause changes in cell membranes that increase oxidative stress and, according to the literature, smoking causes low concentrations of antioxidants in plasma [6, 32]. This metabolism is indirectly affected by the chronic use of cigarettes through this decrease in plasma levels of antioxidants [31, 32].

A change in choroid thickness in short-term smokers and a decrease in choroid thickness in chronic smokers has been reported [34, 35]. It is also believed that smoking causes an imbalance in the neurotransmission of acetylcholine, dopamine and glutamate and deficiencies in the functioning or conformation of receptors, thus being able to modify visual processing [28, 36].

One study suggest that chronic smokers had fewer hexagonal cells than in the non-smoking group. This may be caused by hypoxia in chronic smokers, which changes the number of hexagonal cells. These results imply that the morphological characteristics of the corneal endothelial cells were affected by smoking [37].

The present study demonstrated that the visual performance of passive smokers was also compromised, and in all analyzes performed, the rates were lower than those observed for active smokers. To the best of our knowledge, this is the first study to demonstrate changes in color vision in passive smokers and that the damage may be greater in this group than in active smokers.

Studies reveal that the visual performance of smokers who consume more than 20 cigarettes a day is worse than smokers who consume less than that, suggesting that the intensity of exposure may be related to the severity of visual damage [38]; this analysis cannot be replicated in the present study since the maximum number of cigarettes consumed per day by our sample was 20. However, this relationship with intensity could be explained by the fact that passive smokers may be exposed to more than one active smoker, which would cause that their contact with smoking was greater. In addition, passive smokers generally begin their exposure at a very early age, many of them when they are still children, at a time when the visual system is still developing, which causes intoxications in this period of life can have a greater impact on individual's health [39].

Our results did not show correlation between time and intensity of exposure with visual performance. This is a common result whenever trying to compare functional losses with absolute values of exposure time. This may be due to the existence of genes that encode enzymes responsible for the metabolism of chemical substances and that the polymorphism modifies absorption and the risk of neurotoxic effects among individuals [40]. Susceptibility factors including age and inter-individual differences in the pattern of chemical substance absorption are involved in metabolism and compensatory processes, which also explains the difference in results between subjects exposed to chemical substances [41].

5. Conclusion

The results of this study indicate that tobacco consumption by active and passive smokers produces deficits in color vision processing that are probably caused by the neurotoxic effects of substances in cigarettes.

However, additional studies are needed to elucidate what are the neurobiological mechanisms underlying, directly or indirectly, this neurointoxication and why the observed changes are greater in secondhand/passive smokers.

The analysis also suggests that passive smokers had greater performance deficits than active smokers, indicating that their exposure to smoking shows more aggressive results than is usually imagined.

Moreover, the results obtained in the present study reinforce the usefulness of psychophysical methods such as those used in this study for tracking possible changes in the visual system even if a subclinical level.

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